Oncology in the Real World: A Daylong Multitumor Educational Symposium in Partnership with the American Oncology Network

A CME/MOC- and NCPD-Accredited Event

Saturday, October 14, 2023
9:30 AM – 5:00 PM PT

RTP
RESEARCH
TO PRACTICE

Agenda

Module 1 — Lymphoma: *Drs Flowers and LaCasce*

Module 2 — Urothelial Bladder Cancer and Renal Cell Carcinoma:
Drs Hutson and Sonpavde

Module 3 — Hepatobiliary and Pancreatic Cancers:
Prof Borad and Dr El-Khoueiry

Module 4 — Gynecologic Cancers: *Drs Monk and Moore*

Module 5 — Multiple Myeloma: *Drs Krishnan and Orlowski*

Module 6 — HER2-Positive and Triple-Negative Breast Cancer:
Drs Hurvitz and McArthur

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Gynecologic Cancers Faculty

Bradley J Monk, MD
Professor
Division of Gynecologic Oncology
University of Arizona College of Medicine
Creighton University School of Medicine
Phoenix, Arizona

Kathleen N Moore, MD, MS
Associate Director, Clinical Research
Virginia Kerley Cade Chair in Developmental Therapeutics
Director, TSET Phase I Drug Unit
Co-Director, Cancer Therapeutics Program
Stephenson Cancer Center at the University of Oklahoma HSC
Associate Director, GOG Partners
Board of Directors, GOG Foundation
Oklahoma City, Oklahoma

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Meet The Professor

Optimizing the Management of Ovarian Cancer

Tuesday, October 17, 2023
5:00 PM – 6:00 PM ET

Faculty

David M O'Malley, MD

Moderator

Neil Love, MD

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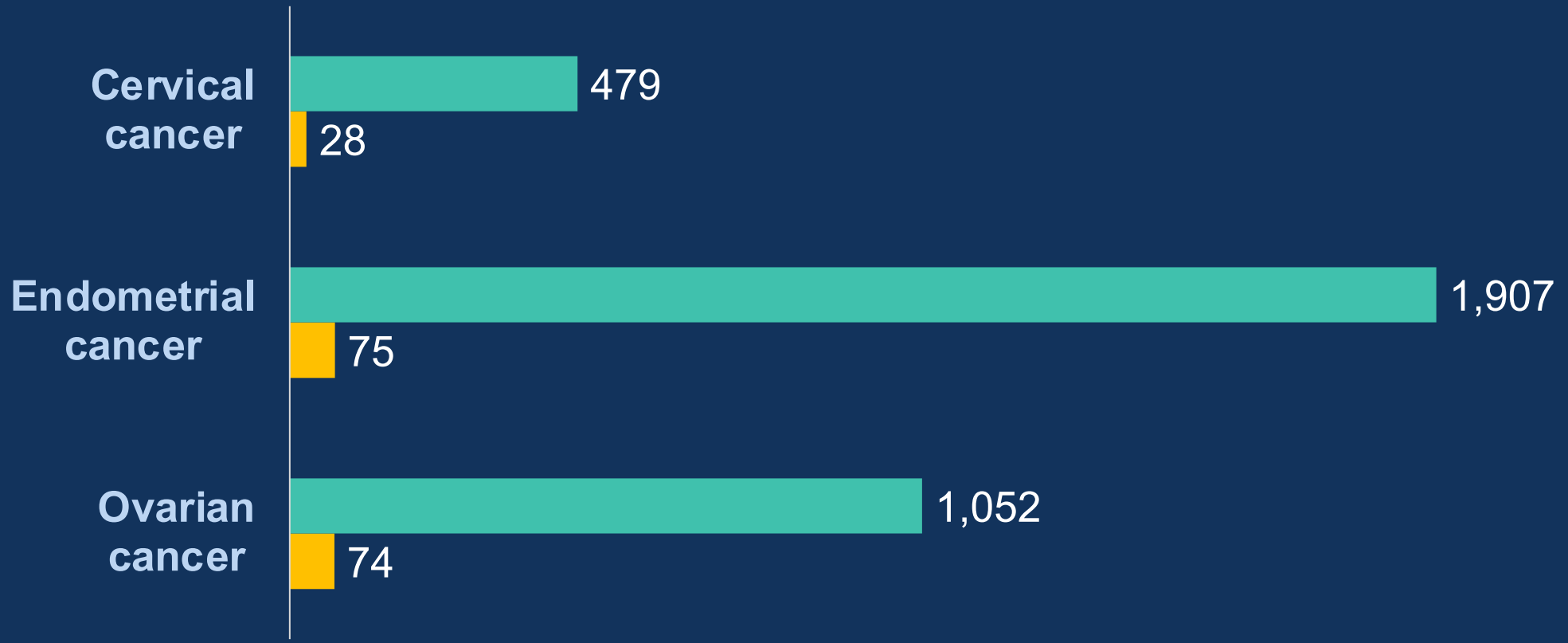
TO PRACTICE

Snapshot of AON Practice
Module 4: Gynecologic



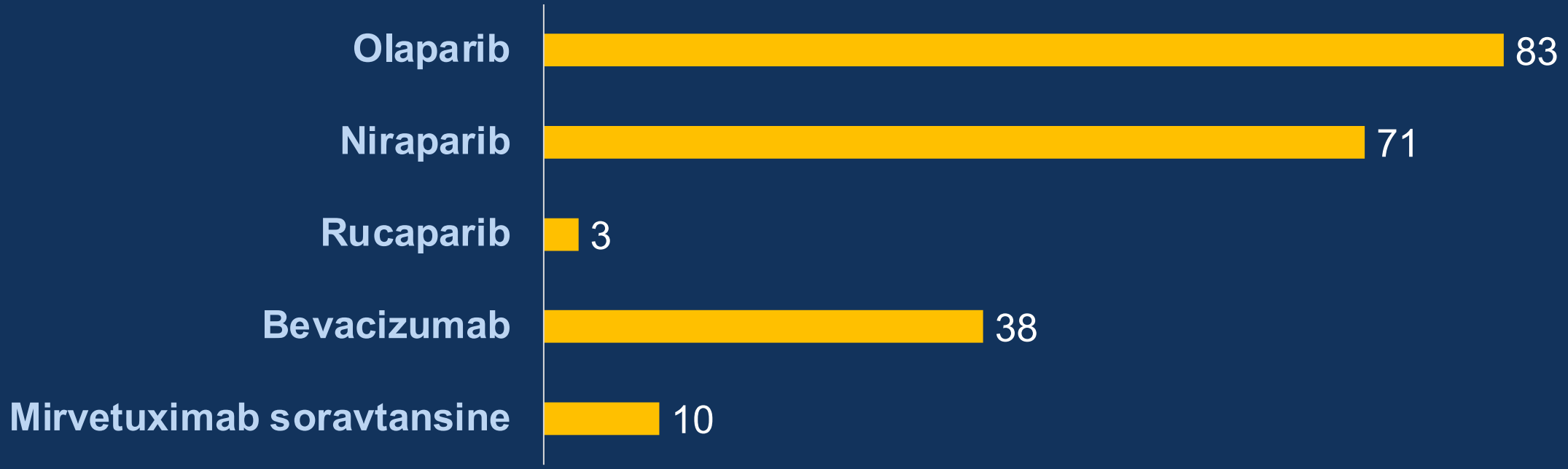
MIBA

THE AON CLINICAL SUMMIT 2023

Collaborate. Innovate. Celebrate.

Snapshot of AON Practice
Ovarian Cancer

Select Treatments Received



Clinical Trial Participation

Number of clinical trials	15
Total patients enrolled	26

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Snapshot of AON Practice
Endometrial Cancer

Select Treatments Received

Clinical Trial Participation

Number of clinical trials	10
Total patients enrolled	14

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Snapshot of AON Practice
Cervical Cancer

Select Treatments Received

Clinical Trial Participation

Number of clinical trials	5
Total patients enrolled	10

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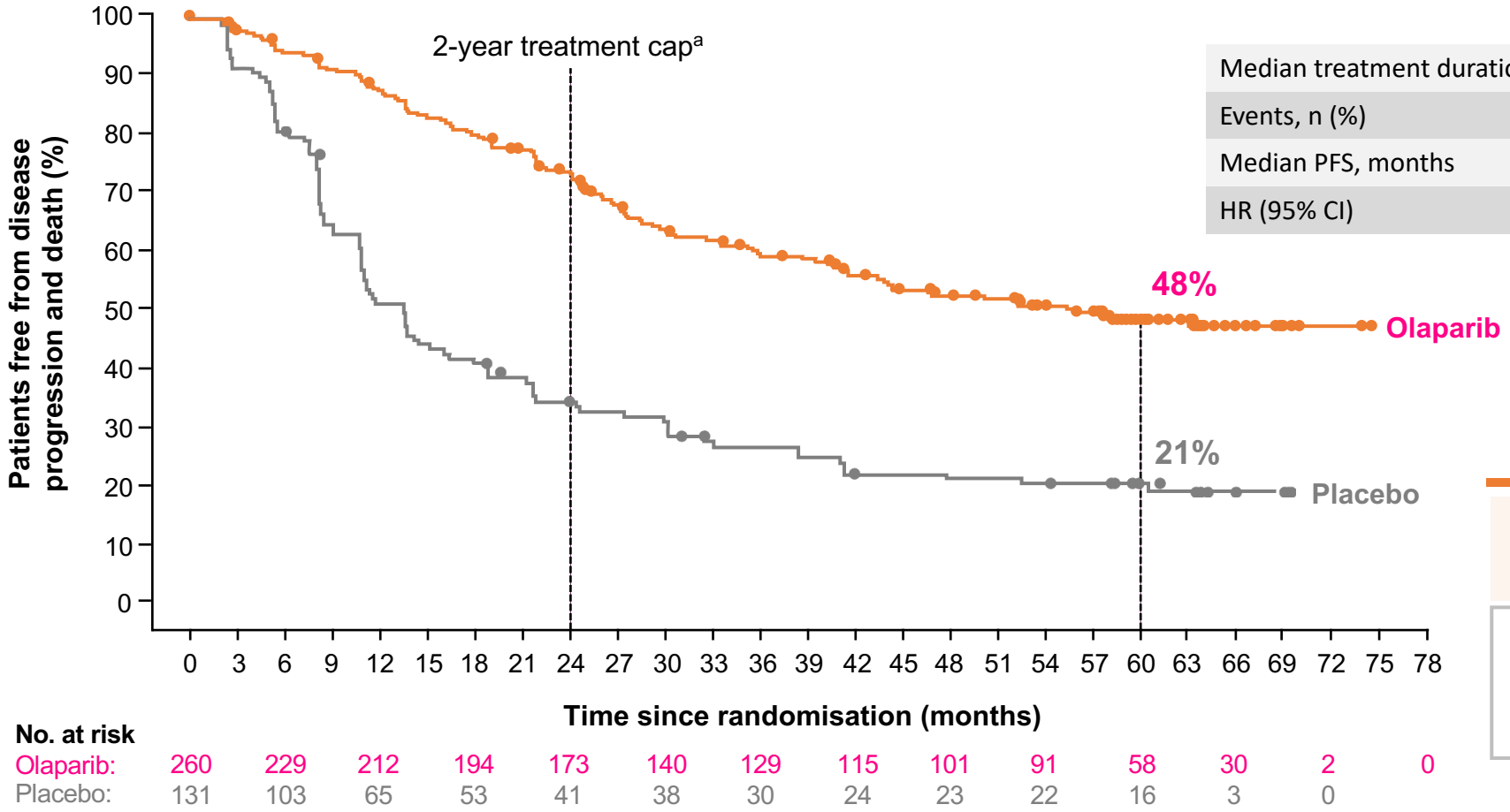
Maintenance therapy for patients with ovarian cancer; Other treatment strategies

Kathleen N. Moore MS MD
Virginia Kerley Cade Chair in Developmental Therapeutics
Professor, Gynecologic Oncology
Associate Director, Clinical Research
Director, TSET/SCRI Phase 1 Clinical Trials Unit
Stephenson Cancer Center at the University of Oklahoma

SOLO-1: PFS benefit of maintenance olaparib was sustained beyond the end of treatment



	Olaparib (n=260)	Placebo (n=131)
Median treatment duration, months	**24.6**	**13.9**
Events, n (%)	**118 (45)**	**100 (76)**
Median PFS, months	**56.0**	**13.8**
HR (95% CI)	**0.33 (0.25, 0.43)**	

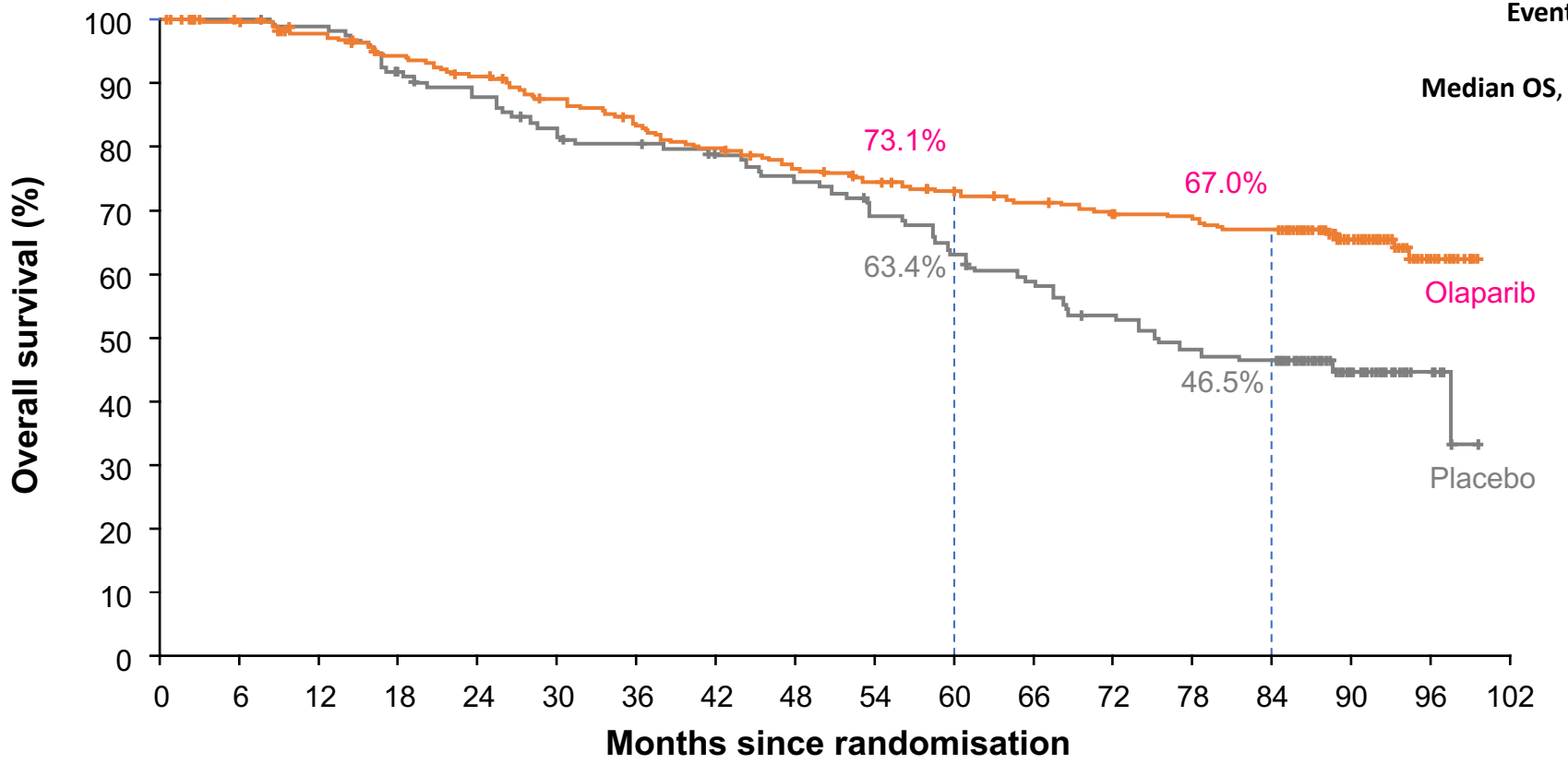
Median PFS difference for olaparib vs placebo: 42.2 months

Median follow-up for PFS:

Olaparib	Placebo
4.8 years	5.0 years

Investigator-assessed by modified RECIST v1.1
[a]Patients who had no evidence of disease at 2 years stopped receiving the trial intervention; patients who had a partial response at 2 years were permitted to continue receiving the trial intervention in a blinded manner; 13 patients (all in the olaparib arm) continued study treatment past 2 years
CI, confidence interval; HR, hazard ratio; PFS, progression-free survival; RECIST, Response Evaluation Criteria In Solid Tumours
Banerjee S, et al. Presented at European Society for Medical Oncology Virtual Congress 2020; 19th–21st September 2020

SOLO-1: Maintenance olaparib provided a clinically meaningful OS benefit



	Olaparib (N=260)	Placebo (N=131)
Events, n (%)	84 (32.3)	65 (49.6)
Median OS, months	**NR**	**75.2**

HR: 0.55 (95% CI: 0.40–0.76)
P=0.0004[a]

44.3% of patients in the placebo group received subsequent PARP inhibitor therapy, compared with 14.6% of patients in the olaparib group

No. at risk

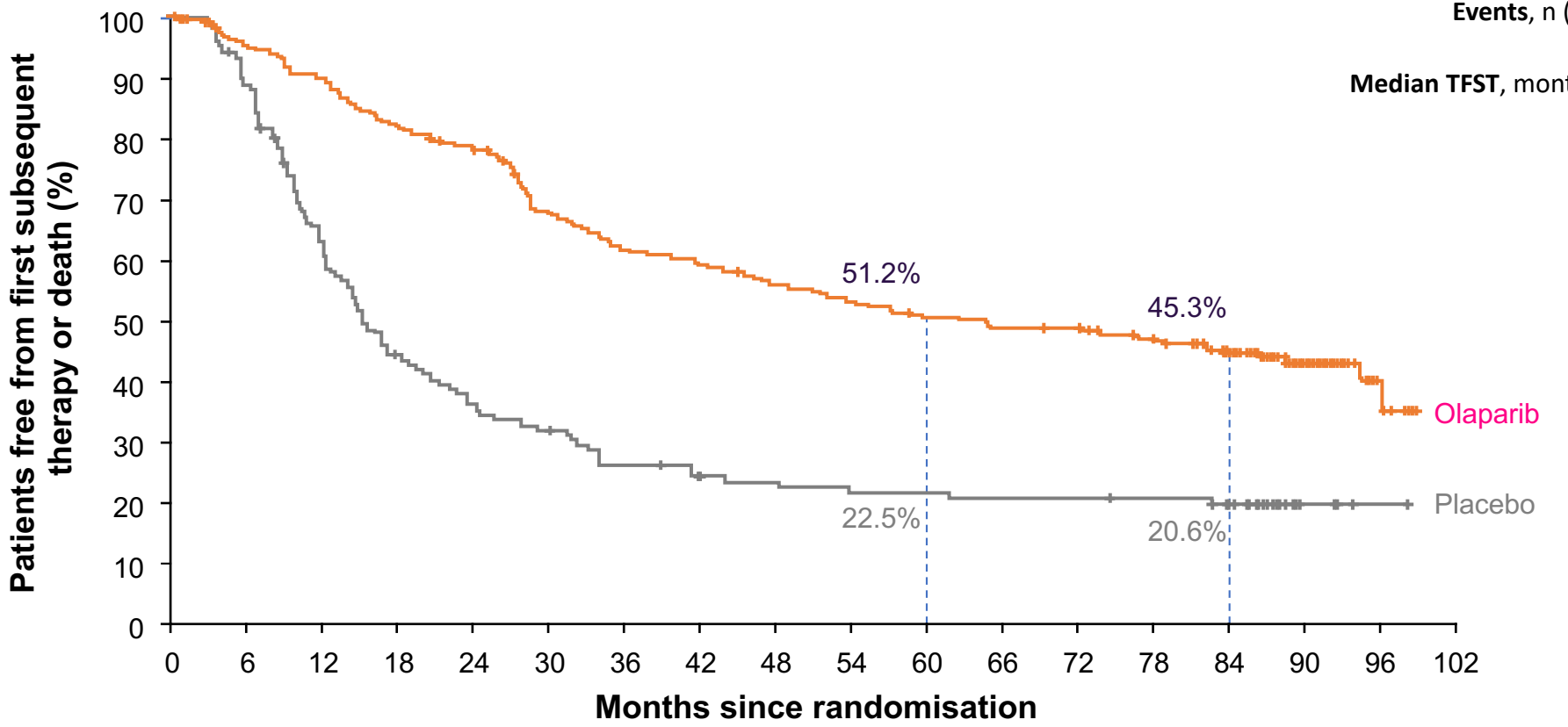
Olaparib	260	252	246	236	227	214	203	194	185	177	170	165	159	157	153	79	21	0
Placebo	131	128	125	114	108	100	97	92	87	80	73	67	60	54	52	21	6	0

CI, confidence interval; HR: hazard ratio; NR, not reached; OS, overall survival; PARP, poly(adenosine diphosphate ribose) polymerase
[a]*P*<0.0001 required to declare statistical significance

DiSilvestro P et al and SOLO-1 Investigators. J Clin Oncol. 2023 Jan 20;41(3):609-617.

SOLO-1: TFST substantially delayed by maintenance olaparib

	Olaparib (N=260)	Placebo (N=131)
Events, n (%)	135 (51.9)	98 (74.8)
Median TFST, months	**64.0**	**15.1**
HR: 0.37 (95% CI: 0.28–0.48)		



No. at risk

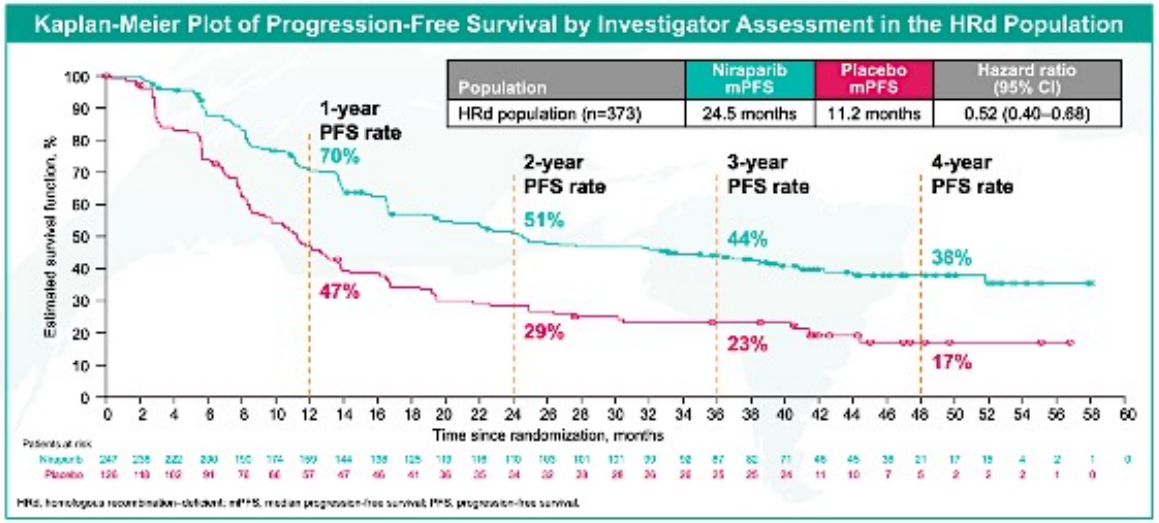
Olaparib	260	240	223	203	190	160	147	141	132	125	119	115	111	102	75	31	5	0
Placebo	131	114	79	55	45	39	32	28	26	25	25	24	24	23	18	4	1	0

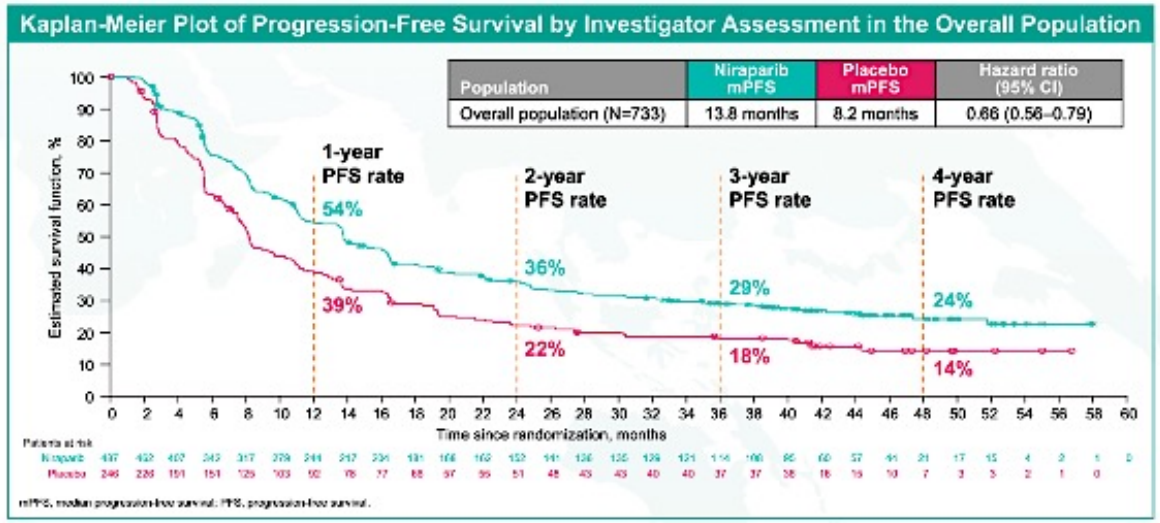
DiSilvestro P et al and SOLO-1 Investigators. J Clin Oncol. 2023 Jan 20;41(3):609-617.

CI, confidence interval; HR: hazard ratio; TFST, time to first subsequent therapy or death

PRIMA Trial – Maintenance Niraparib: Updated Long-Term PFS (Investigator Assessed)

November 17, 2021, Clinical Cutoff Date





- At the time of the updated clinical cutoff date, 16.3% and 11.1% of patients were receiving niraparib or placebo, respectively
- Niraparib treatment significantly extended IA PFS compared with placebo in both the HRd and overall populations
- Updated long-term IA PFS results were also consistent with BICR PFS results from the primary analysis
- OS remains immature at 41.2% for the overall population

IGCS 2022 ANNUAL GLOBAL MEETING

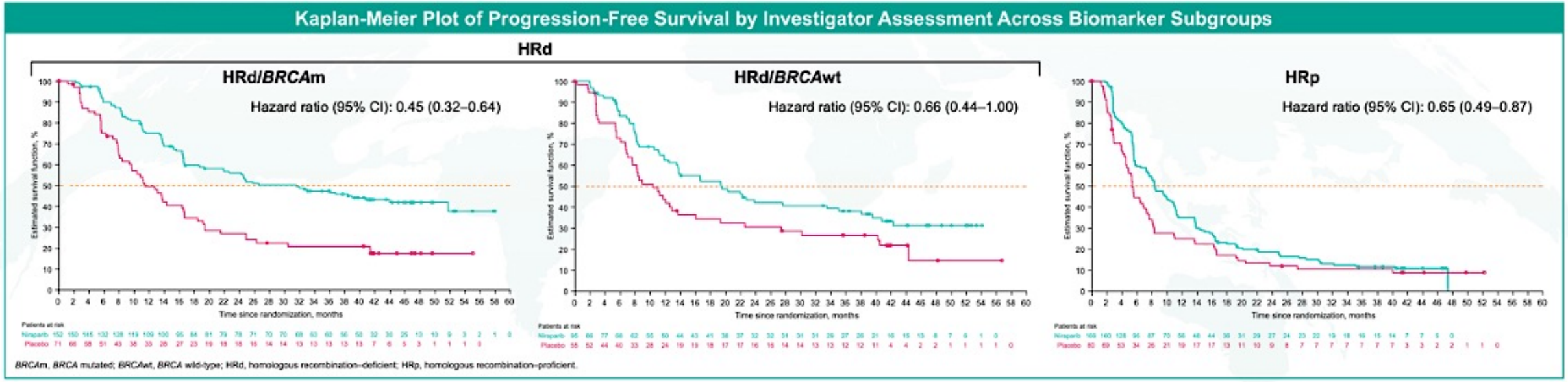
BICR, blinded independent central review; HRd, homologous recombination–deficient; IA, investigator assessed; mPFS, median progression-free survival; OS, overall survival; PFS, progression-free survival.

González-Martín A et al. IGCS 2022;Abstract S005/1753. González-Martín A et al. *Eur J Cancer* 2023;189:112908.

RTP RESEARCH TO PRACTICE

PRIMA – Maintenance Niraparib: PFS Across Biomarker Subgroups (Investigator Assessed)

November 17, 2021, Clinical Cutoff Date



- Niraparib treatment increased PFS duration compared with placebo treatment across biomarker subgroups
- The greatest treatment benefit was seen in patients with HRd tumors that were *BRCA*m

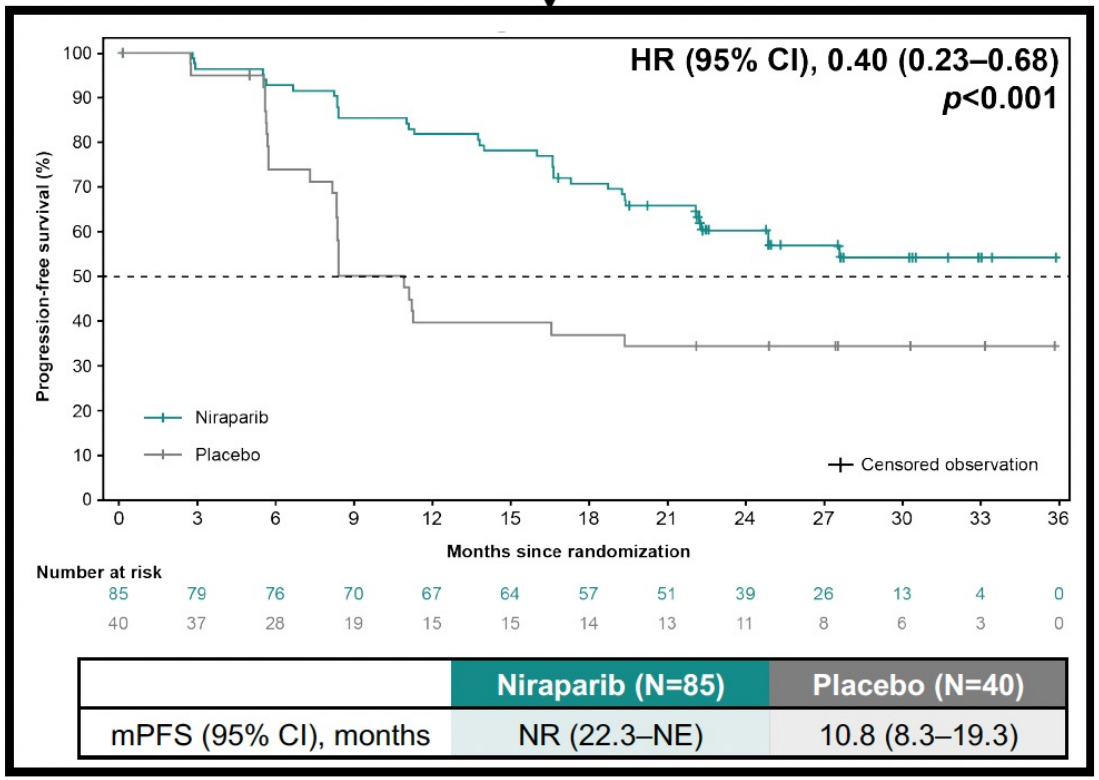
IGCS 2022 ANNUAL GLOBAL MEETING

González-Martín A et al. IGCS 2022;Abstract S005/1753. González-Martín A et al. *Eur J Cancer* 2023;189:112908.

RTP RESEARCH TO PRACTICE

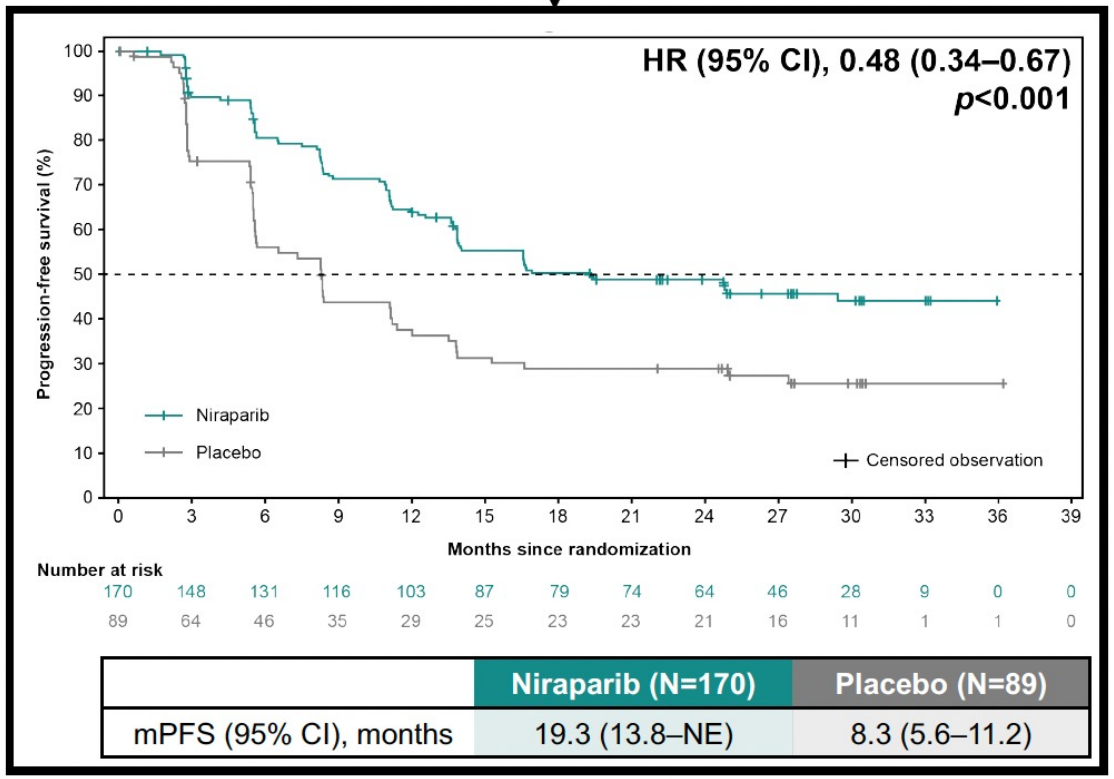
PRIME Trial – Maintenance Niraparib: PFS Benefit by Germline BRCA Mutation (gBRCAmut) Status

g*BRCA*mut



	Niraparib (N=85)	Placebo (N=40)
mPFS (95% CI), months	NR (22.3–NE)	10.8 (8.3–19.3)

Non-g*BRCA*mut



	Niraparib (N=170)	Placebo (N=89)
mPFS (95% CI), months	19.3 (13.8–NE)	8.3 (5.6–11.2)

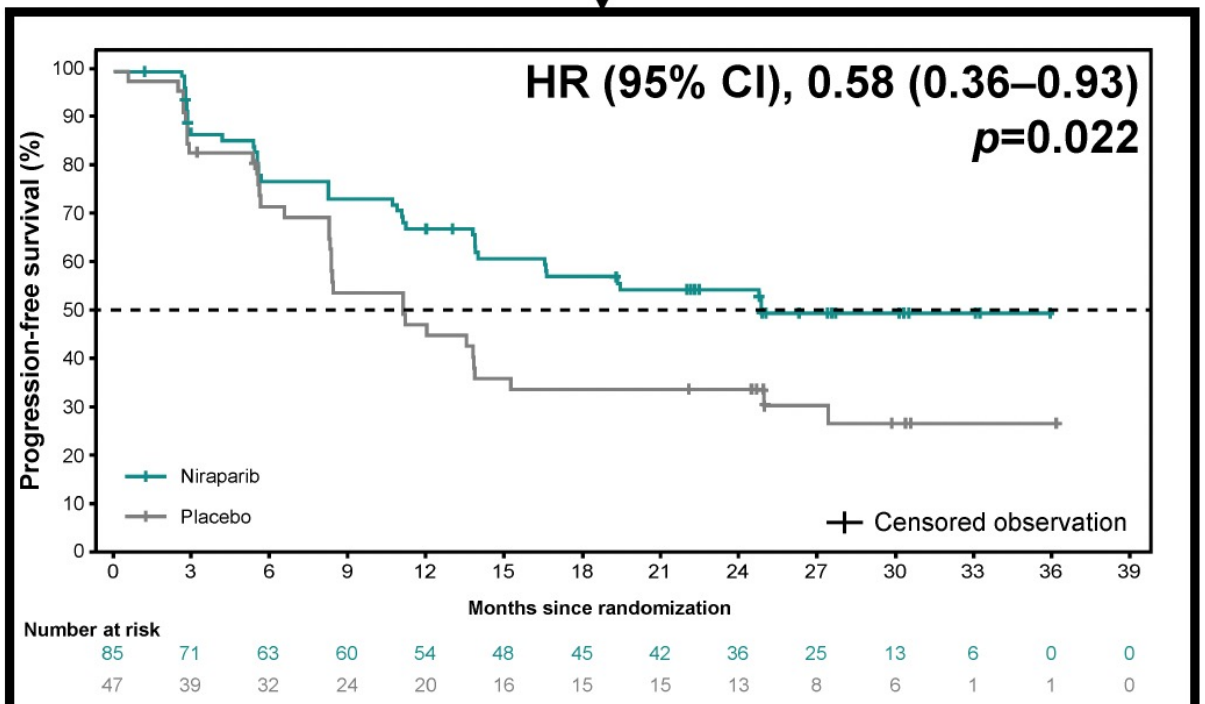
- Median PFS has not been yet reached for the g*BRCA*mut population.
- The benefit of niraparib in the non-g*BRCA*mut population is confirmed.

Li N et al. SGO 2022;Abstract LBA5; Li N et al. *JAMA Oncol* 2023;[Online ahead of print].

RTP RESEARCH TO PRACTICE

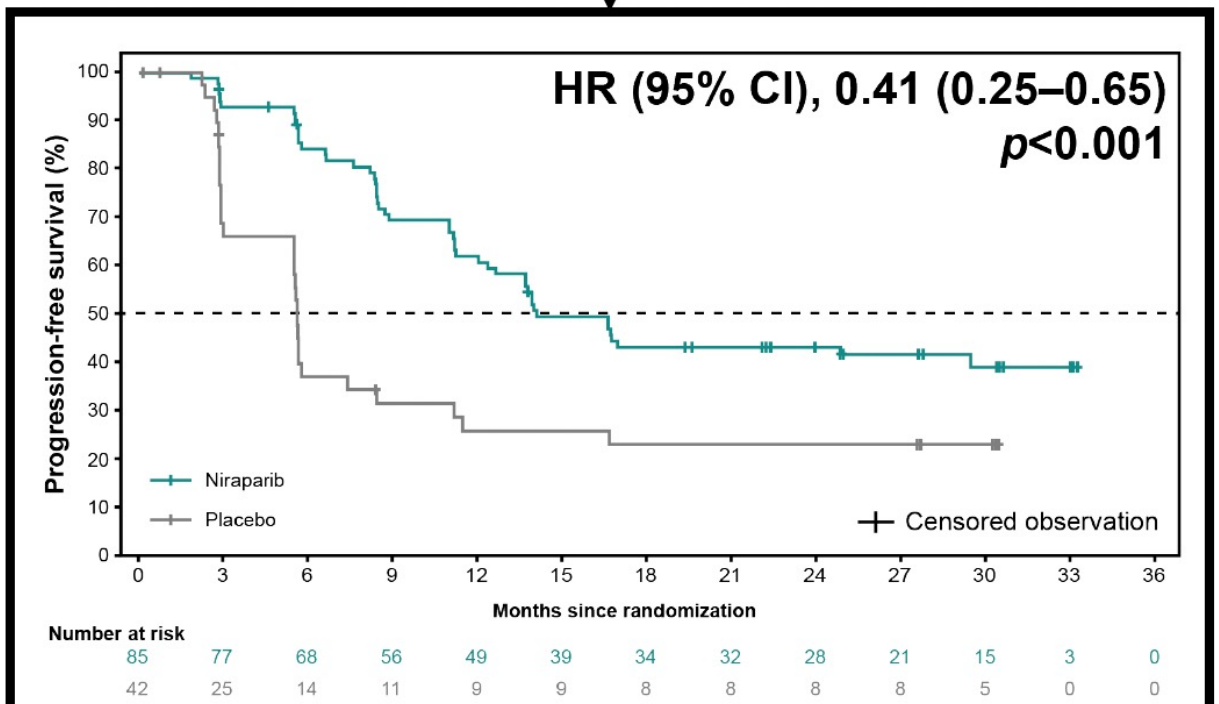
PRIME – Maintenance Niraparib: PFS Benefit by HRD Status in the Non-gBRCAmut Subgroup

Non-g*BRCA*mut/HRd



	Niraparib (N=85)	Placebo (N=47)
mPFS (95% CI), months	24.8 (14.0–NE)	11.1 (8.3–13.8)

Non-g*BRCA*mut/HRp



	Niraparib (N=85)	Placebo (N=42)
mPFS (95% CI), months	14.0 (11.9–NE)	5.5 (2.9–7.3)

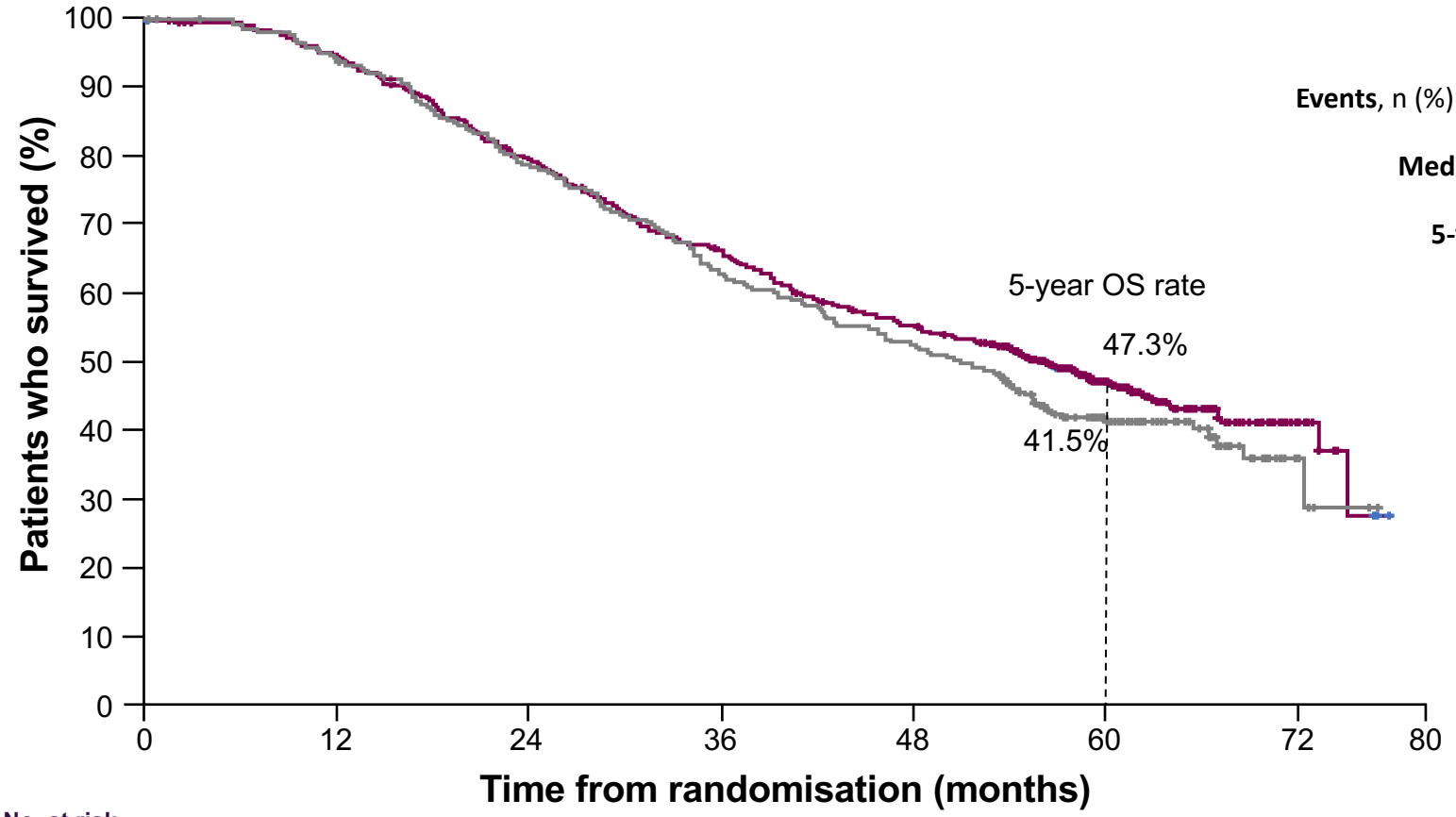
HRD = homologous recombination deficiency

Li N et al. SGO 2022;Abstract LBA5.

RTP RESEARCH TO PRACTICE

PAOLA-1: OS analysis at 5 years: ITT population

Median duration of follow-up for OS, months (IQR)	Olaparib + bev: 61.7 (57.5–67.0)	Placebo + bev: 61.9 (58.1–66.8)



	Olaparib + bevacizumab (N=537)	Placebo + bevacizumab (N=269)
Events, n (%) [55% maturity]	288 (53.6)	158 (58.7)
Median OS, months	**56.5**	**51.6**
5-year OS rate, %	**47.3**	**41.5**

HR: 0.92 (95% CI: 0.76–1.12); ***P*=0.4118**

Patients receiving a PARP inhibitor during any subsequent treatment
Olaparib + bevacizumab: **19.6%**(105/537)
Placebo + bevacizumab: **45.7%** (123/269)

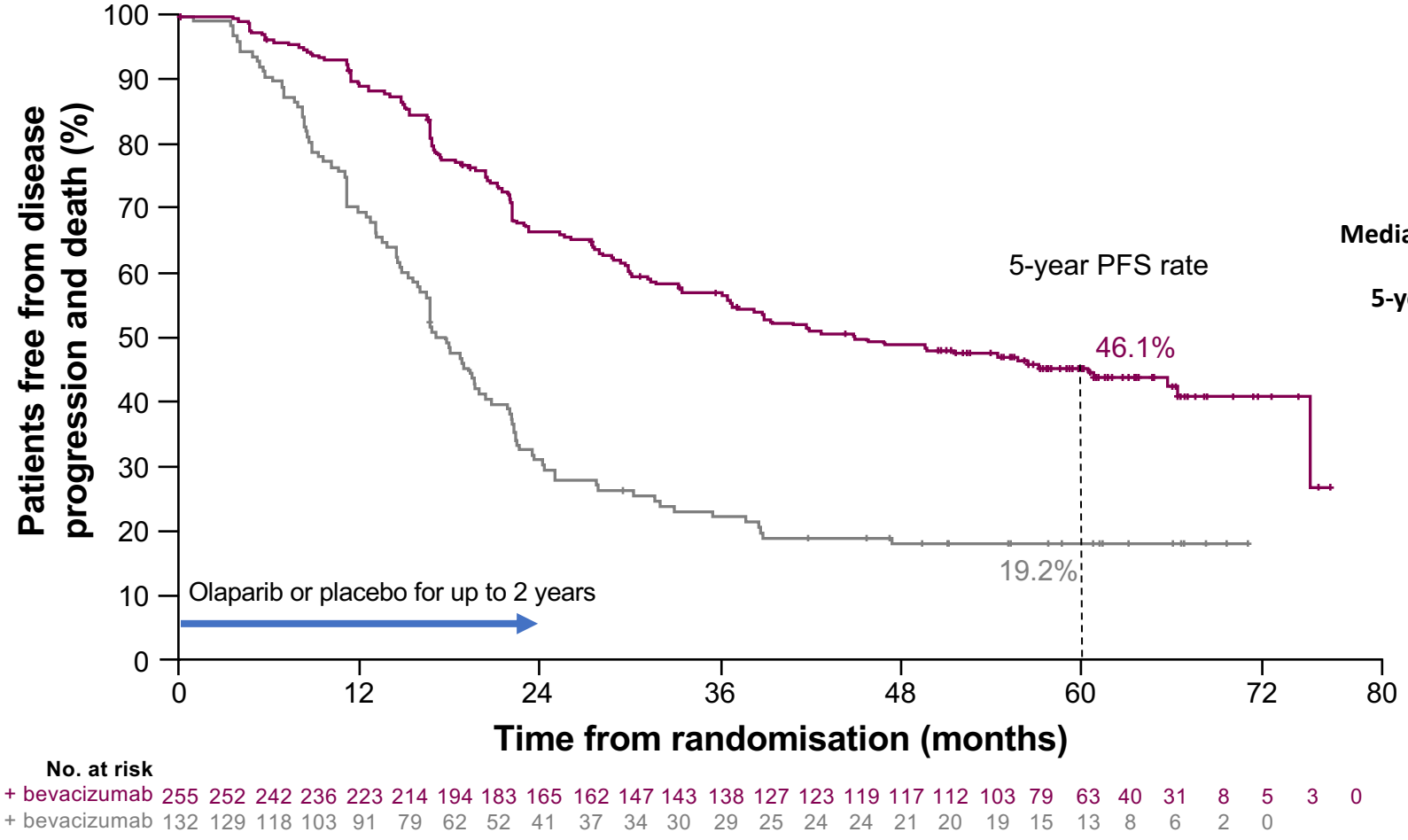
No. at risk

Olaparib + bevacizumab	537	530	528	517	503	480	463	440	420	398	376	357	347	329	308	295	286	276	262	217	169	113	82	40	19	4	0
Placebo + bevacizumab	269	267	264	261	250	242	229	220	208	199	188	179	166	160	154	146	139	132	121	96	76	51	37	20	5	2	0

CI, confidence interval; HR, hazard ratio; ITT, intention to treat; OS, overall survival; PARP, poly(adenosine diphosphate ribose) polymerase

Ray-Coquard I, et al. Presented at European Society for Medical Oncology Annual Meeting, 9–13 September, 2022; Abstract #LBA29. Ray-Coquard I et al. *Ann Oncol*. 2023;34(8):681-692.

PAOLA-1: Updated PFS at 5 years: HRD-positive population[a]



No. at risk																									
Olaparib + bevacizumab	255	252	242	236	223	214	194	183	165	162	147	143	138	127	123	119	117	112	103	79	63	40	31	8	5	3	0
Placebo + bevacizumab	132	129	118	103	91	79	62	52	41	37	34	30	29	25	24	24	21	20	19	15	13	8	6	2	0		

	Olaparib + bevacizumab (N=255)	Placebo + bevacizumab (N=132)
Events, n (%)	136 (53.3)	104 (78.8)
Median PFS, months	**46.8**	**17.6**
5-year PFS rate, %	**46.1**	**19.2**

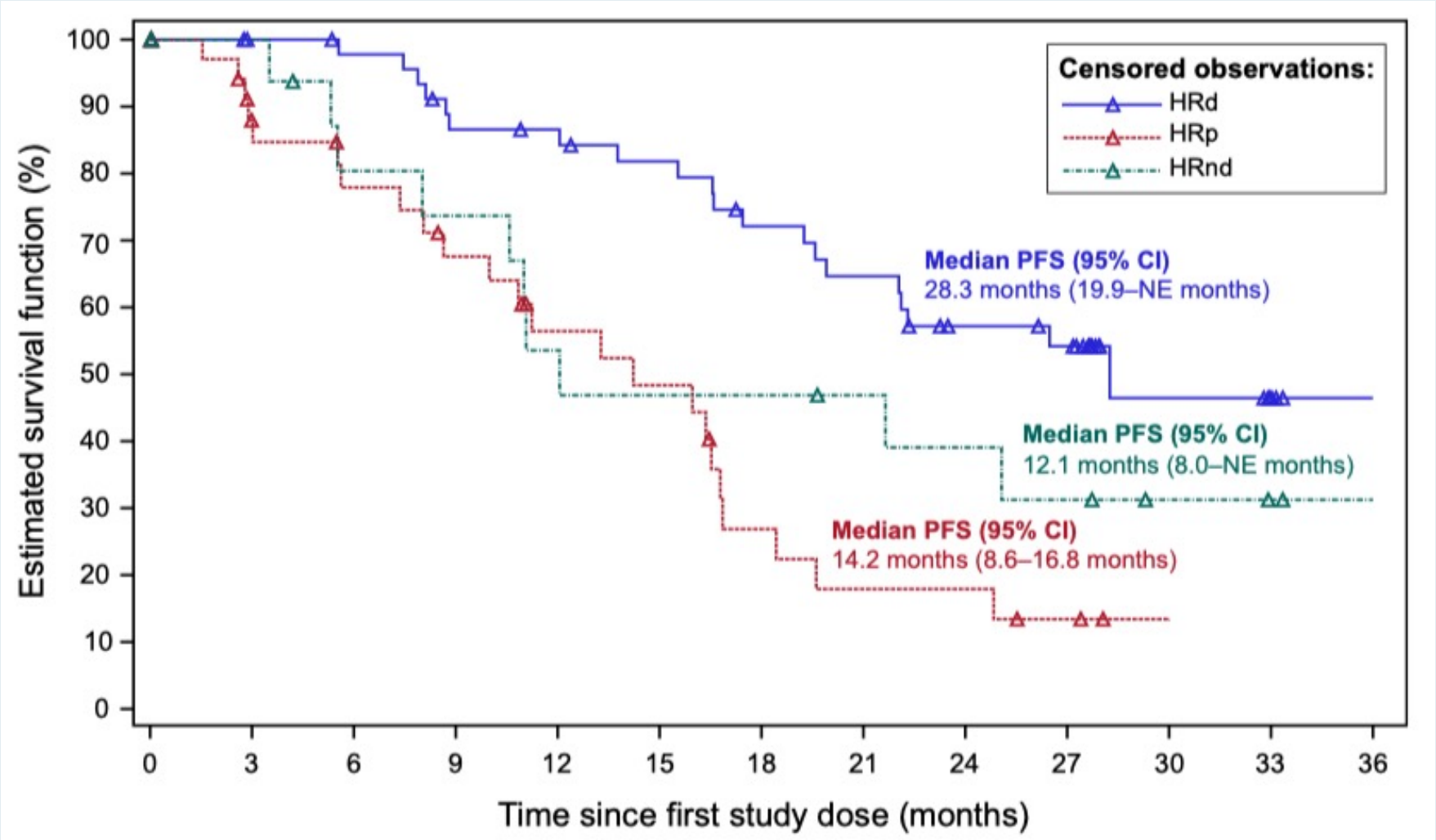
HR: 0.41 (95% CI: 0.32–0.54)

[a]Descriptive analysis; PFS by investigator-assessment (modified RECIST v1.1)

CI, confidence interval; HR, hazard ratio; HRD, homologous recombination deficiency; PFS, progression-free survival

Ray-Coquard I, et al. Presented at European Society for Medical Oncology Annual Meeting, 9–13 September, 2022; Abstract #LBA29. Ray-Coquard I et al. *Ann Oncol*. 2023;34(8):681-692.

OVARIO Trial – Maintenance Niraparib/Bevacizumab: Investigator-Assessed PFS by HRD Status

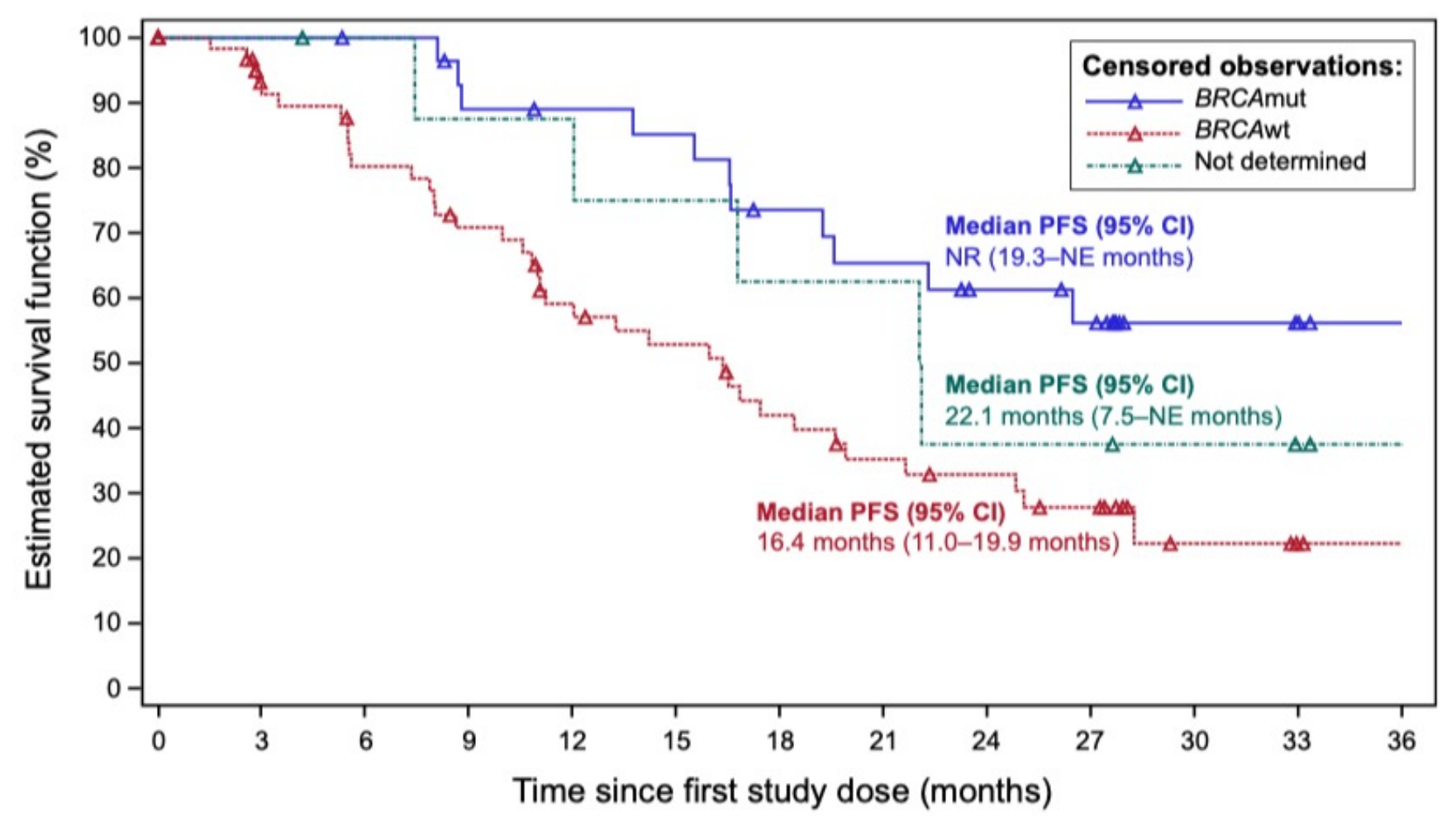


HRd = homologous recombination deficient; HRp = homologous recombination proficient; HRnd = HRD status not determined

Hardesty MM et al. *Gynecol Oncol* 2022;166(2):219-29.

RTP RESEARCH TO PRACTICE

OVARIO – Maintenance Niraparib/Bevacizumab: Investigator-Assessed PFS by BRCA Mutation Status

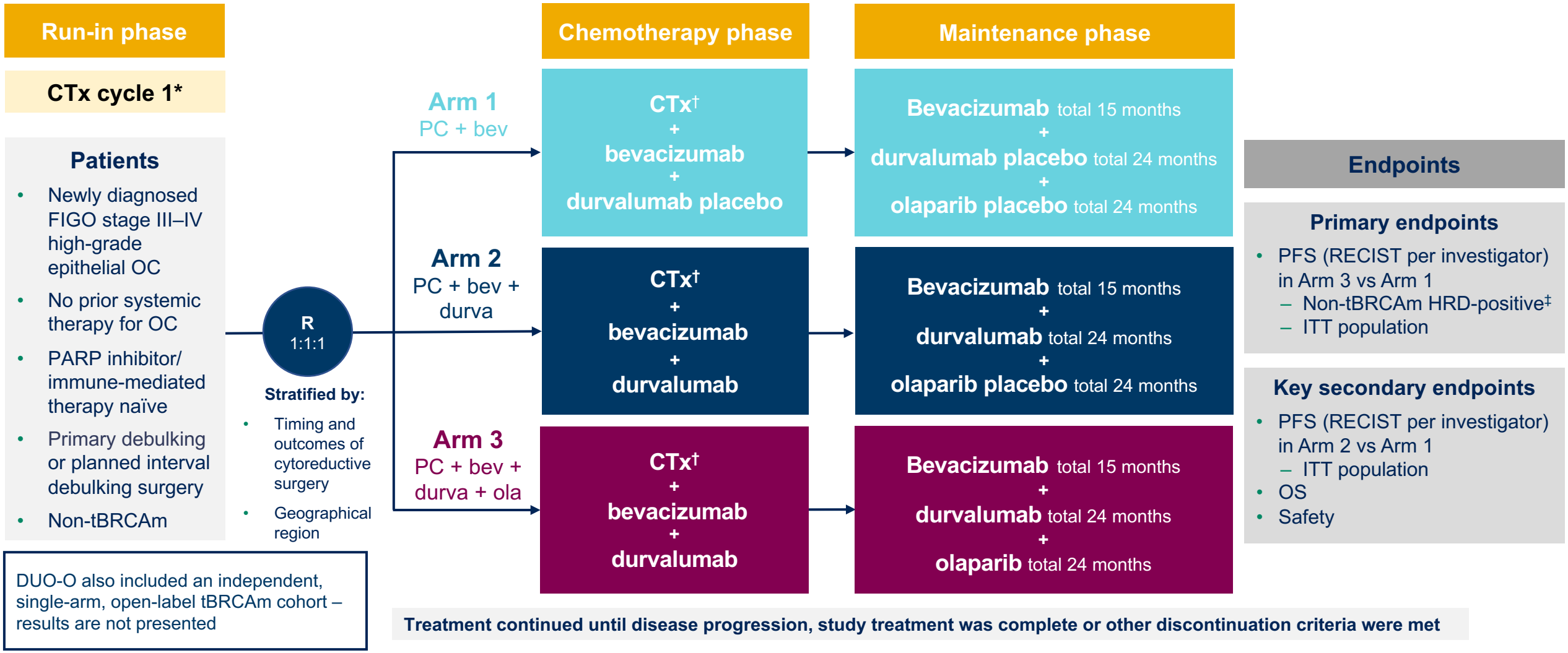


BRCAmut = BRCA mutation; BRCAwt = BRCA wild type

Hardesty MM et al. *Gynecol Oncol* 2022;166(2):219-29.

RTP RESEARCH TO PRACTICE

DUO-O study design

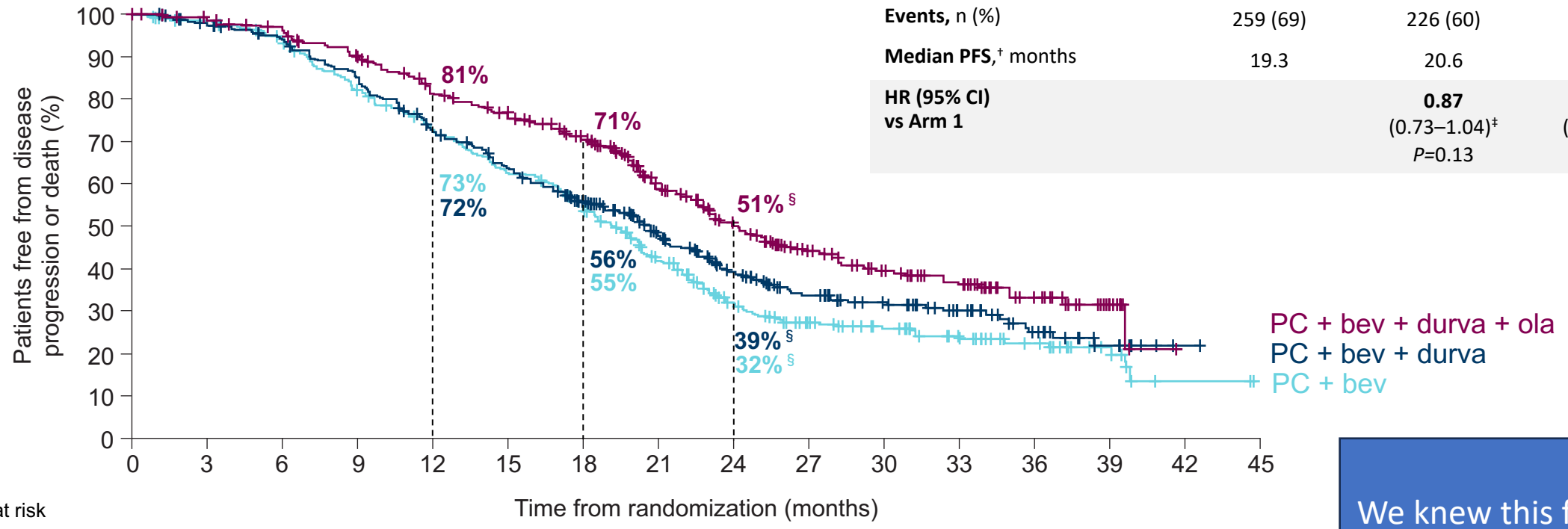


Dosing and schedule: bevacizumab (15 mg/kg IV q3w); durvalumab (1120 mg IV q3w); olaparib (300 mg po bid); chemotherapy: paclitaxel 175 mg/m^2 IV q3w and carboplatin at AUC5 or AUC6 IV q3w. PFS interim analysis DCO: December 5, 2022.
*With or without bevacizumab according to local practice; †Cycles 2–6; ‡Genomic instability score ≥42 assessed prospectively by Myriad MyChoice CDx assay.
AUC, area under the curve; bev, bevacizumab; bid, twice daily; CTx, chemotherapy; DCO, data cutoff; durva, durvalumab; FIGO, International Federation of Gynecology and Obstetrics; HRD, homologous recombination deficiency; ITT, intent-to-treat; IV, intravenous; ola, olaparib; OS, overall survival; PC, paclitaxel/carboplatin; po, by mouth; q3w, every 3 weeks; R, randomization; RECIST, Response Evaluation Criteria for Solid Tumors.

Dr Philipp Harter

PFS: ITT population

	Arm 1 PC + bev N=378	Arm 2 PC + bev + durva N=374	Arm 3 PC + bev + durva + ola N=378
Median follow-up,* months	25.5	23.1	23.3
Events, n (%)	259 (69)	226 (60)	193 (51)
Median PFS,† months	19.3	20.6	24.2
HR (95% CI) vs Arm 1		**0.87** (0.73–1.04)‡ *P*=0.13	**0.63** (0.52–0.76)‡ *P*<0.0001



Patients at risk

Arm 1	378	363	341	297	260	223	189	130	87	63	51	35	23	11	2	0
Arm 2	374	354	336	301	254	221	180	130	93	70	54	39	23	11	1	0
Arm 3	378	366	351	323	286	266	228	163	123	84	65	52	27	9	0	

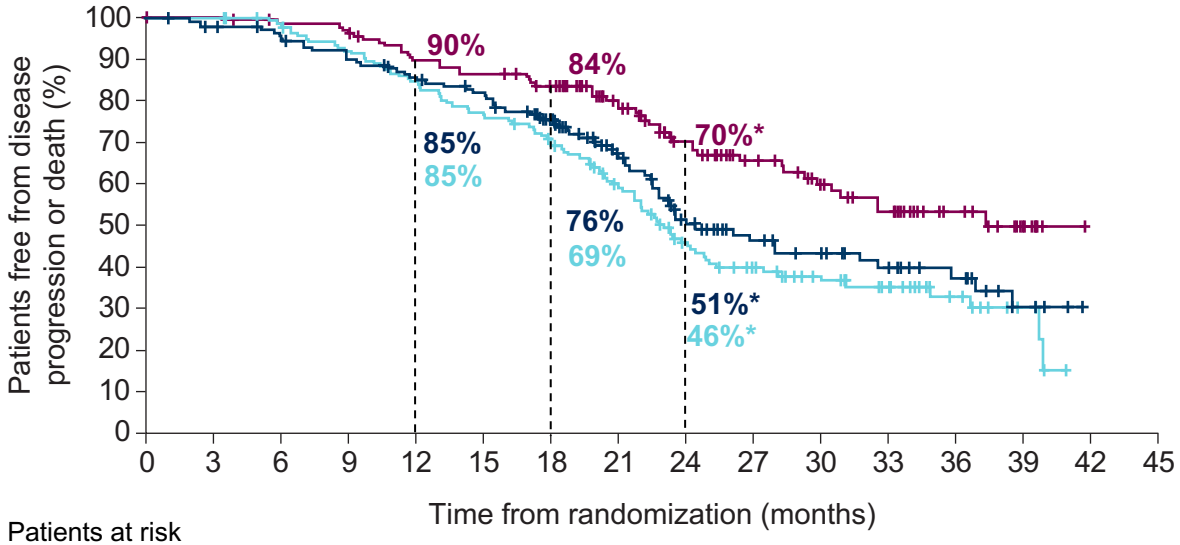
We knew this from IMagyn050

*In censored patients; †Medians and rates were estimated by KM method; ‡HR and CI were estimated from a stratified Cox proportional hazards model. Model stratified by timing and outcome of cytoreductive surgery and geographical region. *P* value from a stratified log rank text; §24-month PFS rates unstable.

Dr Philipp Harter

Subgroup analysis of PFS by HRD status

Non-tBRCAm HRD-positive

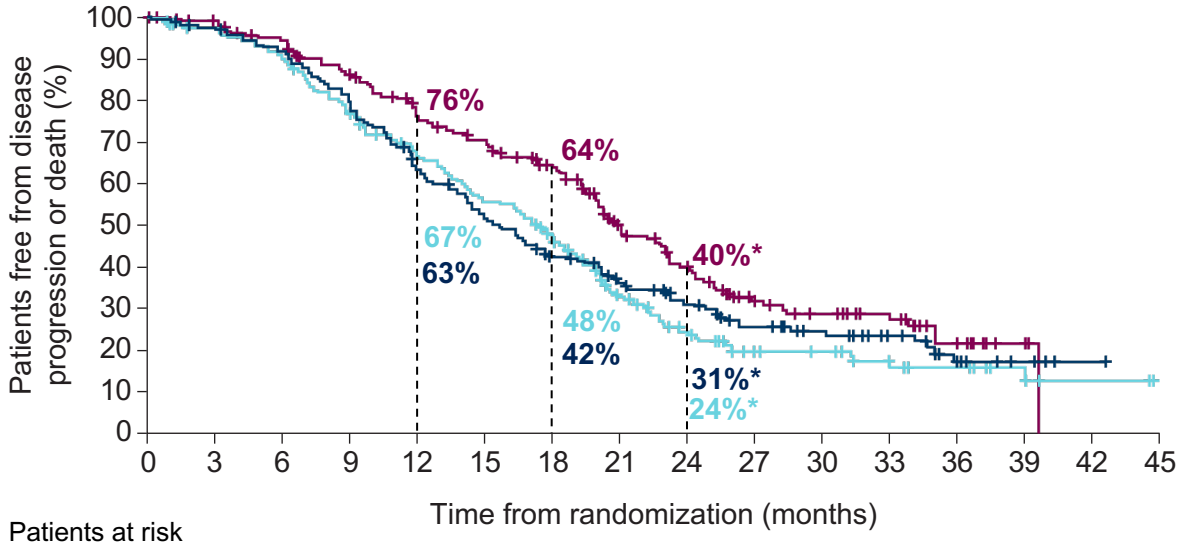


Patients at risk

Arm 1	143	141	136	126	116	105	93	73	52	41	31	22	13	6	0
Arm 2	148	142	137	128	118	112	94	66	45	34	28	21	15	7	0
Arm 3	140	138	135	131	120	116	107	84	63	49	39	32	17	6	0

	Arm 1 PC + bev N=143	Arm 2 PC + bev + durva N=148	Arm 3 PC + bev + durva + ola N=140
Events, n (%)	86 (60)	69 (47)	49 (35)
Median PFS, months†	23.0	24.4‡	37.3‡
HR (95% CI) vs Arm 1		**0.82** (0.60–1.12)§	**0.51** (0.36–0.72)§

HRD-negative



Patients at risk

Arm 1	216	203	188	159	135	112	92	55	34	21	19	12	9	5	2	0
Arm 2	199	189	177	153	120	97	76	59	45	33	25	17	8	4	1	0
Arm 3	211	202	190	169	145	132	111	75	57	33	26	20	10	3	0	

	Arm 1 PC + bev N=216	Arm 2 PC + bev + durva N=199	Arm 3 PC + bev + durva + ola N=211
Events, n (%)	157 (73)	142 (71)	127 (60)
Median PFS, months†	17.4	15.4	20.9
HR (95% CI) vs Arm 1		**0.94** (0.75–1.18)§	**0.68** (0.54–0.86)§

*24-month PFS rates unstable; †Medians and rates were estimated by KM method; ‡Median PFS in HRD-positive subgroup Arm 3 and Arm 2 unstable; §HR and CI were estimated from an unstratified Cox proportional hazards model.

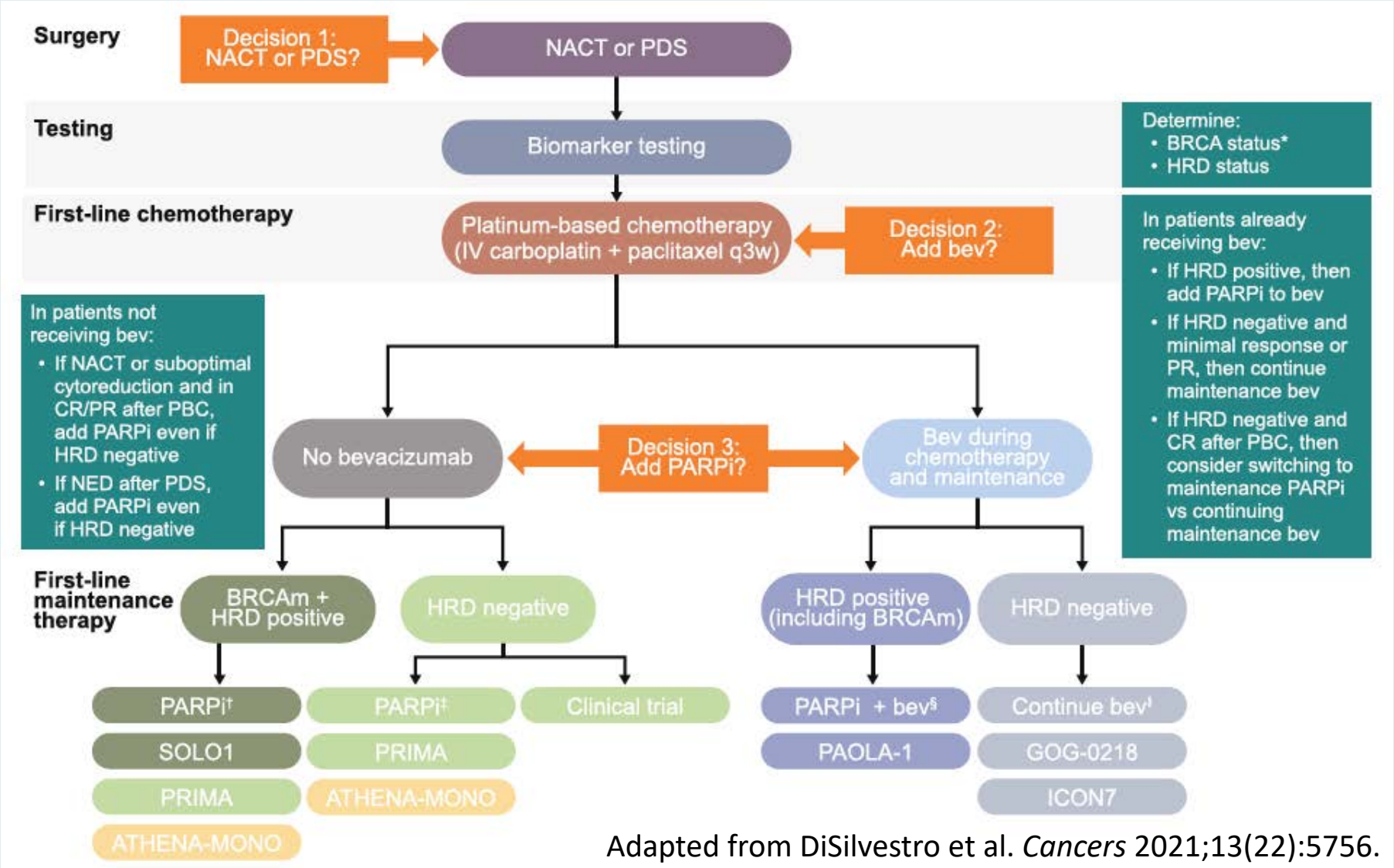
Dr Philipp Harter

Addition of CPI will have to wait for one of these to result…..

Trial	Size	Anti-angiogenic	PARPi	ICI	Start	Estimated Primary Completion
FIRST[a] ENGOT-OV44	1405	± Bevacizumab	Niraparib	Dostarlimab	Oct 2018	Jan 2023
DUO-O[b] ENGOT-OV46	~1254	Bevacizumab	Olaparib	Durvalumab	Jan 2019	June 2023
ATHENA[c] GOG-3020 ENGOT-OV45	~1000	-	Rucaparib	Nivolumab	May 2018	Dec 2024
ENGOT-OV43[d] KEYLYNK-001	~1086	± Bevacizumab	Olaparib	Pembrolizumab	Dec 2018	Aug 2025

- a. ClinicalTrials.gov. NCT03602859; b. ClinicalTrials.gov. NCT03737643; c. ClinicalTrials.gov. NCT03522246; d. NCT03740165.

Proposed Treatment Algorithm for Newly Diagnosed Ovarian Cancer



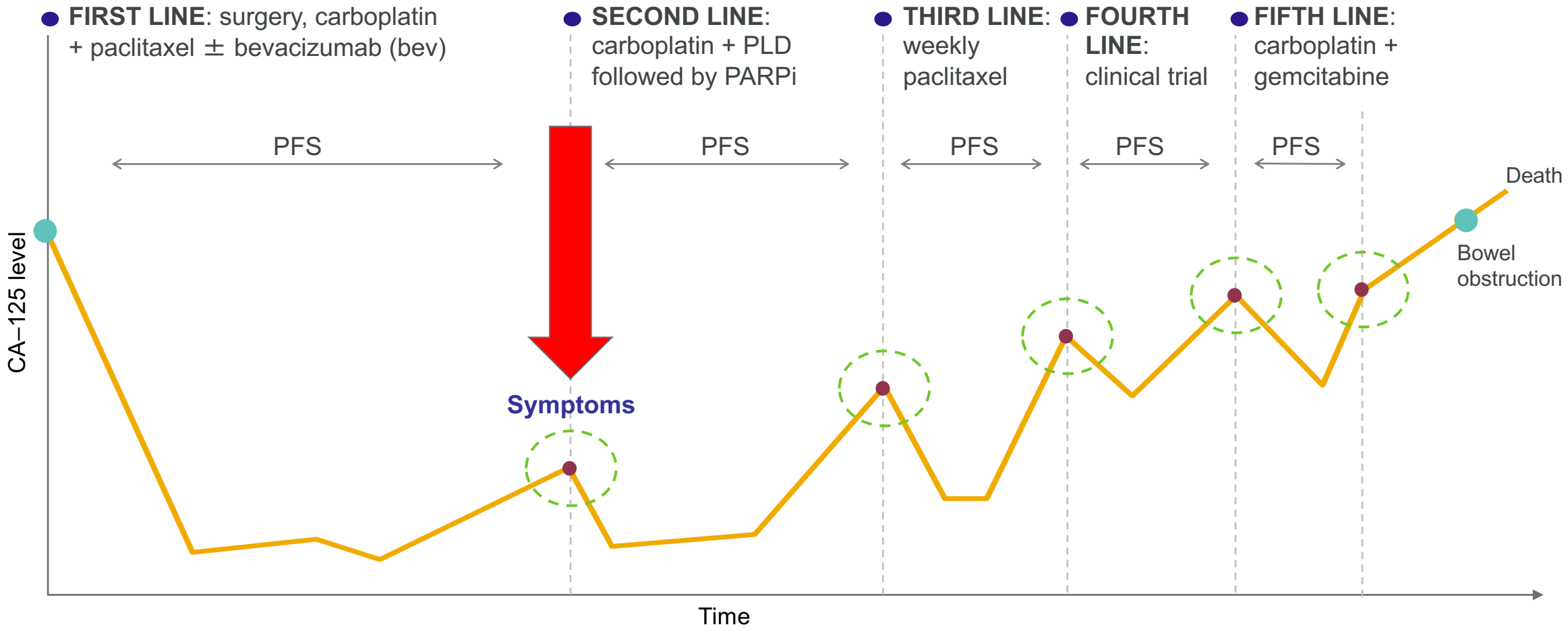
Adapted from DiSilvestro et al. *Cancers* 2021;13(22):5756.

NACT = neoadjuvant chemotherapy; PDS = primary debulking surgery; HRD = homologous recombination deficiency

O'Malley DM et al. *Target Oncol* 2023;18(4):471-503.

RTP RESEARCH TO PRACTICE

Now that we may be using all our best agents “up front” what do we do here?….



PARPi, PARP inhibitor; PFS, progression-free survival; PLD, pegylated liposomal doxorubicin; SOC, standard of care.
Ledermann JA et al. *Ann Oncol.* 2013;24(Suppl 6):vi24-vi32.

Other therapeutic options for recurrent PROC per the NCCN Guidelines[a] updated January 2023

Other recommended regimens[1]

Cytotoxic therapy[b]

- Capecitabine
- Carboplatin[c]
- Carboplatin/docetaxel[c]
- Carboplatin/paclitaxel (weekly)[c]
- Carboplatin/gemcitabine ± bevacizumab[c,d]
- Carboplatin/liposomal doxorubicin ± bevacizumab[c,d]
- Carboplatin/paclitaxel ± bevacizumab[c,d]
- Cyclophosphamide
- Doxorubicin
- Gemcitabine/cisplatin
- Ifosfamide
- Irinotecan
- Ixabepilone + bevacizumab (cat 2B)
- Melphalan
- Oxaliplatin
- Paclitaxel
- Paclitaxel, albumin bound
- Pemetrexed
- Sorafenib/topotecan
- Vinorelbine

Targeted therapy

(single agents)[e]

- Niraparib (cat 3)[f]
- Olaparib (cat 3)[g]
- Pazopanib (cat 2B)
- Rucaparib (cat 3)[h]

Hormone therapy

- Aromatase inhibitors
- Leuprolide acetate
- Megestrol acetate
- Tamoxifen

Useful in certain circumstances[1]

Cytotoxic therapy

- Carboplatin/paclitaxel (for age >70)[c]
- Carboplatin/paclitaxel, albumin bound (for confirmed taxane hypersensitivity)[c]

Immunotherapy

- Dostarlimab-gxly (for dMMR/MSI-H tumors)[i]
- Pembrolizumab (for patients with MSI-H or dMMR solid tumors or TMB-H tumors ≥10 mutations/megabase)[i]

Hormone therapy

- Fulvestrant for LGSOC

Targeted therapy

- Dabrafenib + trametinib (*BRAF* V600E–positive tumors)[i]
- Entrectinib or larotrectinib (*NTRK* gene fusion–positive tumors)[i]
- Mirvetuximab soravtansine-gynx + bevacizumab (for FRα-expressing tumors) (cat 2B)[i]
- Selpercatinib (for *RET* gene fusion-positive tumors)[i]
- Trametinib or binimetinib (cat 2B) for LGSOC

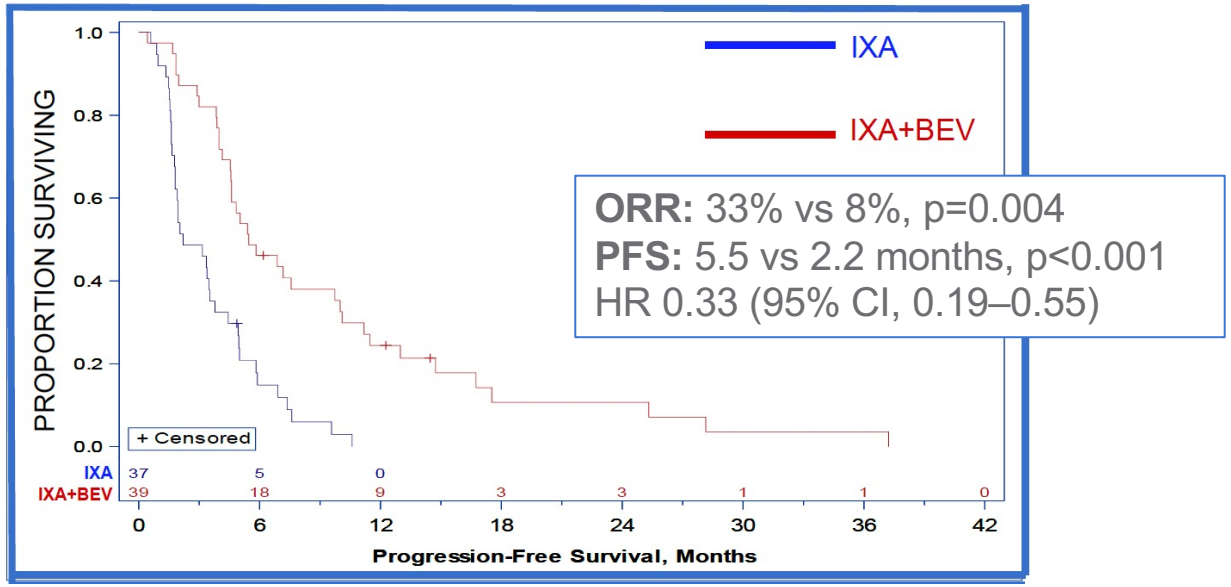
[a] Acceptable recurrence therapies for epithelial ovarian (including LCOC), fallopian tube, and primary peritoneal cancer; chemotherapy has not been shown to be beneficial in ovarian borderline epithelial tumors.[1] [b] Many of these single-agent cytotoxic therapy options have not been tested in patients who have been treated with modern chemotherapy regimens.[1] [c] Do not use in platinum-refractory disease. [d] Contraindicated for patients at increased risk of GI perforation. [e] FDA approvals for PARP inhibitor use as monotherapy for highly pretreated *BRCA*m or HRD+ ovarian cancer have recently been withdrawn.[2] [f] For patients treated with ≥3 prior chemotherapy regimens and whose cancer is associated with HRD.[1] [g] For patients with deleterious g*BRCA* mutation who received ≥2 lines of chemotherapy.[1] [h] For patients with tumors that are *BRCA*m who have been treated with ≥2 lines of chemotherapy.[1] [i] Validated molecular testing should be performed in a CLIA-approved facility using the most recent available tumor tissue. Tumor molecular analysis is recommended to include, at a minimum, tests to identify potential benefit from targeted therapeutics that have tumor-specific or tumor-agnostic benefit including, but not limited to, *BRCA1/2*, HRD status, MSI, MMR, TMB, *BRAF*, *FRα*, *RET*, *NTRK*, if prior testing did not include these markers.[1]

BRAF V600E, replacement of valine 600 with glutamic acid in B-Raf protein kinase; *BRCA*(m), BRCA DNA repair associated gene (mutated); Cat, category; CLIA, Clinical Laboratory Improvement Amendments; dMMR, mismatch repair deficient; FRα, folate receptor alpha; g*BRCA*, germline BRCA DNA repair associated gene mutation; HR, homologous recombination; HRD, homologous recombination deficient; LGSOC, low-grade serous ovarian carcinoma; MSI-H, high microsatellite instability; NCCN, National Comprehensive Cancer Network® (NCCN®); *NTRK*, neurotrophic tyrosine receptor kinase; PROC, platinum-resistant ovarian cancer; RET, proto-oncogene C-Ret; TMB-H, high tumor mutational burden.

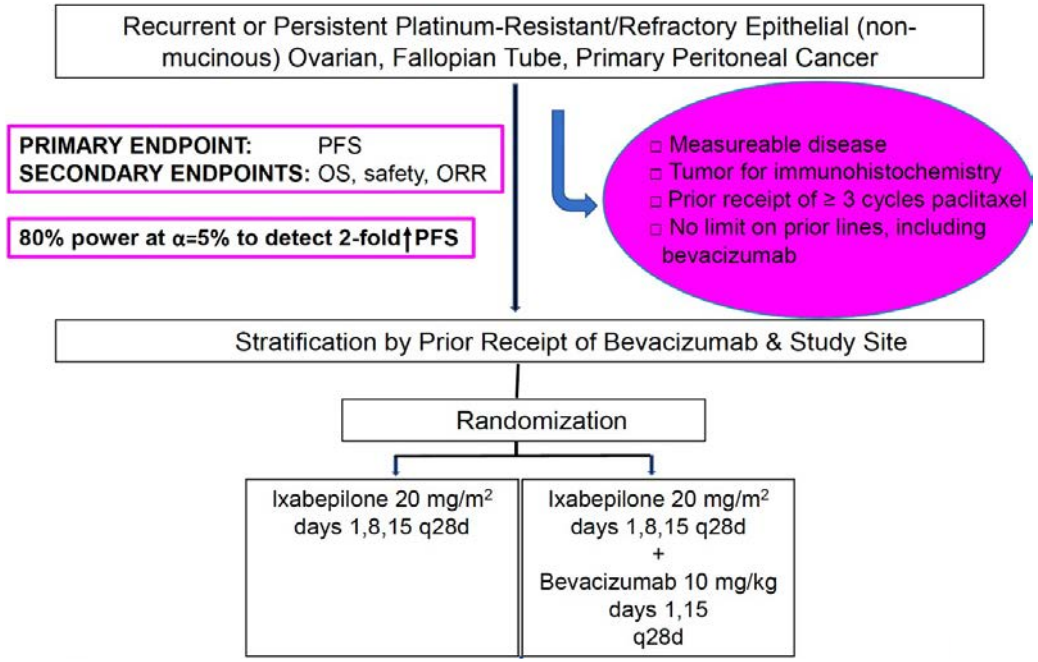
1. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer V.1.2023. Last updated December 22, 2022. Accessed January 9, 2023.
2. Tew WP et al. *J Clin Oncol*. 2022;40(33):3878–3881.

Ixabepilone + bevacizumab

- Ixabepilone (epothilone B analog)
  - Microtubule-stabilizing agent
- FDA approved for breast cancer (2007)
  - monotherapy for tumors resistant/refractory to anthracyclines, taxanes, capecitabine
  - in combination with capecitabine for tumors not suitable for treatment with anthracyclines/taxane



ORR: 33% vs 8%, p=0.004
PFS: 5.5 vs 2.2 months, p<0.001
HR 0.33 (95% CI, 0.19–0.55)

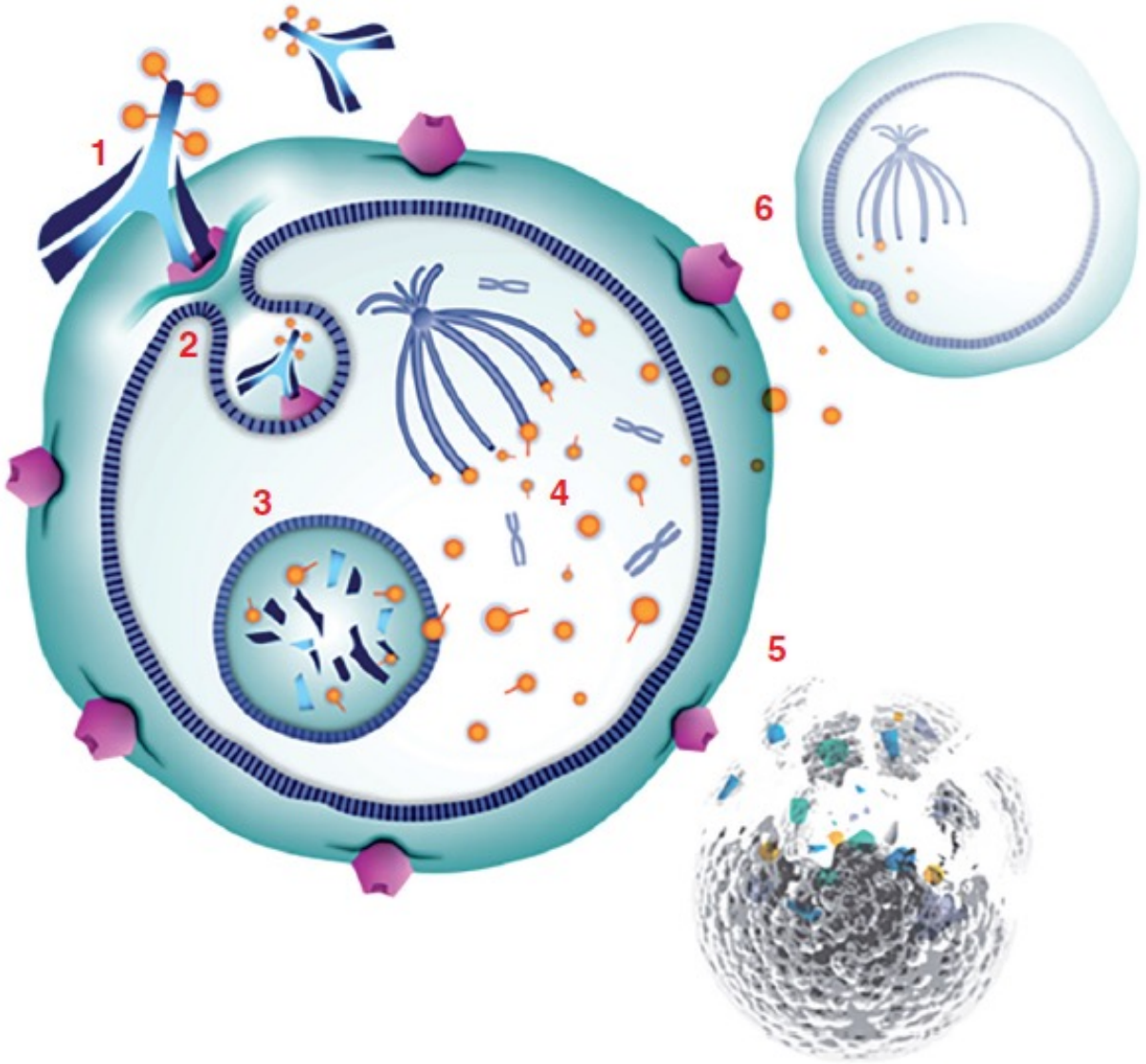


- Dose-limiting toxicities:
  - Peripheral neuropathy, neutropenia, fatigue
- IXA+Bev more likely to experience
  - HTN (36% vs 8%, p=0.005)
  - Peripheral neuropathy (51% vs 19%, p=0.004)

Bev, bevacizumab; HTN, hypertension; IXA, ixabepilone; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; q28d, every 28 days.

1. Roque DM et al, *Br J Cancer*. 2022;126(12):1695-1703. 2. Roque DM, et al, 2021 SGO Virtual Annual Meeting on Women's Cancer. Abstract 11570.

Mirvetuximab Soravtansine: Mechanism of Action



(1) Mirvetuximab soravtansine binds with high affinity to FRα expressed on the tumor cell surface

(2) The antibody-drug conjugate (ADC)/receptor complex becomes internalized via antigen-mediated endocytosis

(3) Lysosomal processing releases active DM4 catabolites from the ADC molecule

(4) These maytansinoid derivatives inhibit tubulin polymerization and microtubule assembly

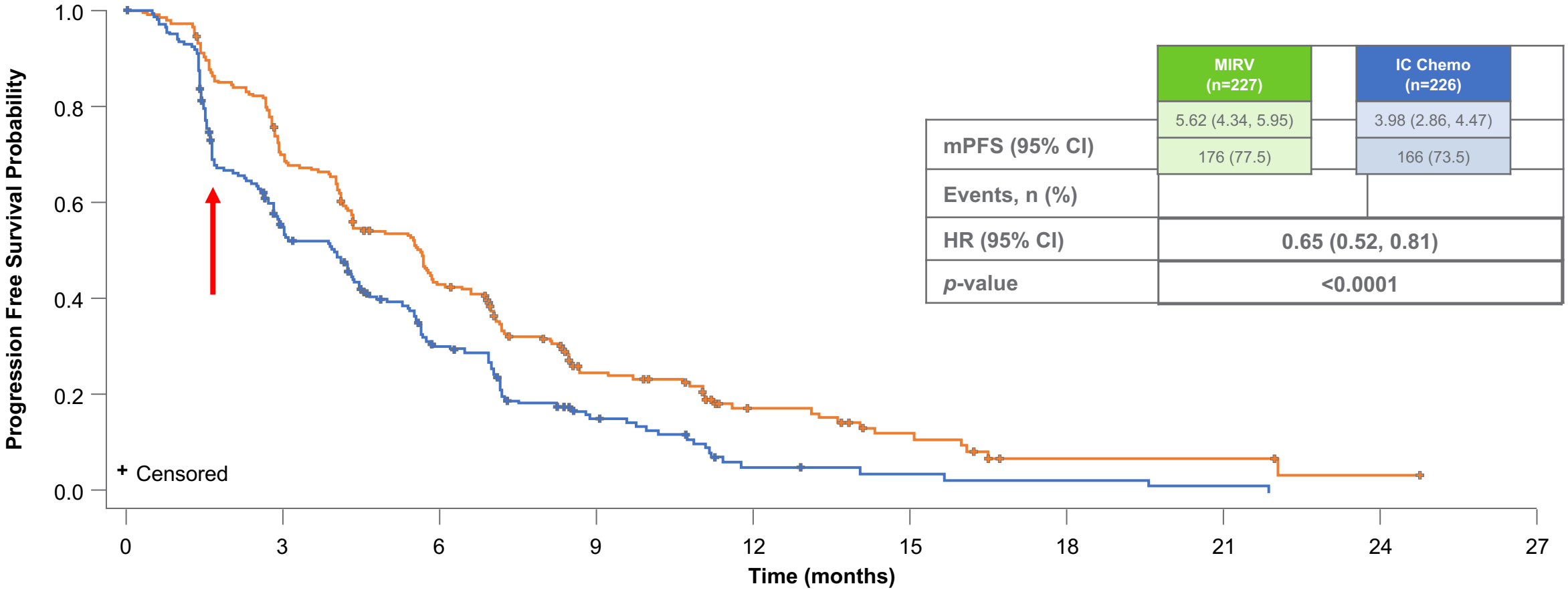
(5) The potent antimitotic effects result in cell-cycle arrest and apoptosis

(6) Active metabolites can also diffuse into neighboring cells and induce further cell death — in other words, bystander killing

Moore K et al. *Future Oncol* 2018:14;123-36.

RTP RESEARCH TO PRACTICE

MIRASOL – Primary Endpoint: Progression-Free Survival by Investigator

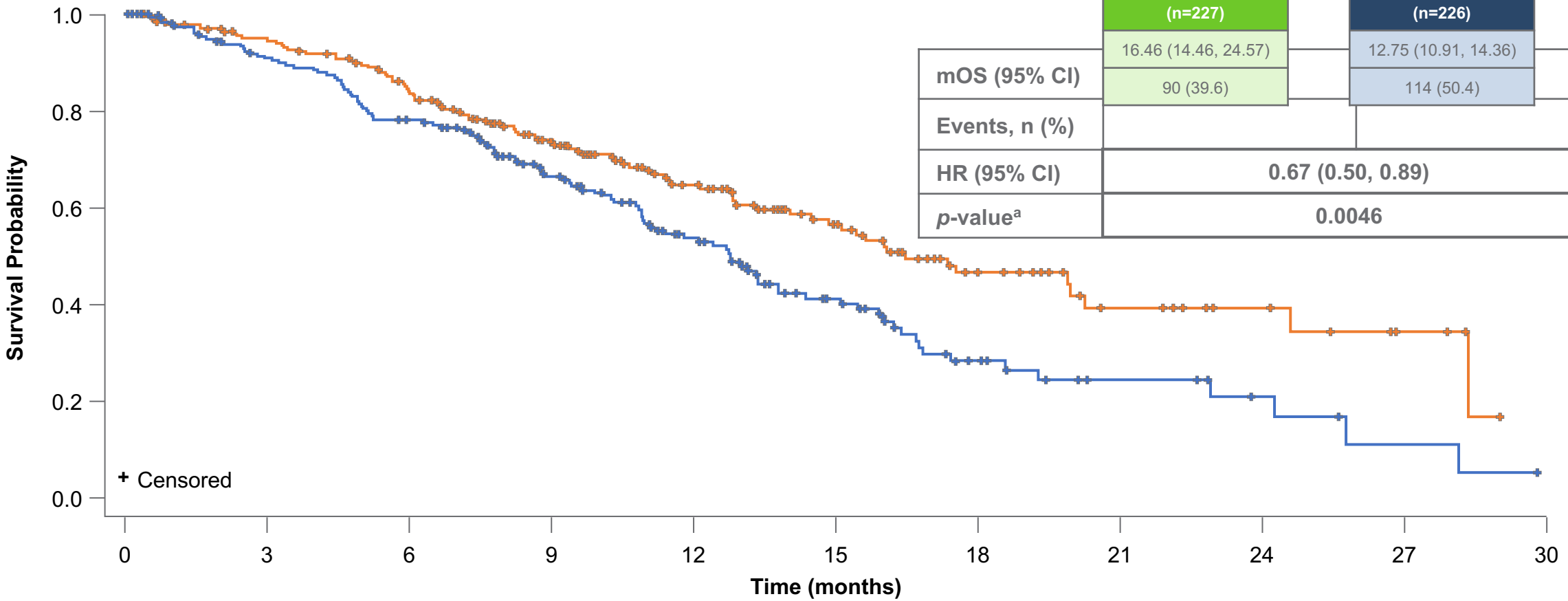


	MIRV (n=227)	IC Chemo (n=226)
mPFS (95% CI)	5.62 (4.34, 5.95)	3.98 (2.86, 4.47)
Events, n (%)	176 (77.5)	166 (73.5)
HR (95% CI)	0.65 (0.52, 0.81)	
p-value	<0.0001	

No. Participants at Risk

MIRV	227	151	89	38	18	10	3	3	1	0
IC Chemo	226	98	48	19	5	3	2	1	0	

MIRASOL – Overall Survival



	MIRV (n=227)	IC Chemo (n=226)
mOS (95% CI)	16.46 (14.46, 24.57)	12.75 (10.91, 14.36)
Events, n (%)	90 (39.6)	114 (50.4)
HR (95% CI)	0.67 (0.50, 0.89)	
p-value[a]	0.0046	

No. Participants at Risk

MIRV	227	204	175	128	82	53	28	15	9	4	0
IC Chemo	226	185	157	107	68	39	18	9	5	2	0

Data cutoff: March 6, 2023; median follow-up time: 13.11 months

MIRV, mirvetuximab soravtansine; IC Chemo, investigator's choice chemotherapy; mOS, median overall survival; CI, confidence interval; HR, hazard ratio.

[a]Overall survival is statistically significant based on pre-specified boundary p-value at interim analysis = 0.01313

PICCOLO

SINGLE-ARM TRIAL FOR MIRVETUXIMAB IN HIGH FRα PATIENTS WITH PLATINUM-SENSITIVE OVARIAN CANCER

Enrollment completed

Global Trial Top Line Results 2024

PRIMARY ENDPOINT
ORR by Investigator

SECONDARY ENDPOINT
DOR by Investigator

ENROLLMENT AND KEY ELIGIBILITY
75 patients
Platinum-sensitive ovarian cancer
2+ prior systemic treatments
At least 2 prior platinum-containing regimens
Prior PARPi required if BRCA+
Appropriate for single-agent therapy

ORR: overall response rate; DOR: duration of response; BRCA: BReast CAncer gene

GLORIOSA

RANDOMIZED PHASE 3 TRIAL FOR MIRVETUXIMAB + BEVACIZUMAB MAINTENANCE IN FRα-HIGH PSOC PATIENTS

TARGET TIMELINES

- Open for Accrual
- Global trial
- POTENTIAL APPROVAL 2026

PRIMARY ENDPOINT

PFS

SECONDARY ENDPOINT

OS by BICR

ENROLLMENT AND KEY ELIGIBILITY

438 patients
Platinum-sensitive ovarian cancer
1 prior systemic treatment
Prior PARPi required if BRCA+
CR, PR, or SD after treatment with platinum-based doublet + bevacizumab required

PRIOR MIRV EXPERIENCE

Strong MIRV/BEV treatment efficacy and tolerability in > 120 patients
FRα high rPSOC, MIRV/BEV has an ORR of 69% and mPFS of 13.3 months

PFS (progression-free survival); BICR (blinded independent central review); OS (overall survival); CR (complete response); PR (partial response); SD (stable disease); BRCA (BReast CAncer gene); MIRV (mirvetuximab soravtansine); DOR: duration of response; ORR: overall response rate

Dr Neil Love | AON Annual Clinical Summit | Saturday, October 14, 2023

Endometrial and Cervical Cancers

Bradley J. Monk, MD, FACS, FACOG
University of Arizona
and Creighton University
Phoenix, USA

Setting the Stage

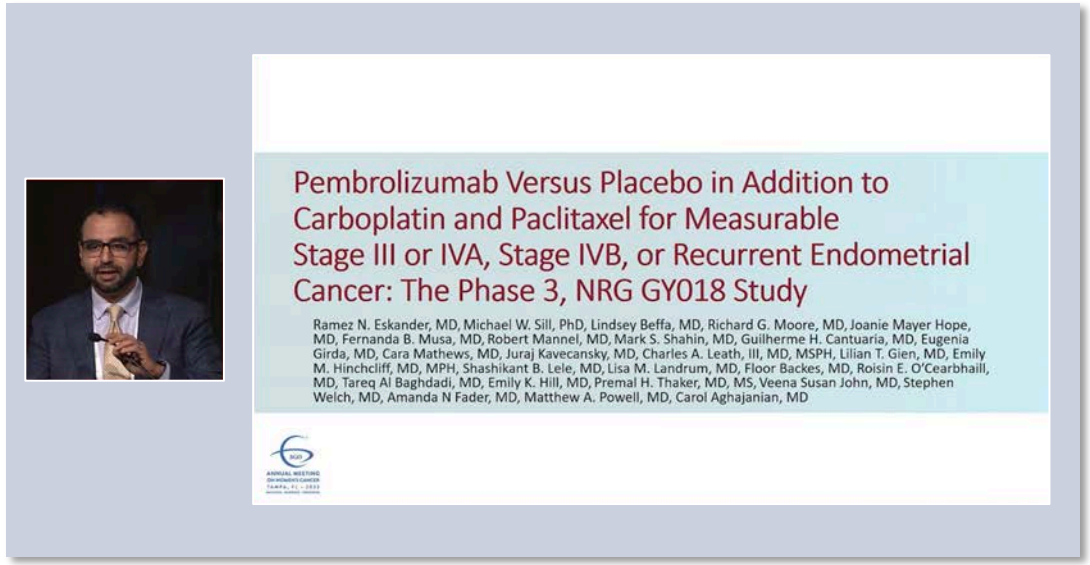
Recent Data From Anti–PD-1 Combination Trials in Primary Advanced or Recurrent Endometrial Cancer

Paradigm-shifting data were presented at SGO[1-2]

Society of Gynecologic Oncology Annual Meeting | Tampa, Florida | March 2023

- Presentation of data from 2 landmark phase 3 EC trials in a late-breaking abstract session
- Concurrently published in *New England Journal of Medicine*

Dr. Mirza presents RUBY Part 1 data[a]



Dr. Eskander presents GY018 data

July 31, 2023: Dostarlimab + chemotherapy approved as 1L treatment for dMMR/MSI-H EC (US)[3]

[a]RUBY Part 1 was also presented at ESMO virtual plenaries, March 2023.
EC = endometrial cancer.

1. Mirza MR, et al. Presented at: SGO; March 25-28, 2023; Tampa, FL, USA. 2. Eskander RN, et al. Presented at: SGO; March 25-28 2023; Tampa, FL, USA. 3. GSK Press Release. https://www.gsk.com/en-gb/media/press-releases/jemperli-plus-chemotherapy-approved-in-us-for-new-indication. Accessed August 23, 2023.

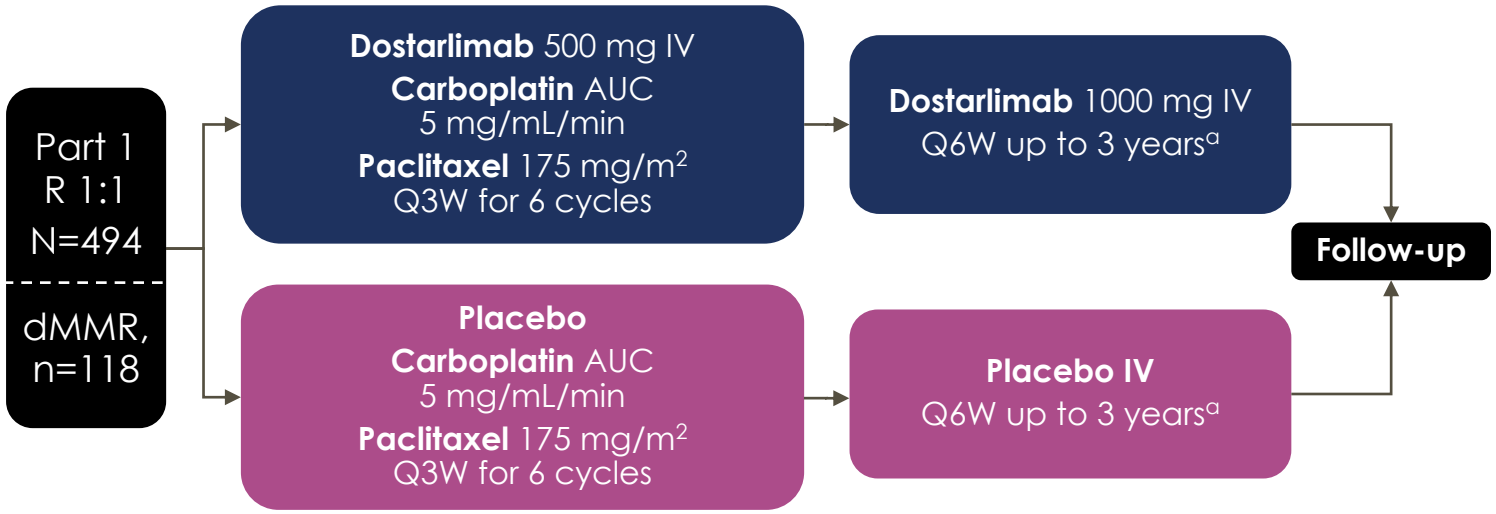
RUBY Part 1 | ENGOT-EN6 | GOG-3031 | NCT03981796[1,2]

Eligible patients

- Histologically or cytologically proven EC with recurrent or advanced disease
- Stage III or IV disease or first recurrence of EC with low potential for cure by use of radiation therapy or surgery alone or in combination
  - Carcinosarcoma, clear cell, serous, or mixed histology
- Naive to systemic therapy or systemic anticancer therapy and recurrence or PD ≥6 months after completing treatment
- ECOG PS 0 or 1
- Adequate organ function

Stratification

- MMR/MSI status
- Prior radiotherapy
- Disease status



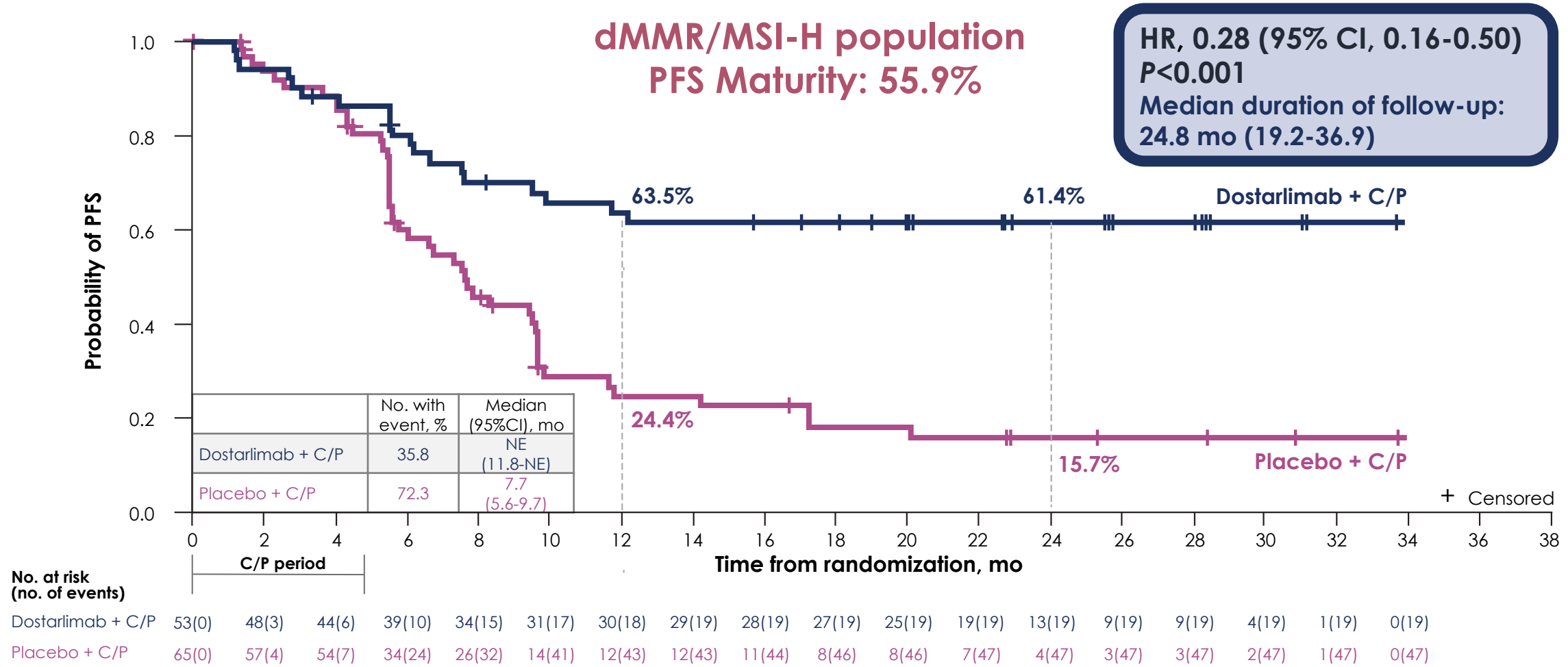
Primary end points: PFS (IA),[b] OS

Secondary end points: PFS (BICR),[c] PFS2, ORR/DOR/DCR,[d] QoL, PK and immunogenicity, safety[e]

[a]Treatment ends after 3 years, PD, toxicity, withdrawal of consent, investigator's decision, or death, whichever occurs first. Continued treatment with dostarlimab or placebo beyond 3 years may be considered after discussion between the sponsor and the investigator. [b]PFS per IA – all patients with recurrent or primary advanced EC (ITT population). [c]PFS by BICR per RECIST v1.1 (not IA) – ITT population and dMMR/MSI-H population. [d]ORR, DOR, and DCR by BICR and IA. [e]All AEs assessed for intensity according to CTCAE v4.03.
AE = adverse event; AUC = area under the plasma or serum concentration-time curve; BICR = blinded independent central radiology review; CTCAE = Common Terminology Criteria for Adverse Events; DCR = disease control rate; dMMR = mismatch repair deficient; DOR = duration of response; EC = endometrial cancer; ECOG PS = Eastern Cooperative Oncology Group performance status; ENGOT = European Network of Gynaecological Oncological Trial Groups; GOG = Gynecologic Oncology Group; IA = investigator-assessed; ITT = intention to treat; IV = intravenously; MMR = mismatch repair; MSI = microsatellite instability; MSI-H = microsatellite instability-high; ORR = objective response rate; OS = overall survival; PD = progressive disease; PFS = progression-free survival; PFS2 = time to second disease progression or death; PK = pharmacokinetics; QoL = quality of life; QXW = every X weeks; R = randomization; RECIST v1.1 = Response Evaluation Criteria in Solid Tumors version 1.1.

1. National Library of Medicine. https://clinicaltrials.gov/ct2/show/NCT03981796. Accessed August 23, 2023. 2. Mirza MR, et al. *N Engl J Med*. 2023;388:2145-2158.

Primary end point: PFS by investigator per RECIST v1.1[1,2]



Adapted from Mirza MR, et al. *N Engl J Med*. 2023;388:2145-2158.

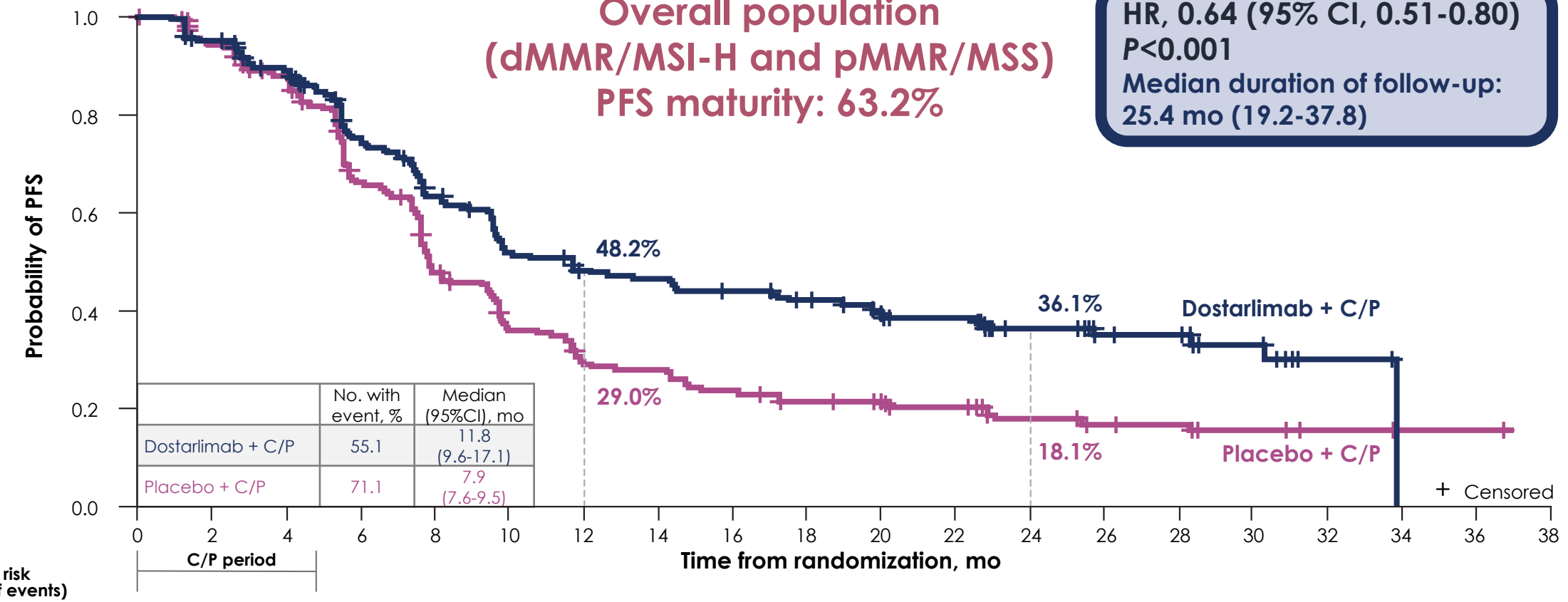
CI = confidence interval; C/P = carboplatin and paclitaxel; dMMR = mismatch repair deficient; HR = hazard ratio; mo = months; MSI-H = microsatellite instability-high; NE = not estimable; PFS = progression-free survival; RECIST v1.1 = Response Evaluation Criteria in Solid Tumors version 1.1.

1. Mirza MR, et al. *N Engl J Med*. 2023;388:2145-2158. 2. Mirza MR, et al. *Ann Oncol*. 2023;34:500-501.

Primary end point: PFS by investigator per RECIST v1.1[1,2]

Overall population (dMMR/MSI-H and pMMR/MSS)
PFS maturity: 63.2%

HR, 0.64 (95% CI, 0.51-0.80)
***P*<0.001**
Median duration of follow-up: 25.4 mo (19.2-37.8)



	No. with event, %	Median (95%CI), mo
Dostarlimab + C/P	55.1	11.8 (9.6-17.1)
Placebo + C/P	71.1	7.9 (7.6-9.5)

No. at risk (no. of events)

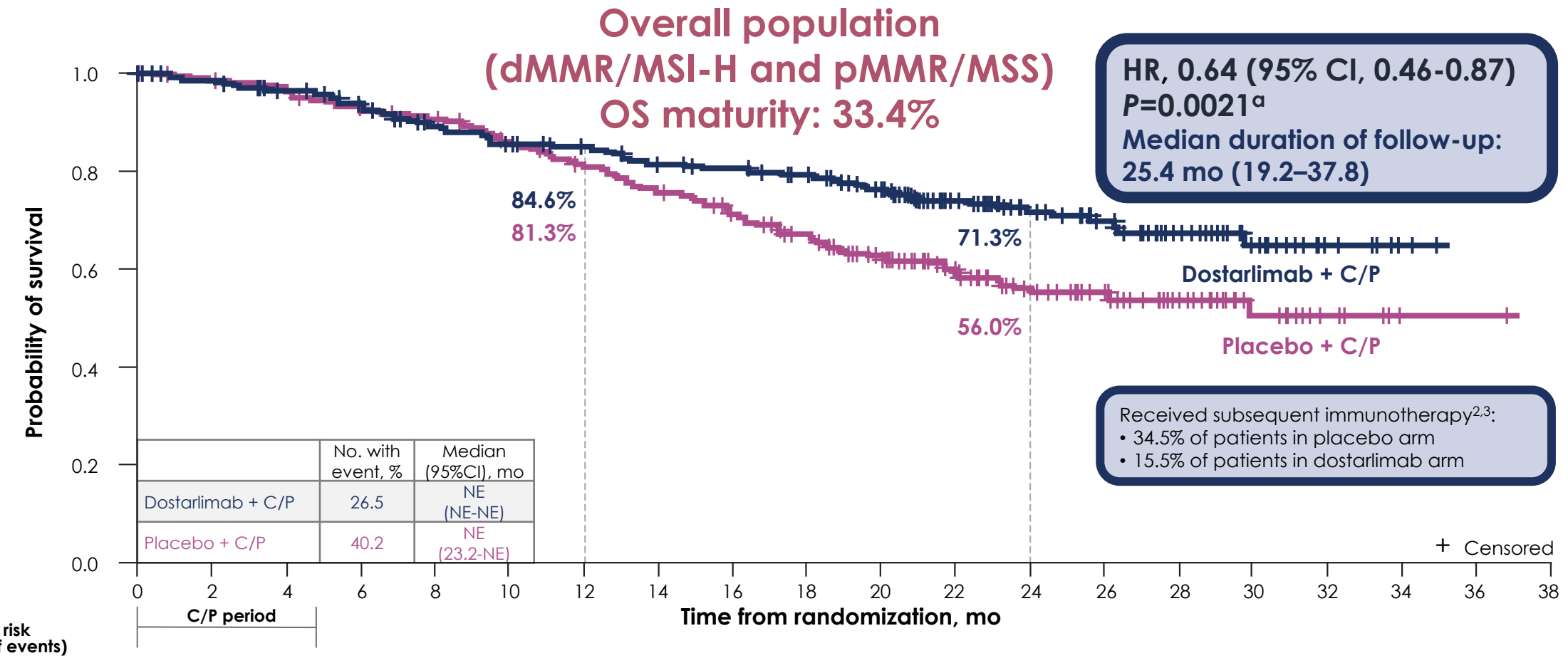
Dostarlimab + C/P	245(0)	220(12)	197(25)	157(55)	130(80)	105(103)	94(110)	90(113)	84(118)	78(122)	66(127)	52(128)	34(131)	23(132)	22(132)	12(133)	2(134)	0(135)	
Placebo + C/P	249(0)	219(14)	200(29)	144(77)	103(115)	74(141)	59(155)	57(157)	48(166)	42(170)	39(170)	32(172)	20(175)	14(176)	13(176)	5(177)	2(177)	1(177)	1(177)	0(177)

Adapted from Mirza MR, et al. *N Engl J Med*. 2023;388:2145-2158.

CI = confidence interval; C/P = carboplatin and paclitaxel; dMMR = mismatch repair deficient; HR = hazard ratio; mo = months; MSI-H = microsatellite instability-high; MSS = microsatellite stable; PFS = progression-free survival; pMMR= mismatch repair proficient; RECIST v1.1 = Response Evaluation Criteria in Solid Tumors version 1.1.

1. Mirza MR, et al. *N Engl J Med*. 2023;388:2145-2158. 2. Mirza MR, et al. *Ann Oncol.* 2023;34:500-501.

Primary end point: OS in overall population[1,2]



No. at risk (no. of events)

Dostarlimab + C/P	245(0)	235(5)	224(8)	214(15)	198(25)	190(33)	183(35)	174(42)	169(44)	162(47)	145(53)	110(57)	83(60)	64(62)	45(64)	25(65)	7(65)	2(65)	0(65)	
Placebo + C/P	249(0)	242(3)	237(7)	226(17)	219(22)	203(35)	189(45)	177(57)	162(68)	147(78)	125(88)	88(93)	65(97)	48(98)	33(99)	15(100)	6(100)	1(100)	1(100)	0(100)

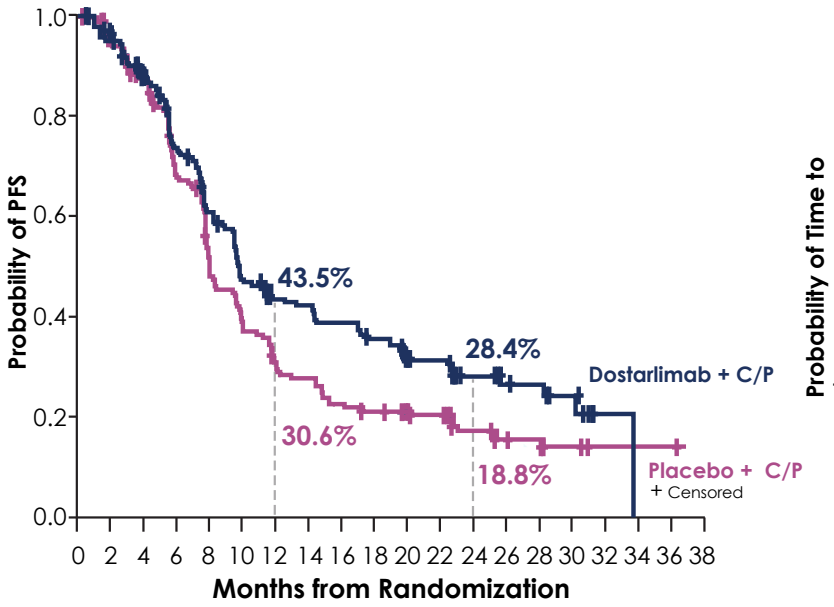
Adapted from Mirza MR, et al. *N Engl J Med*. 2023;388:2145-2158.

[a]*P*≤0.00177 required to declare statistical significance at first interim analysis.
CI = confidence interval; C/P = carboplatin and paclitaxel; dMMR = mismatch repair deficient; HR = hazard ratio; mo = months; MSI-H = microsatellite instability-high; MSS = microsatellite stable; NE = not estimable; OS = overall survival; pMMR = mismatch repair proficient.
1. Mirza MR, et al. *N Engl J Med*. 2023;388:2145-2158. 2. Mirza MR, et al. *Ann Oncol*. 2023;34:500-501.

Efficacy end points assessed in pMMR/MSS patients[1]

PFS

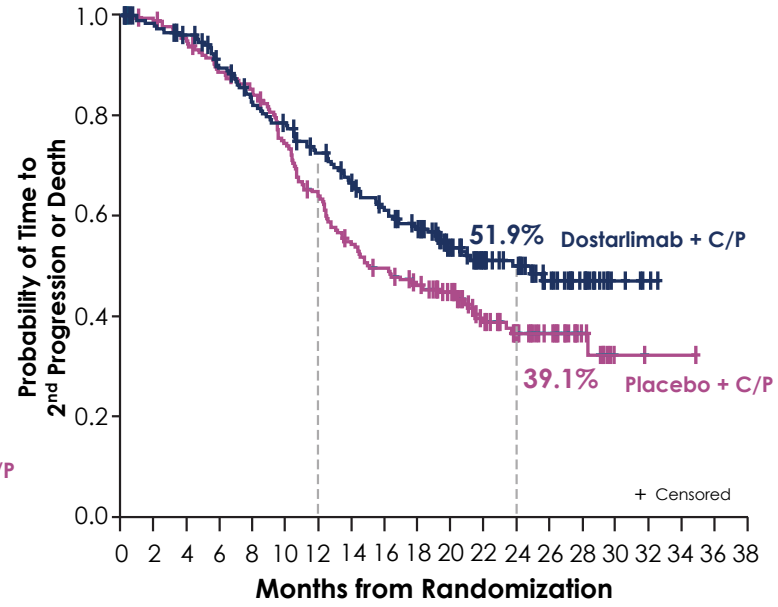
HR 0.76
(95% CI, 0.59-0.98)



Adapted from Mirza MR, et al. *N Engl J Med*. 2023;388:2145-2158.

PFS2

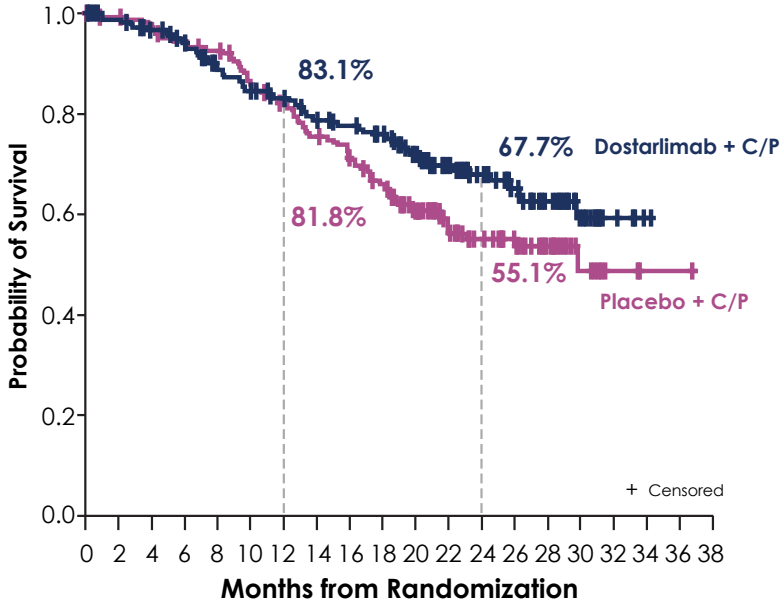
HR 0.71
(95% CI, 0.54-0.95)



Adapted from Mirza MR, et al. *N Engl J Med*. 2023;388:2145-2158.

OS

HR 0.73
(95% CI, 0.52-1.02)



Adapted from Mirza MR, et al. *N Engl J Med*. 2023;388:2145-2158.

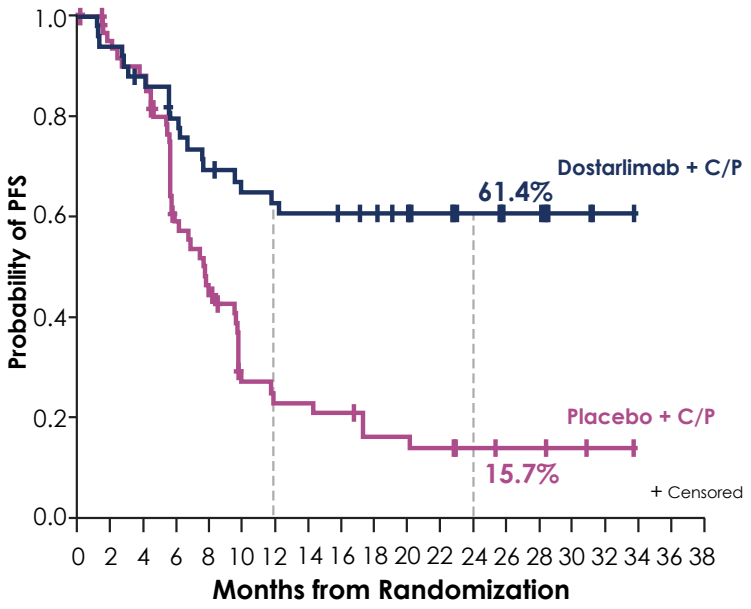
CI = confidence interval; C/P = carboplatin and paclitaxel; HR = hazard ratio; MSS = microsatellite stable; PFS = progression-free survival; PFS2 = progression-free survival 2; pMMR = mismatch repair proficient; OS = overall survival.

1. Mirza MR, et al. *N Engl J Med* 2023;388:2145-2158.

Efficacy end points assessed in dMMR/MSI-H patients[1]

PFS

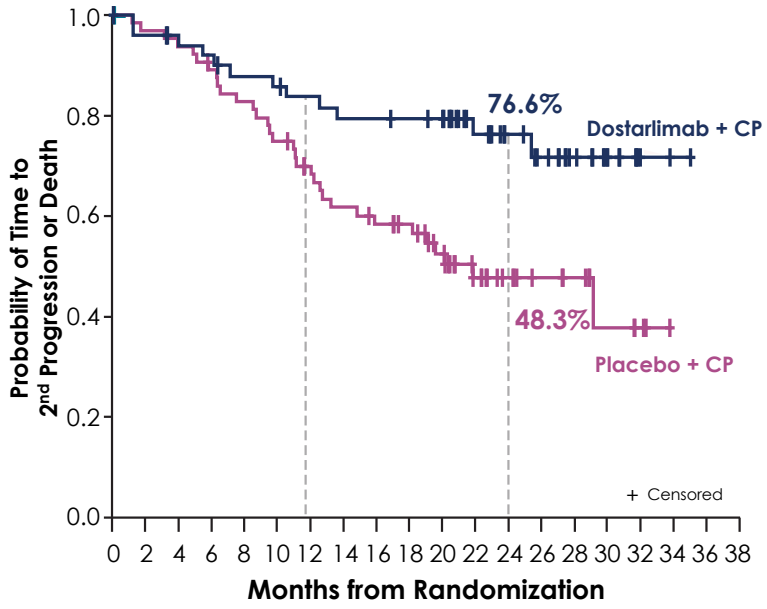
HR 0.28
(95% CI, 0.16-0.50)
***P*<0.001**



Adapted from Mirza MR, et al. *N Engl J Med*. 2023;388:2145-2158.

PFS2

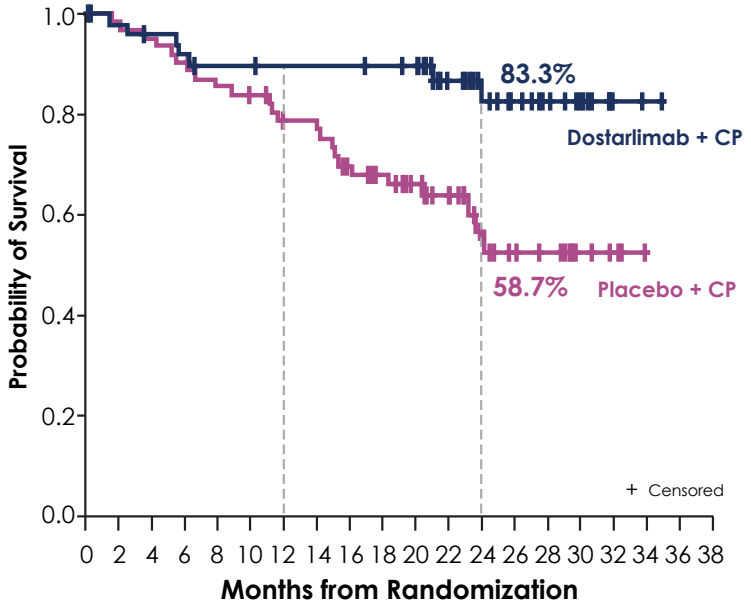
HR 0.37
(95% CI, 0.19-0.73)



Adapted from Mirza MR, et al. *N Engl J Med*. 2023;388:2145-2158.

OS

HR 0.30
(95% CI, 0.13-0.70)



Adapted from Mirza MR, et al. *N Engl J Med*. 2023;388:2145-2158.

CI = confidence interval; C/P = carboplatin and paclitaxel; dMMR = deficient mismatch mutation repair; HR = hazard ratio; MSI-H = microsatellite instability-high; OS = overall survival; PFS = progression-free survival; PFS2 = progression-free survival 2.

1. Mirza MR, et al. *N Engl J Med* 2023;388:2145-2158.

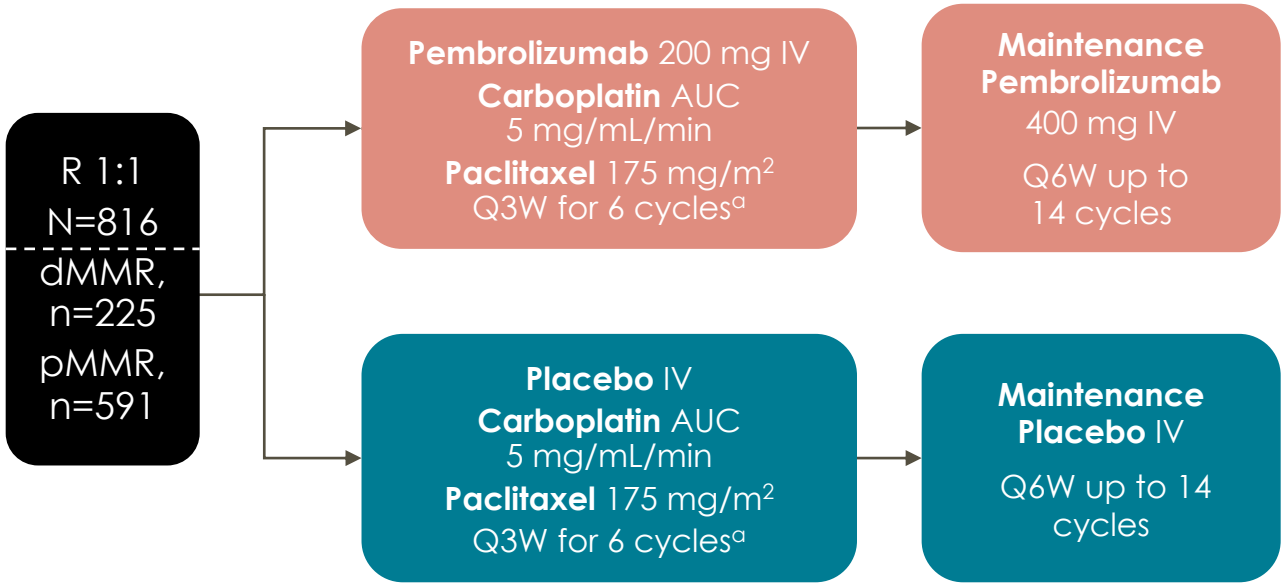
GY018 | KEYNOTE-868 | NCT03914612[1,2]

Eligible patients

- Histologically confirmed recurrent or advanced (stage III, IVA, or IVB) EC
- ECOG PS of 0-2
- Results of institutional MMR IHC testing
- Submission of tumor specimens for centralized MMR IHC testing
- No prior chemotherapy treatment for EC
- Prior adjuvant chemotherapy allowed if completed ≥12 months before enrollment

Stratification

- MMR status
- ECOG PS (0, 1 or 2)
- Prior chemotherapy (yes/no)



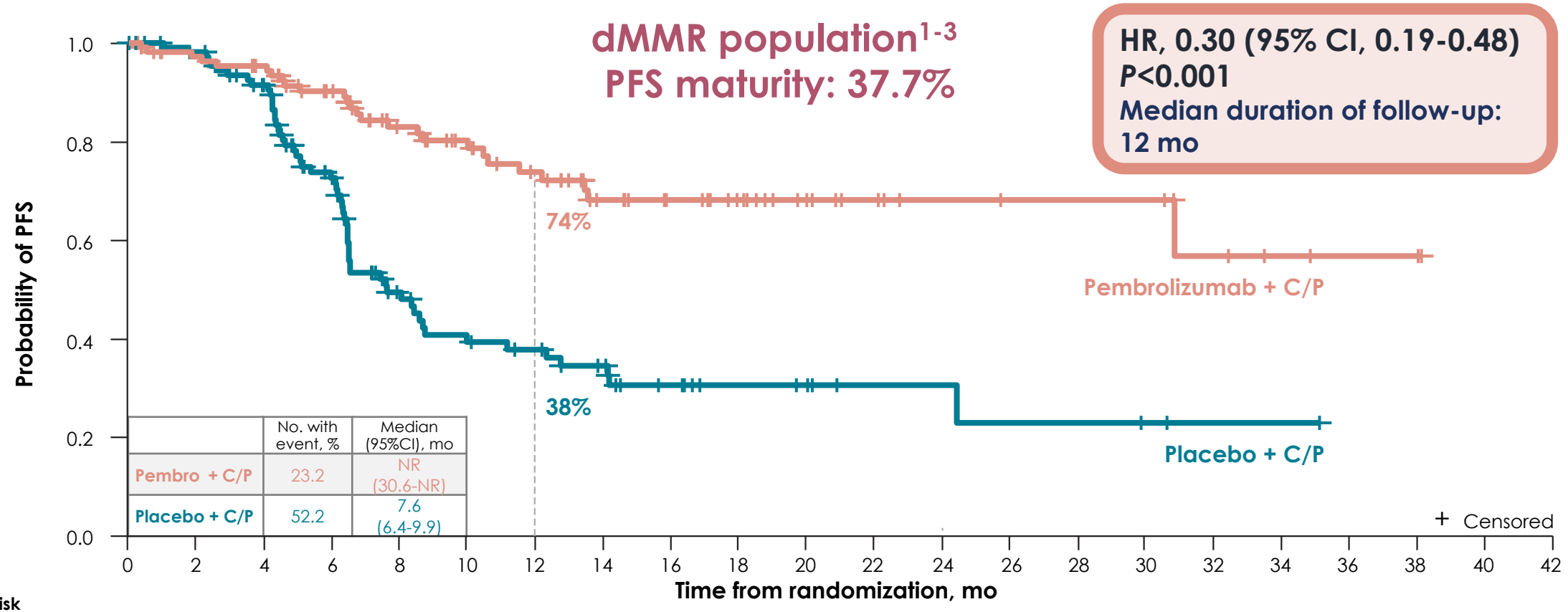
Primary end point: PFS (IA)

Secondary end points: AEs, ORR, DOR, OS, QoL, concordance between institutional MMR IHC and centralized MMR IHC

[a]Patients with SD or PR who still have measurable disease may continue treatment for up to 10 cycles (if deemed necessary by the treating physician) in the absence of disease progression or unacceptable toxicity.
AE = adverse event; AUC = area under the plasma or serum concentration-time curve; dMMR = mismatch repair deficient; DOR = duration of response; EC = endometrial cancer; ECOG PS = Eastern Cooperative Oncology Group performance status; IA = investigator-assessed; IHC = immunohistochemistry; IV = intravenously; MMR = mismatch repair; ORR = objective response rate; OS = overall survival; PFS = progression-free survival; pMMR = mismatch repair proficient; PR = partial response; QoL = quality of life; QXW = every X weeks; R = randomization; SD = stable disease.

1. National Library of Medicine. https://clinicaltrials.gov/ct2/show/NCT03914612. Accessed August 23, 2023. 2. Eskander RN, et al. *N Engl J Med*. 2023;388:2159-2170.

GY018 primary end point: PFS by investigator per RECIST v1.1



No. at risk (no. of events)

Placebo + C/P	113(2)	62(24)	24(35)	8(47)	4(51)	2(52)	0(54)	
Pembro + C/P	112(1)	80(22)	44(46)	22(65)	9(78)	8(79)	2(84)	0(86)

Adapted from Eskander RN, et al. *N Engl J Med*. 2023;388:2159-2170.

Data cutoff date: December 16, 2022.

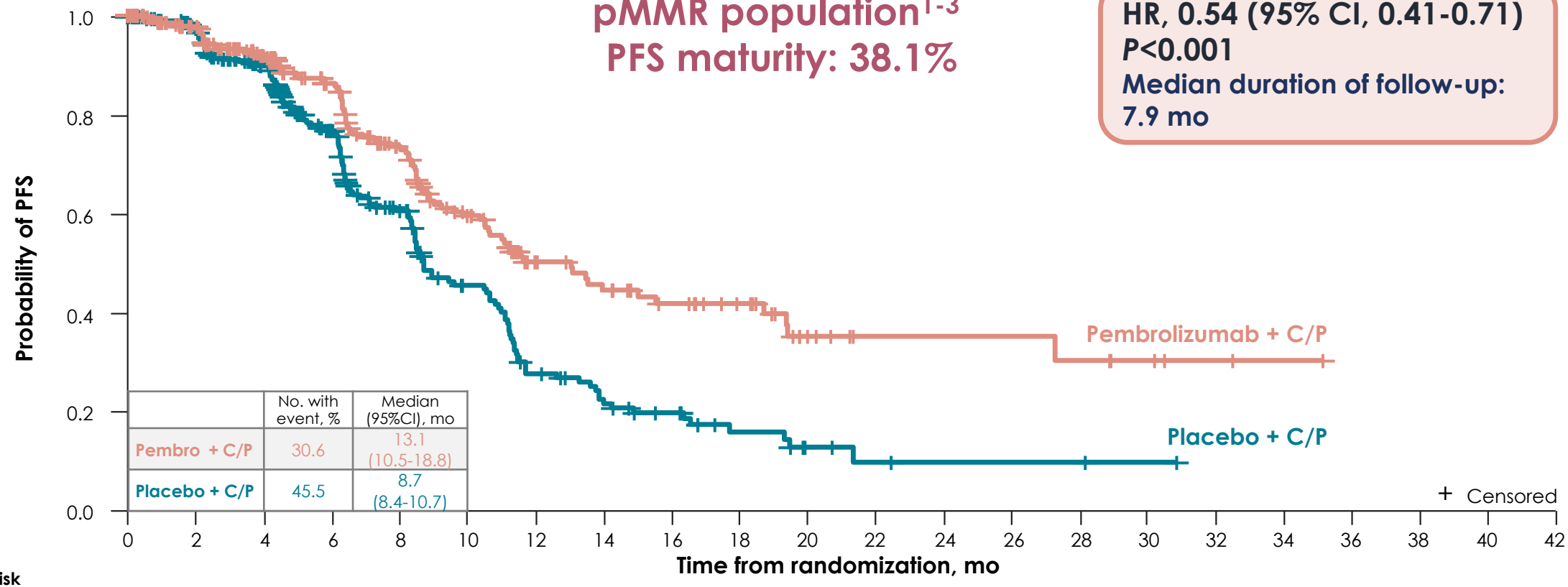
CI = confidence interval; C/P = carboplatin and paclitaxel; dMMR = mismatch repair deficient; HR = hazard ratio; mo = months; NR = not reached; Pembro = pembrolizumab; PFS = progression-free survival; RECIST v1.1 = Response Evaluation Criteria in Solid Tumors version 1.1.

1. Eskander RN, et al. *N Engl J Med*. 2023;388:2159-2170. 2. Eskander RN, et al. Presented at: SGO; March 25-28 2023; Tampa, FL, USA. 3. Arend RC, et al. Presented at: SGO; March 25-28, 2023; Tampa, FL, USA.

GY018 primary end point: PFS by investigator per RECIST v1.1

pMMR population[1-3]
PFS maturity: 38.1%

HR, 0.54 (95% CI, 0.41-0.71)
***P*<0.001**
Median duration of follow-up: 7.9 mo



	No. with event, %	Median (95%CI), mo
Pembro + C/P	30.6	13.1 (10.5-18.8)
Placebo + C/P	45.5	8.7 (8.4-10.7)

No. at risk (no. of events)

Placebo + C/P	292(14)	129(115)	33(141)	10(152)	2(157)	1 (158)	0(159)
Pembro + C/P	290(15)	150(112)	45(167)	20(185)	7(195)	3(198)	0(201)

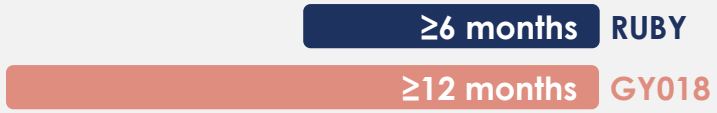
Adapted from Eskander RN, et al. *N Engl J Med*. 2023;388:2159-2170.

Data cutoff date: December 16, 2022.
CI = confidence interval; C/P = carboplatin and paclitaxel; dMMR = mismatch repair deficient; HR = hazard ratio; mo = months; Pembro = pembrolizumab; PFS = progression-free survival; RECIST v1.1 = Response Evaluation Criteria in Solid Tumors version 1.1.

1. Eskander RN, et al. *N Engl J Med*. 2023;388:2159-2170. 2. Eskander RN, et al. Presented at: SGO; March 25-28 2023; Tampa, FL, USA. 3. Arend RC, et al. Presented at: SGO; March 25-28, 2023; Tampa, FL, USA.

RUBY Part 1 and GY018: Key differences in study design[1-4]

Time Since Chemotherapy for Recurrent Patients



Histology – Carcinosarcoma

RUBY	GY018
~10%	Not included

Primary End Points

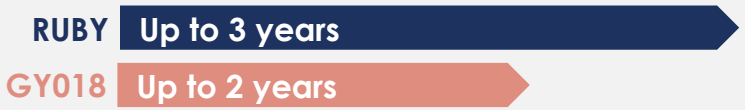
RUBY	PFS by IA (dMMR/MSI-H and ITT), OS (ITT)
GY018	PFS by IA (dMMR and pMMR)

Chemotherapy Duration

QoL Measurement

	Instruments Used	Assessed Population
RUBY	EORTC QLQ-C30, EORTC QLQ-EN24, EQ-5D-5L	dMMR/MSI-H and ITT
GY018	FACT-En-TOI, FACT-GOG-NTX, PROMIS, single-item survey	pMMR[a]

ICI Treatment Duration



There are no completed direct head-to-head trials of these products in EC. There are inherent limitations in cross-study comparisons; caution should be exercised in comparing trials. This slide is for information purposes only and is not intended to imply or infer the noninferiority or superiority of any product, in terms of efficacy or safety.

[a]Treatment information was unblinded February 3, 2023, and patients were asked to continue to complete PRO and QoL questionnaires.

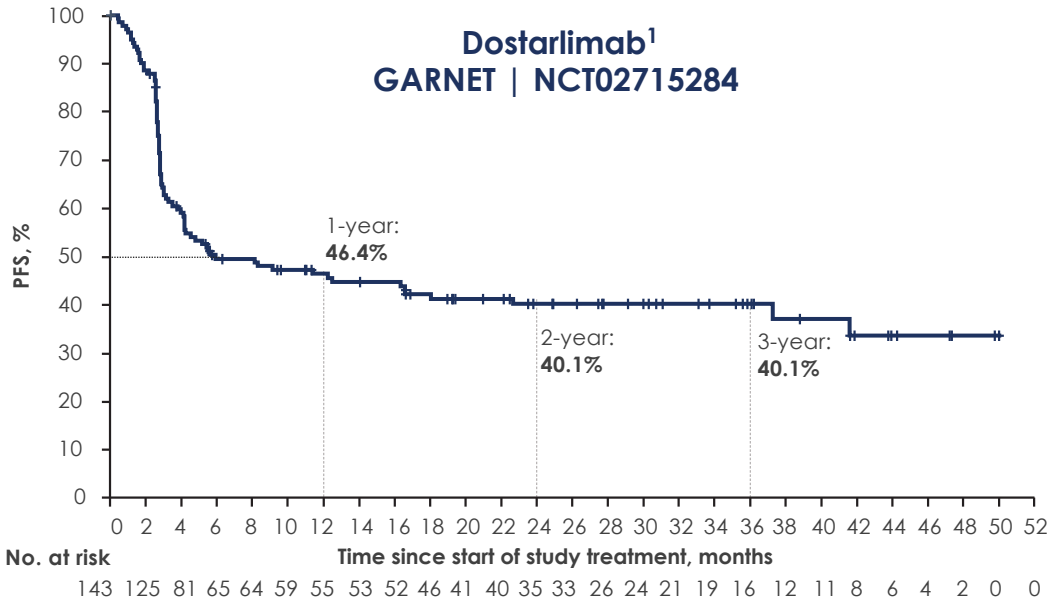
dMMR = mismatch repair deficient; EC = endometrial cancer; EORTC = European Organization for Research and Treatment of Cancer; EQ-5D-5L = European Quality of Life scale, 5-dimension, 5 level; FACT-En-TOI = Trial Outcome Index of the Functional Assessment of Cancer Therapy – Endometrial; ; FACT-GOG-NTX = Functional Assessment of Cancer Therapy/Gynecologic Oncology Group – Neurotoxicity subscale; FDA = US Food and Drug Administration; IA = Investigator assessed; ICI = immune checkpoint inhibitor; ITT = intention-to-treat; MSI-H = microsatellite instability-high; OS = overall survival; PFS = progression free survival; pMMR = mismatch repair proficient; PRO = patient reported outcome; PROMIS = Patient-Reported Outcomes Measurement Information System; QLQ-C30 = Quality of Life Questionnaire Core 30; QLQ-EN24 = Quality of Life Questionnaire-Endometrial Cancer Module; QoL = quality of life.

1. National Library of Medicine. https://clinicaltrials.gov/ct2/show/NCT03981796, Accessed August 23, 2023. 2. Mirza MR, et al. *N Engl J Med*. 2023; 388:2145-2158. 3. National Library of Medicine. https://clinicaltrials.gov/ct2/show/NCT03914612, Accessed August 23, 2023. 4. Eskander RN, et al. *N Engl J Med*. 2023; 388:2159-2170.

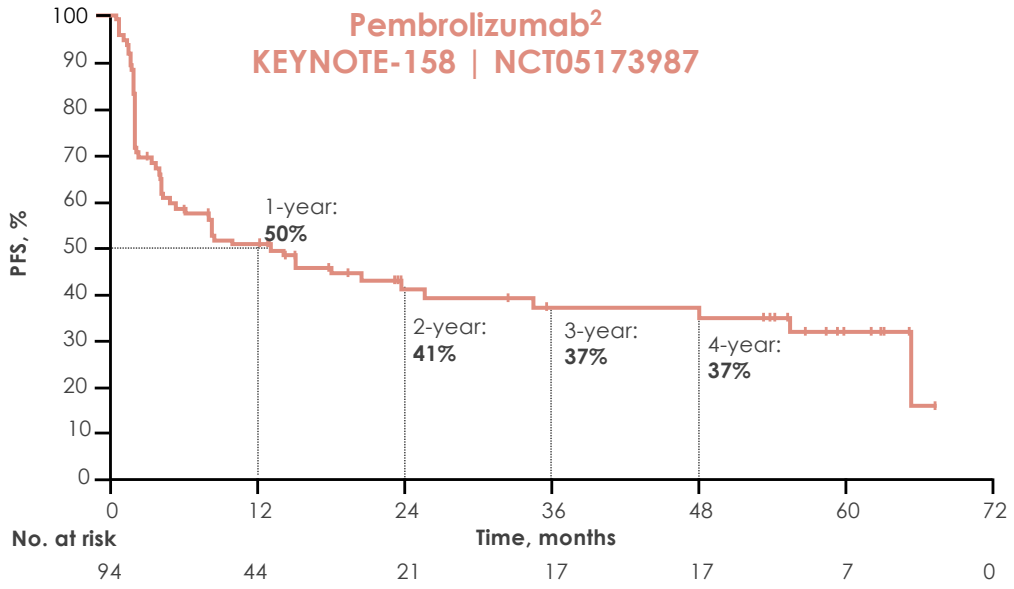
Are patients with dMMR/MSI-H EC potential candidates for de-escalation?

PFS in patients with dMMR/MSI-H EC treated with dostarlimab (GARNET) and pembrolizumab (KEYNOTE-158)

Dostarlimab[1] and pembrolizumab[2] demonstrated durable antitumor activity in patients with advanced or recurrent dMMR/MSI-H EC that had progressed following platinum-based therapy



Adapted from Oaknin A et al. *Clin Cancer Res.* 2023;CCR-22-3915.



Adapted from O'Malley DM, et al. *Ann Oncol.* 2022;33(suppl_7):S796-S797.

The most common TRAEs (>10% of patients) were diarrhea, asthenia, fatigue, and nausea

The most common TRAEs (>10% of patients) were pruritus, fatigue, diarrhea, arthralgia, hypothyroidism, nausea, and rash

There are no completed direct head-to-head trials of these products in EC. There are inherent limitations in cross-study comparisons; caution should be exercised in comparing trials. This slide is for information purposes only and is not intended to imply or infer the noninferiority or superiority of any product, in terms of efficacy or safety.

CI = confidence interval; dMMR = mismatch repair deficient; EC = endometrial cancer; MSI-H = microsatellite instability-high; PFS = progression-free survival; TRAE = treatment-related adverse event.

1. Oaknin A et al. *Clin Cancer Res.* 2023;CCR-22-3915. 2. O'Malley DM, et al. *Ann Oncol.* 2022;33(suppl_7):S796-S797.

Do all dMMR patients need chemotherapy?

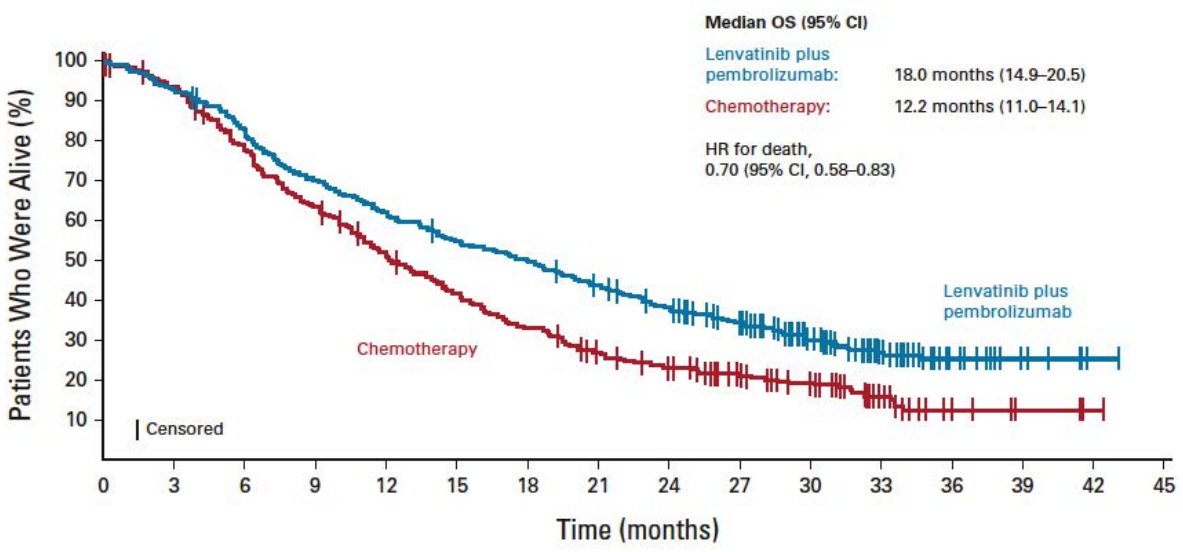
Drug	Dostarlimab	Pembrolizumab
Name	**DOMENICA[1]**	**KEYNOTE-C93[2]**
ClinicalTrials.gov	NCT05201547	NCT05173987
N	260	280
Randomization	1:1 (open-label)	1:1 (open-label)
Experimental treatment	Dostarlimab	Pembrolizumab
Control treatment	C/P	C/P
PD-1 dosing	Q3W, C1–C4 then Q6W	Q6W
Primary end points	PFS (BICR)	PFS (BICR), OS

BICR = blinded independent central review; C = cycle; C/P = carboplatin and paclitaxel; dMMR = mismatch repair deficient; EC = endometrial cancer; OS = overall survival; PD-1 = programmed cell death protein-1; PFS = progression-free survival; QXW = every X weeks.

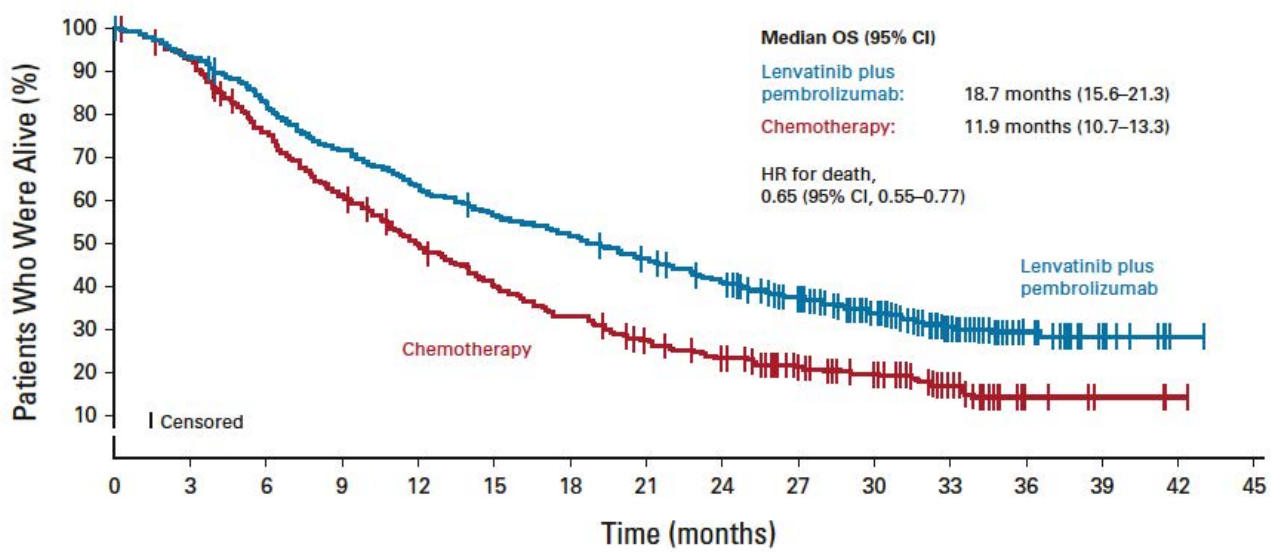
1. National Library of Medicine. https://clinicaltrials.gov/ct2/show/NCT05201547. Accessed Aug 8, 2023. 2. National Library of Medicine. https://clinicaltrials.gov/ct2/show/NCT05173987. Accessed Aug 8, 2023.

KEYNOTE-775 (Study 309): Overall Survival with Lenvatinib in Combination with Pembrolizumab for Previously Treated Advanced Endometrial Cancer

pMMR population



All comers population



pMMR = mismatch repair proficient; OS = overall survival

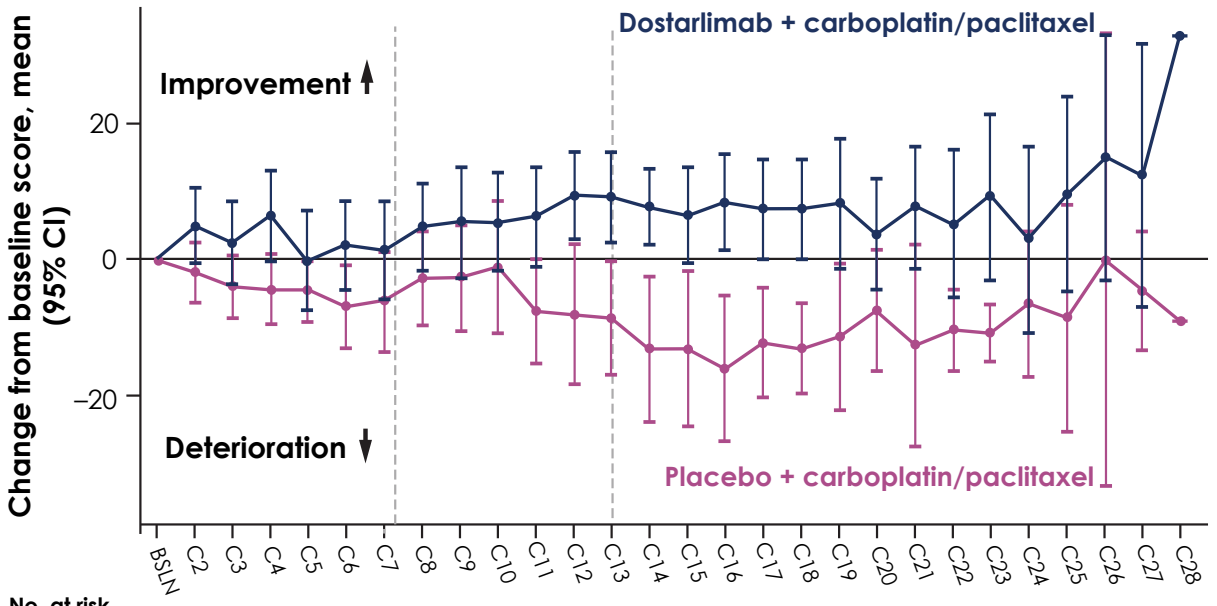
Makker V et al. *J Clin Oncol* 2023 June 1;41(16):2904-10.

What do we know about the impact on the QoL of patients treated with immunotherapy plus chemotherapy?

RUBY Part 1: Patient-reported outcomes

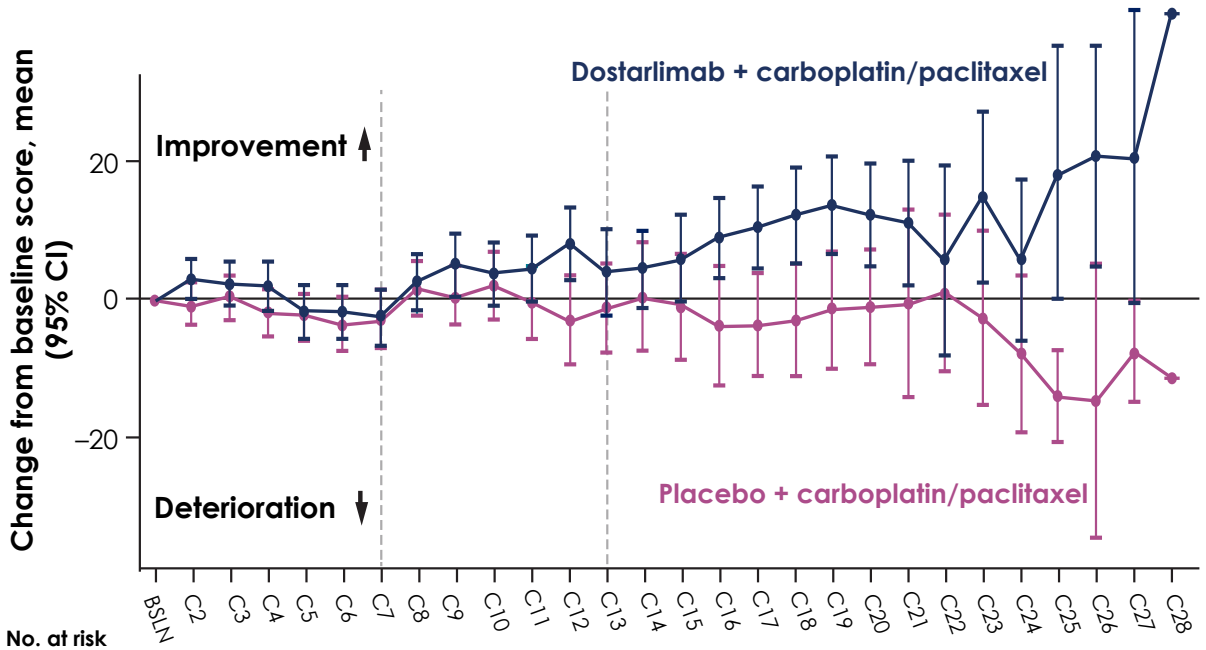
EORTC QLQ-C30 Global Quality of Life Score[1-3]

dMMR/MSI-H



No. at risk	BSLN	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12	C13	C14	C15	C16	C17	C18	C19	C20	C21	C22	C23	C24	C25	C26	C27	C28
Dostarlimab + C/P	51	49	47	46	46	43	39	36	34	34	31	29	27	25	25	25	22	17	15	12	11	9	8	7	5	4	1	
Placebo + C/P	64	61	58	59	57	54	48	39	31	27	19	14	14	13	11	10	9	9	9	8	5	4	4	2	2	2	1	

Overall



No. at risk	BSLN	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12	C13	C14	C15	C16	C17	C18	C19	C20	C21	C22	C23	C24	C25	C26	C27	C28
Dostarlimab + C/P	238	228	219	213	205	196	178	153	140	125	106	93	85	79	75	70	69	55	47	41	31	25	20	14	13	8	5	2
Placebo + C/P	242	232	224	219	210	204	181	151	132	105	82	68	57	55	50	46	41	40	36	31	24	19	17	11	6	5	3	2

Adapted from Mirza MR, et al. *N Engl J Med*. 2023;388:2145-2158.

BSLN = baseline; C = cycle; CI = confidence interval; C/P = carboplatin and paclitaxel; dMMR = mismatch repair deficient; EORTC-QLQ-C30 = European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; MSI-H = microsatellite instability high.

1. Mirza MR, et al. Presented at: SGO; March 25-28, 2023; Tampa, FL, USA. 2. Mirza MR, et al. *Ann Oncol.* 2023;34:500-501. 3. Mirza MR, et al. *N Engl J Med.* 2023;388:2145-2158.

New Combinations and Novel Targets: Ongoing Research in Endometrial Cancer

Efficacy of anti-PD-L1 agents is currently being evaluated in Phase 3 studies for patients with EC

Drug	Atezolizumab	Durvalumab
Name	**ATTEND[1,2]**	**DUO-E[3,4]**
ClinicalTrials.gov	NCT03603184	NCT04269200
N	550	699
Randomization	2:1	1:1:1
Experimental treatment	Atezolizumab + C/P	Durvalumab + C/P then durvalumab
		Durvalumab + C/P then durvalumab + olaparib
Control treatment	Placebo + C/P	Placebo + C/P then placebo
PD-1/L1 dosing	Q3W	Q3W, cycles 1-6 then Q4W
Primary end points	PFS, OS	PFS (IA)

"Durvalumab plus olaparib and durvalumab alone both significantly improved progression-free survival in advanced endometrial cancer when added to chemotherapy. DUO-E is the first global Phase 3 trial of immunotherapy plus PARP inhibition to demonstrate clinical benefit in this setting."[5]

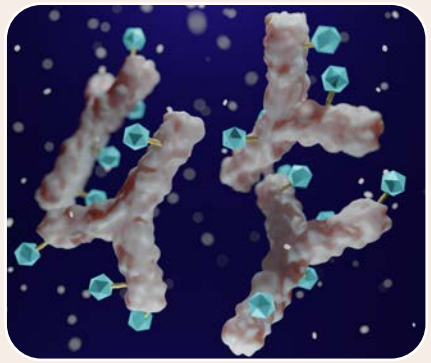
– May 2023 Press Release

C = cycle; C/P = carboplatin and paclitaxel; dMMR = mismatch repair deficient; ECOG PS = Eastern Cooperative Oncology Group performance status; FIGO = Fédération Internationale de Gynécologie et d'Obstétrique; IA = investigator assessed; OS = overall survival; PARP = poly (ADP-ribose) polymerase; PD-1 = programmed cell death protein-1; PD-L1 = programmed death-ligand 1; PFS = progression-free survival; QXW = every X weeks.

1. National Library of Medicine. https://clinicaltrials.gov/ct2/show/NCT03603184. Accessed August 23, 2023. 2. Colombo N, et al. *Ann Oncol*. 2020;31:S647. 3. National Library of Medicine. https://clinicaltrials.gov/ct2/show/NCT04269200. Accessed August 23, 2023. 4. Westin SN, et al. *J Clin Oncol*. 2020;38:TPS6108. 5. AstraZeneca Press Release. https://www.astrazeneca.com/media-centre/press-releases/2023/imfinzi-lynparza-prolonged-pfs-in-endometrial-cancer.html. Accessed August 23, 2023.

What other methods are being evaluated?

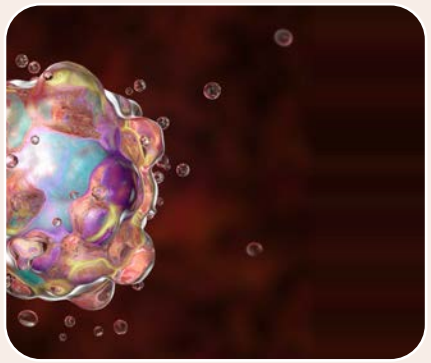
Targeting HER2



Trastuzumab deruxtecan:
DESTINY (phase 2)[1]

Trastuzumab ± C/P:
NCT01367002 (phase 2)[2]

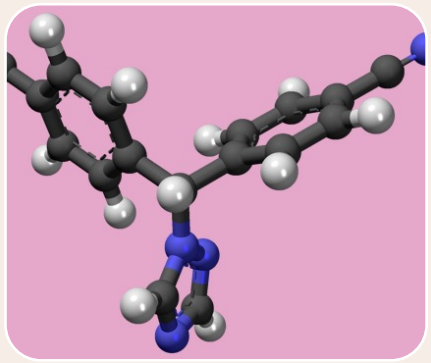
Kickstarting apoptosis



Selinexor:
SIENDO (phase 3)[3]; xport-EC-042 (phase 3)[4]

Navtemadlin:
EURUS (phase 2/3)[5]

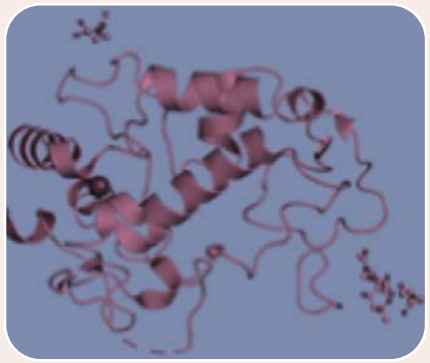
Revisiting endocrine therapy



Letrozole + palbociclib:
PALEO (phase 2)[6]

Letrozole + lerociclib and letrozole:
GOG-3075 (phase 3)[7]

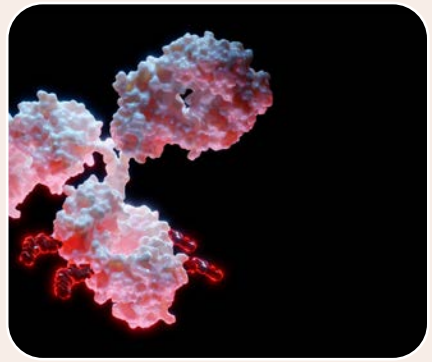
FR-a inhibition



Mirvetuximab soravtansine + gemcitabine:
NCT02996825 (phase 1)[8]

Farletuzumab ecteribulin:
NCT03386942 (phase 1)[9]

Inhibiting TROP-2



Sacituzumab govitecan:
NCT04251416 (phase 2)[10]

FR-α = folate receptor alpha; HER2 = human epidermal growth factor 2; TROP-2 = Trophoblast cell surface antigen 2.

1. Meric-Bernstam F, et al. *J Clin Oncol.* 2023;41(suppl_17):LBA3000. 2. Fader AN, et al. *Clin Cancer Res.* 2020;26:3928-3935. 3. Makker V, et al. *J Clin Oncol.* 2022;40:5511-5511. 4. Vergote IB, et al. *J Clin Oncol.* 2023;41(16_suppl):TPS5627-TPS5627. 5. National Library of Medicine. https://clinicaltrials.gov/ct2/show/NCT05797831. Accessed August 23, 2023. 6. Mirza MR, et al. *Ann Oncol.* 2020;31(s4):S1160. 7. National Library of Medicine. https://clinicaltrials.gov/ct2/show/NCT05712941. Accessed August 23, 2023. 8. National Library of Medicine. https://clinicaltrials.gov/ct2/show/NCT02996825. Accessed August 23, 2023. 9. National Library of Medicine. https://clinicaltrials.gov/ct2/show/NCT03386942. Accessed August 23, 2023. 10. Santin A, et al. *J Clin Oncol.* 2023;41(suppl_16):abst 5599.

Conclusion

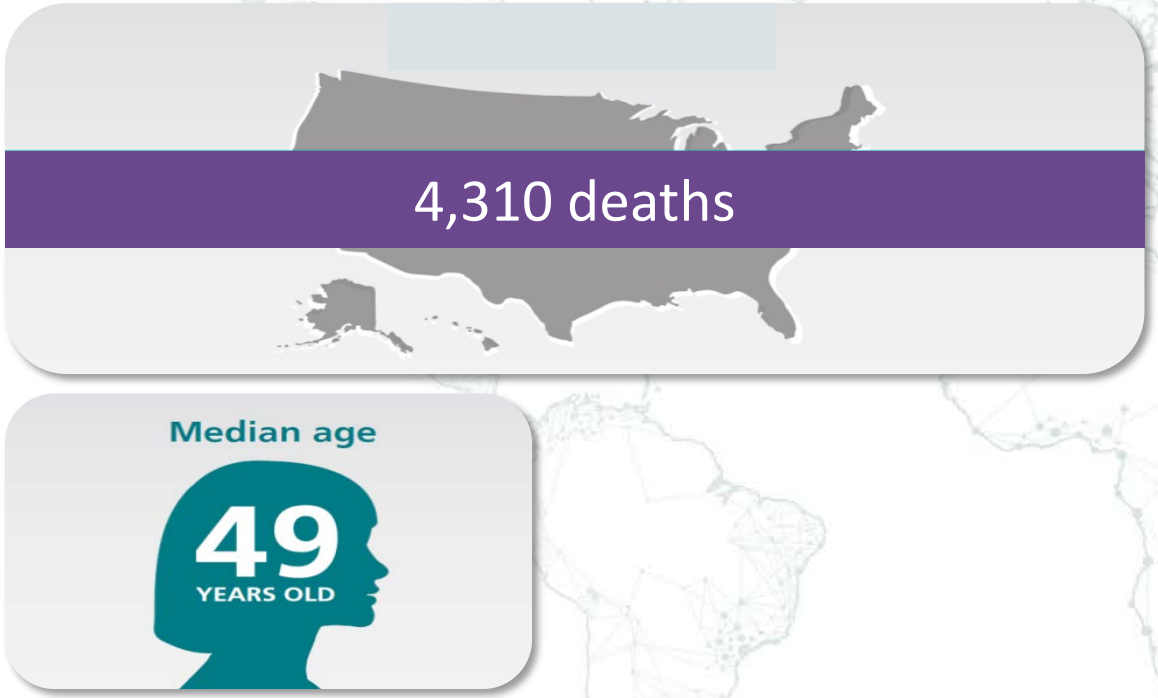
Conclusions

- Addition of a PD-1 inhibitor to standard-of-care chemotherapy in patients with primary advanced/recurrent EC resulted in a substantial and unprecedented benefit in dMMR/MSI-H patients, compared with chemotherapy alone[1,2]
- Benefit was also seen in pMMR patients[1]
- Additional biomarker analyses and combinations with ICIs may help to address the remaining unmet need in this population[3-5]
- Other novel agents and biomarkers are being explored and may provide additional treatment options in targeted patient populations[6-10]
- 2023 marks the beginning of an era of potential breakthroughs in EC that could shift the treatment paradigm and improve outcomes for more patients with this type of cancer[11]

dMMR = mismatch repair deficient; ICI = immune checkpoint inhibitor; MSI = microsatellite instability; MSI-H = microsatellite instability-high; PD-1 = programmed cell death protein-1; pMMR = mismatch repair proficient.

1. Mirza MR, et al. *N Engl J Med*. 2023;388:2145-2158. 2. Eskander RN, et al. *N Engl J Med*. 2023;388:2159-2170. 3. Mirza MR, et al. *Ann Oncol.* 2021;32:S770-S771. 4. Marth C, et al. *Int J Gynecol Cancer.* 2022;32:93-100. 5. Westin SN, et al. *J Clin Oncol*. 2020;38:TPS6108. 6. National Library of Medicine. https://clinicaltrials.gov/ct2/show/NCT04482309. Accessed August 23, 2023. 7. National Library of Medicine. https://clinicaltrials.gov/ct2/show/NCT03555422. Accessed August 23, 2023. 8. National Library of Medicine. https://clinicaltrials.gov/ct2/show/NCT05797831. Accessed August 23, 2023. 9 . Mirza MR, et al. *Ann Oncol*. 2020;31(s4):S1160 10. National Library of Medicine. https://clinicaltrials.gov/ct2/show/NCT04251416. Accessed August 23, 2023. 11. GSK Press Release. https://www.gsk.com/en-gb/media/press-releases/jemperli-plus-chemotherapy-approved-in-us-for-new-indication. Accessed August 23, 2023.

An Estimated 13,960 Cases of Invasive Cervical Cancer in the US in 2023[2]



- ✓ **Death rate in 2016 (2.2 per 100,000) was less than half that in 1975 (5.6 per 100,000)**
- ✓ **From 2007 to 2016, the death rate decreased by about 1% per year in women >50 years of age and older, but was stable in <50**

1) Cancer statistics, 2023. Rebecca L. Siegel et al. First published: 12 January 2023. CA: A Cancer Journal for CliniciansVolume 73, Issue 1 p. 17-48
https://doi.org/10.3322/caac.21763

Incremental Improvements in Survival (OS) in Treating Metastatic and Recurrent Cervical Cancer with Combinations and Biomarkers

Chemotherapy backbone (platinum + taxane) [2009]

Adding bevacizumab [2014]

Adding pembrolizumab in biomarker positive (PD-L1 22c3) [2023]

GOG 204 established the global standard with a median OS of 12.9 months[1]

ORR = 29%

GOG 240 added bevacizumab in eligible patients with a median OS of 17.5 months[2]

ORR = 48%

KN-826 added pembrolizumab in PD-L1 positive (CPS ≥1%) median OS 28.6 months

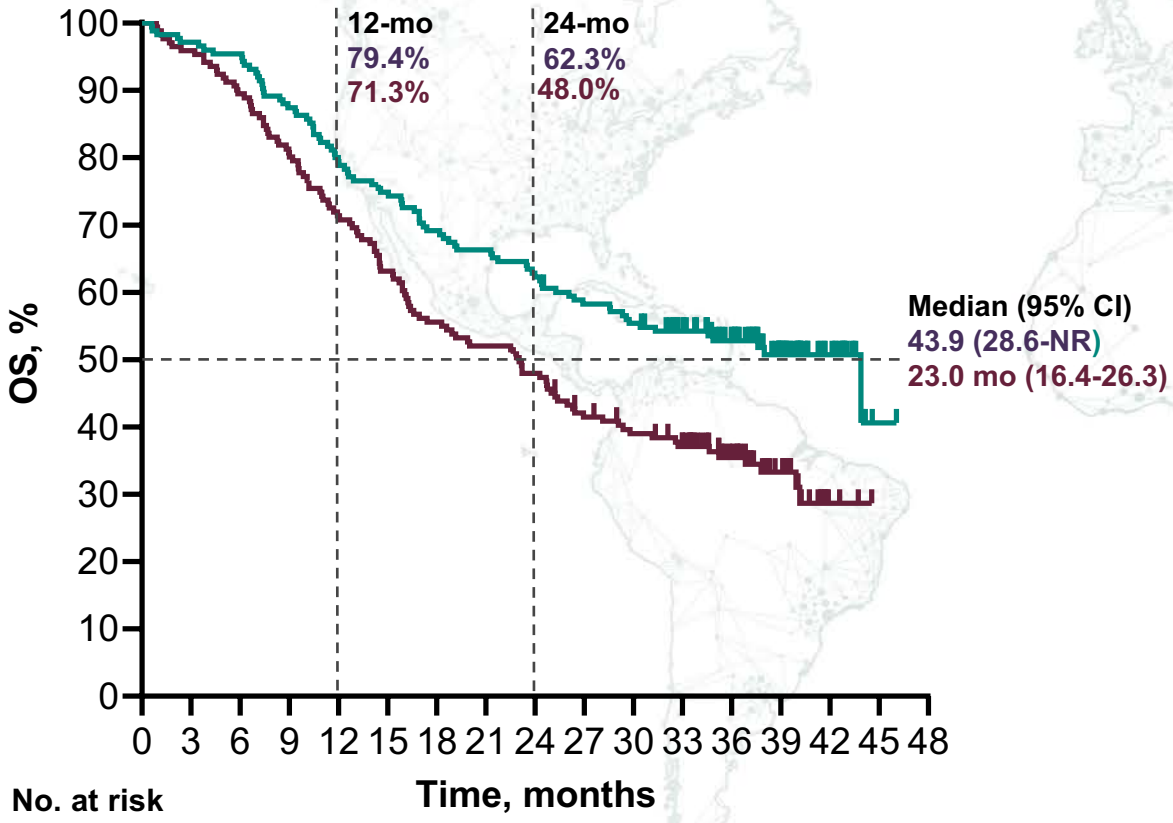
ORR = 69%

1. J Clin Oncol. 2009 Oct 1;27(28):4649-55.
2. Lancet. 2017 Oct 7;390(10103):1654-1663.
3. KEYNOTE-826 Final analysis. Presented at ASCO, 2023

OS by Bevacizumab Use, PD-L1 CPS ≥1 Population

With Bevacizumab (N=346)

	n/N	Events	HR (95% CI)
Pembro arm	85/175	48.6%	0.60 (0.45-0.79)
Placebo arm	113/171	66.1%	

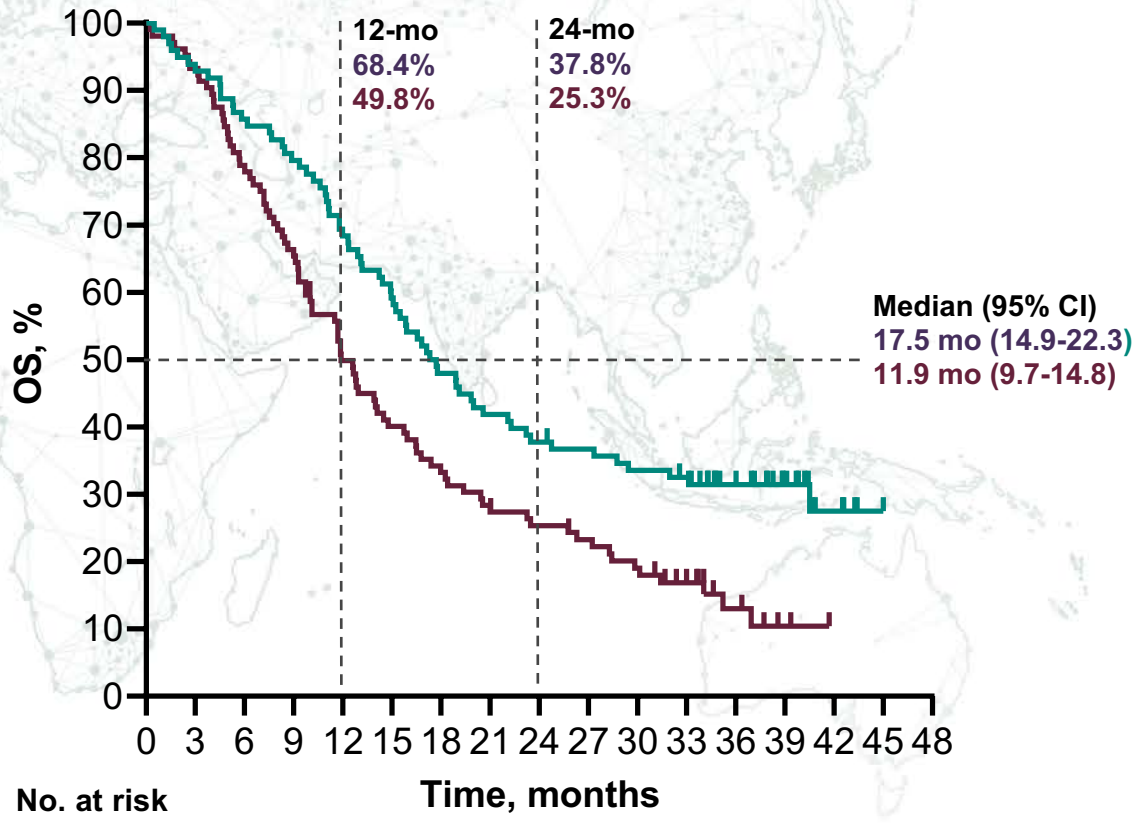


No. at risk

175	170	167	153	139	131	121	116	109	101	96	86	69	39	17	1	0
171	164	153	138	122	108	95	89	82	69	63	56	39	22	3	0	0

Without Bevacizumab (N=202)

	n/N	Events	HR (95% CI)
Pembro arm	68/98	69.4%	0.61 (0.44-0.85)
Placebo arm	88/104	84.6%	



No. at risk

98	91	84	78	67	58	47	41	37	35	32	30	21	13	5	1	0
104	97	82	69	51	41	34	28	25	22	18	12	6	2	0	0	0

Data cutoff date: October 3, 2022.

Phase 3 KEYNOTE-A18 Trial Meets Primary Endpoint of Progression-Free Survival (PFS) in Patients With Newly Diagnosed High-Risk Locally Advanced Cervical Cancer

7/19/2023

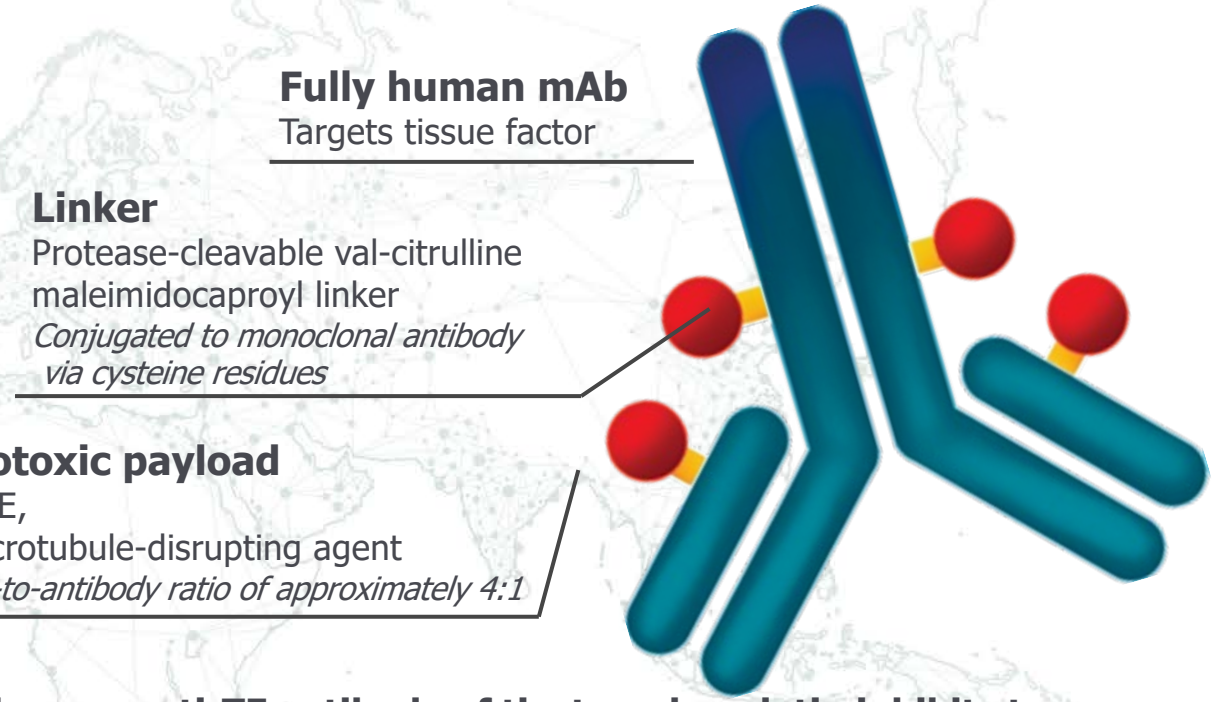
Pembrolizumab plus concurrent chemoradiotherapy demonstrated statistically significant and clinically meaningful improvement in PFS versus concurrent chemoradiotherapy alone in these patients

Today [it was] announced that the Phase 3 KEYNOTE-A18 trial, also known as ENGOT-cx11/GOG-3047, investigating pembrolizumab in combination with external beam radiotherapy (EBRT) plus concurrent chemotherapy, followed by brachytherapy (also known as concurrent chemoradiotherapy) met one of its primary endpoints of progression-free survival (PFS) as treatment for newly diagnosed patients with high-risk locally advanced cervical cancer. At a prespecified interim analysis conducted by an independent Data Monitoring Committee, pembrolizumab in combination with concurrent chemoradiotherapy showed a statistically significant and clinically meaningful improvement in PFS versus concurrent chemoradiotherapy alone.

A favorable trend in overall survival (OS), the trial's other primary endpoint, was also observed for pembrolizumab plus concurrent chemoradiotherapy compared to concurrent chemoradiotherapy alone; however, these OS data were not mature at the time of this interim analysis. The trial is continuing and follow-up of OS is ongoing.

Tisotumab Vedotin: (3rd Landmark Discovery)

- Transmembrane receptor for coagulation factor VII/VIIa[a-c]:
  - Expressed on subendothelial vessel wall cells
- Normal physiological conditions[a-c]:
  - Central role in initiation of the extrinsic pathway of the coagulation cascade
- In oncogenesis[a-c]:
  - Role in tumor angiogenesis, proliferation, metastases, thrombotic events



The human anti-TF antibody of tisotumab vedotin inhibits tumor proliferation pathways with minimal impact on clotting cascade

Antigen[a]	Gynecologic malignancy	Expression frequency
Tissue factor	Ovarian cancer	23.8% to 100%
	Uterine cancer	100%
	Cervical cancer	**94% to 100%**

- mAb, monoclonal antibody; MMAE, Monomethyl auristatin E; TF, tissue factor.

Coleman R, et al. Presented at: ESMO 2020; September 19-21, 2020. Abstract LBA32.

a. Versteeg HH, et al. Semin Thromb Hemost. 2015;41:747-755; b. van den Berg YW, et al. Blood. 2012;119:924-932; c. Chu AJ. Int J Inflam. 2011;2011:367284; d. Forster Y, et al. Clin Chim Acta. 2006;364:12-21; e. Cocco E, et al. BMC Cancer. 2011;11:263; f. Ruf W, et al. J Thromb Haemost. 2011;9(Suppl 1):306-315; g. Jacobs, et al. J Clin Oncol. 2012;30(15_suppl; abstr e16022).

Bringing TV to the Clinic in 2-L

2-L TV Approved by FDA on September 20, 2021

GOG-3057/ENGOT-cx12/innovaTV 301: Trial Study Design

Companies Announce Tisotumab Vedotin-tftv Improved Overall Survival in Patients With Recurrent or Metastatic Cervical Cancer Compared With Chemotherapy Alone

09/04/2023

BOTHELL, Wash. & COPENHAGEN, Denmark--(BUSINESS WIRE)-- The manufacturers' of tisotumab vedotin announced today that the Phase 3 innovaTV 301 global trial in recurrent or metastatic cervical cancer patients with disease progression on or after front-line therapy who received tisotumab vedotin-tftv, compared with chemotherapy alone, met its primary endpoint of overall survival (OS). An Independent Data Monitoring Committee determined that OS crossed the pre-specified efficacy boundary at interim analysis. The key secondary endpoints of investigator-assessed progression-free survival and objective response rate also demonstrated statistical significance. The safety profile of tisotumab vedotin in innovaTV 301 was consistent with the known safety profile of tisotumab vedotin as presented in the U.S. prescribing information, and no new safety signals were observed.

The results of innovaTV 301/ENGOT cx-12/GOG 3057, a global, randomized, open-label Phase 3 trial, add to the previous results of innovaTV 204, which served as the basis for the accelerated approval of tisotumab vedotin in the U.S. Subject to discussions with regulatory authorities, the results from innovaTV 301 are intended to serve as the pivotal confirmatory trial for the U.S. accelerated approval and support global regulatory applications. The innovaTV 301 China extension study has been initiated and continues to enroll patients.

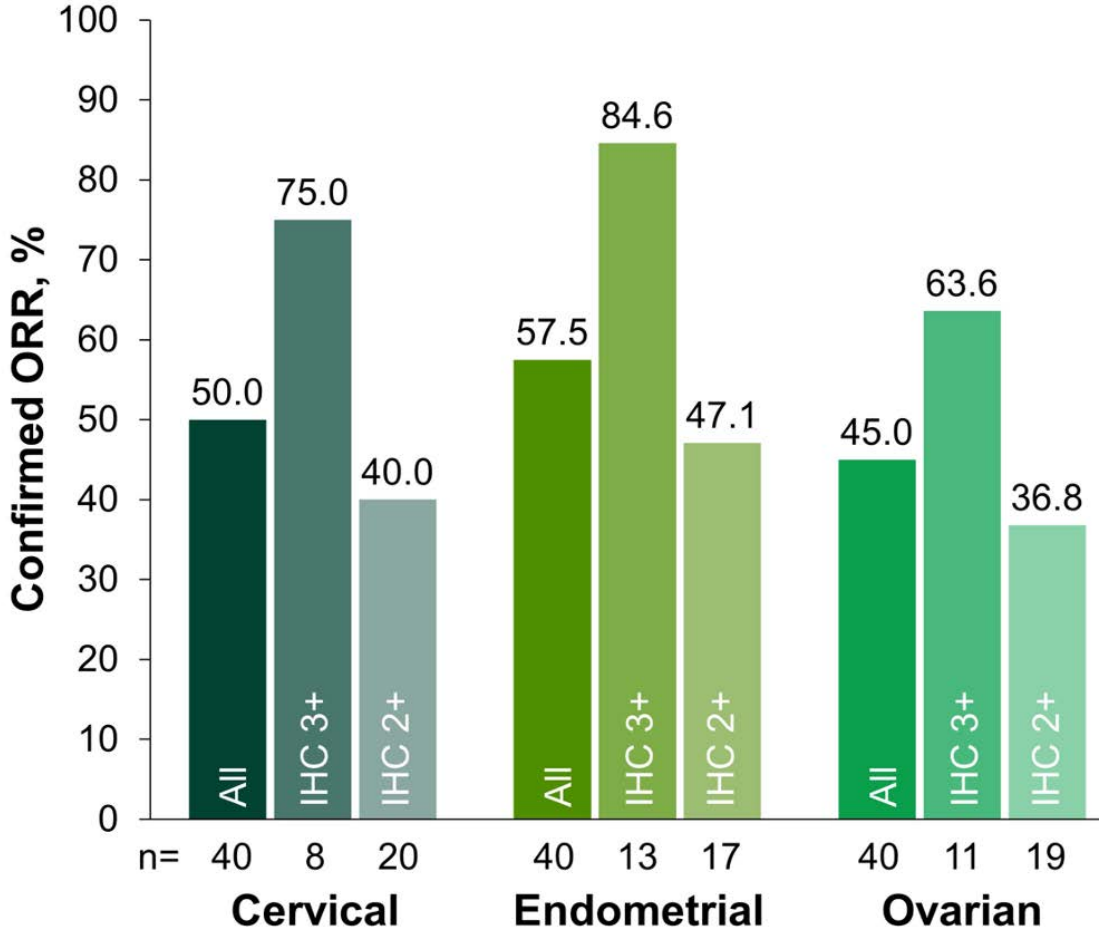
"Tisotumab vedotin is the only U.S. Food and Drug Administration-approved therapy in second-line recurrent or metastatic cervical cancer regardless of biomarker status, tumor histology and prior therapy," said Roger Dansey, M.D., President of Research and Development and Chief Medical Officer. "Demonstrating a survival benefit with the results of innovaTV 301 is a critical milestone in our efforts to ensure more adults living with advanced cervical cancer have an approved treatment option."

"With limited options for advanced cervical cancer patients who have progressed after front-line therapy, there is a need for therapeutic options with new mechanisms of action, particularly those with a demonstrated survival benefit," said Jan van de Winkel, Ph.D., Chief Executive Officer. "These results provide hope for patients with recurrent or metastatic cervical cancer."

Results of the Phase 3 innovaTV 301 clinical trial will be submitted for presentation at an upcoming medical congress and discussed with regulatory authorities.

DESTINY-PanTumor02: Activity of T-DXd in Gynecologic Cohorts

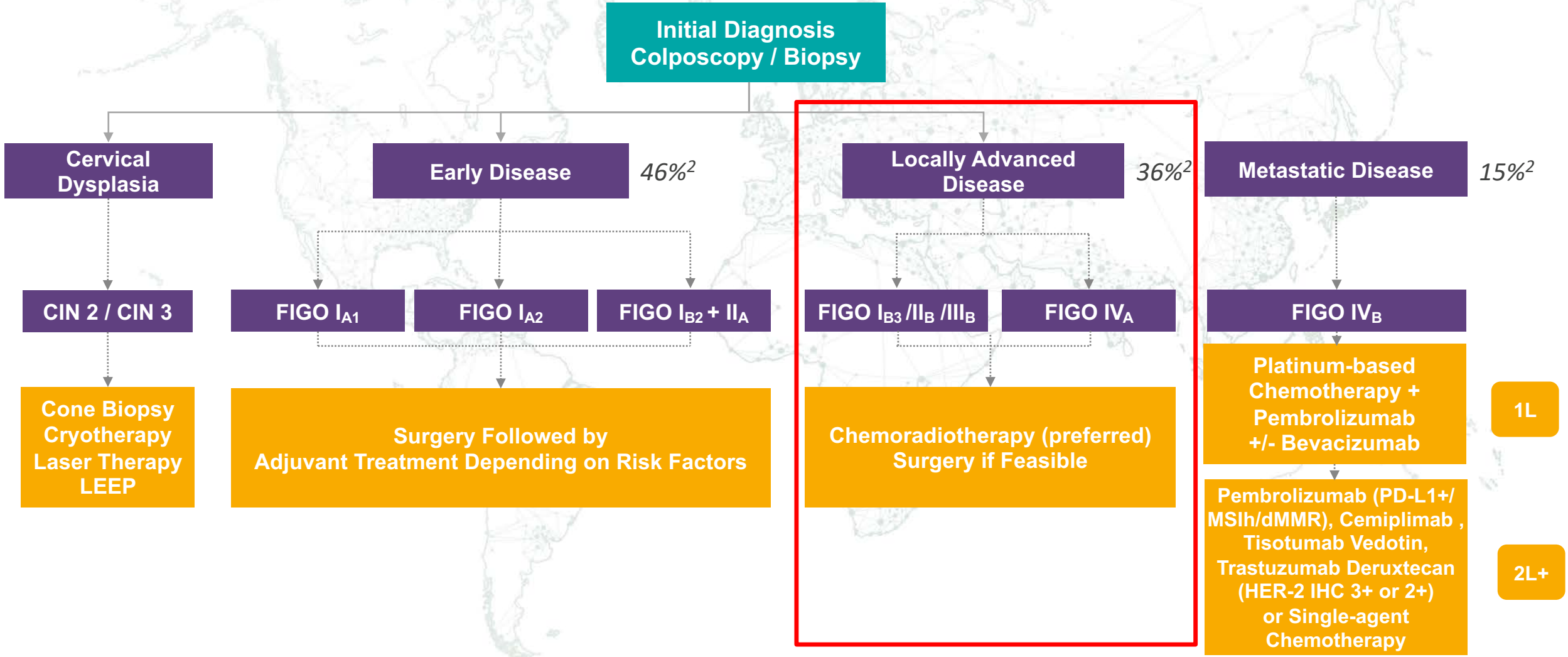
		Cervical (n=40)	Endometrial (n=40)	Ovarian (n=40)
Investigator assessment				
ORR, n (%)		**20 (50.0)**	**23 (57.5)**	**18 (45.0)**
Best overall response, n (%)	Complete response	2 (5.0)	7 (17.5)	4 (10.0)
	Partial response	18 (45.0)	16 (40.0)	14 (35.0)
	Stable disease	12 (30.0)	13 (32.5)	14 (35.0)
	PD	7 (17.5)	4 (10.0)	7 (17.5)



ORR = objective response rate

Meric-Bernstam F et al. ASCO 2023;Abstract LBA3000.

Cervical cancer: Summary of treatment



LEEP: Loop Electrosurgical Excision Procedure; PD-L1: Programmed Cell Death Ligand-1; MSIh: Microsatellite Instability High; dMMR: deficient Mismatch Repair

1. National Comprehensive Cancer Network. NCCN Cervical Cancer Guidelines version 1.2023. https://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf. Accessed 10 June 2023; 2. National Cancer Institute. SEER Cancer Stat Facts: Cervical Cancer. https://seer.cancer.gov/statfacts/html/cervix.html. Accessed 10 March 2023

Oncology in the Real World: A Daylong Multitumor Educational Symposium in Partnership with the American Oncology Network

A CME/MOC- and NCPD-Accredited Event

Saturday, October 14, 2023
9:30 AM – 5:00 PM PT

RTP
RESEARCH
TO PRACTICE

Agenda

Module 1 — Lymphoma: *Drs Flowers and LaCasce*

Module 2 — Urothelial Bladder Cancer and Renal Cell Carcinoma:
Drs Hutson and Sonpavde

Module 3 — Hepatobiliary and Pancreatic Cancers:
Prof Borad and Dr El-Khoueiry

Module 4 — Gynecologic Cancers: *Drs Monk and Moore*

Module 5 — Multiple Myeloma: *Drs Krishnan and Orlowski*

Break: 3:30 PM – 3:50 PM

Module 6 — HER2-Positive and Triple-Negative Breast Cancer:
Drs Hurvitz and McArthur

RTP
RESEARCH
TO PRACTICE

Multiple Myeloma Faculty

Amrita Krishnan, MD
Director of the Judy and Bernard Briskin Center for Multiple Myeloma Research
Professor of Hematology/Hematopoietic Cell Transplantation
City of Hope Cancer Center
Duarte, California

Robert Z Orlowski, MD, PhD
Florence Maude Thomas Cancer Research Professor
Department of Lymphoma and Myeloma
Professor, Department of Experimental Therapeutics
Director, Myeloma Section
Division of Cancer Medicine
The University of Texas
MD Anderson Cancer Center
Houston, Texas

RTP
RESEARCH
TO PRACTICE

Snapshot of AON Practice
Module 5: Multiple Myeloma

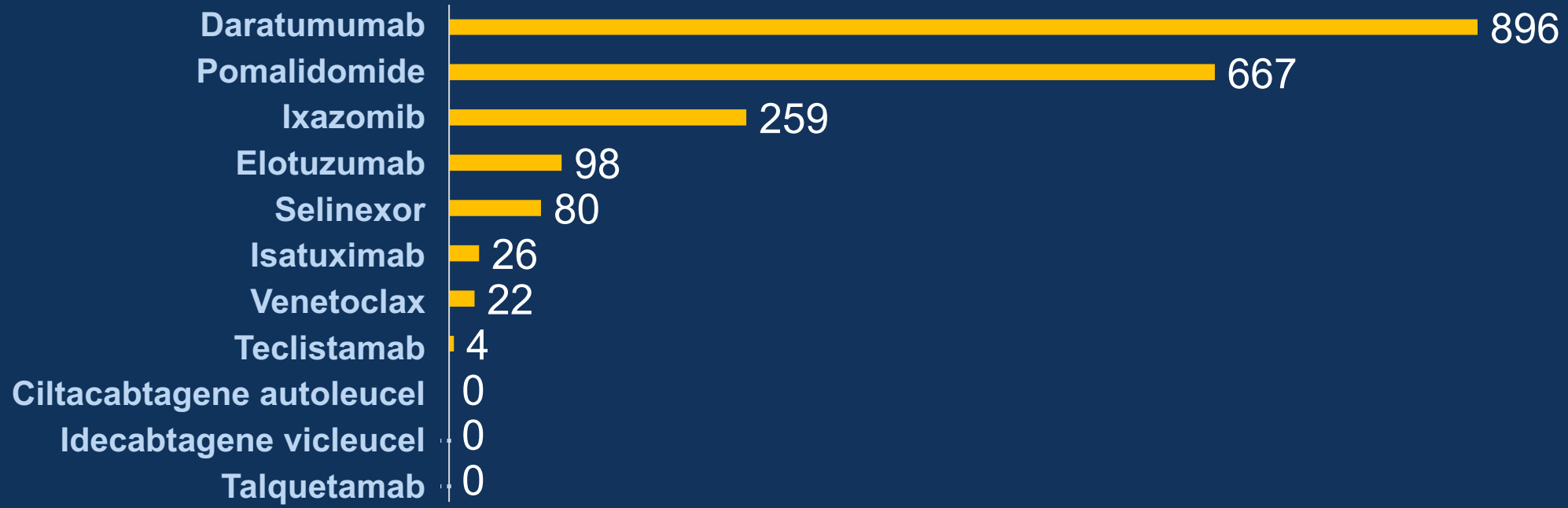
MIBA

THE AON CLINICAL SUMMIT 2023

Collaborate. Innovate. Celebrate.

Snapshot of AON Practice
Multiple Myeloma

Select Treatments Received



Clinical Trial Participation

Number of clinical trials	28
Total patients enrolled	109

MIBA

THE AON CLINICAL SUMMIT 2023

Collaborate. Innovate. Celebrate.

Optimizing the Current Management of Multiple Myeloma

Robert Z. Orlowski, M.D., Ph.D.

Director, Myeloma Section, & Deputy Chair, Department of Lymphoma/Myeloma

Florence Maude Thomas Cancer Research Professor

Principal Investigator, MD Anderson SCOR in High Risk Plasma Cell Dyscrasias

Chair, SWOG Myeloma Committee

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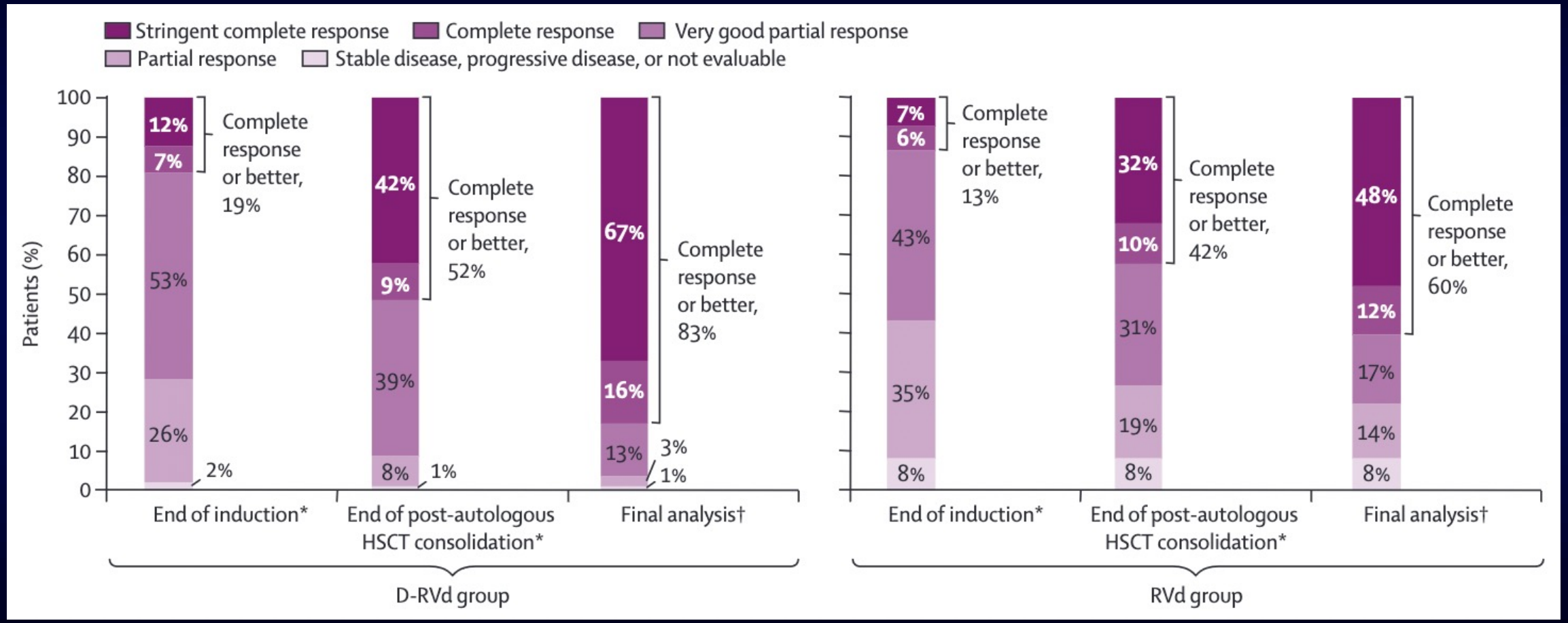
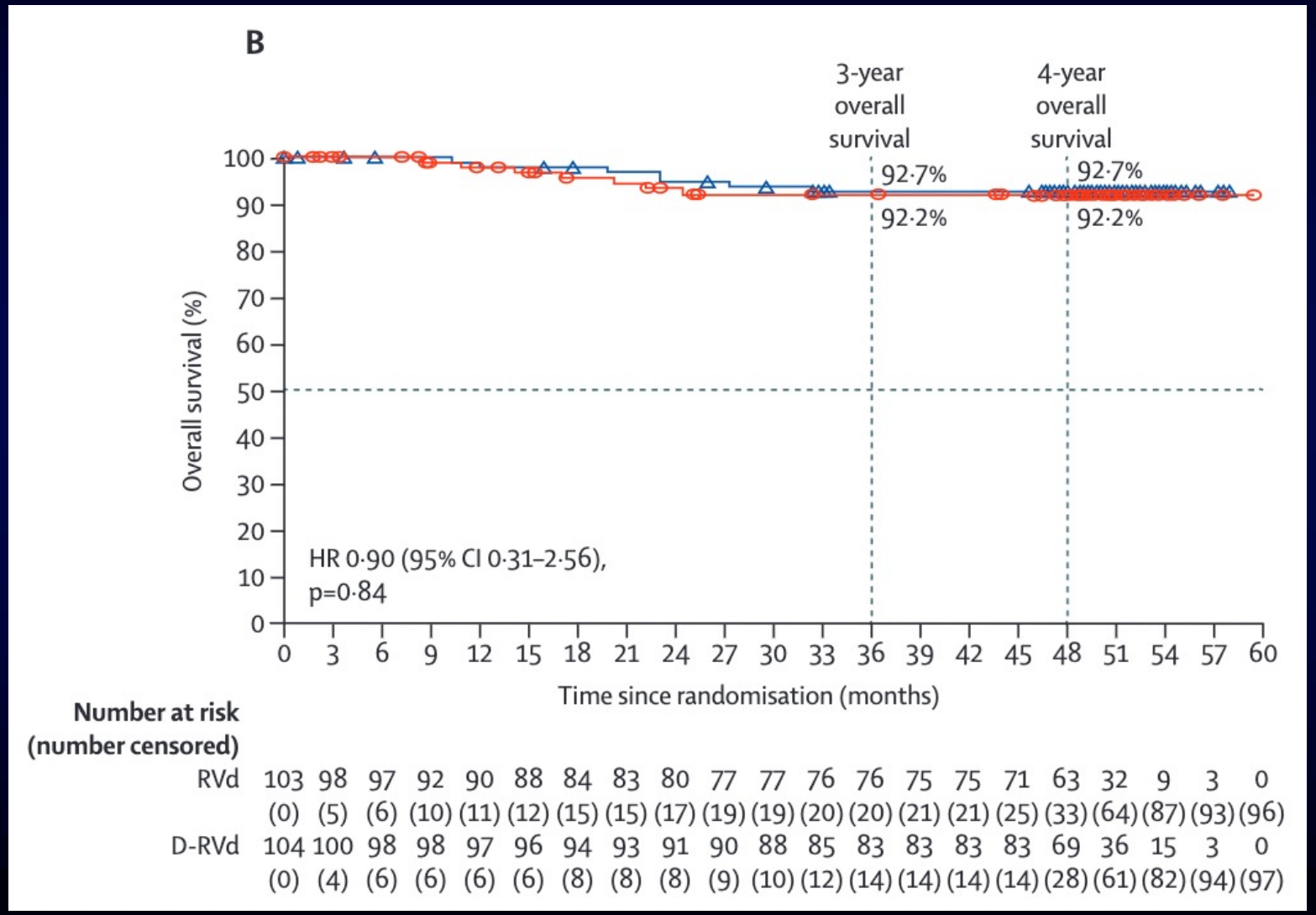
Daratumumab Adverse Events in Induction

	D-RVd group (n=99)				RVd group (n=102)			
	Grade 1–2	Grade 3	Grade 4	Grade 5	Grade 1–2	Grade 3	Grade 4	Grade 5
Haematological								
Anaemia	28 (28%)	9 (9%)	0	0	27 (26%)	5 (5%)	1 (1%)	0
Thrombocytopenia	28 (28%)	4 (4%)	12 (12%)	0	27 (26%)	4 (4%)	5 (5%)	0
Leukopenia	22 (22%)	8 (8%)	9 (9%)	0	22 (22%)	6 (6%)	2 (2%)	0
Neutropenia	17 (17%)	32 (32%)	14 (14%)	0	18 (18%)	21 (21%)	2 (2%)	0
Lymphopenia	8 (8%)	13 (13%)	10 (10%)	0	6 (6%)	20 (20%)	3 (3%)	0
Non-haematological								
Hypokalaemia	24 (24%)	3 (3%)	1 (1%)	0	24 (24%)	3 (3%)	0	0
Hypocalcaemia	17 (17%)	0	0	0	12 (12%)	2 (2%)	1 (1%)	0
Pneumonia	11 (11%)	11 (11%)	1 (1%)	1 (1%)	4 (4%)	14 (14%)	0	0
Hyperkalaemia	6 (6%)	1 (1%)	0	0	1 (1%)	0	1 (1%)	0
Cellulitis	6 (6%)	0	1 (1%)	0	3 (3%)	1 (1%)	0	0
Hypophosphataemia	5 (5%)	9 (9%)	1 (1%)	0	6 (6%)	11 (11%)	0	0
Hyperuricaemia	4 (4%)	0	0	0	6 (6%)	0	1 (1%)	0
Acute kidney injury	2 (2%)	2 (2%)	2 (2%)	0	4 (4%)	3 (3%)	0	0
Atrial fibrillation	1 (1%)	0	1 (1%)	0	3 (3%)	0	0	0
Increased blood creatine phosphokinase	1 (1%)	0	0	0	0	0	1 (1%)	0
Atrial tachycardia	1 (1%)	0	0	0	0	0	1 (1%)	0
Sepsis	0	1 (1%)	2 (2%)	0	0	1 (1%)	0	0
Drug reaction with eosinophilia and systemic symptoms	0	0	0	0	0	1 (1%)	1 (1%)	0
Septic shock	0	0	0	0	0	0	1 (1%)	0
Cerebrovascular accident	0	0	0	0	0	0	1 (1%)	0
Systemic inflammatory response syndrome	0	0	0	0	0	0	1 (1%)	0
Death	0	0	0	0	0	0	0	1 (1%)

Response Data



Durability: PFS & OS



Isatuximab Adverse Events in Induction

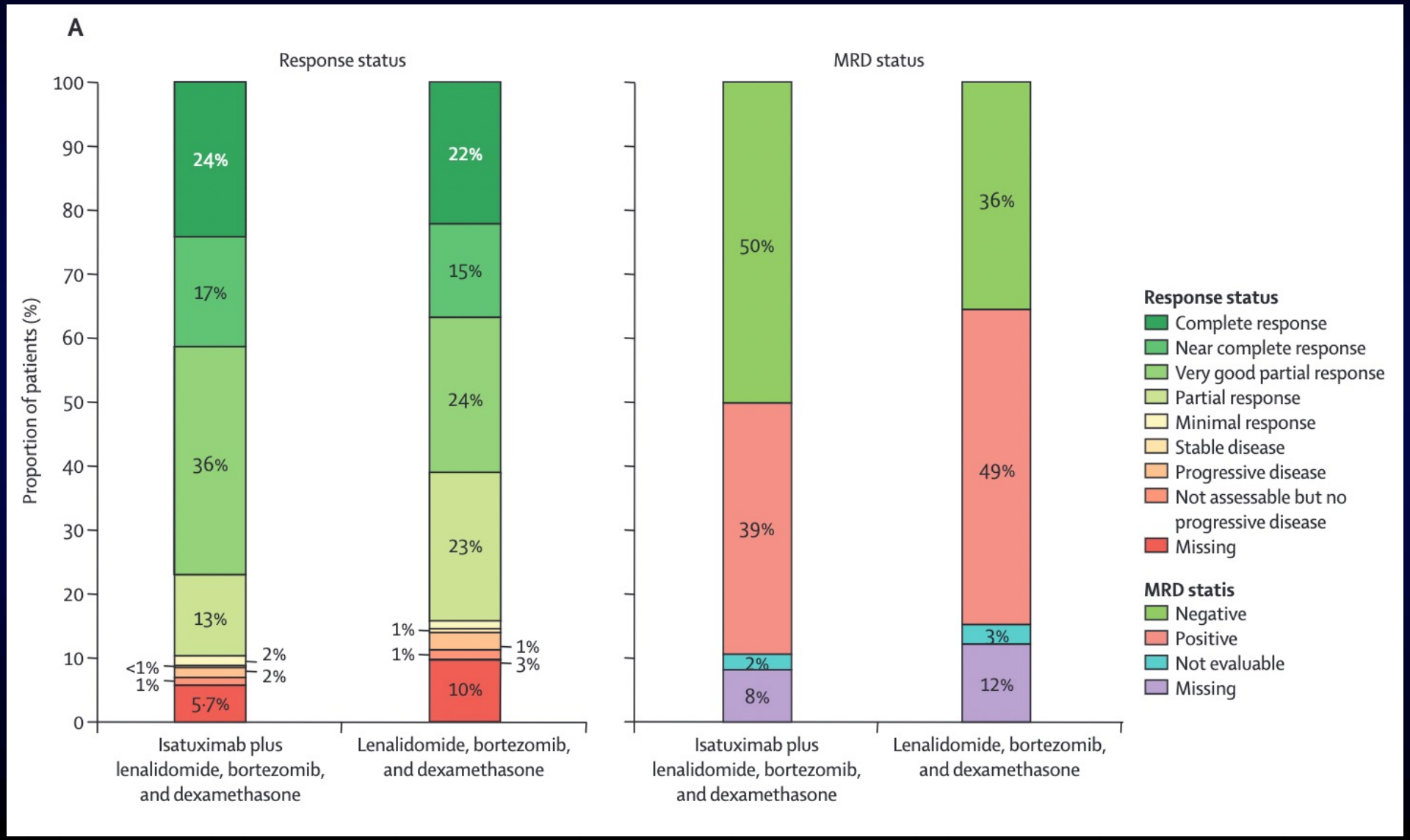
Clinical Trial > Lancet Haematol. 2022 Nov;9(11):e810-e821.

	Isatuximab group (n=330)				Control group (n=328)			
	Grade 1 or 2*	Grade 3	Grade 4	Grade 3 or 4	Grade 1 or 2*	Grade 3	Grade 4	Grade 3 or 4
Any adverse event†	152 (46%)	184 (56%)	70 (21%)	208 (63%)	132 (40%)	180 (55%)	48 (15%)	199 (61%)
Investigations (SOC)‡	0	49 (15%)	30 (9%)	79 (24%)	1 (<1%)	48 (15%)	29 (9%)	77 (23%)
Blood and lymphatic system disorders (SOC)	0	58 (18%)	27 (8%)	85 (26%)	0	44 (13%)	11 (3%)	55 (17%)
Infections and infestations (SOC)	44 (13%)	36 (11%)	4 (1%)	40 (12%)	43 (13%)	29 (9%)	3 (1%)	32 (10%)
Nervous system disorders (SOC)	69 (21%)	32 (10%)	1 (<1%)	33 (10%)	80 (24%)	26 (8%)	1 (<1%)	27 (8%)
Gastrointestinal disorders (SOC)	7 (2%)	22 (7%)	5 (2%)	27 (8%)	6 (2%)	28 (9%)	2 (1%)	30 (9%)
Metabolism and nutrition disorders (SOC)	0	8 (2%)	4 (1%)	12 (4%)	0	21 (6%)	5 (2%)	26 (8%)
Cardiac disorders (SOC)	5 (2%)	12 (4%)	1 (<1%)	13 (4%)	2 (1%)	5 (2%)	0	5 (2%)
Specific haematological adverse events§								
Leukocytopenia	0	19 (6%)	8 (2%)	27 (8%)	0	10 (3%)	3 (1%)	13 (4%)
Neutropenia	0	51 (15%)	27 (8%)	77 (23%)	0	18 (5%)	6 (2%)	23 (7%)
Lymphopenia	0	35 (11%)	13 (4%)	48 (15%)	0	38 (12%)	27 (8%)	65 (20%)
Anaemia	0	13 (4%)	0	13 (4%)	0	18 (5%)	2 (1%)	20 (6%)
Thrombocytopenia	1 (<1%)	13 (4%)	8 (2%)	21 (6%)	0	9 (3%)	6 (2%)	15 (5%)
Specific non-haematological adverse events§								
Peripheral neuropathy	68 (21%)	21 (6%)	1 (<1%)	22 (7%)	80 (24%)	24 (7%)	1 (<1%)	25 (8%)
Thromboembolic events	14 (4%)	8 (2%)	0	8 (2%)	10 (3%)	4 (1%)	0	4 (1%)
Infusion-related reactions¶	39 (12%)	2 (<1%)	1 (<1%)	3 (1%)	..	..	..	..
Serious adverse events†								
Any serious adverse event	32 (10%)	78 (24%)	23 (7%)	92 (28%)	40 (12%)	85 (26%)	12 (4%)	93 (28%)

Collaborators, Affiliations + expand

PMID: 36328040 DOI: 10.1016/S2352-3026(22)00263-0

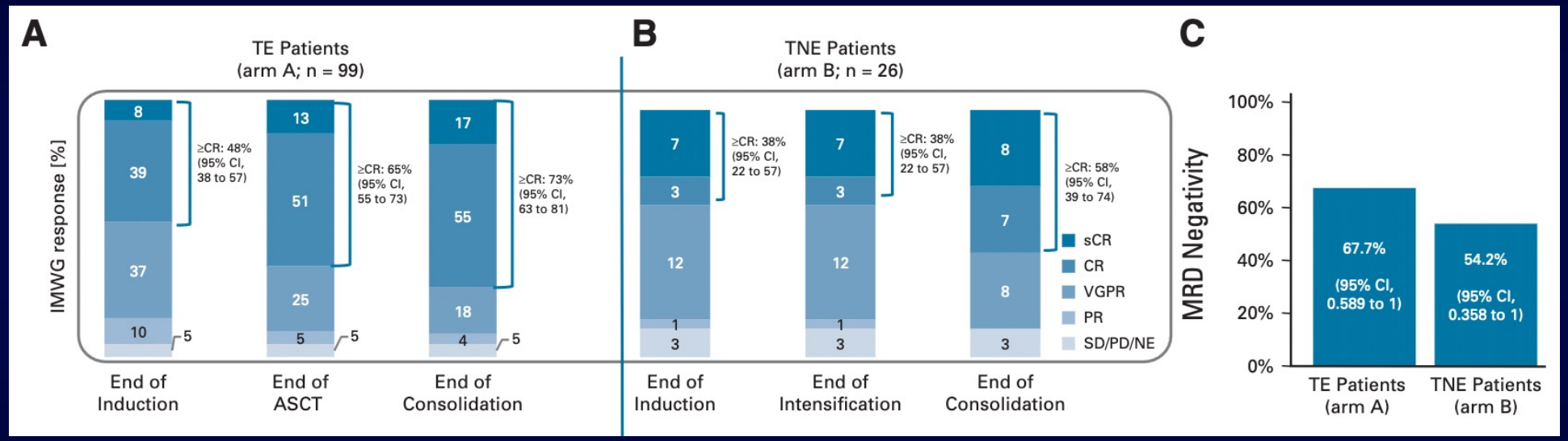
Response & MRD Status



Isatuximab & Carfilzomib Induction

	TE Patients (n = 97), %		TNE Patients (n = 25), %	
AE	AE All Grades	AE Grade ≥3	AE All Grades	AE Grade ≥3
Patients with any AE	93.8	78.4	88	72
Hematologic				
Neutropenia	41.2	39.2	28	28
Leukopenia	25.8	24.7	4	4
Thrombocytopenia	27.8	26.8	20	16
Anemia	14.4	14.4	20	12
Nonhematologic				
Infection (total)	60.8	27.8	48	28
Gastrointestinal	19.6	9.3	28	4
Neuropathy	35.1	2.1	16	4
Cardiac	11.3	2.1	20	20
Hypertension	14.4	10.3	16	8
Renal	8.2	6.2	16	8
Infusion-related reaction	26.8	1	16	0

Response Data



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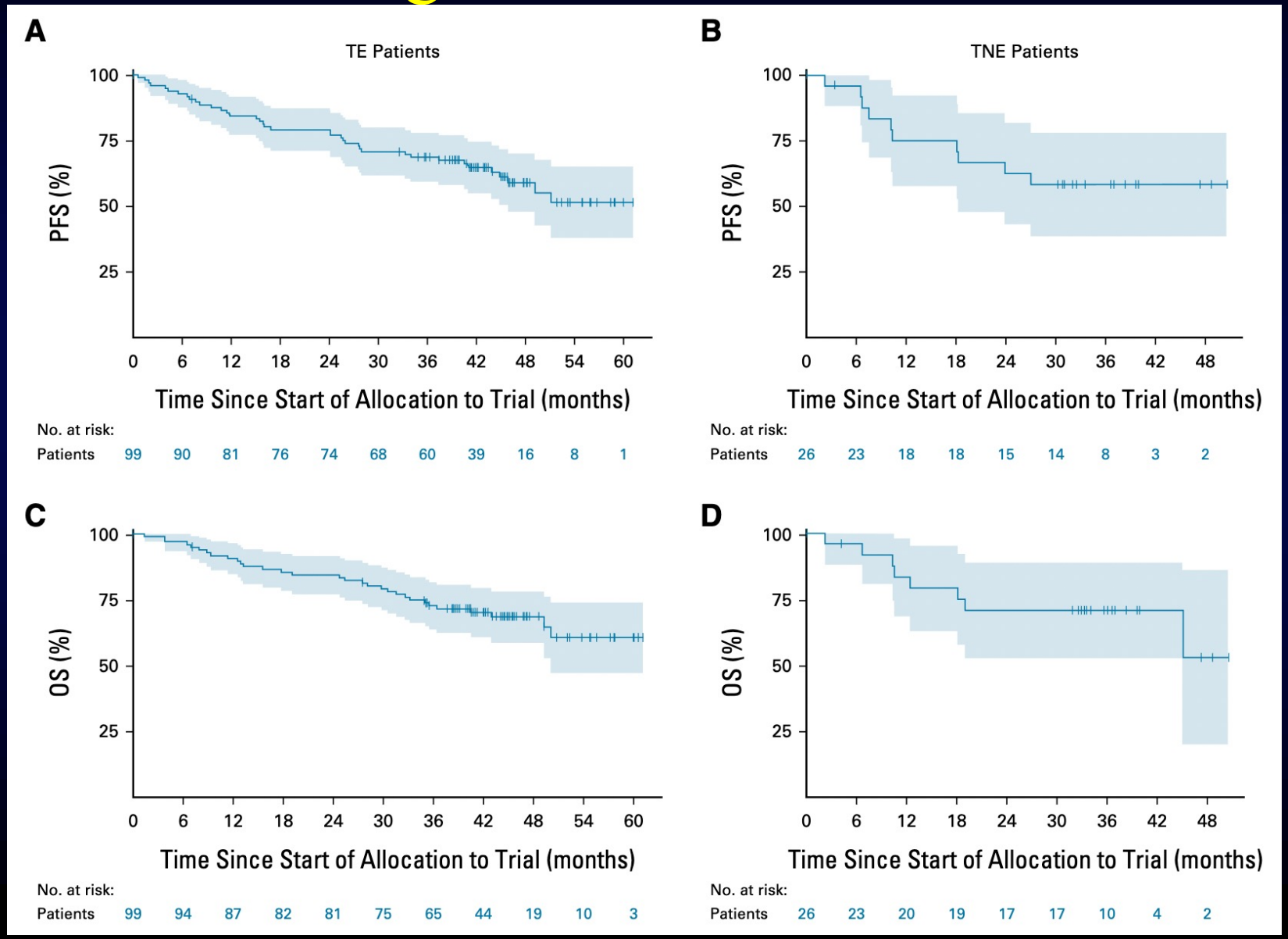
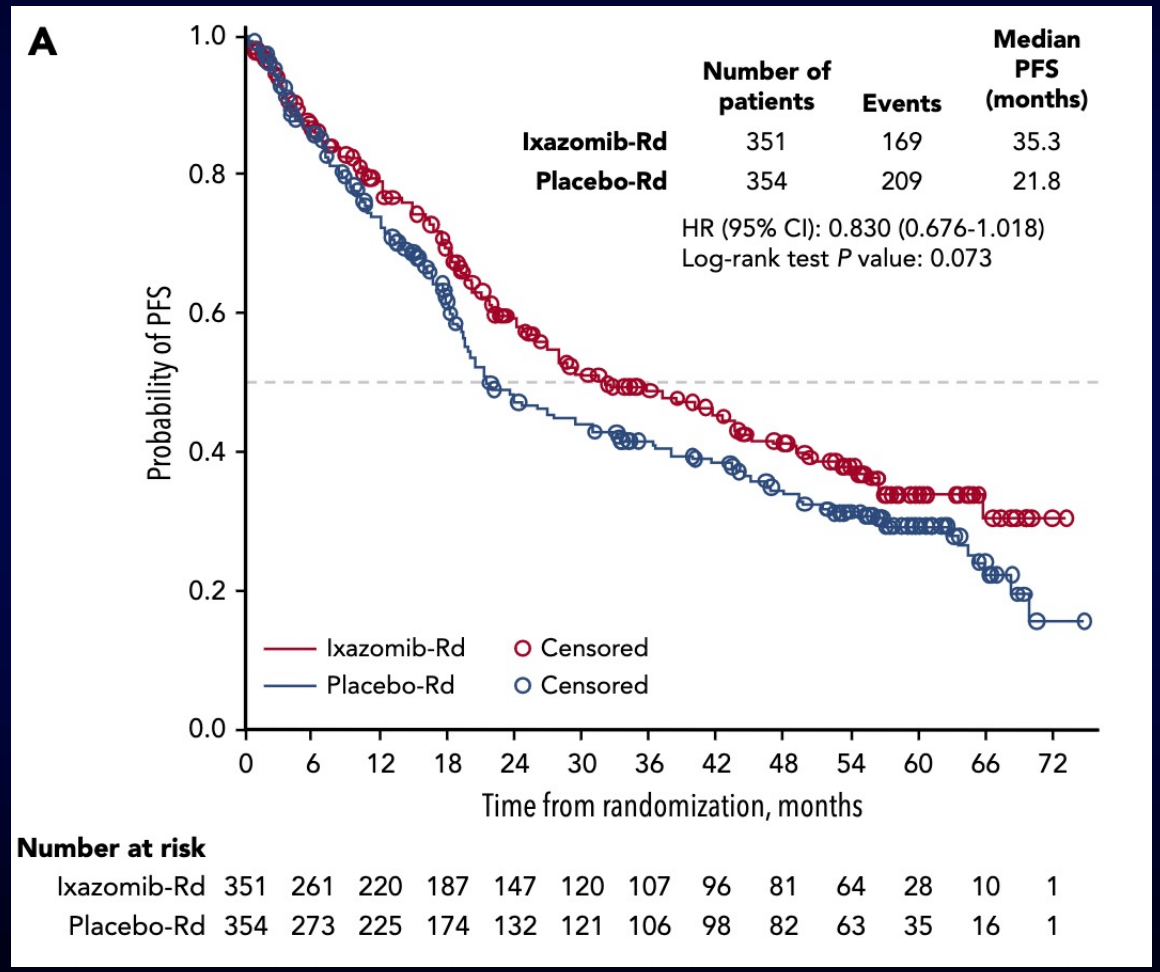
Longer Term Outcomes

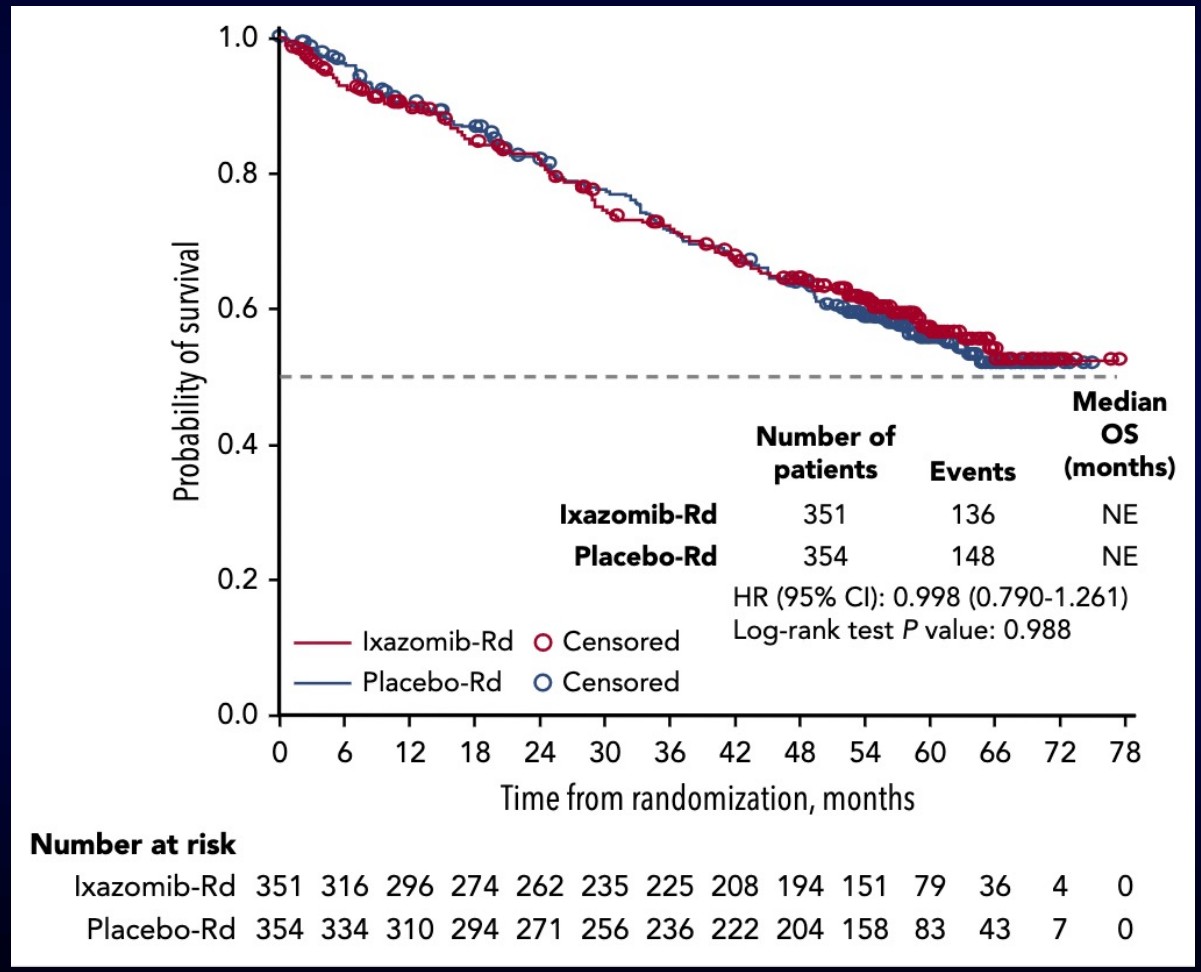


Ixazomib Adverse Events in Induction Therapy

	Ixazomib-Rd (N = 354)		Placebo-Rd (N = 349)	
MedDRA preferred term, n (%)	Any grade	Grade ≥3	Any grade	Grade ≥3
Diarrhea	216 (61.0)	35 (9.9)	161 (46.1)	7 (2.0)
Rash*	199 (56.2)	59 (16.7)	130 (37.2)	26 (7.4)
Peripheral edema	172 (48.6)	4 (1.1)	117 (33.5)	4 (1.1)
Constipation	151 (42.7)	4 (1.1)	144 (41.3)	3 (0.9)
Nausea	131 (37.0)	5 (1.4)	97 (27.8)	1 (0.3)
Peripheral neuropathy*	120 (33.9)	8 (2.3)	96 (27.5)	4 (1.1)
Fatigue	109 (30.8)	14 (4.0)	106 (30.4)	14 (4.0)
Anemia	108 (30.5)	56 (15.8)	108 (30.9)	62 (17.8)
Vomiting	105 (29.7)	4 (1.1)	46 (13.2)	2 (0.6)
Cardiac arrhythmias*,†	81 (22.9)	37 (10.5)	74 (21.2)	26 (7.4)
Thrombocytopenia*	73 (20.6)	47 (13.3)	33 (9.5)	16 (4.6)
Neutropenia*	71 (20.1)	60 (16.9)	104 (29.8)	94 (26.9)
Pneumonia	62 (17.5)	36 (10.2)	46 (13.2)	26 (7.4)
Acute renal failure*	58 (16.4)	23 (6.5)	65 (18.6)	26 (7.4)
Hypotension*	41 (11.6)	8 (2.3)	29 (8.3)	7 (2.0)
Heart failure*,‡	32 (9.0)	15 (4.2)	21 (6.0)	10 (2.9)
Liver impairment*,§	31 (8.8)	9 (2.5)	27 (7.7)	9 (2.6)
Myocardial infarction*,‖	11 (3.1)	6 (1.7)	9 (2.6)	8 (2.3)
Encephalopathy*,§	8 (2.3)	3 (0.8)	7 (2.0)	4 (1.1)
New primary malignancies	43 (12.1)		40 (11.5)	

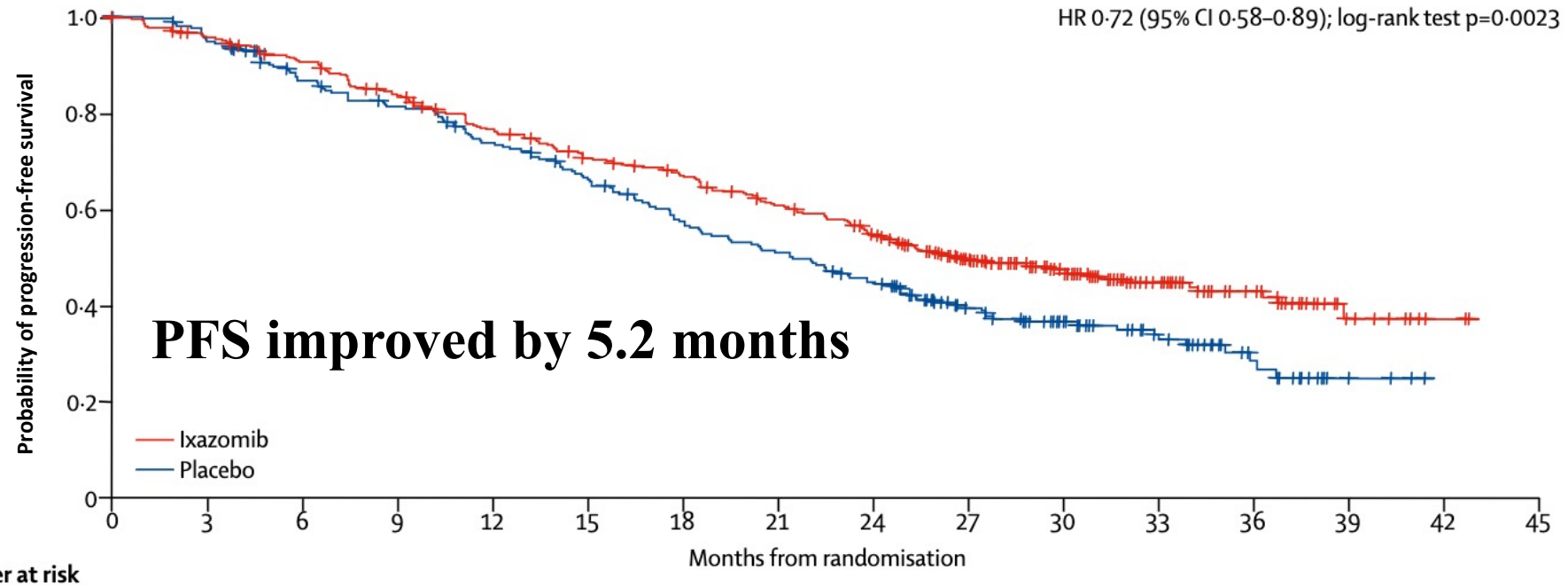
PFS but not OS Benefit





Ixazomib as a Maintenance Post-ASCT

Clinical Trial > Lancet. 2019 Jan 19;393(10168):253-264.



Number at risk (number censored)															
Ixazomib	395	363	340	311	279	255	238	213	187	135	93	56	35	9	3	0
	(0)	(15)	(19)	(22)	(26)	(30)	(33)	(37)	(41)	(76)	(112)	(146)	(165)	(188)	(194)	(197)
Placebo	261	238	210	195	174	153	130	117	100	69	46	32	15	3	0	0
	(0)	(10)	(18)	(20)	(22)	(25)	(27)	(27)	(29)	(50)	(68)	(78)	(91)	(102)	(105)	(105)

PMID: 30545780 DOI: 10.1016/S0140-6736(18)33003-4

Ixazomib TEEM Maintenance

Adverse Event	Ixazomib Group (n = 426)			Placebo Group (n = 276)		
	Any Grade	Grade 3	Grade 4	Any Grade	Grade 3	Grade 4
Common hematologic TEAEs of any cause						
Thrombocytopenia[a]	20 (4.7)	9 (2.1)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)
Neutropenia[a]	10 (2.3)	8 (1.9)	1 (0.2)	9 (3.3)	4 (1.4)	0 (0.0)
Common nonhematologic TEAEs of any cause						
GI disorders (MedDRA SOC)	222 (52.1)	22 (5.2)	0 (0.0)	93 (33.7)	7 (2.5)	0 (0.0)
Nausea	114 (26.8)	2 (0.5)	0 (0.0)	22 (8.0)	0 (0.0)	0 (0.0)
Vomiting	103 (24.2)	7 (1.6)	0 (0.0)	12 (4.3)	2 (0.7)	0 (0.0)
Diarrhea	99 (23.2)	8 (1.9)	0 (0.0)	34 (12.3)	2 (0.7)	0 (0.0)
Infections and infestations (MedDRA SOC)[b]	206 (48.4)	28 (6.6)	0 (0.0)	104 (37.7)	12 (4.3)	0 (0.0)
Upper respiratory tract infection	67 (15.7)	2 (0.5)	0 (0.0)	30 (10.9)	1 (0.4)	0 (0.0)
Rash[a]	109 (25.6)	12 (2.8)	0 (0.0)	29 (10.5)	0 (0.0)	0 (0.0)
Peripheral neuropathy[a]	83 (19.5)	7 (1.6)	0 (0.0)	30 (10.9)	0 (0.0)	0 (0.0)
Back pain	61 (14.3)	1 (0.2)	0 (0.0)	31 (11.2)	1 (0.4)	0 (0.0)
Arthralgia	49 (11.5)	2 (0.5)	0 (0.0)	20 (7.2)	2 (0.7)	0 (0.0)
Pyrexia	48 (11.3)	1 (0.2)	0 (0.0)	14 (5.1)	0 (0.0)	1 (0.4)
Fatigue	46 (10.8)	6 (1.4)	0 (0.0)	28 (10.1)	1 (0.4)	0 (0.0)
Other TEAEs of clinical interest						
Cardiac arrhythmias[a,c]	18 (4.2)	6 (1.4)	0 (0.0)	13 (4.7)	2 (0.7)	0 (0.0)
Heart failure[a,d]	5 (1.2)	2 (0.5)	0 (0.0)	4 (1.4)	1 (0.4)	1 (0.4)
Hypotension[a]	10 (2.3)	0 (0.0)	0 (0.0)	3 (1.1)	0 (0.0)	0 (0.0)
Liver impairment[a]	19 (4.5)	6 (1.4)	0 (0.0)	7 (2.5)	3 (1.1)	0 (0.0)
Myocardial infarction[a,e]	1 (0.2)	0 (0.0)	1 (0.2)	4 (1.4)	1 (0.4)	0 (0.0)
Renal impairment[a,f]	16 (3.8)	4 (0.9)	4 (0.9)	5 (1.8)	0 (0.0)	0 (0.0)
Herpes zoster	13 (3.1)	1 (0.2)	0 (0.0)	2 (0.7)	0 (0.0)	0 (0.0)
In patients receiving antiviral prophylaxis	1/274 (0.4)	0 (0.0)	0 (0.0)	0/167 (0.0)	0 (0.0)	0 (0.0)
In patients not receiving prophylaxis	12/152 (7.9)	1/152 (0.7)	0 (0.0)	2/109 (1.8)	0 (0.0)	0 (0.0)
New primary malignant tumor	22 (5.2)	—		17 (6.2)	—	

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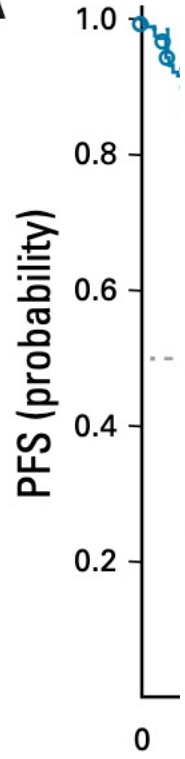
A

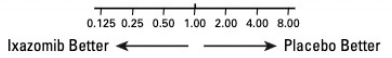


No. at risk:

Ixazomib	425			4	0	0
Placebo	281			3	1	0

B

Subgroup	No. of Patients with PFS Events (of total patients) Ixazomib	Placebo	Median PFS (months) Ixazomib	Placebo	HR (95% CI)
All patients (n = 706)	228 of 425	198 of 281	17.4	9.4	0.659 (0.542 to 0.801)
Age at time of random assignment					
< 75 years (n = 432)*	141 of 261	123 of 171	17.7	9.3	0.615 (0.480 to 0.788)
≥ 75 years (n = 274)*	87 of 164	75 of 110	16.7	10.6	0.738 (0.537 to 1.014)
Prior PI exposure					
Yes (n = 566)*	187 of 342	152 of 224	16.8	11.1	0.743 (0.597 to 0.924)
No (n = 140)*	41 of 83	46 of 57	24.1	7.7	0.395 (0.251 to 0.622)
Preinduction ISS stage					
I or II (n = 465)*	144 of 281	128 of 184	17.4	10.6	0.641 (0.503 to 0.816)
III (n = 241)*	84 of 144	70 of 97	16.6	7.8	0.695 (0.499 to 0.967)
Response to initial therapy					
CR or VGPR (n= 438)*	116 of 263	112 of 175	25.6	12.9	0.586 (0.449 to 0.765)
PR (n= 268)*	112 of 162	86 of 106	10.2	6.5	0.756 (0.566 to 1.010)
Age					
< 65 years (n = 68)†	25 of 37	24 of 31	11.5	8.3	0.569 (0.297 to 1.090)
≥ 65 years and < 75 years (n = 365)†	116 of 224	100 of 141	17.9	9.3	0.632 (0.480 to 0.833)
≥ 75 years (n = 273)†	87 of 164	74 of 109	16.7	10.2	0.742 (0.539 to 1.021)
Sex					
Male (n = 377)	129 of 222	113 of 155	15.3	8.3	0.700 (0.539 to 0.909)
Female (n = 329)	99 of 203	85 of 126	20.3	12.5	0.620 (0.457 to 0.842)
Race					
White (n = 557)	178 of 330	167 of 227	16.9	9.2	0.602 (0.483 to 0.751)
Asian (n = 102)	31 of 63	23 of 39	20.3	14.8	0.826 (0.458 to 1.491)
Other or not reported (n = 27)	9 of 17	5 of 10	22.0	18.7	3.152 (0.356 to 27.875)
Region					
Asia-Pacific (n = 118)	36 of 70	32 of 48	18.7	10.7	0.793 (0.471 to 1.337)
Europe/Middle East/Africa (n = 505)	164 of 304	143 of 201	16.9	9.3	0.635 (0.503 to 0.801)
Other (n = 83)	28 of 51	23 of 32	17.4	9.2	0.672 (0.337 to 1.343)
Frailty status					
Fit (n = 284)	91 of 172	83 of 112	18.6	8.5	0.530 (0.387 to 0.727)
Unfit (n = 245)	80 of 147	67 of 98	17.6	10.6	0.746 (0.526 to 1.058)
Frail (n = 170)	54 of 102	47 of 68	15.4	11.1	0.733 (0.481 to 1.117)
Prior IMiD exposure					
Yes (n = 231)	72 of 137	73 of 94	18.9	8.7	0.498 (0.350 to 0.708)
No (n = 475)	156 of 288	125 of 187	16.6	10.6	0.734 (0.575 to 0.936)
ISS stage at initial diagnosis					
I (n = 178)†	52 of 112	43 of 66	20.3	14.5	0.741 (0.479 to 1.148)
II (n = 279)†	90 of 165	84 of 114	15.7	9.4	0.555 (0.403 to 0.765)
III (n = 249)†	86 of 148	71 of 101	17.7	7.9	0.712 (0.510 to 0.993)
Revised ISS stage at initial diagnosis					
I (n = 86)	21 of 54	22 of 32	21.8	8.0	0.531 (0.278 to 1.015)
II (n = 347)	121 of 204	107 of 143	15.4	9.3	0.667 (0.508 to 0.876)
III (n = 92)	36 of 58	24 of 34	15.3	7.8	0.966 (0.544 to 1.714)
Unclassifiable (n = 181)	50 of 109	45 of 72	18.6	14.2	0.644 (0.407 to 1.019)
Response at study entry					
CR (n = 163)†	31 of 98	29 of 65	40.5	26.7	0.760 (0.434 to 1.332)
VGPR (n = 306)†	97 of 175	102 of 131	17.6	8.7	0.550 (0.410 to 0.737)
PR (n = 194)†	82 of 121	60 of 73	11.1	7.4	0.702 (0.491 to 1.004)
Cytogenetic risk‡					
High risk (n = 122)	51 of 74	36 of 48	10.1	9.6	1.011 (0.631 to 1.621)
Standard risk (n = 465)	142 of 275	139 of 190	17.9	9.2	0.617 (0.484 to 0.787)
Unclassifiable (n = 119)	35 of 76	23 of 43	22.0	14.3	0.735 (0.401 to 1.347)
Cytogenetic risk¶					
Expanded high risk (n = 241)	101 of 150	72 of 91	10.8	8.3	0.765 (0.550 to 1.063)
Standard risk (n = 256)	70 of 148	77 of 108	18.7	9.3	0.550 (0.388 to 0.780)
Unclassifiable (n = 209)	57 of 127	49 of 82	26.7	14.2	0.645 (0.424 to 0.983)
Reason for transplantation ineligibility					
Age (n = 617)	195 of 373	170 of 244	17.6	9.9	0.651 (0.526 to 0.805)
Other (n = 70)	28 of 43	20 of 27	14.8	9.3	0.783 (0.413 to 1.484)



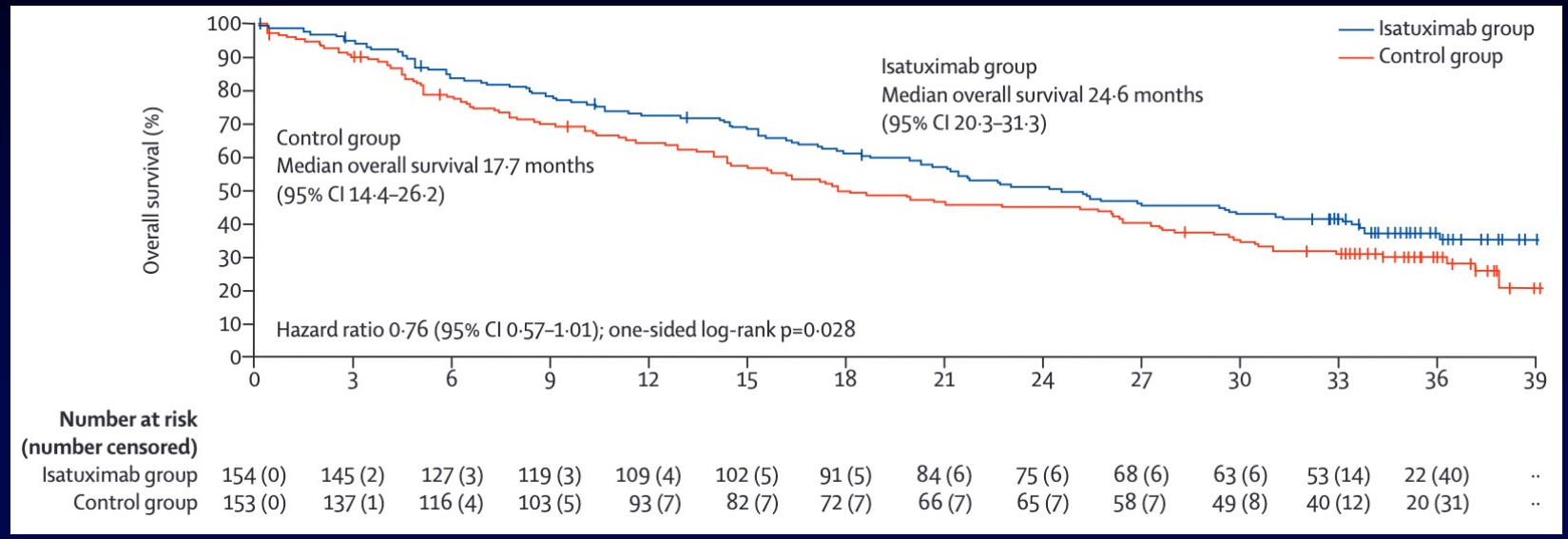
Median PFS (months)
17.4
9.4

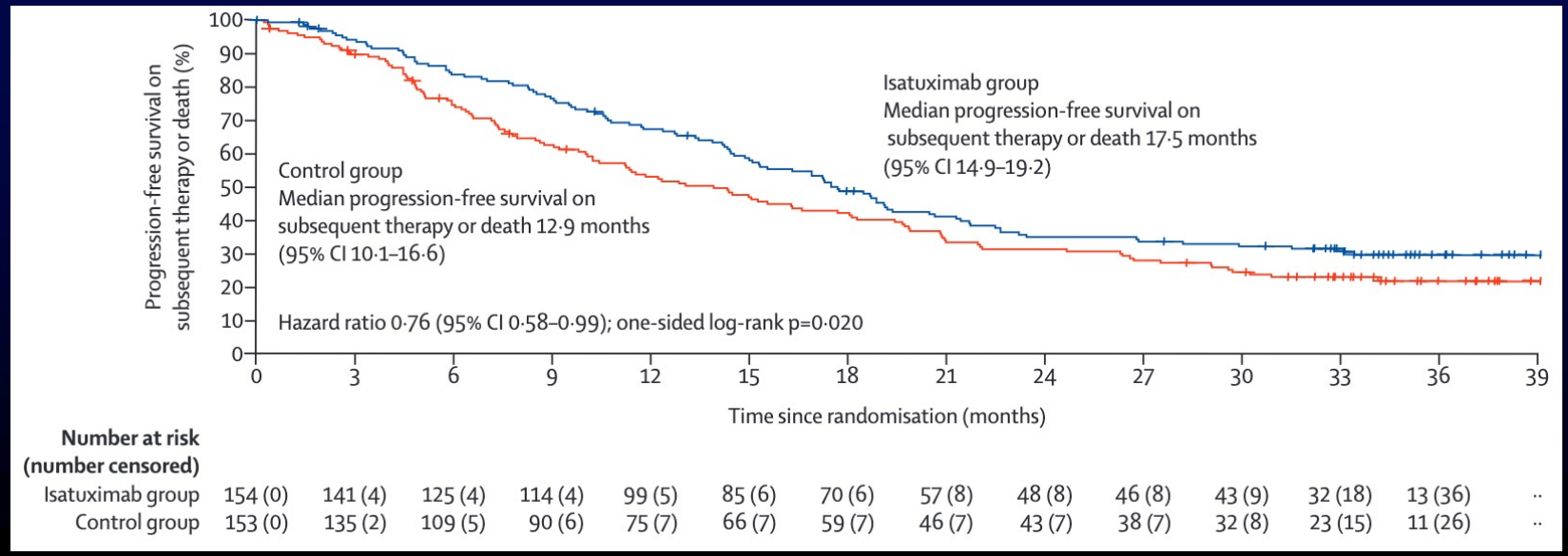
xazomib
Placebo
42 45 48

Isatuximab in ARROW vs. ICARIA Update

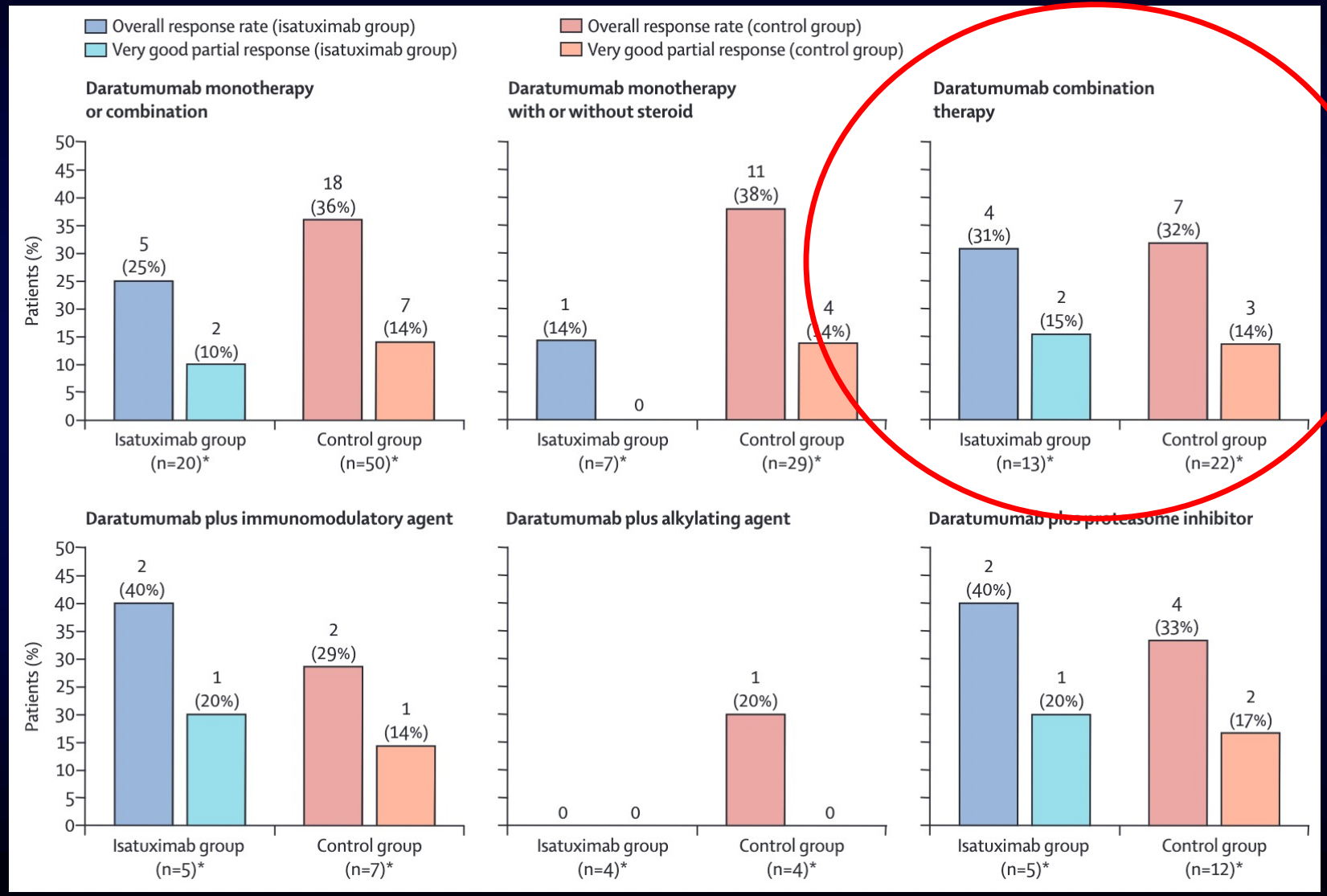
	Isatuximab group (n=152)				Control group (n=149)			
	Grade 1–2	Grade 3	Grade 4	Grade 5	Grade 1–2	Grade 3	Grade 4	Grade 5
Any class	142 (93%)	125 (82%)	69 (45%)	14 (9%)	138 (94%)	95 (64%)	50 (34%)	15 (10%)
Infusion-related reaction	54 (36%)	2 (1%)	2 (1%)	0	2 (1%)*	0	0	0
Upper respiratory tract infection	50 (33%)	5 (3%)	0	0	28 (19%)	2 (1%)	0	0
Diarrhoea	46 (30%)	3 (2%)	0	0	32 (22%)	2 (1%)	0	0
Bronchitis	36 (24%)	7 (5%)	0	0	16 (11%)	1 (1%)	0	0
Oedema peripheral	29 (19%)	2 (1%)	0	0	18 (12%)	0	0	0
Fatigue	27 (18%)	6 (4%)	0	0	32 (22%)	0	0	0
Constipation	25 (16%)	0	0	0	30 (20%)	0	0	0
Back pain	25 (16%)	4 (3%)	0	0	24 (16%)	2 (1%)	0	0
Dyspnoea	23 (15%)	7 (5%)	0	0	13 (9%)	2 (1%)	0	0
Nausea	23 (15%)	0	0	0	14 (10%)	0	0	0
Pyrexia	23 (15%)	4 (3%)	0	0	19 (13%)	2 (1%)	0	0
Nasopharyngitis	21 (14%)	0	0	0	10 (7%)	0	0	0
Asthenia	21 (14%)	5 (3%)	0	0	26 (18%)	4 (3%)	0	0
Vomiting	18 (12%)	2 (1%)	0	0	6 (4%)	0	0	0
Decreased appetite	17 (11%)	2 (1%)	0	0	8 (5%)	1 (1%)	0	0
Headache	16 (11%)	0	0	0	9 (6%)	0	0	0
Muscle spasms	15 (10%)	1 (1%)	0	0	16 (11%)	0	0	0
Arthralgia	14 (9%)	3 (2%)	0	0	15 (10%)	1 (1%)	0	0
Neutropenia	1 (1%)	52 (34%)	46 (30%)	1 (1%)	6 (4%)	33 (22%)	26 (17%)	0
Pneumonia	14 (9%)	34 (22%)	3 (2%)	0	12 (8%)	29 (20%)	2 (1%)	1 (1%)
Febrile neutropenia	0	16 (11%)	2 (1%)	0	0	4 (3%)	1 (1%)	0
Lower respiratory tract infection	5 (3%)	8 (5%)	0	0	5 (3%)	4 (3%)	0	0
Anaemia	2 (1%)	7 (5%)	0	0	1 (1%)	1 (1%)	0	0
Cataract	8 (5%)	7 (5%)	0	0	6 (4%)	4 (3%)	0	0
Thrombocytopenia	3 (2%)	6 (4%)	17 (11%)	0	0	8 (5%)	14 (9%)	0
Urinary tract infection	14 (9%)	6 (4%)	1 (1%)	1 (1%)	13 (9%)	1 (1%)	0	1 (1%)

OS & PFS2


Isatuximab group
Control group
Overall survival (%)
Isatuximab group
Median overall survival 24·6 months
(95% CI 20·3–31·3)
Control group
Median overall survival 17·7 months
(95% CI 14·4–26·2)
Hazard ratio 0·76 (95% CI 0·57–1·01); one-sided log-rank p=0·028
Number at risk
(number censored)
Isatuximab group 154 (0) 145 (2) 127 (3) 119 (3) 109 (4) 102 (5) 91 (5) 84 (6) 75 (6) 68 (6) 63 (6) 53 (14) 22 (40)
Control group 153 (0) 137 (1) 116 (4) 103 (5) 93 (7) 82 (7) 72 (7) 66 (7) 65 (7) 58 (7) 49 (8) 40 (12) 20 (31)


Progression-free survival on subsequent therapy or death (%)
Isatuximab group
Median progression-free survival on
subsequent therapy or death 17·5 months
(95% CI 14·9–19·2)
Control group
Median progression-free survival on
subsequent therapy or death 12·9 months
(95% CI 10·1–16·6)
Hazard ratio 0·76 (95% CI 0·58–0·99); one-sided log-rank p=0·020
Time since randomisation (months)
Number at risk
(number censored)
Isatuximab group 154 (0) 141 (4) 125 (4) 114 (4) 99 (5) 85 (6) 70 (6) 57 (8) 48 (8) 46 (8) 43 (9) 32 (18) 13 (36)
Control group 153 (0) 135 (2) 109 (5) 90 (6) 75 (7) 66 (7) 59 (7) 46 (7) 43 (7) 38 (7) 32 (8) 23 (15) 11 (26)

Giving Dara-based Therapy After Isa

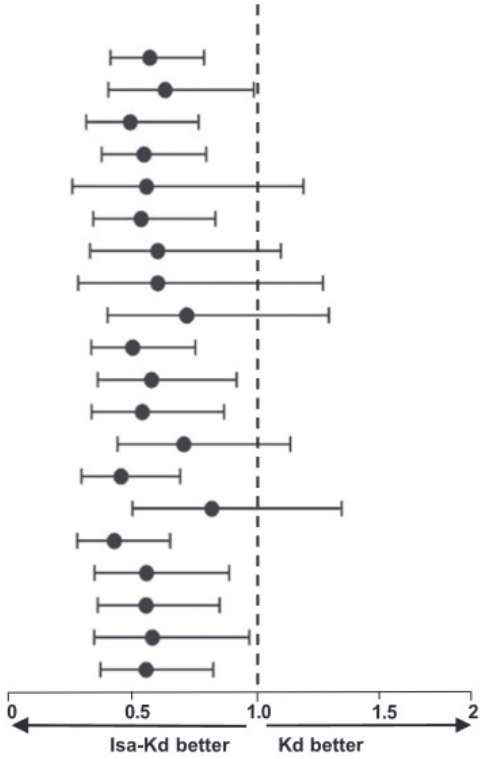


Isatuximab in RRMM: TEAEs Update

n (%)	Isa-Kd (*n* = 177)		Kd (*n* = 122)	
	All grades	Grade ≥ 3	All grades	Grade ≥ 3
Most common TEAEs (preferred terms), in ≥ 20% of patients in the Isa-Kd arm				
Infusion reaction	81 (45.8)	1 (0.6)	4 (3.3)	0
Diarrhea	70 (39.5)	5 (2.8)	39 (32.0)	3 (2.5)
Hypertension	67 (37.9)	40 (22.6)	43 (35.2)	28 (23.0)
Upper respiratory tract infection	66 (37.3)	6 (3.4)	33 (27.0)	2 (1.6)
Fatigue	56 (31.6)	10 (5.6)	25 (20.5)	1 (0.8)
Dyspnea	54 (30.5)	10 (5.6)	27 (22.1)	1 (0.8)
Pneumonia	48 (27.1)	33 (18.6)	26 (21.3)	15 (12.3)
Back pain	45 (25.4)	3 (1.7)	26 (21.3)	1 (0.8)
Insomnia	45 (25.4)	11 (6.2)	30 (24.6)	3 (2.5)
Bronchitis	43 (24.3)	4 (2.3)	15 (12.3)	1 (0.8)
Arthralgia	39 (22.0)	4 (2.3)	15 (12.3)	2 (1.6)
Cough	39 (22.0)	0	17 (13.9)	0
Asthenia	36 (20.3)	4 (2.3)	20 (16.4)	4 (3.3)
Selected TEAEs				
Cardiac failure[a]	15 (8.5)	8 (4.5)	9 (7.4)	5 (4.1)
Second primary malignancy[b,c]	16 (9.0)	8 (4.5)	9 (7.4)	5 (4.1)
Skin cancer	11 (6.2)	2 (1.1)	4 (3.3)	1 (0.8)
Solid tumor, non-skin cancer	7 (4.0)	6 (3.4)	5 (4.1)	3 (2.5)
Hematologic malignancy	0	0	1 (0.8)	1 (0.8)
Not specified	1 (0.6)	1 (0.6)	0	0

Updated PFS Data (ITT)

Subgroup		Isa-Kd Events/total	Kd Events/total	Hazard ratio (95% CI)
All patients		86/179	77/123	0.576 (0.418–0.792)
Age	<65 years	43/88	38/66	0.637 (0.410–0.990)
	≥65 years	43/91	39/57	0.497 (0.321–0.771)
Baseline eGFR (MDRD)	≥60 mL/min/1.73 m²	55/122	60/93	0.553 (0.382–0.801)
	<60 mL/min/1.73 m²	23/43	10/18	0.562 (0.266–1.189)
ISS staging at study entry	I	39/89	43/71	0.541 (0.350–0.837)
	II	34/63	17/31	0.608 (0.336–1.099)
	III	13/26	16/20	0.607 (0.290–1.268)
High-risk cytogenetic status	Yes	26/42	21/31	0.724 (0.406–1.290)
	No	50/114	48/77	0.508 (0.341–0.758)
1q21+	Yes	39/75	35/52	0.582 (0.368–0.923)
	No	39/84	33/55	0.546 (0.342–0.873)
Number of prior lines of therapy (IRT)	1	41/80	31/55	0.712 (0.445–1.138)
	>1	45/99	46/68	0.460 (0.302–0.698)
Prior PI treatment*	Yes	43/81	26/47	0.824 (0.506–1.343)
	No	43/98	51/76	0.434 (0.286–0.657)
Prior IMiD treatment*	Yes	37/81	37/62	0.562 (0.355–0.892)
	No	49/98	40/61	0.560 (0.367–0.854)
Refractory to lenalidomide	Yes	31/57	30/42	0.586 (0.353–0.972)
	No	55/122	47/81	0.560 (0.378–0.829)



Number at Risk

Isa-Kd	179	164	151	136	127	114	108	95	88	81	75	72	64	62	50	18	1
Kd	123	108	99	85	73	63	53	43	39	32	29	23	21	16	10	3	2

Neil Love, MD

Paul G Richardson, MD

8-30-2023

Selinexor Combination Response RRMM

	Selinexor, bortezomib, and dexamethasone group (n=195)		Bortezomib and dexamethasone group (n=204)*	
	Any grade†	Grade 3–4	Any grade‡	Grade 3–4
Haematological adverse events				
Thrombocytopenia	117 (60%)	77 (39%)	55 (27%)	35 (17%)
Anaemia	71 (36%)	31 (16%)	47 (23%)	20 (10%)
Neutropenia	29 (15%)	17 (9%)	12 (6%)	7 (3%)
Non-haematological adverse events				
Fatigue	82 (42%)	26 (13%)	37 (18%)	2 (1%)
Nausea	98 (50%)	15 (8%)	20 (10%)	0
Diarrhoea	63 (32%)	12 (6%)	51 (25%)	1 (<1%)
Peripheral neuropathy§	63 (32%)	9 (5%)	96 (47%)	18 (9%)
Decreased appetite	69 (35%)	7 (4%)	11 (5%)	0
Weight loss	51 (26%)	4 (2%)	25 (12%)	2 (1%)
Asthenia	48 (25%)	16 (8%)	27 (13%)	9 (4%)
Constipation	33 (17%)	0	35 (17%)	3 (1%)
Cough	35 (18%)	1 (1%)	30 (15%)	0
Insomnia	31 (16%)	2 (1%)	32 (16%)	4 (2%)
Back pain	30 (15%)	1 (1%)	29 (14%)	2 (1%)
Pneumonia¶	35 (18%)	24 (12%)	34 (17%)	21 (10%)
Pyrexia	30 (15%)	3 (2%)	22 (11%)	2 (1%)
Cataract	42 (22%)	17 (9%)	13 (6%)	3 (1%)
Vomiting	40 (21%)	8 (4%)	9 (4%)	0
Peripheral oedema	23 (12%)	1 (1%)	26 (13%)	0
Dyspnoea	18 (9%)	1 (1%)	27 (13%)	5 (2%)
Bronchitis	24 (12%)	3 (2%)	20 (10%)	1 (<1%)
Upper respiratory tract infection	35 (18%)	5 (3%)	30 (15%)	1 (<1%)

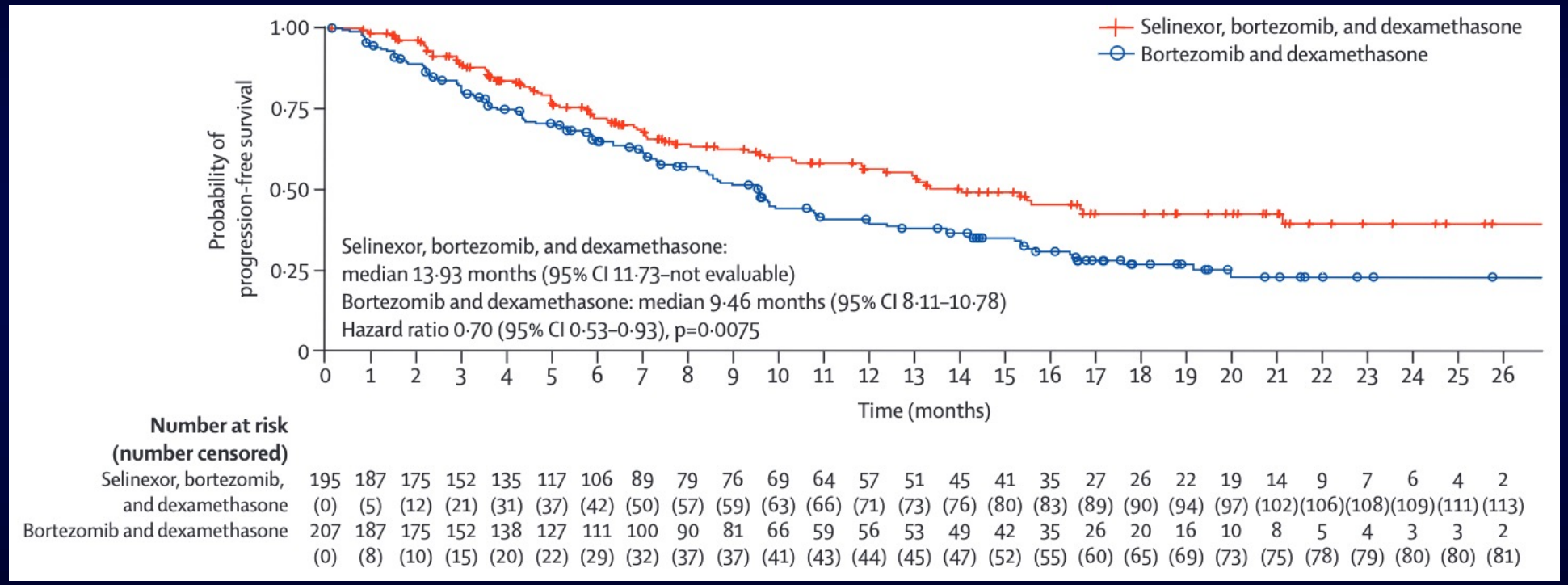
14;396(10262):1563-1573.

	Selinexor, bortezomib, and dexamethasone group (n=195)	Bortezomib and dexamethasone group (n=207)
Overall response rate*	149 (76·4% [69·8–82·2])	129 (62·3% [55·3–68·9])
Best overall response†		
Stringent complete response	19 (10%)	13 (6%)
Complete response	14 (7%)	9 (4%)
Very good partial response	54 (28%)	45 (22%)
Partial response	62 (32%)	62 (30%)
Minimal response	16 (8%)	20 (10%)
Stable disease	25 (13%)	40 (19%)
Progressive disease	1 (1%)	10 (5%)
Non-evaluable	4 (2%)	8 (4%)
Negative status for minimal residual disease‡	9 (5%)	8 (4%)

nan [46], Meletios A Dimopoulos [47],
asi [49]

-6736(20)32292-3

Longer Term Outcomes



Number at risk (number censored)																											
Selinexor, bortezomib, and dexamethasone	195 (0)	187 (5)	175 (12)	152 (21)	135 (31)	117 (37)	106 (42)	89 (50)	79 (57)	76 (59)	69 (63)	64 (66)	57 (71)	51 (73)	45 (76)	41 (80)	35 (83)	27 (89)	26 (90)	22 (94)	19 (97)	14 (102)	9 (106)	7 (108)	6 (109)	4 (111)	2 (113)
Bortezomib and dexamethasone	207 (0)	187 (8)	175 (10)	152 (15)	138 (20)	127 (22)	111 (29)	100 (32)	90 (37)	81 (37)	66 (41)	59 (43)	56 (44)	53 (45)	49 (47)	42 (52)	35 (55)	26 (60)	20 (65)	16 (69)	10 (73)	8 (75)	5 (78)	4 (79)	3 (80)	3 (80)	2 (81)

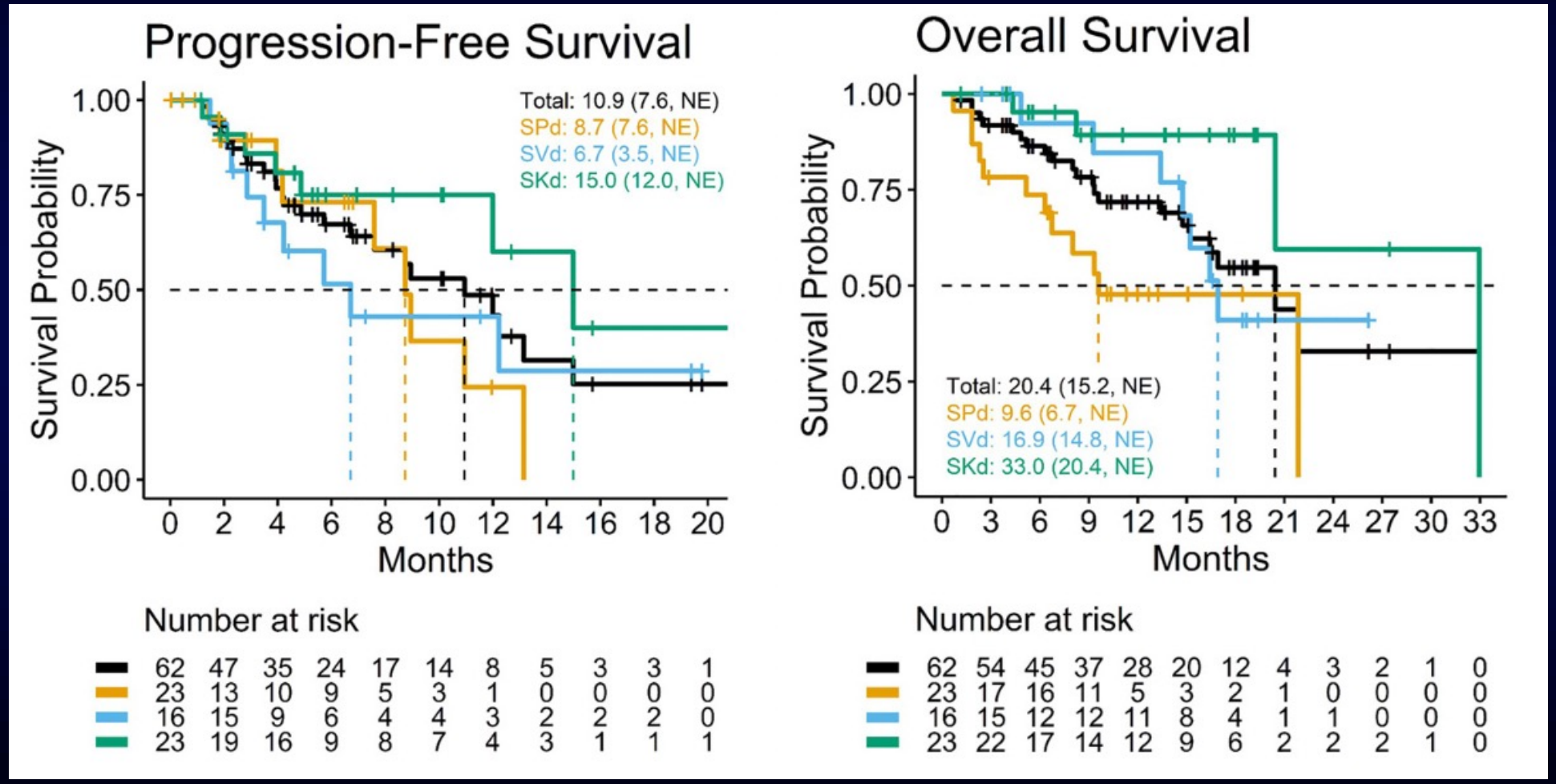
Selinexor Response Rates After α-CD38s

Table 4 Efficacy of Selinexor-Containing Triplets

	SPd	SVd	SKd	All Patients
Overall response rate, n/N (%)				
All patients	12/23 (52.2)	9/16 (56.3)	15/23 (65.2)	36/62 (58.1)
Patients with αCD38 mAb in their most recent prior line	7/13 (53.8)	6/11 (54.5)	10/17 (58.8)	23/41 (56.1)
Patients naive or nonrefractory to the third drug in the Sd-based triplet	7/12 (58.3)	6/9 (66.7)	14/22 (63.6)	27/43 (62.8)
Refractory to the third drug in the Sd-based triplet	5/11 (45.5)	3/7 (42.9)	1/1 (100.0)	9/19 (47.4)
Patients without high-risk cytogenetics	5/10 (50.0)	3/9 (33.3)	3/8 (37.5)	11/27 (40.7)
Patients with high-risk cytogenetics[a]	7/13 (53.8)	6/7 (85.7)	12/15 (80.0)	25/35 (71.4)
Clinical benefit rate, n/N (%)				
All patients	16/23 (69.6)	12/16 (75.0)	17/23 (73.9)	45/62 (72.6)
Patients with αCD38 mAb in their most recent prior line	8/13 (61.5)	9/11 (81.8)	11/17 (64.7)	28/41 (68.3)
Patients naive or nonrefractory to the third drug in the Sd-based triplet	9/12 (75.0)	8/9 (88.9)	16/22 (72.7)	33/43 (76.7)
Refractory to the third drug in the Sd-based triplet	7/11 (63.6)	4/7 (57.1)	1/1 (100.0)	12/19 (63.2)
Patients without high-risk cytogenetics	6/10 (60.0)	6/9 (66.7)	4/8 (50.0)	16/27 (59.3)
Patients with high-risk cytogenetics[a]	10/13 (76.9)	6/7 (85.7)	13/15 (86.7)	29/35 (82.9)

Free article

Longer Term Outcomes



THE UNIVERSITY OF TEXAS MD Anderson Cancer Center Making Cancer History®

Take Home Messages

- Quads based on CD38 mAbs (+PI, Len, dex) standards of care for induction therapy
  - Dara-CyBorD in AL; Dara-VTd, Dara-VMP
  - May consider Car as partner PI for high-risk disease
  - Sequencing of Dara & Isa not yet clear, though Isa may have better activity against amp 1q21
- Maintenance with Len is SOC post-ASCT
  - S1803 Len ± Dara
  - Consider Ixa if Len-intolerant or in TIE MM

Take Home Messages II

- Isatuximab-based triplets (with pom or car) show strong efficacy in early relapse
  - sc isa is on the way
  - May be able to give Dara-based combo after Isa, especially if you do a class switch with partner drug
- Selinexor-based triplets are an important option post-CD38 triplets
  - May be displaced by bispecifics when earlier line data become available

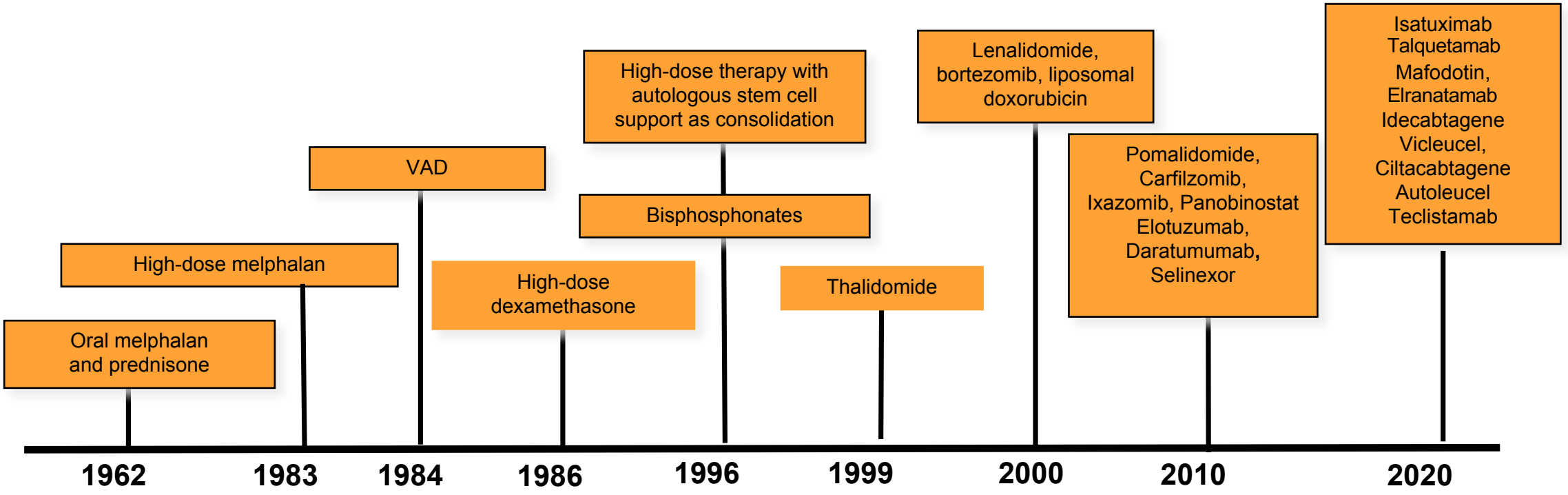
CART and Bispecific Therapy; Venetoclax in MM

Amrita Krishnan MD FACP

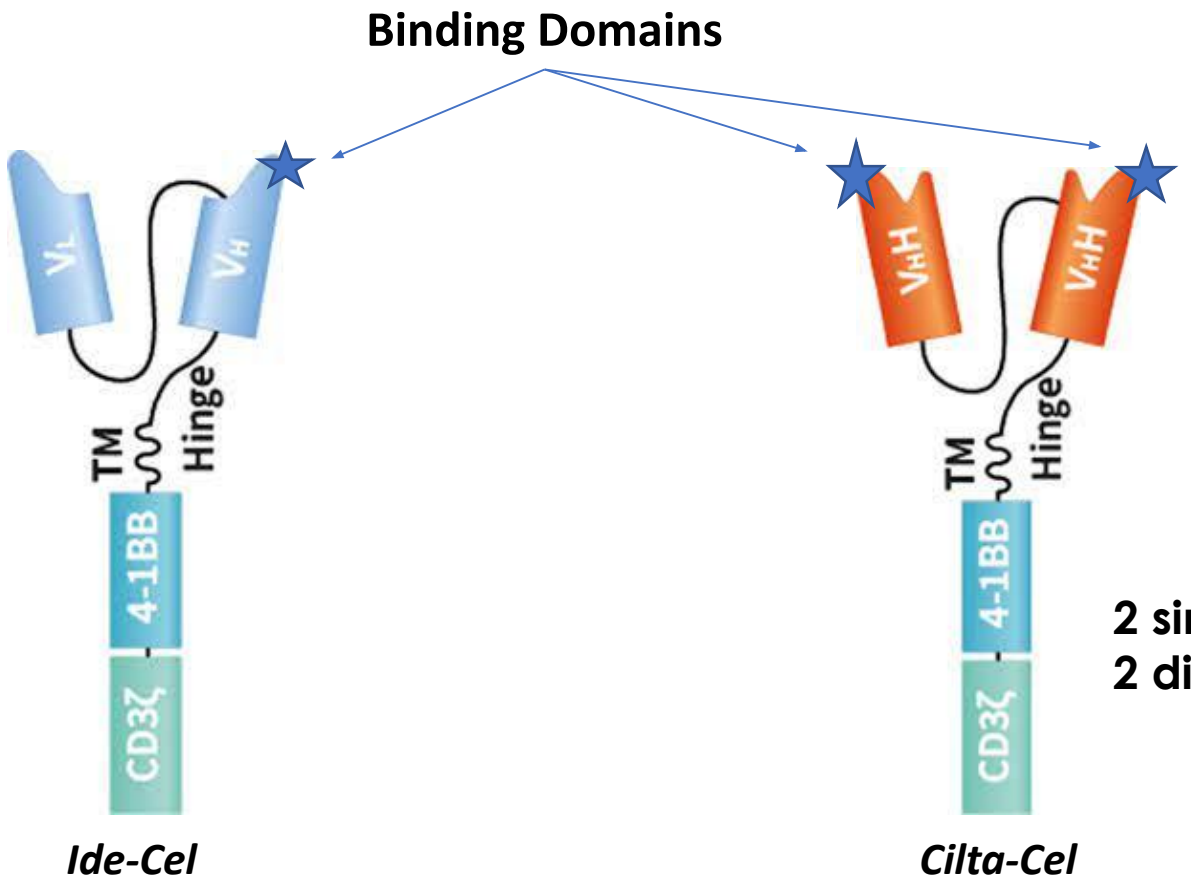
Director of Hematology City of Hope Orange County

Director Judy and Bernard Briskin Center for Myeloma

Evolution of Myeloma Therapy

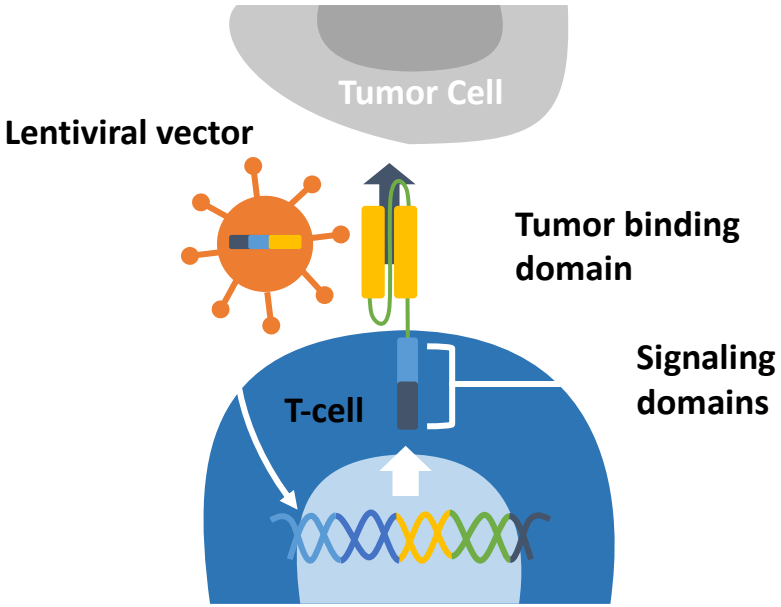


CAR T: Ide-Cel vs Cilta-Cel

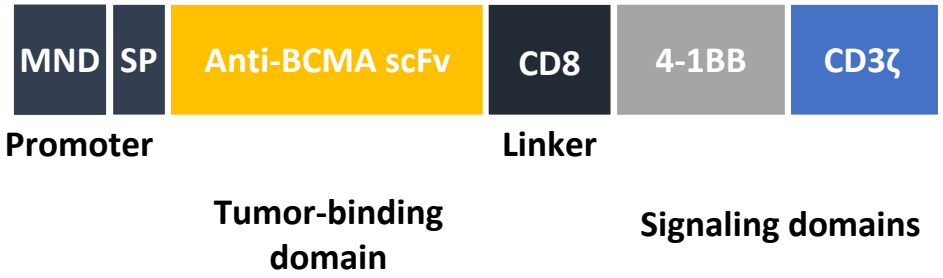


2 single domain antibodies targeting
2 different epitopes of BCMA

Phase II KarMMa: Idecabtagene Vicleucel in R/R MM



Idecabtagene CAR design



Patients with R/R MM and ≥3 prior regimens each with ≥2 consecutive cycles, prior IMiD, PI, and anti-CD38 mAb, and refractory to last therapy by IMWG criteria
(N = 158)

Leukapheresed
n = 140

Idecabtagene vicleucel (n = 128)
150 x 10^6 CAR T-cells (n = 4)
300 x 10^6 CAR T-cells (n = 70)
450 x 10^6 CAR T-cells (n = 54)

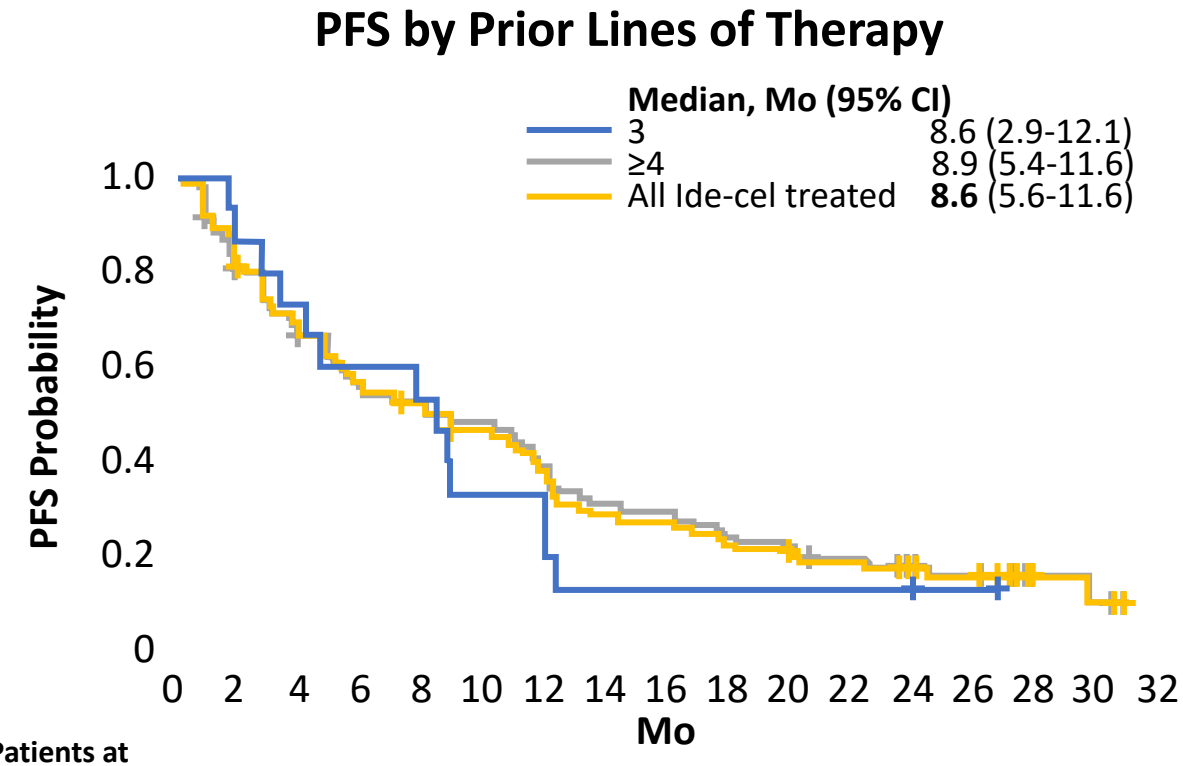
Median Follow-up, Mo
150 x 10^6 CAR T-cells: 18.0
300 x 10^6 CAR T-cells: 15.8
450 x 10^6 CAR T-cells: 12.4
Overall: 24.8

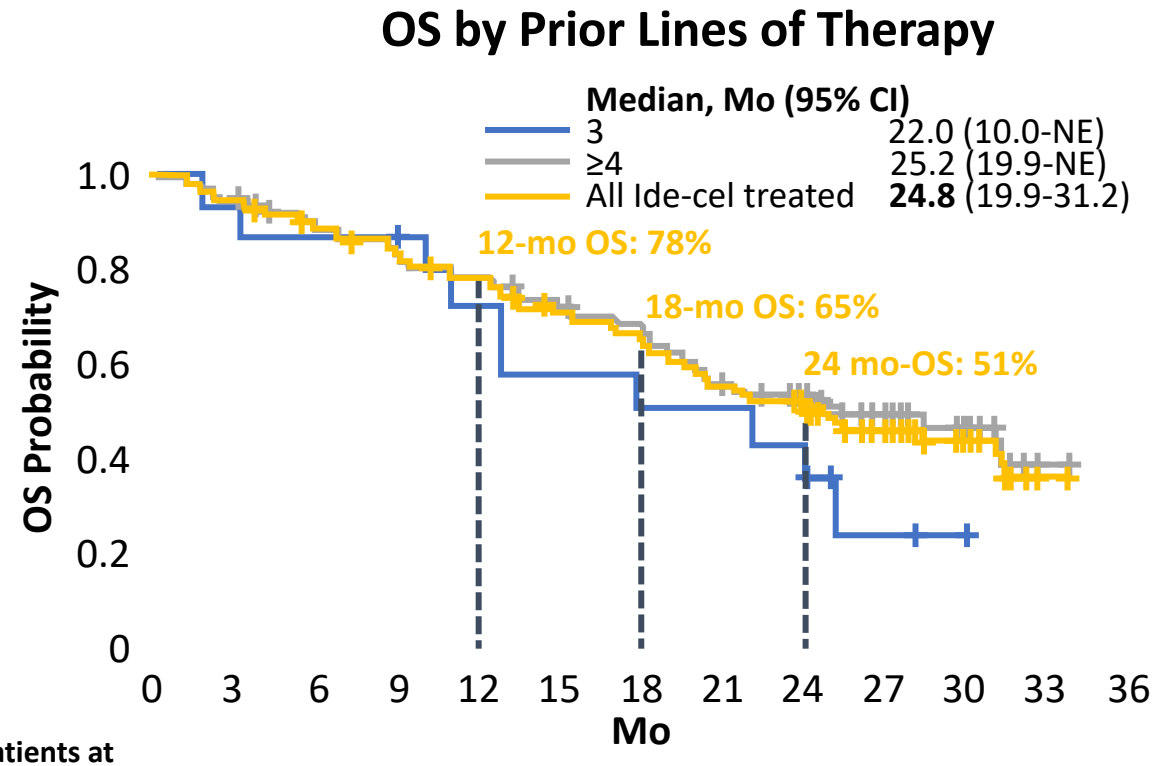
- **Primary endpoint:** ORR
- **Secondary endpoints:** CRR, safety, DoR, PFS, OS, PK, MRD, QoL, HEOR
- **Exploratory endpoints:** immunogenicity, BCMA expression/loss, cytokines, T-cell immunophenotype, GEP in BM

Baseline characteristics:
- High-risk cytogenetics: 35%
- Extramedullary disease: 39%
- Median no. of prior therapies: 6 (range: 3-16)
- Triple refractory: 84%

Anderson. ASCO 2021. Abstr 8016. Munshi. NEJM. 2021;384:705.

KarMMa: PFS and OS With Ide-cel in R/R MM





- Update at ASCO 2021 with median f/u of 24.8 mo

Anderson. ASCO 2021. Abstr 8016.

CARTITUDE-1: Trial Schema and Study Endpoints

Primary endpoints

- Phase 1b: Safety and dose
- Phase 2: Overall response rate (ORR)

Secondary endpoints

- PFS
- OS
- Minimal residual disease (MRD) negativity at 10^{-5}

Key eligibility criteria

- Progressive multiple myeloma per International Myeloma Working Group criteria
- Eastern Cooperative Oncology Group performance status 0 or 1
- Measurable disease
- ≥3 prior LOT or double-refractory to a PI and IMiD
- Prior PI, IMiD, and anti-CD38 mAb exposure

Lin Y, et al. ASCO 2023. Abstract 8009.

CARTITUDE-1: PFS by CR and Sustained MRD Negativity

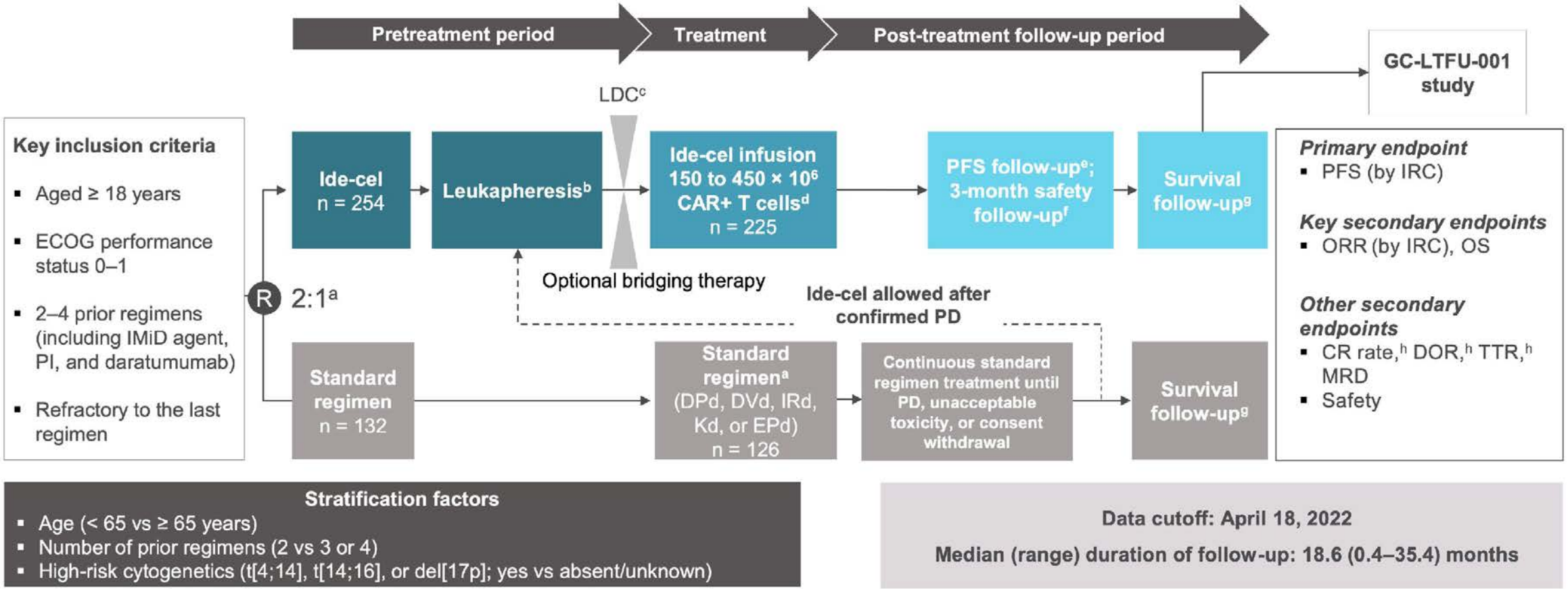
Subgroups	mPFS (95% CI), mo	30-mo PFS rate	36-mo PFS rate
All patients	34.9 (25.2–NE)	54.2%	47.5%
≥CR[a]	38.2 (34.9–NE)	66.8%	59.8%
12-mo sustained MRD negativity[b]	NR (NE–NE)	74.9%	NE
12-mo sustained MRD-negative ≥CR[b]	NR (NE–NE)	78.5%	NE

[a]Patients had ≥CR at any time during the study, assessed by computerized algorithm. [b]Patients who were MRD evaluable had a baseline clone identified, sufficient follow-up for assessment, and ≥2 MRD-negative assessments 12 months apart, with no MRD-positive samples in that interval. mPFS, median progression-free survival; NR, not reached.

Lin Y, et al. ASCO 2023. Abstract 8009.

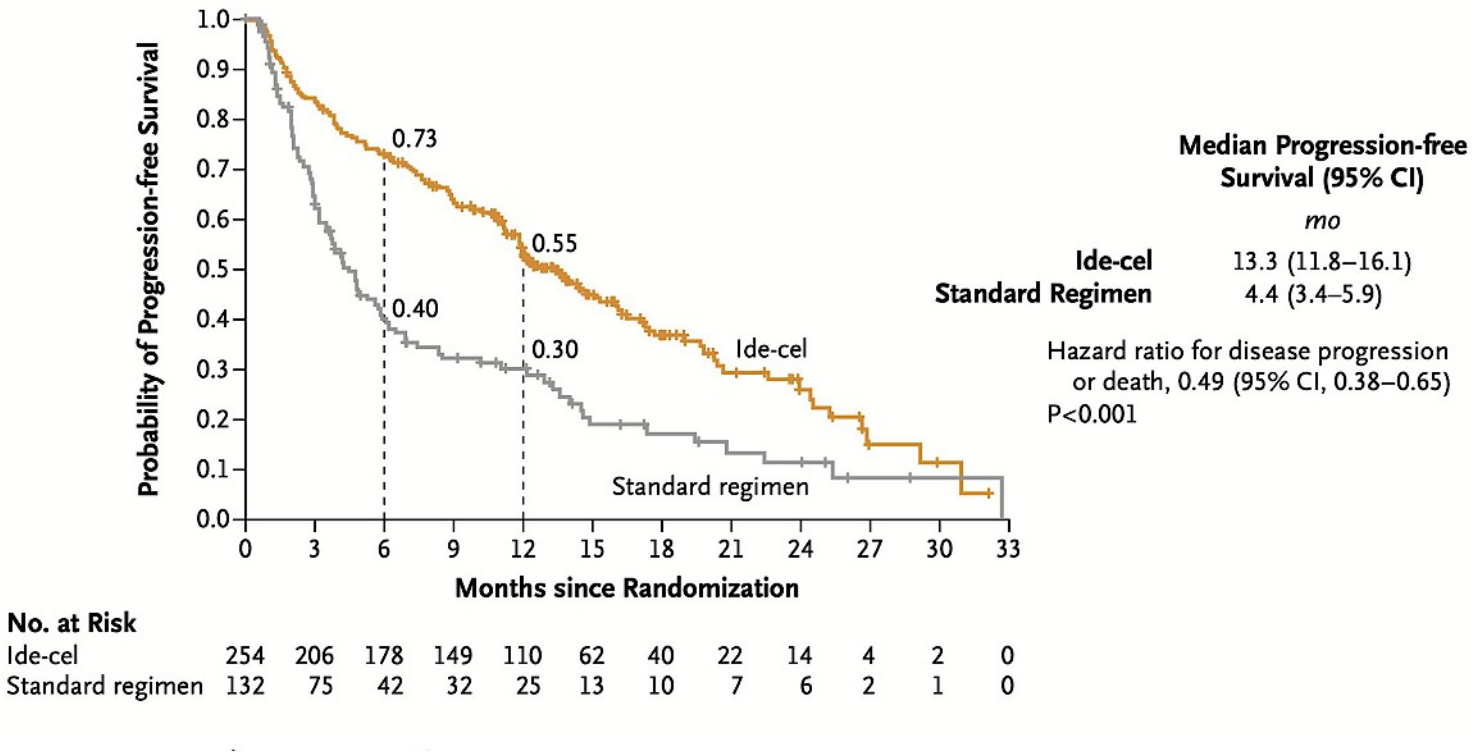
KarMMa-3 Ide-Cel Phase 3

First phase III study of anti-BCMA CAR T-cells in multiple myeloma
2-4 prior lines. including IMiD, PI, and daratumumab (triple class exposed)
2:1 randomization



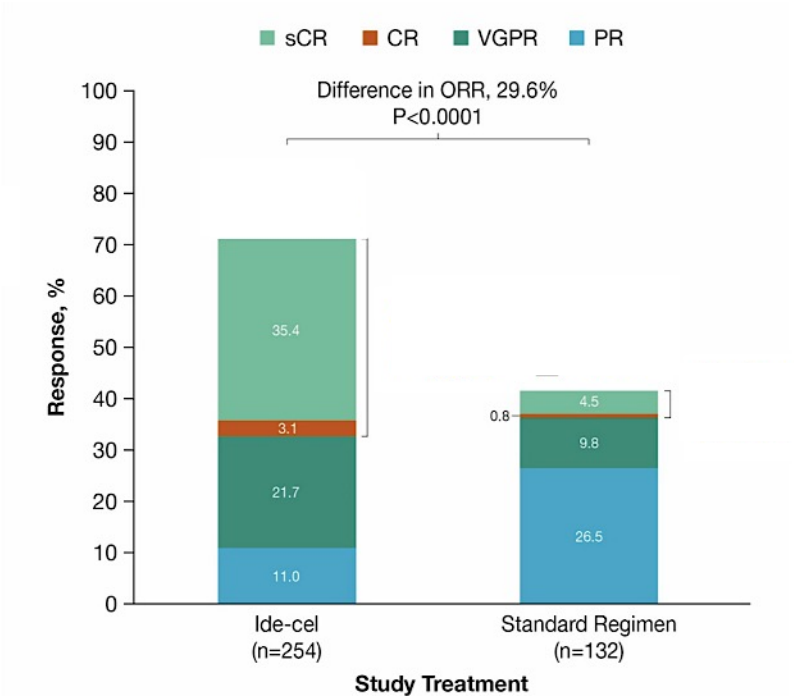
Rodriguez-Otero P, et al. European CAR T-Cell Meeting 2023. Abstract BA02-7.

KarMMa-3: Results



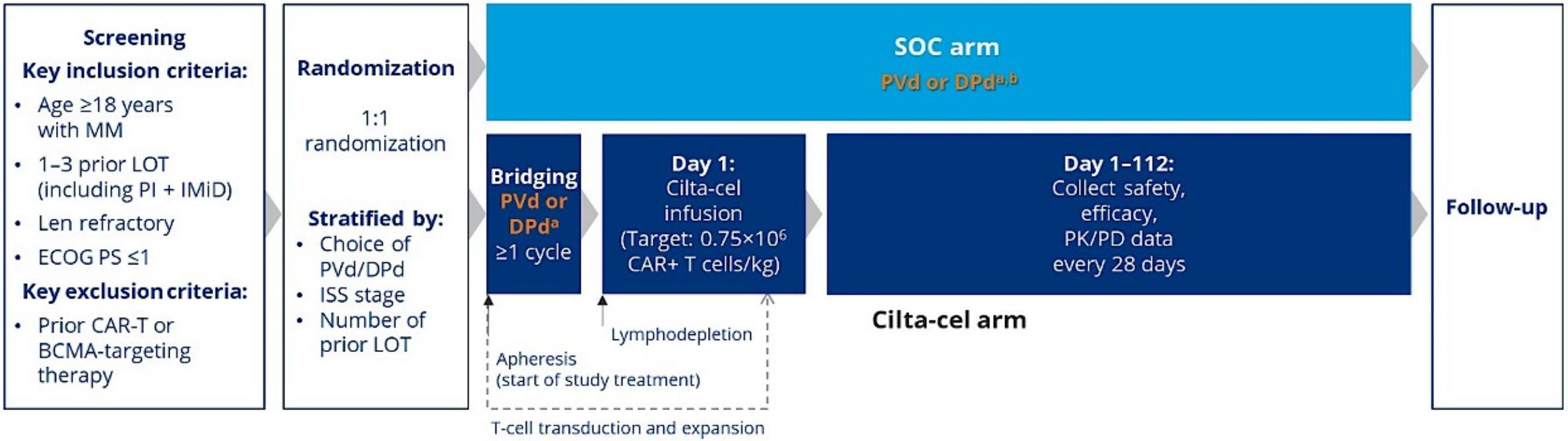
	Median Progression-free Survival (95% CI)
	mo
Ide-cel	13.3 (11.8–16.1)
Standard Regimen	4.4 (3.4–5.9)

Hazard ratio for disease progression or death, 0.49 (95% CI, 0.38–0.65)
P<0.001



Rodriguez-Otero P, et al. *N Engl J Med.* 2023; 388:1002-1014.

CARTITUDE-4: Cilta-Cel Phase 3



Primary endpoint

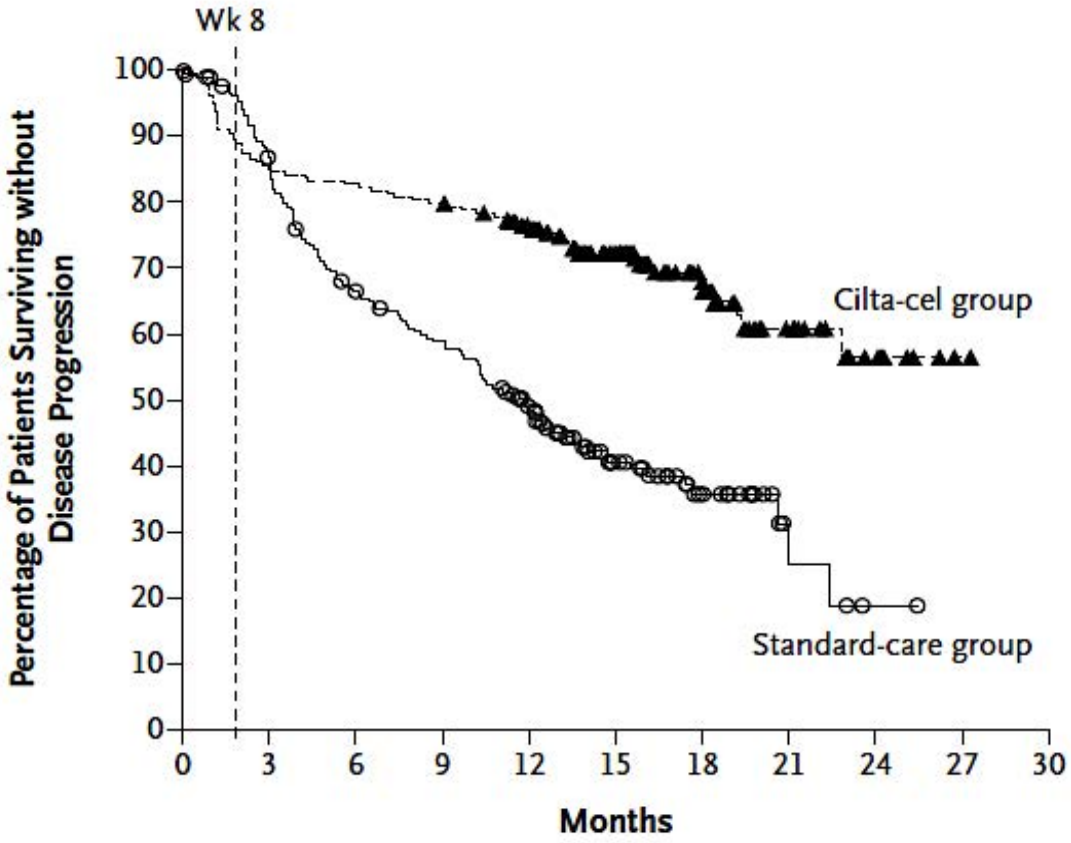
- PFS[c]

Secondary endpoints

- Efficacy: ≥CR, ORR, MRD negativity, OS
- Safety
- PROs

Dhakal B, et al. ASCO 2023. Abstract LBA106; San-Miguel J, et al. *N Engl J Med.* 2023 Jul 27;389(4):335-47.

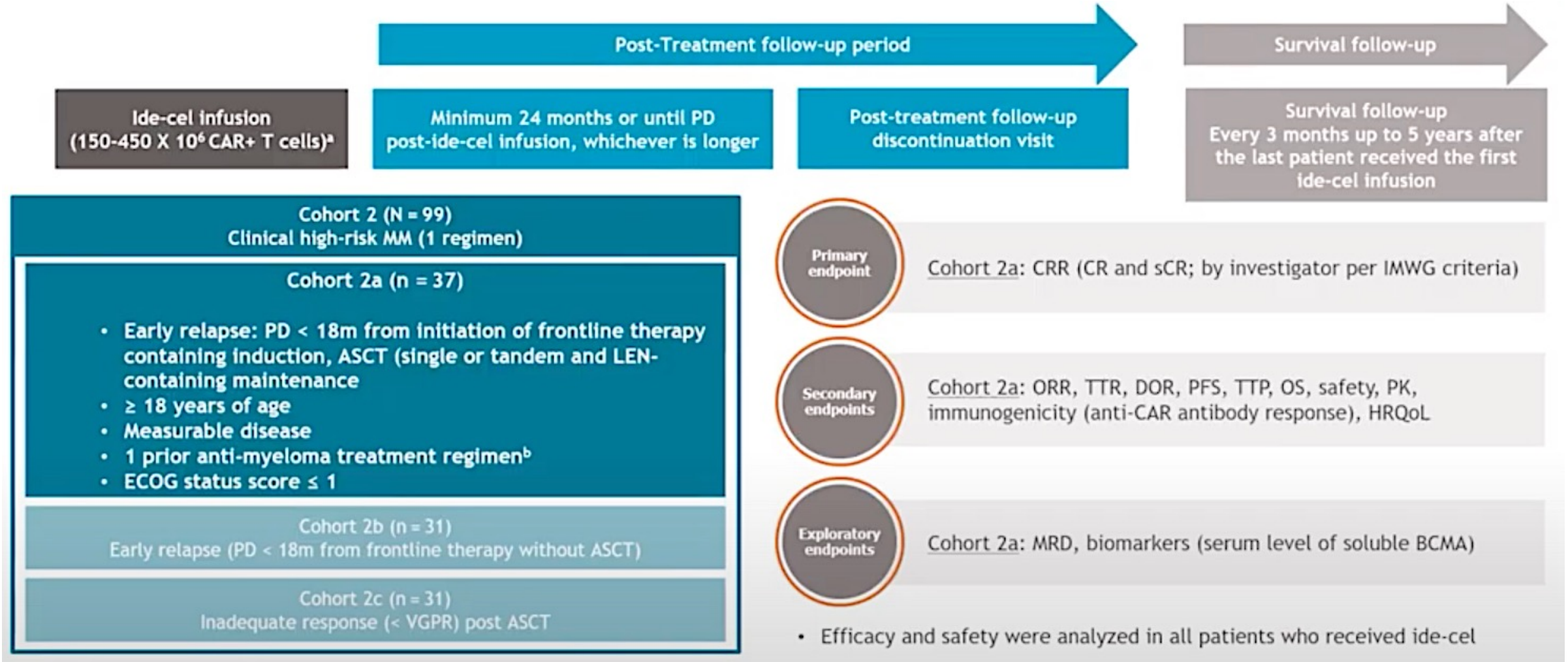
CARTITUDE-4: PFS (ITT population)



	Cilta-cel (n = 208)	SoC (n = 211)
Median PFS, mo	NR	11.8
	HR: 0.26; *P* < 0.0001)	
12-mo PFS, %	76	49

San-Miguel J, et al. *N Engl J Med.* 2023 Jul 27;389(4):335-47.

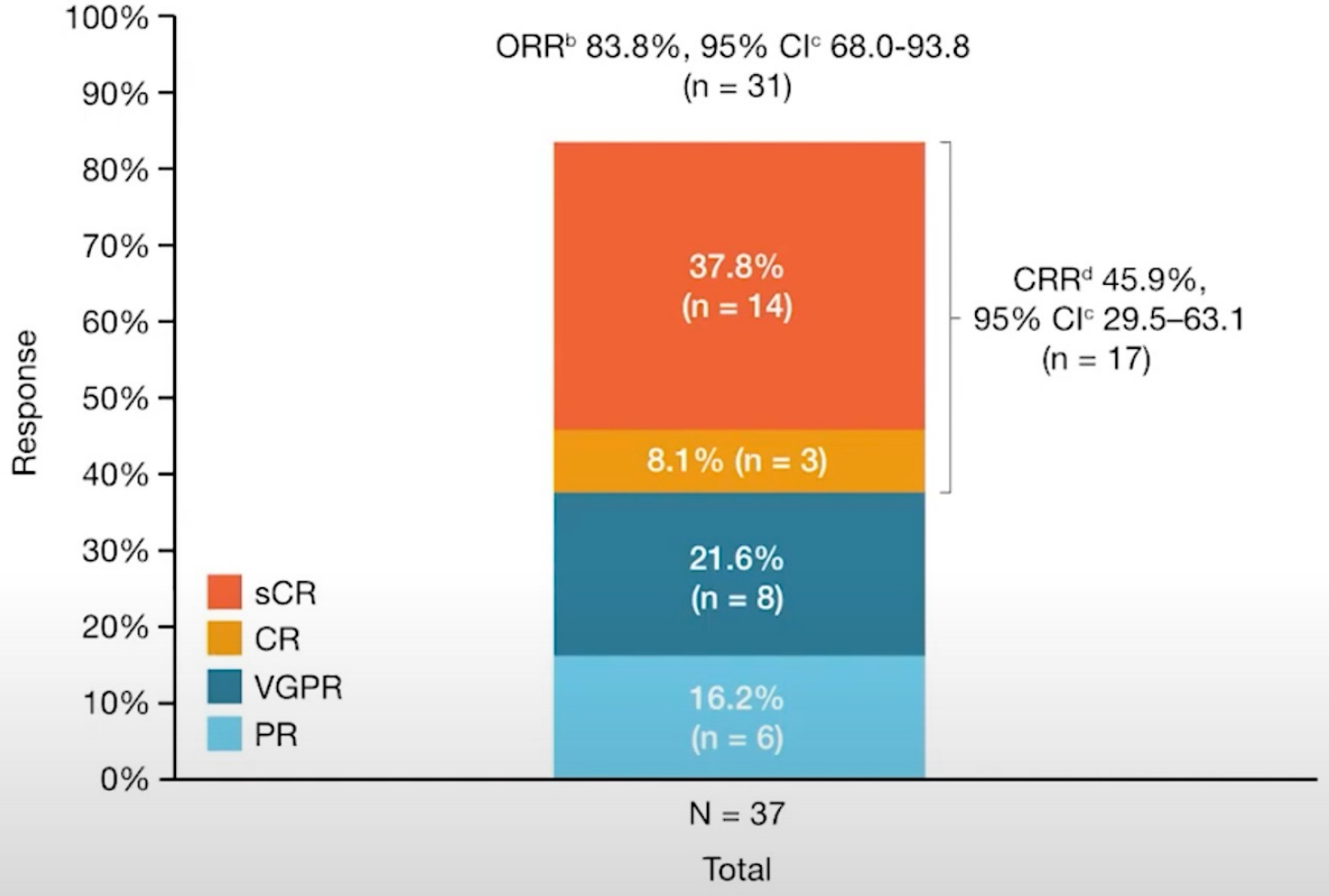
KarMMa-2: Cohort 2 Study Design



Usmani S et al. ASH 2022. Abstract 361.

KarMMa-2: Best Overall Response

- Primary endpoint was met, with 45.9% achieving ≥ CR ($P < 0.0001$)
- ORR was 83.8% (95% CI 68.0-93.8)
- Median time to first response[a] was 1.0 month (range 0.9-2.9 months)



Usmani S et al. ASH 2022. Abstract 361.

Cilta-Cel: Phase III Trials in Newly Diagnosed MM

CARTITUDE-5: Transplant not intended/not eligible.
N = 650 planned. Patient enrollment began August 2021

CARTITUDE-6: Transplant eligible.
N = 750 planned

Key Eligibility Criteria

- MM per IMWG criteria
- ECOG PS 0 or 1
- Measurable disease
- Not considered for HDCT with ASCT
- No prior BCMA therapy
- Clinical laboratory values of:
  - Hb ≥8.0 g/dL[a]
  - Platelets ≥75×10⁹/L
  - ALC ≥0.3×10⁹/L
  - ANC ≥1.0×10⁹/L[b]
  - ALT/AST ≤3×ULN
  - eGFR ≥40 mL/min/1.73 m²
  - Total bilirubin ≤2×ULN[c]

Primary Outcome

- PFS

Key Secondary Outcomes

- Sustained MRD-negative CR[d]
- MRD-negative CR at 9 months
- Overall MRD-negative CR
- OS
- CR or better
- PFS2
- Time to next antimyeloma therapy
- Safety

Screening
(up to 28 days)

Pre-randomization treatment
VRd (6 cycles of 21 days)

1:1 Randomization
(Estimated N=650)

Arm A: VRd + Rd

VRd
(2 cycles of 21 days)

Rd (maintenance)
(21-day cycles until confirmed PD or unacceptable toxicity)

Arm B: VRd + Cilta-cel

Bridging therapy post apheresis
VRd
(2 cycles of 21 days)

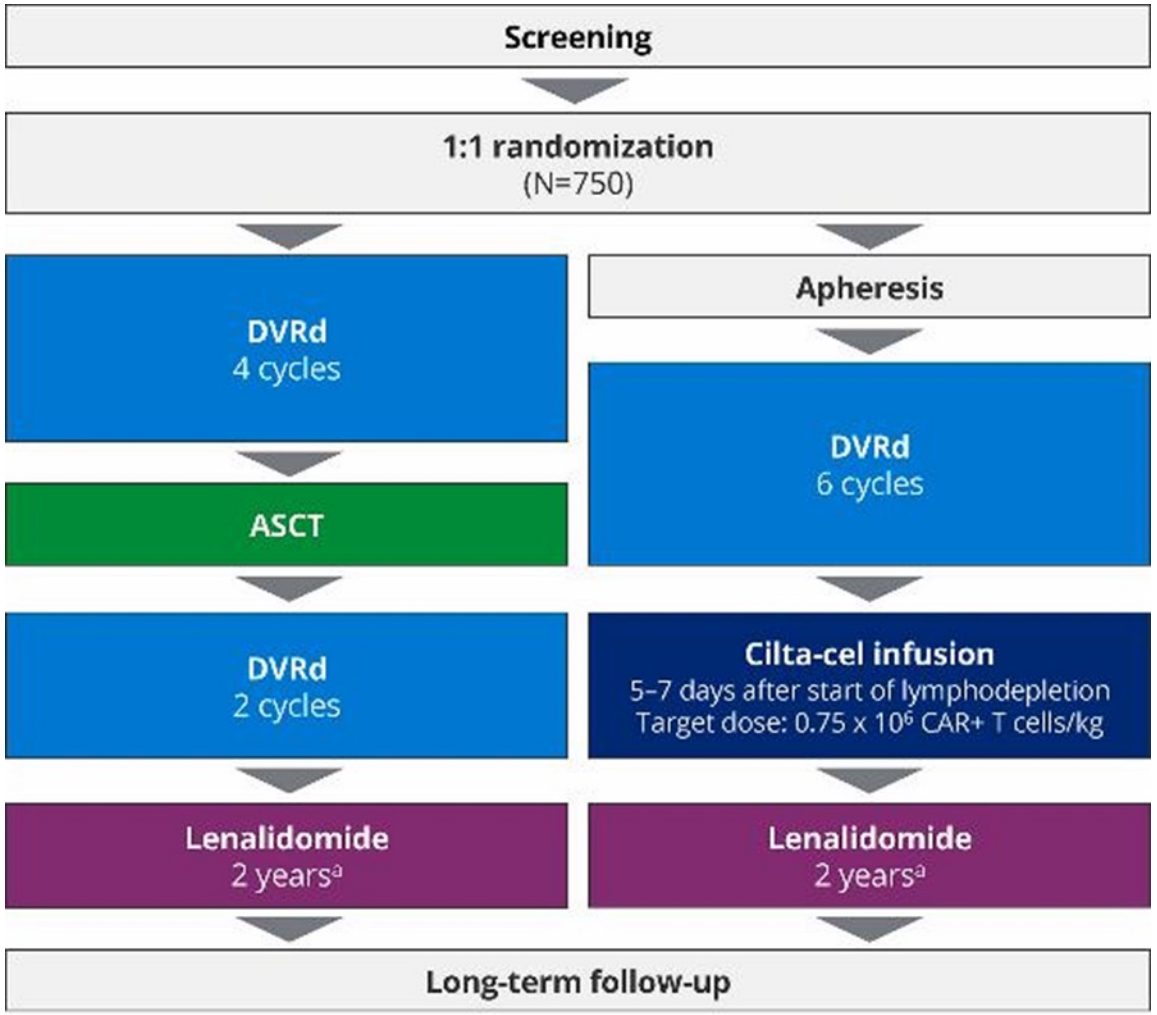
Conditioning regimen (3 days)
Cy (300 mg/m² IV) + Flu (30 mg/m² IV)

Cilta-cel infusion
Target: 0.75×10⁶ CAR+ viable T cells/kg

Follow-up

Assessments

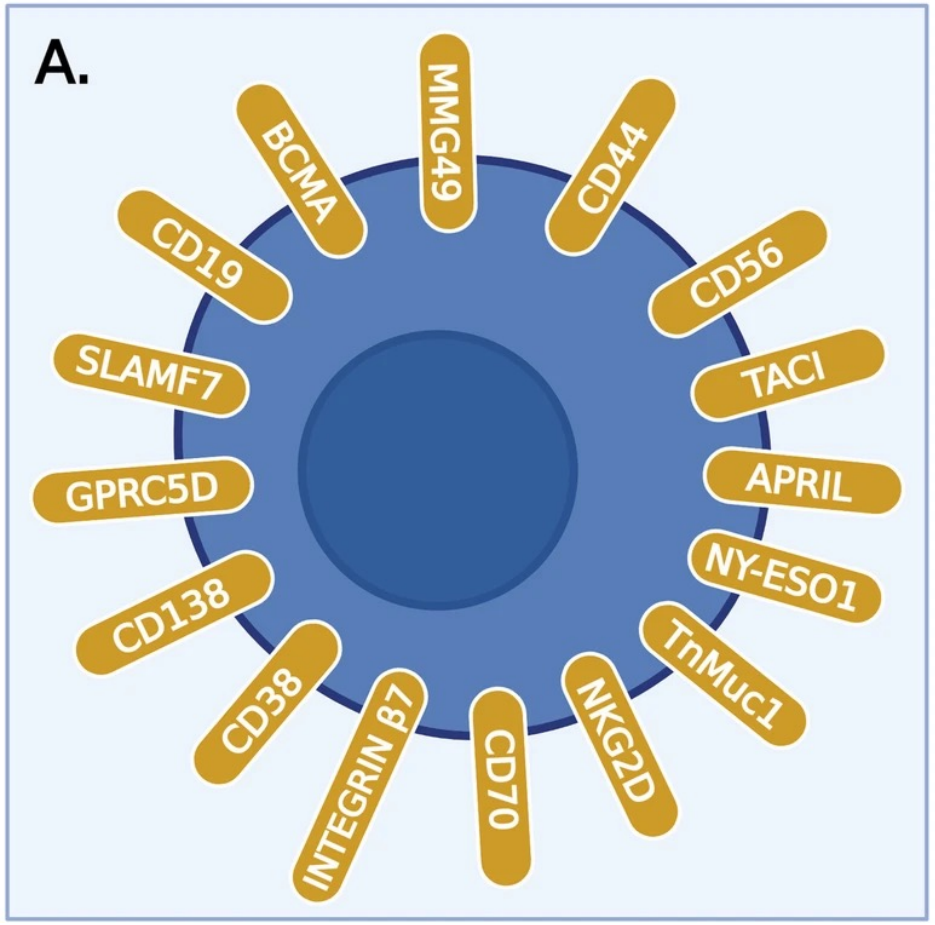
- PROs
- Vital signs
- Safety evaluations
- ECG
- PK



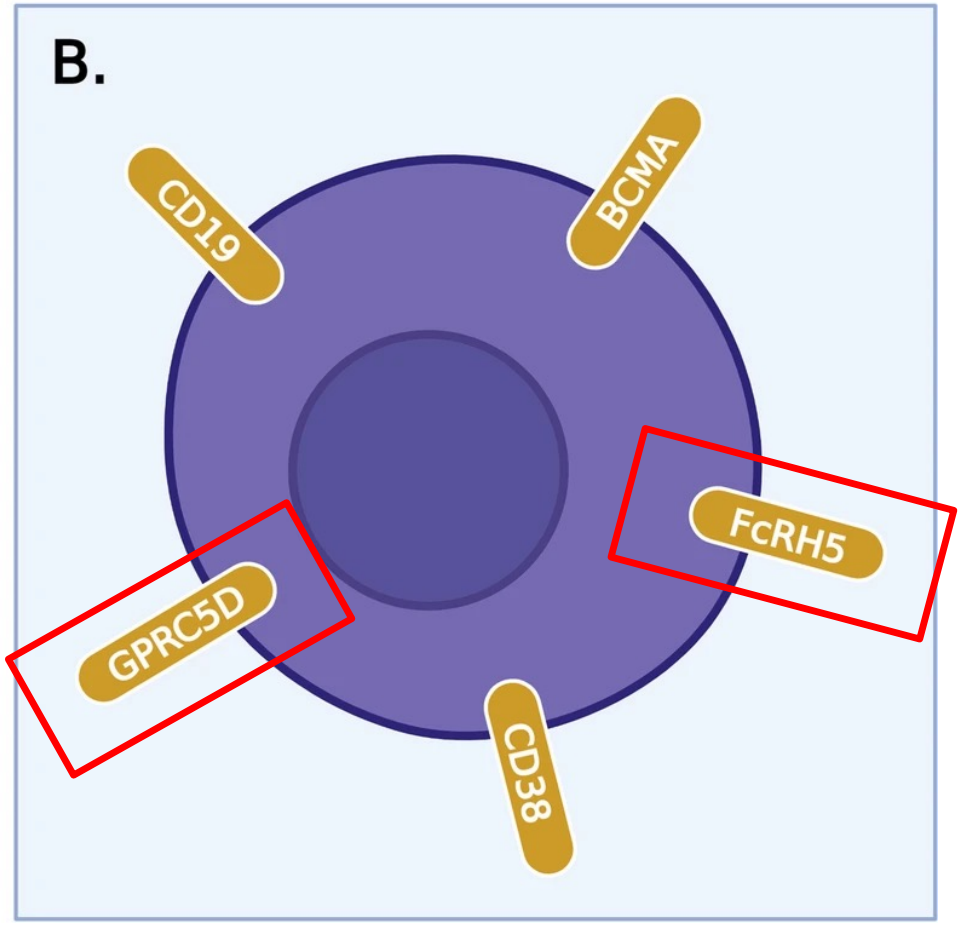
[a]Patients benefiting from therapy have the option to continue lenalidomide therapy until progressive disease per investigator's discretion after benefit-risk assessment and review by the medical monitor.

Bispecifics

CAR/TCR T cell trials

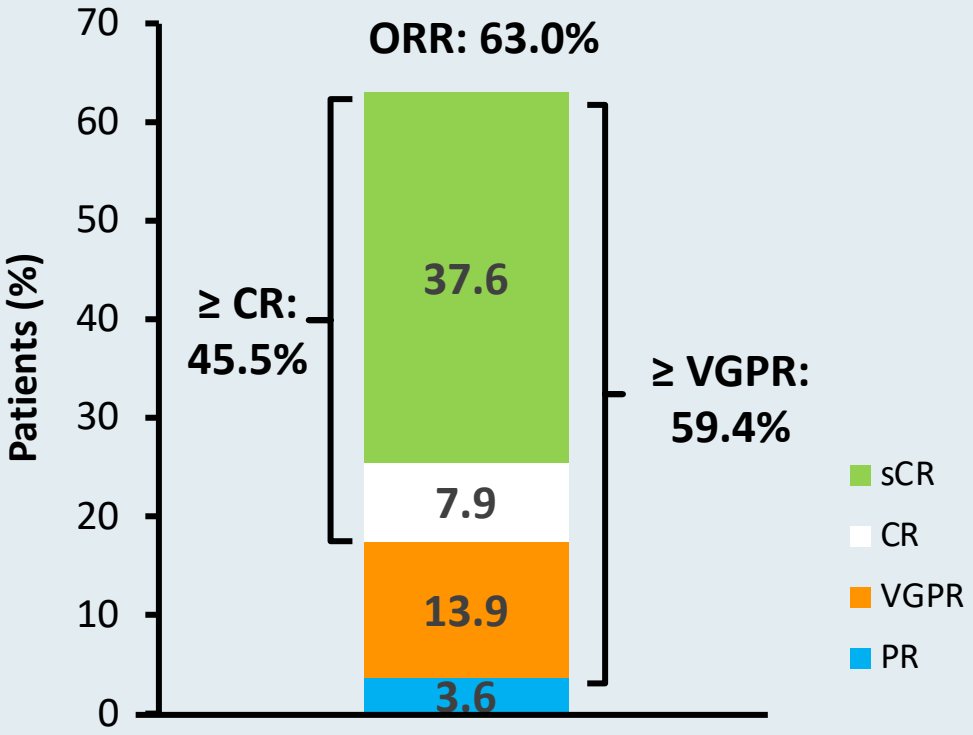


BsAb trials

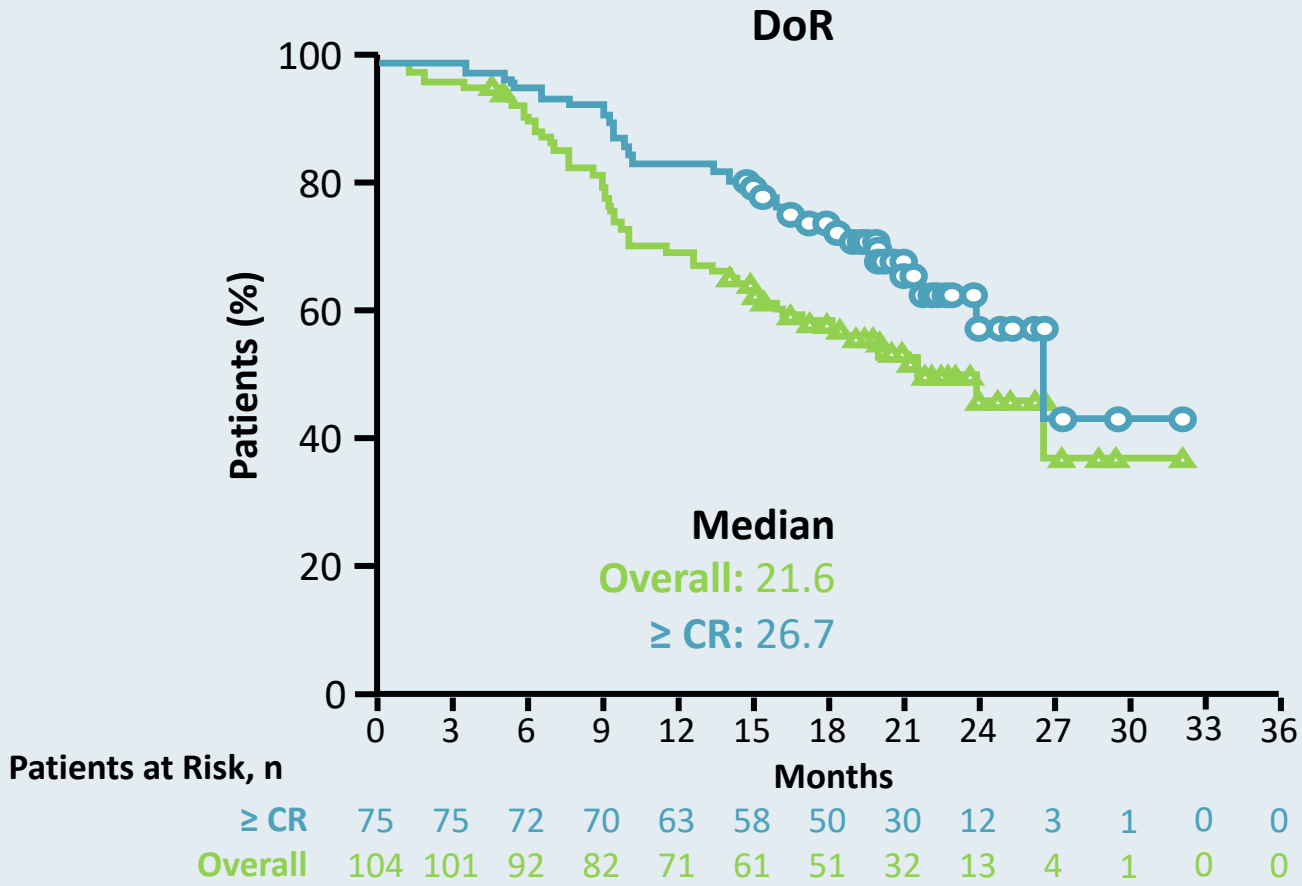


Kegyes et al, J Hematol Oncol 2022

MajesTEC-1 Update: Response and Duration of Response (DoR)



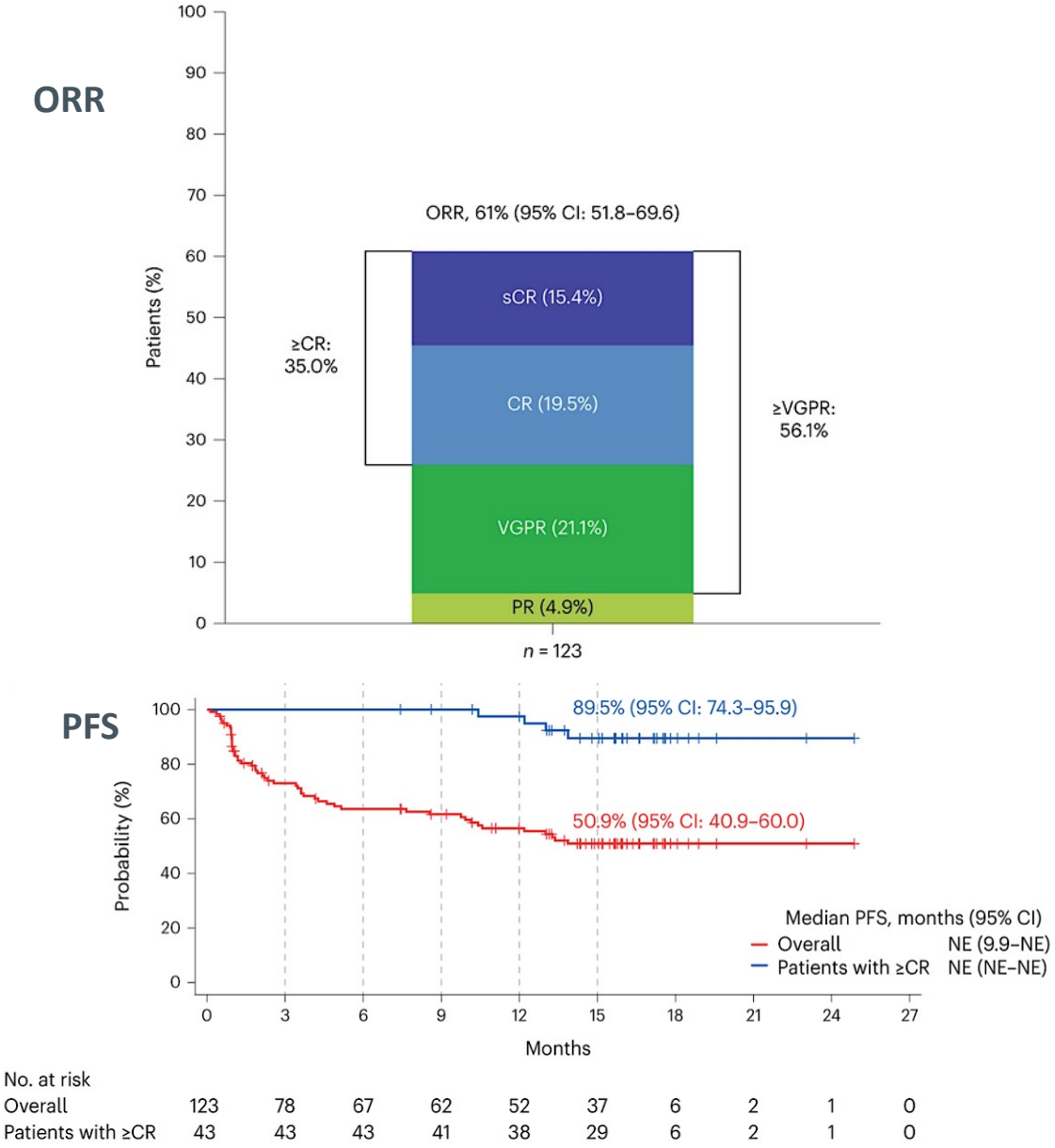
Patient Subgroup	ORR, % (n/N)
≤3 prior lines of treatment	74.4 (32/43)
>3 prior lines of treatment	59.0 (72/122)
High-risk cytogenetics and/or EMD	53.3 (32/60)



van de Donk N et al. ASCO 2023;Abstract 8011.

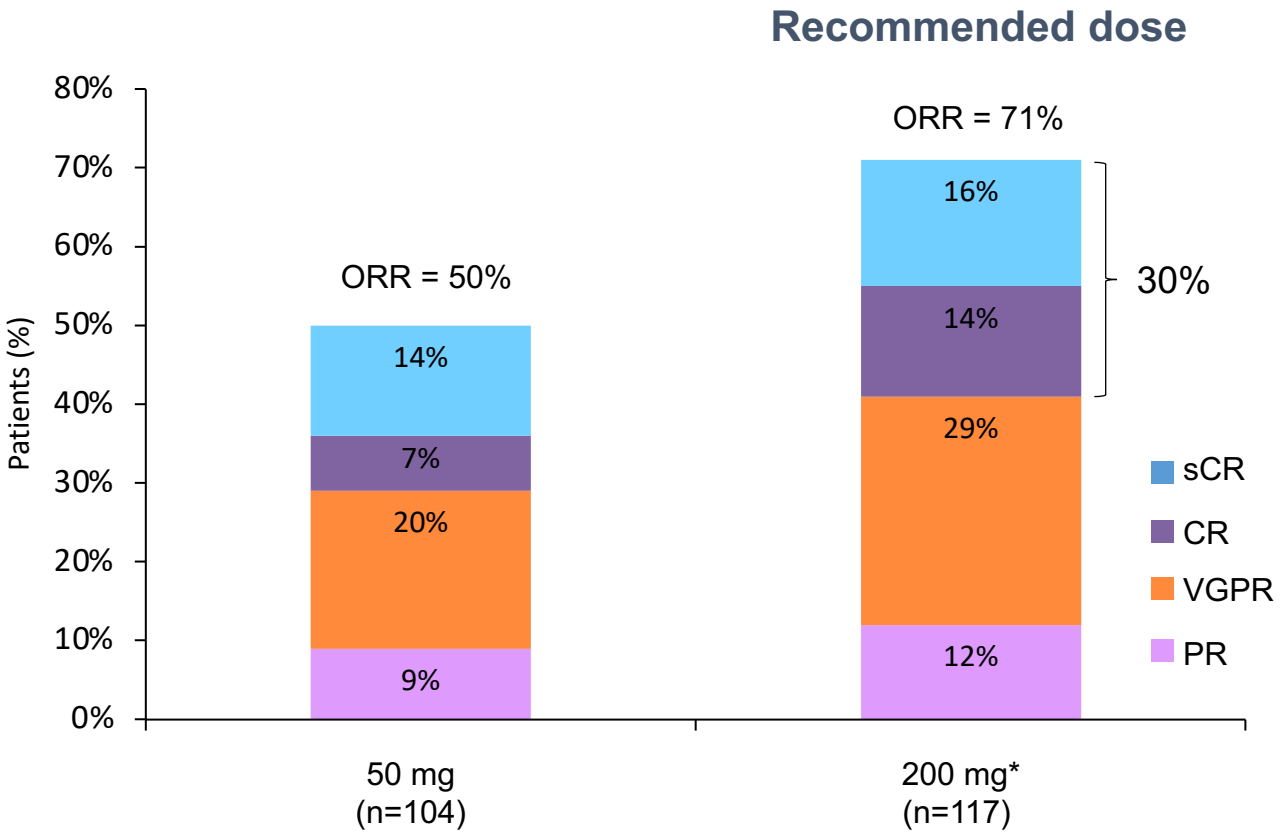
MagnetisMM-3: Elranatamab Phase I

- **Cohort A: no prior BCMA (n = 123)**
  - 2 step-up priming doses (12 mg, 32 mg) → weekly (76 mg)
  - After 6 cycles, responders → q2 weeks
- **Median prior lines 5 (2–22)**
  - 96.7% TCR, 42.3% PCR
- **25% hrFISH, 31.7% EMD**
- **ORR 61, 35% CR or better**
- **At a median follow-up of 14.7 months**
  - mDOR: NR (15-month rate 71.5%)
  - PFS: NR (15-month rate 50.9%)
  - OS: NR (15-month rate 56.7%)
- CRS 57.7% (no G3/4), ICANS 3.4% (no G3/4)
- Motor (17.1%) and sensory (13.8%) neuropathy
- All-grade infections 69.9% (39.8% G3/4); 43% received IVIG



Lesokhin AM, et al. *Nat Med*. 2023;10.1038/s41591-023-02528-9.

LINKER-MM1: Linvoseltamab Phase 2



- Median duration of follow-up:
  - 50 mg – 7.7 months (range 0.3–31.3)
  - 200 mg* – 5.6 months (range 0.2–28.2)
- At the recommended dose (200 mg):
  - ORR 71%
  - VGPR or better in 59%
  - 77 (66%) patients on the 200 mg dose remain on study
- Based on earlier results, responses may deepen over time
- Among patients with CR or sCR with available MRD data (N = 46), 54.3%‡ were MRD negative at 10^{-5}

Data cut-off: 28 Feb 2023. *Includes patients from dose escalation and dose expansion parts of the study. ‡MRD data include clonoSEQ and Euroflow. 8 patients had missing data due to missing specimens or specimen quality
ORR, objective response rate; PR, partial response; sCR, stringent CR; VGPR, very good partial response.

Lee HC et al. ASCO 2023;Abstract 8006.

BCMAxCD3

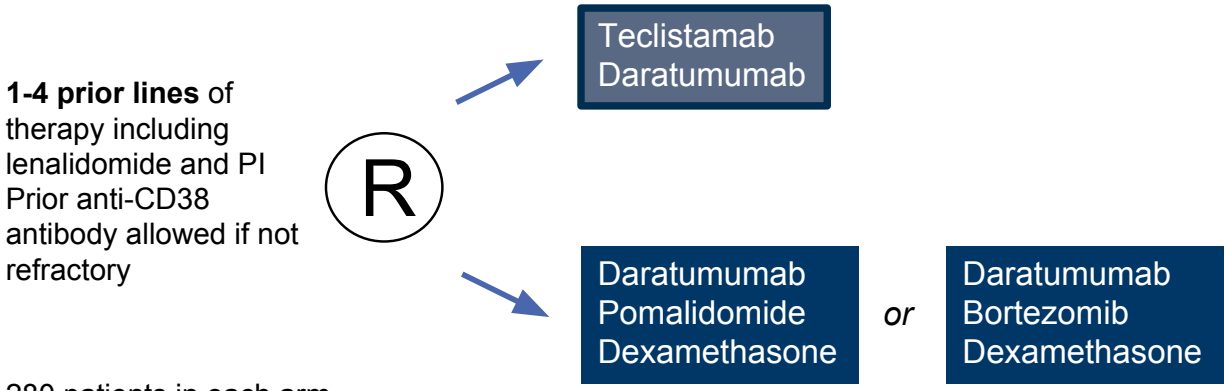
Bispecific Antibody	Teclistamab (JNJ-64007957)	Elranatamab (PF-06863135)	Linvoseltamab (REGN5458)	ABBV-383	Alnuctamab BMS-93269	HPN217
Structure/Function	Humanized antibody	Humanized antibody	Veloci-Bi® platform fully human antibody	Low CD3 affinity fully human antibody	Humanize antibody 2 BCMA + 1 CD3	Trispecific 50kDa (albumin)
Treatment	Weekly SC	Weekly SC	Weekly IV	IV q3w	Qwk -> Q4wk SQ	Q2wk IV
Patients	n= 165	n= 123	n= 252	n= 174	n= 68	n= 62
Median prior lines	5	5	5	5	4	6
Triple-class refractory	78%	97%	81%	80%	63%	76%
ORR at RP2d RP2D (n)	63% 1.5 mg/kg SC (n=165)	61% 76 mg SQ (n=123)	64% 200 mg IV (n=58)	58-61% 40 to 60 mg IV (n=52; n=59)	65% 30 mg SQ (n=26)	73% ?12 or 24 mg (n=13)
PFS	11.3 mos (8.8-17.1)	NE @ 12 mos	NR	13.7 or 11.2 mos	NR	NR
DOR	18.4 mos (14.9-NE)	NE @12 mos	89% @ 6 mos	NE	NE	NR
Median f/u	14.1 mos	10.4 mos	3.2 mos	6.8	4.6 mos	
AEs, (All/(Gr 3+);						
CRS	72% (0.6%)	58% (0%)	44% (1%)	60% (1%)	53% (0%)	27 (0%)
Infections	76% (45%)	67% (35%)	54% (29%)	(22%)	34% (9%)	45% (16%)
Neutropenia	71% (64%)	48% (48%)	25% (23%)	34% (26%)	37%(32%)	16% (13%)
Anemia	52% (37%)	48% (37%)	36% (31%)	37% (16%)	38%(25%)	44% (34%)
Thrombocytopenia	40% (21%)	26% (24%)	18% (6%)	29% (11%)	24%(9%)	NR
Neuro	Neurotoxicity 15% (0.1)	NR/ PN?	ICANS 2% (1%)	5% (0.1%)	ICANS 3 (0%)	16% (0%)
# Deaths	68/(41 due to PD)	21 (/11 due to PD)	NR	46	1	NR
Hypogamma/IVIg	75%//39%	75%/40%	NR	NR		

Moreau P et al. *N Engl J Med*. 2022;387(6):495-505. Bahlis NJ et al. 2022 ASH. Abstract 97. Bumma N et al. 2022 ASH. Abstract 1936. Voorhees PM et al. 2022 ASH. Abstract 1919. Wong SW et al. 2022 ASH. Abstract 162. Abdallah AO et al. 2022 ASH. Abstract 3240. D'Souza A et al. *J Clin Oncol*. 2022;40(31):3576-3586.

Moving BCMA Bispecifics Into Early Relapse

MajesTEC-3. Teclistamab

Adapted from Mateos M-V et al., ASCO 2022

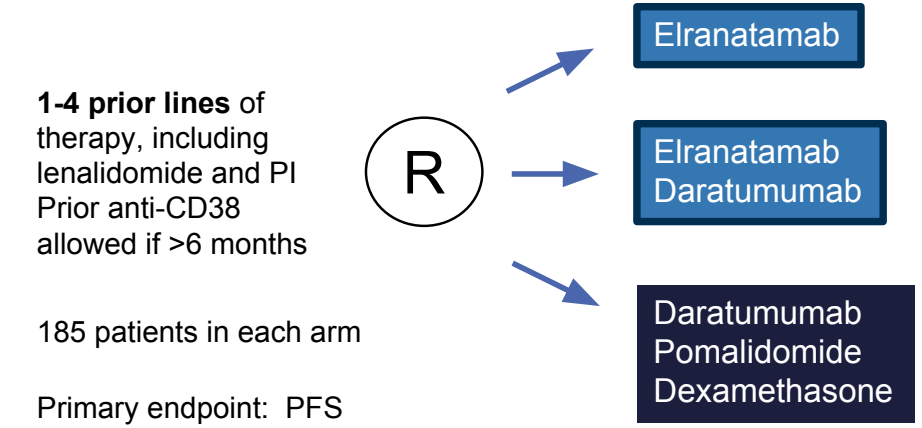


280 patients in each arm

Primary endpoint: PFS

MagnetisMM-5. Elranatamab

Adapted from Grosicki S et al., ASCO 2022

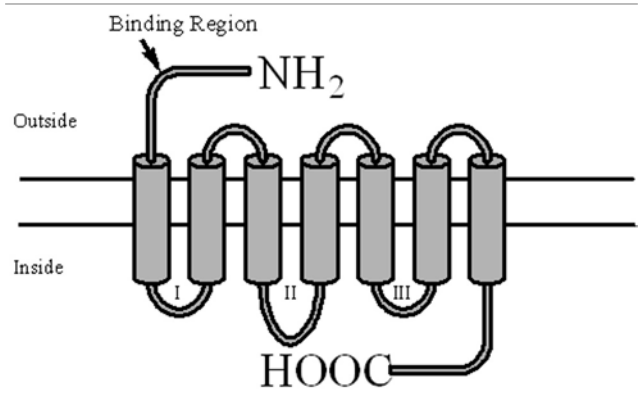


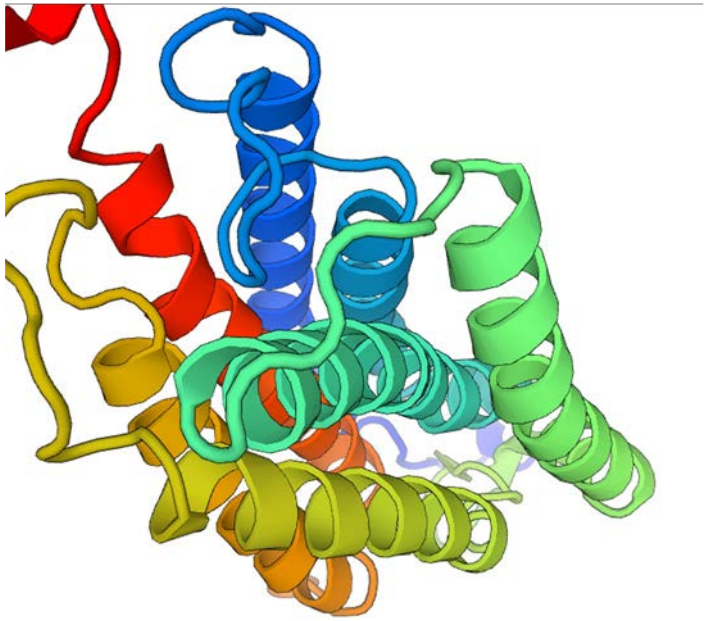
185 patients in each arm

Primary endpoint: PFS

GPRC5D

- G-protein coupled receptor family C group 5 (GPRC5D) is an orphan receptor with no known ligands or functions in human (and human cancer)
- GPRC5D has seven transmembrane segments and is expressed in cell membranes
- The GPRC5D gene that is mapped on chromosome12p13.3 contains three exons and spans about 9.6 kb. The large first exon encodes the seven-transmembrane domain
- Biological function in MM not known, but GPRC5D described to be associated with poor prognosis and high tumour load (plasma cell number) in MM patients[1, 2, 3]
- Talquetamab received accelerated approval for 5L+ RRMM in August 2023
- At least 3 CAR T therapies targeting GPRC5D are in development

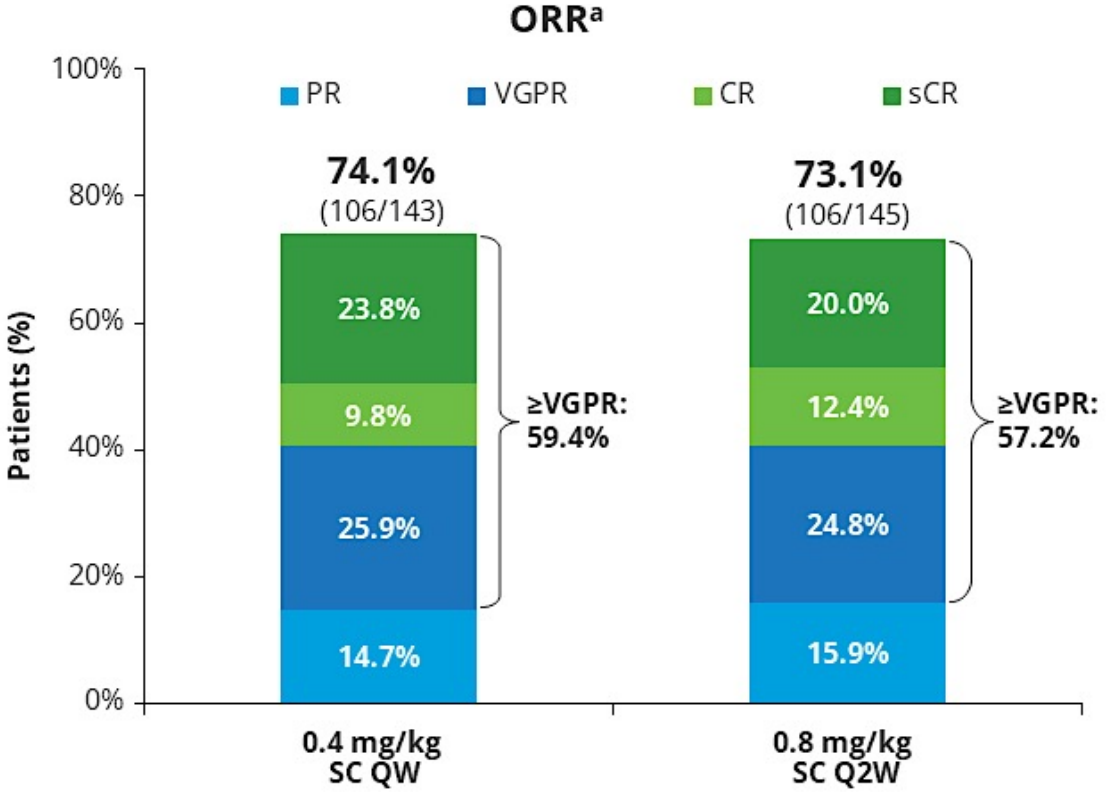


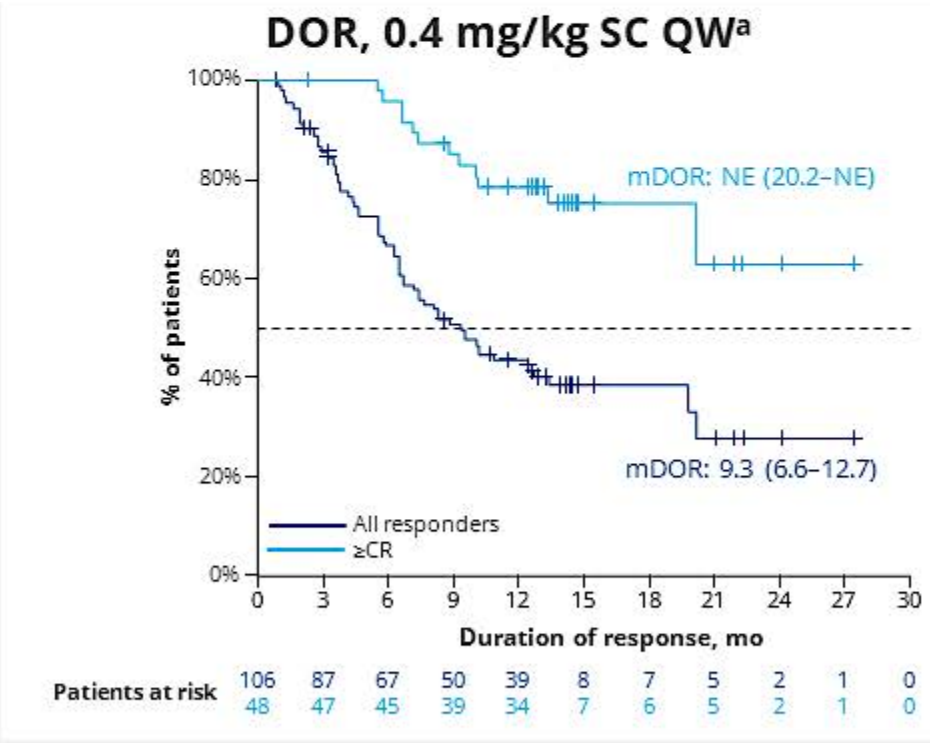


[1]Venkateshaiah, Blood 2013; [2]Atamaniuk, ESCI 2012; [3]Cohen, Hematology 2013;

MonumenTAL-1: phase 2 expansion of talquetamab in RRMM

- Dose: 0.4 mg/kg SQ qwk (n=143) or 0.8 mg/kg SQ q2wks (n=145)
- Med 5 priors, 72% TCR, 25% PDR, 25% EMD. 13% prior belantamab
- Med f/up 14.9 and 8.6 mos





mPFS: 7.5 months (95% CI: 5.7–9.4; 33% censored)

Schinke et al, ASCO 2023, # 8036; Chari et al, ASH 2022, #157

MonumenTAL-1: phase 2 expansion of talquetamab in RRMM

AEs (≥20% of any RP2D cohort), n (%)	0.4 mg/kg SC QW[a] (n=143) mFU, 11.0 months[b]		0.8 mg/kg SC Q2W[a] (n=145) mFU, 5.1 months[c]	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Anemia	64 (44.8)	45 (31.5)	57 (39.3)	36 (24.8)
Neutropenia	49 (34.3)	44 (30.8)	41 (28.3)	32 (22.1)
Lymphopenia	40 (28.0)	37 (25.9)	38 (26.2)	37 (25.5)
Thrombocytopenia	39 (27.3)	29 (20.3)	39 (26.9)	24 (16.6)
CRS	113 (79.0)	3 (2.1)	105 (72.4)	1 (0.7)
Skin-related AEs[d]	80 (55.9)	0	98 (67.6)	1 (0.7)
Nail-related AEs[e]	74 (51.7)	0	63 (43.4)	0
Dysgeusia[f]	69 (48.3)	NA	67 (46.2)	NA
Rash-related AEs[g]	56 (39.2)	2 (1.4)	39 (26.9)	8 (5.5)
Weight decreased	57 (39.9)	3 (2.1)	47 (32.4)	2 (1.4)
Pyrexia	53 (37.1)	4 (2.8)	35 (24.1)	1 (0.7)
Asthenia	37 (25.9)	3 (2.1)	13 (9.0)	2 (1.4)
Dry mouth	36 (25.2)	0	53 (36.6)	0
Diarrhea	34 (23.8)	3 (2.1)	32 (22.1)	0
Dysphagia	34 (23.8)	0	33 (22.8)	3 (2.1)
Fatigue	32 (22.4)	5 (3.5)	29 (20.0)	1 (0.7)
Decreased appetite	25 (17.5)	2 (1.4)	29 (20.0)	2 (1.4)

ICANS in 10-11% (1-2% grade 3)

Infections

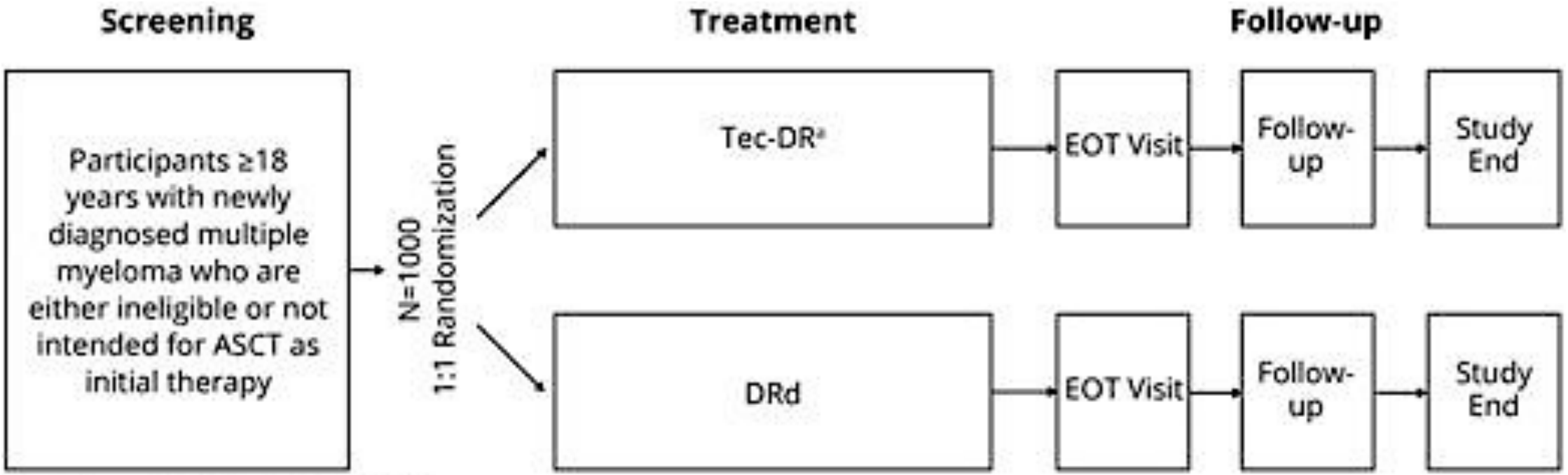
- At 0.4 mg/kg QW and 0.8 mg/kg Q2W:
  - Infections occurred in 57.3% and 50.3%
    - Grade 3/4 in 16.8% and 11.7%
  - 5 (3.5%)[d] and 4 (2.8%)[e] patients had opportunistic infections
  - 13 (9.1%) and 16 (11.0%) patients had COVID-19
    - 2 patients died from COVID-19
- 13.3% and 9.7% of patients received IVIg, respectively

- **Low rates of discontinuation due to AEs** with QW (4.9%) and Q2W (6.2%) schedules
- At time of data cut-off, no patients in these cohorts died due to drug-related AEs

Schinke et al, ASCO 2023, # 8036; Chari et al, ASH 2022, #157

Frontline Trials With Bispecifics

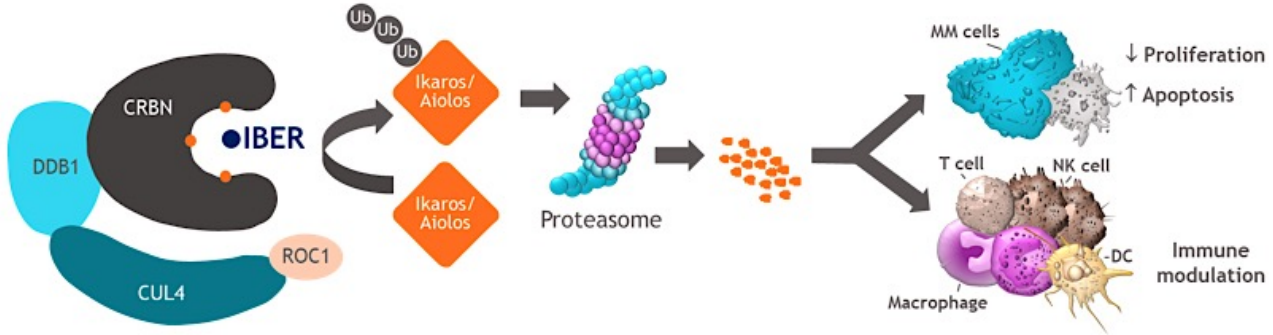
MajesTEC-7 Study Design



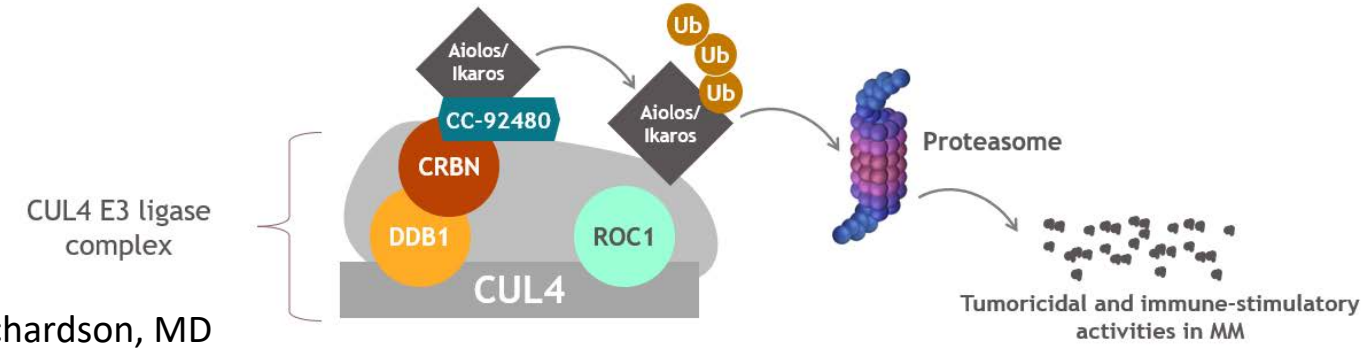
[a]Dexamethasone will also be administered for Cycles 2 to 4.
ASCT, autologous stem cell transplantation; DRd, daratumumab SC, lenalidomide, and dexamethasone; EOT, end of treatment; SC, subcutaneous; Tec-DR, teclistamab, daratumumab SC and lenalidomide.

CELMoDs

- IBER is an oral, potent, novel CELMoD™ compound that co-opts CRBN to enable enhanced degradation of target proteins, including Ikaros and Aiolos
  - IBER induces potent direct antimyeloma and immune-stimulatory activity in preclinical models
  - IBER is active in LEN- and POM-resistant myeloma cell lines and enhances cell-mediated killing through immune stimulation



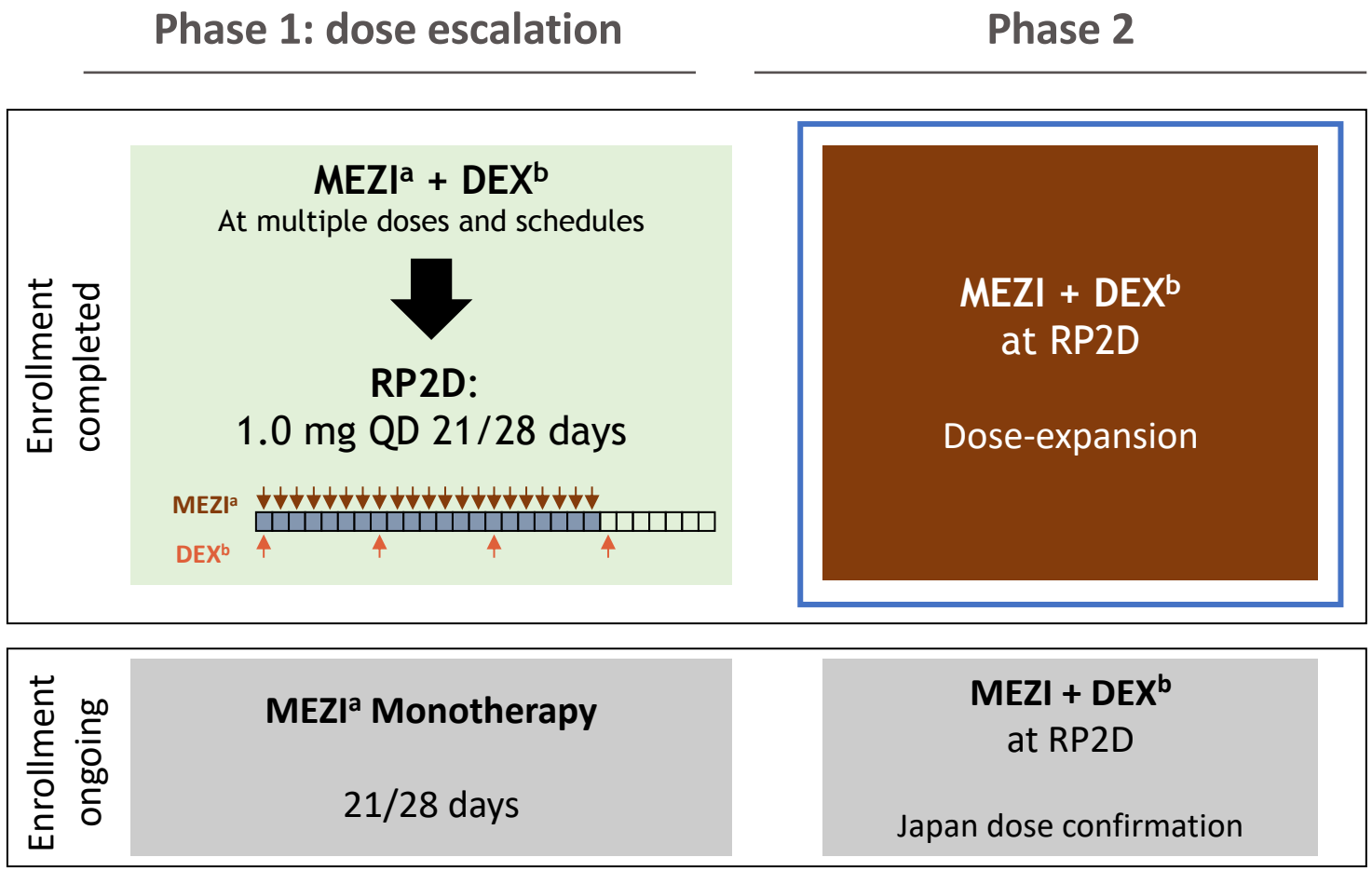
- Mezigdomide (CC-92480): a potent, novel CELMoD™ agent designed for rapid and maximal degradation of target proteins, including Ikaros and Aiolos
  - Enhanced direct antimyeloma and immune-stimulatory activities in preclinical models
  - Potent antiproliferative and tumoricidal activity in MM cell lines, including those LEN- and POM-resistant
  - Marked synergistic effects with SoC therapies, such as DEX, PIs, and mAbs
- Mezigdomide (CC-92480) is being evaluated in active clinical trials in MM



Content courtesy of Paul G. Richardson, MD

CC-92480-MM-001 study design and objective

- **Phase 1/2 trial evaluating MEZI alone or in combination with DEX in pts with RRMM[1]**
- **In phase 1, the RP2D of MEZI in combination with DEX was selected at 1 mg QD for 21/28 days[2]**
- **In phase 1, the ORR at the RP2D was 54.5%[2]**
- **Objective: to report efficacy and safety of the MEZI + DEX dose-expansion cohort**



Richardson PG, et al. ASCO 2020; Abstract 8500; Richardson PG et al. *N Engl J Med* 2023 Sep 14;389(11):1009-22.

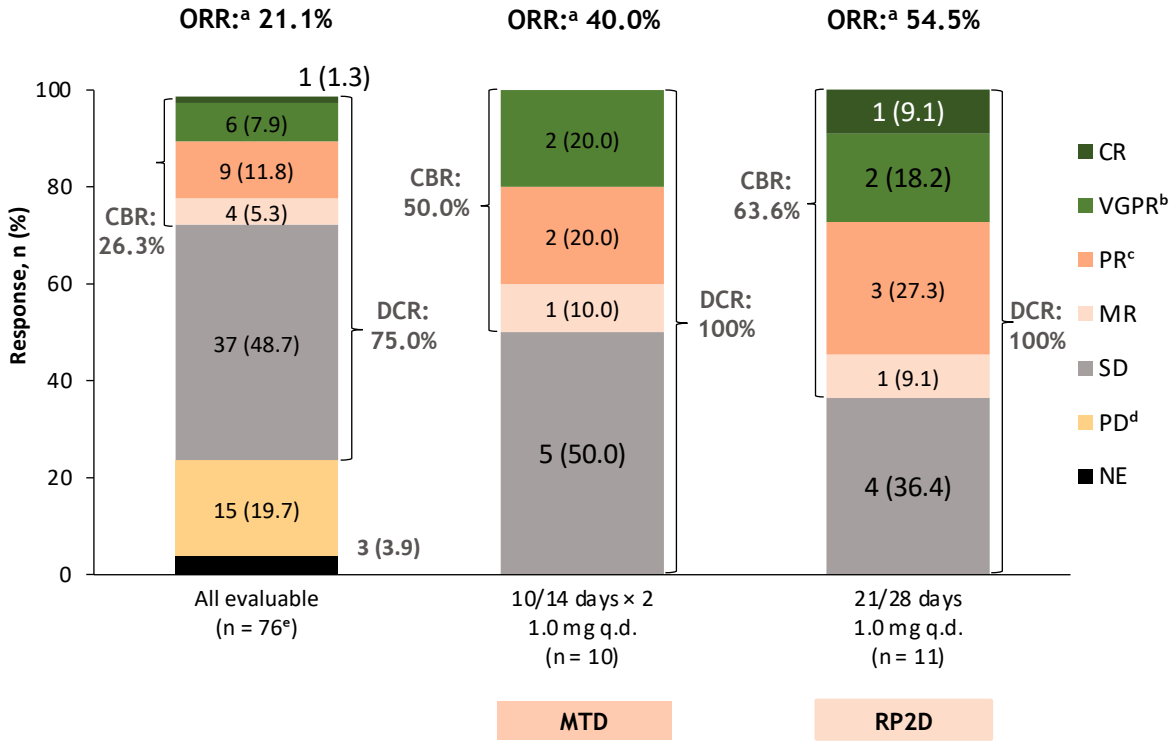
A first-in-human phase 1 trial assessed dose, safety, PK and preliminary efficacy of mezigdomide + dexamethasone in heavily pre-treated RRMM

Baseline characteristics: Median age 66 years; time since diagnosis 7.2 years; ISS stage ≥ II (67.1%); EMP (36.8%)

Prior therapies: Median prior therapies 6; lenalidomide-refractory (73.7%); pomalidomide-refractory (78.9%), PI-refractory (73.7%), anti-CD38 mAb-refractory (69.7%)
50% of patients were triple class refractory

Primary endpoint: Assess PK and safety, and define the MTD/RP2D

Common (> 20% all grade) TEAEs and events of interest, n (%)	All doses (N = 76)	
	Grade 3	Grade 4
Neutropenia	23 (30.3)	26 (34.2)
Febrile neutropenia	4 (5.3)	1 (1.3)
Anemia	24 (31.6)	-
Thrombocytopenia	5 (6.6)	7 (9.2)
Fatigue	7 (9.2)	-
Pyrexia	3 (3.9)	-
Peripheral sensory neuropathy	-	-
Diarrhea	1 (1.3)	-
Nausea	1 (1.3)	-
Deep vein thrombosis	-	-
Infections	25 (32.9)	2 (2.6)
Pneumonia[f]	11 (14.5)	-



Richardson PG, et al. ASCO 2020; Abstract 8500; Richardson PG et al. *N Engl J Med* 2023 Sep 14;389(11):1009-22.

First Results From the Randomized Portion of a Phase 2 Study of Venetoclax Plus Carfilzomib-Dexamethasone vs Carfilzomib-Dexamethasone in Patients With t(11;14)-Positive Relapsed/Refractory Multiple Myeloma

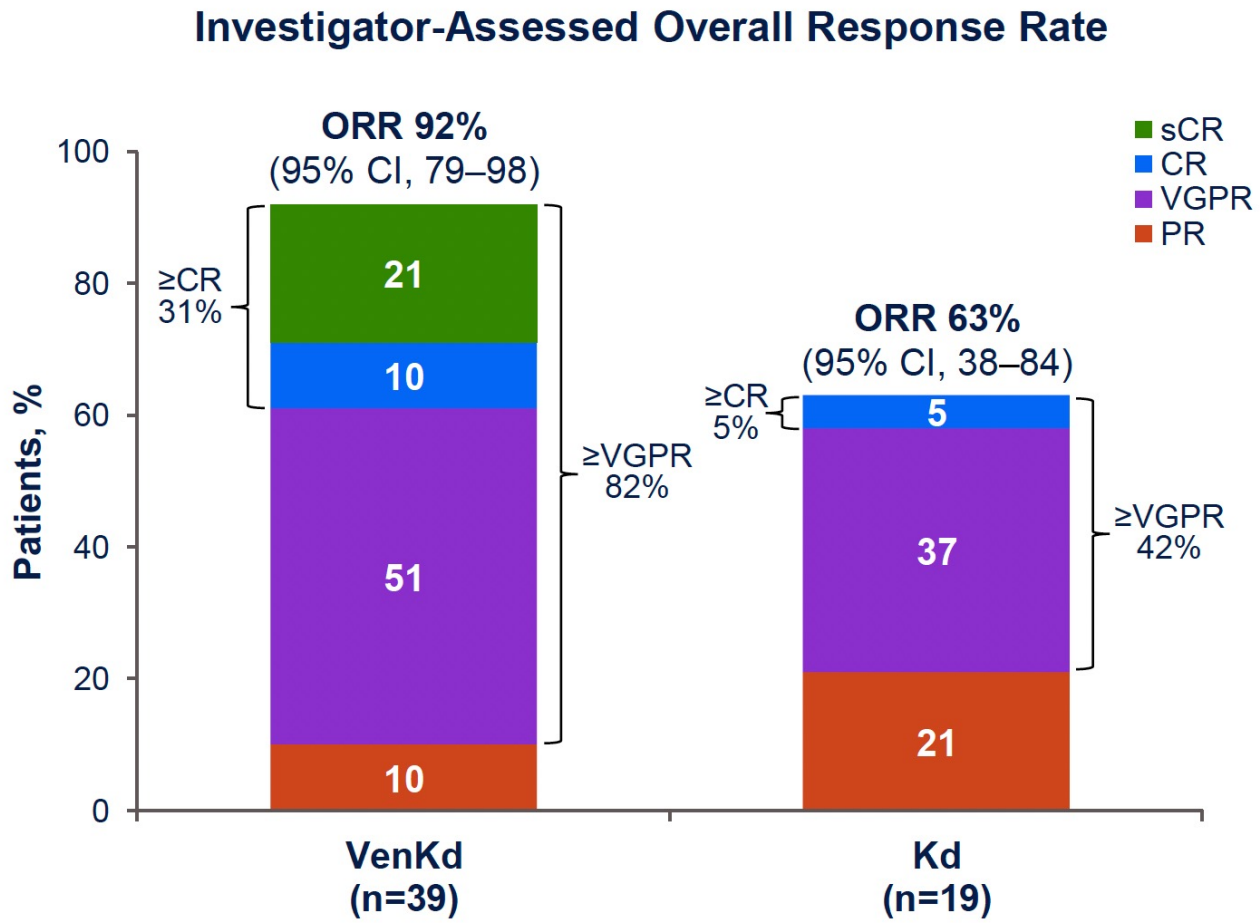
Jonathan L. Kaufman, MD[1]; Cristina Gasparetto, MD[2]; Tibor Kovacsovics, MD[3]; Gabor Mikala, MD, PhD[4]; Tamás Masszi, MD, PhD[5]; Laura Rosiñol, MD, PhD[6]; Wojciech Janowski, MBBS[7]; Albert Oriol, MD, PhD[8]; Maika Onishi, MD, MAS[9]; Zhuangzhuang Liu, PhD[10]; Mohamed Badawi, PhD[10]; Jeremy A. Ross, PhD[10]; Rajvineeth K. Pothacamury, MD[10]; Orlando F. Bueno, MD, PhD[10]; Edyta Dobkowska, MD[11]; Edward A. Stadtmauer, MD[12]*; and Luciano J. Costa, MD, PhD[13]*

*Authors contributed equally

[1]Department of Hematology and Medical Oncology, Winship Cancer Institute of Emory University, Atlanta, GA, USA; [2]Division of Hematologic Malignancies and Cellular Therapy, Department of Medicine, Duke University School of Medicine, Durham, NC, USA; [3]Division of Hematology and Hematologic Malignancies, Huntsman Cancer Institute, University of Utah School of Medicine, Salt Lake City, UT, USA; [4]Department of Hematology and Stem Cell Transplantation, South Pest Central Hospital, National Institute for Hematology and Infectious Diseases, Budapest, Hungary; [5]Department of Haematology and Stem Cell Transplantation, St. István and St. László Hospital, Department of Internal Medicine and Hematology, Semmelweis University, Budapest, Hungary; [6]Amyloidosis and Myeloma Unit, Department of Hematology, Hospital Clínic de Barcelona, IDIBAPS, Barcelona, Spain; [7]Department of Haematology, Calvary Mater Newcastle, Waratah, New South Wales, Australia; [8]Catalan Institute of Oncology and Josep Carreras Institute, Hospital Germans Trias i Pujol, Badalona, Barcelona, Spain; [9]Genentech, Inc, South San Francisco, CA, USA; [10]AbbVie, Inc, North Chicago, IL, USA; [11]Pharmacyclics Switzerland GmbH, An AbbVie Company, Schaffhausen, Switzerland; [12]Division of Hematology and Oncology, University of Pennsylvania Abramson Cancer Center, Philadelphia, PA, USA; [13]Division of Hematology/Oncology, University of Alabama at Birmingham, Birmingham, AL, USA

International Myeloma Society Annual Meeting, September 27-30, 2023, Athens, Greece

Addition of venetoclax to Kd produced an overall response rate of 92% in patients with t(11;14)-positive RRMM



CR, complete response; Kd, carfilzomib + dexamethasone; ORR, overall response rate; PR, partial response; RRMM, relapsed/refractory multiple myeloma; sCR, stringent CR; Ven400Kd, venetoclax 400 mg + carfilzomib + dexamethasone; Ven800Kd, venetoclax 800 mg + carfilzomib + dexamethasone; VenKd, venetoclax + carfilzomib + dexamethasone; VGPR, very good PR.

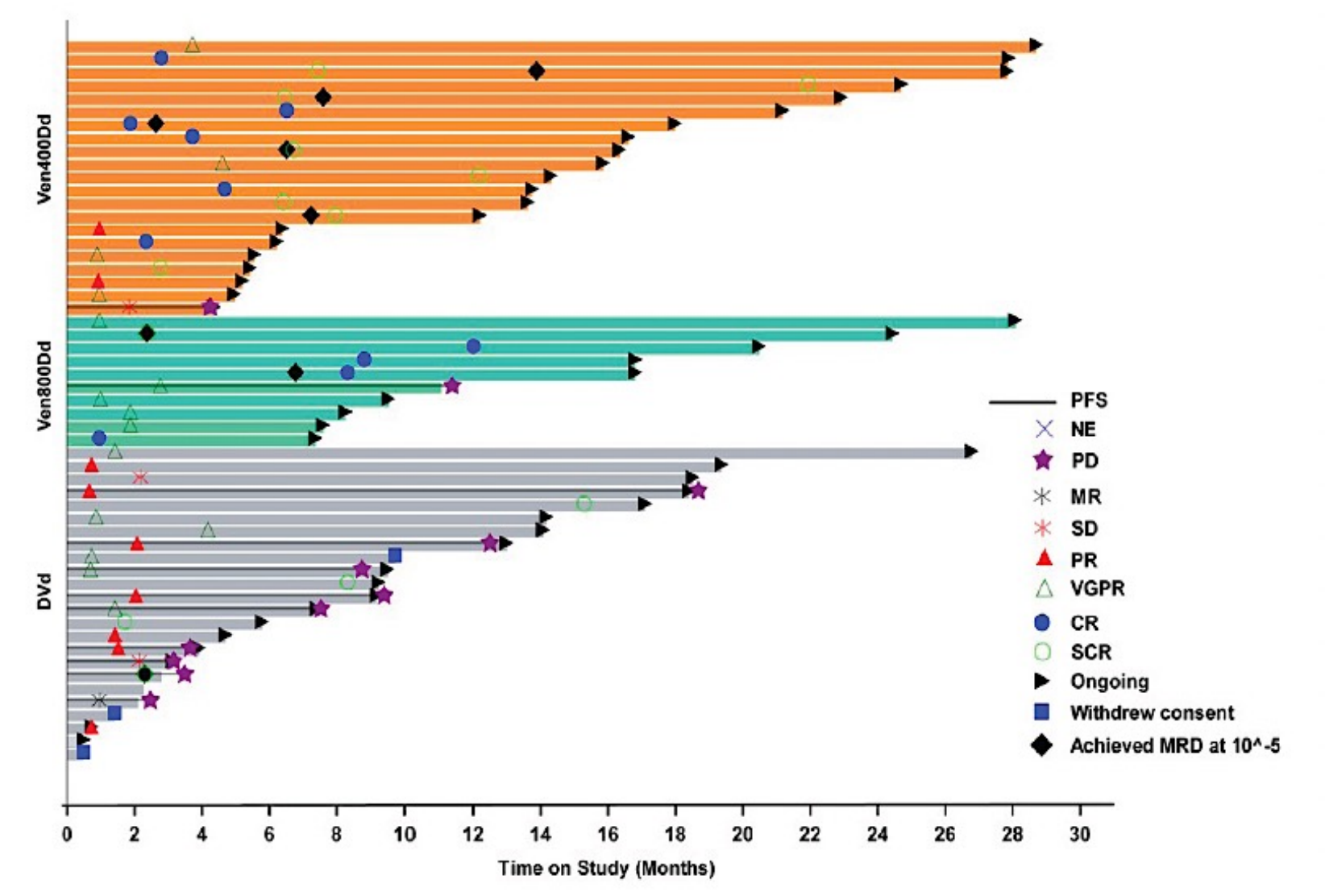
Kaufman JL et al. IMS 2023;Abstract OA-29.

ASH 2022 Abstract 3232

An Updated Safety and Efficacy Analysis of Venetoclax Plus Daratumumab and Dexamethasone in an Expansion Cohort of a Phase 1/2 Study of Patients With t(11;14) Relapsed/Refractory Multiple Myeloma

Jonathan L. Kaufman,[1] Hang Quach,[2] Rachid Baz,[3] Annette Juul Vangsted,[4] Shir-Jing Ho,[5] Simon J. Harrison,[6] Torben Plesner,[7] Philippe Moreau,[8] Simon Gibbs,[9] Eva Medvedova,[10] Muhammad Jalaluddin,[11] Jeremy A. Ross,[11] Leanne L Fleming,[11] Yan Luo,[11] Nizar J. Bahlis[12]

Venetoclax, Daratumumab and Dexamethasone (VenDd) Responses

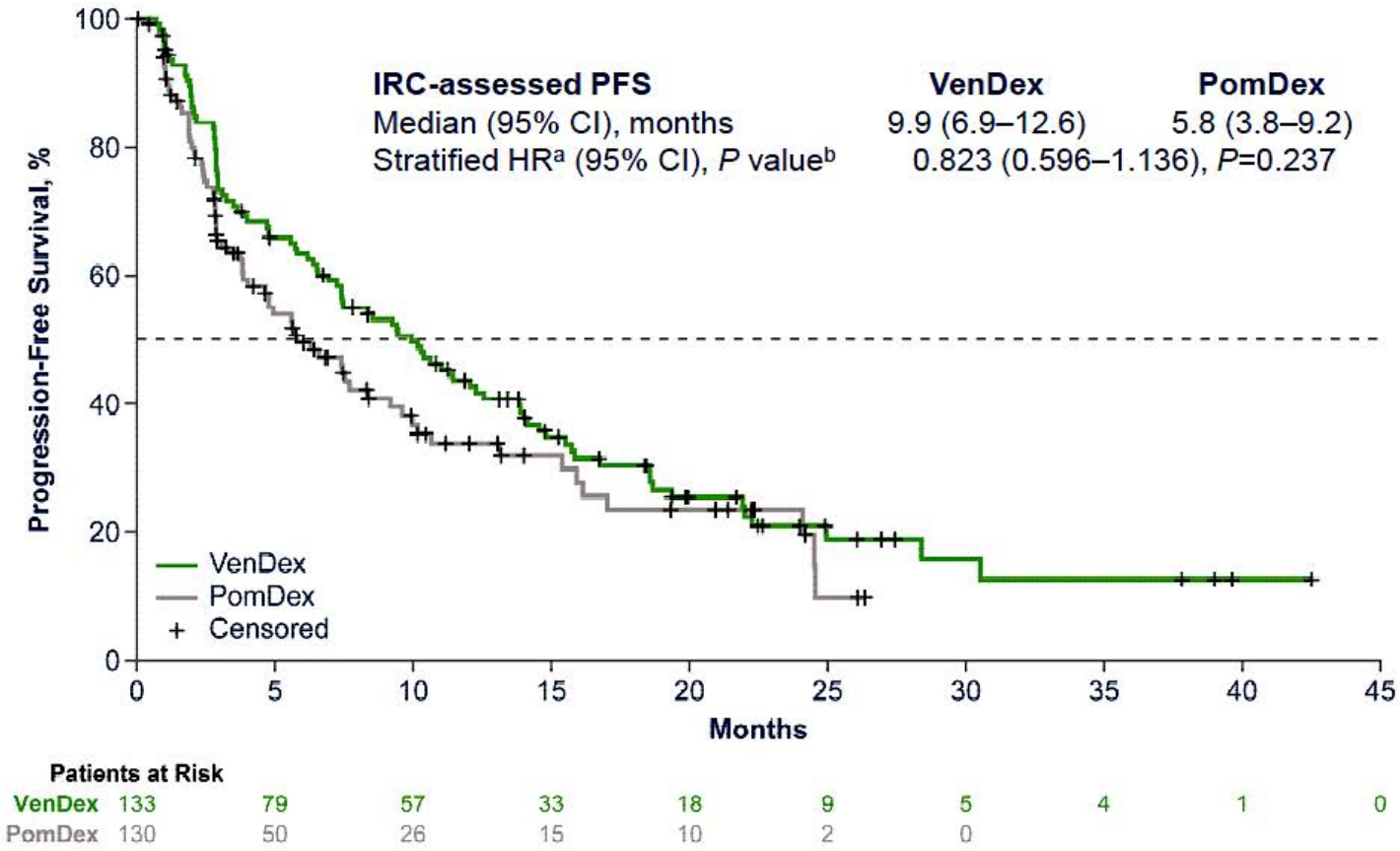


Kaufman JL et al. ASH 2022;Abstract 3232.

RTP RESEARCH TO PRACTICE

CANOVA Trial Primary Endpoint: PFS with Venetoclax/Dexamethasone versus Pomalidomide/Dexamethasone for t(11;14) Relapsed/Refractory MM

- The median follow-up time was 24.9 months for VenDex and 25.6 months for PomDex
- The concordance[c] between IRC- and investigator-assessed PFS was 94%



[a]HR for PFS was determined by a stratified Cox proportional hazard model. [b]*P* value was determined by stratified log-rank test. [c]The overall concordance rate was defined as the percentage of patients who had PD by both IRC and investigator and patients who were non-PD by both IRC and investigator among all patients.
HR, hazard ratio; IRC, independent review committee; PD, progressive disease; PFS, progression-free survival; PomDex, pomalidomide and dexamethasone; VenDex, venetoclax and dexamethasone.

Mateos M-V et al. IMS 2023;Abstract OA-52.

RTP RESEARCH TO PRACTICE

Oncology in the Real World: A Daylong Multitumor Educational Symposium in Partnership with the American Oncology Network

A CME/MOC- and NCPD-Accredited Event

Saturday, October 14, 2023
9:30 AM – 5:00 PM PT

RTP
RESEARCH
TO PRACTICE

We are taking a short break!

The program will resume at 3:50 PM PT

Up Next…

Drs Sara Hurvitz and Heather McArthur discuss the management of HER2-positive and triple-negative breast cancer

RTP
RESEARCH
TO PRACTICE

Oncology in the Real World: A Daylong Multitumor Educational Symposium in Partnership with the American Oncology Network

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Saturday, October 14, 2023
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RTP
RESEARCH
TO PRACTICE

Agenda

Module 1 — Lymphoma: *Drs Flowers and LaCasce*

Module 2 — Urothelial Bladder Cancer and Renal Cell Carcinoma:
Drs Hutson and Sonpavde

Module 3 — Hepatobiliary and Pancreatic Cancers:
Prof Borad and Dr El-Khoueiry

Module 4 — Gynecologic Cancers: *Drs Monk and Moore*

Module 5 — Multiple Myeloma: *Drs Krishnan and Orlowski*

Module 6 — HER2-Positive and Triple-Negative Breast Cancer:
Drs Hurvitz and McArthur

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RESEARCH
TO PRACTICE

HER2-Positive and Triple-Negative Breast Cancer Faculty

Sara A Hurvitz, MD, FACP
Professor
Senior Vice President
Clinical Research Division
Fred Hutchinson Cancer Center
Head, Division of Hematology/Oncology
UW Medicine
Seattle, Washington

Heather McArthur, MD, MPH
Associate Professor
Department of Internal Medicine
Clinical Director, Breast Cancer Program
Komen Distinguished Chair in
Clinical Breast Cancer Research
UT Southwestern Medical Center
Dallas, Texas

RTP
RESEARCH
TO PRACTICE

Snapshot of AON Practice
Module 6: Breast Cancer

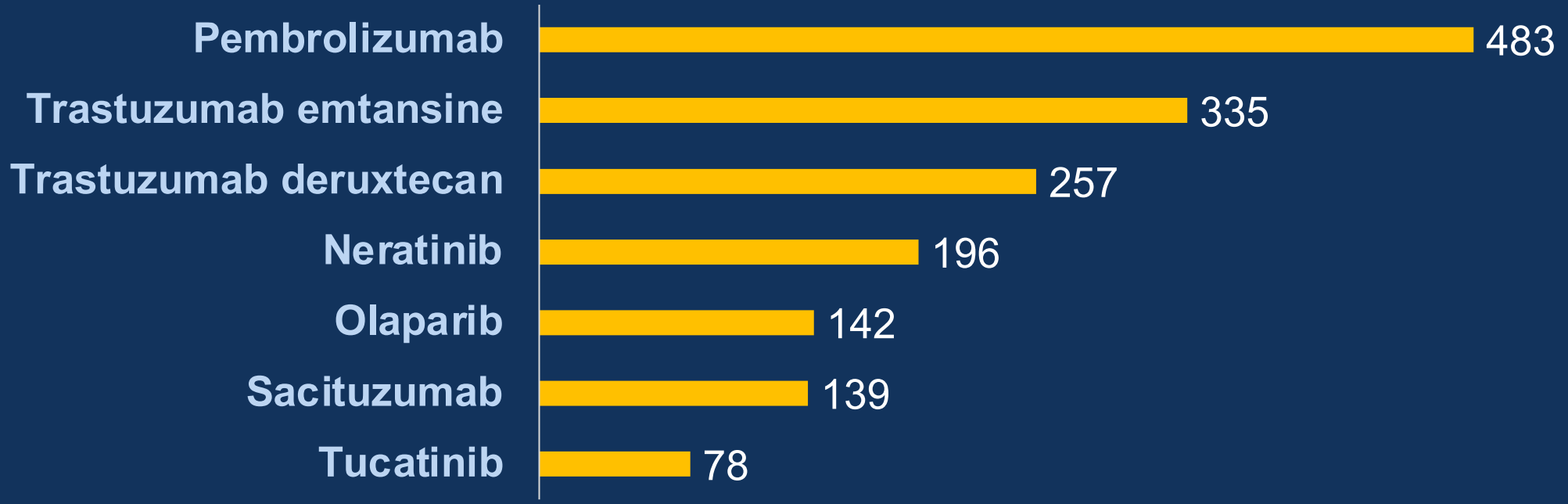
MIBA

THE AON CLINICAL SUMMIT 2023

Collaborate. Innovate. Celebrate.

Snapshot of AON Practice
Breast Cancer

Select Treatments Received



Clinical Trial Participation

Number of clinical trials	41
Total patients enrolled	124

MIBA

THE AON CLINICAL SUMMIT 2023

Collaborate. Innovate. Celebrate.

UT Southwestern
Medical Center

Triple Negative Breast Cancer

Heather McArthur, MD, MPH
Clinical Director, Breast Cancer
Komen Distinguished Chair in Clinical Breast Cancer Research
Associate Professor
UT Southwestern, Dallas, TX
Heather.McArthur@utsouthwestern.edu
@hmcarthur

KEYNOTE-355 Study Design (NCT02819518)

- paclitaxel
- nab-paclitaxel
- gemcitabine/carboplatin

Key Eligibility Criteria

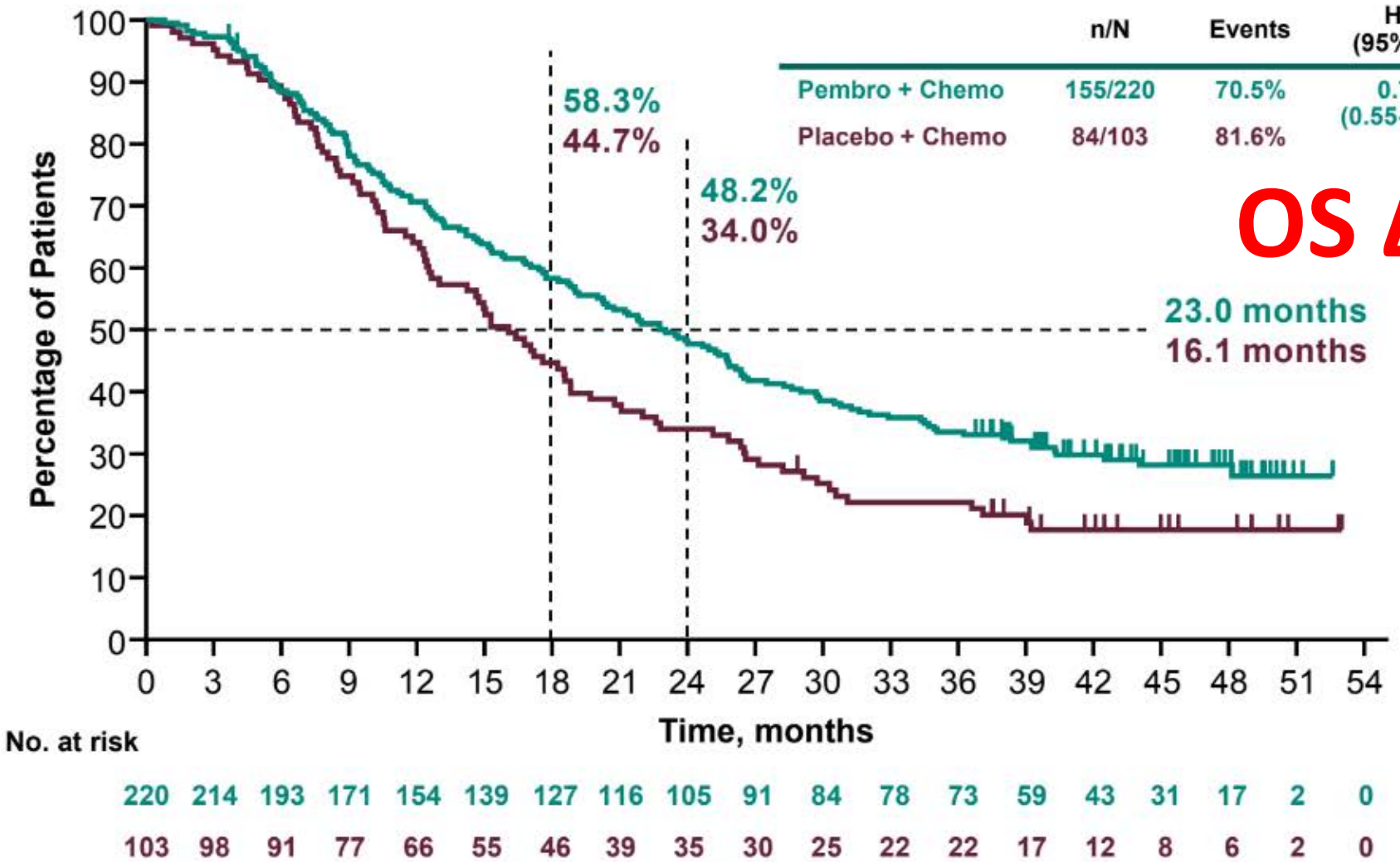
- Age ≥18 years
- Central determination of TNBC and PD-L1 expression
- Previously untreated locally recurrent inoperable or metastatic TNBC
- Completion of treatment with curative intent ≥6 months prior to first disease recurrence
- ECOG performance status 0 or 1
- Life expectancy ≥12 weeks from randomization
- Adequate organ function
- No systemic steroids
- No active CNS metastases
- No active autoimmune disease

Stratification Factors:

- Chemotherapy on study (taxane vs gemcitabine/carboplatin)
- PD-L1 tumor expression (CPS ≥1 vs CPS <1)
- Prior treatment with same class chemotherapy in the neoadjuvant or adjuvant setting (yes vs no)

Rugo et al. Abstract LBA16, ESMO 2021

Overall Survival: PD-L1 CPS ≥10



	n/N	Events	HR (95% CI)	P-value (one-sided)
Pembro + Chemo	155/220	70.5%	0.73 (0.55-0.95)	0.0093[a]
Placebo + Chemo	84/103	81.6%		

OS Δ ~7mo

[a]Prespecified *P* value boundary of 0.0113 met.
Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors. Data cutoff: June 15, 2021.

Rugo et al. Abstract LBA16, ESMO 2021; Cortes J et al. NEJM 2022;387(3):217-226.

KEYNOTE-522

Eligibility

- Newly diagnosed TNBC (central confirmation)
- T1c N+ or T≥2 N0-2
- PD-L1+ or PD-L1-

Stratification

- T1/T2 vs T3/T4
- N0 vs N+
- Carboplatin Q1W vs Q3W

N = 1,174

R

Neoadjuvant chemo **+ pembrolizumab**

Neoadjuvant chemo **+ placebo**

Surgery

Adjuvant **pembrolizumab** 9 cycles

Adjuvant **placebo** 9 cycles

Within 3-6 weeks

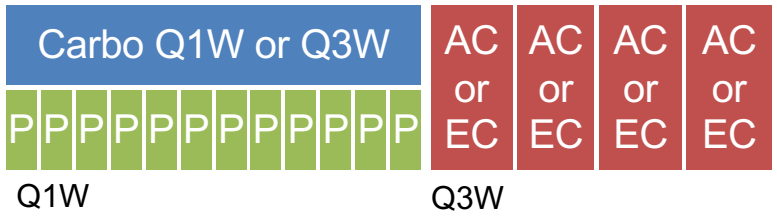
Primary endpoints

- pCR rate (ypT0/Tis ypN0)
- EFS

Secondary endpoints

- Alternative pCR rate (ypT0 ypN0)
- pCR rate in PD-L1+
- EFS in PD-L1+
- OS

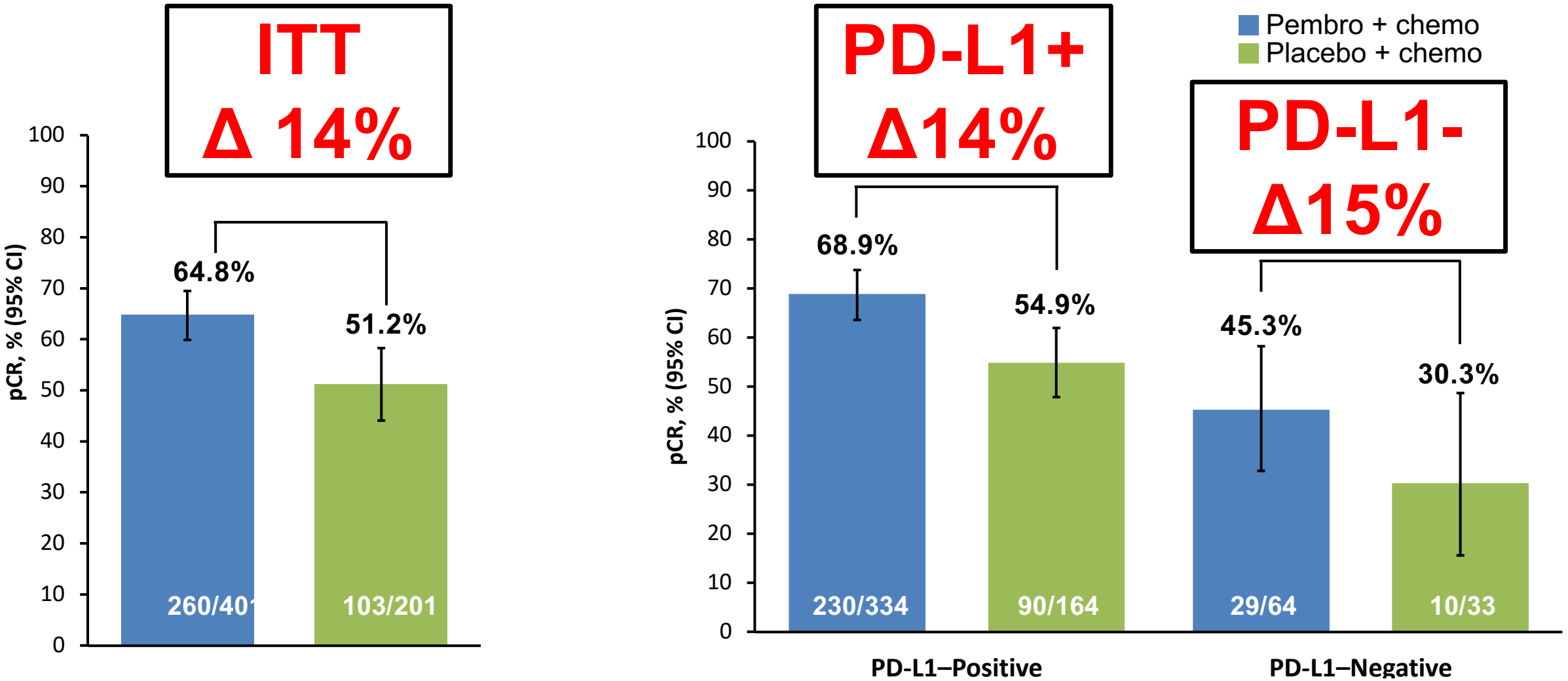
Study Treatment



Paclitaxel 80 mg/m^2 IV weekly
Carboplatin weekly (AUC 1.5) or Q3W (AUC5)
Doxorubicin 60 mg/m^2 IV Q3W
(Epirubicin 90 mg/m^2 IV Q3W)
Cyclophosphamide 600 mg/m^2 IV Q3W
Pembrolizumab 200 mg IV Q3W

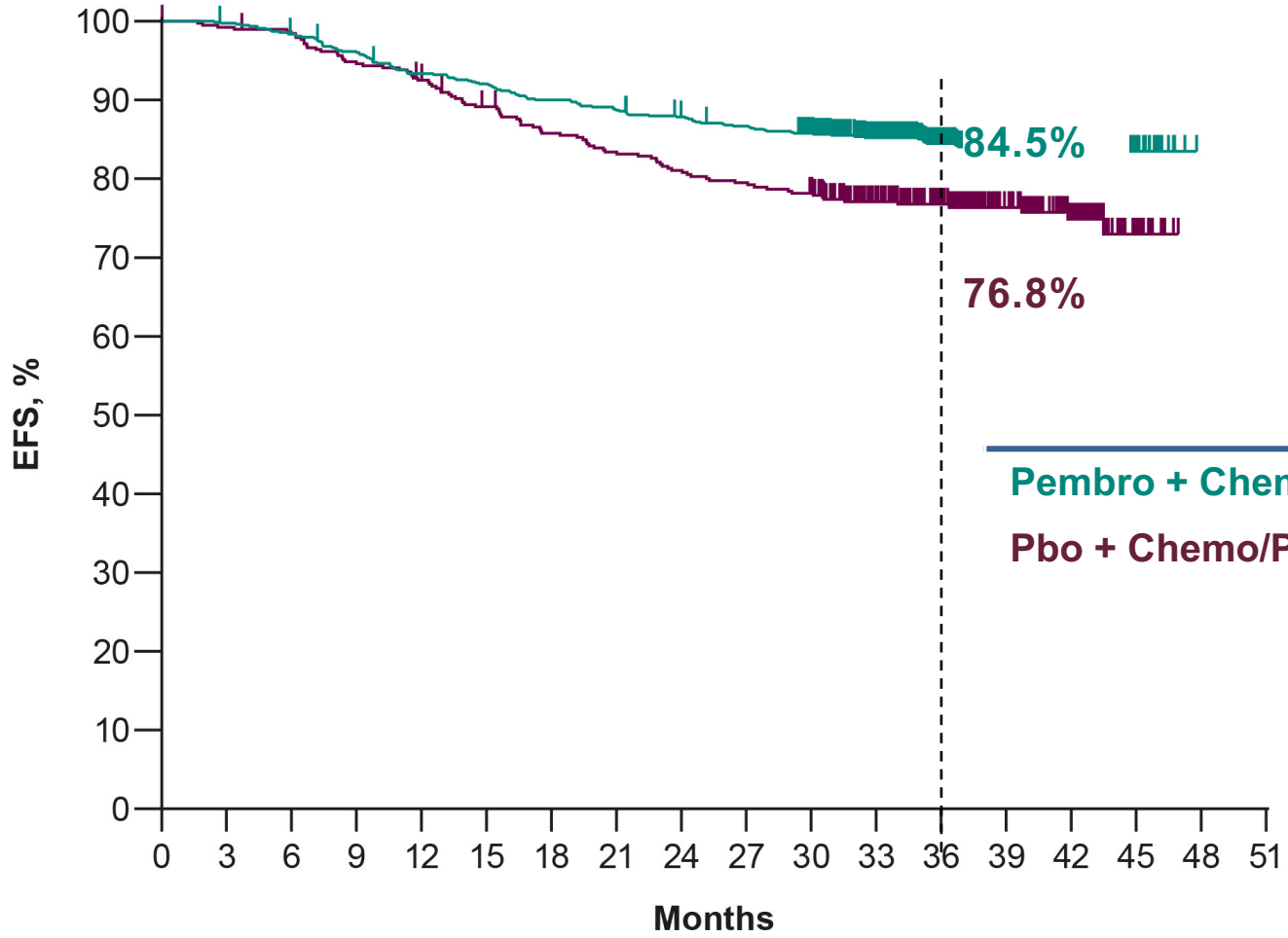
Schmid P et al. NEJM 2020

KEYNOTE-522: pCR at IA1



Schmid et al. NEJM 2020

KEYNOTE-522: EFS update at IA4 (39.1mo)



Δ7.7%

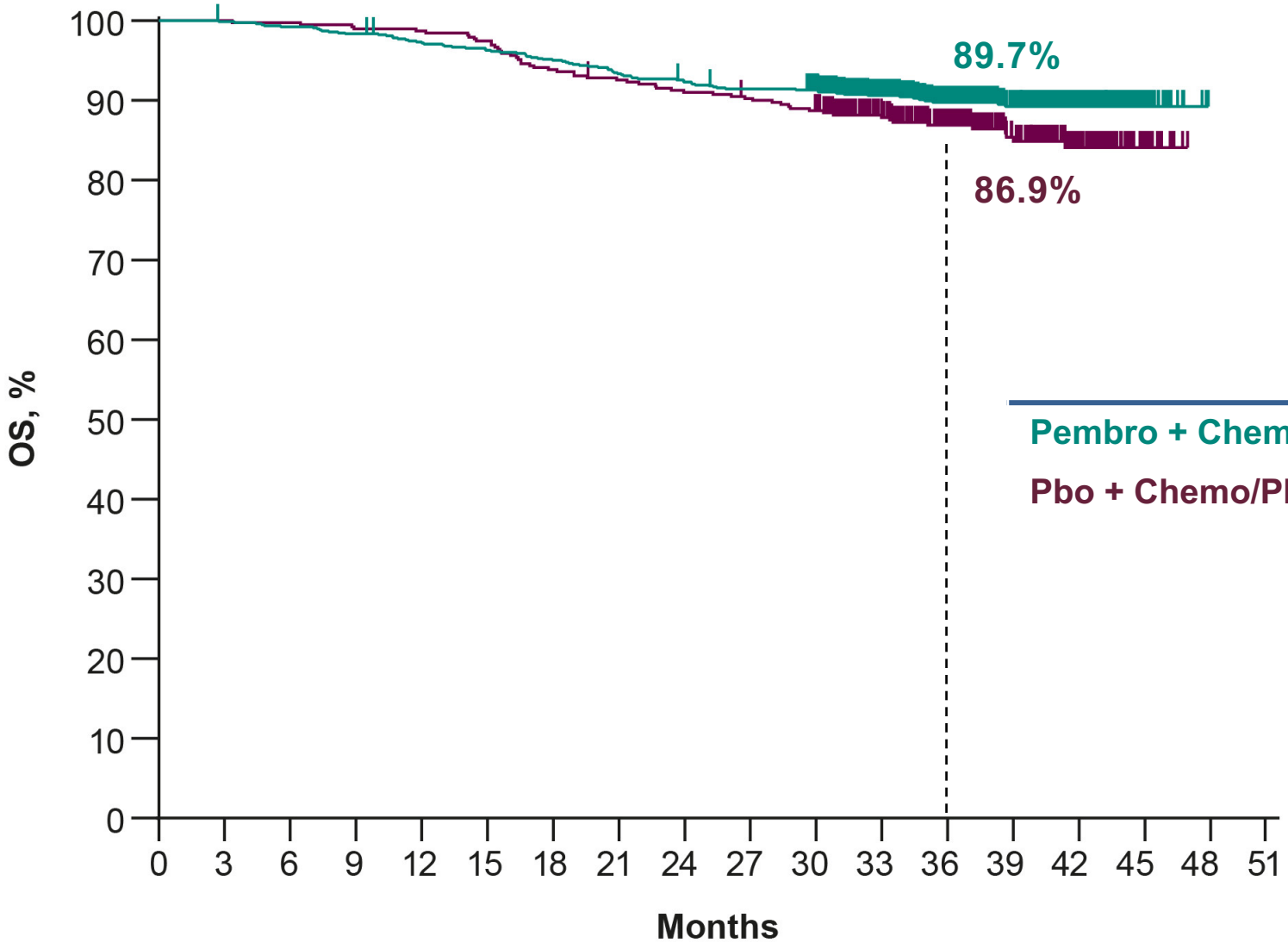
	Events	HR (95% CI)	*P*-value
Pembro + Chemo/Pembro	15.7%	0.63	0.00031
Pbo + Chemo/Pbo	23.8%		

No. at Risk

Pembro + Chemo/Pembro	784	781	769	751	728	718	702	692	681	671	652	551	433	303	165	28	0	0
Pbo + Chemo/Pbo	390	386	382	368	358	342	328	319	310	304	297	250	195	140	83	17	0	0

Schmid et al. ESMO 2021.
Schmid et al. NEJM 2022

Overall Survival



	Events	HR (95% CI)	*P*-value
Pembro + Chemo/Pembro	10.2%	0.72 (0.51-1.02)	0.03214
Pbo + Chemo/Pbo	14.1%		

Schmid et al. ESMO 2021.
Schmid et al. NEJM 2022

g*BRCA* Mutations May Occur in Both HR+/HER2- and TNBC Subtypes

TNBC
14% g*BRCA*mut[3]
≈34,000 patients[1,2]
≈4,800 patients[1-3,a]

HR+/HER2-
5% g*BRCA*mut[3]
≈205,000 patients[1,2]
≈10,000 patients[1-3,a]

Most g*BRCA* mutations (>80%) are found in patients with HER2-negative disease[1-3]

1. https://seer.cancer.gov/statfacts/html/breast-subtypes.html. 2. Howlader N et al. *J Natl Cancer Inst.* 2014;106. 3. Tung N et al. *J Clin Oncol.* 2016;34:1460-1468.

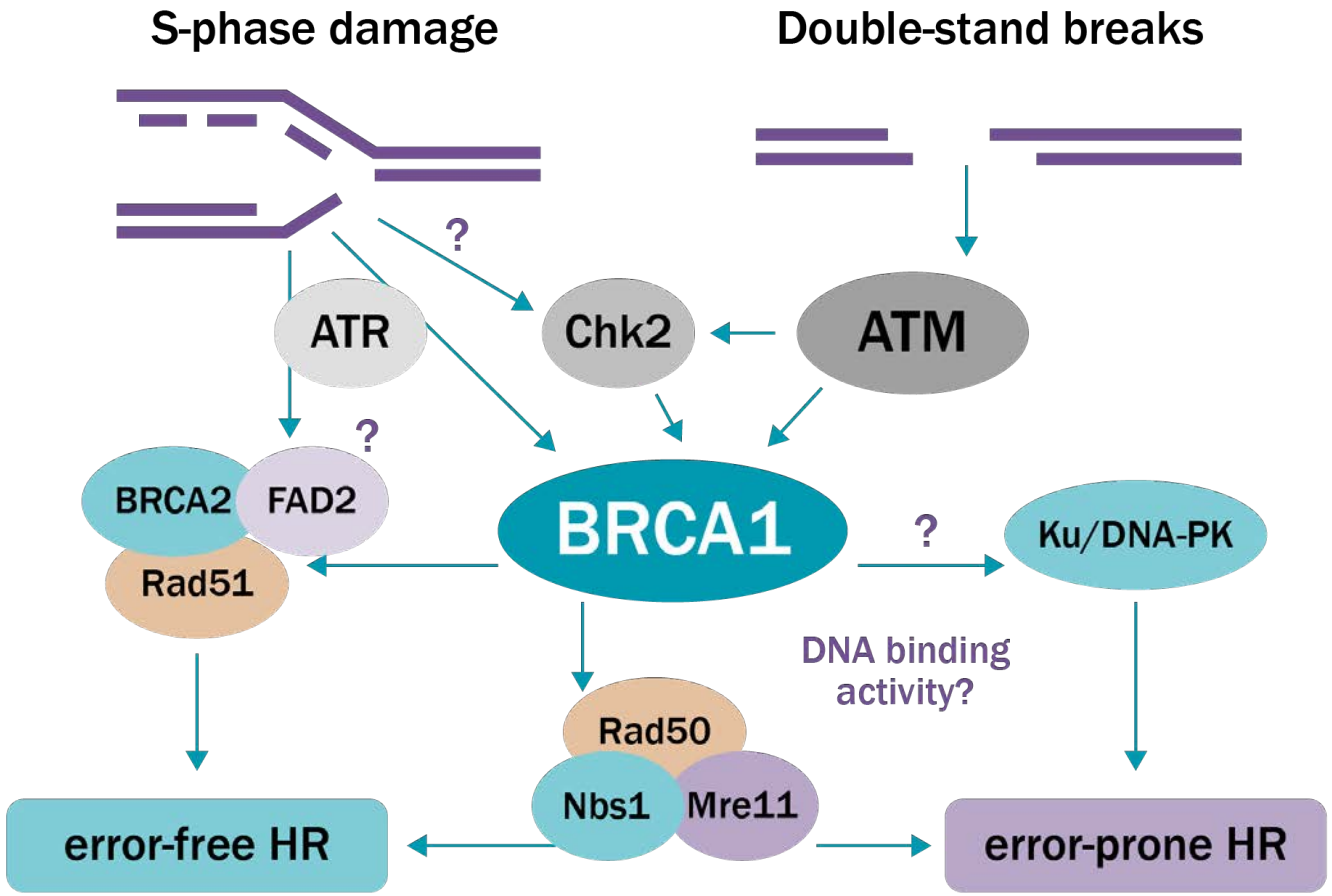
DNA Damage Repair Deficiency as a Target

In normal cells, BRCA1 can help repair damaged DNA or destroy cells if DNA cannot be repaired[1]

- Especially critical in repair of DNA double-strand breaks

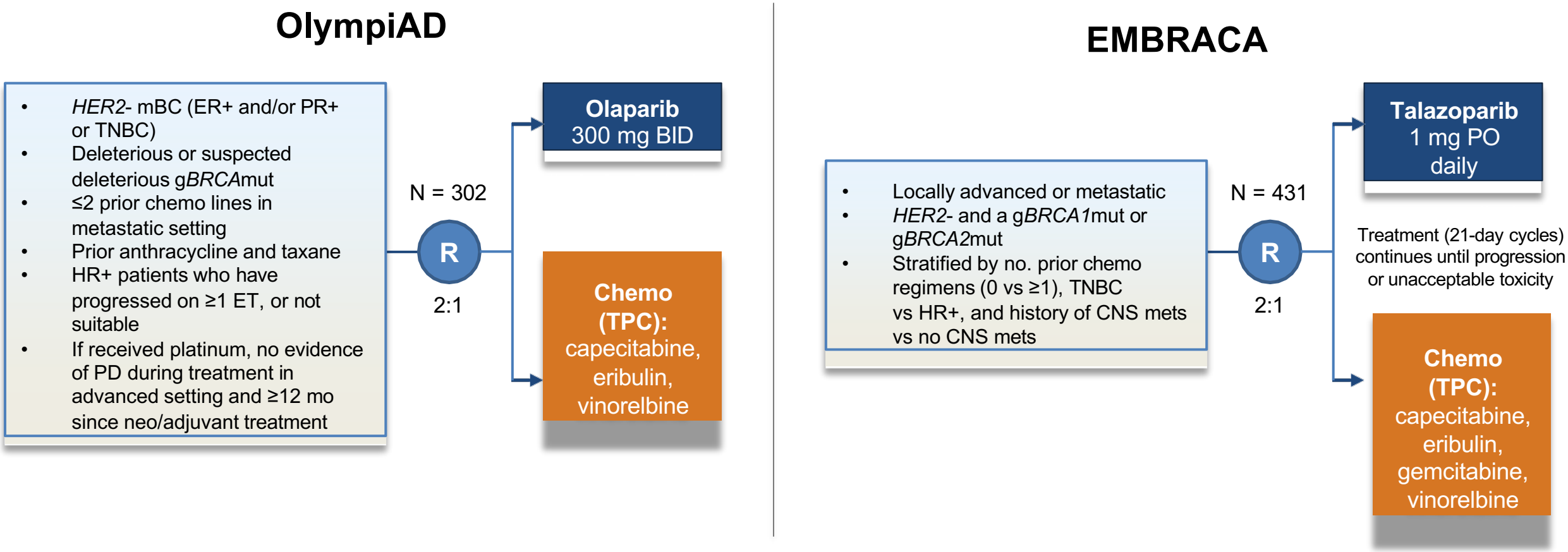
If BRCA1 or BRCA2 are mutated, damaged DNA may not be repaired properly, and damaged cells can multiply out of control[2]

Role of BRCA1 in DNA Repair and S-phase Arrest[1]



1. Zhang J, et al. *Mol Cancer Res*. 2005;3:531-539. 2. Yoshida K, et al. *Cancer Sci*. 2004;95(11):866-871.

Phase 3 PARPi Trials in Metastatic Breast Cancer: OlympiAD and EMBRACA Study Designs



OlympiAD and EMBRACA: phase 3 trials, PARPi vs standard nonplatinum chemo (first to third line)

Robson M et al. *N Engl J Med.* 2017;377:523-533.
Litton JK et al. *N Engl J Med.* 2018;379:753-763.

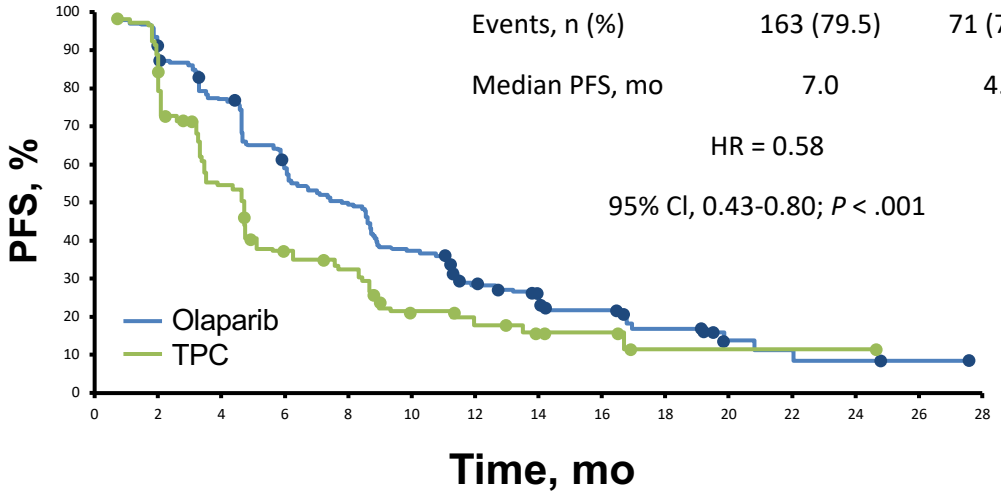
PARPi for MBC in g*BRCA* Carriers

OlympiAD

	Olaparib (n = 205)	TPC (n = 97)
Events, n (%)	163 (79.5)	71 (73.2)
Median PFS, mo	7.0	4.2

HR = 0.58

95% CI, 0.43-0.80; *P* < .001



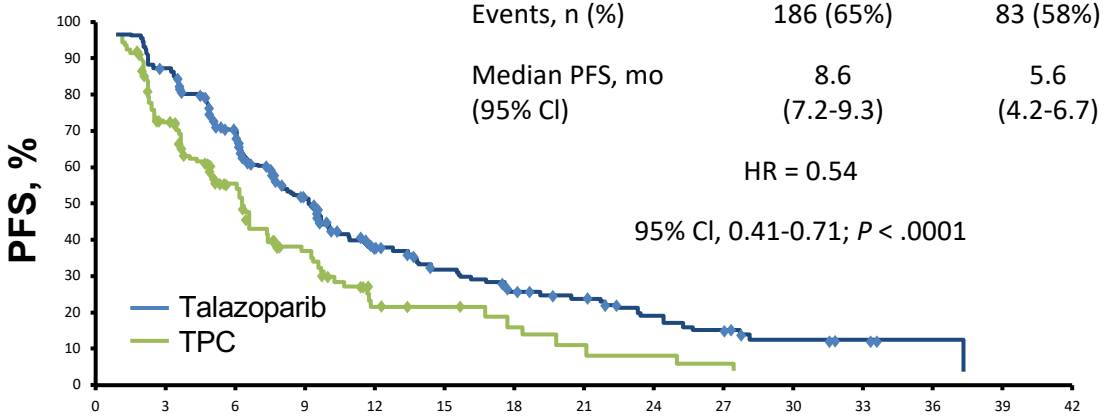
No. at Risk															
Olaparib	205	177	154	107	94	69	40	23	21	11	4	3	2	1	0
TPC	97	63	44	25	21	11	8	4	4	1	1	1	1	0	0

EMBRACA

	Talazoparib (n = 287)	TPC (n = 144)
Events, n (%)	186 (65%)	83 (58%)
Median PFS, mo (95% CI)	8.6 (7.2-9.3)	5.6 (4.2-6.7)

HR = 0.54

95% CI, 0.41-0.71; *P* < .0001



No. at Risk															
Talazoparib	287 (0/0)	229 (50/50)	148 (53/103)	91 (34/137)	55 (17/154)	42 (9/154)	29 (9/172)	23 (2/174)	16 (5/179)	12 (4/183)	5 (2/185)	3 (0/185)	1 (0/185)	0 (0/186)	0 (0/186)
TPC	144 (0/0)	68 (41/41)	34 (20/61)	22 (8/69)	9 (7/76)	8 (0/76)	4 (3/79)	2 (0/81)	1 (1/82)	0 (1/83)	0 (1/83)	0 (1/83)	0 (1/83)	0 (1/83)	0 (1/83)

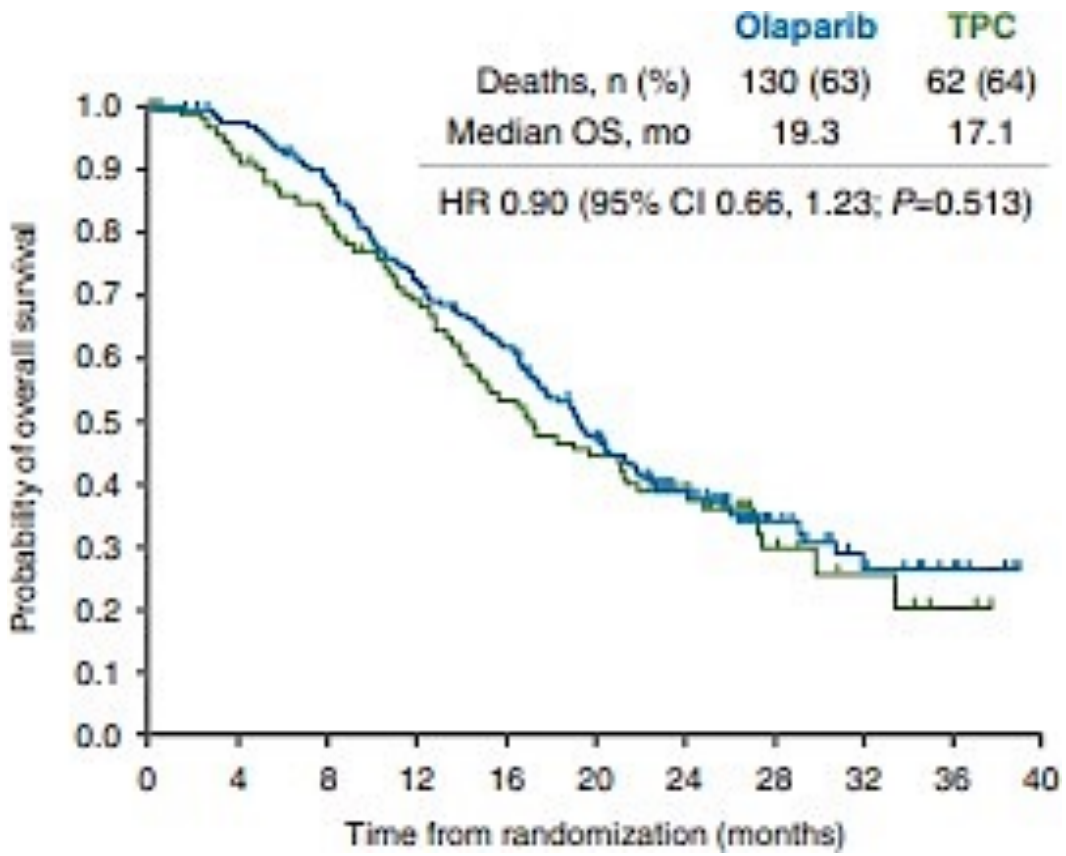
In both studies, PARPi resulted in

- Significant ↑ PFS (HR 0.58 and 0.54)
- Significant ↑ HR-QoL
- No improvement in OS

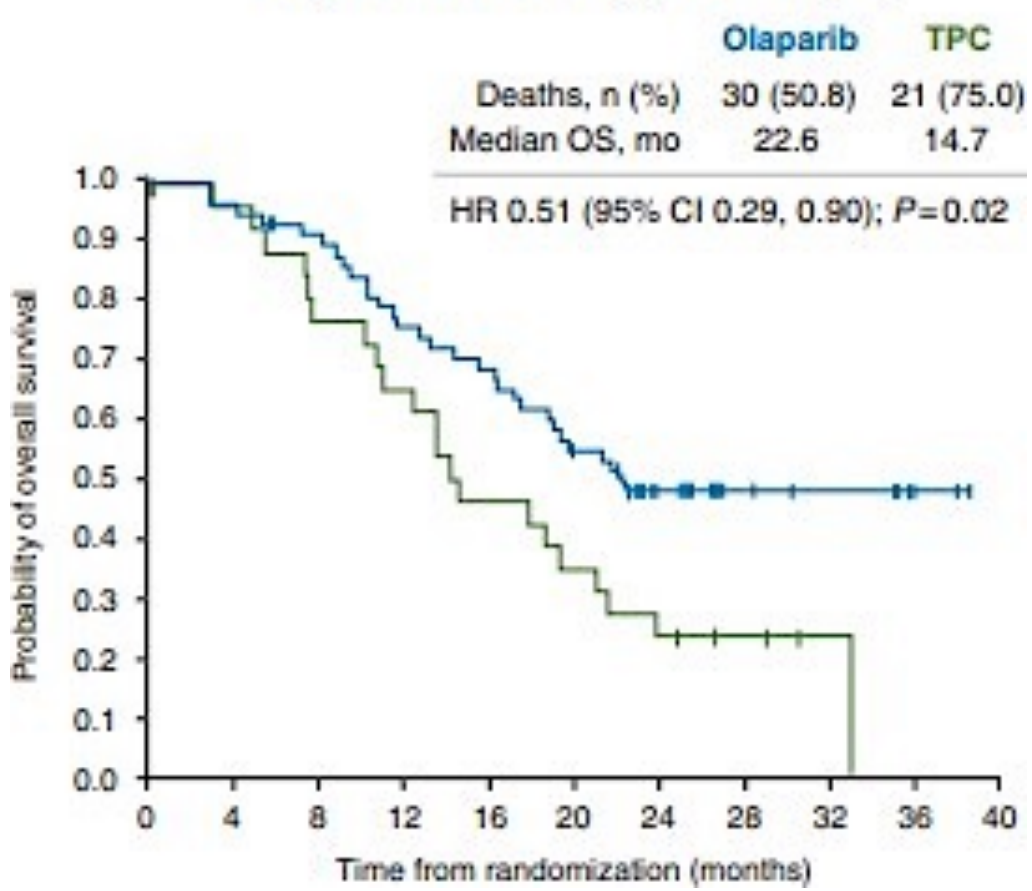
Robson M et al. *N Engl J Med.* 2017;377:523-533.
Litton JK et al. *N Engl J Med.* 2018;379:753-763.

OlympiAD OS

ITT



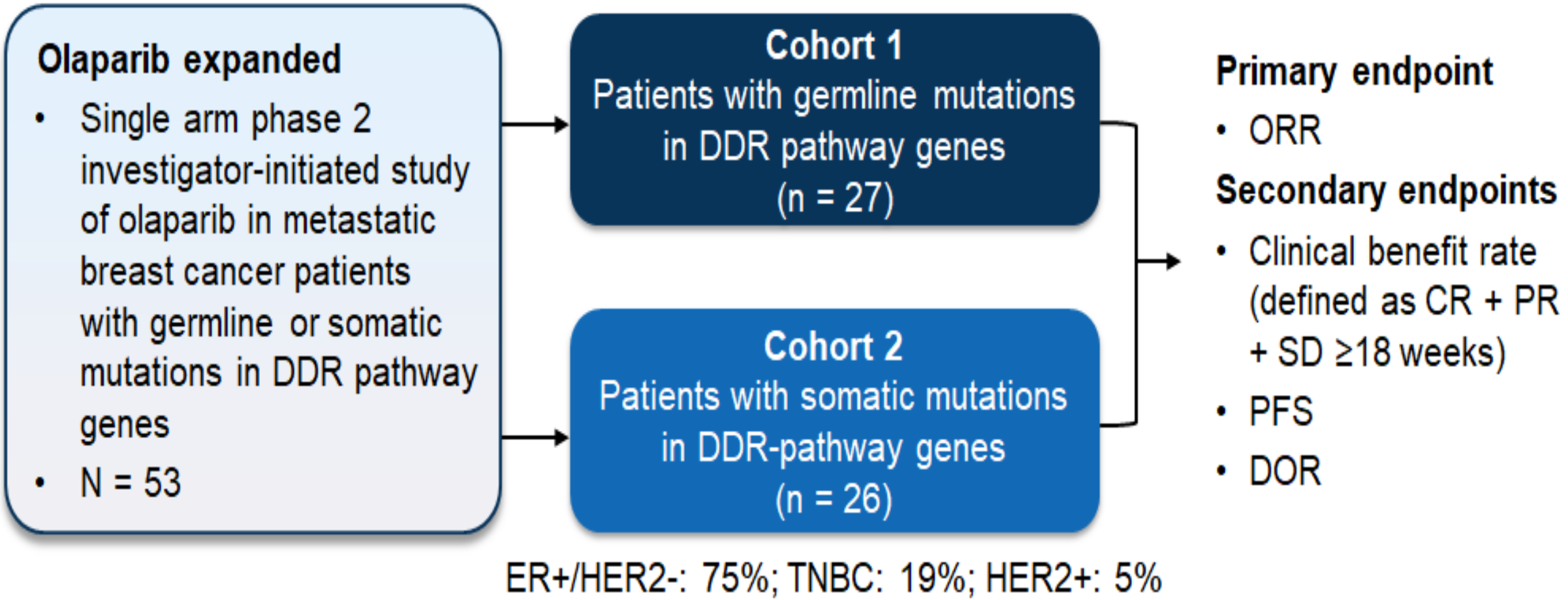
No prior chemo for MBC



Robson M. et al. Ann Oncol 2019; Robson ME et al. Eur J Cancer 2023

TBCRC 048: Phase 2 Olaparib Monotherapy in mBC Patients With Germline/Somatic Mutations in DDR Pathway Genes

Study Design

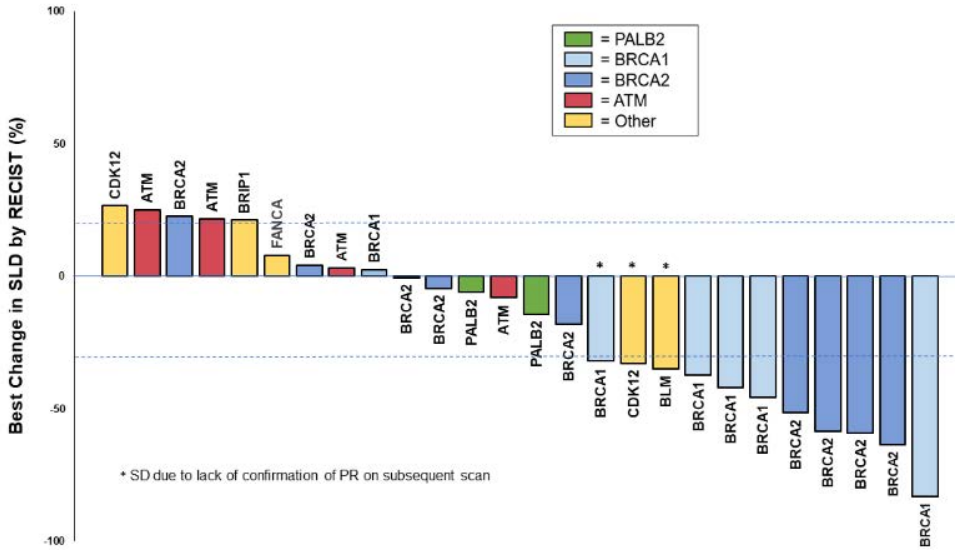


[a] 1 s*PALB2*- lost to follow-up after 1st tumor assessment with skin and tumor marker response. [b] Includes patient from cohort 1 with s*BRCA1* and g*CHEK2*.
[c] Not included: patient with both g*CHEK2* and s*BRCA1*; patient with g*ATM* and g*PALB2*.

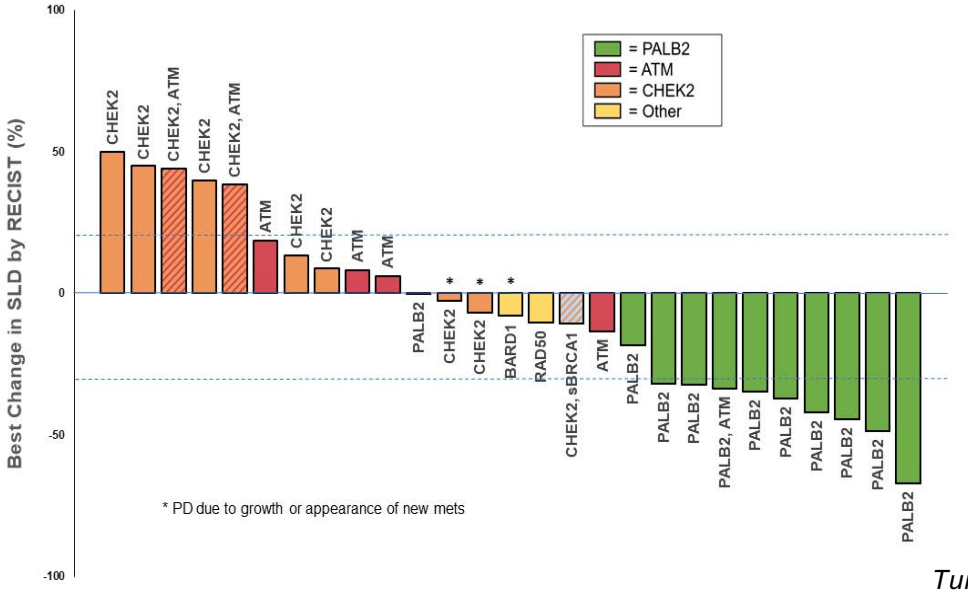
1. Tung NM et al. 2020 American Society of Clinical Oncology Annual Meeting (ASCO 2020). Abstract 1002.

PARPi in Other Types of HR Deficiency: TBCRC 048

Olaparib in somatic BRCA1/2 mt and non BRCA1/2 germline mutations



Somatic BRCA1/2 mt (5-10% in TNBC) 50% RR (8/16)



Germline PALB2 mt 82% RR (9/11)

Gene	Germline N	Somatic N	RR	% RR
BRCA1	**--**	**6**	**4/6**	**67%**
BRCA2	**--**	**10**	**4/10**	**40%**
PALB2	**11**	**2**	**9/13 (all g)**	**69%**
CHEK2*	9	0	0	0
ATM*	5	4	0	0
RAD50	1	0	0	0
CDK12	**0**	**2**	**1/2**	**50%**
BARD1	1	0	0	0
BLM1	**0**	**1**	**1/1**	**50%**
BRIP1	0	1	0	0
FANCA	0	1	0	0

* 1 pt gCHEK2 + gATM

Tung N et al. JCO 2020

Talazoparib Beyond BRCA

A phase II trial of talazoparib monotherapy in *BRCA1* and *BRCA2* wild-type patients with advanced HER2-negative breast cancer or other solid tumors with a mutation in homologous recombination (HR) pathway genes

Joshua J. Gruber[1,2], Anosheh Afghahi[3], Alyssa Hatton[1], Danika Scott[1], Alex McMillan[1], James M. Ford[1,2], Melinda L. Telli[1]

Departments of Medicine[1] and Genetics[2], Stanford University School of Medicine

Department of Medicine[3], University of Colorado

PRESENTED AT: 2019 ASCO ANNUAL MEETING #ASCO19

PRESENTED BY: Joshua Gruber, MD, PhD

Best Overall Response and Overall Response Rate (ORR)
Breast cancer

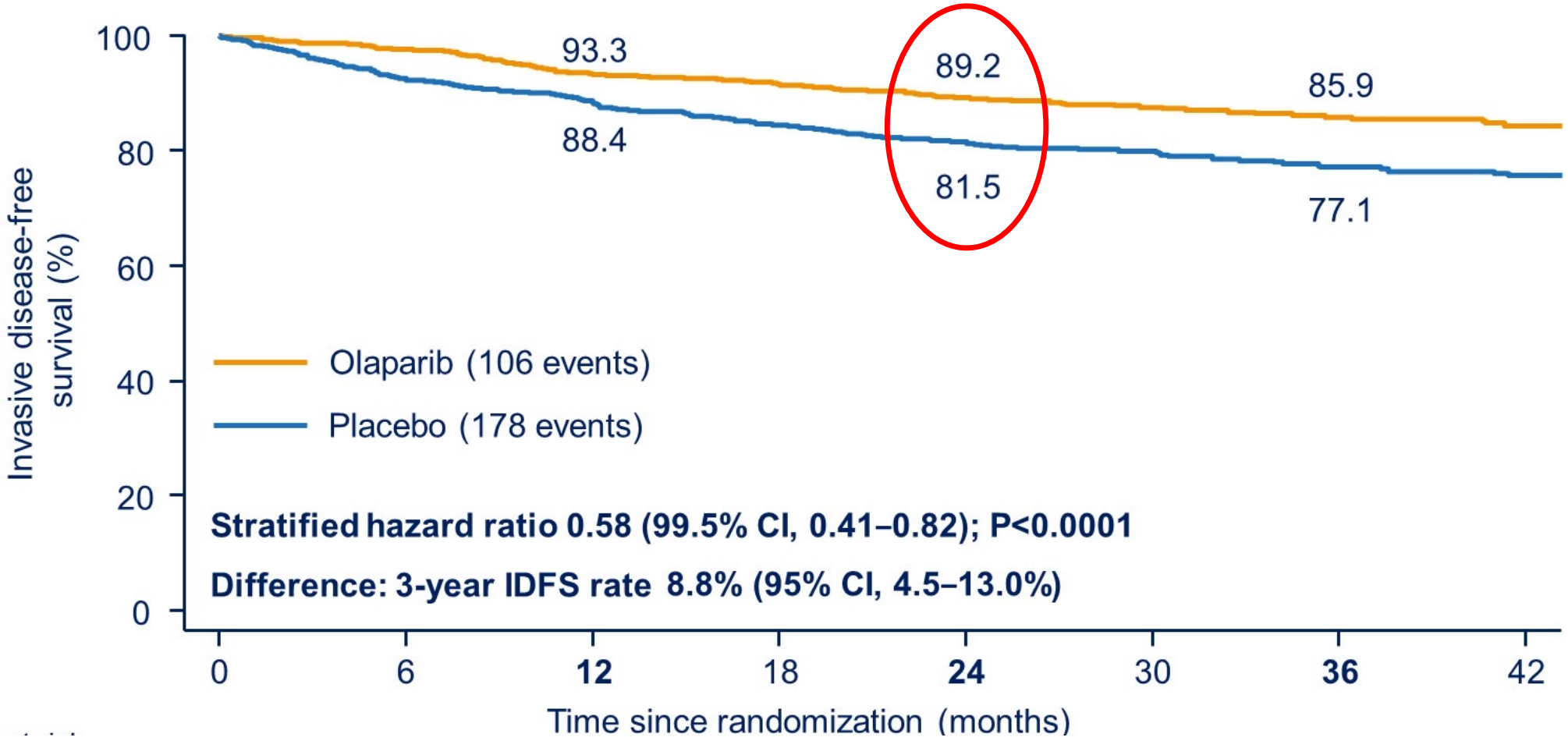
Best Response	Response Rate, n (%) Efficacy Evaluable (N=13)
Complete Response (CR)	0 (0%)
Partial Response (PR)	4 (31%)
Stable Disease (SD)	6 (46%)
Progressive Disease (PD)	3 (23%)
ORR (CR+PR)	4 (31%)
CBR (CR+PR+SD ≥ 6 months)	7 (54%)

ORR = 4/13 evaluable = **31%**
- 4 PR
  - gPALB2
  - gPALB2
  - gPALB2
  - gCHEK2/gFANCA/sPTEN

CBR = CR+PR+SD ≥ 6 months = 7/13 = **54%**
- SD ≥ 6 months
  - gPALB2 (-23.4%)
  - sPTEN (0%)
  - sATR (0%)

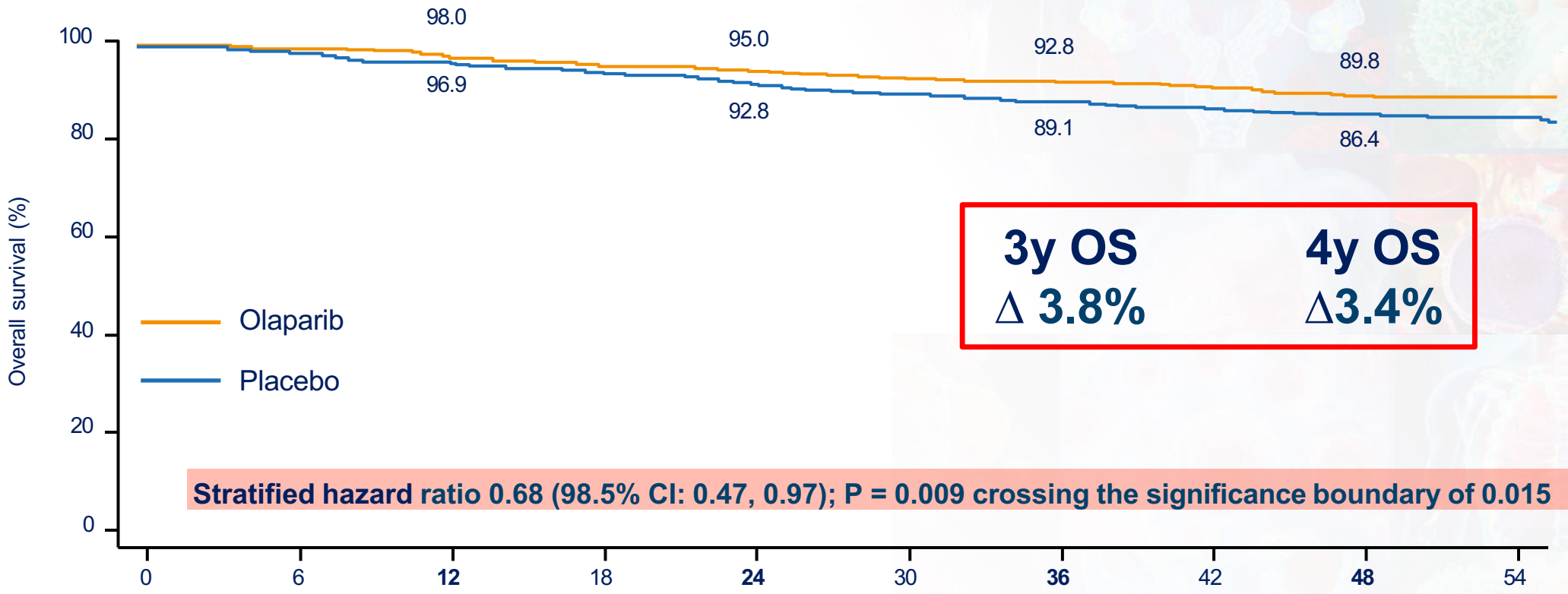
OlympiA

~5% of breast cancer patients carry gBRCA1/2 mutation
~82% TNBC on OlympiA



Tutt et al. ASCO 2021.
Tutt et al. NEJM 2021.

OlympiA OS

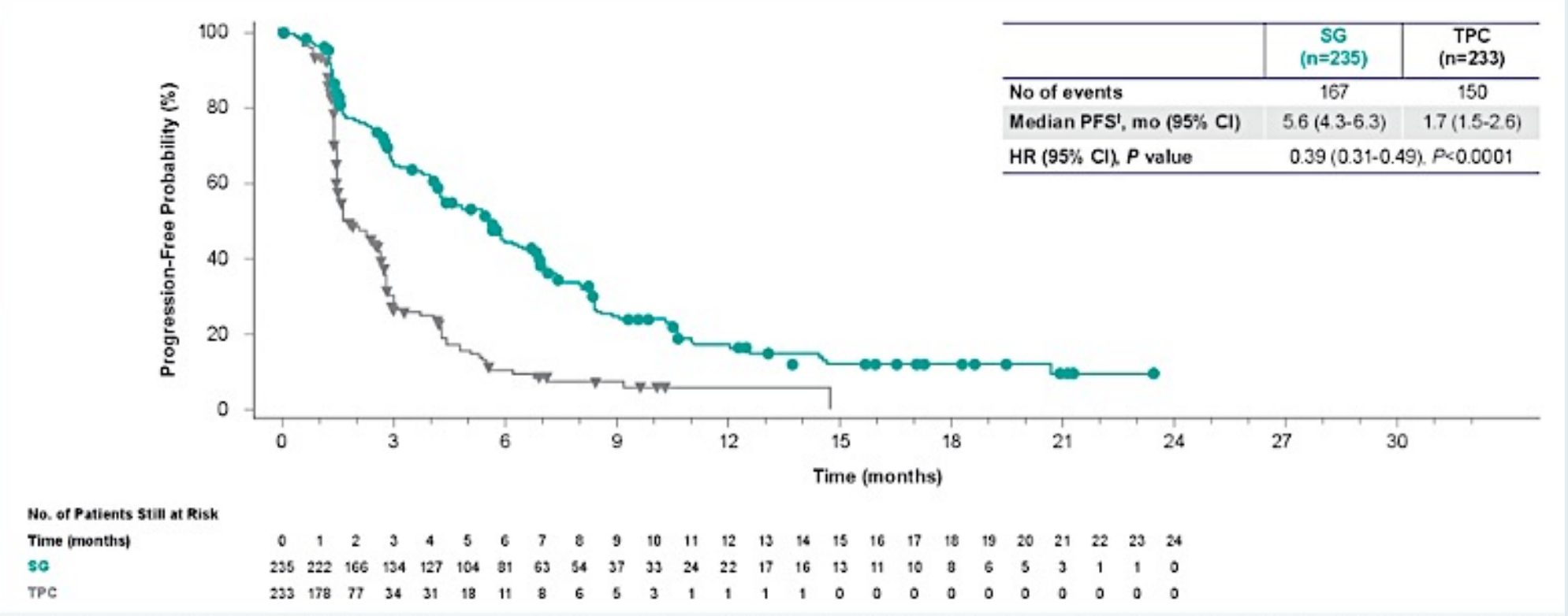


No. at risk

Olaparib	921	862	844	809	773	672	560	437	335	228
Placebo	915	868	843	808	752	647	530	423	333	218

Tutt et al, *Annals of Oncology*, March 2022

ASCENT Final Analysis: Progression-Free Survival with Sacituzumab Govitecan for mTNBC — Brain Metastasis-Negative Population



	SG (n=235)	TPC (n=233)
No of events	167	150
Median PFS[1], mo (95% CI)	5.6 (4.3-6.3)	1.7 (1.5-2.6)
HR (95% CI), *P* value	0.39 (0.31-0.49), *P*<0.0001	

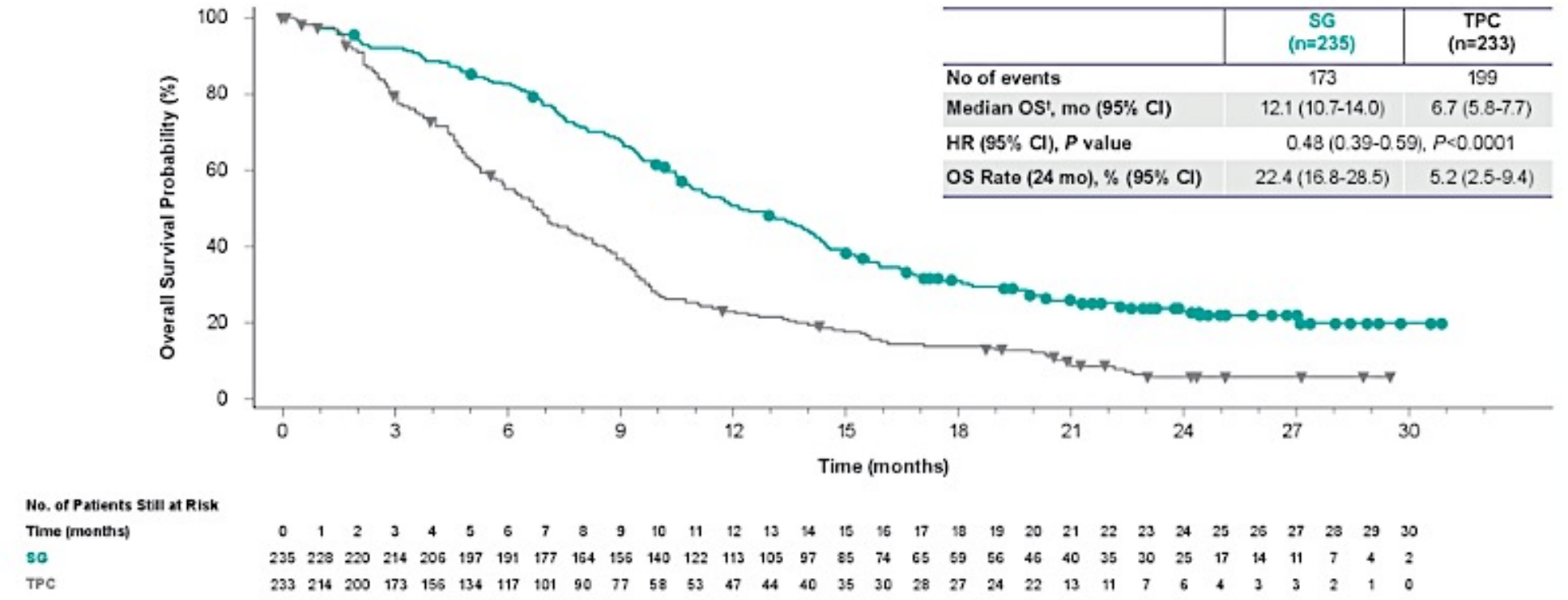
mTNBC = metastatic triple-negative breast cancer; SG = sacituzumab govitecan; TPC = treatment of physician's choice; PFS = progression-free survival

- The clinical benefit of SG over TPC in the ITT population was consistent with that in the brain metastasis-negative population:
  - Median PFS of 4.8 mo vs 1.7 mo (HR 0.41, $p < 0.0001$)

Bardia A et al. ASCO 2022;Abstract 1071.

RTP RESEARCH TO PRACTICE

ASCENT Final Analysis: Overall Survival with Sacituzumab Govitecan for mTNBC — Brain Metastasis-Negative Population



SG = sacituzumab govitecan; TPC = treatment of physician's choice; OS = overall survival

- The clinical benefit of SG over TPC in the ITT population was consistent with that in the brain metastasis-negative population:
  - Median OS of 11.8 mo vs 6.9 mo (HR 0.51, $p < 0.0001$)

Bardia A et al. ASCO 2022;Abstract 1071.

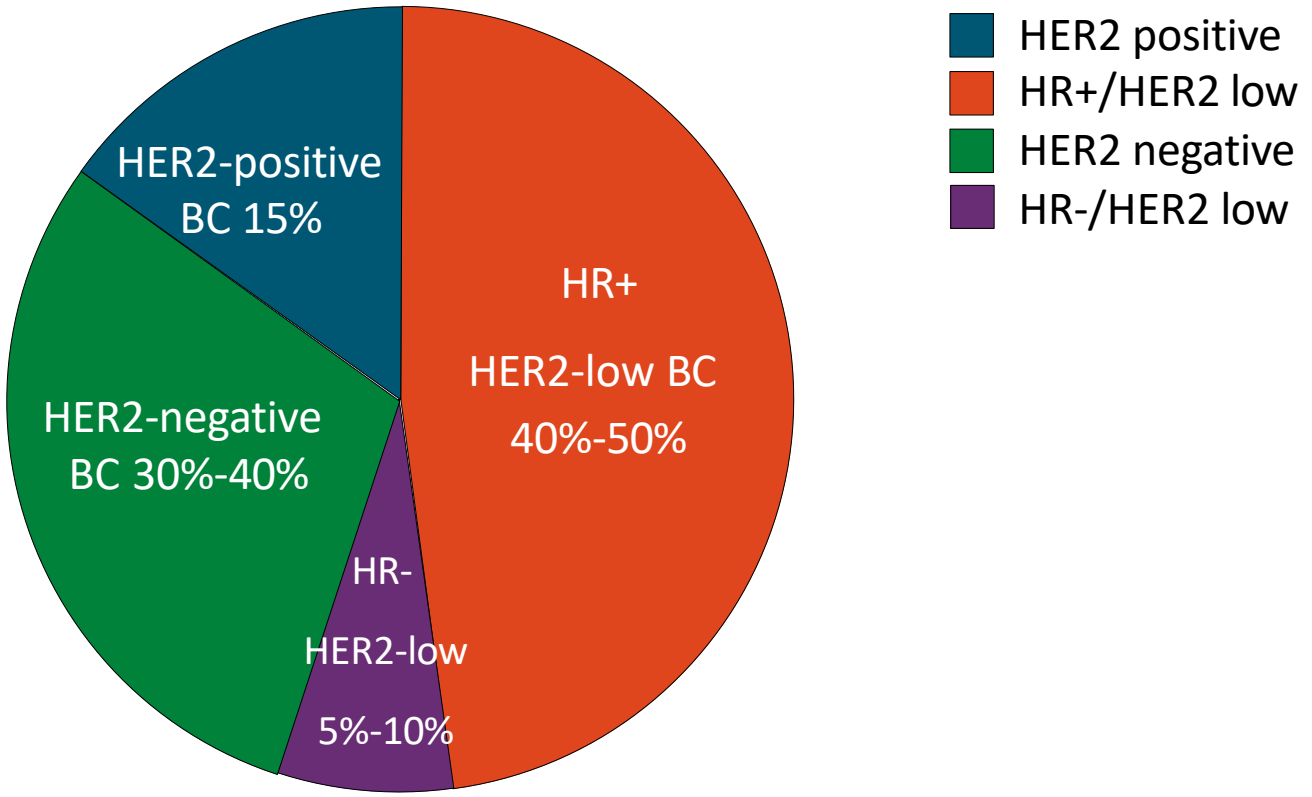
RTP RESEARCH TO PRACTICE

ASCENT Final Analysis: Treatment-Related Adverse Events (TRAEs) — All Grades, >20%; Grade 3 or 4, >5% of Patients

TRAE*		SG (n=258)			TPC (n=224)		
		All grade (%)	Grade 3 (%)	Grade 4 (%)	All grade (%)	Grade 3 (%)	Grade 4 (%)
Hematologic	Neutropenia†	163 (63)	88 (34)	45 (17)	96 (43)	45 (20)	29 (13)
	Anemia	89 (35)	20 (8)	0	53 (24)	11 (5)	0
	White blood cell count decreased	33 (13)	18 (7)	2 (1)	22 (10)	9 (4)	2 (1)
	Febrile neutropenia	15 (6)	12 (5)	3 (1)	5 (2)	4 (2)	1 (<1)
Gastrointestinal	Diarrhea	153 (59)	28 (11)	0	27 (12)	1 (<1)	0
	Nausea	147 (57)	6 (2)	1 (<1)	59 (26)	1 (<1)	0
	Vomiting	75 (29)	3 (1)	1 (<1)	23 (10)	1 (<1)	0
Other	Alopecia	119 (46)	0	0	35 (16)	0	0
	Fatigue	115 (45)	8 (3)	0	68 (30)	12 (5)	0

Bardia A et al. ASCO 2022;Abstract 1071.

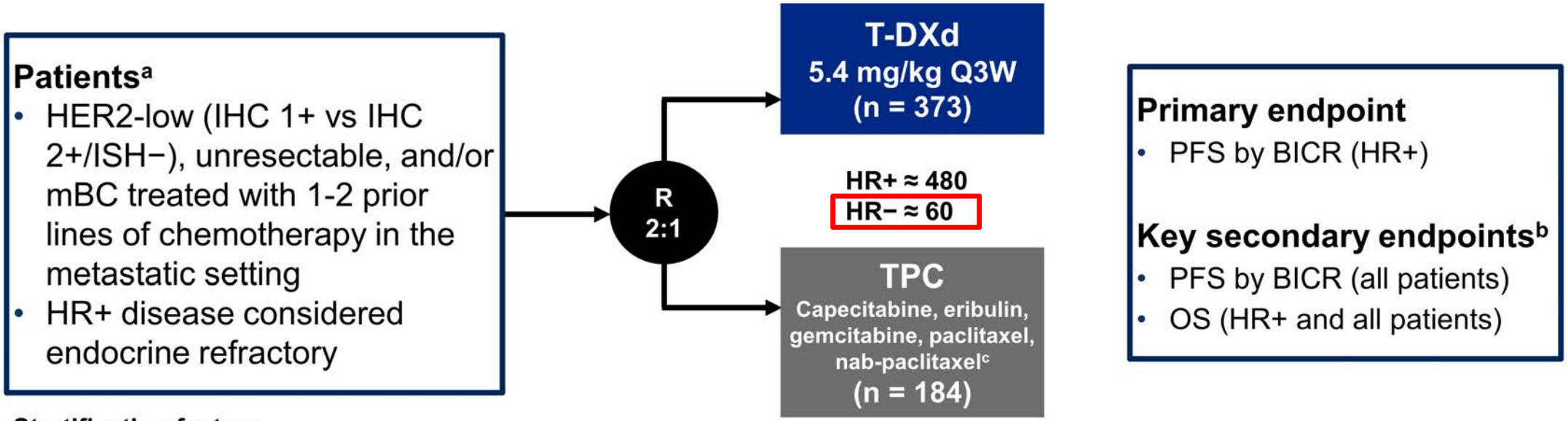
HER2-Low Breast Cancer (IHC 1+, or 2+ and ISH Negative)



Adapted from: Tarantino. JCO.2020;38:1951.

DESTINY-Breast04: First Randomized Phase 3 Study of T-DXd for HER2-low mBC

An open-label, multicenter study (NCT03734029)



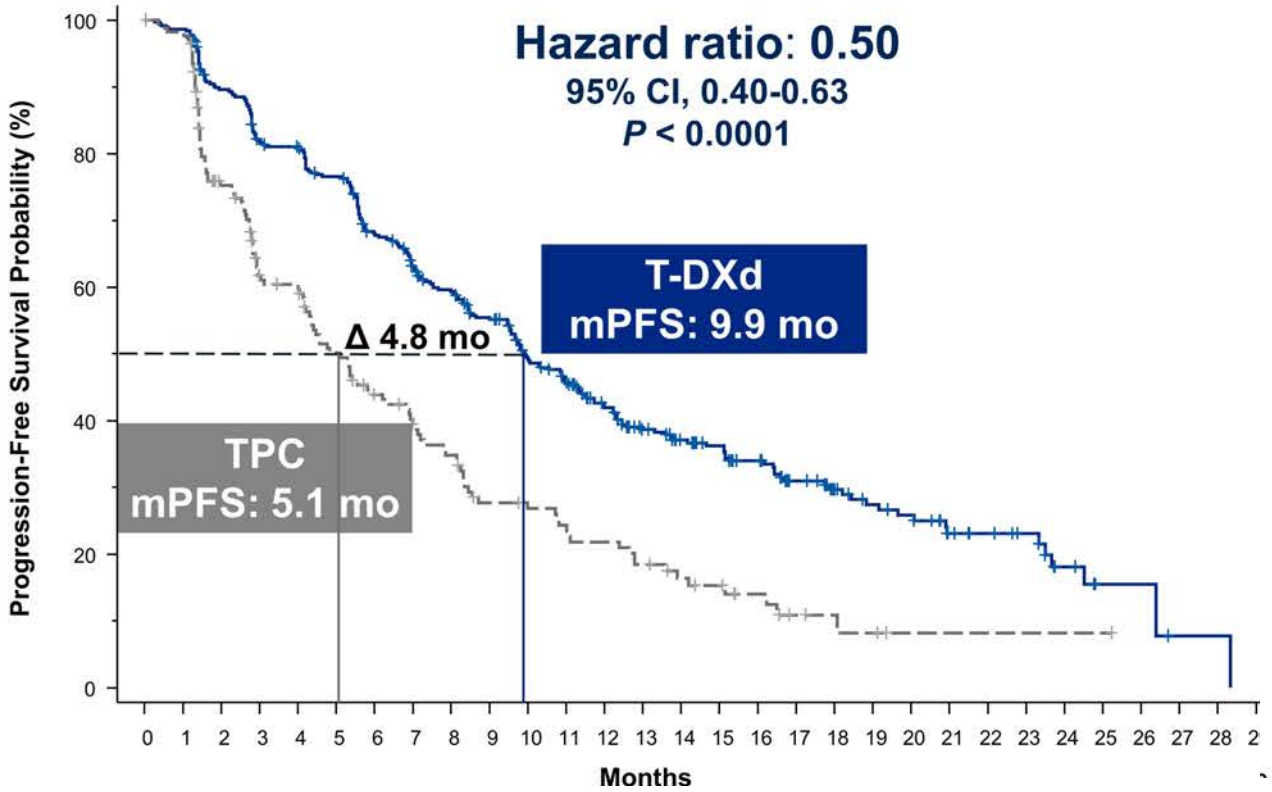
Stratification factors

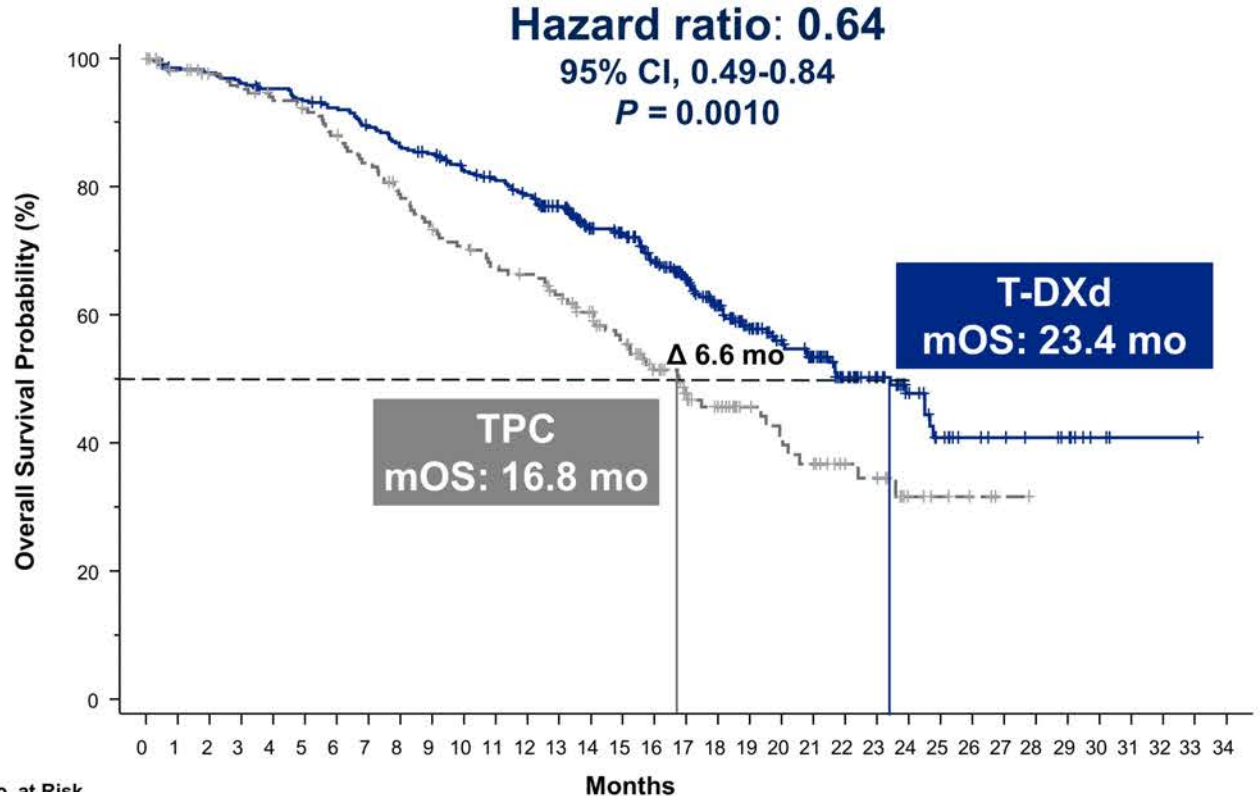
- Centrally assessed HER2 status[d] (IHC 1+ vs IHC 2+/ISH−)
- 1 versus 2 prior lines of chemotherapy
- HR+ (with vs without prior treatment with CDK4/6 inhibitor) versus HR−

ASCO/CAP, American Society of Clinical Oncology/College of American Pathologists; BICR, blinded independent central review; CDK, cyclin-dependent kinase; DOR, duration of response; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; IHC, immunohistochemistry; ISH, in situ hybridization; mBC, metastatic breast cancer; OS, overall survival; PFS, progression-free survival; Q3W, every 3 weeks; R, randomization; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.

[a]If patients had HR+ mBC, prior endocrine therapy was required. [b]Other secondary endpoints included ORR (BICR and investigator), DOR (BICR), PFS (investigator), and safety; efficacy in the HR− cohort was an exploratory endpoint. [c]TPC was administered according to the label. [d]Performed on adequate archived or recent tumor biopsy per ASCO/CAP guidelines using the VENTANA HER2/new (4B5) investigational use only [IOU] Assay system.

PFS and OS in All Patients

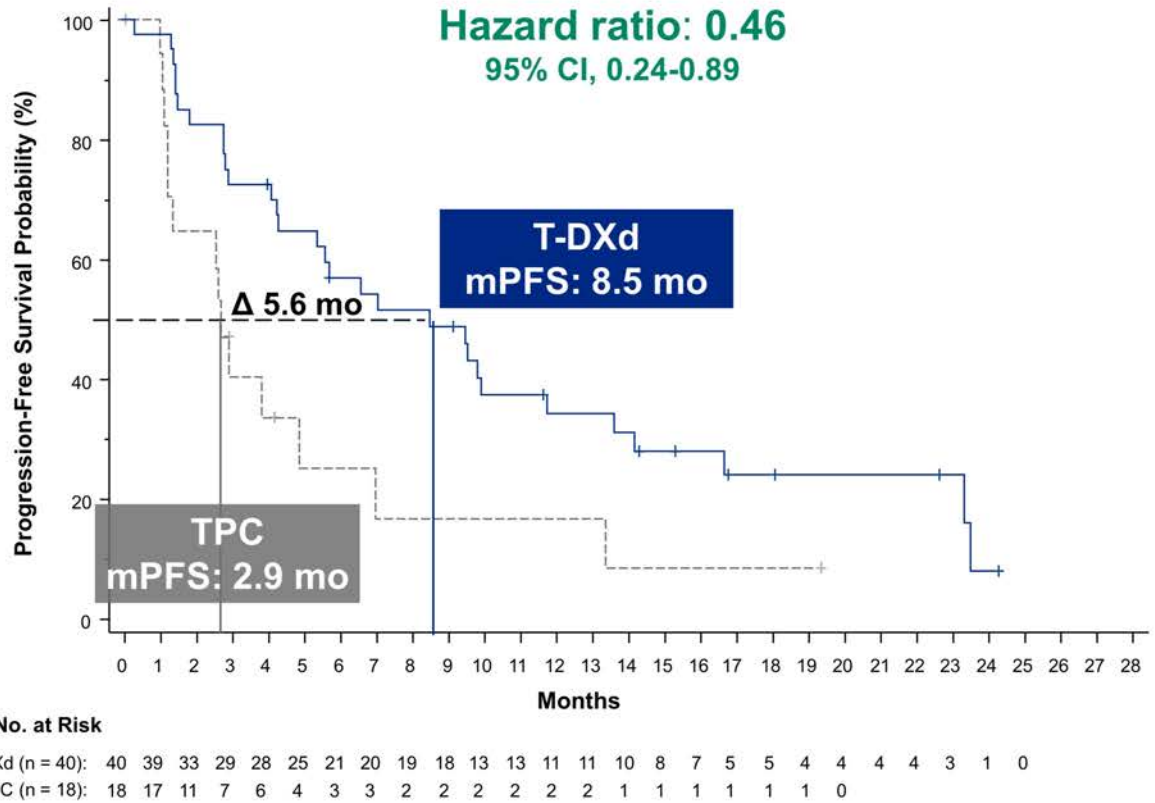




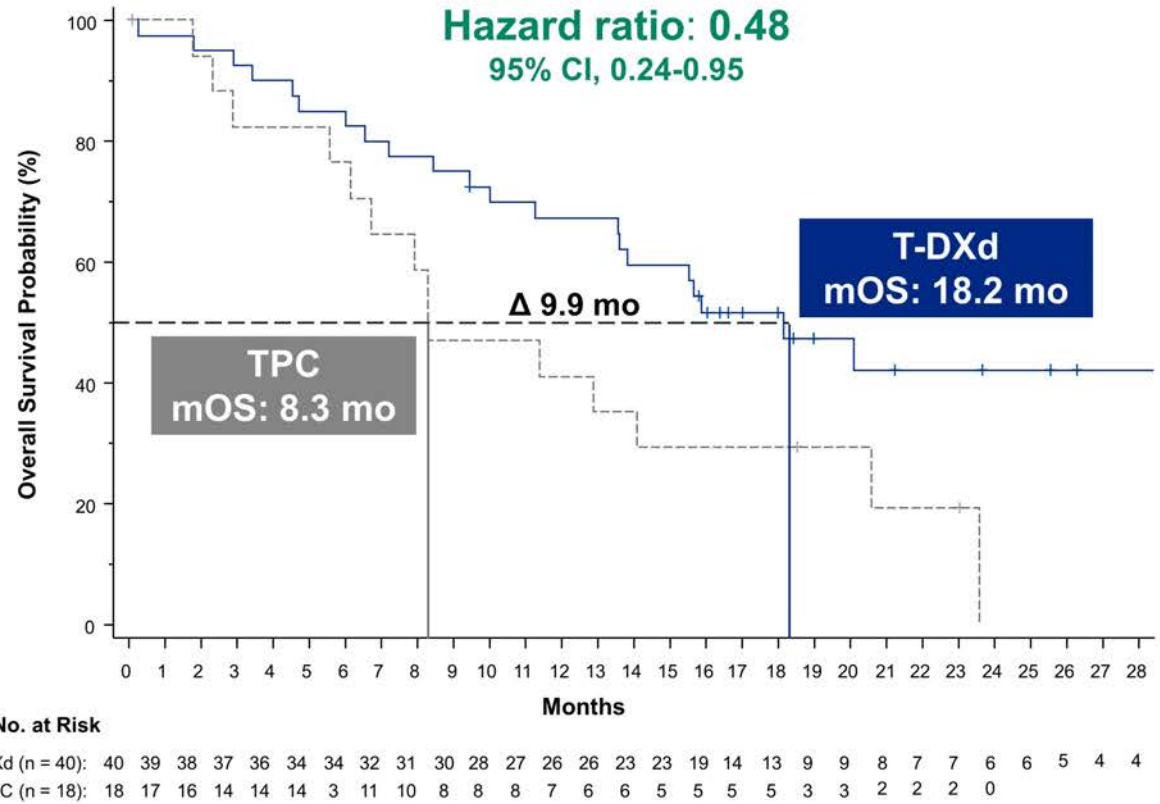
Modi et al ASCO 2022
Modi et al NEJM 2022

PFS and OS in HR− (Exploratory Endpoints)

PFS



OS



HR, hormone receptor; mOS, median overall survival; mPFS, median progression-free survival; OS, overall survival; PFS, progression-free survival; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.
For efficacy in the hormone receptor–negative cohort, hormone receptor status is based on data from the electronic data capture corrected for misstratification.

NOVEL PAYLOADS

First generation ADCs

e.g. T-DM1

Next-generation ADCs

- ↑ therapeutic index
- bystander effect;
- ↑ tissue agnostic profile.

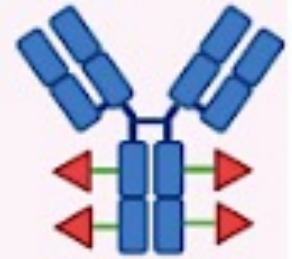
e.g. T-DXd

1) Bispecific ADCs

2) Dual-payload ADCs

3) ADCs with immune-stimulating payloads

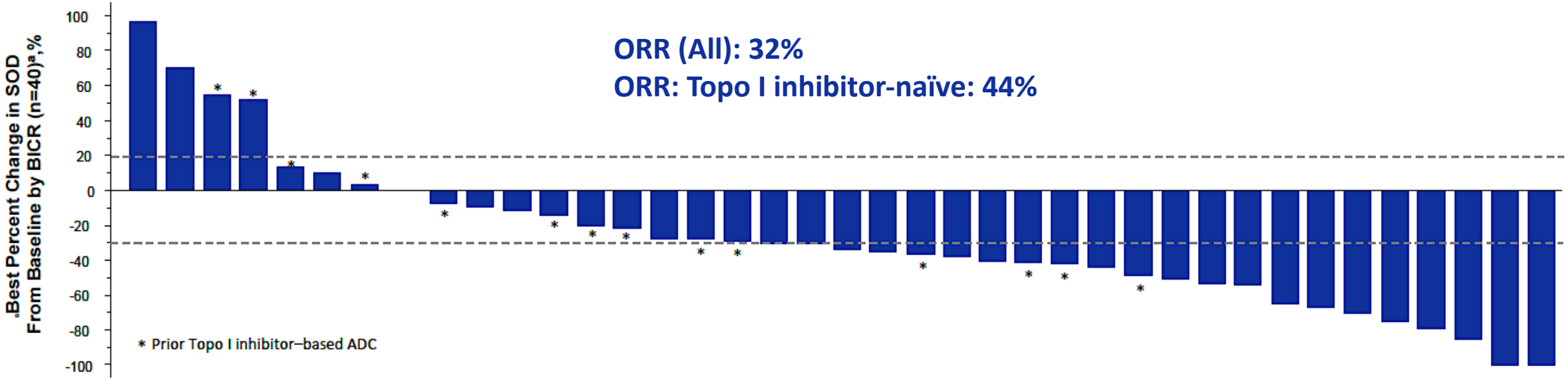
(e.g. TLR8 agonist)



4) Radionuclide ADCs

Adapted from Tarantino et al. Ca Cancer J Clin 2022;72:165-82.

Phase I TROPION-PanTumor01 Study: Response and Survival with Datopotamab Deruxtecan for mTNBC



	All patients (N = 44)	Topo I inhibitor-naïve (N = 30)
Median PFS	4.4 mo	7.3 mo
Median OS	13.5 mo	14.3 mo

Bardia A et al. SABCS 2022;Abstract P6-10-03.

RTP RESEARCH TO PRACTICE

Phase I TROPION-PanTumor01 Study: All Cause Treatment-Emergent Adverse Events (TEAEs) with Datopotamab Deruxtecan

TEAEs, n (%)	N=44	
	Any grade	Grade ≥3
Any TEAE	**44 (100)**	**23 (52)**
Stomatitis	32 (73)	5 (11)
Nausea	29 (66)	1 (2)
Vomiting	17 (39)	2 (5)
Alopecia	16 (36)	NA
Fatigue	15 (34)	3 (7)
Headache	11 (25)	0
Constipation	10 (23)	0
Decreased neutrophil count	9 (20)	1 (2)
Pyrexia	8 (18)	0
Cough	8 (18)	0
Decreased lymphocyte count	8 (18)	3 (7)
Anemia	7 (16)	1 (2)
Decreased appetite	7 (16)	0
Hypokalemia	7 (16)	0
Diarrhea	7 (16)	0
Rash	7 (16)	0
Dry eye	7 (16)	0

Bardia A et al. SABCS 2022;Abstract P6-10-03.

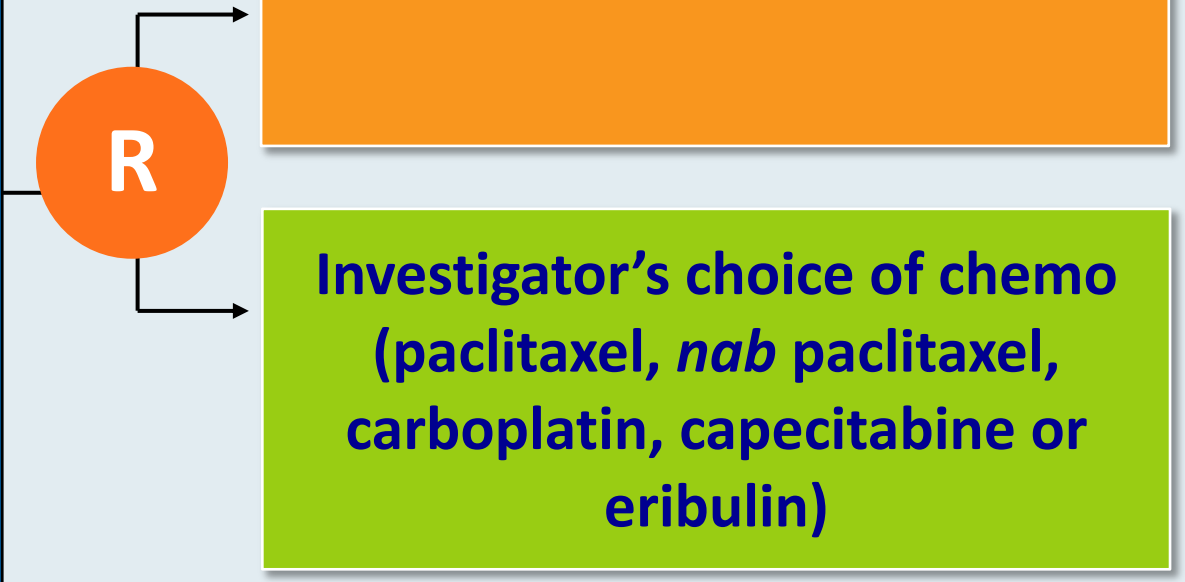
TROPION-Breast02 Phase III Study Design

Estimated enrollment (N = 600)

Estimated primary completion: Dec 2025

Eligibility

- Previously untreated HR-negative, HER2-negative locally advanced, unresectable or metastatic TNBC
- PD-L1-negative or PD-L1-positive but relapsed after prior ICI for localized BC, or comborbidities precluding ICI, or no regulatory access to pembrolizumab



ICI = immune checkpoint inhibitor

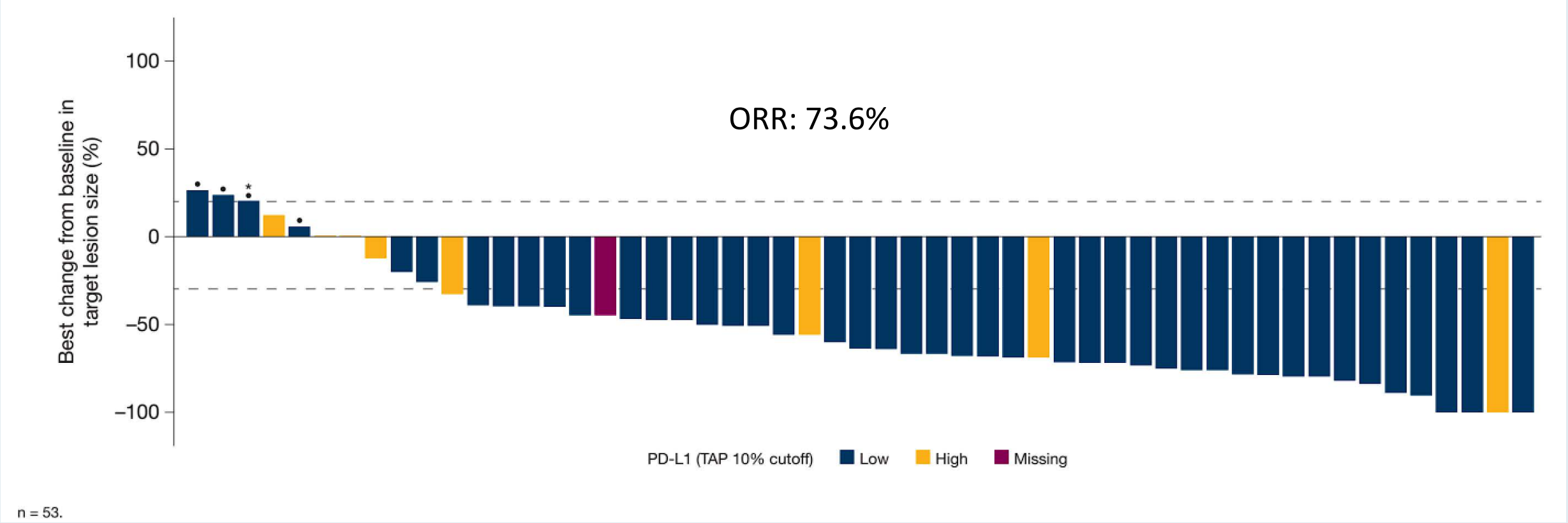
Coprimary endpoints: PFS by BICR, OS

Secondary endpoints: ORR, DoR, PFS (investigator), DCR TFST, TSST, PFS2, others

www.clinicaltrials.gov. NCT05374512. Accessed October 2023.

RTP RESEARCH TO PRACTICE

Phase Ib/II BEGONIA Study: Antitumor Activity of Dato-DXd and Durvalumab for Unresectable Locally Advanced or Metastatic TNBC



Schmid P et al. SABCS 2022;Abstract PD11-09.

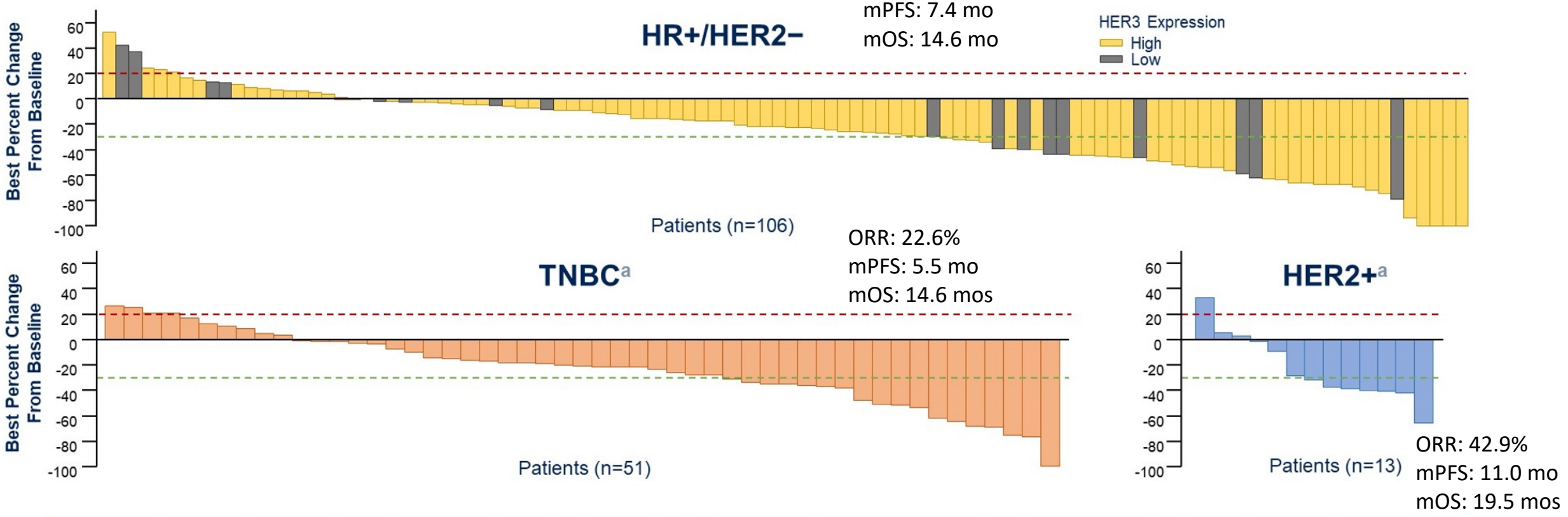
RTP RESEARCH TO PRACTICE

BEGONIA: Safety Summary with Dato-DXd and Durvalumab

	N=61
Common AEs (≥20% patients, any grade)	
Nausea	35 (57.4)
Stomatitis	34 (55.7)
Alopecia	28 (45.9)
Fatigue, constipation	24 (39.3) each
Rash	17 (27.9)
Vomiting	13 (21.3)
Any Grade 3/4 AE	25 (41.0)
Any serious AE	10 (16.4)
AE leading to dose interruption	27 (44.3)
AE leading to death[b]	1 (1.6)
Durvalumab dose delay	25 (41.0)
Dato-DXd dose delay	23 (37.7)
Dato-DXd dose reduction	12 (19.7)

Schmid P et al. SABCS 2022;Abstract PD11-09.

Phase I/II Study of Patritumab Deruxtecan for HER3-Expressing Metastatic Breast Cancer



HER3-DXd induced a clinically meaningful decrease in tumor size by BICR in most patients across BC subtypes.[b]

Krop IE et al. ASCO 2022;Abstract 1002; Krop IE et al. *J Clin Oncol* 2023;[Online ahead of print].

RTP RESEARCH TO PRACTICE

Phase I/II Study of Patritumab Deruxtecan for HER3-Expressing Metastatic Breast Cancer: Overall Safety and ILD

Patients	4.8 mg/kg (n = 48)	6.4 mg/kg (n = 98)	All Doses (N = 182)
Any TEAE, No. (%)	47 (97.9)	98 (100)	181 (99.5)
Associated with discontinuation	5 (10.4)	8 (8.2)	18 (9.9)[a]
Associated with dose reduction	6 (12.5)	22 (22.4)	35 (19.2)
Associated with drug interruption	23 (47.9)	57 (58.2)	100 (54.9)
Associated with death	1 (2.1)	6 (6.1)	7 (3.8)[b]
Serious TEAE	13 (27.1)	36 (36.7)	60 (33.0)
Grade ≥3 TEAE, No. (%)	31 (64.6)	80 (81.6)	130 (71.4)
Treatment-related TEAE, No. (%)	47 (97.9)	97 (99.0)	180 (98.9)
Associated with death	0	1 (1.0)[c]	1 (0.5)[c]
Grade ≥3	27 (56.3)	76 (77.6)	120 (65.9)
Serious TEAE	7 (14.6)	23 (23.5)	38 (20.9)

- Treatment-related interstitial lung disease (ILD) occurred in 12 patients (6.6%); the majority of cases were Grade 1 or 2
  - Grade 3 ILD: 3 (1.6%)
  - Grade 5 ILD: 1 (0.5%, cause of death according to central adjudication was deemed not related to ILD by the treating investigator)

Krop IE et al. *J Clin Oncol* 2023;[Online ahead of print].

RTP RESEARCH TO PRACTICE

A Taste of ESMO….

LBA18 - Pembrolizumab or placebo plus chemotherapy followed by pembrolizumab or placebo for early-stage TNBC: Updated EFS results from the phase 3 KEYNOTE-522 study

LBA19 - Event-free survival (EFS) analysis of neoadjuvant taxane/carboplatin with or without atezolizumab followed by an adjuvant anthracycline regimen in high-risk triple negative breast cancer (TNBC): NeoTRIP Michelangelo randomized study

LBA20 - A randomized, double-blind trial of nivolumab (NIVO) vs placebo (PBO) with neoadjuvant chemotherapy (NACT) followed by adjuvant endocrine therapy (ET) ± NIVO in patients (pts) with high-risk, ER+ HER2– primary breast cancer (BC)

LBA21 - KEYNOTE-756: Phase 3 study of neoadjuvant pembrolizumab (pembro) or placebo (pbo) + chemotherapy (chemo), followed by adjuvant pembro or pbo + endocrine therapy (ET) for early-stage high-risk ER+/HER2– breast cancer

HER2+ Breast Cancer

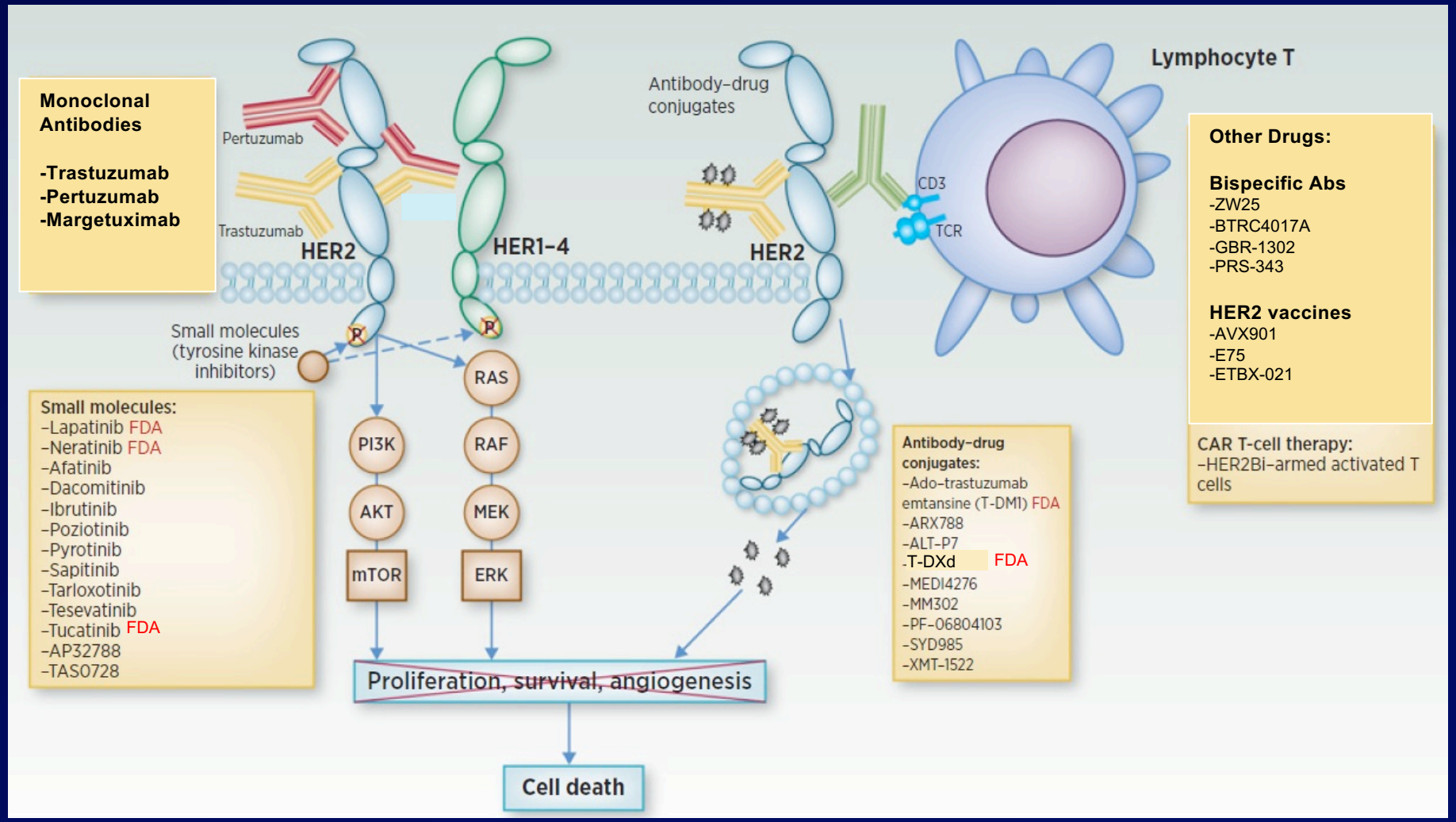
Sara A. Hurvitz, MD, FACP

Professor of Medicine
Head, Division of Hematology/Oncology,
University of Washington School of Medicine
Senior Vice President, Clinical Research Division,
Fred Hutchinson Cancer Center

Fred Hutch Cancer Center

UNIVERSITY of WASHINGTON

The Expanding Armamentarium of Agents for HER2+ Breast Cancer



PI3K = phosphoinositide-3 kinase; AKT = a serine/threonine kinase; mTOR = mammalian target of rapamycin.

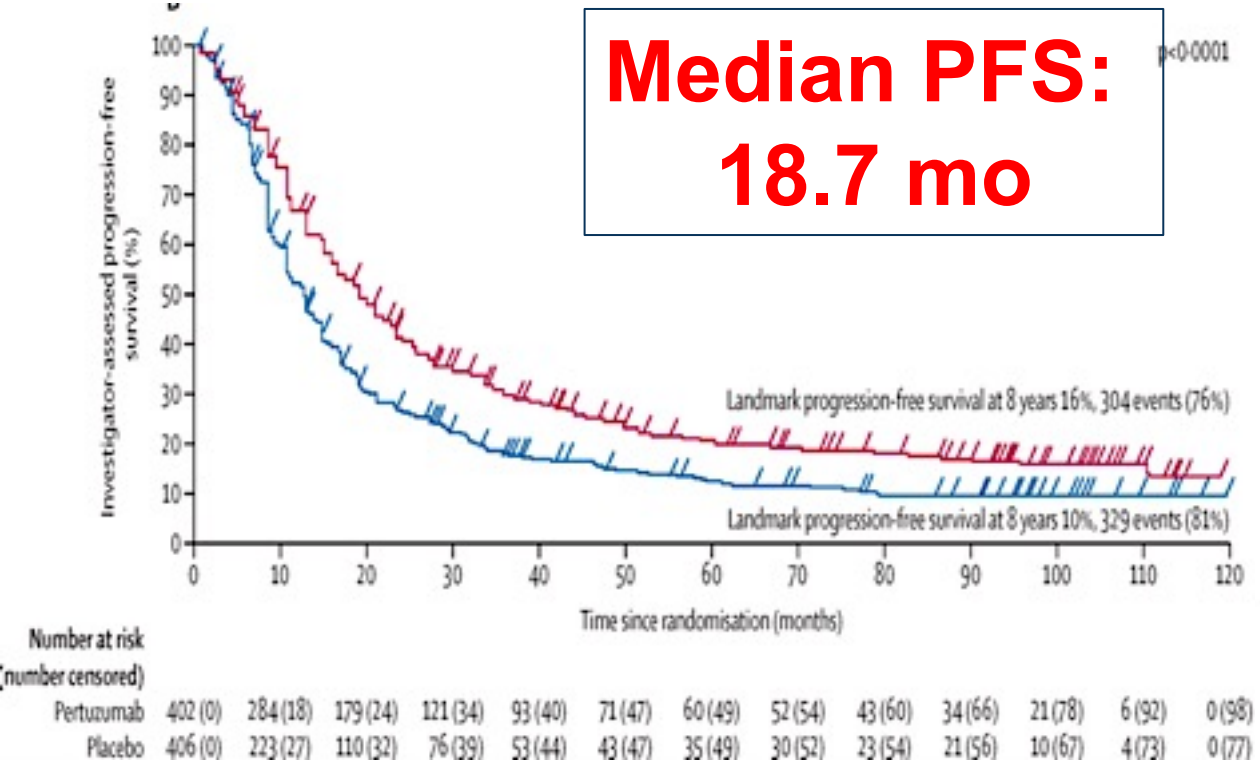
Meric-Bernstam F, et al. *Clin Cancer Res.* 2019;25:2033-2041.

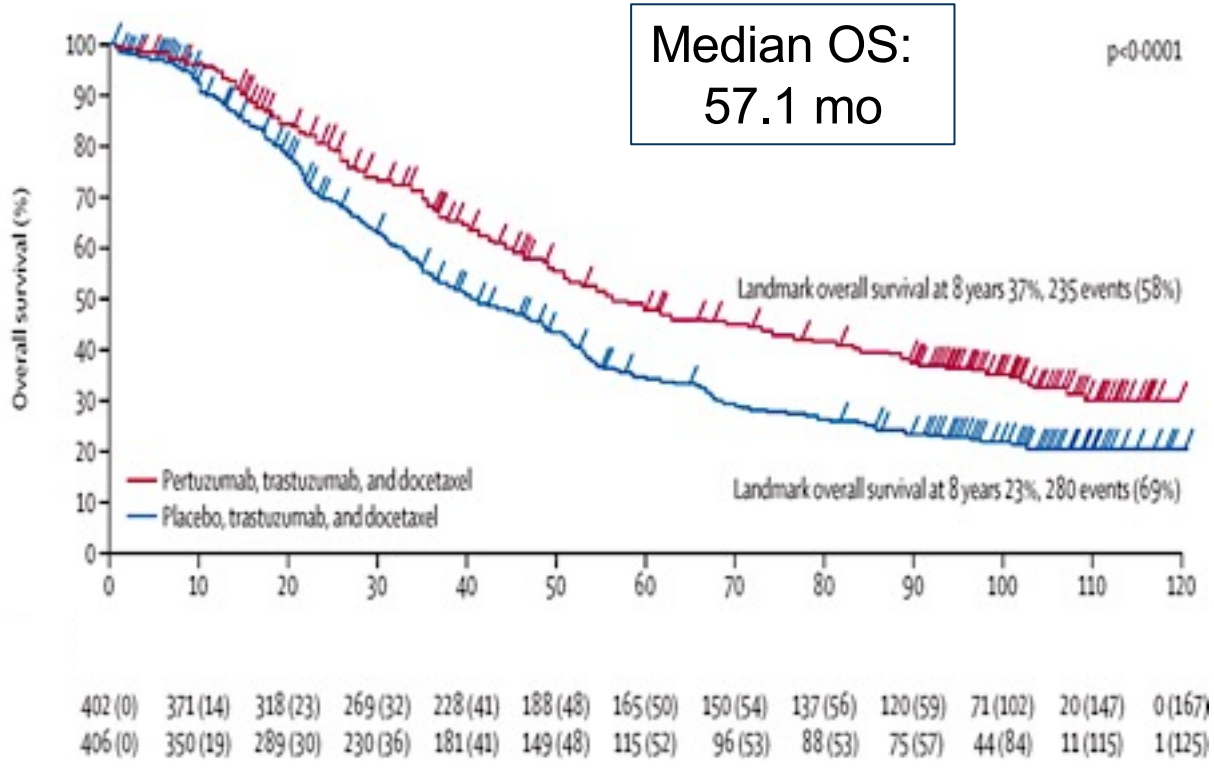
1st Line Metastatic Breast Cancer

Pertuzumab plus Trastuzumab (HP) plus Chemo

CLEOPATRA End-of-Study Results:
Adding Pertuzumab to Taxane + Trastuzumab Improves PFS and OS

(median follow-up ~100 months)





Swain S, et al. Lancet Oncol. 2020;21:519-530.

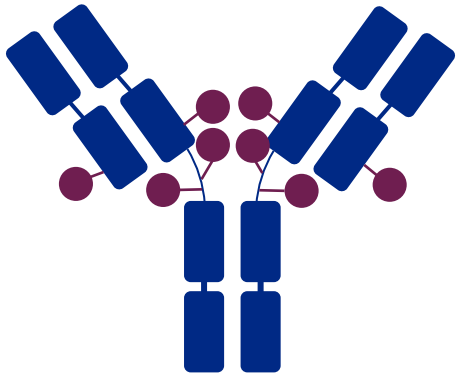
Second Line Therapy
(after trastuzumab/taxane)

Trastuzumab Deruxtecan (T-DXd): a Novel HER2 ADC

Characteristic Differences Between T-DXd and T-DM1

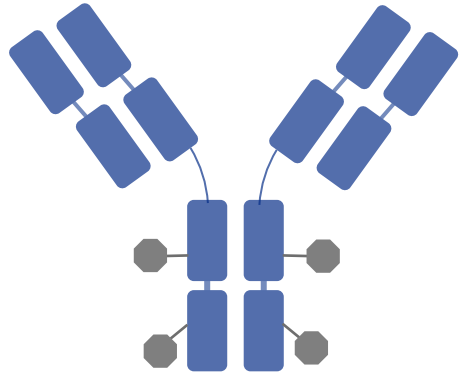
HER2 Targeting ADCs with similar mAB Backbone

Trastuzumab deruxtecan (T-DXd)[1]



T-DXd[1-4]	ADC Attributes	T-DM1[4-6]
Topoisomerase I inhibitor	**Payload MoA**	Anti-microtubule
~8:1	**Drug-to-antibody ratio**	~3.5:1
Yes	**Tumor-selective cleavable linker?**	No
Yes	**Evidence of bystander anti-tumor effect?**	No

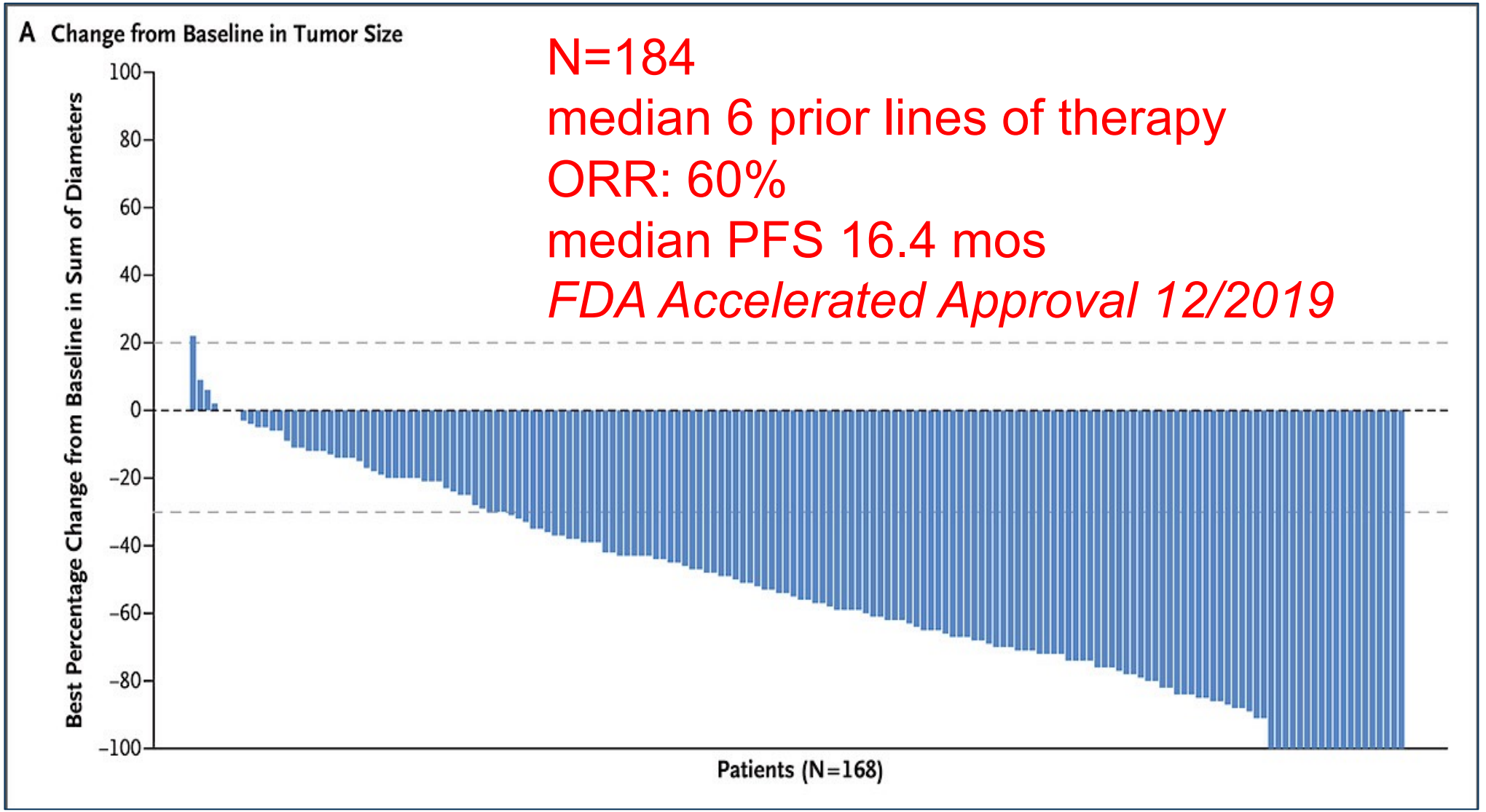
Trastuzumab emtansine (T-DM1)[1]



Abbreviations: ADC, antibody-drug conjugate; MoA, mechanism of action.

1. Cortes J, et al. Abstract LBA-1. Presented at: ESMO 2021 Annual Meeting; September 16-21, 2021. 2. Nakada T et al. *Chem Pharm Bull (Tokyo).* 2019;67:173-85. 3. Ogitani Y et al. *Clin Cancer Res.* 2016;22:5097-108. 4. Trail PA et al. *Pharmacol Ther.* 2018;181:126-42. 5. Ogitani Y et al. *Cancer Sci.* 2016;107:1039-46. 6. LoRusso PM et al. *Clin Cancer Res*. 2011;17:6437-47.

DESTINY-Breast01 Phase II single arm study: Response to Trastuzumab Deruxtecan



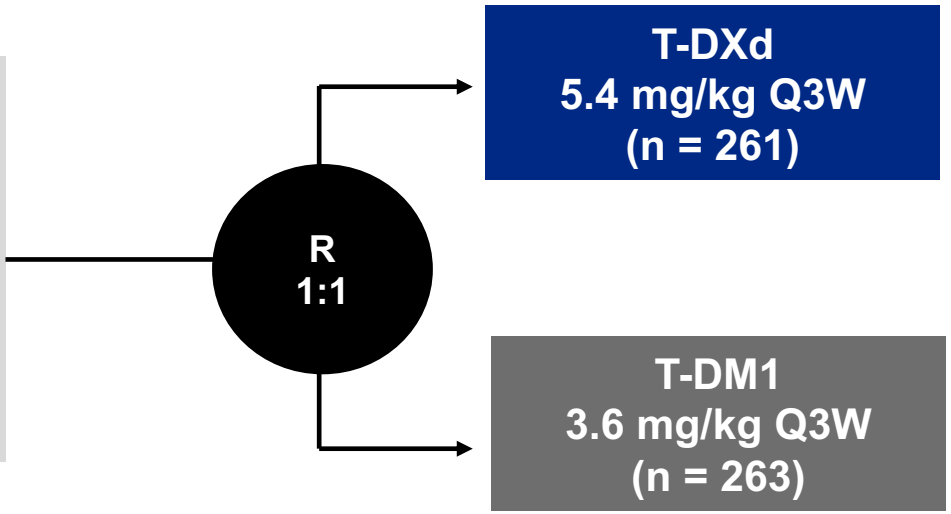
Modi et al. N Engl J Med 2020;382:610-621.

DESTINY-Breast03

Randomized, open-label, multicenter study (NCT03529110)

Patients (N = 524)

- Unresectable or metastatic HER2-positive[a] breast cancer
- Previously treated with trastuzumab and a taxane in metastatic or (neo)adjuvant setting with recurrence within 6 months of therapy[b]



Primary endpoint

- PFS (BICR)

Key secondary endpoint

- OS[c]

Secondary endpoints

- ORR (BICR and investigator)
- DoR (BICR)
- Safety

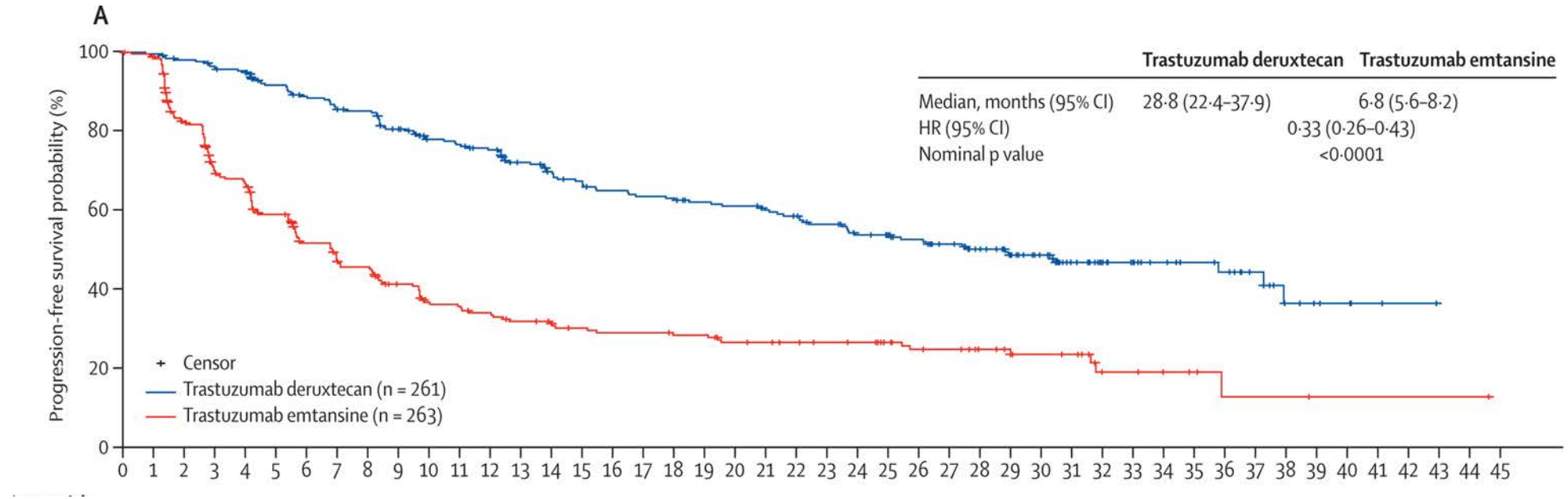
Stratification factors

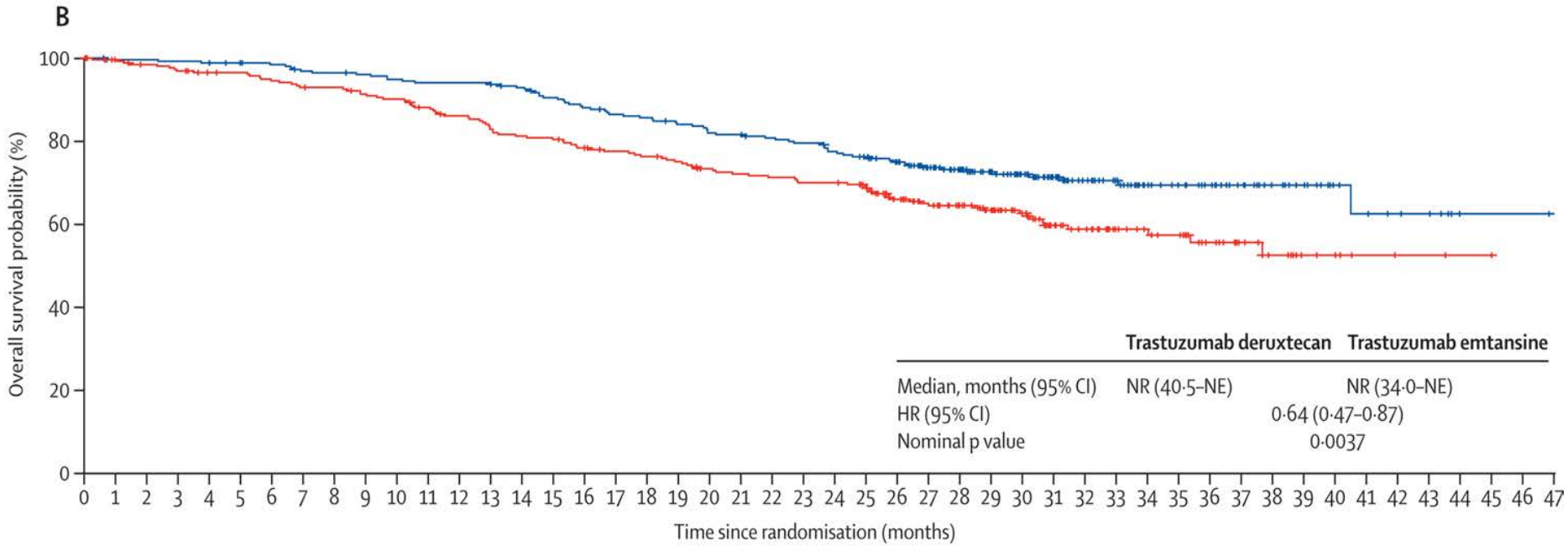
- Hormone receptor status
- Prior treatment with pertuzumab
- History of visceral disease

The prespecified OS interim analysis was planned with 153 events.[d] At the time of data cutoff (July 25, 2022), 169 OS events were observed and the *P* value to achieve statistical significance was 0.013

BICR, blinded independent central review; DoR, duration of response; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; Q3W, every 3 weeks; R, randomization; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.

[a]HER2 IHC 3+ or IHC 2+/ISH+ based on central confirmation. [b]Progression during or within 6 months after completing adjuvant therapy involving trastuzumab and a taxane. [c]80% powered at 2-sided significance level of 5%. [d]Information fraction of 61%, with a *P* value boundary to reach statistical significance of 0.008. The *P* value was recalculated based on the actual OS events at the data cutoff.

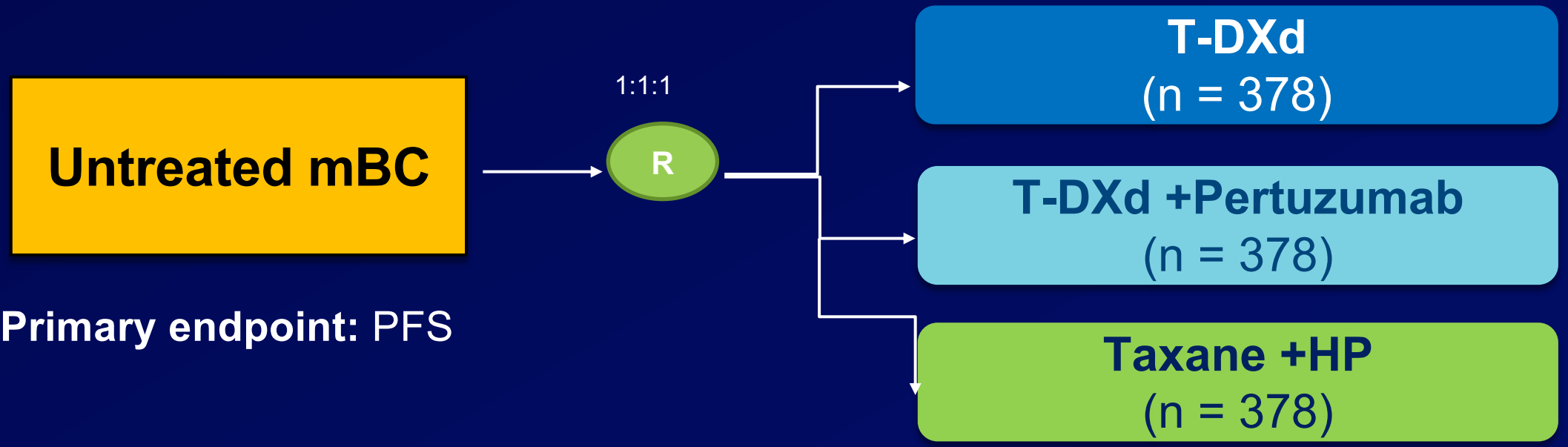




https://doi.org/10.1016/S0140-6736(22)02420-5

First line Standard May Soon Change

DESTINY-Breast09 (NCT04784715): 1st Line Trial in HER2+ MBC



Primary endpoint: PFS

- **But how will QoL compare after taxane is dropped in THP arm?**

Third Line Therapy
(after T-DM1)

DESTINY-Breast02

Randomized phase 3, open-label, multicenter study (NCT03523585)

Key eligibility criteria[a]
- Centrally confirmed HER2-positive (IHC 3+ or IHC 2+/ISH+) unresectable or metastatic breast cancer
- Documented radiographic progression after most recent treatment
- Previously treated with T-DM1

Stratification factors
- Hormone receptor status
- Prior treatment with pertuzumab
- History of visceral disease

R 2:1

T-DXd
5.4 mg/kg Q3W
(n = 406)

TPC
Per label (n = 202)
- Trastuzumab / Capecitabine

or
- Lapatinib / Capecitabine

Primary endpoint
- PFS (BICR[b])

Key secondary endpoint
- OS

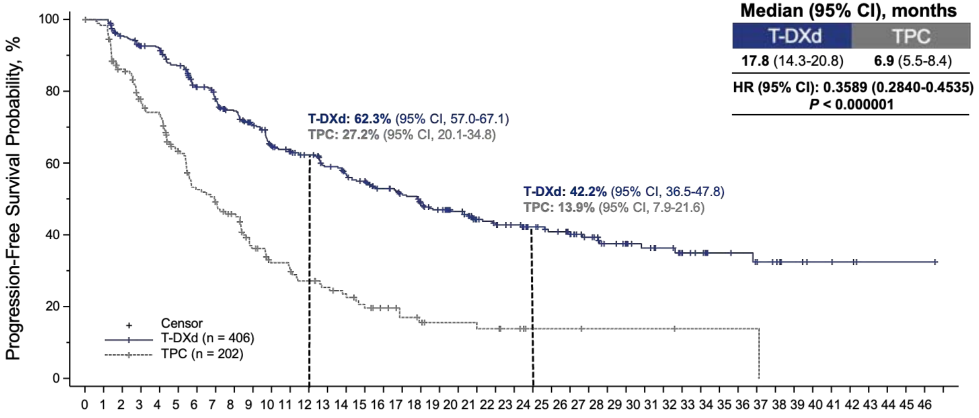
Secondary endpoints
- ORR (BICR[b])
- DoR (BICR[b])
- PFS (investigator)
- Safety

Exploratory endpoints
- CBR (BICR[b])
- PFS2[c] (investigator)

Median F/U ~20m

DESTINY-Breast02

Primary Endpoint: PFS by BICR



Patients still at risk

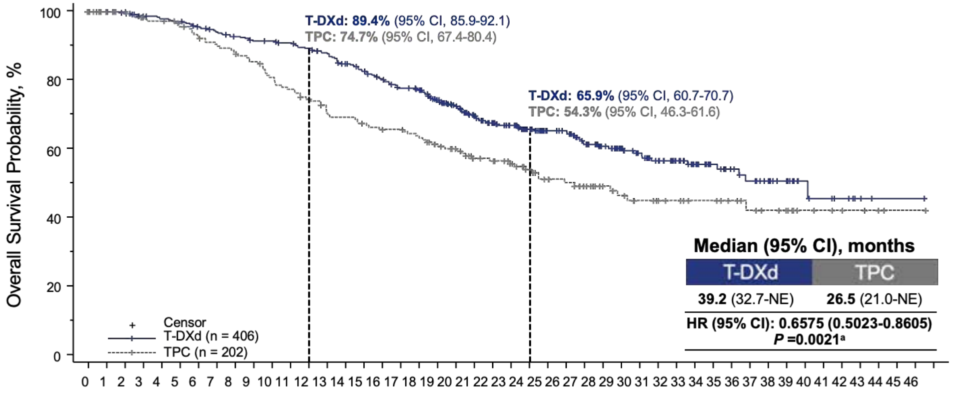
Arm	Months 0–46
T-DXd (406)	406 400 374 359 355 330 296 278 260 239 213 203 194 179 170 161 149 141 132 119 109 88 83 76 65 60 55 47 38 35 31 27 23 19 15 14 12 10 6 4 4 3 1 1 1 1 0
TPC (202)	202 180 148 126 118 95 78 72 64 48 39 37 32 28 24 20 17 13 11 9 9 8 8 6 3 3 3 2 2 2 2 2 1 1 1 1 1 0

BICR, blinded independent central review; HR, hazard ratio; mo, month; PFS, progression-free survival; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.

Krop. SABCS 2022. Abstr GS2-01.

DESTINY-Breast02

Key Secondary Endpoint: OS



Patients still at risk

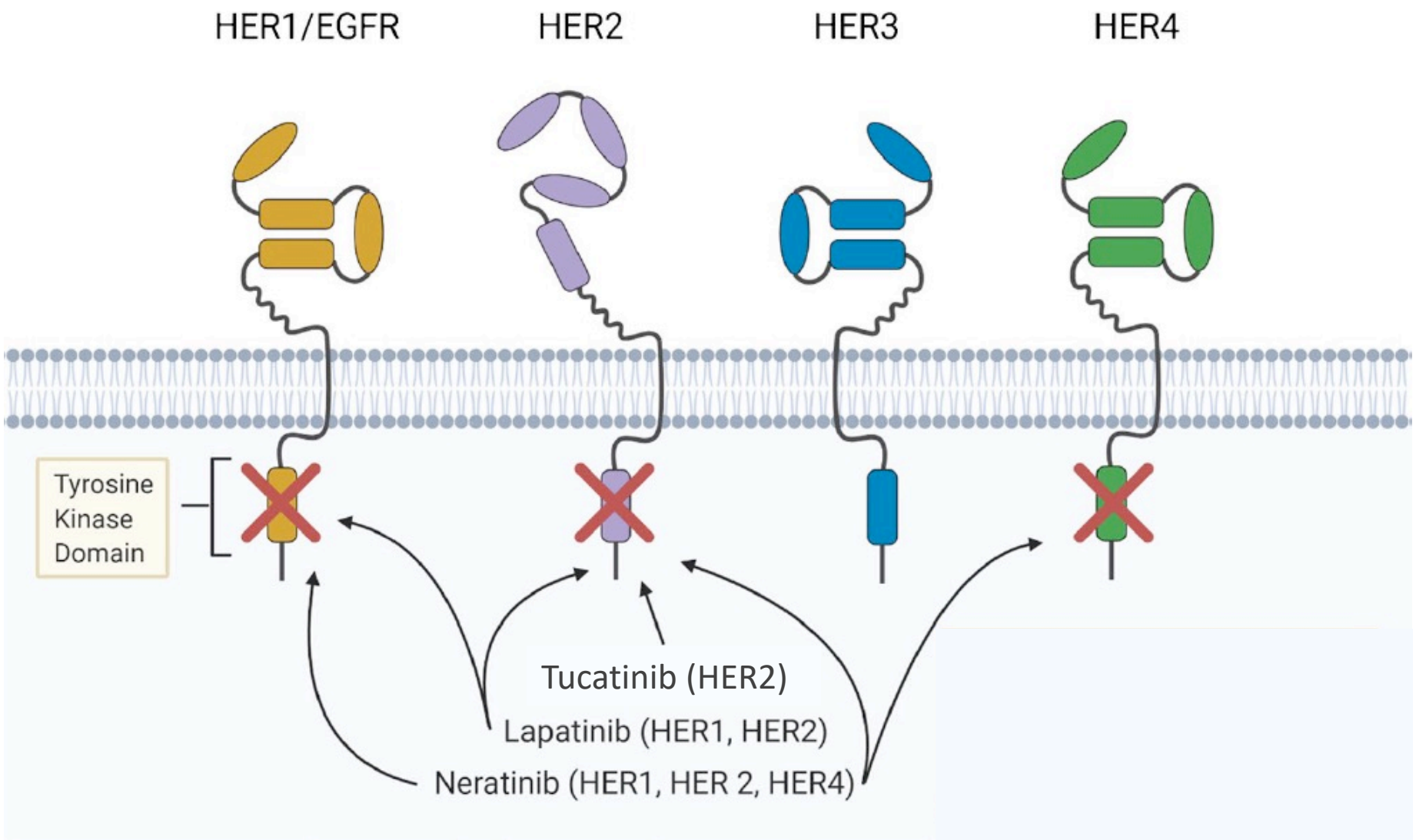
Arm	Months 0–46
T-DXd (406)	406 404 400 390 385 382 374 366 357 352 350 346 339 331 317 306 295 282 277 257 234 215 196 183 160 144 139 122 104 93 82 72 63 51 40 34 29 25 19 10 8 6 3 1 1 1 0
TPC (202)	202 192 187 182 178 173 167 161 157 151 142 136 130 124 118 114 111 110 106 95 89 79 76 72 61 53 50 46 38 33 29 28 25 22 22 18 15 13 12 7 6 5 4 3 1 1 0

In the TPC arm
- **69.3% (140/202) of patients received a new systemic anticancer treatment**
- **25.7% (52/202) of patients received T-DXd in the post-trial setting**

[a]The boundary for statistical significance is 0.0040. HR, hazard ratio; mo, month; NE, not estimable; OS, overall survival; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.

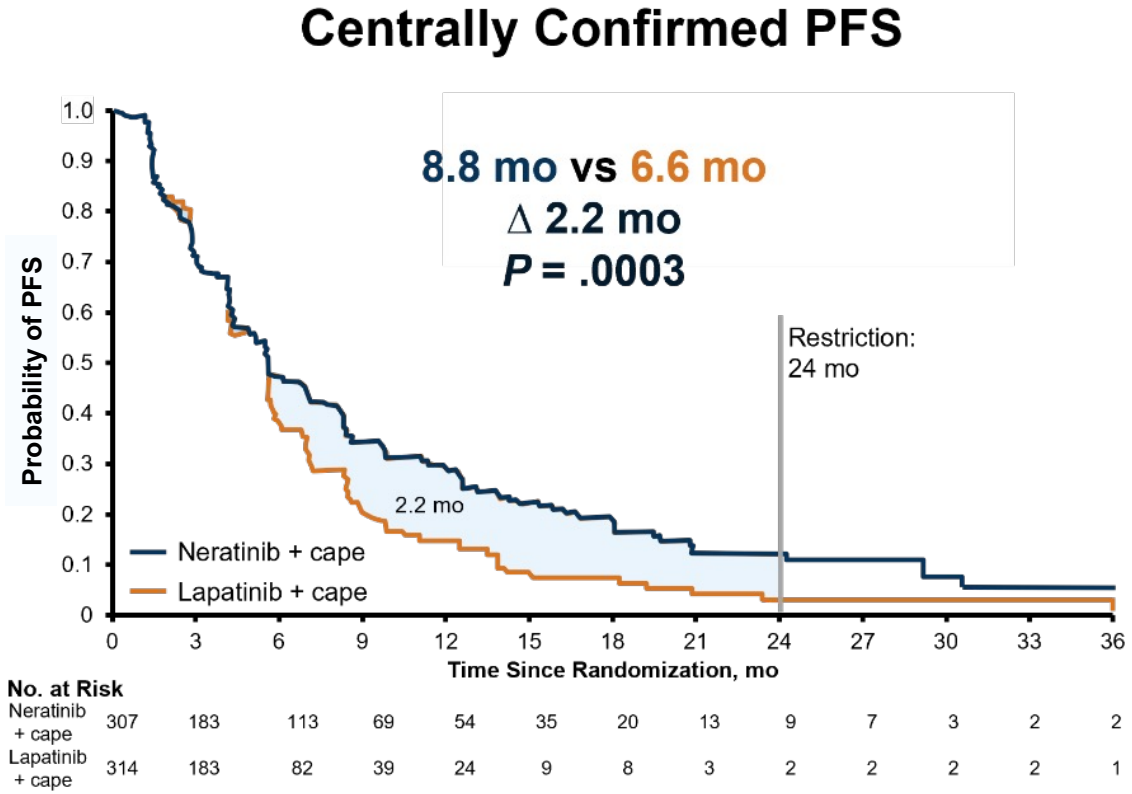
Krop. SABCS 2022. Abstr GS2-01.

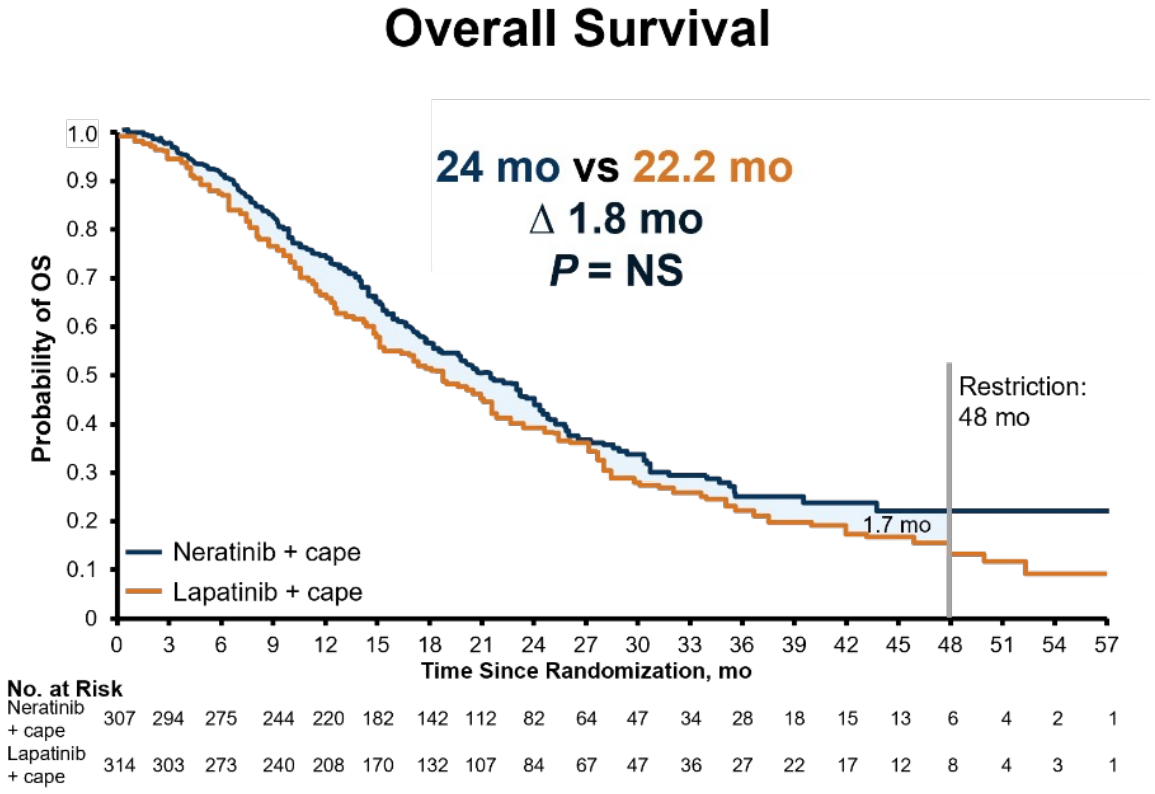
HER2-targeted tyrosine kinase inhibitors



1. Dent SF, et al. Curr Oncol Rep. 2021;23:128. 2. Murthy R, et al. Lancet Oncol. 2018;19:880-888.

Neratinib+Capecitabine: NALA Trial Results





- 1-y PFS: **29%** vs 15%
- ORR: **33%** vs 27% (*P* = .1201)
- Median DOR: **8.5 mo** vs 5.6 mo (HR = 0.50, 95% CI, 0.33-0.74; *P* = .0004)
- Fewer interventions for CNS dz occurred with N+C VS. L+C (22.8% vs. 29.2%, *P*=0.043).

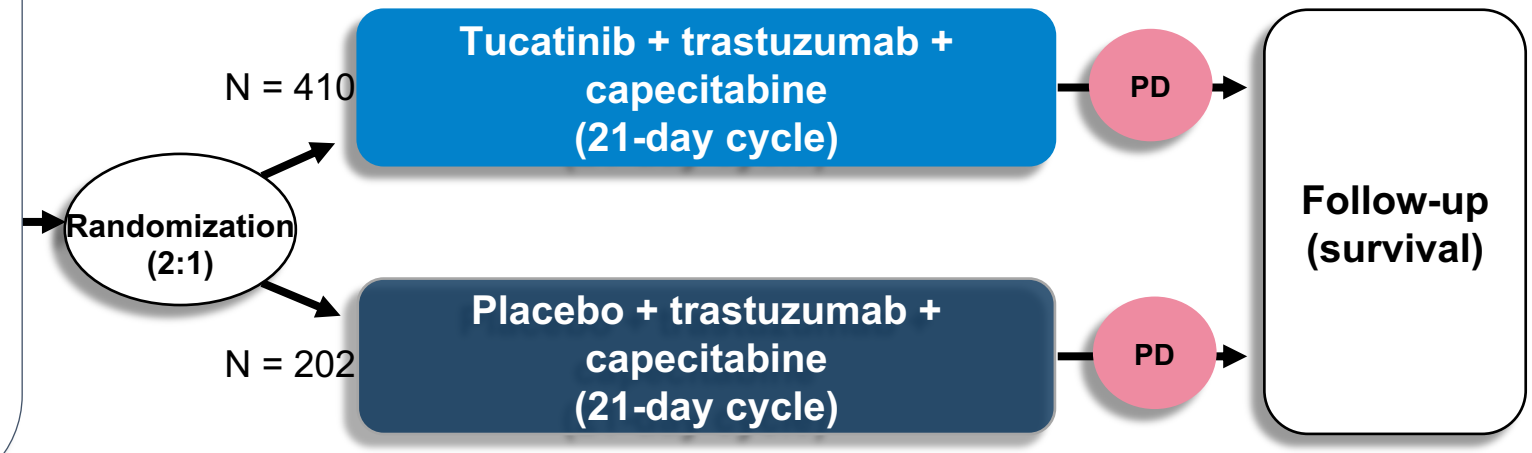
Saura C, et al. J Clin Oncol. 2020; 38(27):3138-49.

HER2CLIMB

Tucatinib + Trastuzumab + Capecitabine vs Placebo + Trastuzumab + Capecitabine

Inclusion criteria

- HER2+ metastatic breast cancer
- Prior treatment with trastuzumab, pertuzumab, and T-DM1
- ECOG 0, 1
- *Brain MRI at baseline*
  - *No evidence of brain metastases, or*
  - *Untreated, previously treated stable, or previously treated progressing, brain metastases not needing immediate local therapy*



Stratification variables

- Presence of brain metastases (yes/no)
- ECOG status (0 or 1)
- Region of the world (US or Canada or rest of world)

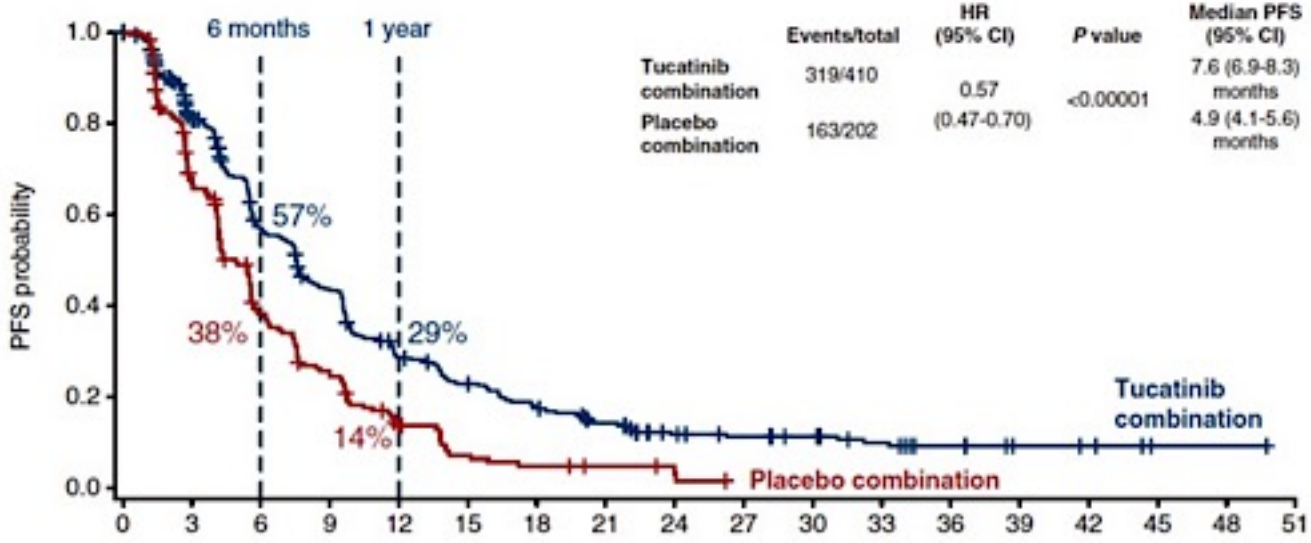
Endpoints

- Primary: PFS (first 480 patients randomized)
- Secondary: OS (total population), PFS among patients with brain metastases, ORR

Notable baseline characteristic: *48% of patients had CNS metastases*

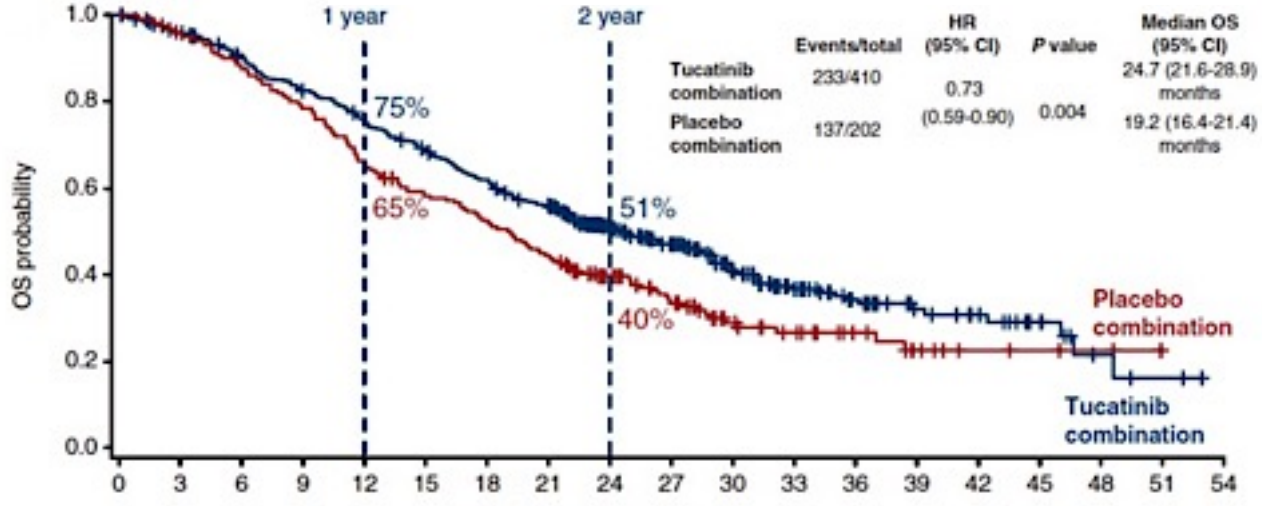
Murthy R, et al. *N Engl J Med.* 2020;382:597-609.

HER2CLIMB: Progression-Free Survival (PFS)



	Events/total	HR (95% CI)	*P* value	Median PFS (95% CI)
Tucatinib combination	319/410	0.57 (0.47-0.70)	<0.00001	7.6 (6.9-8.3) months
Placebo combination	163/202			4.9 (4.1-5.6) months

Final Overall Survival Analysis



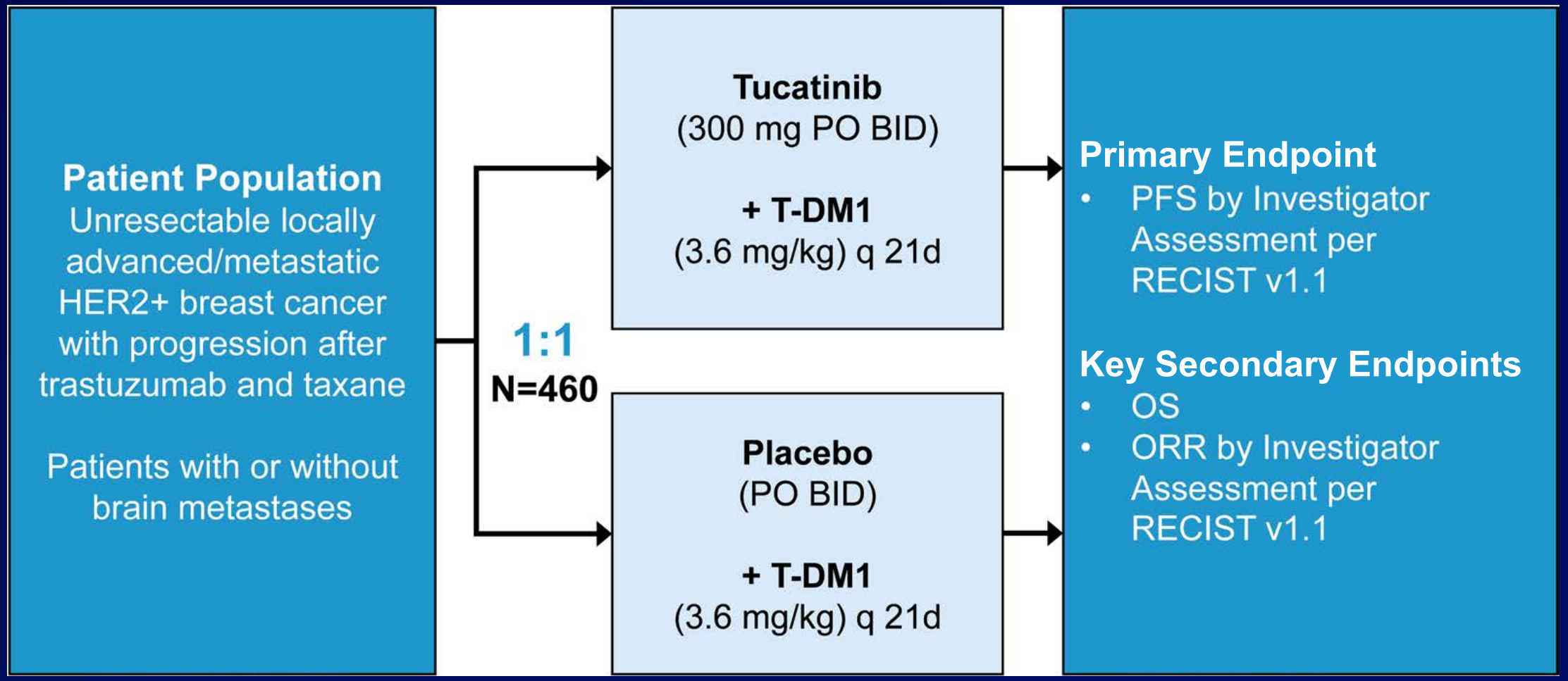
	Events/total	HR (95% CI)	*P* value	Median OS (95% CI)
Tucatinib combination	233/410	0.73 (0.59-0.90)	0.004	24.7 (21.6-28.9) months
Placebo combination	137/202			19.2 (16.4-21.4) months

Patients at risk

Tucatinib combination	410	387	356	325	295	268	241	214	153	122	81	56	38	24	19	11	4	2	0
Placebo combination	202	191	174	156	129	114	103	87	63	47	28	21	14	8	4	3	2	0	0

Curigliano G et al. *Ann Oncol* 2022;33(3):321-29.

HER2CLIMB-02: A Randomized, Double-Blind, Phase 3 Study of Tucatinib or Placebo With T-DM1 for Metastatic HER2+ Breast Cancer



Hurvitz S et al. ESMO 2020

Phase III Trial of Tucatinib in Combination with Ado-Trastuzumab Emtansine Meets Primary Endpoint of Progression-Free Survival in Patients with Previously Treated HER2-Positive Metastatic Breast Cancer

Press Release: August 16, 2023

"[The manufacturer] today announced that the Phase 3 HER2CLIMB-02 clinical trial of tucatinib in combination with the antibody-drug conjugate ado-trastuzumab emtansine met its primary endpoint of progression-free survival (PFS). Patients in the trial had unresectable locally advanced or metastatic human epidermal growth factor receptor 2-positive (HER2-positive) breast cancer and had received previous treatment with a taxane and trastuzumab. Overall survival (OS) data, a secondary endpoint, are not yet mature. Discontinuations due to adverse events were more common in the combination arm of the trial, but no new safety signals emerged for the combination.

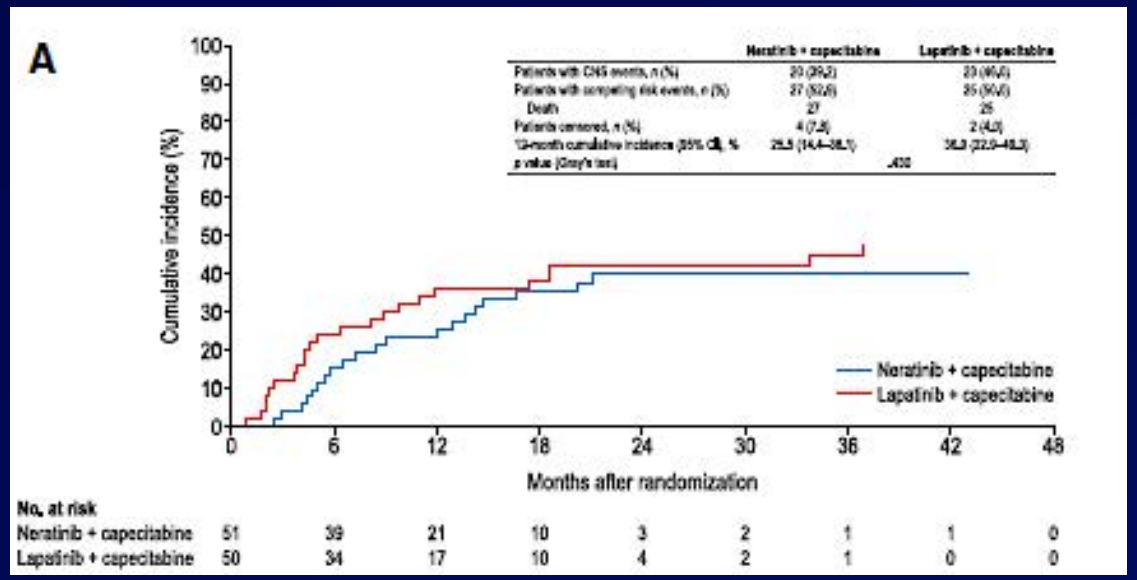
'We are encouraged by these results for tucatinib in combination with trastuzumab in metastatic HER2-positive breast cancer, including in patients with brain metastases,' said Roger Dansey, President of Research and Development and Chief Medical Officer…. 'We plan to present the HER2CLIMB-02 data at an upcoming medical meeting and discuss the results with the FDA.'"

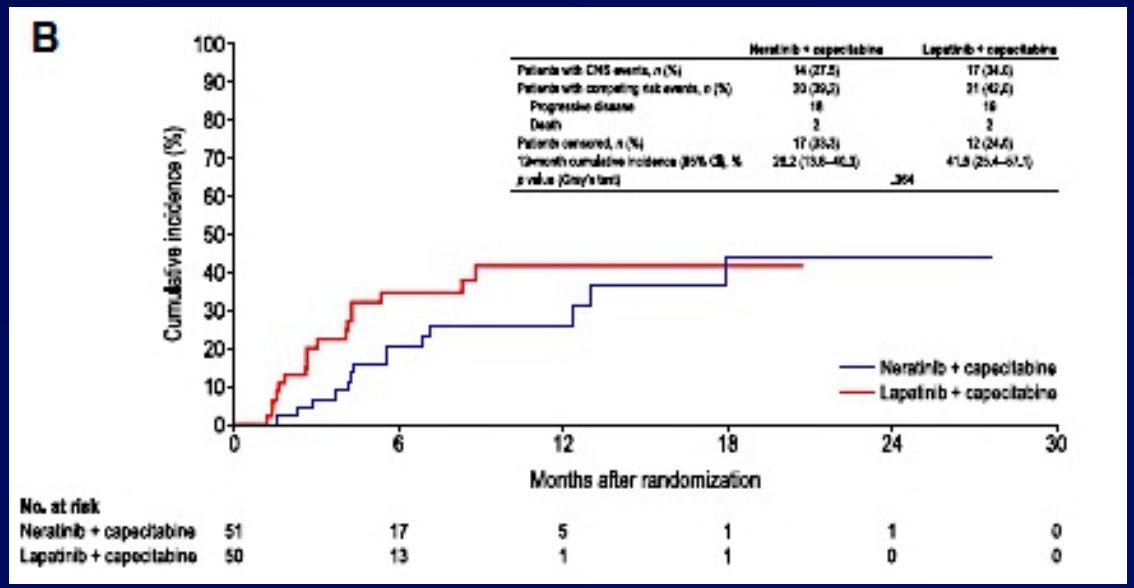
https://investor.seagen.com/press-releases/news-details/2023/Seagen-Phase-3-Trial-of-TUKYSA-tucatinib-in-Combination-with-Antibody-Drug-Conjugate-ado-trastuzumab-emtansine-Meets-Primary-Endpoint-of-Progression-Free-Survival-in-Patients-with-Previously-Treated-HER2-Positive-Metastatic-Breast-Cancer/default.aspx

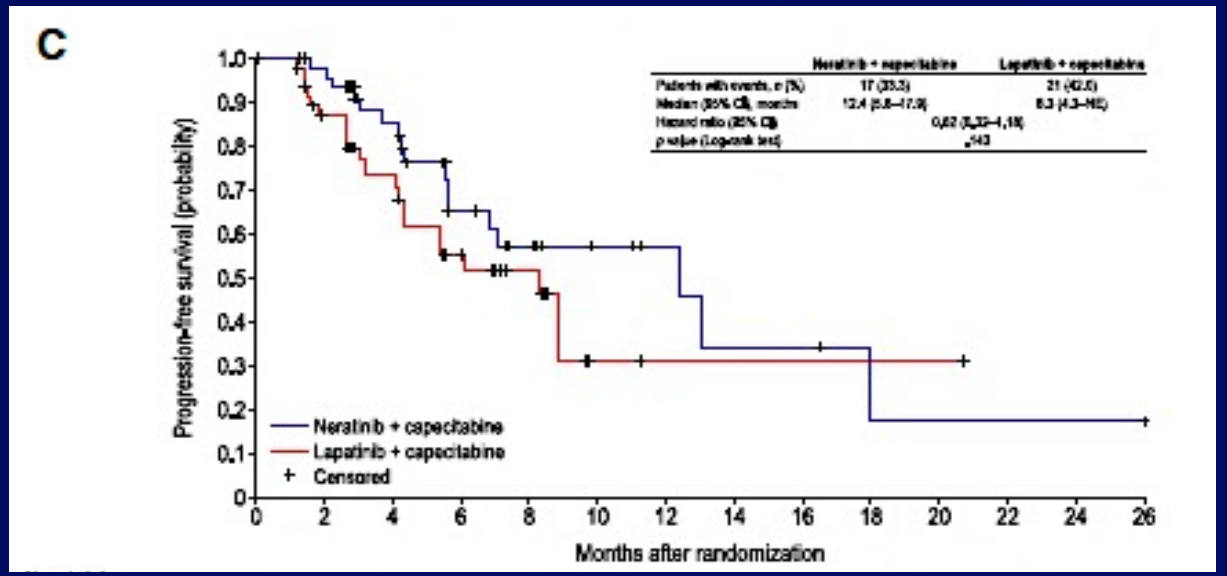
RTP RESEARCH TO PRACTICE

Considerations for patients with CNS metastases

Time to intervention (A), Time to Progression of CNS Disease (B) and CNS Progression Free Survival (NALA)



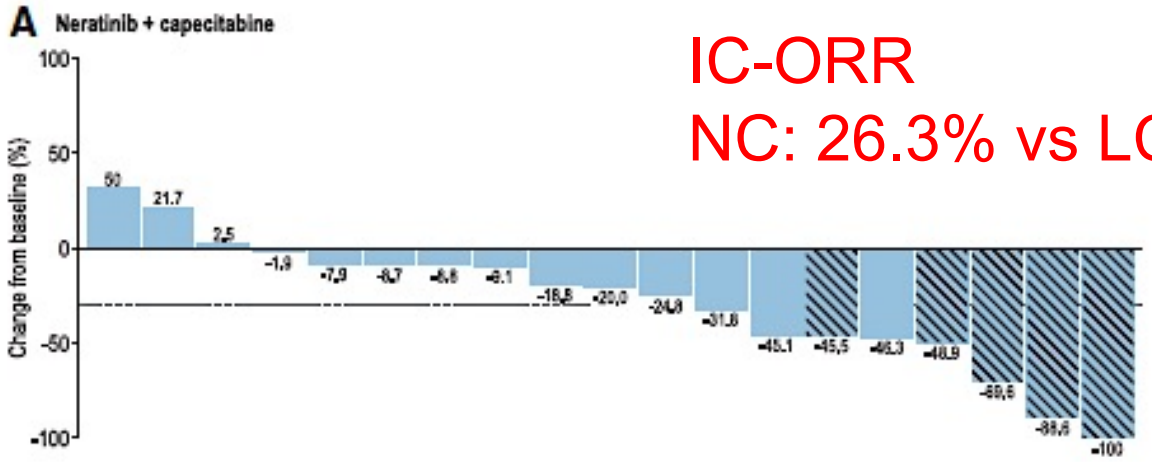


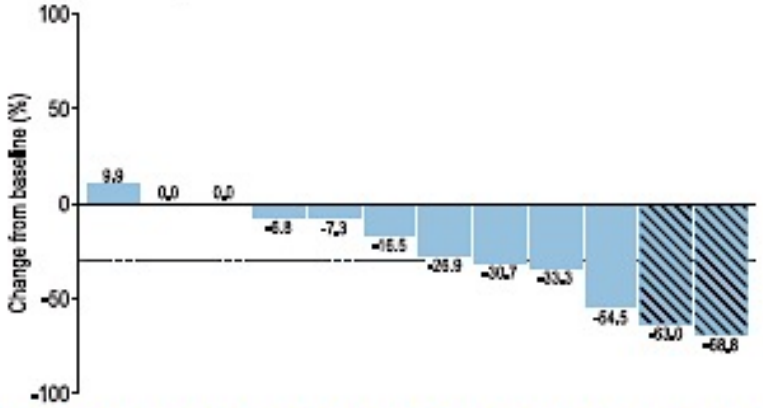


Hurvitz S et al The Oncologist 2021

Intracranial responses in NALA with neratinib or lapatinib plus capecitabine in patients with brain metastases

IC-ORR
NC: 26.3% vs LC: 15.4%





	N+C (n = 19)	L+C (n = 13)
Best overall intracranial response (unconfirmed), n (%)		
Complete response	1 (5.3)	0 (0.0)
Partial response	7 (36.8)	5 (38.5)
Stable disease	9 (47.4)	6 (46.2)
Disease progression	2 (10.5)	1 (7.7)
Not evaluable	0 (0.0)	1 (7.7)
Intracranial objective response (confirmed), n (%)	5 (26.3)	2 (15.4)
Objective response rate (95% CI)	26.3 (9.1–51.2)	15.4 (1.9–45.4)
Difference (95% CI)	10.9 (−23.3 to 40.1)	

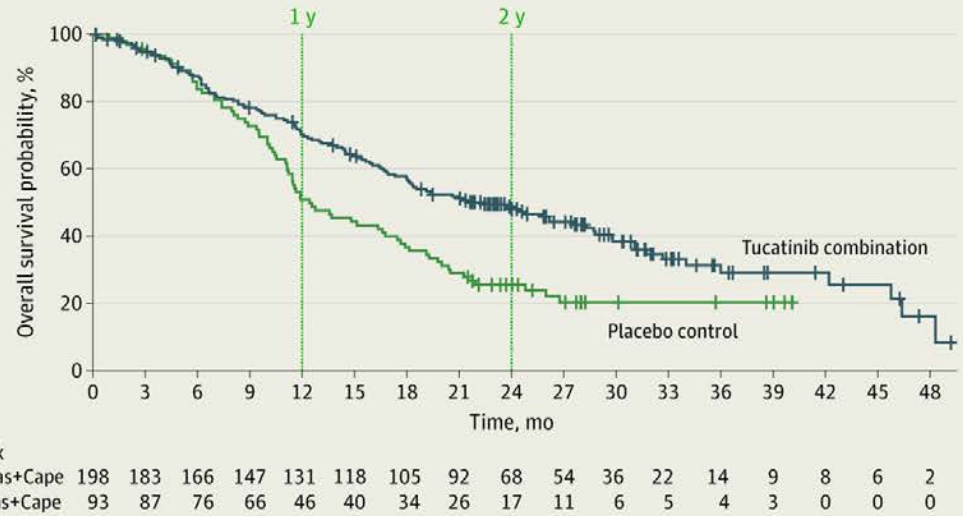
Figure 4. Best changes in intracranial tumor size from baseline for patients with target CNS lesions at screening per local assessment. Hatched bar indicates patient has confirmed response. Note: One patient in the lapatinib plus capecitabine group did not have a follow-up assessment and is not included in Fig. 4B.
Abbreviations: CI, confidence interval; CNS, central nervous system; L + C, lapatinib + capecitabine; N + C, neratinib plus capecitabine.

Hurvitz S et al The Oncologist 2021

Outcomes in HER2CLIMB in patients with CNS metastases

FINDINGS

Median OS was longer in the tucatinib-combination group compared with the placebo-combination group



Median OS:

21.6 mo (95% CI, 18.1-28.5 mo) in tucatinib-combination group

12.5 mo (95% CI, 11.2-16.9 mo) in placebo-combination group

Table. Confirmed Intracranial Responses in Patients With Active Brain Metastases and Measurable Intracranial Lesions at Baseline

Intracranial response	Tucatinib combination (n = 55)[a]	Placebo combination (n = 20)[b]
Patients with objective response of confirmed complete response or partial response, No.	26	4
Confirmed ORR-IC, % (95% CI)	47.3 (33.7-61.2)	20.0 (5.7-43.7)
DOR-IC, median (95% CI), mo[c]	8.6 (5.5-10.3)	3.0 (3.0-10.3)

Abbreviations: DOR-IC, duration of intracranial response; ORR-IC, intracranial objective response rate.

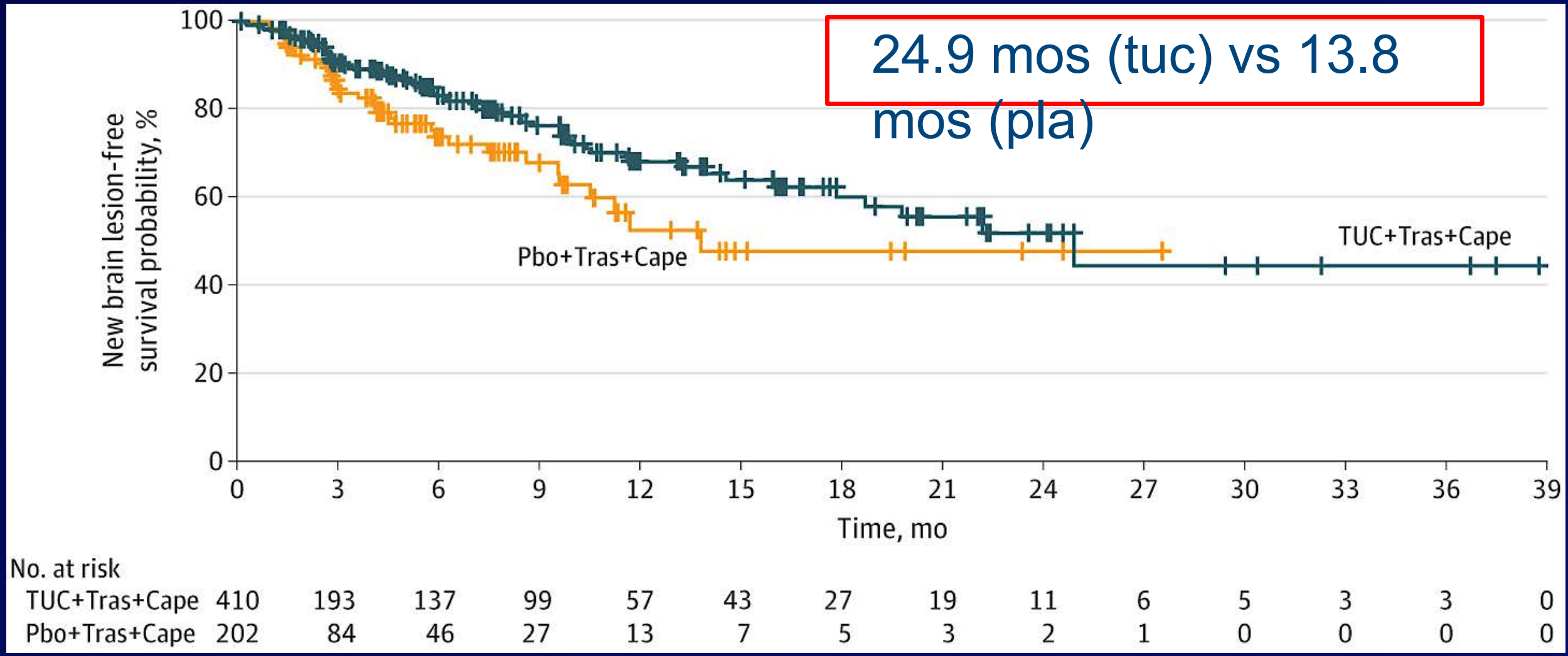
[a] Tucatinib, trastuzumab, and capecitabine.

[b] Placebo, trastuzumab, and capecitabine.

[c] Calculated with the complementary log-log transformation method.

Lin, et al. JAMA Oncol. 2023;9(2):197-205. doi:10.1001/jamaoncol.2022.5610

Outcomes in HER2CLIMB in patients with CNS metastases: New Brain Lesion–Free Survival



Lin, et al. JAMA Oncol. 2023;9(2):197-205. doi:10.1001/jamaoncol.2022.5610

T-DXd in Patients With HER2+ MBC and Brain Metastases

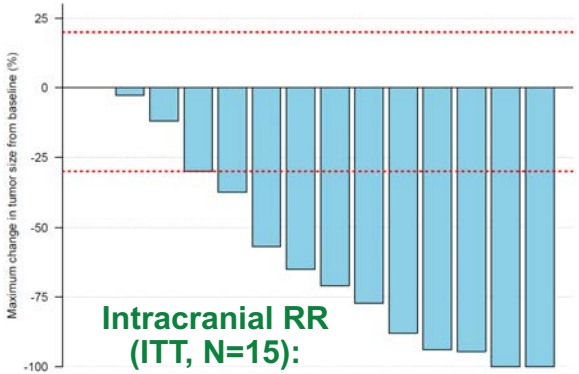
Single-Arm Phase 2 Trial in Patients With Active Brain Metastases: TUXEDO-1[1]

Key Eligibility Criteria

- HER2+ MBC
- Brain metastases either recently diagnosed or recently progressed after local therapy

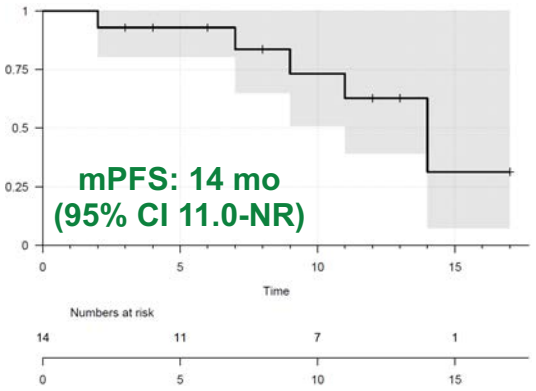
T-DXd: 5.4 mg/kg q3w
Until progression or unacceptable toxicity

Primary Endpoint: Intracranial Response Rate



Intracranial RR (ITT, N=15): 73.3%

Secondary Endpoint: PFS



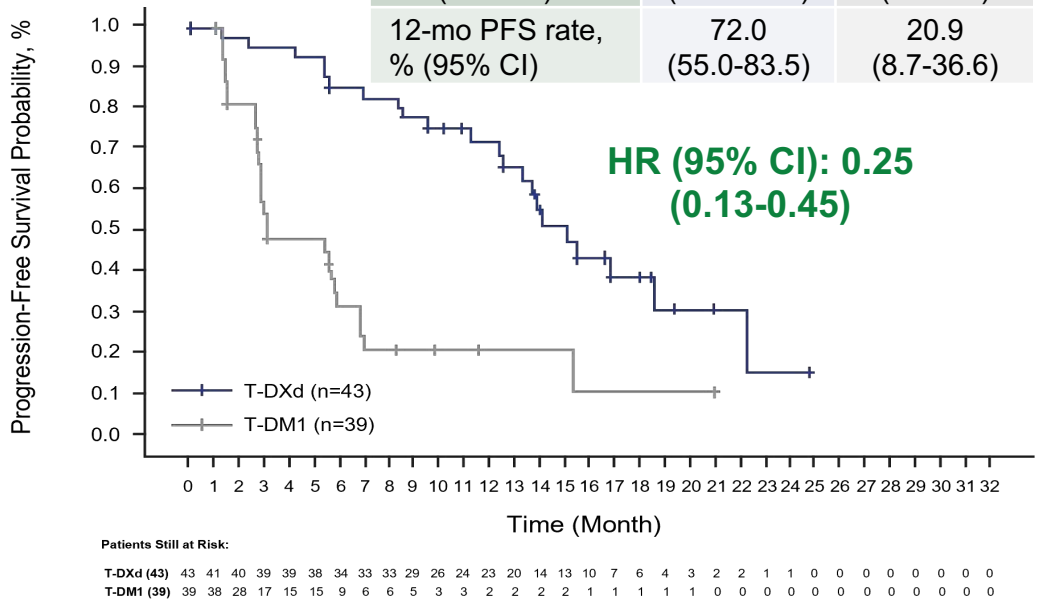
mPFS: 14 mo (95% CI 11.0-NR)

Safety: AEs of special interest

- Ejection fraction decrease in 1 patient (grade 3)
- ILD in 1 patient (grade 2)
- Grade 5 urosepsis in 1 patient (deemed unrelated)

DESTINY-Breast03 Subgroup Analysis: PFS in Stable Brain Metastases[2]

	T-DXd	T-DM1
mPFS, mo (95% CI)	15.0 (12.5-22.2)	3.0 (2.8-5.8)
12-mo PFS rate, % (95% CI)	72.0 (55.0-83.5)	20.9 (8.7-36.6)



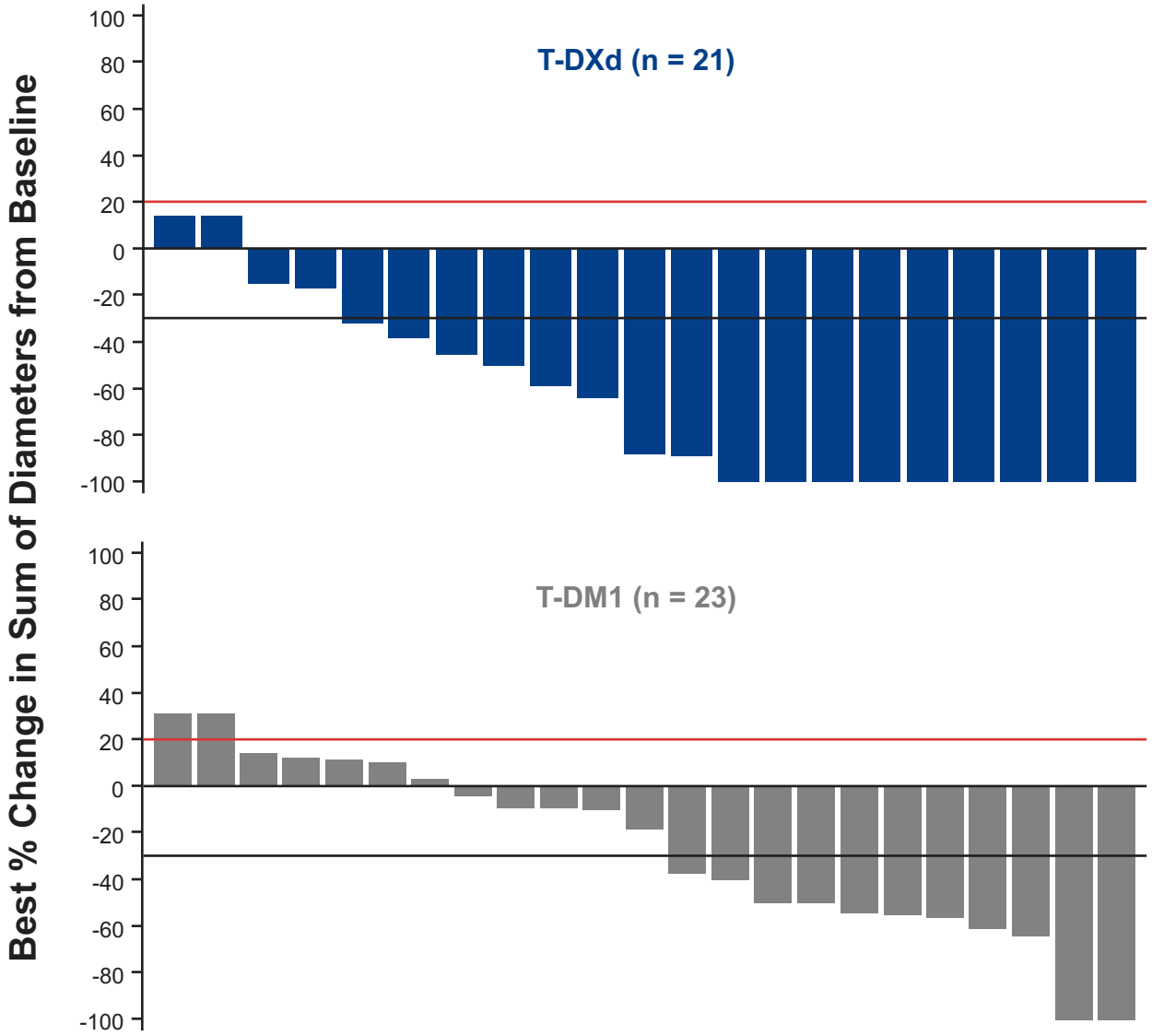
HR (95% CI): 0.25 (0.13-0.45)

At data cutoff, in patients with BM at baseline, PD was observed:

- In 21/43 treated with T-DXd versus 27/39 treated with T-DM1
  - In the brain in 9/21 treated with T-DXd versus 11/27 treated with T-DM1

1. Bartsch R, et al. *Nat Med*. 2022;28(9):1840-1847. **2.** Hurvitz SA, et al. SABCS 2021. Abstract GS3-01.

Intracranial Response per BICR using RECIST 1.1



	T-DXd (n = 36)	T-DM1 (n = 36)
Best Overall Response, n (%)[a]		
CR	10 (27.8)	1 (2.8)
PR	13 (36.1)	11 (30.6)
Non-CR/Non-PD	6 (16.7)	7 (19.4)
SD	4 (11.1)	7 (19.4)
PD	1 (2.8)	8 (22.2)
Not Evaluable	0	1 (2.8)
Missing	2 (5.6)	1 (2.8)
Subjects with Objective Response of CR or PR, n	23	12

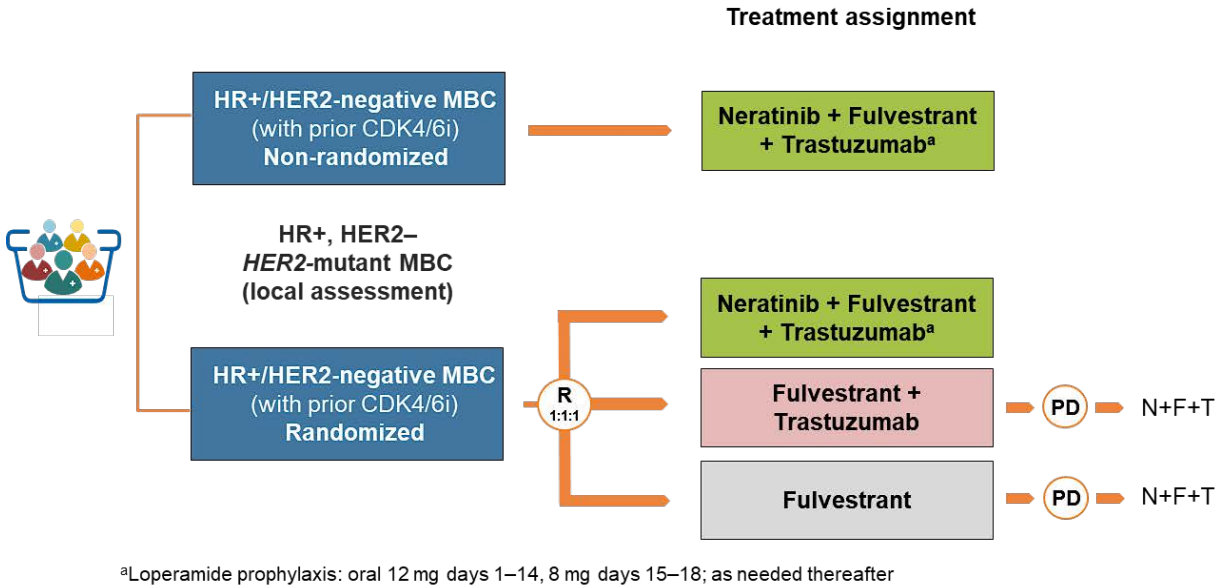
CR, complete response; DCR, disease control rate; mDOR, median duration of response; PD, progressive disease; PR, partial response; SD, stable disease; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.
Table includes target and non-target lesions. Only patients with target lesion assessments are eligible for inclusion in waterfall.
Red line at 20% indicates progressive disease; black line at -30% indicates partial response.
[a]Denominator for percentages is the number of subjects in the full analysis set with brain metastases tumor assessment

1. Hurvitz SA et al Presented at: SABCS 2021 Annual Meeting;

HER2 Mutation: Combinations needed for improved efficacy and durability

SUMMIT (NCT01953926): ER+ HER2- *ERBB2* mut Cohort

***HER2* mutation: 8% ER+ MBC**
15%: met ILC



[a]Loperamide prophylaxis: oral 12 mg days 1–14, 8 mg days 15–18; as needed thereafter

***HER2*-mutant MBC**

Primary endpoint

- Confirmed objective response rate (ORR; RECIST v1.1, centrally assessed)

Secondary endpoints

- Confirmed ORR (investigator-assessed)
- Duration of response (DOR)
- Clinical benefit rate (CBR)
- Progression-free survival (PFS)
- Safety and PROs

Treatment Regimen	ORR	PFS (months)	DOR (months)
Neratinib (n=23)	17%	3.6	6.5
Neratinib + Fulvestrant (n=47)	**30%**	**5.4**	**9.2**
Neratinib + Fulvestrant +Trastuzumab (n=51)	**35.3%**	**8.2**	**14.3**

Addition of T to N prolongs suppression of HER3 phosphorylation in HR+, HER2-negative, *HER2*-mutant breast cancer cell line model

- Tucatinib + Trastuzumab Basket Study (NCT04579380)
- BDTX0819 Potent and Selective Inhibitor of the Allosteric Oncogenic ErbB Family (NCT04209465)
- Trastuzumab Deruxtecan: DESTINY-pantumor01 (NCT04639219)

Jhaveri et al SABCS 2021; Jhaveri et al ASCO 2022; Jhaveri et al Ann of Oncol 2023

Courtesy of Komal Jhaveri, MD

Oncology in the Real World: A Daylong Multitumor Educational Symposium in Partnership with the American Oncology Network

A CME/MOC- and NCPD-Accredited Event

Saturday, October 14, 2023
9:30 AM – 5:00 PM PT

RTP
RESEARCH
TO PRACTICE

Meet The Professor

Optimizing the Management of Ovarian Cancer

Tuesday, October 17, 2023
5:00 PM – 6:00 PM ET

Faculty

David M O'Malley, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Breast Cancer

A 3-Part CME Satellite Symposium Series Held in Conjunction with the 2023 San Antonio Breast Cancer Symposium®

ER-Positive Metastatic Breast Cancer

Tuesday, December 5, 2023

7:15 PM – 9:15 PM CT

Localized HER2-Negative Breast Cancer

Wednesday, December 6, 2023

7:15 PM – 9:15 PM CT

HER2-Low Breast Cancer

Thursday, December 7, 2023

7:15 PM – 8:45 PM CT

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Hematologic Cancers

A 4-Part CME Friday Satellite Symposium Series Preceding the 65th ASH Annual Meeting and Exposition

Friday, December 8, 2023

Follicular, Mantle Cell and Hodgkin Lymphoma
7:30 AM – 10:00 AM PT

Diffuse Large B-Cell Lymphoma
11:30 AM – 1:30 PM PT

Chronic Lymphocytic Leukemia
3:15 PM – 5:15 PM PT

Multiple Myeloma
7:00 PM – 9:00 PM PT

Moderator
Neil Love, MD

RTP RESEARCH TO PRACTICE

JOIN US IN 2024 FOR THE RETURN OF

The Annual
National General Medical Oncology Summit

A Multitumor CME/MOC- and NCPD-Accredited Educational Conference Developed in Partnership with Florida Cancer Specialists and Research Institute

MARCH 22-24, 2024

JW Marriott Miami Turnberry

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Please complete the postevent survey now available on the meeting iPads.

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The survey will remain open for 5 minutes after the meeting ends.

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In-person attendees: Please refer to the program syllabus for the CME/MOC and NCPD credit link or QR code.

Online/Zoom attendees: The CME/MOC and NCPD credit link is posted in the chat room.

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