Meet The Professor

Optimizing the Management of Head and Neck and Thyroid Cancers

Tuesday, September 20, 2022
5:00 PM – 6:00 PM ET

Faculty

Robert Haddad, MD

Moderator

Neil Love, MD

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Commercial Support

This activity is supported by educational grants from Bayer HealthCare Pharmaceuticals and Coherus BioSciences.

Dr Love — Disclosures

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Dr Haddad — Disclosures

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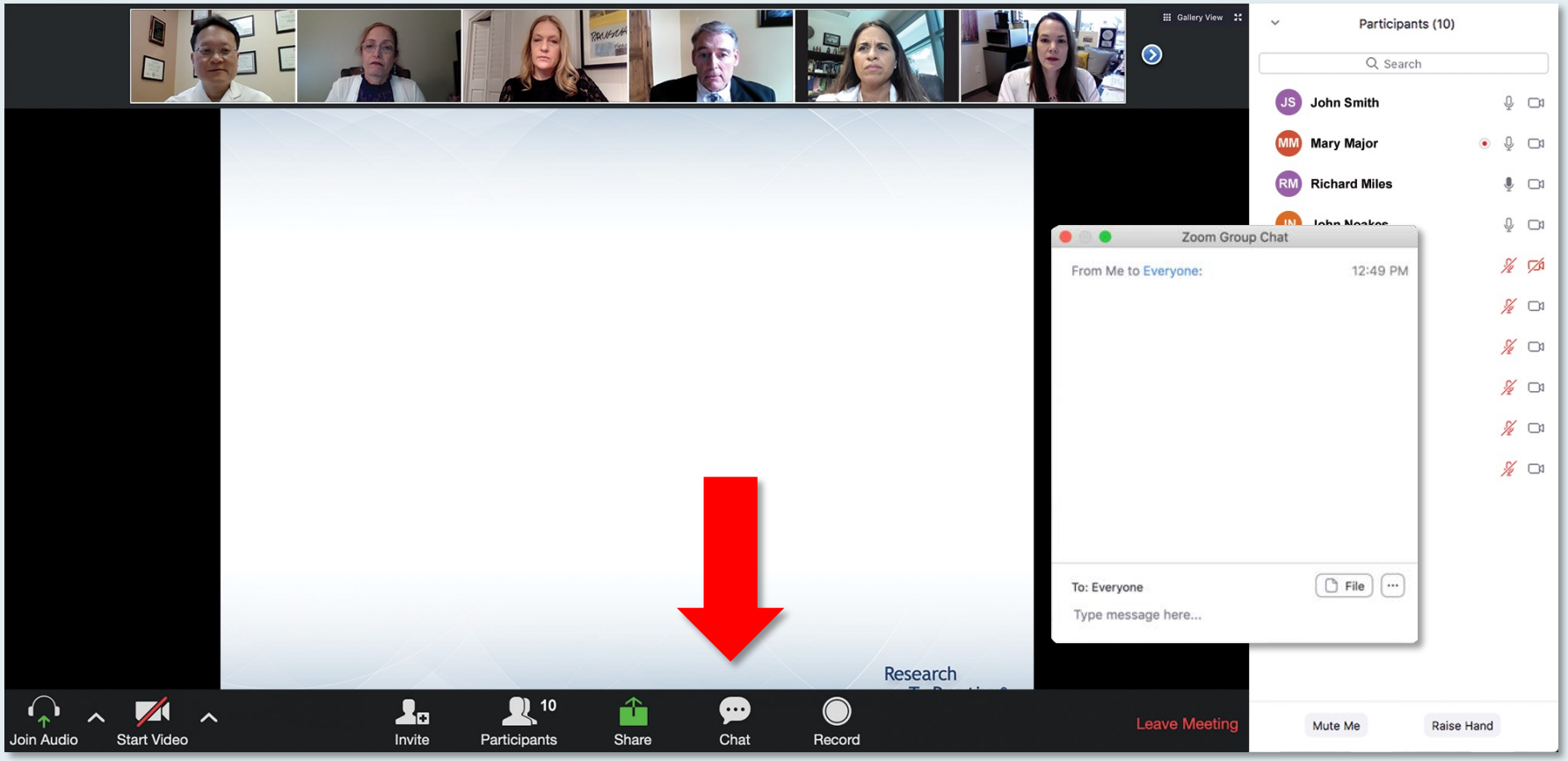

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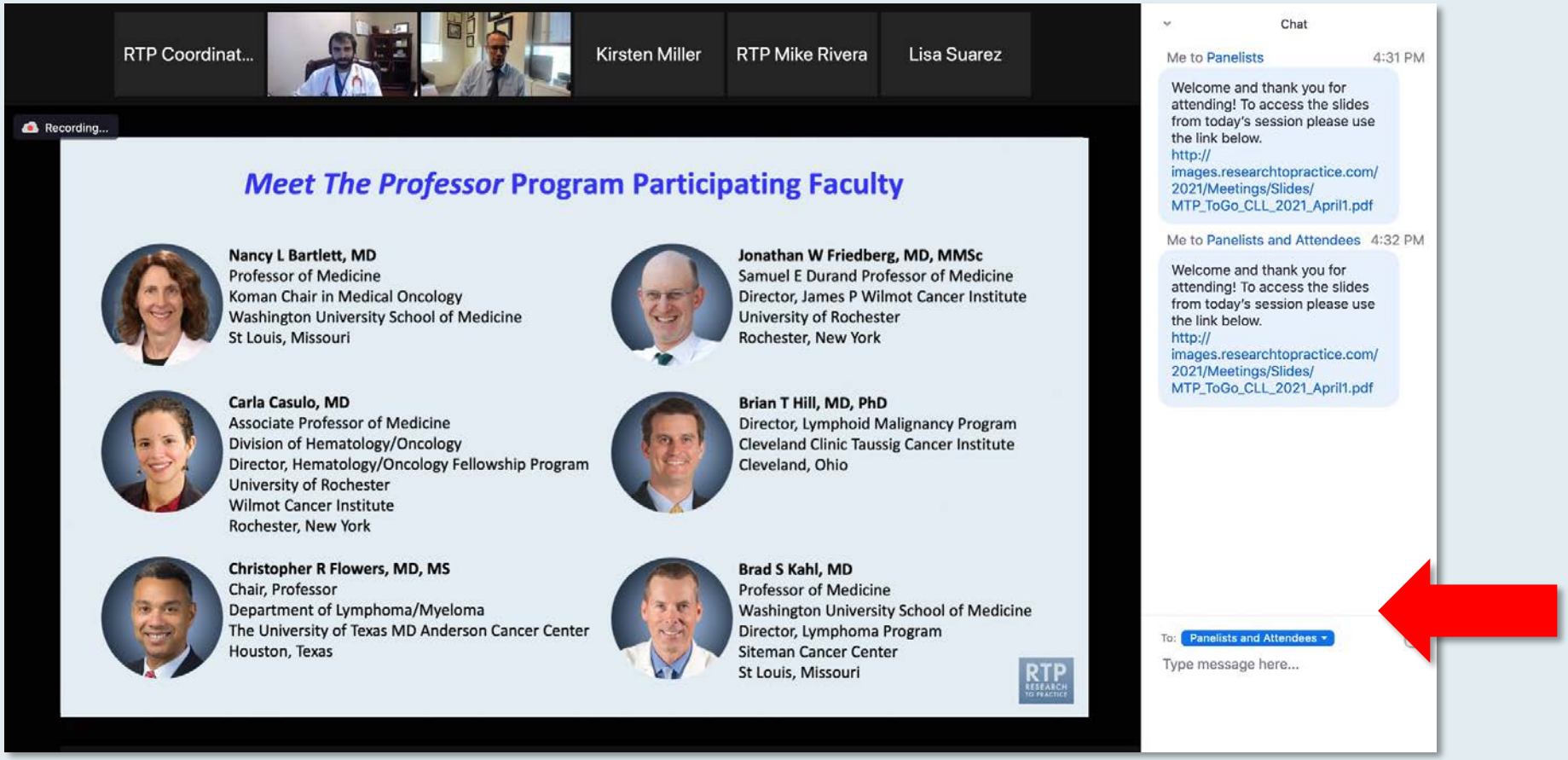
Expand chat submission box



Drag the white line above the submission box up to create more space for your message.

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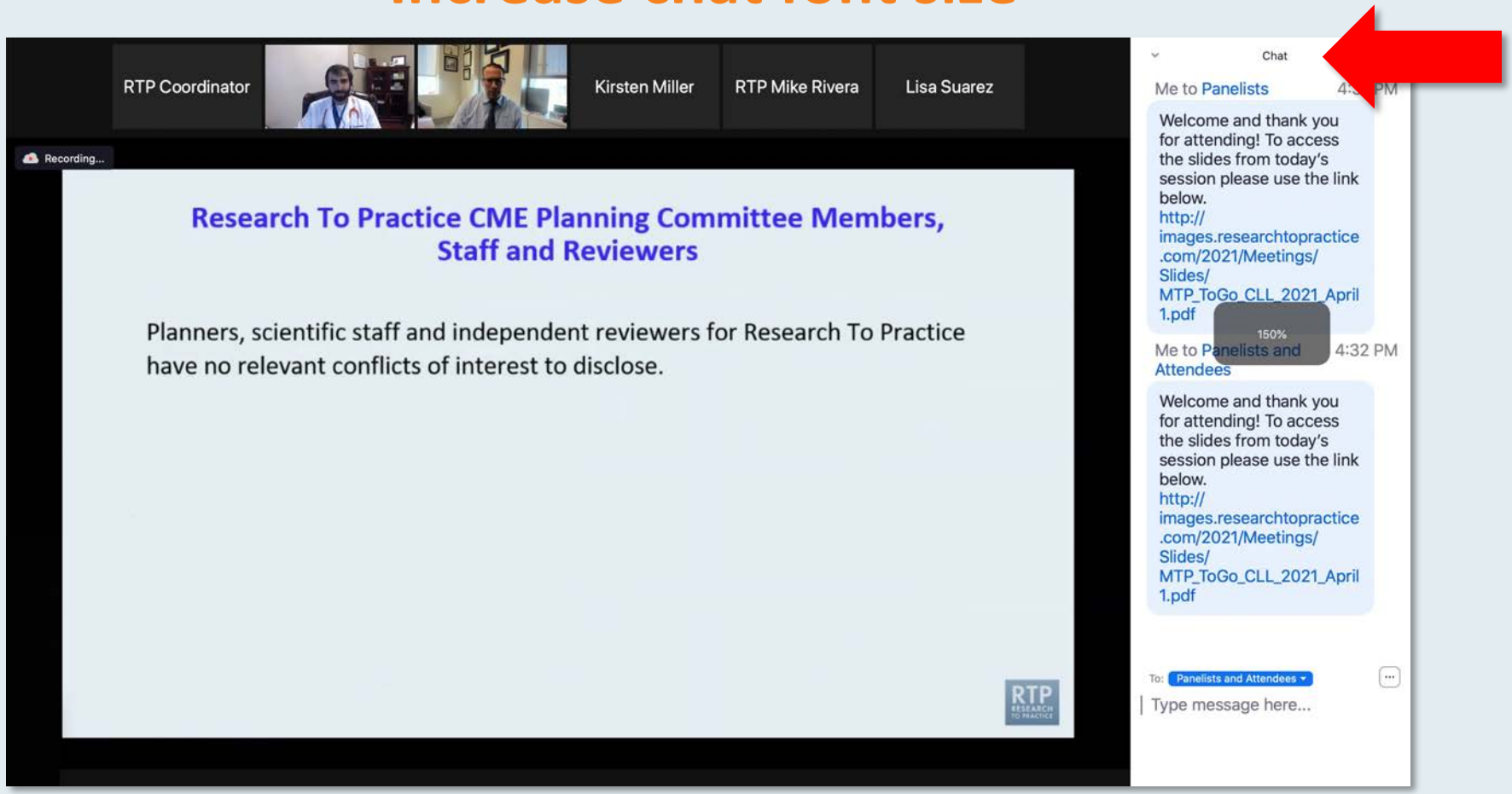

Press Command (for Mac) or Control (for PC) and the + symbol.
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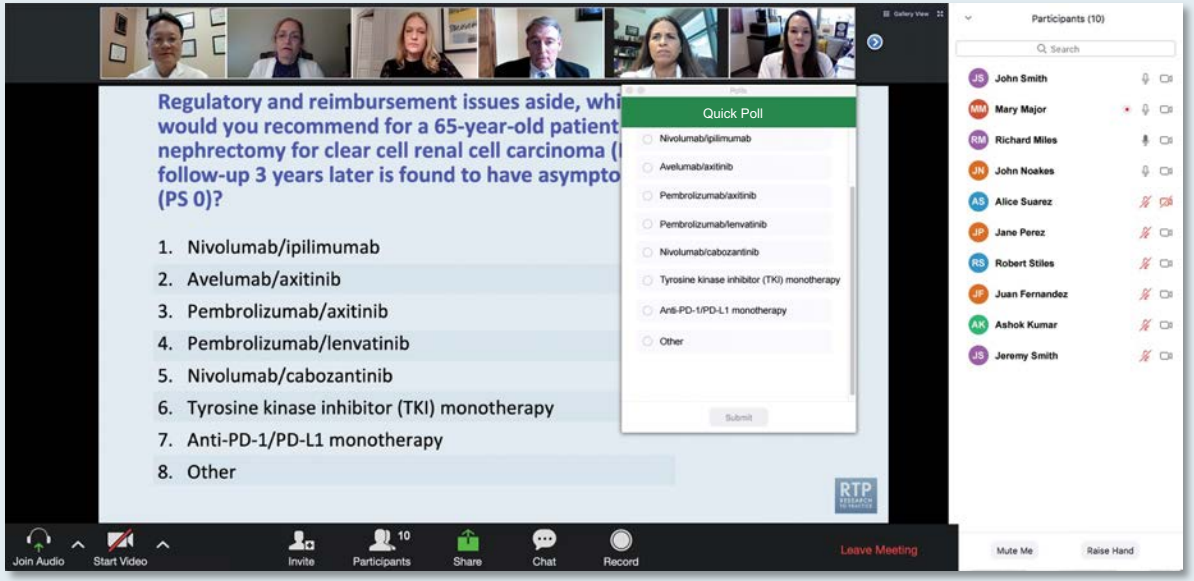

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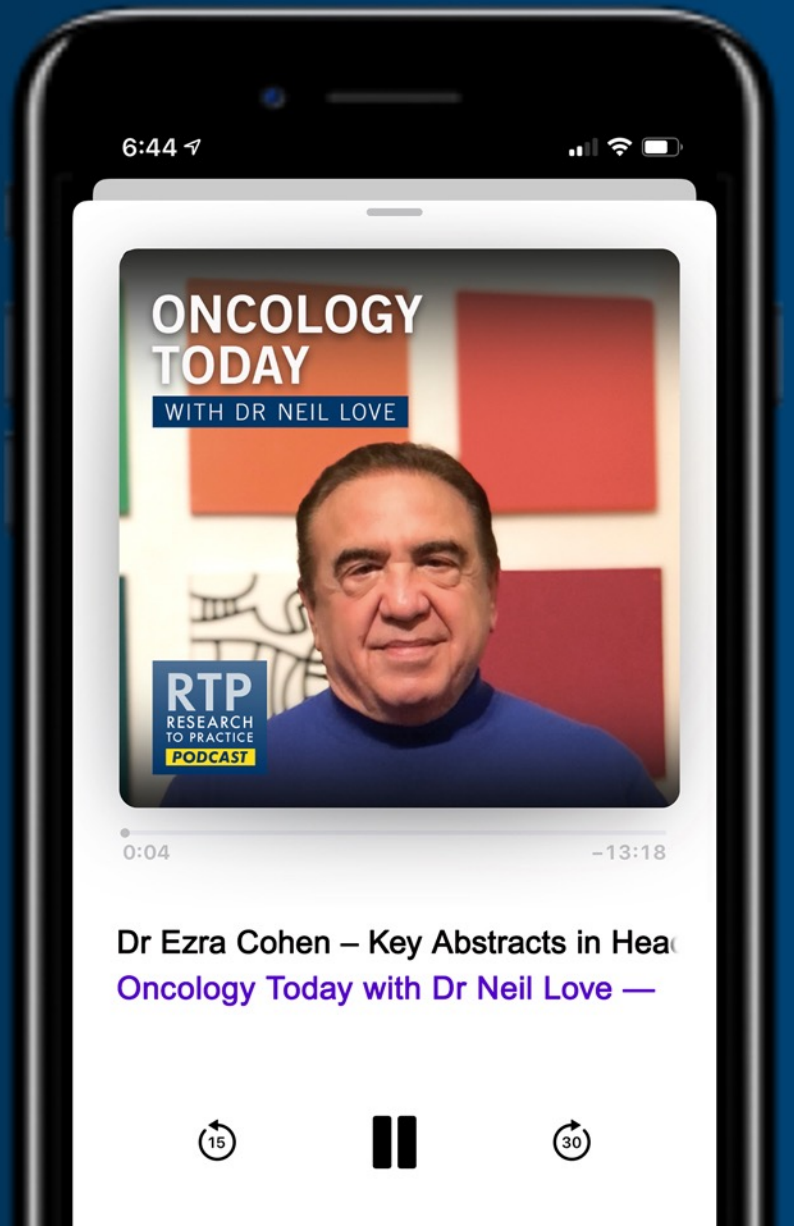

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Optimizing the Management of Small Cell Lung Cancer

Wednesday, September 21, 2022
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Thursday, October 6, 2022
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Sagar Lonial, MD

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The Clinical Implications of Key Recent Data Sets in Oncology: A Daylong Multitumor Educational Symposium in Partnership with Florida Cancer Specialists

Saturday, October 22, 2022

7:30 AM – 5:30 PM ET

JW Marriott Orlando| Orlando, Florida

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Matthew P Goetz, MD
Ian E Krop, MD, PhD
Ann S LaCasce, MD, MMSc
Corey J Langer, MD
Prof Georgina Long, AO, BSc, PhD, MBBS
Christine M Lovly, MD, PhD
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8:30 AM – 9:30 AM ET

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Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.

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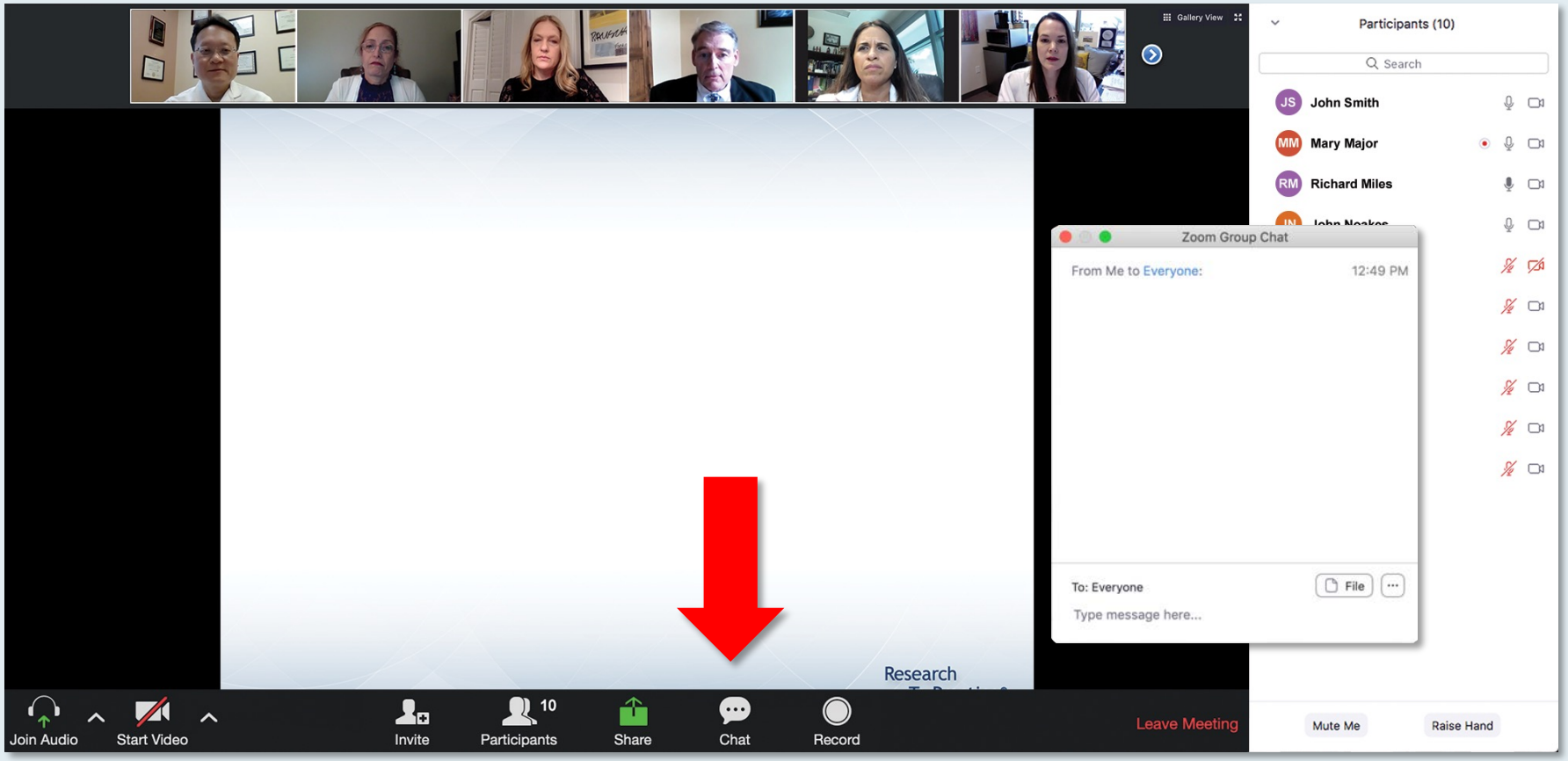

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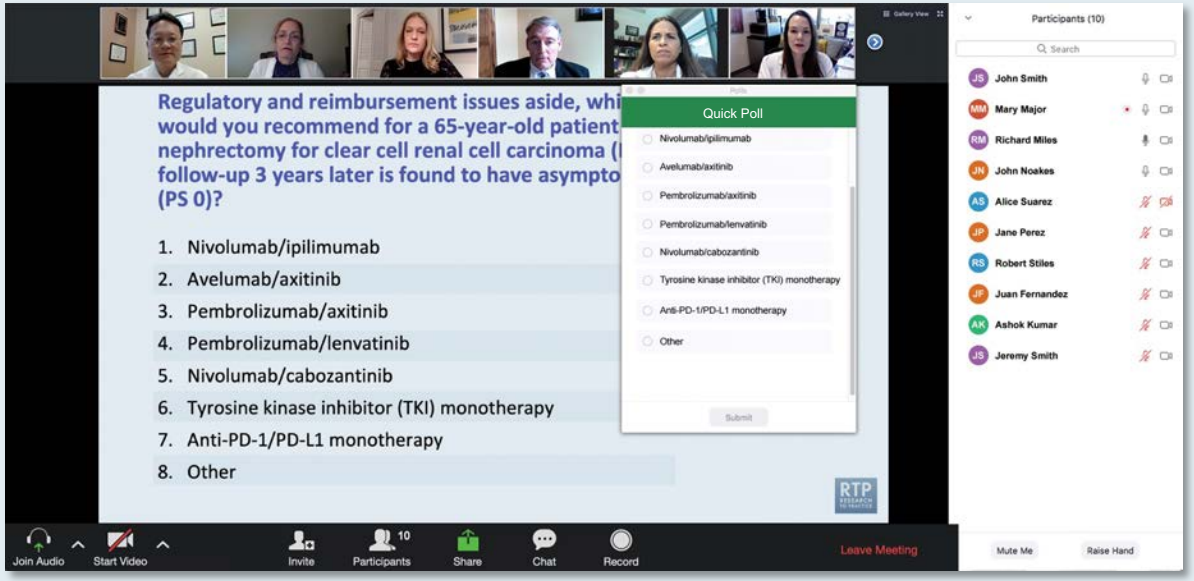

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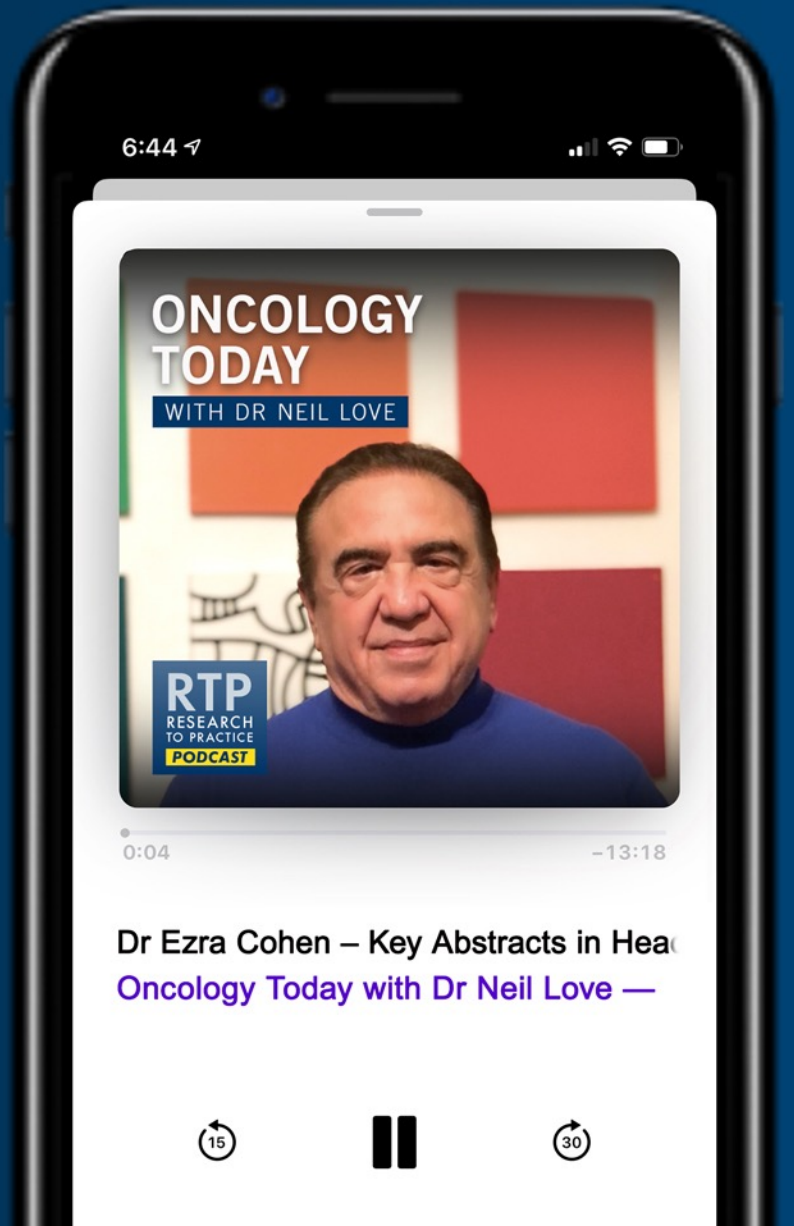

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Dr Haddad — Disclosures

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Ezra Cohen, MD
Chief, Division of Hematology-Oncology
Department of Medicine, UC San Diego
Co-Director, San Diego Center for Precision Immunotherapy
Co-Director, IEM Center for Engineering in Cancer
Associate Director for Clinical Sciences
Moores Cancer Center at UC San Diego Health
Co-Leader, Solid Tumor Therapeutics Program
Co-Director, Hanna and Mark Gleiberman Head and Neck Cancer Center
La Jolla, California

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Spencer H Bachow, MD
Lynn Cancer Institute
Boca Raton, Florida

Neil Morganstein, MD
Atlantic Health System
Summit, New Jersey

Mamta Choksi, MD
Florida Cancer Specialists
New Port Richey, Florida

Erik Rupard, MD
The Reading Hospital
West Reading, Pennsylvania

Meet The Professor with Dr Haddad

MODULE 1: ESMO 2022

MODULE 2: Needle in a Haystack

MODULE 3: Head and Neck Cancer

MODULE 4: Thyroid Cancer

MODULE 5: Journal Club with Dr Haddad

MODULE 6: Appendix

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MODULE 4: Thyroid Cancer

MODULE 5: Journal Club with Dr Haddad

MODULE 6: Appendix

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Lancet 2021;398(10318):2289-99.

Seminar

Head and neck cancer

Mayur D Mody, James W Rocco, Sue S Yom, Robert I Haddad, Nabil F Saba

Regulatory and reimbursement issues aside, which of the following would be your most likely first-line systemic treatment recommendation for a patient with metastatic squamous cell carcinoma of the head and neck and a PD-L1 CPS of <1?

- Chemotherapy
- Chemotherapy + cetuximab
- Chemotherapy + pembrolizumab
- Chemotherapy + pembrolizumab + cetuximab
- Other
- I'm not sure

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Regulatory and reimbursement issues aside, which of the following would be your most likely first-line systemic treatment recommendation for a symptomatic patient with metastatic squamous cell carcinoma and a PD-L1 CPS of 20?

- Chemotherapy
- Chemotherapy + cetuximab
- Chemotherapy + pembrolizumab
- Chemotherapy + pembrolizumab + cetuximab
- Pembrolizumab
- Other
- I'm not sure

ESMO 2022;Abstract 659MO.

Pembrolizumab With or Without Chemotherapy For First-Line Treatment of Recurrent/Metastatic Head and Neck Squamous Cell Carcinoma: 5-year Results from KEYNOTE-048

Makoto Tahara[1]; Richard Greil[2]; Danny Rischin[3]; Kevin J. Harrington[4]; Barbara Burtness[5]; Gilberto de Castro[6]; Amanda Psyrri[7]; Irene Brana[8]; Prakash Neupane[9]; Åse Bratland[10]; Thorsten Fuereder[11]; Brett G.M. Hughes[12]; Ricard Mesia[13]; Nuttapong Ngamphaiboon[14]; Tamara Rordorf[15]; Wan Zamaniah Wan Ishak[16]; Jianxin Lin[17]; Burak Gumuscu[17]; Nati Lerman[17]; Denis Soulières[18]

[1]National Cancer Center Hospital East, Kashiwa, Japan; [2]Paracelsus Medical University Salzburg Cancer Research Institute and Cancer Cluster, Salzburg, Austria; [3]Peter MacCallum Cancer Institute University of Melbourne, Melbourne, VIC, Australia; [4]The Institute of Cancer Research, London, United Kingdom; [5]Yale School of Medicine, New Haven, CT, USA; [6]Instituto do Cancer de Sao Paulo—ICESP, São Paulo, Brazil; [7]National and Kapodistrian University of Athens, Attikon University Hospital, Athens, Greece; [8]Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; [9]University of Kansas Medical Center, Kansas City, MO, USA; [10]Oslo University Hospital, Oslo, Norway; [11]Medical University of Vienna/General Hospital Vienna, Vienna, Austria; [12]Royal Brisbane & Women's Hospital, and University of Queensland, Herston, QLD, Australia; [13]Catalan Institute of Oncology, Barcelona, Spain; [14]Ramathibodi Hospital, Mahidol University, Ratchatewi, Bangkok, Thailand, [15]University Hospital, Zurich, Switzerland; [16]University Malaya, Kuala Lumpur, Wilayah Persekutuan, Malaysia; [17]Merck & Co., Inc., Rahway, NJ, USA; [18]CHUM, Montréal, Quebec, Canada

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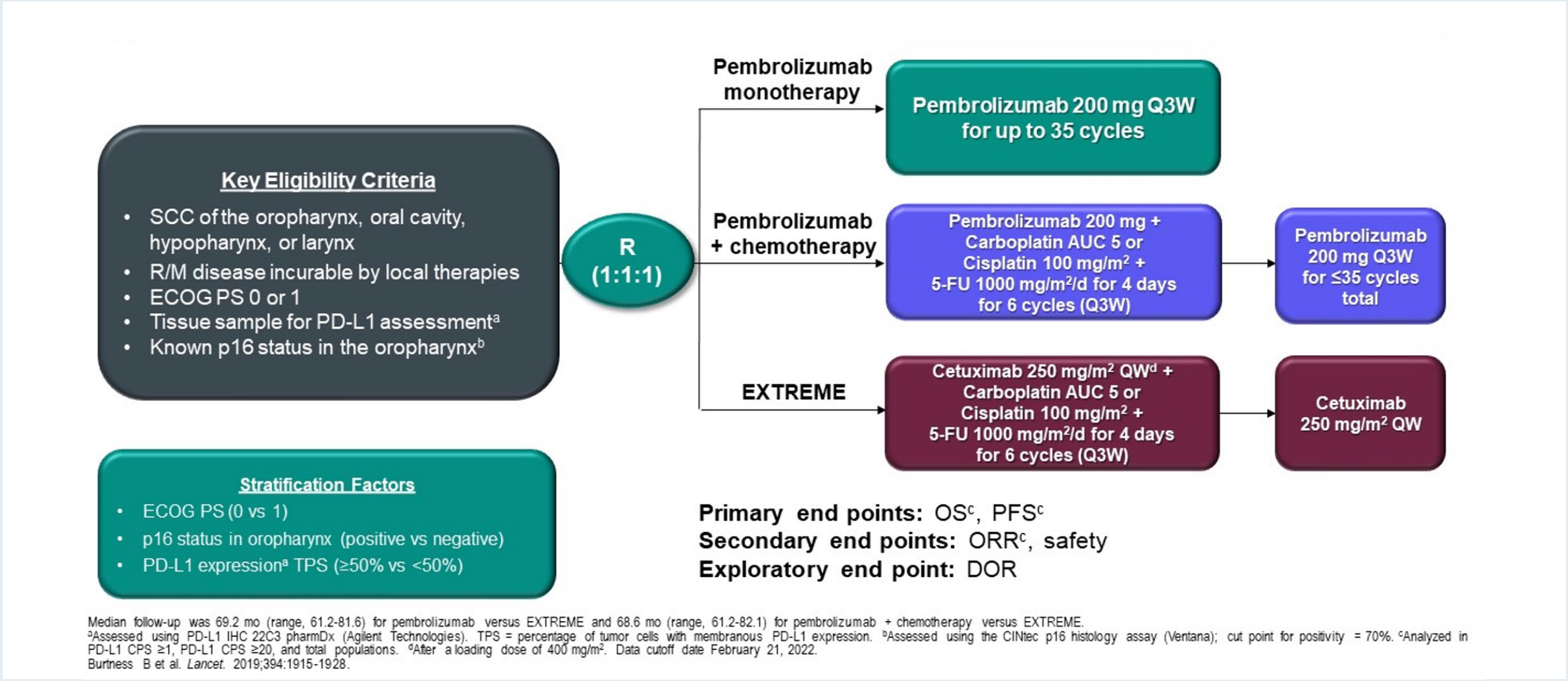
KEYNOTE-048 Phase III Study Design

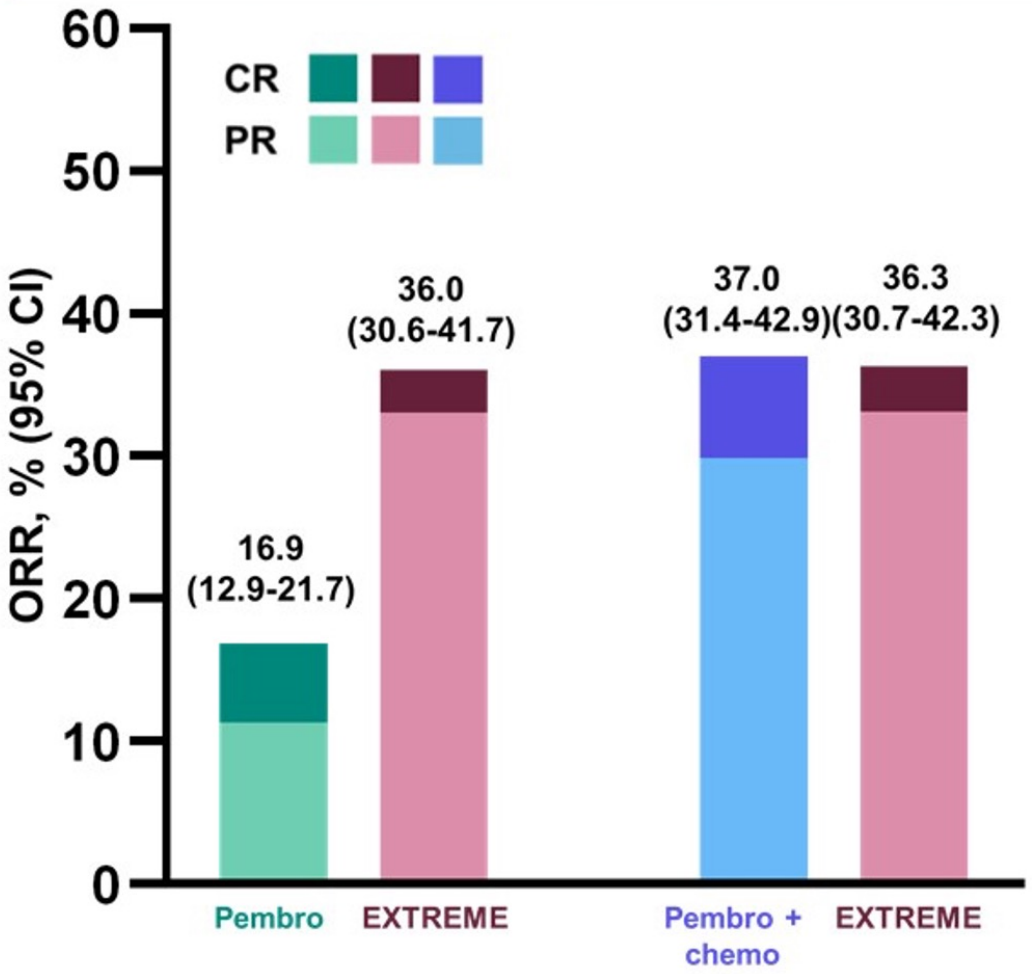


Median follow-up was 69.2 mo (range, 61.2-81.6) for pembrolizumab versus EXTREME and 68.6 mo (range, 61.2-82.1) for pembrolizumab + chemotherapy versus EXTREME. [a]Assessed using PD-L1 IHC 22C3 pharmDx (Agilent Technologies). TPS = percentage of tumor cells with membranous PD-L1 expression. [b]Assessed using the CINtec p16 histology assay (Ventana); cut point for positivity = 70%. [c]Analyzed in PD-L1 CPS ≥1, PD-L1 CPS ≥20, and total populations. [d]After a loading dose of 400 mg/m². Data cutoff date February 21, 2022.
Burtness B et al. *Lancet*. 2019;394:1915-1928.

SCC = squamous cell carcinoma; OS = overall survival; PFS = progression-free survival; ORR = objective response rate; DOR = duration of response

Tahara M et al. ESMO 2022;Abstract 659MO.

KEYNOTE-048: Objective Response Rate and Duration of Response by BICR in the ITT Population



	Pembro vs EXTREME		Pembro + chemo vs EXTREME	
	Pembro n = 301	EXTREME n = 300	Pembro + chemo n = 281	EXTREME n = 278
DOR, median (range), mo	22.6 (1.5+ to 75.5+)	4.5 (1.2+ to 73.9+)	6.7 (1.6+ to 73.8+)	4.3 (1.2+ to 66.5+)

BICR = blinded independent central review; CR = complete response; PR = partial response; ORR = objective response rate; DOR = duration of response

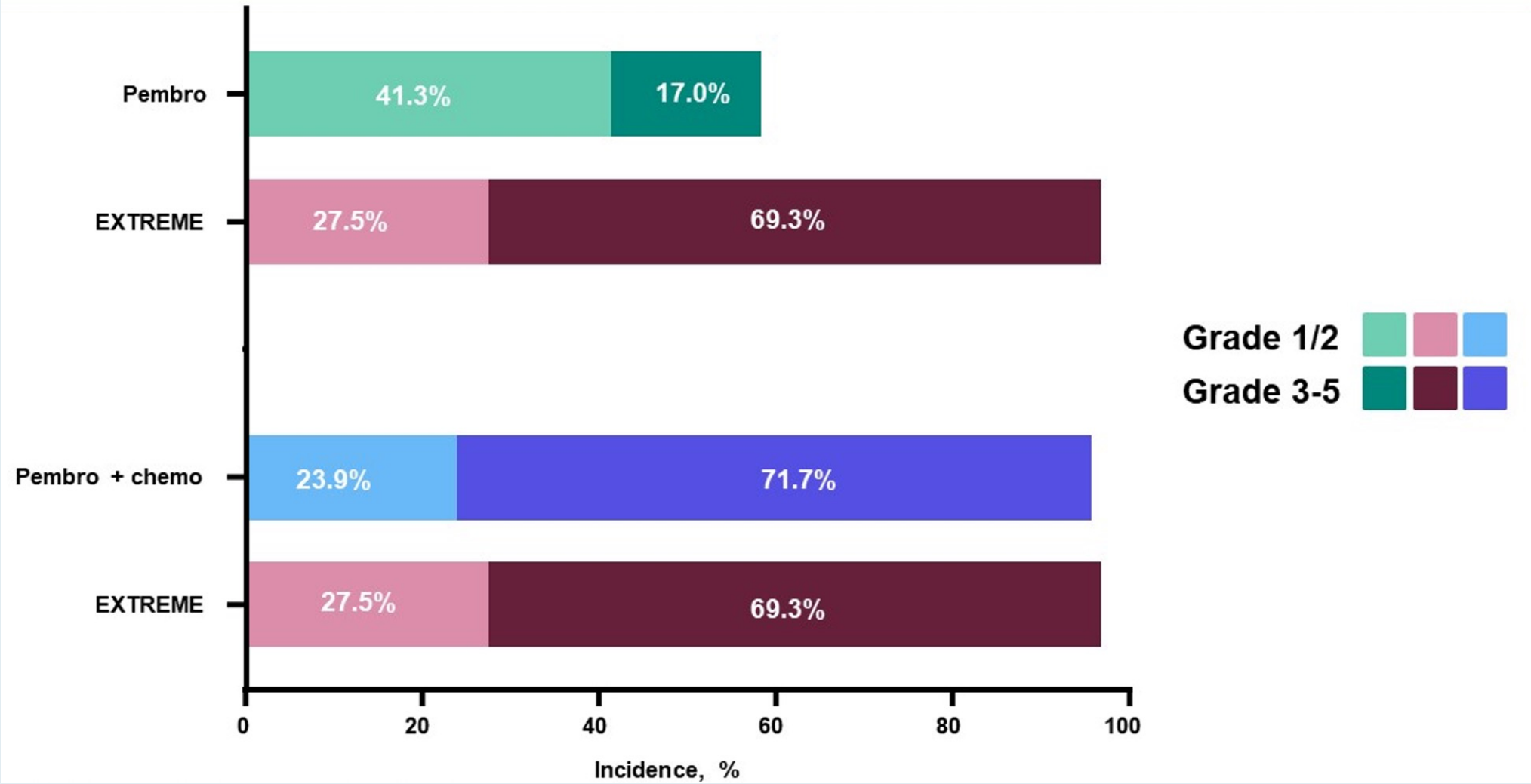
Tahara M et al. ESMO 2022;Abstract 659MO.

KEYNOTE-048: Objective Response Rate and Duration of Response by PD-L1 Status

	Pembro vs EXTREME		Pembro + chemo vs EXTREME	
	Pembro	EXTREME	Pembro + chemo	EXTREME
CPS ≥1, n	257	255	242	235
ORR, % (95% CI)	19.1 (14.5-24.4)	34.9 (29.1-41.1)	38.0 (31.9-44.5)	35.7 (29.6-42.2)
DOR, median, (range) mo	23.4 (1.5+ to 75.5+)	4.5 (1.2+ to 73.9+)	6.7 (1.6+ to 73.8+)	4.3 (1.2+ to 66.5+)
CPS ≥20, n	133	122	126	110
ORR, % (95% CI)	23.3 (16.4-31.4)	36.1 (27.6-45.3)	45.2 (36.4-54.3)	38.2 (29.1-47.9)
DOR, median, (range) mo	23.4 (2.7 to 75.5+)	4.3 (1.2+ to 38.2+)	7.1 (2.1+ to 73.8+)	4.2 (1.2+ to 38.2+)

Tahara M et al. ESMO 2022;Abstract 659MO.

KEYNOTE-048: Treatment-Related Adverse Events Summary



Tahara M et al. ESMO 2022;Abstract 659MO.

KEYNOTE-048 Conclusions

- With an extended follow-up of 5 years, first-line pembrolizumab monotherapy and pembrolizumab + chemotherapy continue to suggest clinical benefit in R/M HNSCC regardless of PD-L1 status
  - 5-year OS rate for overall ITT population
    - 14.4% versus 6.5% for pembrolizumab monotherapy versus EXTREME
    - 16.0% versus 5.2% for pembrolizumab + chemotherapy versus EXTREME
  - DOR remained longer with pembrolizumab or pembrolizumab + chemotherapy than with EXTREME
  - Safety was consistent with that of previous reports[1]
- Results from this study further support treatment with pembrolizumab and pembrolizumab + chemotherapy as first-line standard of care in R/M HNSCC

Tahara M et al. ESMO 2022;Abstract 659MO.

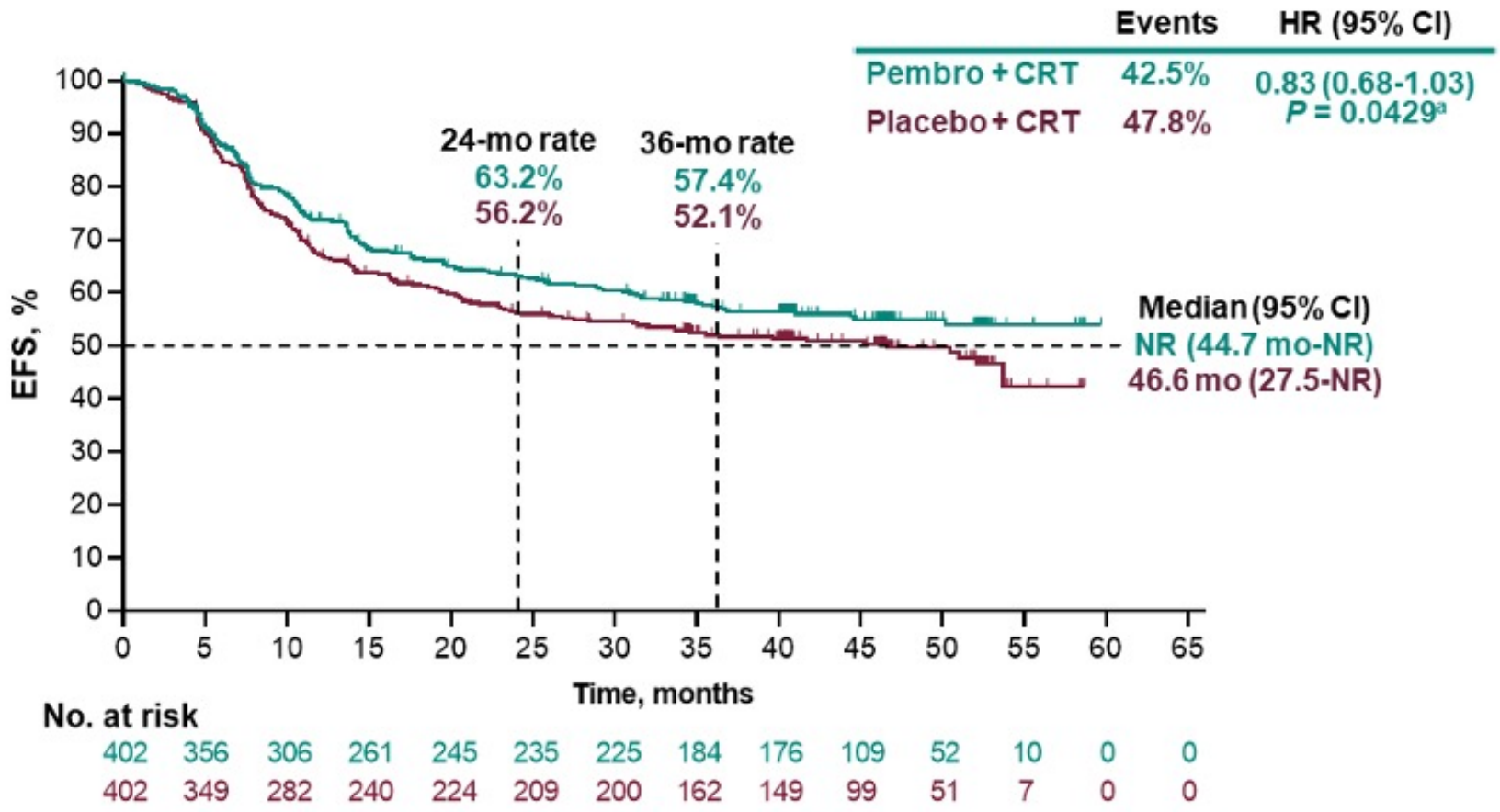
ESMO 2022; Abstract LBA5

Primary Results of the Phase 3 KEYNOTE-412 Study: Pembrolizumab Plus Chemoradiation Therapy (CRT) vs Placebo Plus CRT for Locally Advanced Head and Neck Squamous Cell Carcinoma

Jean-Pascal Machiels[1], Yungan Tao[2], Barbara Burtness[3], Makoto Tahara[4], Danny Rischin[5], Gustavo V. Alves[6], Iane Pinto Figueiredo Lima[7], Brett G.M. Hughes[8], Yoann Pointreau[9], Sercan Aksoy[10], Simon Laban[11], Richard Greil[12], Martin Burian[13], Marcin Hetnal[14], Lisa Licitra[15], Ramona Swaby[16], Yayan Zhang[17], Burak Gumuscu[17], Behzad Bidadi[17], Lillian L. Siu[18]

[1]Cliniques universitaires Saint-Luc and Institut de Recherche Clinique et Expérimentale (Pole MIRO), UCLouvain, Brussels, Belgium; [2]Institut Gustave Roussy, Villejuif, France; [3]Yale University School of Medicine and Yale Cancer Center, New Haven, CT, USA; [4]National Cancer Center Hospital East, Kashiwa, Japan; [5]Peter MacCallum Cancer Centre and the University of Melbourne, Melbourne, Australia; [6]Centro Integrado de Pesquisa em Oncologia, Hospital Nossa Senhora da Conceição, Porto Alegre, Brazil; [7]CRIO Centro Regional Integrado de Oncologia, Fortaleza-CE, Brazil; [8]Royal Brisbane and Women's Hospital and University of Queensland, Brisbane, Queensland, Australia; [9]Centre Jean Bernard, Le Mans, France; [10]Hacettepe University, Cancer Institute, Ankara, Turkey; [11]Ulm University Medical Center, Head & Neck Cancer Center of the Comprehensive Cancer Center Ulm, Department of Otorhinolaryngology, Head & Neck Surgery, Ulm, Germany; [12]Paracelsus Medical University, Salzburg Cancer Research Institute, and Cancer Cluster Salzburg, Salzburg, Austria; [13]Krankenhaus der Barmherzigen Schwestern Linz, Linz, Austria; [14]Andrzej Frycz Modrzewski Krakow University, Amethyst Radiotherapy Centre, Rydygier Hospital, Krakow, Poland; [15]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; University of Milan, Milan, Italy.; [16]Merck & Co., Inc., Rahway, NJ, USA (currently at Carisma Therapeutics, Philadelphia, PA, USA); [17]Merck & Co., Inc., Rahway, NJ, USA; [18]Princess Margaret Cancer Centre, University of Toronto, Toronto, Canada.

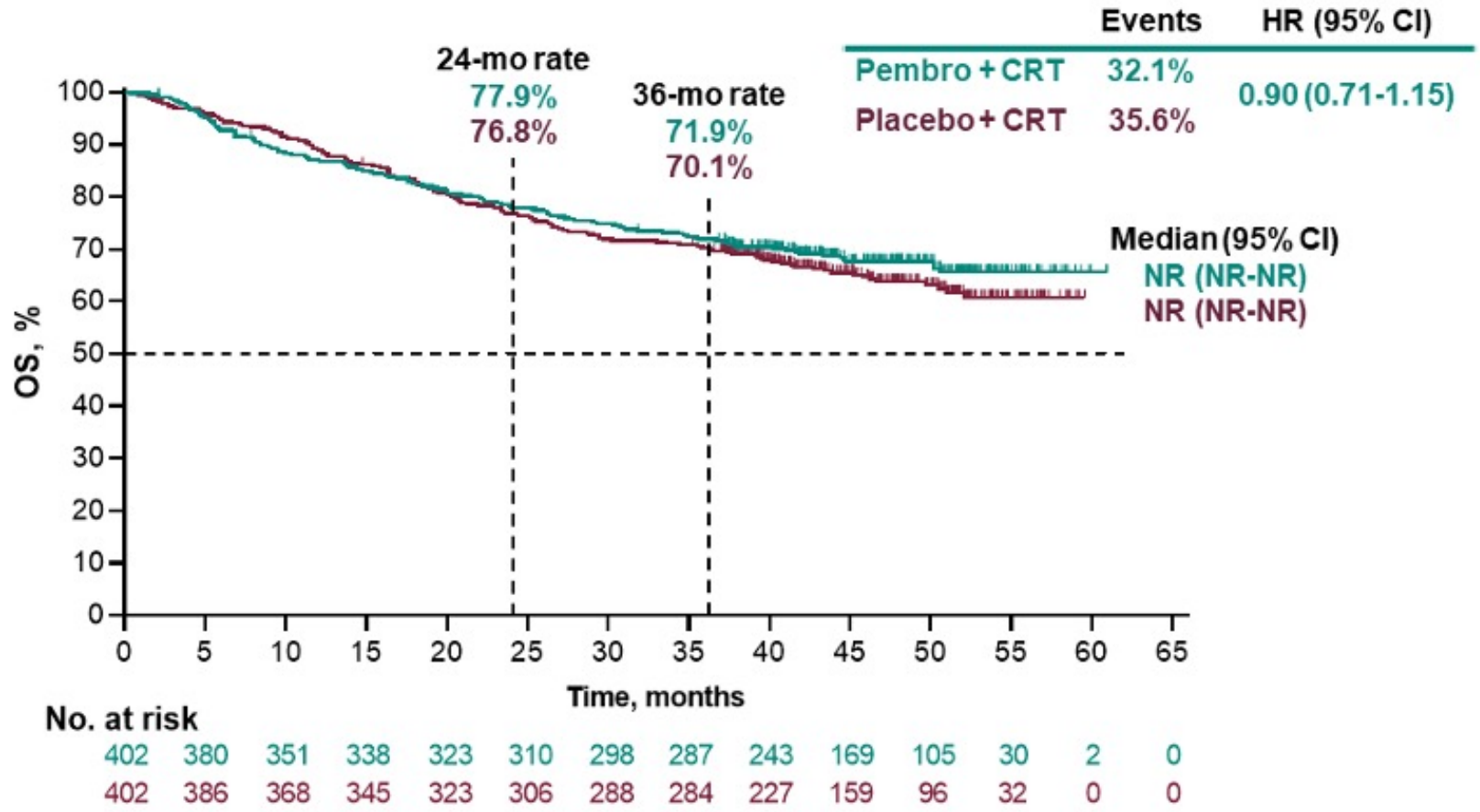
Event-Free Survival, ITT Population



[a]*P* value did not meet the superiority threshold of one-sided α of 0.0242.
Data cutoff date: May 31, 2022.

Machiels J-P et al. ESMO 2022;Abstract LBA5.

Overall Survival, ITT Population



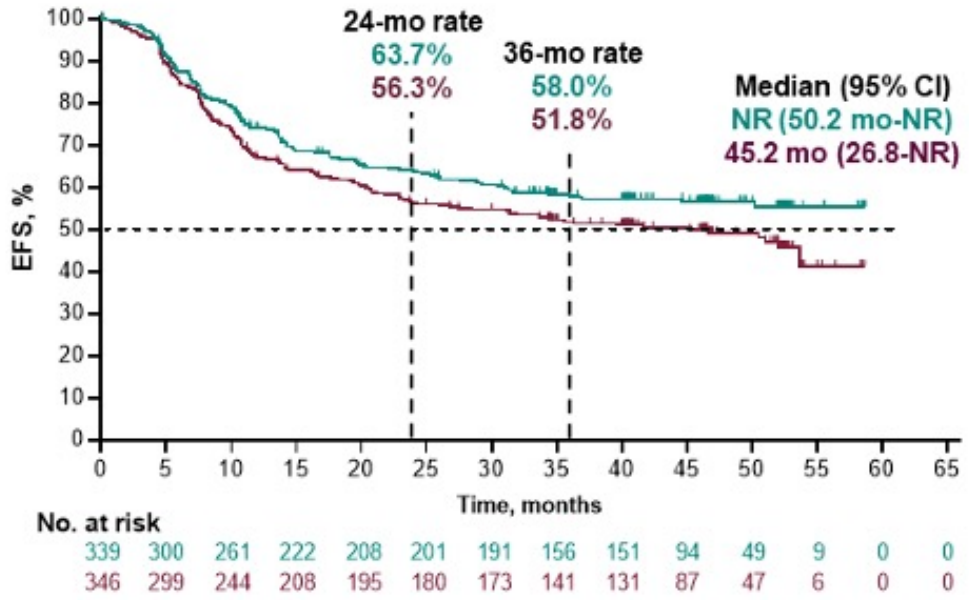
Data cutoff date: May 31, 2022.

Machiels J-P et al. ESMO 2022;Abstract LBA5.

EFS and OS in Patients With PD-L1 CPS ≥1 (Prespecified Subgroup Analysis)

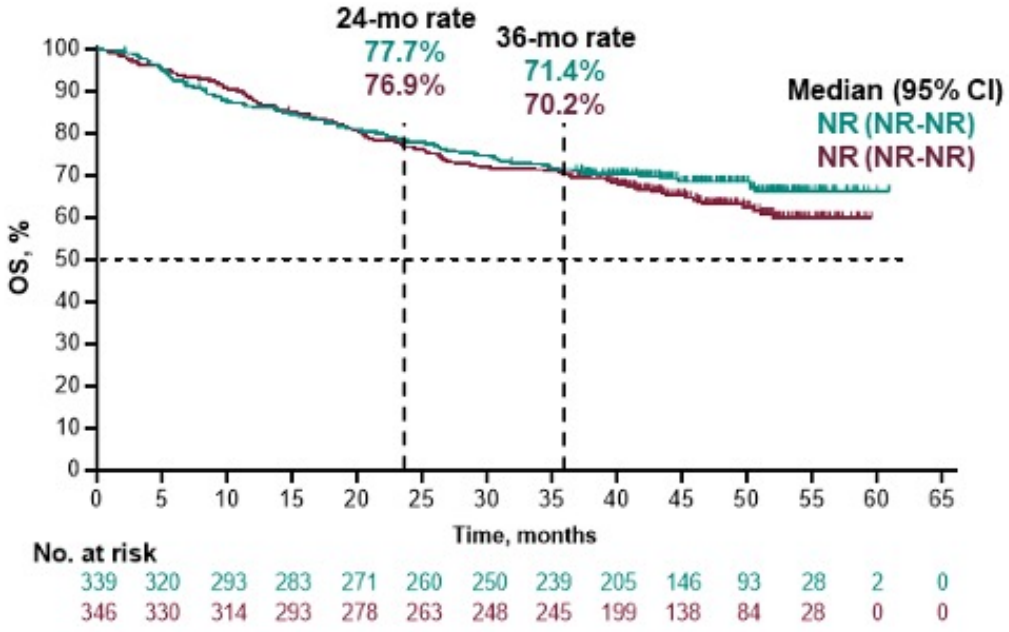
EFS

	Events	HR (95% CI)
Pembro + CRT	41.6%	0.80 (0.64-1.00)
Placebo + CRT	48.6%	



OS

	Events	HR (95% CI)
Pembro + CRT	31.6%	0.88 (0.68-1.14)
Placebo + CRT	36.1%	



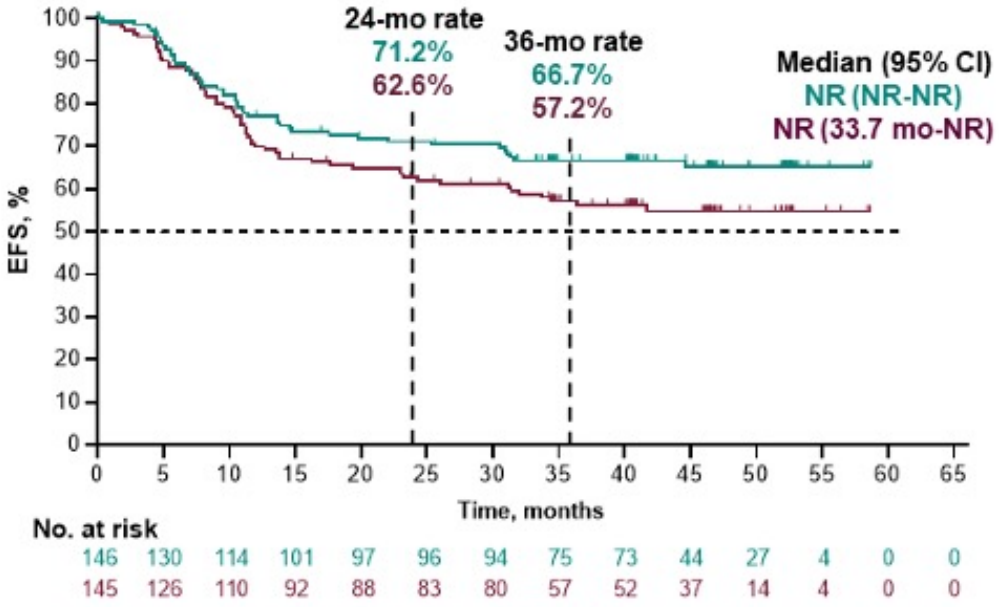
Data cutoff date: May 31, 2022.

Machiels J-P et al. ESMO 2022;Abstract LBA5.

EFS and OS in Patients With PD-L1 CPS ≥20 (Post Hoc Analysis)

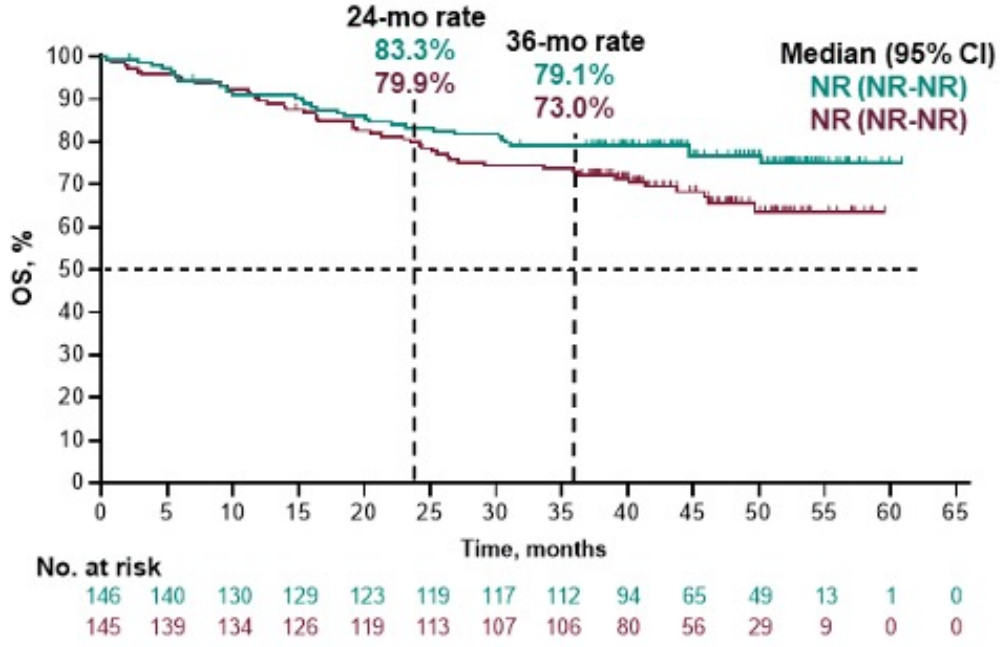
EFS

	Events	HR (95% CI)
Pembro + CRT	32.2%	0.73 (0.49-1.06)
Placebo + CRT	42.1%	



OS

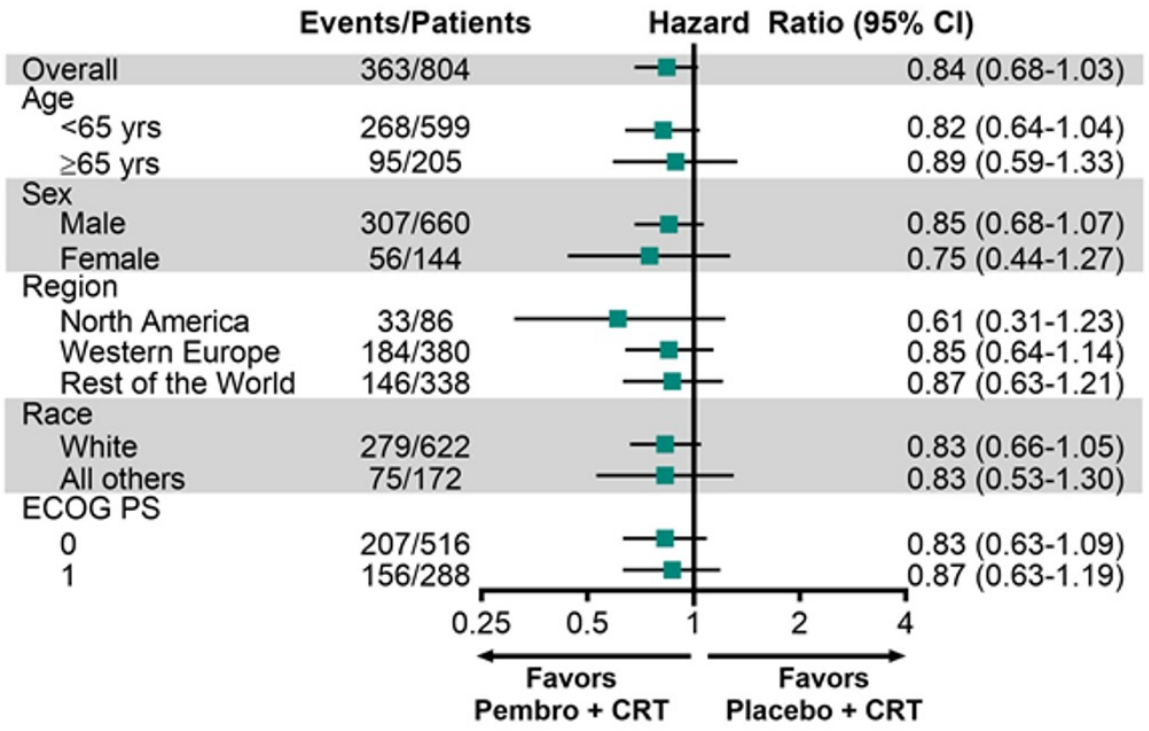
	Events	HR (95% CI)
Pembro + CRT	22.6%	0.67 (0.43-1.04)
Placebo + CRT	32.4%	

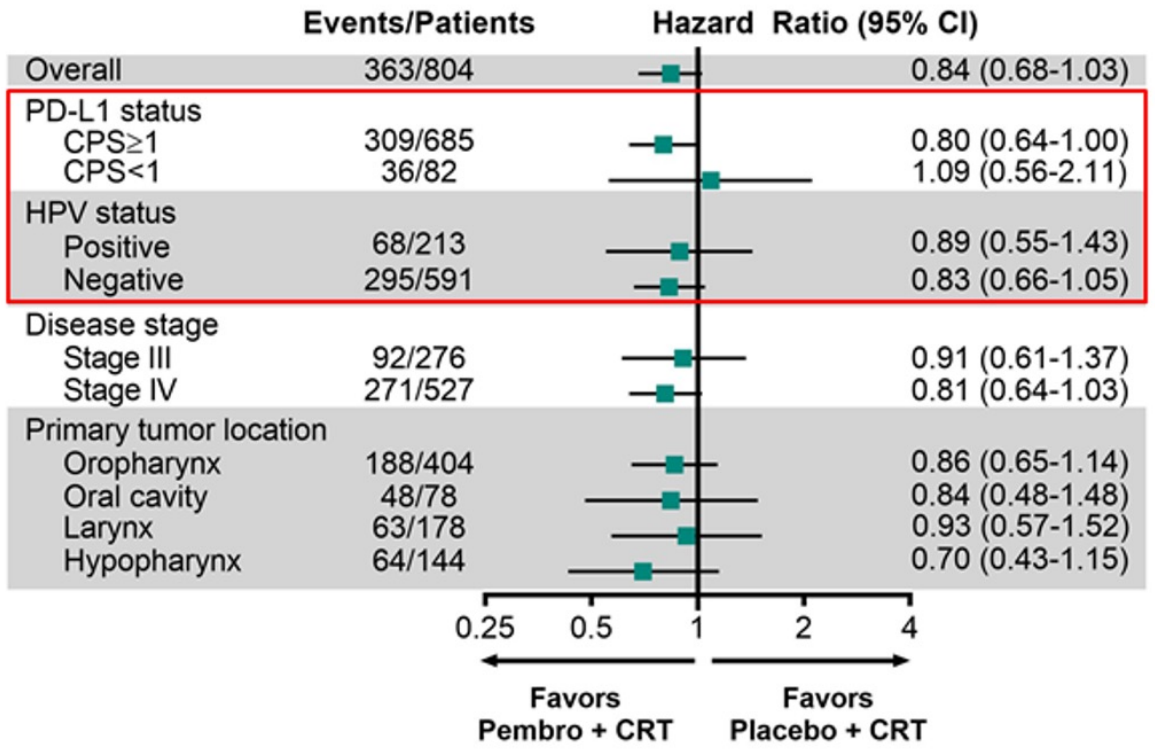


Data cutoff date: May 31, 2022.

Machiels J-P et al. ESMO 2022;Abstract LBA5.

KEYNOTE-412: EFS in Prespecified Subgroups (ITT)





Machiels J-P et al. ESMO 2022;Abstract LBA5.

RTP RESEARCH TO PRACTICE

Summary and Conclusions

- Pembrolizumab plus CRT was associated with a favorable trend toward improved EFS vs placebo plus CRT in patients with LA HNSCC (HR, 0.83; *P* = 0.0429)
  - The difference did not reach statistical significance (superiority threshold, one-sided *P* = 0.0242)
  - 24-mo EFS rate: 63.2% vs 56.2%
- PD-L1 expression[a] may be an informative predictive biomarker
  - CPS ≥1: 24-mo EFS rate, 63.7% vs 56.3%; 36-mo OS rate, 71.4% vs 70.2%
  - CPS ≥20: 24-mo EFS rate, 71.2% vs 62.6%; 36-mo OS rate, 79.1% vs 73.0% (post hoc analysis)
- No new safety signals with the combination of pembrolizumab plus CRT
- LA HNSCC remains a challenging disease to treat

[a]Measured by CPS using PD-L1 IHC 22C3 pharmDx.

Machiels J-P et al. ESMO 2022;Abstract LBA5.

PARIS 2022 ESMO congress

Presidential Symposium 2

Medical Oncologist's Point of View

LBA 4, 5, 6 and 7

James Larkin

Royal Marsden NHS Foundation Trust / Institute of Cancer Research
London UK

Why did KN 412 miss the primary endpoint?

- Chemotherapy + anti-PD1 has benefit in advanced disease, so why the difference?
- There is a signal here, particularly in the high PD-L1 group, consistent with the (also negative) Javelin 100 study, although caution required comparing avelumab (anti-PD-L1) with pembrolizumab (anti-PD1)
- Is there an issue with treatment schedule? e.g. PACIFIC in NSCLC is an analogous (positive) trial where checkpoint inhibition was given after chemoradiotherapy
- Is there an issue with lymph node RT when combining with checkpoint inhibitors? RT is the central component of treatment in this setting but could it be modified?
- As already suggested, a better understanding of integrating checkpoint inhibition with radiotherapy in terms of timing, fields, dose and fractionation is needed

Larken J. ESMO 2022.

Meet The Professor with Dr Haddad

MODULE 1: ESMO 2022

MODULE 2: Needle in a Haystack

- Dr Cohen: 51-year-old man presents with metastatic anaplastic thyroid cancer

MODULE 3: Head and Neck Cancer

MODULE 4: Thyroid Cancer

MODULE 5: Journal Club with Dr Haddad

MODULE 6: Appendix

RTP
RESEARCH
TO PRACTICE

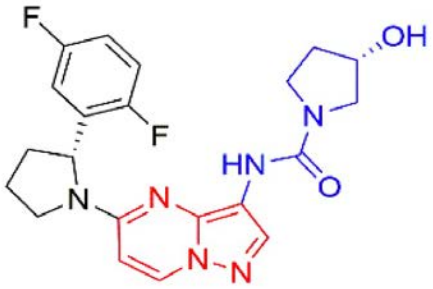
Case Presentation: 51-year-old man presents with metastatic anaplastic thyroid cancer

Dr Ezra Cohen (La Jolla, California)

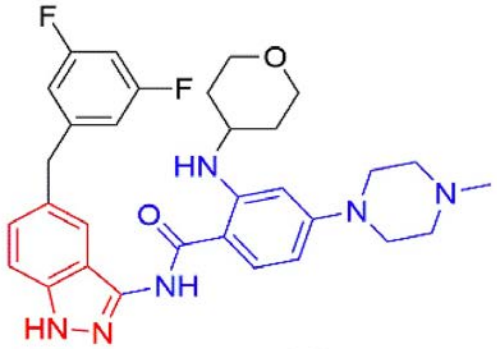
RTP RESEARCH TO PRACTICE

FDA Approved and Investigational TRK Inhibitors for Patients with Solid Tumors with NTRK Gene Fusions

FDA-approved first-generation NTRK gene fusion inhibitors

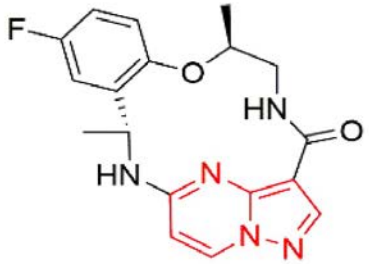


Larotrectinib
MW 428.44

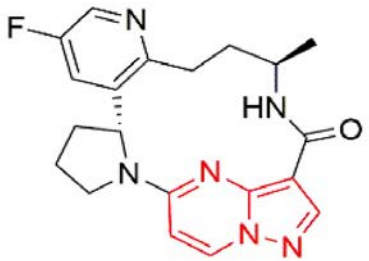


Entrectinib
MW 560.65

Second-generation investigational NTRK gene fusion inhibitors



Repotrectinib
MW 355.37



Selitrectinib
MW 380.43

Larotrectinib: FDA approval 11/26/2018

- Based on LOXO-TRK-14001, SCOUT and NAVIGATE

Entrectinib: FDA approval 8/15/2019

- Based on ALKA, STARTRK-1 and STARTRK-2

Repotrectinib* and selitrectinib

- Next-generation TRK tyrosine kinase inhibitors with a compact macrocyclic structure that binds completely inside the ATP binding pocket even in the presence of mutations

* Breakthrough therapy designation: 10/6/2021

Besse B et al. AACR-NCI-EORTIC Virtual International Conference 2021;Abstract LB6546.
Larotrectinib PI, rev 3/2021; Entrectinib PI, rev 7/2022; https://www.tptherapeutics.com/news-releases/news-release-details/turning-point-therapeutics-granted-breakthrough-therapy

TRK Inhibitor Activity in Solid Tumors with NTRK Gene Fusions – Data from the Registrational Studies

	Larotrectinib (LOXO-TRK-14001, SCOUT, NAVIGATE) (N = 244)	Entrectinib (ALKA, STARTRK-1, STARTRK-2) (N = 150)
Median age	38	58.5
NTRK fusion NTRK1 NTRK2 NTRK3	 46% 3% 51%	Not reported
Prior lines of systemic therapy 0 1 ≥2	 27% 28% 44%	 34% 29% 37%
ORR (CR)	69% (21%)	61% (17%)
Median DoR	33 mo	20 mo
Median PFS	29 mo	14 mo
Median OS	Not reached	37 mo

Drilon A et al. ASCO 2022;Abstract 3100. Krzakowski M et al. ASCO 2022;Abstract 3099.

Genetic Alterations Associated with Different Histotypes of Thyroid Cancer

	PTC	FTC	PDTC	ATC	MTC
AKT	1%	1%-2.6%	-	0%-3%	-
BRAF	**61.7%**	**1.7%**	**19%-33%**	**19%-45%**	-
DICER1	2.7%	5.1%	-	1.1%	-
EIF1AX	1.5%	5.1%	10%	9%	0.6%
HRAS	2%	7%	5%	6%	9.3%-15.8%
KRAS	1.3%	4%	2%	0%-5%	3.0%-6.2%
NRAS	6%	17%-57%	21%	18%	0.6%-1%
PAX8-PPARγ	0.8%	12%-53%	4%	0	-
PI3KCA	-	5.5%	2%	18%	-
PTEN	1%	7.1%	4%	15%	1%
RET	**-**	**-**	**-**	**-**	**55.8%**
RET/PTC	**6.8%**	**0**	**14%**	**0**	**Very rare**
SWI/SNF	-	-	6%	18%-36%	-
TERT promoter	9.4%	-	33%-40%	43%-73%	-
TP53	6%	5.1%-9.7%	0%-8%	43%-78%	1.2%
NTRK-Fusion	2-19%	-	-	-	-
TSHR	2%	10.3%	2%	6%	0.6%

Brose MS. ASCO 2022 Education Session. Prete A et al. *Front Endocrinol (Lausanne)* 2020;11:102.

RTP RESEARCH TO PRACTICE

Considerations for RET and TRK Fusion Testing Methodologies

FISH	• Current standard for detection of gene fusions; break-apart probes preferred to fusion probes • Difficulties in FISH interpretation: pericentric fusions, close proximity of several possible partner genes to fusion gene (RET or TRK) • Limitation: not optimal for extensive and multiplex screening, or when recognition of fusion partner influences clinical decisions
RT-PCR	• Can detect fusion transcripts and identify fusion partner if primer for specific partner is present • Limitation: imbalance assay for unknown fusion partner is highly dependent on expression of partner and may not be reliable
DNA NGS	• NGS panel sequencing can identify fusions if specifically designed to examine introns • Limitations: limited sensitivity for detection of fusion genes and no information on effective transcription of rearranged *RET or TRK* genes
RNA NGS	• Targeted RNA-based assays are method of choice for *RET* and TRK fusion screening; allows detection of gene fusions with complex rearrangements • Limitation: assessment of RNA quality is crucial to ensure accuracy; poor preanalytical conditions may affect assay

Brose MS. ASCO 2022 Education Session. Bell C et al. *Ann Oncol* 2021:32(3):337-50.

Lancet Oncol 2020;21(4):531-40.

Larotrectinib in patients with TRK fusion-positive solid tumours: a pooled analysis of three phase 1/2 clinical trials

David S Hong, Steven G DuBois, Shivaani Kummar, Anna F Farago, Catherine M Albert, Kristoffer S Rohrberg, Cornelis M van Tilburg, Ramamoorthy Nagasubramanian, Jordan D Berlin, Noah Federman, Leo Mascarenhas, Birgit Geoerger, Afshin Dowlati, Alberto S Pappo, Stefan Bielack, François Doz, Ray McDermott, Jyoti D Patel, Russell J Schilder, Makoto Tahara, Stefan M Pfister, Olaf Witt, Marc Ladanyi, Erin R Rudzinski, Shivani Nanda, Barrett H Childs, Theodore W Laetsch, David M Hyman, Alexander Drilon**

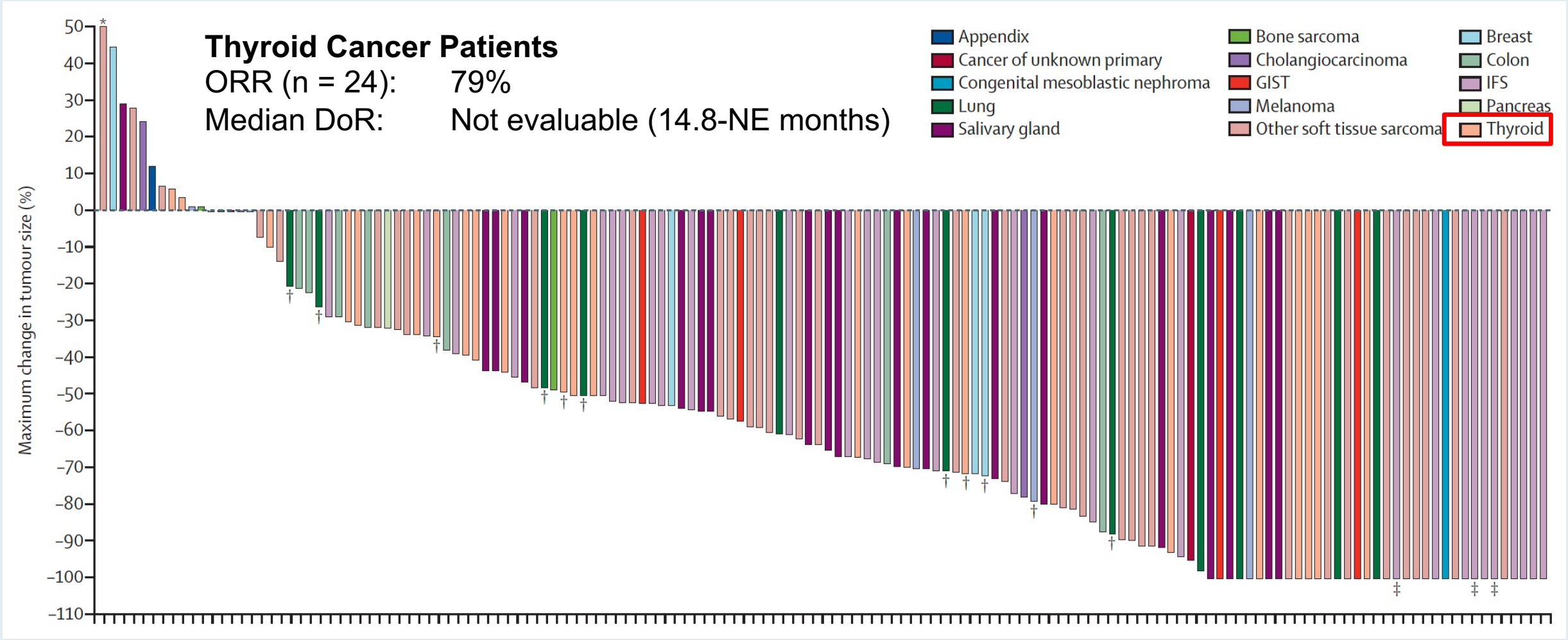
Clinical Characteristics of Patients in 3 Pooled Phase I/II Studies

	All patients (n=159)
Study*	
Adult phase 1	12 (8%)
Paediatric phase 1/2	50 (31%)
Adolescents and adult phase 2 basket study	97 (61%)
Sex	
Male	77 (48%)
Female	82 (52%)
Age	
Median, years	43·0 (6·5–61)
Range	<1 month to 84 years
Age group distribution, years	
<1	24 (15%)
1 to <18	28 (18%)
18 to <65	77 (48%)
≥65	30 (19%)

Tumour type	
Soft tissue sarcoma	
Infantile fibrosarcoma	29 (18%)
Gastrointestinal stromal tumour	4 (3%)
Other	36 (23%)
Thyroid	26 (16%)
Salivary gland	21 (13%)
Lung	12 (8%)
Colon	8 (5%)
Melanoma	7 (4%)
Breast	5 (3%)
Bone sarcoma	2 (1%)
Cholangiocarcinoma	2 (1%)
Pancreas	2 (1%)
Appendix	1 (<1%)
Congenital mesoblastic nephroma	1 (<1%)
Hepatocellular	1 (<1%)
Prostate	1 (<1%)
Unknown primary	1 (<1%)

Hong DS et al. *Lancet Oncol* 2020;21(4):531-40.

Waterfall Plot of Maximum Percent Change in Tumor Size with Larotrectinib in Patients with Solid Tumors with TRK Fusions



Hong DS et al. *Lancet Oncol* 2020;21(4):531-40.

Lancet Oncol 2020;21(2):271-82.

Entrectinib in patients with advanced or metastatic *NTRK* fusion-positive solid tumours: integrated analysis of three phase 1–2 trials

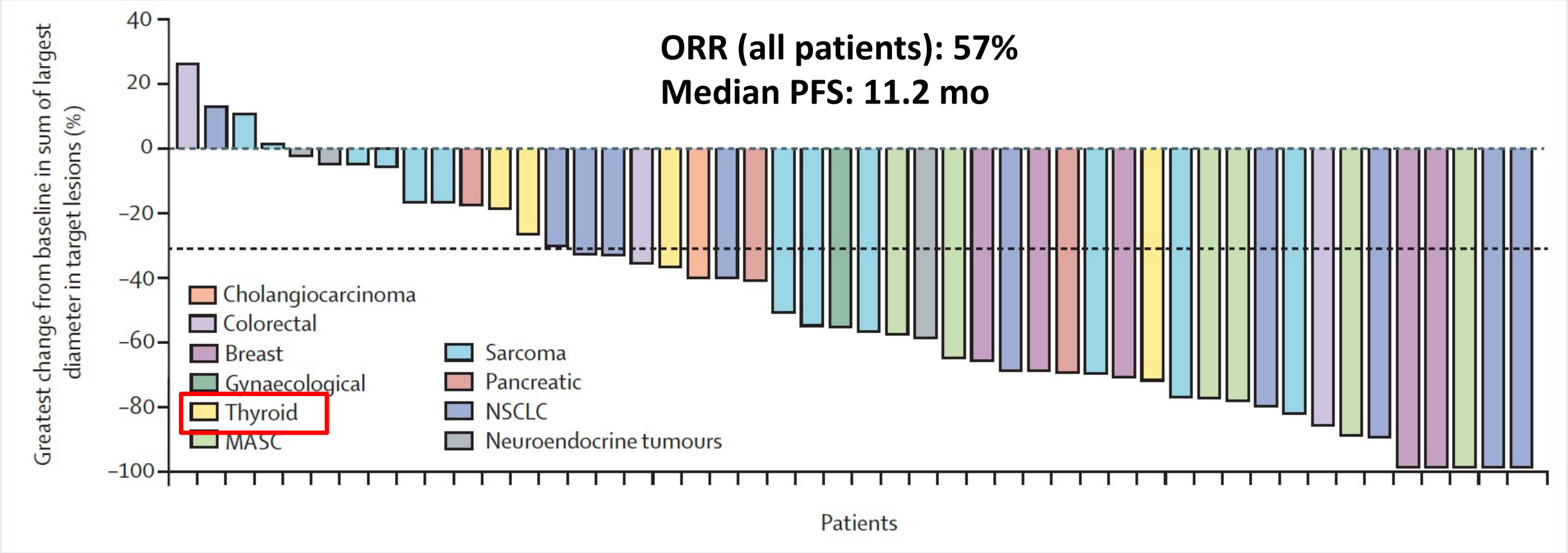
Robert C Doebele, Alexander Drilon*, Luis Paz-Ares, Salvatore Siena, Alice T Shaw, Anna F Farago, Collin M Blakely, Takashi Seto, Byung Chul Cho, Diego Tosi, Benjamin Besse, Sant P Chawla, Lyudmila Bazhenova, John C Krauss, Young Kwang Chae, Minal Barve, Ignacio Garrido-Laguna, Stephen V Liu, Paul Conkling, Thomas John, Marwan Fakih, Darren Sigal, Herbert H Loong, Gary L Buchschacher Jr, Pilar Garrido, Jorge Nieva, Conor Steuer, Tobias R Overbeck, Daniel W Bowles, Elizabeth Fox, Todd Riehl, Edna Chow-Maneval, Brian Simmons, Na Cui, Ann Johnson, Susan Eng, Timothy R Wilson, George D Demetri, on behalf of the trial investigators*

Entrectinib for Advanced or Metastatic Solid Tumors with NTRK Fusions (ALKA, STARTRK-1, STARTRK-2)

	All patients in *NTRK* gene fusion-positive efficacy-evaluable population (n=54)
Age, years	58 (48–67)
Tumour type	
Sarcoma‡	13 (24%)
NSCLC	10 (19%)
Mammary analogue secretory carcinoma (salivary)	7 (13%)
Breast	6 (11%)
Thyroid	5 (9%)
Colorectal	4 (7%)
Neuroendocrine	3 (6%)
Pancreatic	3 (6%)
Gynaecological	2 (4%)
Ovarian	1 (2%)
Endometrial	1 (2%)
Cholangiocarcinoma	1 (2%)

Doebele RC et al. *Lancet Oncol* 2020;21(2):271-82.

Entrectinib for Advanced or Metastatic Solid Tumors with NTRK Fusions (ALKA, STARTRK-1, STARTRK-2)



Doebele RC et al. *Lancet Oncol* 2020;21(2):271-82.

Oncologist 2022 May 10;[Online ahead of print].

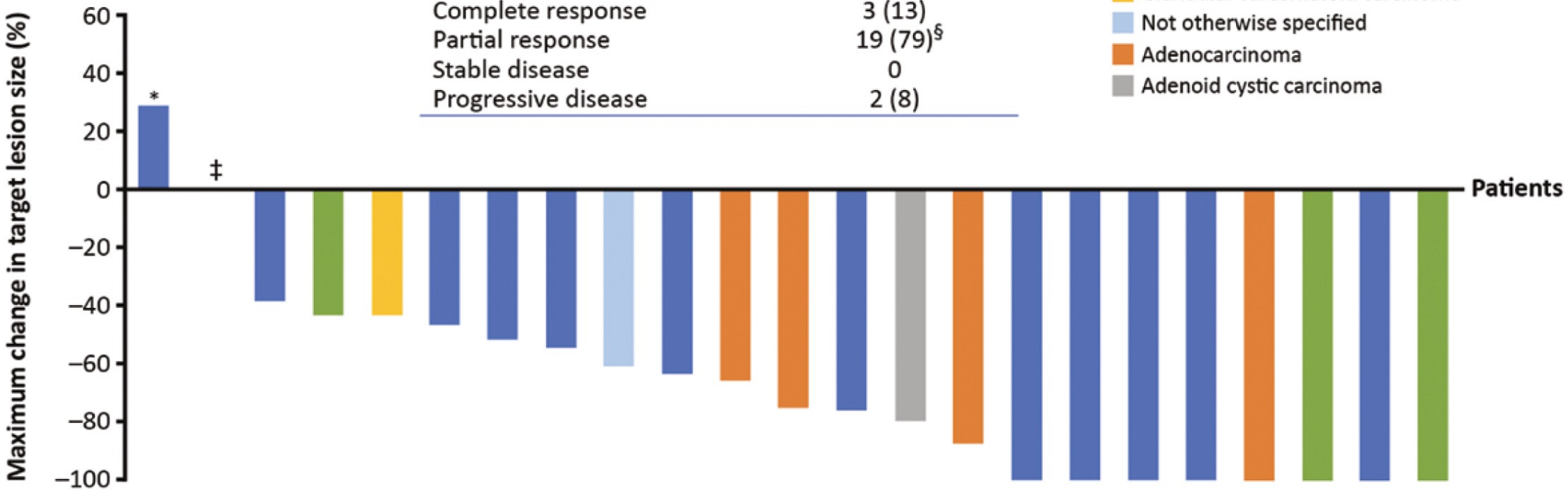
Original Article

Larotrectinib Treatment for Patients With TRK Fusion-Positive Salivary Gland Cancers

Xiuning Le[1,*], Christina Baik[2], Jessica Bauman[3], Jill Gilbert[4], Marcia S. Brose[5], Juneko E. Grilley-Olson[6], Tejas Patil[7], Ray McDermott[8,9], Luis E. Raez[10], Jennifer M. Johnson[5], Lin Shen[11], Makoto Tahara[12], Alan L. Ho[13,14], Ricarda Norenberg[15], Laura Dima[16], Nicoletta Brega[17], Alexander Drilon[13,14], David S. Hong[1]

Maximum Change in Target Lesion Size and Response After Treatment with Larotrectinib

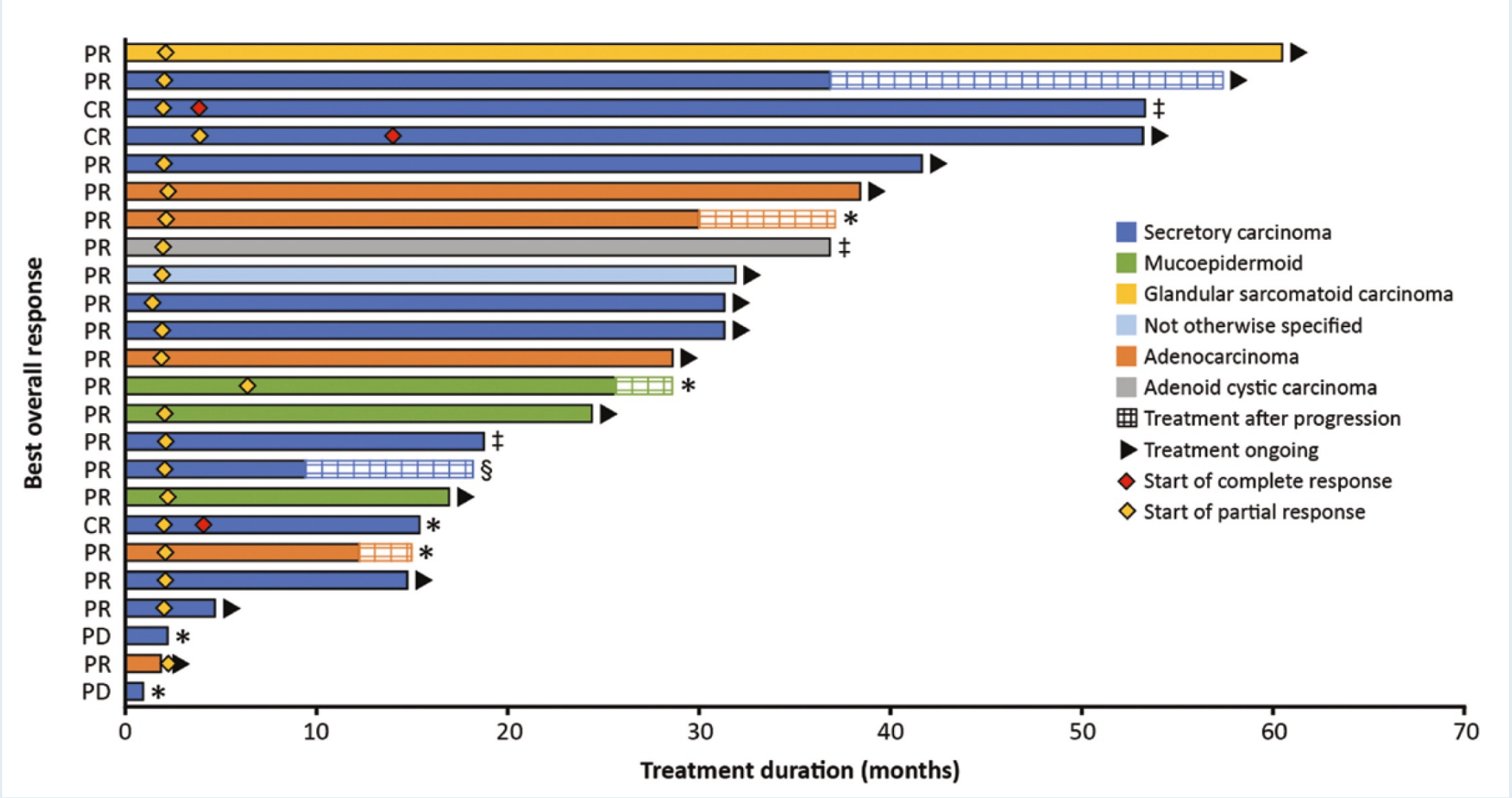
	N = 24
ORR, % (95% CI)	92 (73–99)
Best overall response, *n* (%)	
Complete response	3 (13)
Partial response	19 (79)[§]
Stable disease	0
Progressive disease	2 (8)



Le X et al. *Oncologist* 2022 May 10;[Online ahead of print].

RTP RESEARCH TO PRACTICE

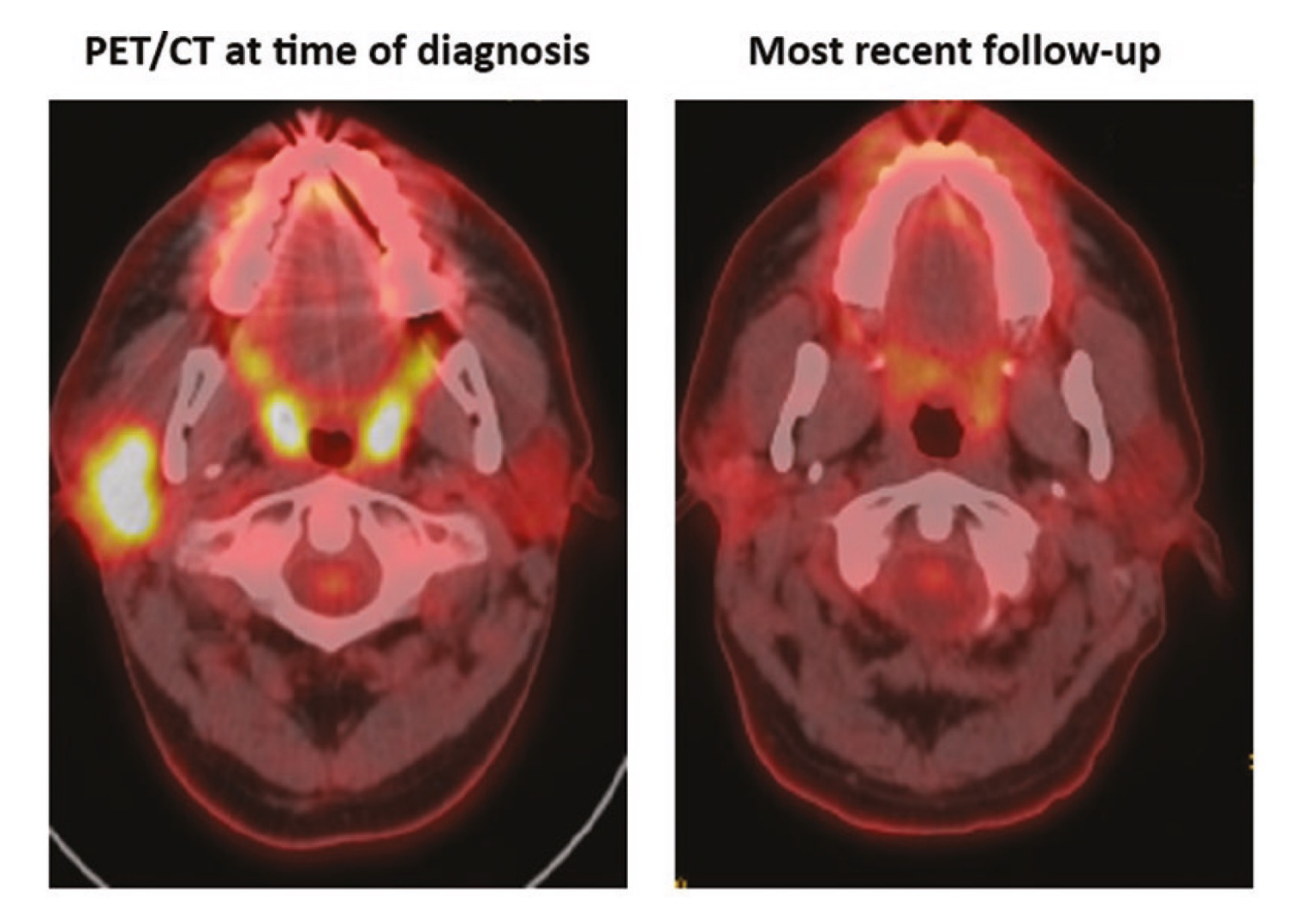
Treatment Duration with Larotectinib for Patients with Salivary Gland Cancer with NTRK Fusions



Le X et al. *Oncologist* 2022 May 10;[Online ahead of print].

RTP RESEARCH TO PRACTICE

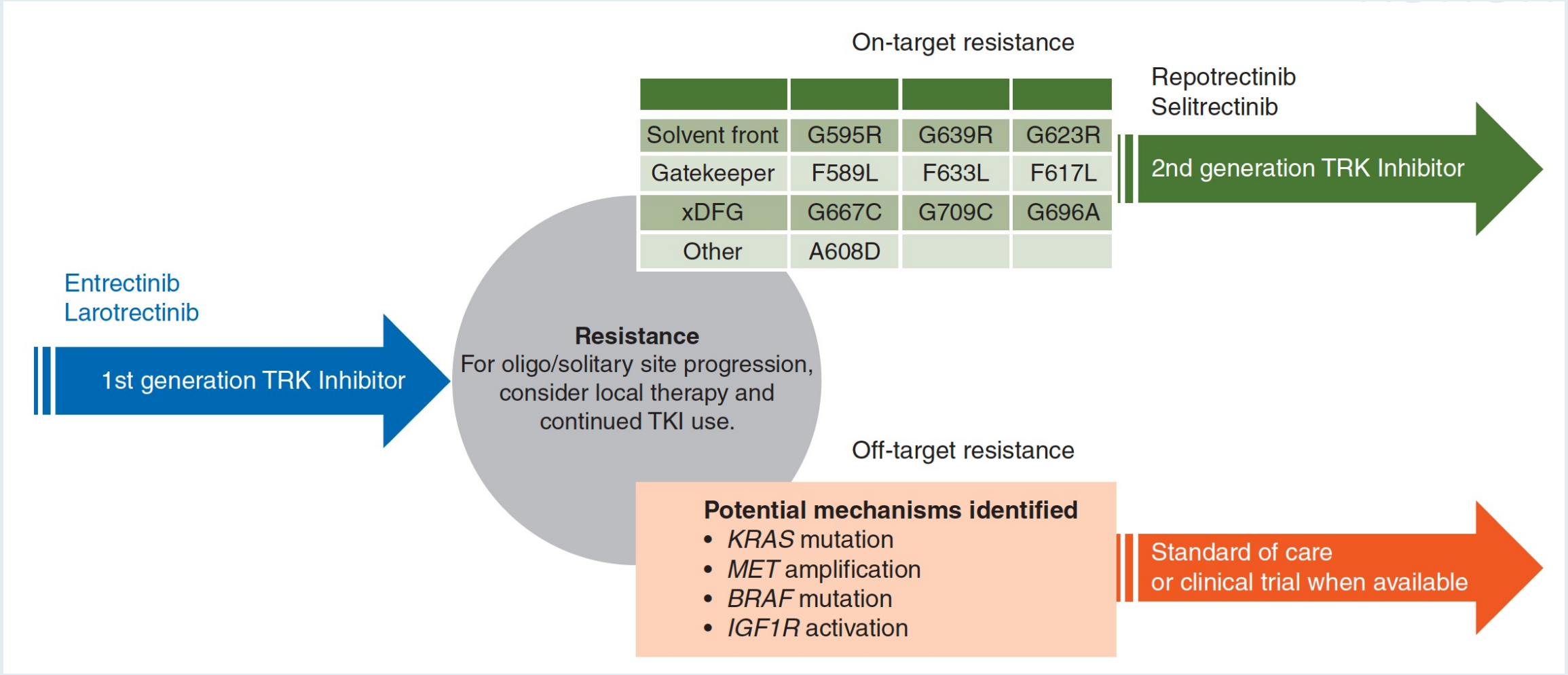
Response to Larotrectinib in a Patient with Secretory Carcinoma of the Salivary Gland with ETV6-NTRK3 Fusion



Le X et al. *Oncologist* 2022 May 10;[Online ahead of print].

RTP RESEARCH TO PRACTICE

Mechanisms of Resistance to NTRK Inhibitors and Sequential Therapy



Drilon A. *Ann Oncol* 2019;30(Suppl 8):23-30.

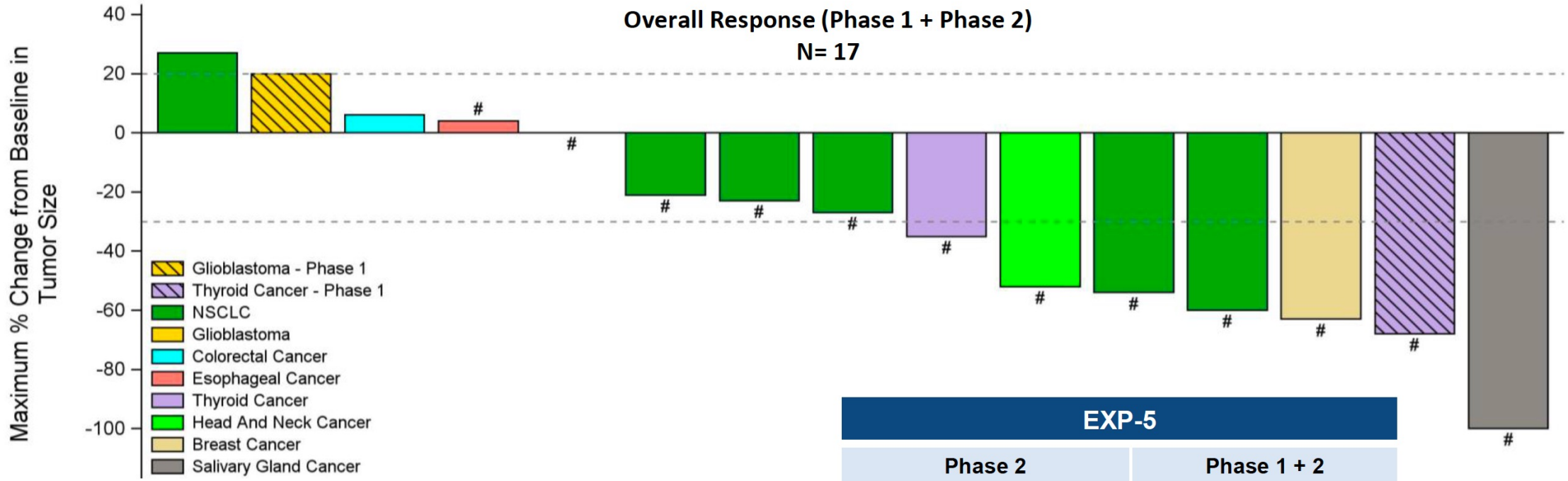
AACR-NCI-EORTC Virtual International Conference on
MOLECULAR TARGETS AND CANCER THERAPEUTICS
October 7-10, 2021

LB #6546

Repotrectinib in patients with *NTRK* fusion-positive advanced solid tumors: update from the registrational phase 2 TRIDENT-1 trial

Benjamin Besse,[1] Christina Baik,[2] Christoph Springfeld,[3] Alice Hervieu,[4] Victor Moreno,[5] Lyudmila Bazhenova,[6] Jessica J. Lin,[7] D. Ross Camidge,[8] Benjamin Solomon,[9] Vamsidhar Velcheti,[10] Young-Chul Kim,[11] Anthonie J. van der Wekken,[12] Enriqueta Felip,[13] Dipesh Uprety,[14] Denise Trone,[15] Shanna Stopatschinskaja,[15] Byoung Chul Cho,[16] Alexander Drilon[17]

TRIDENT-1: Preliminary Efficacy with Repotrectinib for TKI-Naïve Advanced Solid Tumors with NTRK Fusions



Patient remains on treatment.
2 patients not displayed due to discontinuing treatment prior to first post-baseline scan.

	EXP-5	
	Phase 2 (N=15)	**Phase 1 + 2 (N=17)**
Confirmed ORR (cORR) (95% CI)	**40%** (16 – 68)	**41%** (18 – 67)
Duration of Response (range in months)	1.9+ – 7.4+ n=6	1.9+ – 7.4+ n=7

Besse B et al. AACR-NCI-EORTC Virtual International Conference 2021;Abstract 6546.

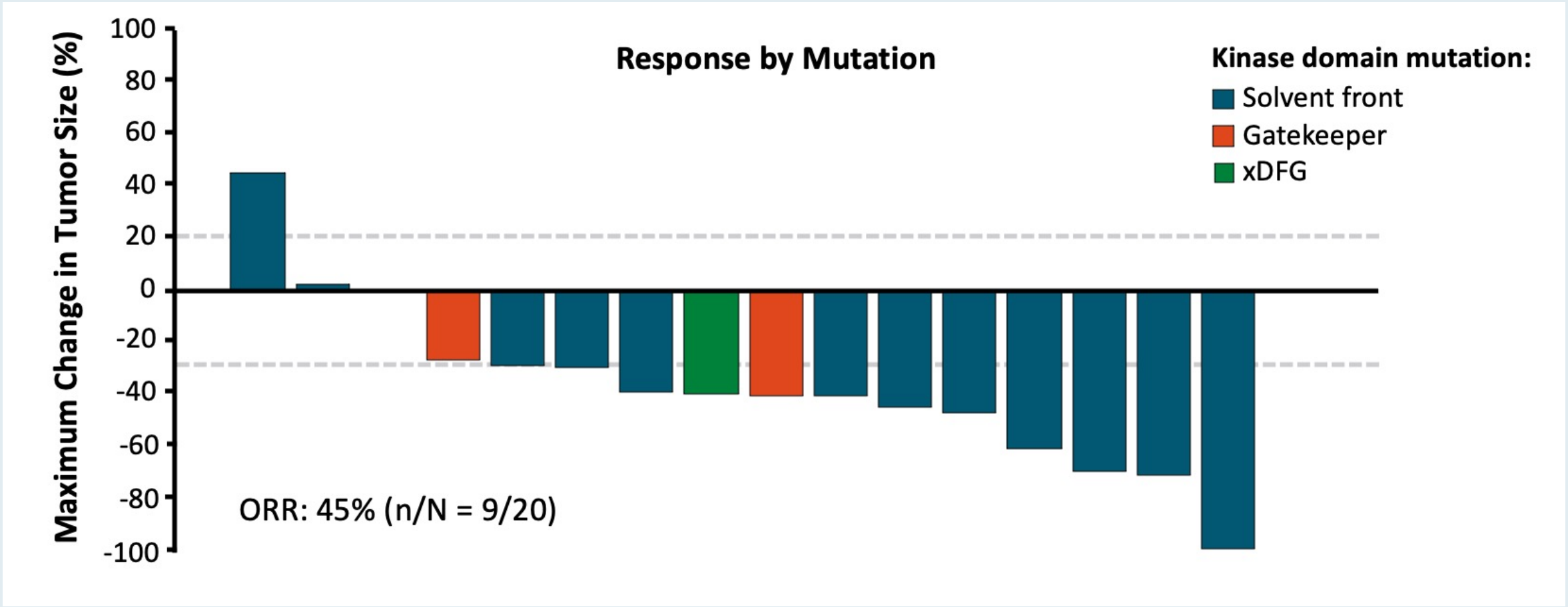
RTP RESEARCH TO PRACTICE

Phase I and Expanded Access Experience of LOXO-195 (BAY 2731954), a Selective Next-Generation TRK Inhibitor (TRKi)

Hyman D et al.

AACR 2019;Abstract CT127.

Activity of Selitrectinib (LOXO-195) in a Phase I/Expanded Access Study for Adults and Children with Progressive Disease or Intolerance to a Prior TRK Inhibitor



Hyman D et al. AACR 2019;Abstract CT127.

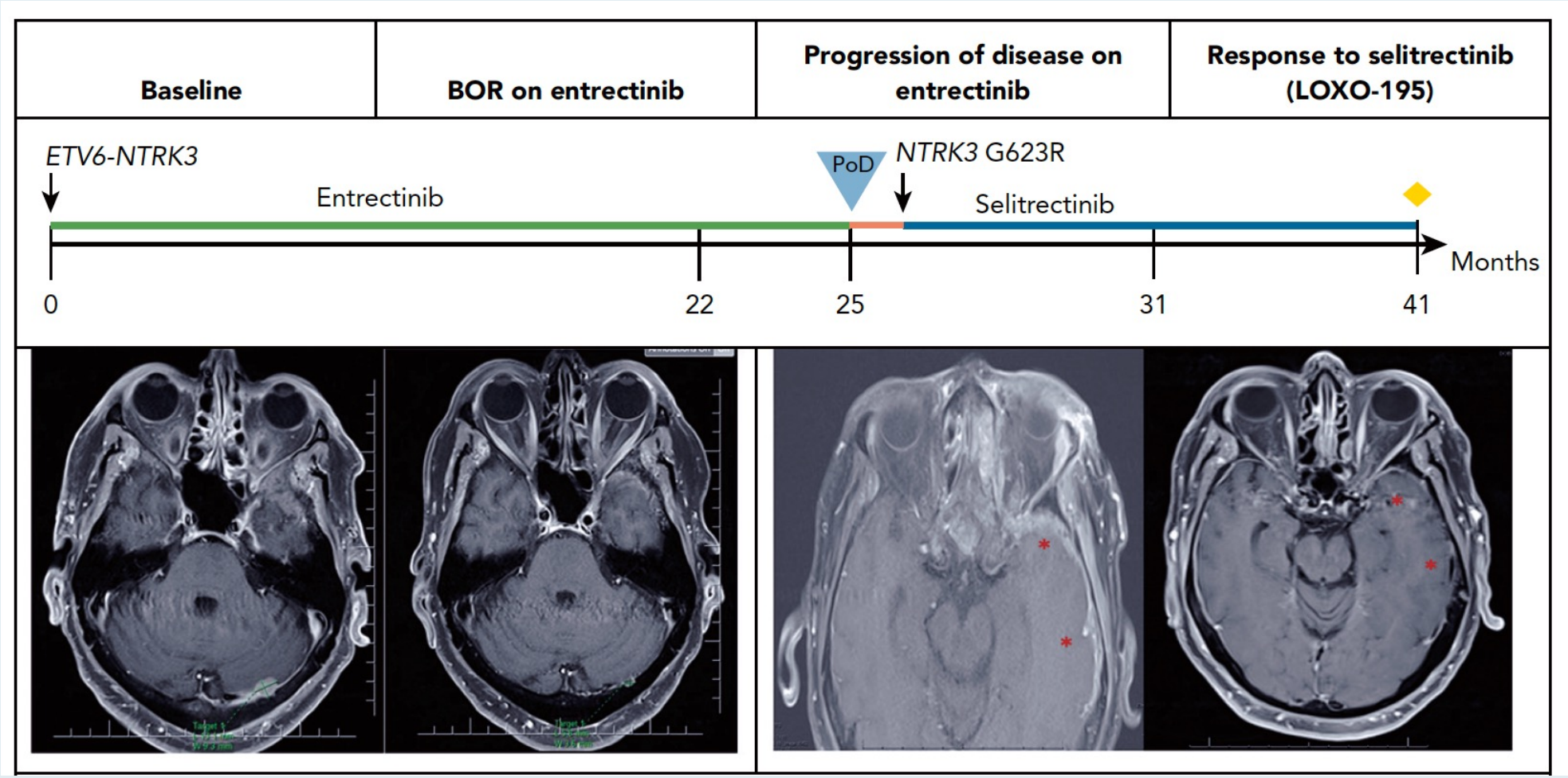
MOLECULAR INSIGHTS IN PATIENT CARE

Clinical Activity of Selitrectinib in a Patient With Mammary Analogue Secretory Carcinoma of the Parotid Gland With Secondary Resistance to Entrectinib

Vaia Florou, MD[1]; Christopher Nevala-Plagemann, MD[1]; Jonathan Whisenant, MD[1]; Patricia Maeda, MD[2]; Glynn W. Gilcrease, MD[1]; and Ignacio Garrido-Laguna, MD, PhD[1]

J Natl Compr Canc Netw 2021;19(5):478-82.

Most Characteristic Imaging Studies Showing Response to Selitrectinib After Disease Progression on Entrectinib



Florou V et al. *J Natl Compr Canc Netw* 2021;19(5):478-82.

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Haddad

MODULE 3: Head and Neck Cancer

- Dr Rupard: 67-year-old man s/p IO therapy for melanoma is diagnosed with Stage I (cN2 N1) p16-positive SCC of the left tonsil
- Dr Cohen: 42-year-old Asian woman s/p cisplatin/RT and gemcitabine/cisplatin for locoregionally advanced nasopharyngeal cancer develops metastatic disease – PD-L1 CPS 10
- Dr Morganstein: 72-year-old man presents with recurrent and rapidly progressing HPV-negative metastatic head and neck cancer
- Dr Choksi: 58-year-old man s/p definitive RT and surgery for locally recurrent SCC of the head and neck presents with worsening shortness of breath
- Dr Bachow: 73-year-old man with a longstanding history of T-cell large granular lymphocytic leukemia presents with metastatic HPV-positive SCC of the left tonsil – PD-L1-negative
- Dr Cohen: 57-year-old man presents with HPV-positive Stage III cancer of the base of the tongue

Case Presentation: 67-year-old man s/p IO therapy for melanoma is diagnosed with Stage I (cN2 N1) p16-positive SCC of the left tonsil

Dr Erik Rupard (West Reading, Pennsylvania)

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Case Presentation: 42-year-old Asian woman s/p cisplatin/RT and gemcitabine/cisplatin for locoregionally advanced nasopharyngeal cancer develops metastatic disease – PD-L1 CPS 10

Dr Ezra Cohen (La Jolla, California)

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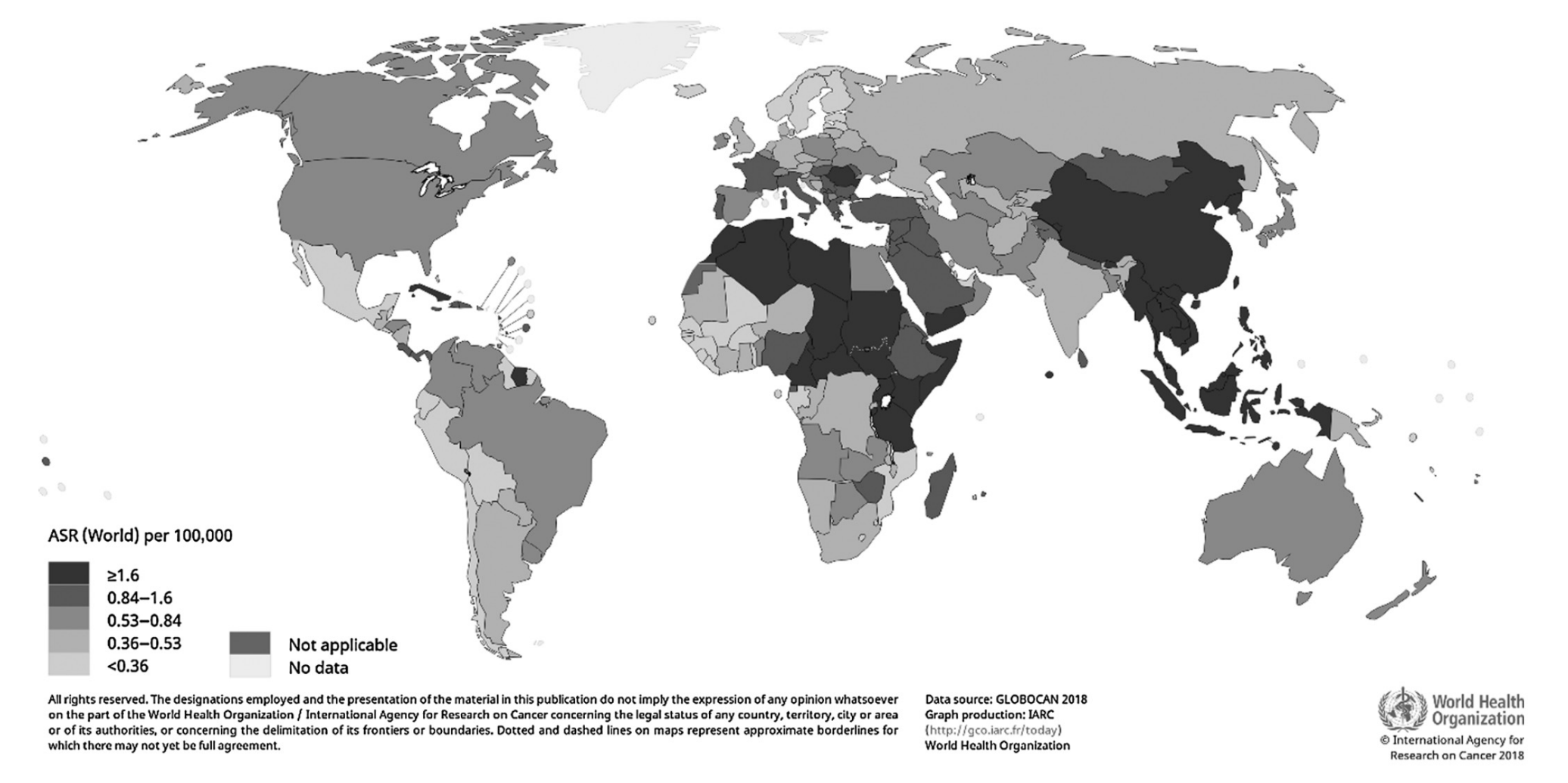
Cancer Epidemiol Biomarkers Prev 2021;30:1035-47.

CANCER EPIDEMIOLOGY, BIOMARKERS & PREVENTION | REVIEW

The Evolving Epidemiology of Nasopharyngeal Carcinoma AC

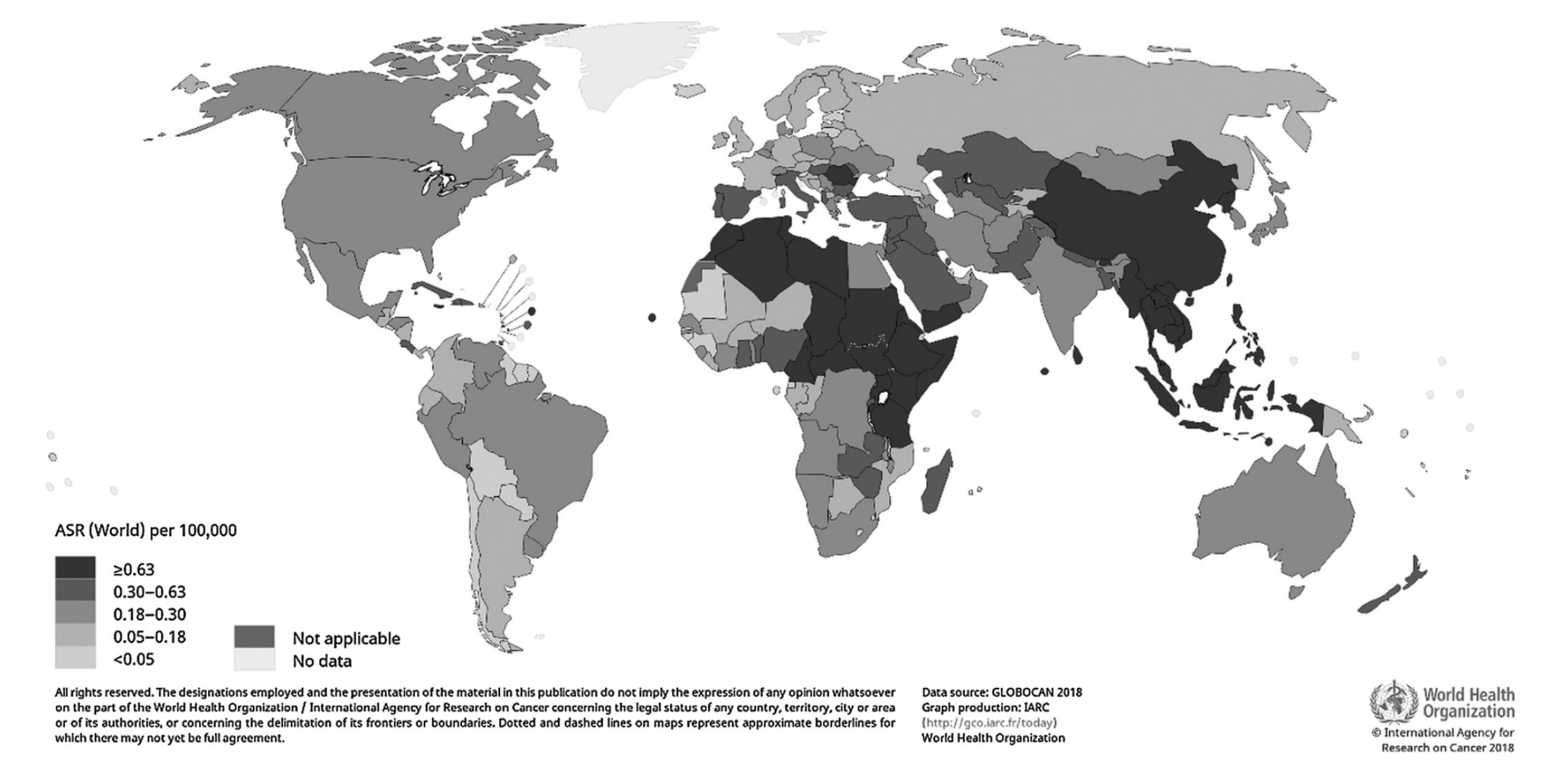
Ellen T. Chang[1,2], Weimin Ye[3], Yi-Xin Zeng[4,5], and Hans-Olov Adami[6,7]

Estimated Age-Standardized (World Population Standard) Incidence Rates of Nasopharyngeal Cancer Among Males by Country



Chang ET et al. *Cancer Epidemiol Biomarkers Prev* 2021;30:1035-47.

Estimated Age-Standardized (World Population Standard) Incidence Rates of Nasopharyngeal Cancer Among Females by Country



Chang ET et al. *Cancer Epidemiol Biomarkers Prev* 2021;30:1035-47.

Cancer Treatment Reviews 109 (2022) 102428

Contents lists available at ScienceDirect

Cancer Treatment Reviews

journal homepage: www.elsevier.com/locate/ctrv

Clinical trial data of Anti–PD-1/PD-L1 therapy for recurrent or metastatic nasopharyngeal Carcinoma: A review

Douglas R. Adkins [a,*], Robert I. Haddad [b]

[a] Division of Medical Oncology and Alvin J. Siteman Cancer Center, Washington University School of Medicine, St. Louis, MO, USA
[b] Department of Medical Oncology, Center for Head & Neck Oncology, Dana-Farber Cancer Institute, Boston, MA, USA

2021 ASCO ANNUAL MEETING **Abstract LBA2.**

JUPITER-02:
The randomized, double-blind, phase 3 study of toripalimab or placebo plus cisplatin and gemcitabine as first-line treatment for recurrent or metastatic nasopharyngeal carcinoma (NPC)

Rui-Hua Xu[1, *], Hai-Qiang Mai[2], Qiu-Yan Chen[2] Dongping Chen[3], Chaosu Hu[4], Kunyu Yang[5], Jiyu Wen[6], Jingao Li[7], Ying-Rui Shi[8], Feng Jin[9], Ruilian Xu[10], Jianji Pan[11], Shenhong Qu[12], Ping Li[13], Chunhong Hu[14], Yi-Chun Liu[15], Yi Jiang[16], Xia He[17], Hung-Ming Wang[18] and Wan-Teck Lim[19], Coherus Biosciences and Shanghai Junshi Biosciences.

[1]Department of Medical Oncology, Sun Yat-Sen University Cancer Center; State Key Laboratory of Oncology in South China; Collaborative Innovation Center of Cancer Medicine, Guangzhou, China; [2] Department of Nasopharyngeal Carcinoma, Sun Yat-Sen University Cancer Center; [3]Affiliated Cancer Hospital & Institute of Guangzhou Medical University, Guangzhou, China; [4]Fudan University Cancer Center, Shanghai, China; [5]Union Hospital Tongji Medical College Huazhong University of Science and Technology, Wuhan, China; [6]Affiliated Hospital of Guangdong Medical University, Zhanjiang, China; [7]Jiangxi Cancer Hospital, Nanchang, China; [8]Hunan Cancer Hospital and the Affiliated Cancer Hospital of Xiangya School of Medicine, Changsha, China; [9]Guizhou Cancer Hospital of Guizhou Medical University, Guiyang China; [10]Shenzhen People's Hospital, Shenzhen, China; [11]Fujian Provincial Cancer Hospital, Fuzhou, China; [12]The People's Hospital of Guangxi Zhuang Autonomous Region, Nanning, China; [13]West China Hospital of Sichuan University, Chengdu, China; [14]The Second Xiangya Hospital of Central South University, Changsha, China; [15]Taichung Veterans General Hospital, Taichung, Taiwan; [16]Cancer Hospital of Shantou University Medical College, Shantou, China; [17]Jiangsu Cancer Hospital, Nanjing, China; [18]Chang Gung Memorial Hospital, Taoyuan, Taiwan; [19]National Cancer Centre, Singapore City, Singapore

ARTICLES *Nat Med* 2021 Sep;27(9):1536-43.
https://doi.org/10.1038/s41591-021-01444-0
nature medicine
Check for updates

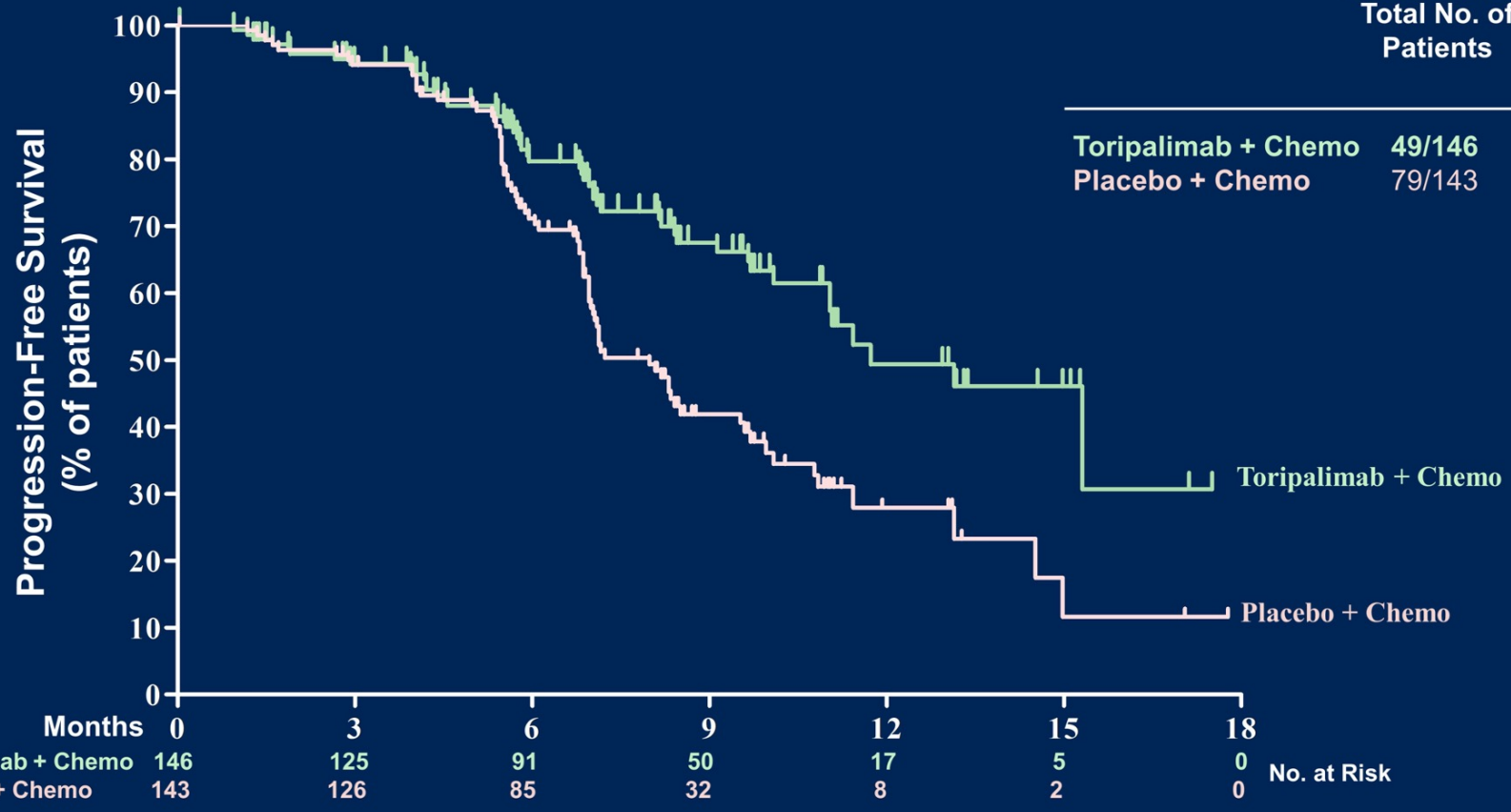
Toripalimab or placebo plus chemotherapy as first-line treatment in advanced nasopharyngeal carcinoma: a multicenter randomized phase 3 trial

Hai-Qiang Mai[1,37], Qiu-Yan Chen[1,37], Dongping Chen[2], Chaosu Hu[3], Kunyu Yang[4], Jiyu Wen[5], Jingao Li[6], Ying-Rui Shi[7], Feng Jin[8], Ruilian Xu[9], Jianji Pan[10], Shenhong Qu[11], Ping Li[12], Chunhong Hu[13], Yi-Chun Liu[14], Yi Jiang[15], Xia He[16], Hung-Ming Wang[17], Wan-Teck Lim[18], Wangjun Liao[19], Xiaohui He[20], Xiaozhong Chen[21], Zhigang Liu[22], Xianglin Yuan[23], Qi Li[24], Xiaoyan Lin[25], Shanghua Jing[26], Yanju Chen[27], Yin Lu[28], Ching-Yun Hsieh[29], Muh-Hwa Yang[30], Chia-Jui Yen[31], Jens Samol[32,33], Hui Feng[34,35], Sheng Yao[34,35], Patricia Keegan[35] and Rui-Hua Xu[36]✉

RTP RESEARCH TO PRACTICE

JUPITER-02: Progression-Free Survival by BIRC

Interim Analysis Data cut-off Date: May 30, 2020



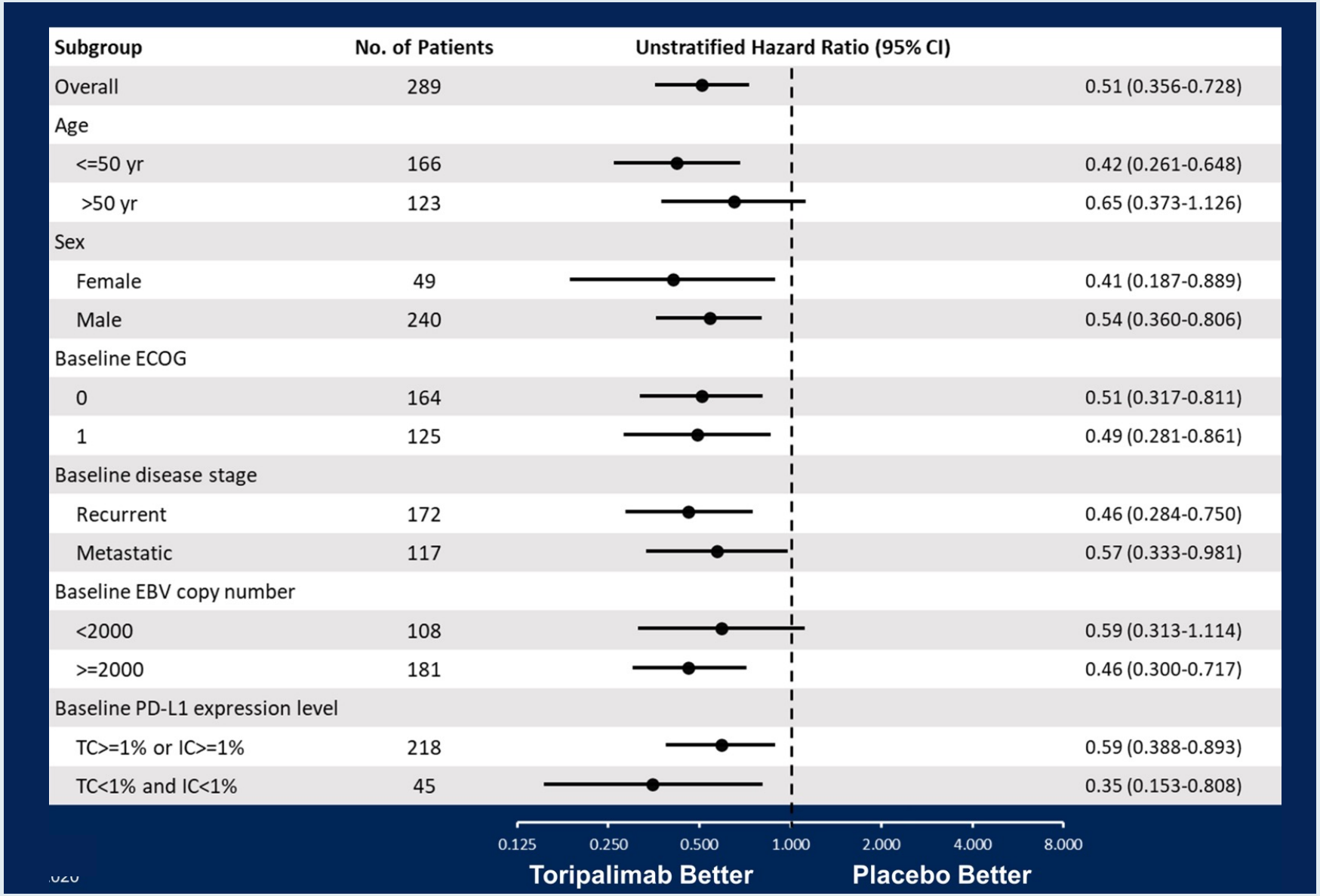
	No. of Events/ Total No. of Patients	Median Progression-free Survival, months (95% CI)	1-Yr Progression-free Survival Rate, % (95% CI)
Toripalimab + Chemo	49/146	11.7 (11.0, NE)	49.4 (36.4, 61.1)
Placebo + Chemo	79/143	8.0 (7.0, 9.5)	27.9 (18.0, 38.8)

Stratified HR for disease progression or death,

0.52 (95% CI 0.36-0.74); P=0.0003

Xu R-H et al. ASCO 2021;Abstract LBA2.

JUPITER-02: Progression-Free Survival by BIRC in Key Subgroups



Xu R-H et al. ASCO 2021;Abstract LBA2.

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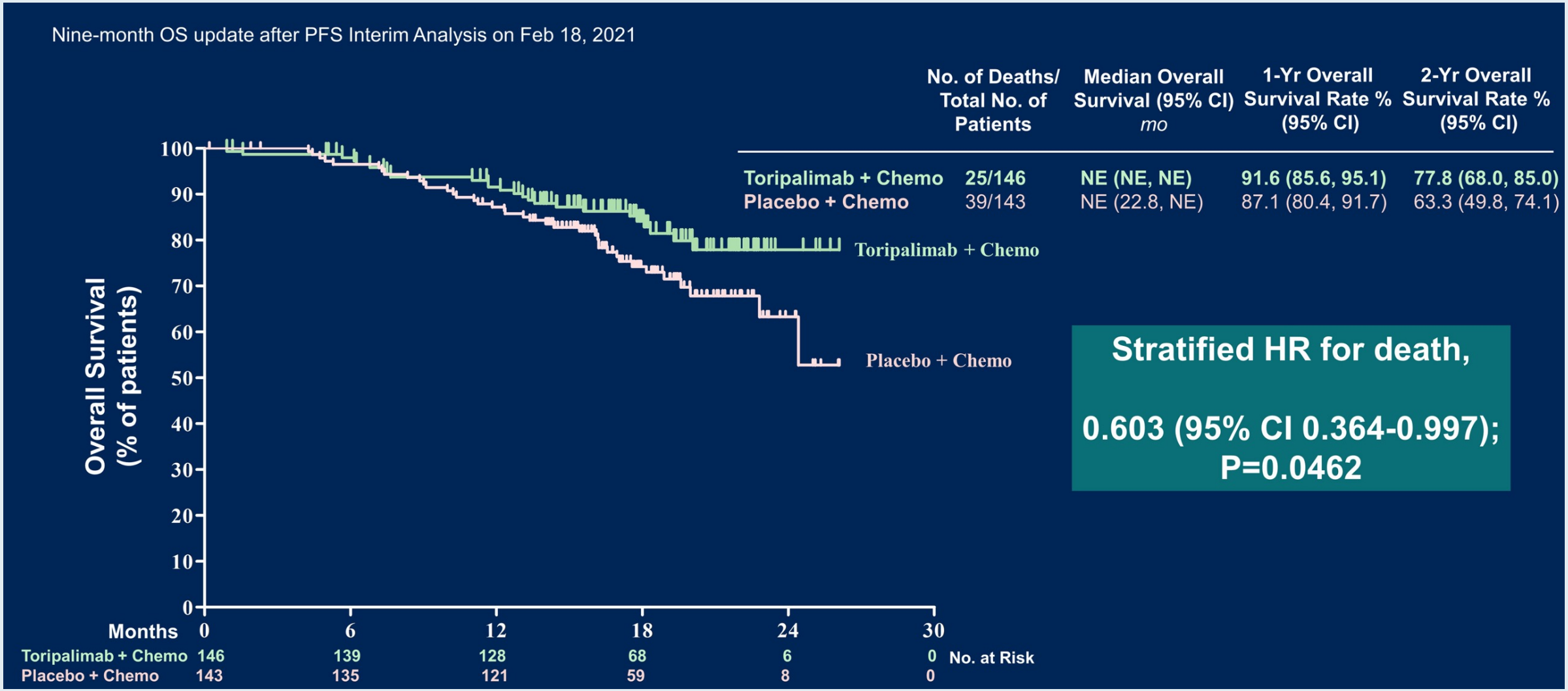
JUPITER-02: Overall Survival Update

Nine-month OS update after PFS Interim Analysis on Feb 18, 2021

	No. of Deaths/ Total No. of Patients	Median Overall Survival (95% CI) *mo*	1-Yr Overall Survival Rate % (95% CI)	2-Yr Overall Survival Rate % (95% CI)
Toripalimab + Chemo	25/146	NE (NE, NE)	91.6 (85.6, 95.1)	77.8 (68.0, 85.0)
Placebo + Chemo	39/143	NE (22.8, NE)	87.1 (80.4, 91.7)	63.3 (49.8, 74.1)



Stratified HR for death,

0.603 (95% CI 0.364-0.997); P=0.0462

Xu R-H et al. ASCO 2021;Abstract LBA2.

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2022 ASCO® ANNUAL MEETING

Presentation 384950.

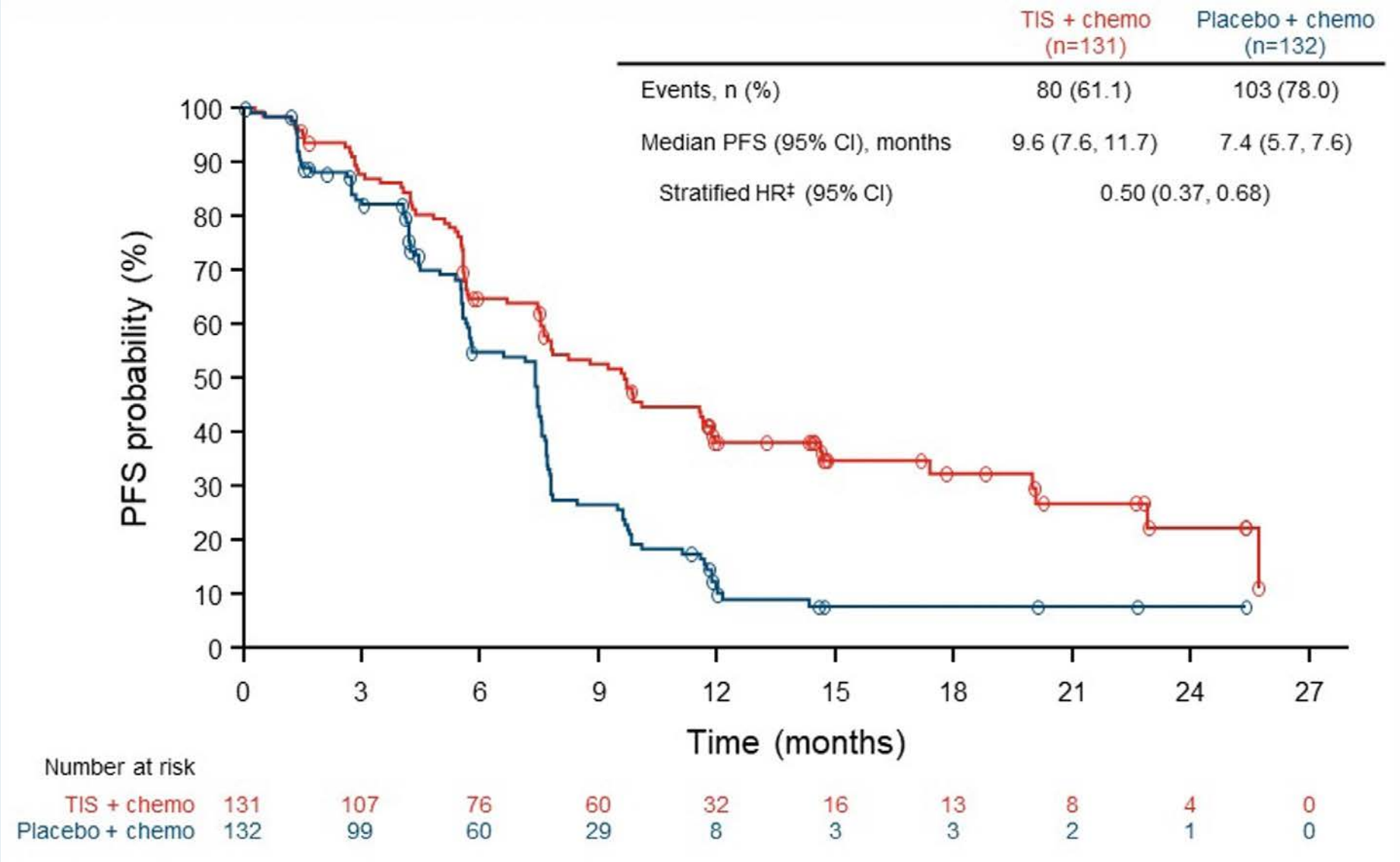
RATIONALE-309: Updated PFS, PFS2, and OS from a Phase 3 double-blind trial of tislelizumab versus placebo, plus chemotherapy, as first-line treatment for recurrent/metastatic nasopharyngeal cancer

Li Zhang, MD[1]

on behalf of Yunpeng Yang,[1] Jianji Pan,[2] Xiaozhong Chen,[3] Yan Sun,[4] Hui Wang,[5] Shenhong Qu,[6] Nianyong Chen,[7] Lizhu Lin,[8] Siyang Wang,[9] Qitao Yu,[10] Guihua Wang,[11] Feng Lei,[12] Jiyu Wen,[13] Chenqi Chen,[14] Yanjie Wu,[14] Shiangjiin Leaw,[14] Wenfeng Fang[1]

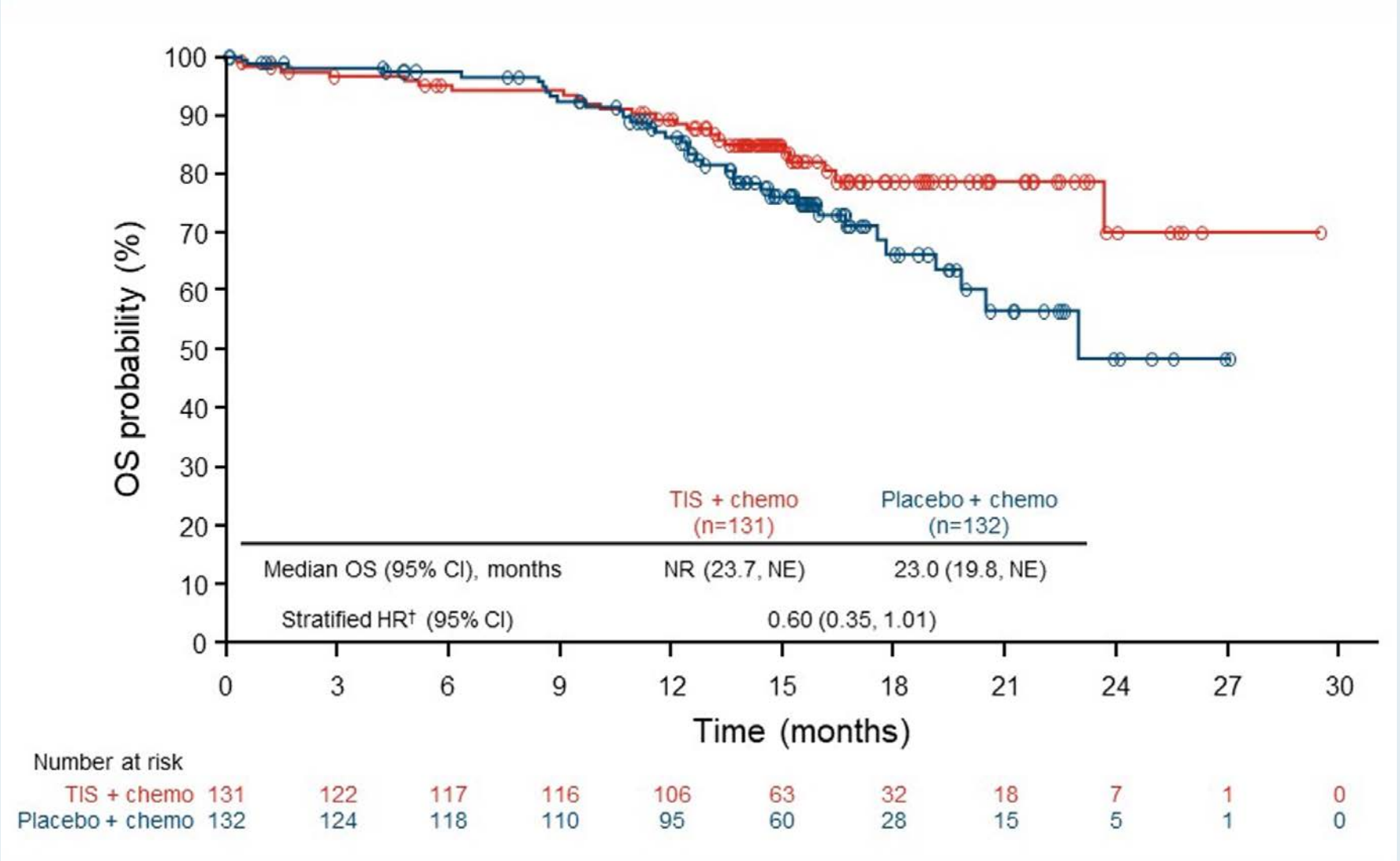
[1]Sun Yat-sen University Cancer Center, Guangzhou, China; [2]Fujian Cancer Hospital, Fuzhou, China; [3]Zhejiang Cancer Hospital, Hangzhou, China; [4]Beijing Cancer Hospital, Beijing, China; [5]Hunan Cancer Hospital, Changsha, China; [6]The People's Hospital of Guangxi Zhuang Autonomous Region, Otolaryngology Department, Nanning, China; [7]West China Hospital of Sichuan University, Chengdu, China; [8]The First Affiliated Hospital of Guangzhou Traditional Chinese Medicine University, Guangzhou, China; [9]The Fifth Affiliated Hospital Sun Yat-sen University, Zhuhai, China; [10]The Affiliated Cancer Hospital of Guangxi Medical University, Nanning, China; [11]Changsha Central Hospital, Changsha, China; [12]The People's Hospital of Zhongshan City, Zhongshan, China; [13]Affiliated Hospital of Guangdong Medical University, Zhanjiang, China; [14]BeiGene (Shanghai) Co., Ltd., Shanghai, China

RATIONALE-309: Updated PFS (Median Follow-Up 15.5 Months)



Zhang L et al. ASCO 2022;Presentation 384950.

RATIONALE-309: Updated Overall Survival



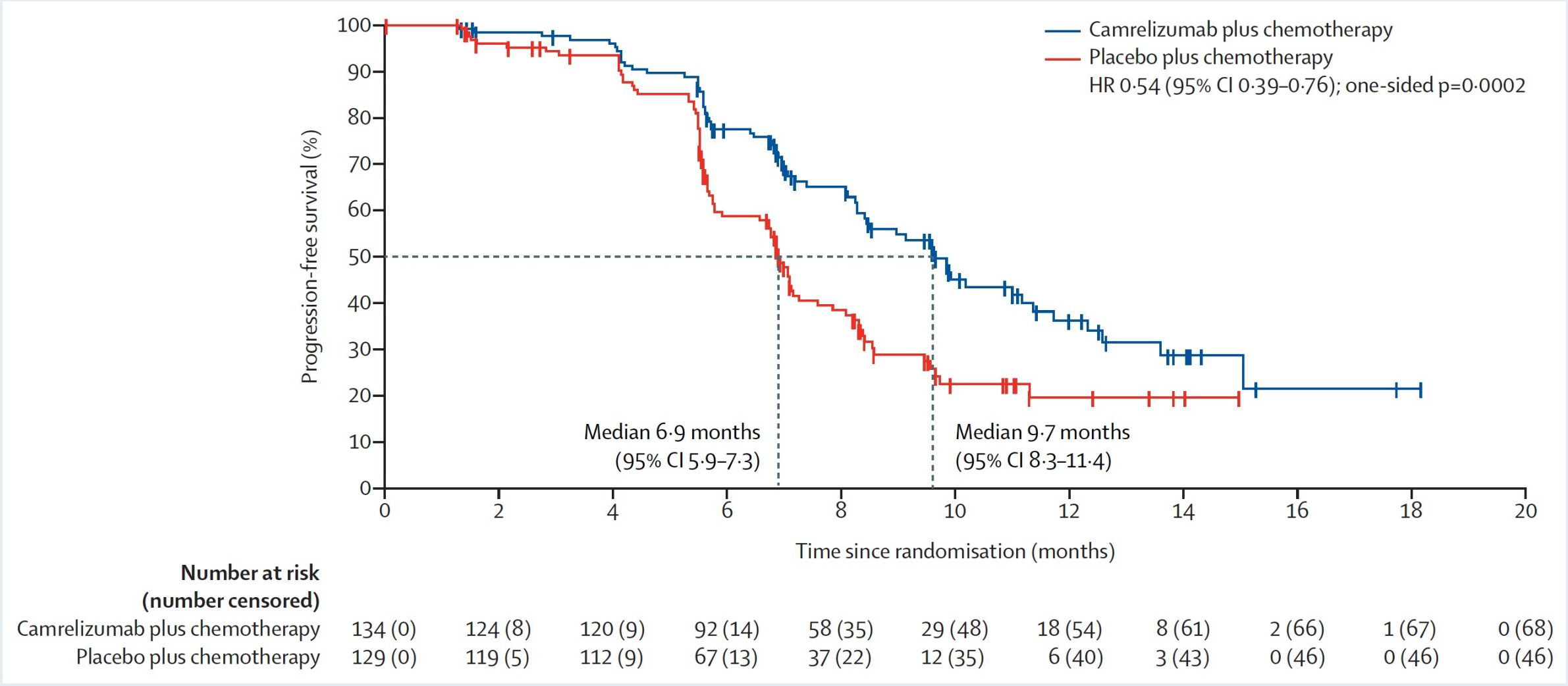
Zhang L et al. ASCO 2022;Presentation 384950.

Lancet Oncol 2021August;22(8):1162-74.

Camrelizumab versus placebo in combination with gemcitabine and cisplatin as first-line treatment for recurrent or metastatic nasopharyngeal carcinoma (CAPTAIN-1st): a multicentre, randomised, double-blind, phase 3 trial

Yunpeng Yang, Song Qu*, Jingao Li*, Chaosu Hu*, Mingjun Xu*, Weidong Li*, Ting Zhou*, Liangfang Shen, Hui Wu, Jinyi Lang, Guangyuan Hu, Zhanxiong Luo, Zhichao Fu, Shenhong Qu, Weineng Feng, Xiaozhong Chen, Shaojun Lin, Weimin Zhang, Xiaojiang Li, Yan Sun, Zhixiong Lin, Qin Lin, Feng Lei, Jianting Long, Jinsheng Hong, Xiaoming Huang, Lingzhi Zeng, Peiguo Wang, Xiaohui He, Ben Zhang, Qing Yang, Xiaojing Zhang, Jianjun Zou, Wenfeng Fang†, Li Zhang†*

CAPTAIN-1st Primary Endpoint: Progression-Free Survival



Number at risk (number censored)											
Camrelizumab plus chemotherapy	134 (0)	124 (8)	120 (9)	92 (14)	58 (35)	29 (48)	18 (54)	8 (61)	2 (66)	1 (67)	0 (68)
Placebo plus chemotherapy	129 (0)	119 (5)	112 (9)	67 (13)	37 (22)	12 (35)	6 (40)	3 (43)	0 (46)	0 (46)	0 (46)

Yang Y et al. *Lancet Oncol* 2021;22(8):1162-74.

Case Presentation: 72-year-old man presents with recurrent and rapidly progressing HPV-negative metastatic head and neck cancer

Dr Neil Morganstein (Summit, New Jersey)

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Case Presentation: 58-year-old man s/p definitive RT and surgery for locally recurrent SCC of the head and neck presents with worsening shortness of breath

Dr Mamta Choksi (New Port Richey, Florida)

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Case Presentation: 73-year-old man with a longstanding history of T-cell large granular lymphocytic leukemia presents with metastatic HPV-positive SCC of the left tonsil – PD-L1-negative

Dr Spencer Bachow (Boca Raton, Florida)

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Case Presentation: 57-year-old man presents with HPV-positive Stage III cancer of the base of the tongue

Dr Ezra Cohen (La Jolla, California)

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Haddad

MODULE 1: ESMO 2022

MODULE 2: Needle in a Haystack

MODULE 3: Head and Neck Cancer

MODULE 4: Thyroid Cancer

- Dr Rupard: 73-year-old man presents with metastatic anaplastic thyroid cancer – PD-L1-positive, mutations in TERT promoter, TP53 and MEN1
- Dr Cohen: 63-year-old man presents with BRAF V600E mutation-positive metastatic papillary thyroid cancer

MODULE 5: Journal Club with Dr Haddad

MODULE 6: Appendix

RTP RESEARCH TO PRACTICE

Case Presentation: 73-year-old man presents with metastatic anaplastic thyroid cancer – PD-L1-positive, mutations in TERT promoter, TP53 and MEN1

Dr Erik Rupard (West Reading, Pennsylvania)

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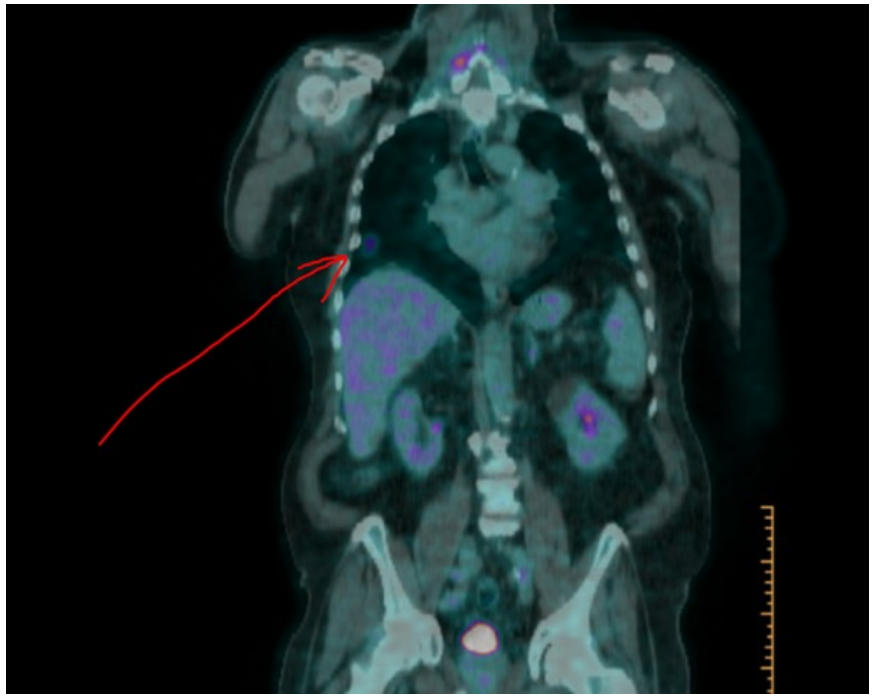
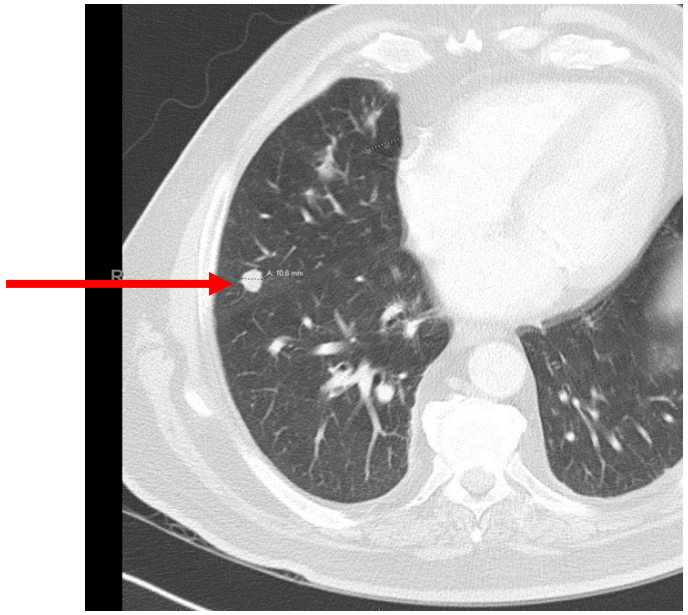
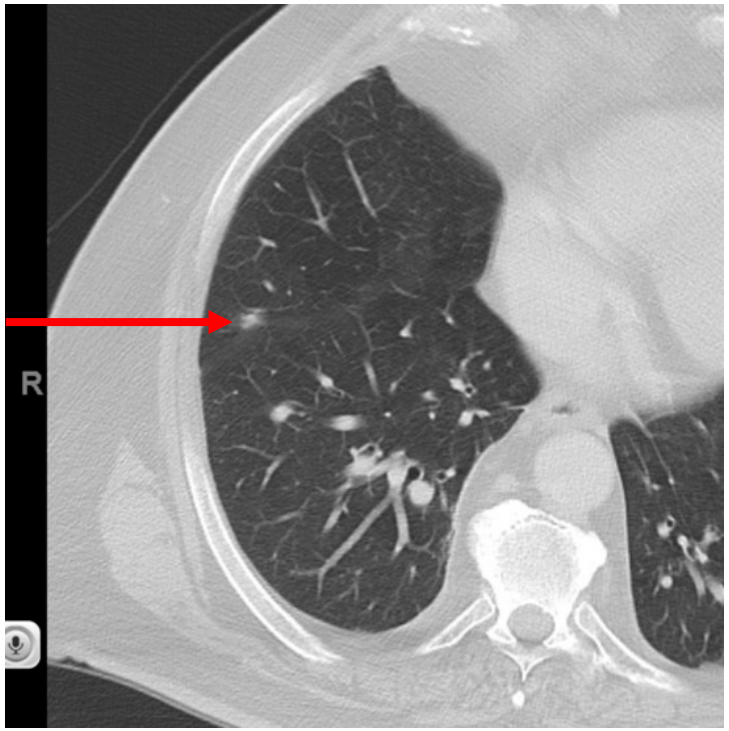
Before Pembrolizumab





After Pembrolizumab



Case Presentation: 63-year-old man presents with BRAF V600E mutation-positive metastatic papillary thyroid cancer

Dr Ezra Cohen (La Jolla, California)

Meet The Professor with Dr Haddad

MODULE 1: ESMO 2022

MODULE 2: Needle in a Haystack

MODULE 3: Head and Neck Cancer

MODULE 4: Thyroid Cancer

MODULE 5: Journal Club with Dr Haddad

MODULE 6: Appendix

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Enhanced Pathologic Tumor Response with Two Cycles of Neoadjuvant Pembrolizumab in Surgically Resectable, Locally Advanced HPV-Negative Head and Neck Squamous Cell Carcinoma (HNSCC)

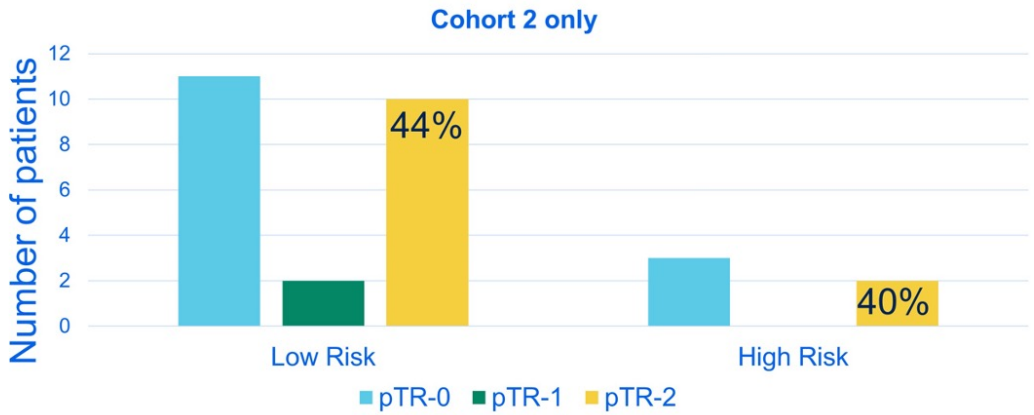
Uppaluri R et al.

ASCO 2021;Abstract 6008.

Post-Surgery Findings

Characteristic	Cohort 2 (N=28)*	
pTR Category**		
pTR-0	14	50.0%
pTR-1	2	7.1%
pTR-2	12	42.9%
Pathologic disease Stage, N (%)		
I-II	5	17.9%
III	5	17.9%
IVA-IVB	18	64.3%
Pathologic risk category (positive margins/ENE)		
High risk	5	17.9%
Intermediate/low risk	23	82.1%

*1 patient enrolled but withdrew from trial- did not have surgery
**3 samples with prelim pTR, pending central review for pTR

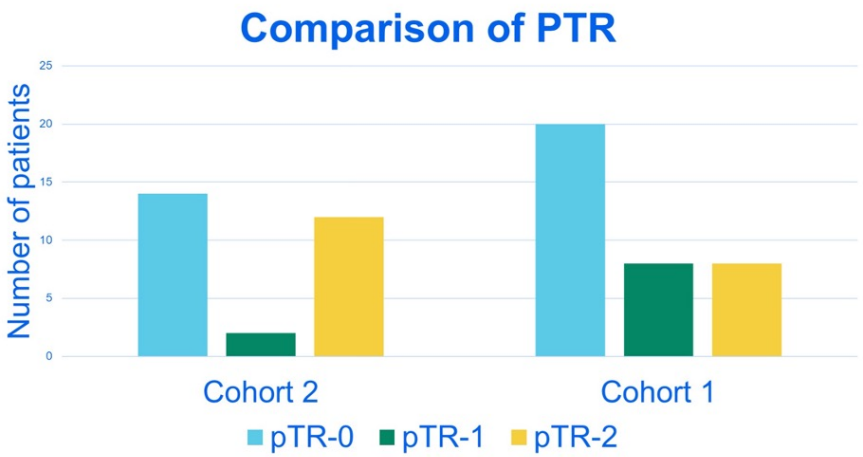


- Any pTR was seen in 14/28 (50%) of patients
- pTR-2 was seen in 42.9% of patients
  -higher than Cohort 1
- pTR-1 rates (7.1%) were lower than Cohort 1
- pTR distributions were similar across risk categories

pTR = pathologic tumor response; ENE = extranodal extension

Uppaluri R et al. ASCO 2021;Abstract 6008.

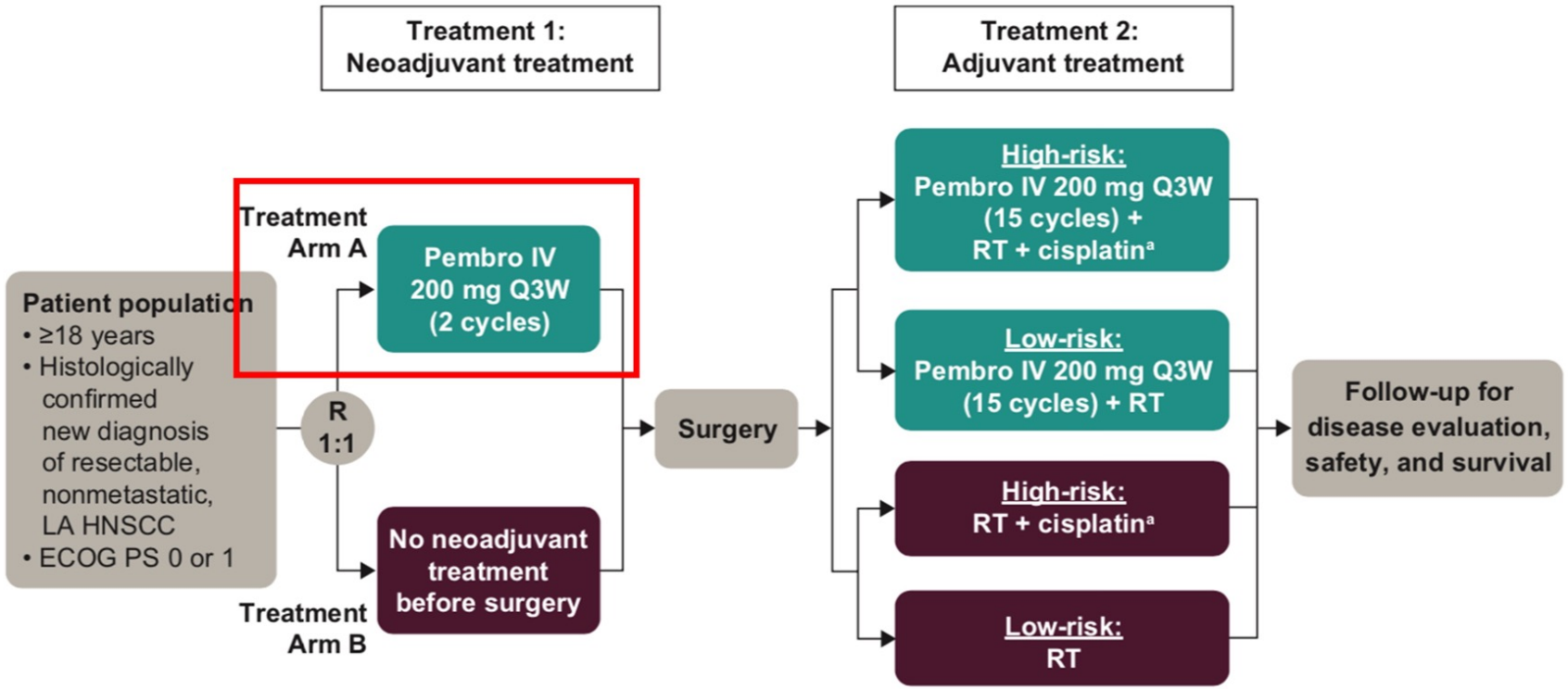
Cohort 1 versus Cohort 2



Characteristic	Cohort 2 (N=28)		Cohort 1 (N=36)		p-value	Diff (95% CI)
pTR Category						
pTR-0	14	50.0%	20	55.6%	0.11	-5.6 (-28.4 to 18.0)
pTR-1	2	7.1%	8	22.2%		-15.1 (-31.8 to 3.6)
pTR-2	12	42.9%	8	22.2%		20.6 (-2.1 to 41.5)
Pathologic risk category (positive margins/ENE)						
High risk	5	17.9%	18	50.0%	0.008	
Intermediate/low risk	23	82.1%	18	50.0%		32.1 (8.6 to 50.6)
Pathologic disease Stage, N (%)						
I-II	5	17.9%	3	8.3%	0.54	9.5 (-7.3 to 28.1)
III	5	17.9%	6	16.7%		1.2 (-17.0 to 21.0)
IVA-IVB	18	64.3%	27	75.0%		-10.7 (-32.3 to 11.3)

Uppaluri R et al. ASCO 2021;Abstract 6008.

Resectable, Locally Advanced Head and Neck Squamous Cell Carcinoma



KEYNOTE-689- testing neoadjuvant/ adjuvant pembrolizumab in HNSCC uses 2 doses pre-operatively

NCT03765918

Uppaluri R et al. ASCO 2021;Abstract 6008.

ORIGINAL ARTICLE

Head Neck 2022;44(6):1442-52.

Association between radiation dose to organs at risk and acute patient reported outcome during radiation treatment for head and neck cancers

Mona Arbab MD[1,2] | Yu-Hui Chen MS[3] | Roy B. Tishler MD, PhD[4] | Lauren Gunasti BS[4] | Jason Glass NP[3] | Jo Ann Fugazzotto NP[4] | Joseph H. Killoran PhD[4] | Rosh Sethi MD, MPH[5] | Eleni Rettig MD[5] | Donald Annino MD, DMD[5] | Laura Goguen MD[5] | Ravindra Uppaluri MD, PhD[5] | Carolyn Hsu MS[6] | Elaine Burke MS[6] | Glenn J. Hanna MD[3] | Jochen Lorch MD, MS[7] | Robert I. Haddad MD[4] | Danielle N. Margalit MD, MPH[4] | Jonathan D. Schoenfeld MD, MPhil, MPH[4]

Baseline and End-of-Treatment Symptom Scores

Symptom	Baseline score		End of treatment score	
	Median	Range	Median	Range
Difficulty swallowing/chewing	0	0–10	6	0–10
Choking/coughing	0	0–10	2	0–10
Problem with mucus in mouth/throat	0	0–8	6	0–10
Difficulty with speech	0	0–8	4	0–10
Dry mouth	1	0–9	6	0–10

Arbab M et al. *Head Neck* 2022;44(6):1442-52.

2021 ESMO congress

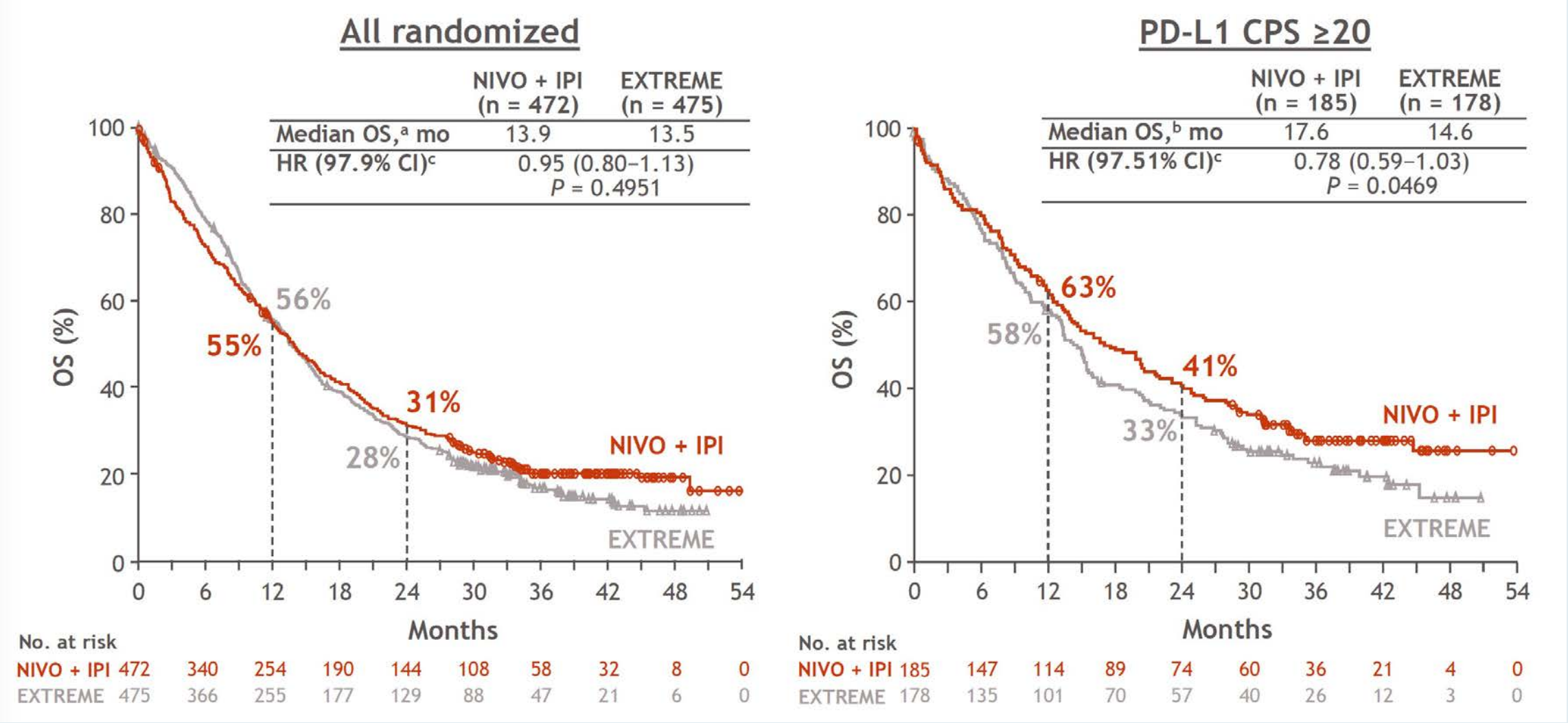
Nivolumab + ipilimumab vs EXTREME regimen as first-line treatment for recurrent/metastatic squamous cell carcinoma of the head and neck: final results of CheckMate 651

Athanassios Argiris,[1,2] Kevin Harrington,[3] Makoto Tahara,[4] Robert L. Ferris,[5] Maura Gillison,[6] Jerome Fayette,[7] Amaury Daste,[8] Piotr Koralewski,[9] Ricard Mesia,[10] Nabil F. Saba,[11] Milena Mak,[12] Miguel Angel Álvarez Avitia,[13] Alexander Guminski,[14] Urs Müller-Richter,[15] Naomi Kiyota,[16] Mustimbo Roberts,[17] Tariq Aziz Khan,[17] Karen Miller-Moslin,[17] Li Wei,[17] Robert Haddad[18]

[1]Hygeia Hospital, Marousi, Greece; [2]Thomas Jefferson University, Philadelphia, PA, USA; [3]Royal Marsden Hospital/The Institute of Cancer Research, London, UK; [4]National Cancer Center Hospital East, Kashiwa, Japan; [5]UPMC Hillman Cancer Center, Pittsburgh, PA, USA; [6]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [7]Centre Léon Bérard, Lyon, France; [8]Hôpital Saint-André, Bordeaux, France; [9]Wojewodzki Szpital Specjalistyczny im. Ludwika Rydygiera w Krakowie, Krakow, Poland; [10]Catalan Institut of Oncology, L'Hospitalet de Llobregat, Barcelona, Spain; [11]Winship Cancer Institute of Emory University, Atlanta, GA, USA; [12]Instituto do Câncer do Estado de São Paulo, Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil; [13]Instituto Nacional De Cancerología, Mexico City, Mexico; [14]Royal North Shore Hospital, Sydney, Australia; [15]University Hospital Würzburg, Bavarian Cancer Research Center (BZKF), Würzburg, Germany; [16]Kobe University Hospital, Kobe, Japan; [17]Bristol Myers Squibb, Princeton, NJ, USA; [18]Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA

Presentation number LBA36

Primary Endpoints: Overall Survival (OS) with Nivolumab (NIVO) + Ipilimumab (IPI) versus EXTREME Regimen



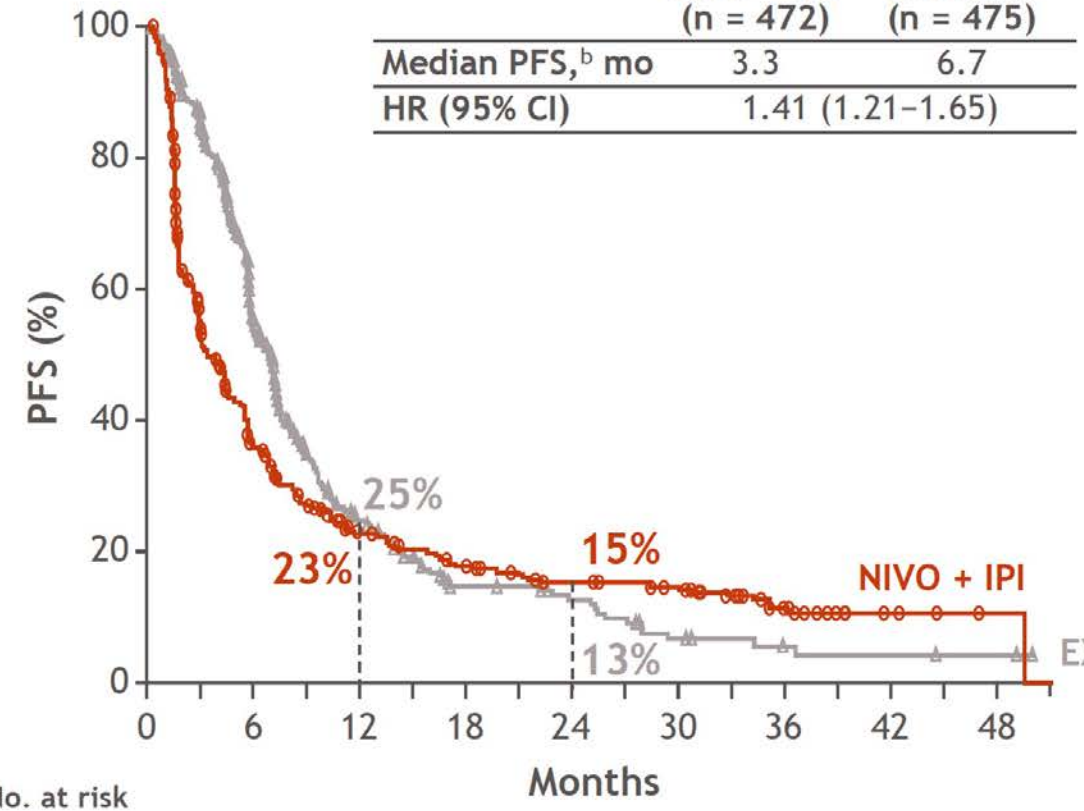
EXTREME regimen: cetuximab + cisplatin/carboplatin + fluorouracil ≤6 cycles, then cetuximab maintenance

Argiris A et al. ESMO 2021;Abstract LBA36.

Efficacy in All Randomized Patients

PFS[a]

	NIVO + IPI (n = 472)	EXTREME (n = 475)
Median PFS,[b] mo	3.3	6.7
HR (95% CI)	1.41 (1.21–1.65)	

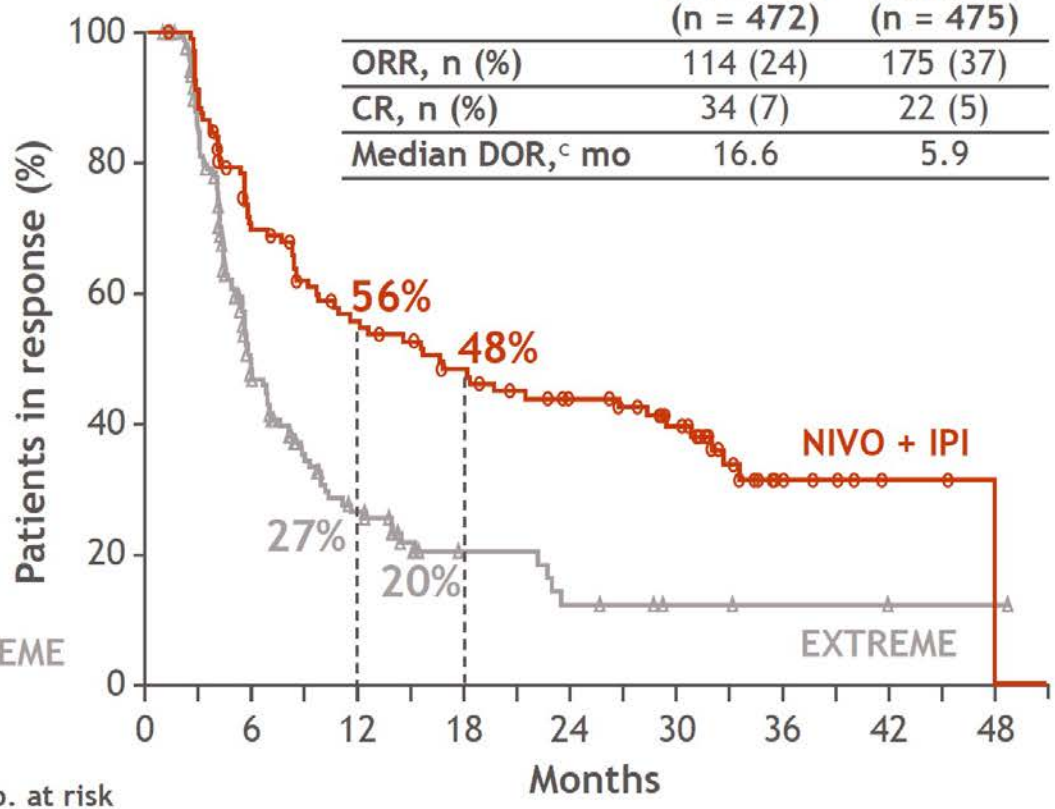


No. at risk

NIVO + IPI	472	142	76	55	42	35	14	5	1	0
EXTREME	475	178	59	24	18	8	4	3	2	0

ORR[a] and DOR[a]

	NIVO + IPI (n = 472)	EXTREME (n = 475)
ORR, n (%)	114 (24)	175 (37)
CR, n (%)	34 (7)	22 (5)
Median DOR,[c] mo	16.6	5.9

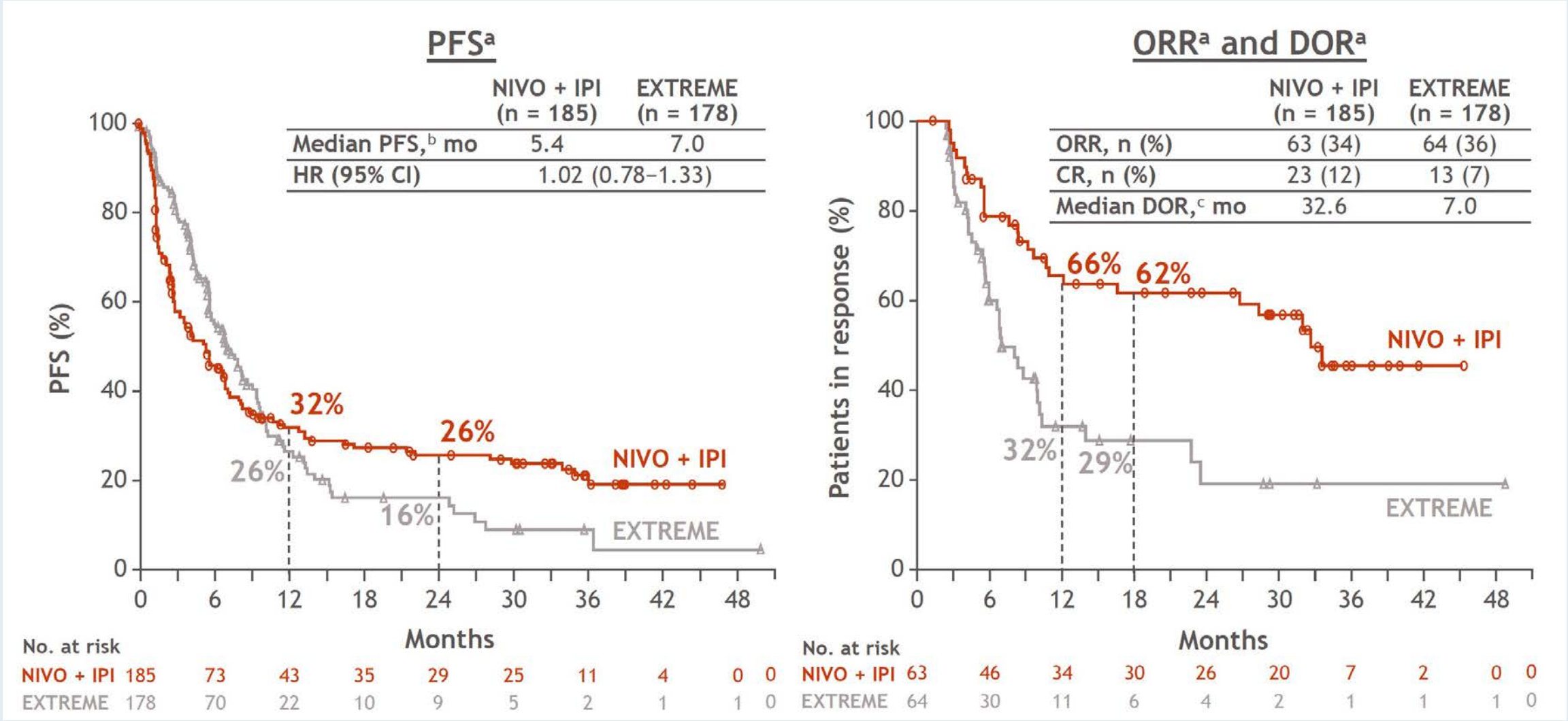


No. at risk

NIVO + IPI	114	73	54	44	35	26	8	3	0	0
EXTREME	175	62	26	10	6	3	2	1	1	0

Argiris A et al. ESMO 2021;Abstract LBA36.

Efficacy in PD-L1 CPS ≥20 Population



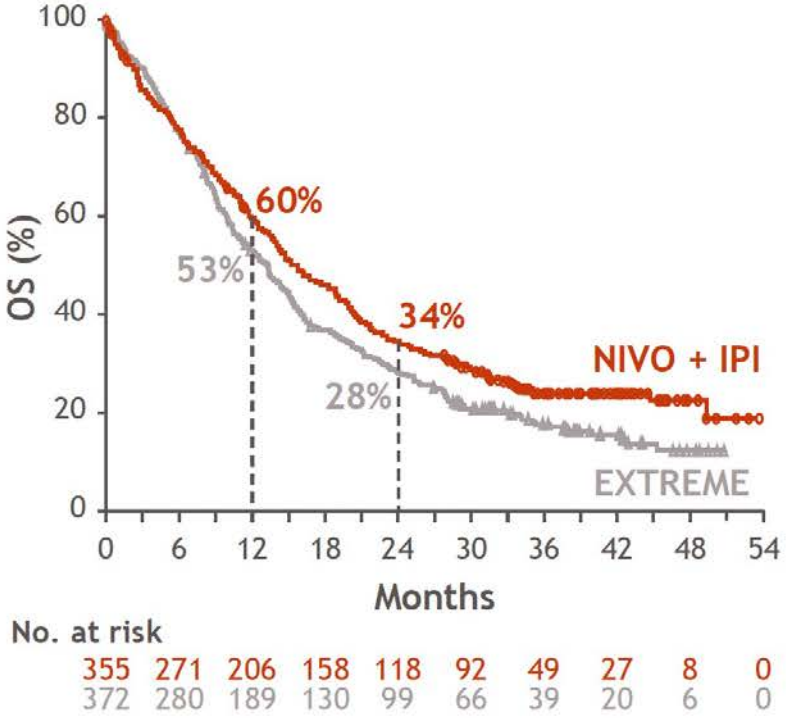
CPS = combined positive score; PFS = progression-free survival; ORR = objective response rate; DOR = duration of response

Argiris A et al. ESMO 2021;Abstract LBA36.

Efficacy in PD-L1 CPS ≥1 Population

OS (secondary endpoint)

	NIVO + IPI (n = 355)	EXTREME (n = 372)
Median OS,[b] mo	15.7	13.2
HR (95% CI)	0.82 (0.69–0.97)	

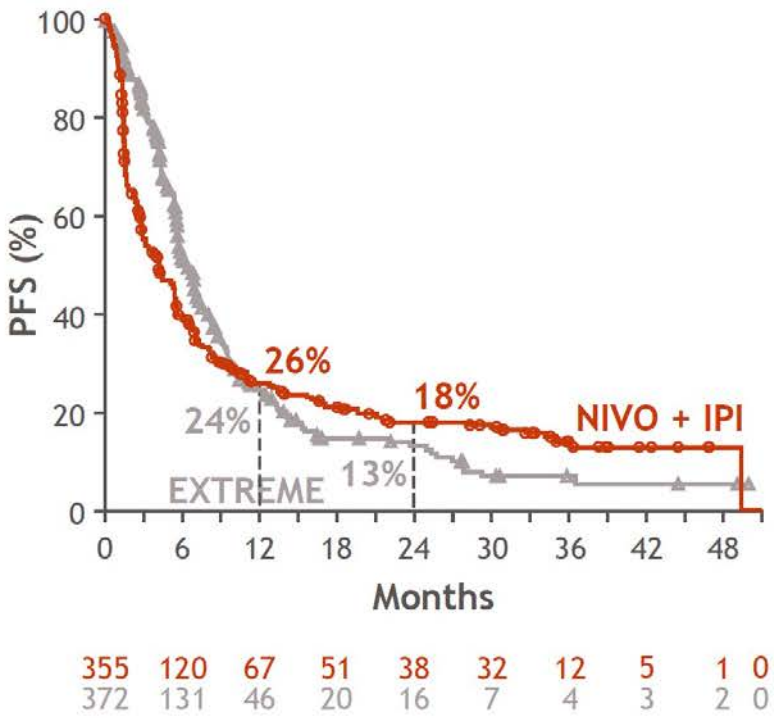


No. at risk

NIVO + IPI	355	271	206	158	118	92	49	27	8	0
EXTREME	372	280	189	130	99	66	39	20	6	0

PFS[a]

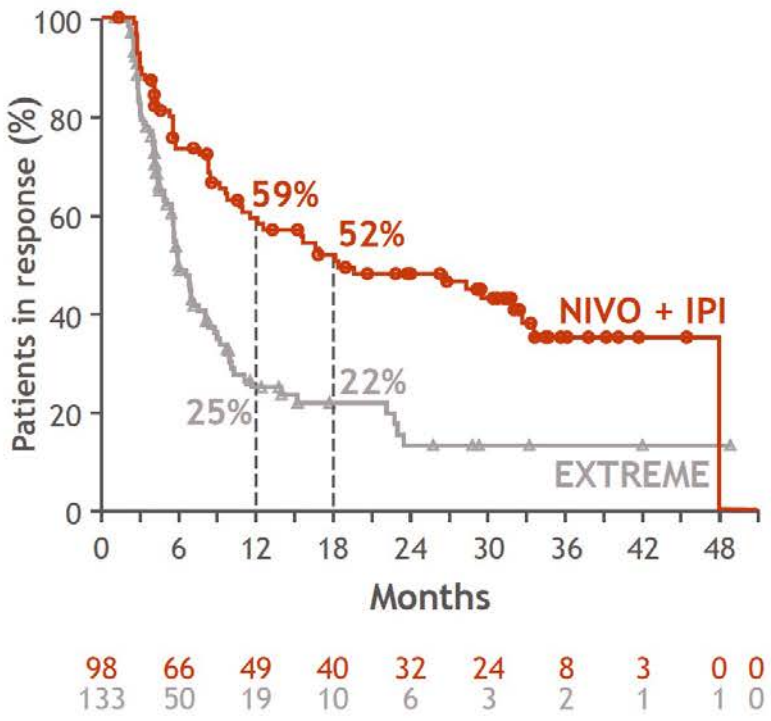
	NIVO + IPI (n = 355)	EXTREME (n = 372)
Median PFS,[c] mo	4.2	6.1
HR (95% CI)	1.23 (1.03–1.47)	



NIVO + IPI	355	120	67	51	38	32	12	5	1	0
EXTREME	372	131	46	20	16	7	4	3	2	0

ORR[a] and DOR[a]

	NIVO + IPI (n = 355)	EXTREME (n = 372)
ORR,[a] n (%)	98 (28)[d]	133 (36)[e]
Median DOR,[f] mo	18.3	6.0



NIVO + IPI	98	66	49	40	32	24	8	3	0	0
EXTREME	133	50	19	10	6	3	2	1	1	0

Argiris A et al. ESMO 2021;Abstract LBA36.

Safety and Exposure Summary for All Patients Receiving Treatment

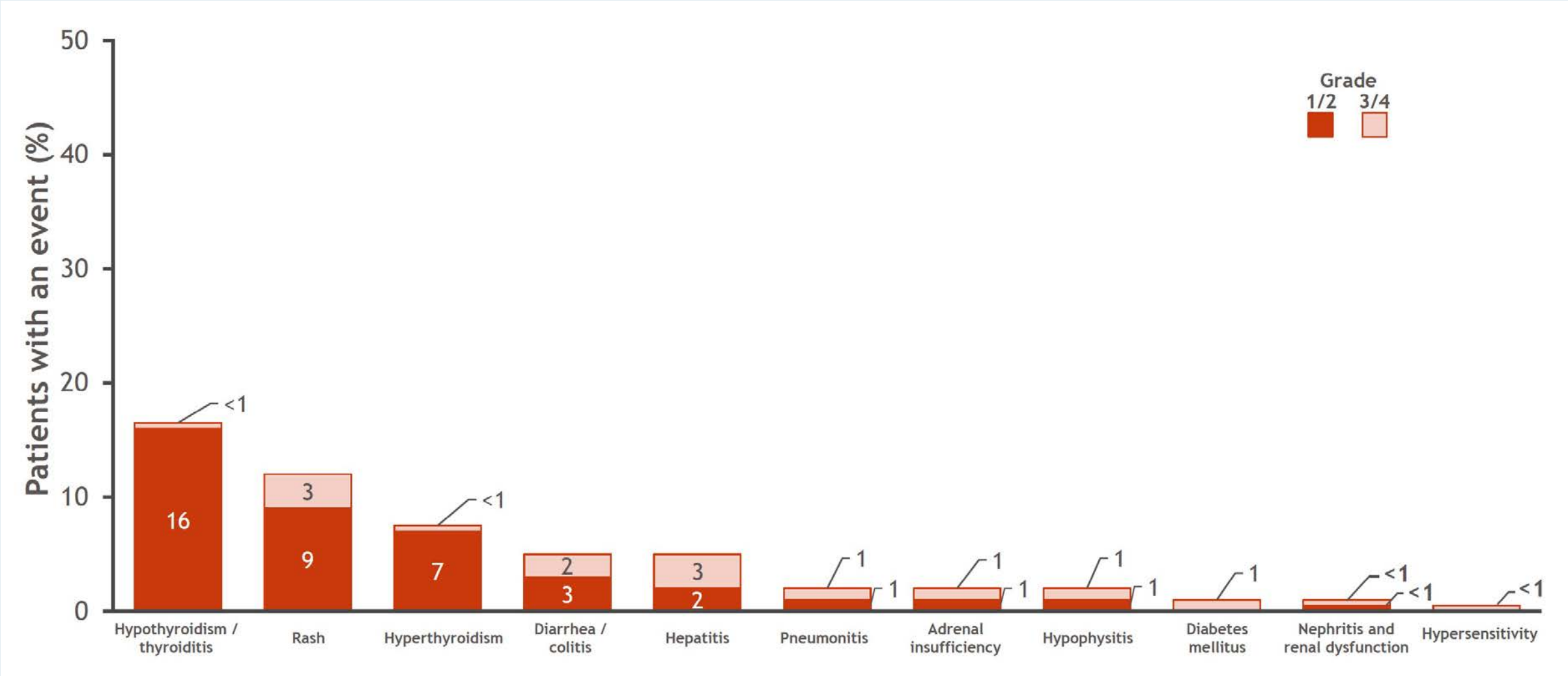
TRAE, %	NIVO + IPI (n = 468)		EXTREME (n = 441)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Any TRAEs	72	28	98	71
TRAEs leading to discontinuation of any component of the regimen	12[a]	10	13	9
Serious TRAEs	16	12	28	24
Treatment-related deaths	1[b]		2[c]	

- Median (range) duration of therapy was 3.8 (<0.1–24.0) months in the NIVO + IPI arm vs 5.0 (<0.1–50.7) months in the EXTREME arm
- Patients in the NIVO + IPI arm received a median (range) of 8 (1–53) doses of NIVO and 3 (1–18) doses of IPI

TRAE = treatment-related adverse event

Argiris A et al. ESMO 2021;Abstract LBA36.

Immune-Mediated Adverse Events with Nivolumab and Ipilimumab



Argiris A et al. ESMO 2021;Abstract LBA36.

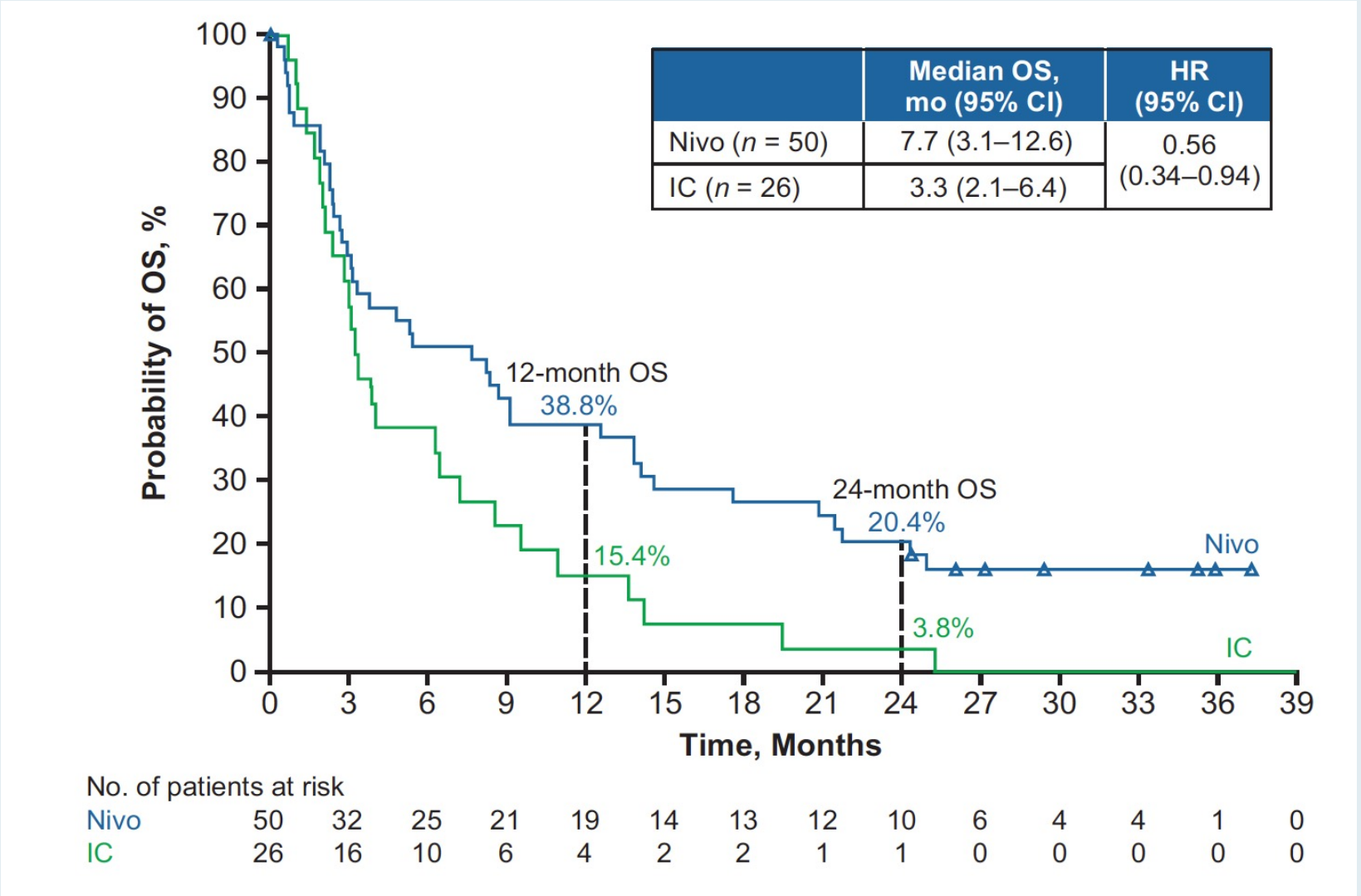
The Oncologist, 2022, **27**, e194–e198
https://doi.org/10.1093/oncolo/oyab036
Advance access publication 15 February 2022
Brief Communication

OXFORD

Long-term Outcomes with Nivolumab as First-line Treatment in Recurrent or Metastatic Head and Neck Cancer: Subgroup Analysis of CheckMate 141

Maura L. Gillison[1,*], George Blumenschein Jr.[1], Jerome Fayette[2], Joel Guigay[3], A. Dimitrios Colevas[4], Lisa Licitra[5], Kevin J. Harrington[6], Stefan Kasper[7], Everett E. Vokes[8], Caroline Even[9], Francis Worden[10], Nabil F. Saba[11], Lara CarmenIglesias Docampo[12], Robert Haddad[13], Tamara Rordorf[14], Naomi Kiyota[15], Makoto Tahara[16], Vijayvel Jayaprakash[17,†], Li Wei[17], Robert L. Ferris[18]

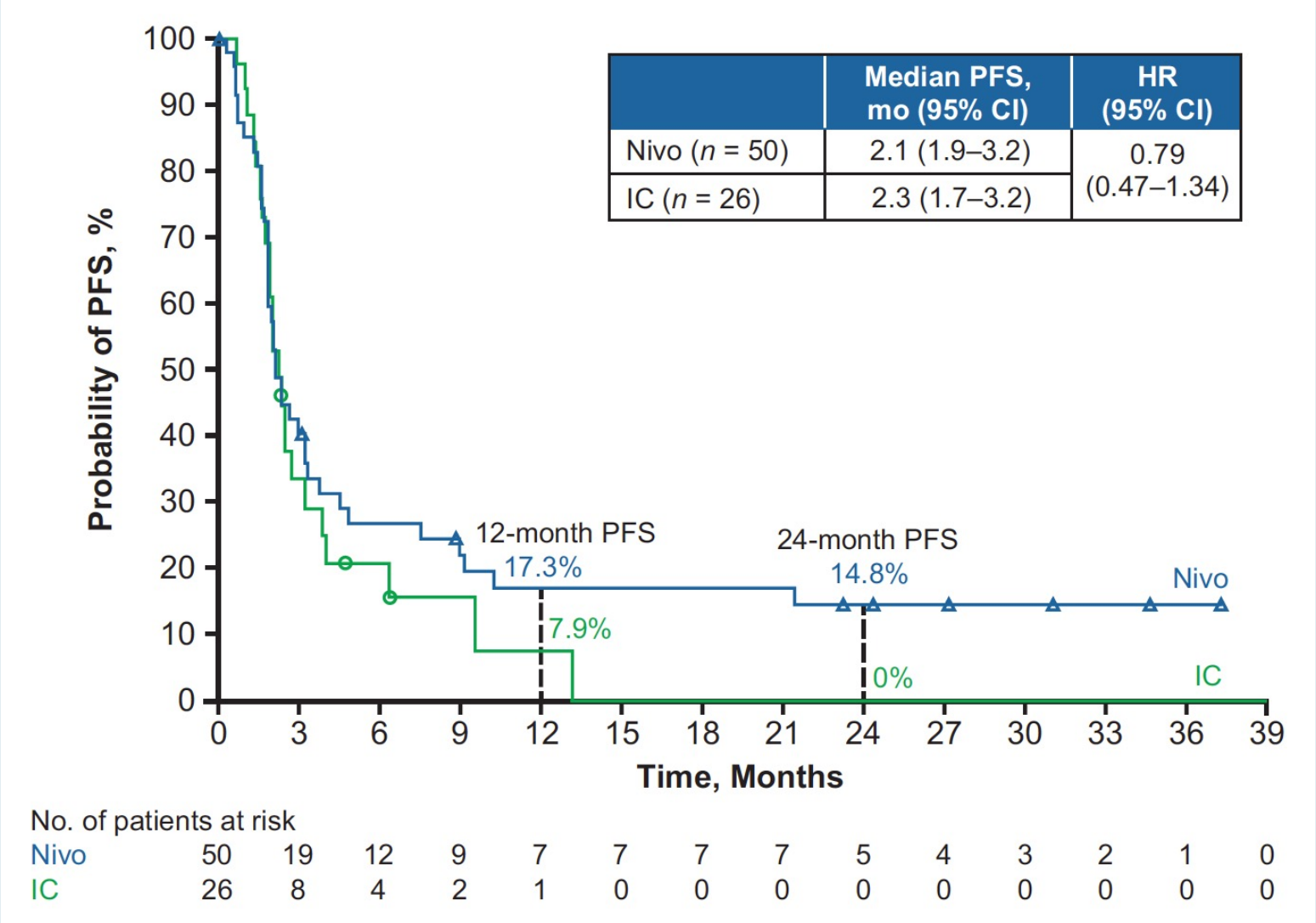
OS Among Patients Randomly Assigned to Nivolumab or Investigator's Choice (IC) as First-Line Treatment for Recurrent or Metastatic SCCHN



SCCHN = squamous cell carcimona of the head and neck

Gillison ML et al. *Oncologist* 2022;27(2):e194-8.

PFS Among Patients Randomly Assigned to Nivolumab or IC as First-Line Treatment for Recurrent or Metastatic SCCHN



	Median PFS, mo (95% CI)	HR (95% CI)
Nivo (*n* = 50)	2.1 (1.9–3.2)	0.79 (0.47–1.34)
IC (*n* = 26)	2.3 (1.7–3.2)	

Gillison ML et al. *Oncologist* 2022;27(2):e194-8.

Open access Original research

Journal for ImmunoTherapy of Cancer

2022 Feb;10(2):e003026

Influence of tumor mutational burden, inflammatory gene expression profile, and PD-L1 expression on response to pembrolizumab in head and neck squamous cell carcinoma

Robert I Haddad ,[1] Tanguy Y Seiwert ,[2] Laura Q M Chow,[3] Shilpa Gupta,[4] Jared Weiss,[5] Iris Gluck,[6] Joseph P Eder,[7] Barbara Burtness,[8] Makoto Tahara,[9] Bhumsuk Keam ,[10] Hyunseok Kang ,[11] Kei Muro,[12] Andrew Albright,[13] Robin Mogg,[13] Mark Ayers,[13] Lingkang Huang,[13] Jared Lunceford,[13] Razvan Cristescu,[13] Jonathan Cheng,[13] Ranee Mehra[14]

Neoadjuvant and Adjuvant Nivolumab and Lirilumab in Patients with Recurrent, Resectable Squamous Cell Carcinoma of the Head and Neck

Hanna GJ et al.

ASCO 2021;Abstract 6053.

Research

JAMA Otolaryngology–Head & Neck Surgery | Original Investigation

Use of Fluoro-[^{18}F]-Deoxy-2-D-Glucose Positron Emission Tomography/ Computed Tomography to Predict Immunotherapy Treatment Response in Patients With Squamous Cell Oral Cavity Cancers

Hina Shah, MD; Yating Wang; Su-Chun Cheng, ScD; Lauren Gunasti; Yu-Hui Chen, MS; Ana Lako, MD; Jeffrey Guenette, MD; Scott Rodig, MD, PhD; Vickie Y. Jo, MD; Ravindra Uppaluri, MD, PhD; Robert Haddad, MD; Jonathan D. Schoenfeld, MD, MPH; Heather A. Jacene, MD

JAMA Otolaryngol Head Neck Surg 2022;148(3):268-76.

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Research

JAMA Oncol 2020;6(10):1563-70.

JAMA Oncology | Original Investigation

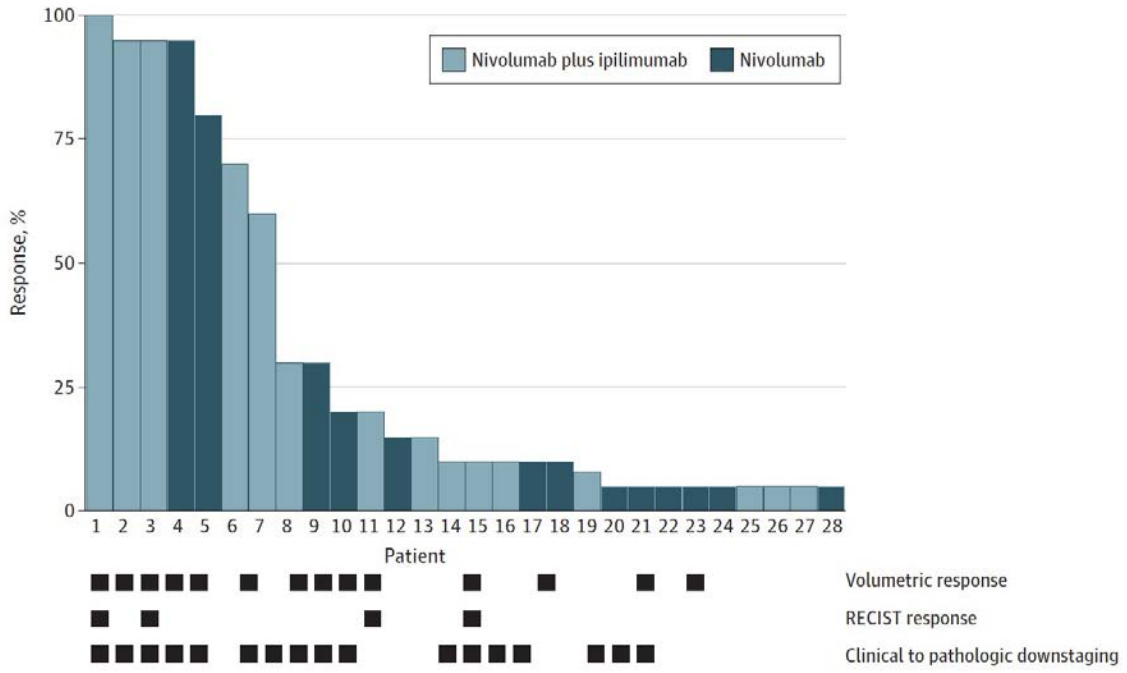
Neoadjuvant Nivolumab or Nivolumab Plus Ipilimumab in Untreated Oral Cavity Squamous Cell Carcinoma

A Phase 2 Open-Label Randomized Clinical Trial

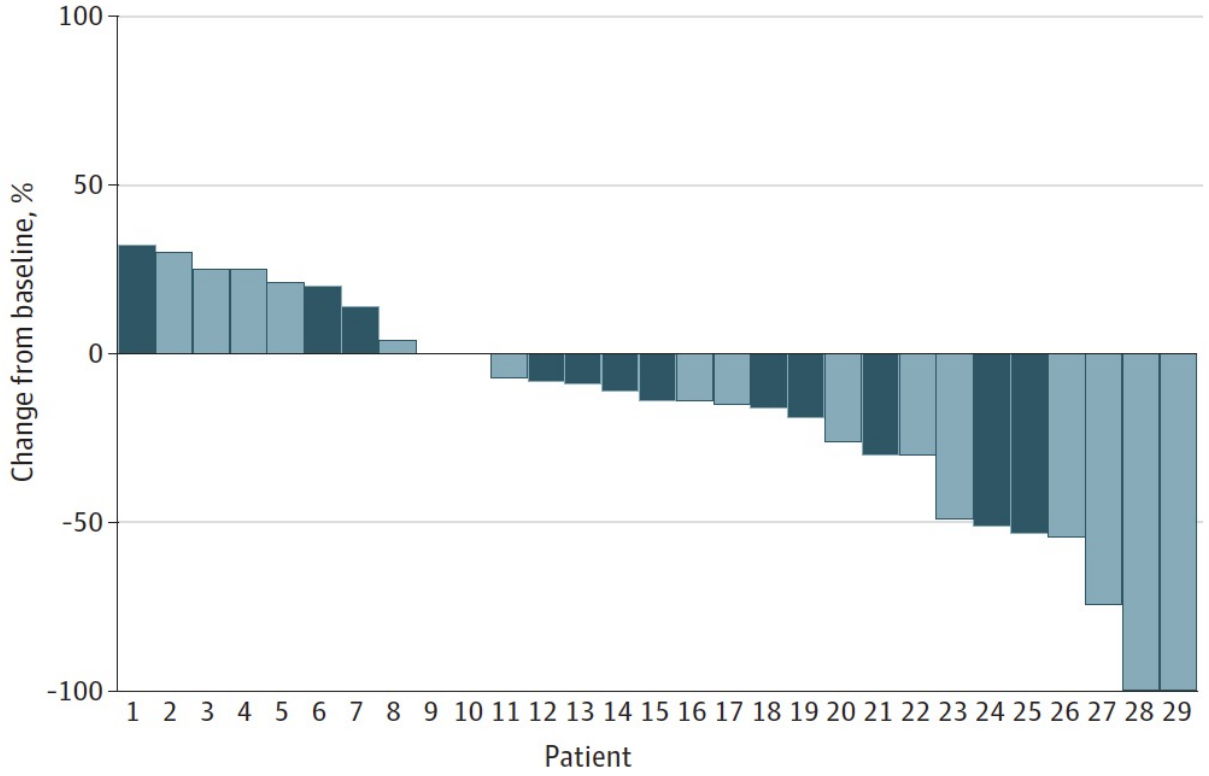
Jonathan D. Schoenfeld, MD, MPH; Glenn J. Hanna, MD; Vickie Y. Jo, MD; Bhupendra Rawal, MS; Yu-Hui Chen, MS; Paul S. Catalano, ScD; Ana Lako, PhD; Zoe Ciantra, BS; Jason L. Weirather, PhD; Shana Criscitiello, BA; Adrienne Luoma, PhD; Nicole Chau, MD; Jochen Lorch, MD, MS; Jason I. Kass, MD, PhD; Donald Annino, MD, DMD; Laura Goguen, MD; Anupam Desai, MD; Brendan Ross, BS; Hina J. Shah, MD; Heather A. Jacene, MD; Danielle N. Margalit, MD, MPH; Roy B. Tishler, MD, PhD; Kai W. Wucherpfennig, MD, PhD; Scott J. Rodig, MD, PhD; Ravindra Uppaluri, MD, PhD; Robert I. Haddad, MD

Summary of Response in Both Treatment Arms

Pathologic Response

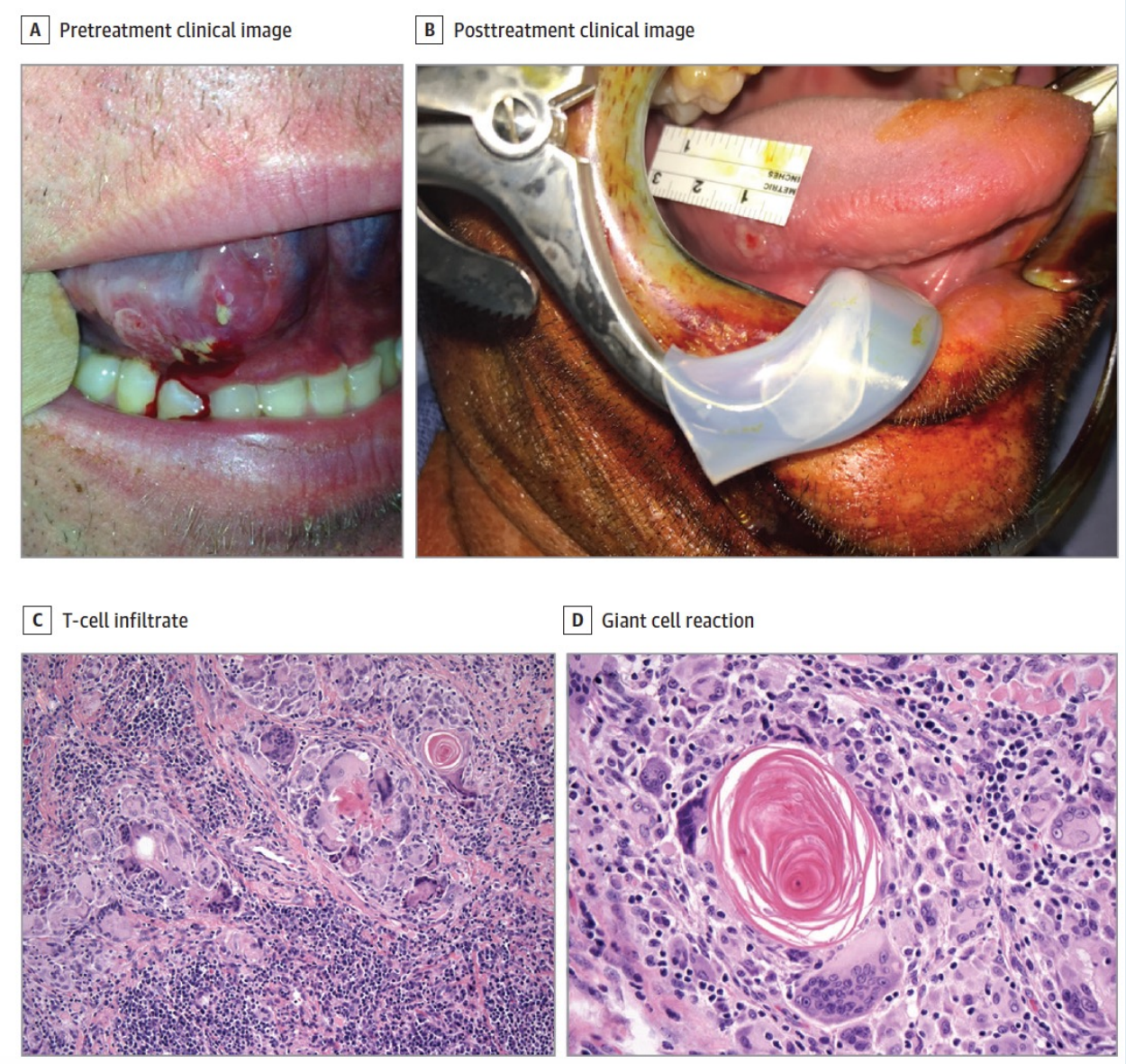


Objective Tumor Response



Schoenfeld JD et al. *JAMA Oncol* 2020;6(10):1563-70.

Clinical and Pathologic Features of Response



Schoenfeld JD et al. *JAMA Oncol* 2020;6(10):1563-70.

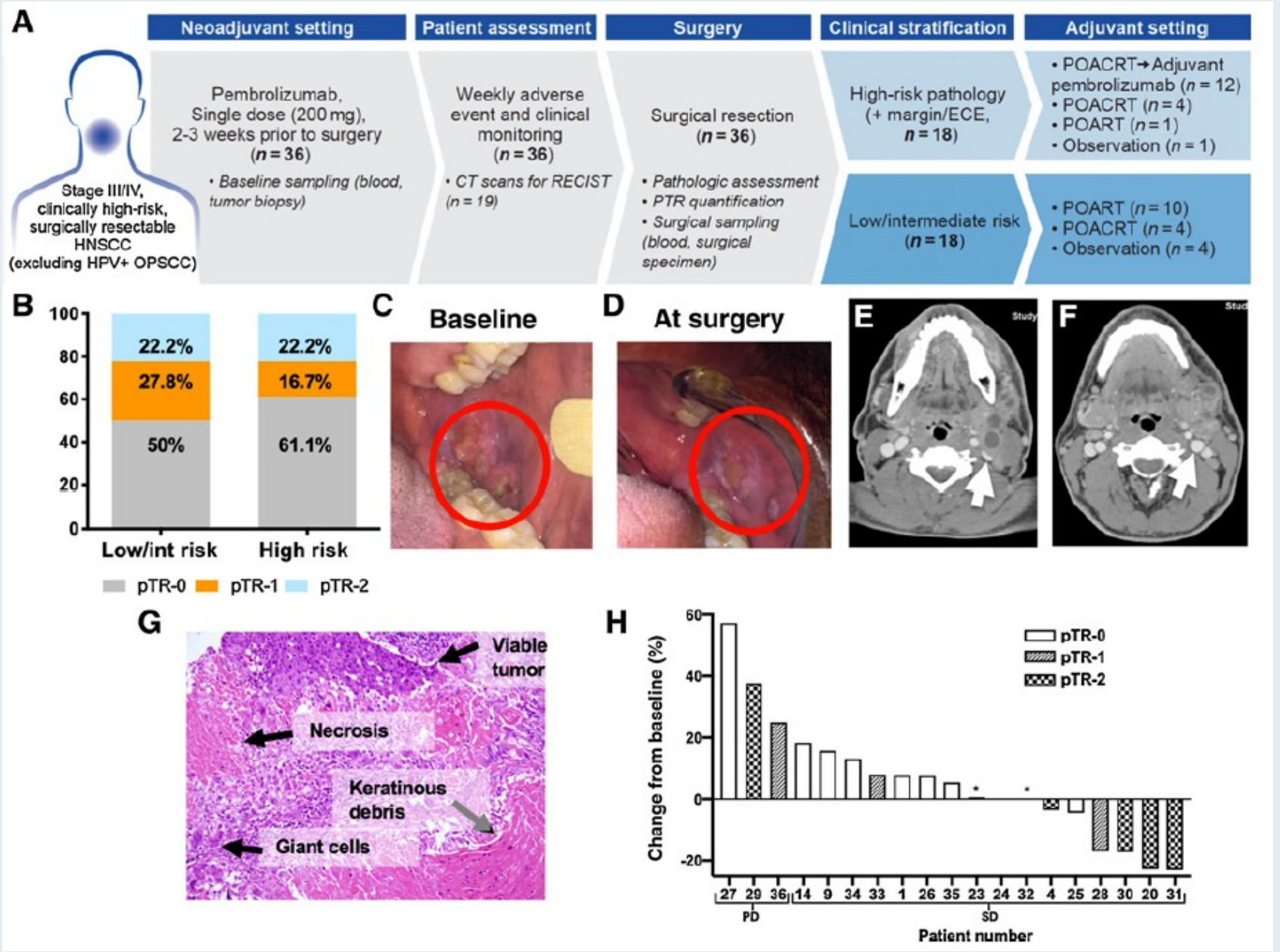
Clin Cancer Res 2021;27(1):357.

CLINICAL CANCER RESEARCH | CLINICAL TRIALS: IMMUNOTHERAPY

Neoadjuvant and Adjuvant Pembrolizumab in Resectable Locally Advanced, Human Papillomavirus–Unrelated Head and Neck Cancer: A Multicenter, Phase II Trial

Ravindra Uppaluri[1,2], Katie M. Campbell[3,4], Ann Marie Egloff[1], Paul Zolkind[5], Zachary L. Skidmore[4], Brian Nussenbaum[5,6], Randal C. Paniello[5,6], Jason T. Rich[5,6], Ryan Jackson[5,6], Patrik Pipkorn[5,6], Loren S. Michel[6,7], Jessica Ley[7], Peter Oppelt[6,7], Gavin P. Dunn[6,8], Erica K. Barnell[3,4], Nicholas C. Spies[4], Tianxiang Lin[5], Tiantian Li[9], David T. Mulder[9], Youstina Hanna[9], Iulia Cirlan[9], Trevor J. Pugh[9,10,11], Tenny Mudianto[2], Rachel Riley[2], Liye Zhou[2], Vickie Y. Jo[1], Matthew D. Stachler[12], Glenn J. Hanna[2], Jason Kass[1,2], Robert Haddad[1,2], Jonathan D. Schoenfeld[2,13], Evisa Gjini[12], Ana Lako[12], Wade Thorstad[6,14], Hiram A. Gay[6,14], Mackenzie Daly[6,14], Scott J. Rodig[12,15], Ian S. Hagemann[16], Dorina Kallogjeri[5], Jay F. Piccirillo[5,6], Rebecca D. Chernock[16], Malachi Griffith[3,4,6,7], Obi L. Griffith[3,4,6,7], and Douglas R. Adkins[6,7]

Trial Profile and Tumor Response



Uppaluri R et al. *Clin Cancer Res* 2021;27(1):357.

Meet The Professor with Dr Haddad

MODULE 1: ESMO 2022

MODULE 2: Needle in a Haystack

MODULE 3: Head and Neck Cancer

MODULE 4: Thyroid Cancer

MODULE 5: Journal Club with Dr Haddad

MODULE 6: Appendix

RTP
RESEARCH
TO PRACTICE

Immunotherapeutic Strategies for Metastatic/Unresectable Head and Neck Cancer

ESMO 2022;Abstract 659MO.

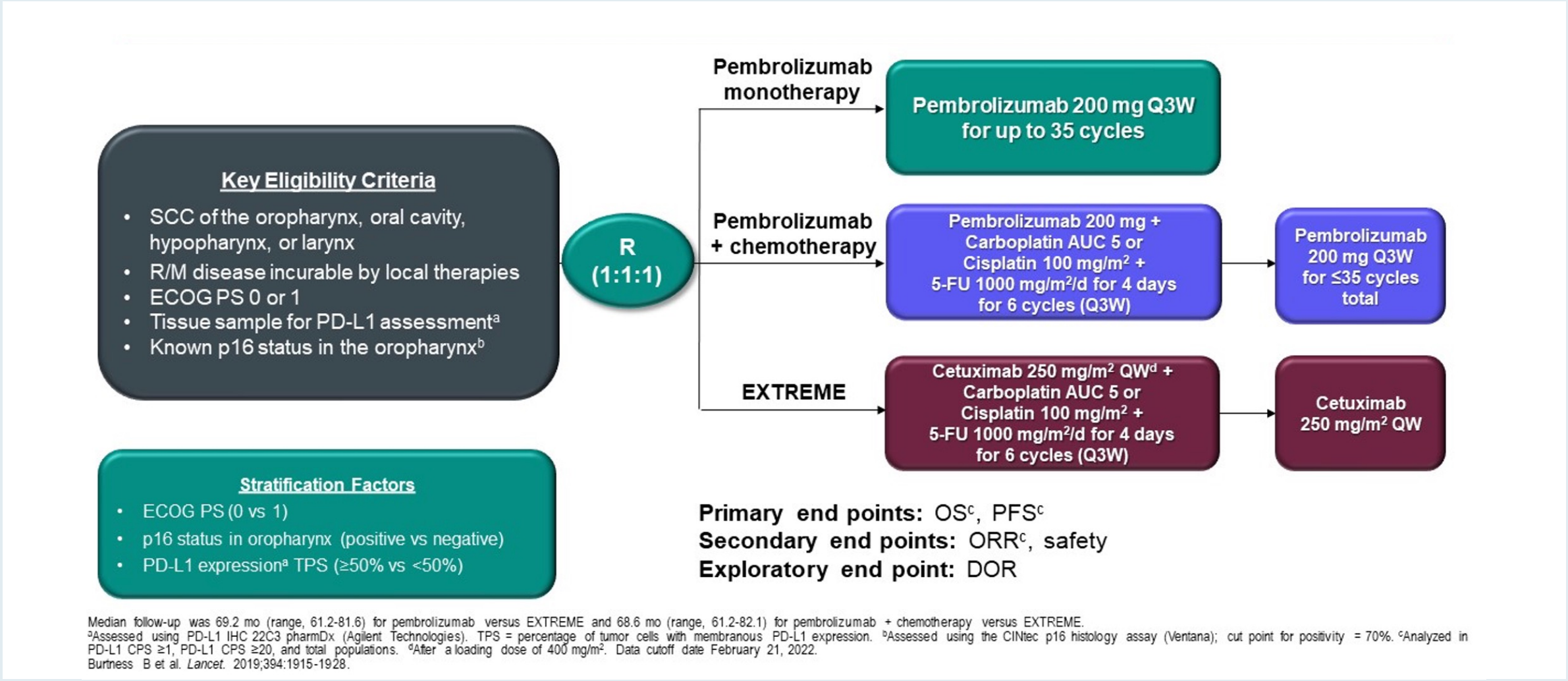
Pembrolizumab With or Without Chemotherapy For First-Line Treatment of Recurrent/Metastatic Head and Neck Squamous Cell Carcinoma: 5-year Results from KEYNOTE-048

Makoto Tahara[1]; Richard Greil[2]; Danny Rischin[3]; Kevin J. Harrington[4]; Barbara Burtness[5]; Gilberto de Castro[6]; Amanda Psyrri[7]; Irene Brana[8]; Prakash Neupane[9]; Åse Bratland[10]; Thorsten Fuereder[11]; Brett G.M. Hughes[12]; Ricard Mesia[13]; Nuttapong Ngamphaiboon[14]; Tamara Rordorf[15]; Wan Zamaniah Wan Ishak[16]; Jianxin Lin[17]; Burak Gumuscu[17]; Nati Lerman[17]; Denis Soulières[18]

[1]National Cancer Center Hospital East, Kashiwa, Japan; [2]Paracelsus Medical University Salzburg Cancer Research Institute and Cancer Cluster, Salzburg, Austria; [3]Peter MacCallum Cancer Institute University of Melbourne, Melbourne, VIC, Australia; [4]The Institute of Cancer Research, London, United Kingdom; [5]Yale School of Medicine, New Haven, CT, USA; [6]Instituto do Cancer de Sao Paulo—ICESP, São Paulo, Brazil; [7]National and Kapodistrian University of Athens, Attikon University Hospital, Athens, Greece; [8]Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; [9]University of Kansas Medical Center, Kansas City, MO, USA; [10]Oslo University Hospital, Oslo, Norway; [11]Medical University of Vienna/General Hospital Vienna, Vienna, Austria; [12]Royal Brisbane & Women's Hospital, and University of Queensland, Herston, QLD, Australia; [13]Catalan Institute of Oncology, Barcelona, Spain; [14]Ramathibodi Hospital, Mahidol University, Ratchatewi, Bangkok, Thailand, [15]University Hospital, Zurich, Switzerland; [16]University Malaya, Kuala Lumpur, Wilayah Persekutuan, Malaysia; [17]Merck & Co., Inc., Rahway, NJ, USA; [18]CHUM, Montréal, Quebec, Canada

RTP RESEARCH TO PRACTICE

KEYNOTE-048 Phase III Study Design

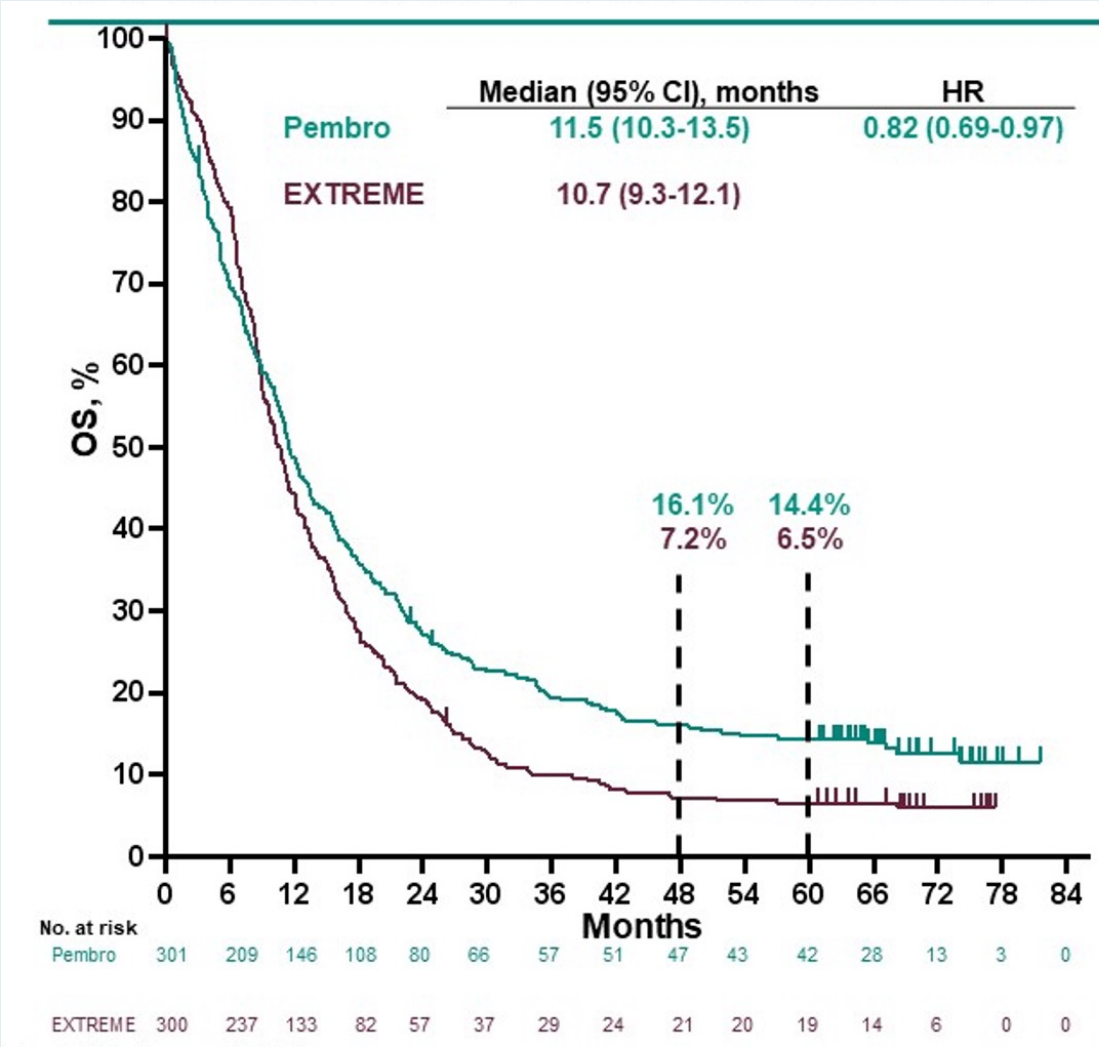


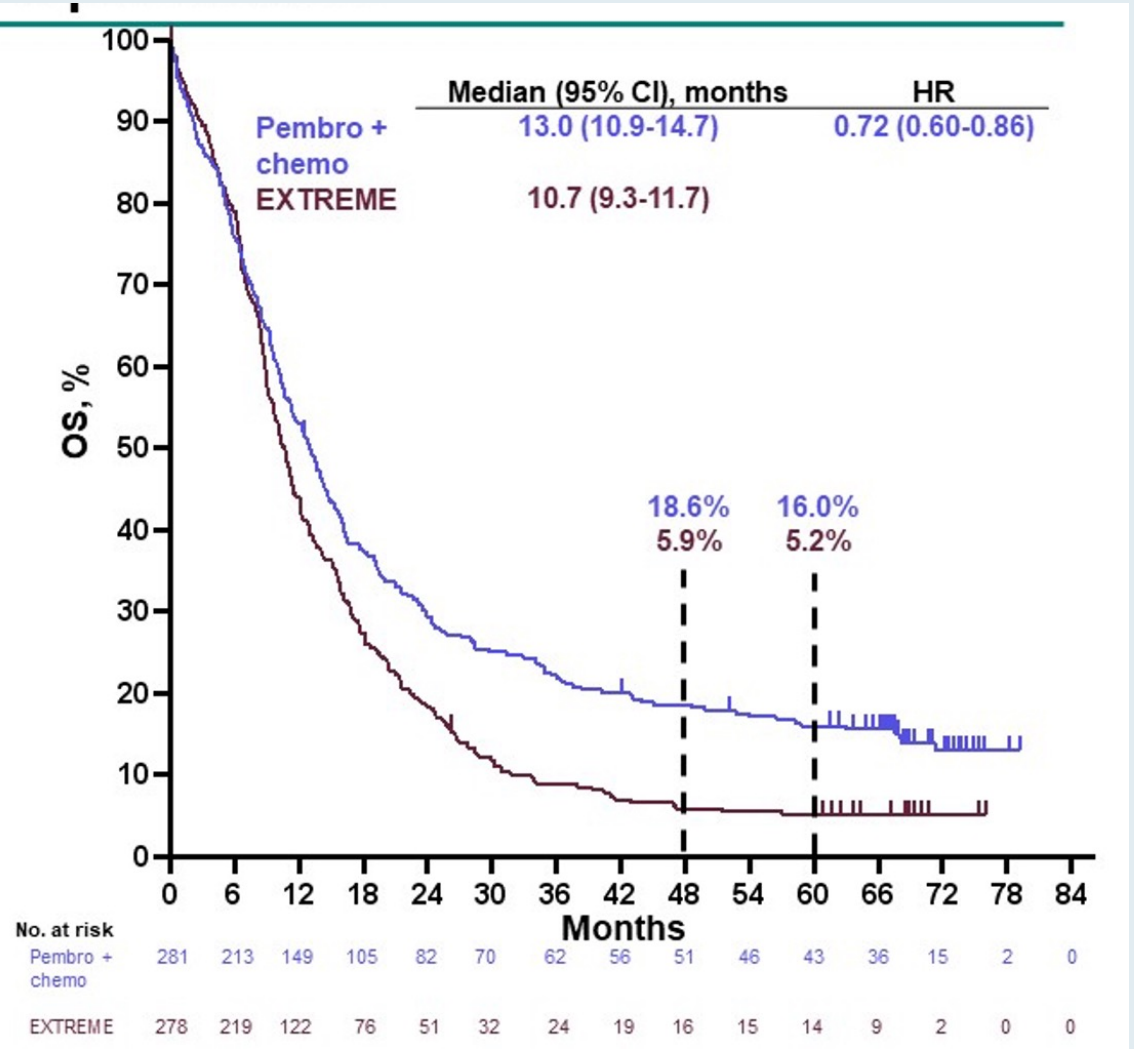
Median follow-up was 69.2 mo (range, 61.2-81.6) for pembrolizumab versus EXTREME and 68.6 mo (range, 61.2-82.1) for pembrolizumab + chemotherapy versus EXTREME. [a]Assessed using PD-L1 IHC 22C3 pharmDx (Agilent Technologies). TPS = percentage of tumor cells with membranous PD-L1 expression. [b]Assessed using the CINtec p16 histology assay (Ventana); cut point for positivity = 70%. [c]Analyzed in PD-L1 CPS ≥1, PD-L1 CPS ≥20, and total populations. [d]After a loading dose of 400 mg/m². Data cutoff date February 21, 2022.
Burtness B et al. *Lancet*. 2019;394:1915-1928.

SCC = squamous cell carcinoma; OS = overall survival; PFS = progression-free survival; ORR = objective response rate; DOR = duration of response

Tahara M et al. ESMO 2022;Abstract 659MO.

KEYNOTE-048: Overall Survival in the ITT Population



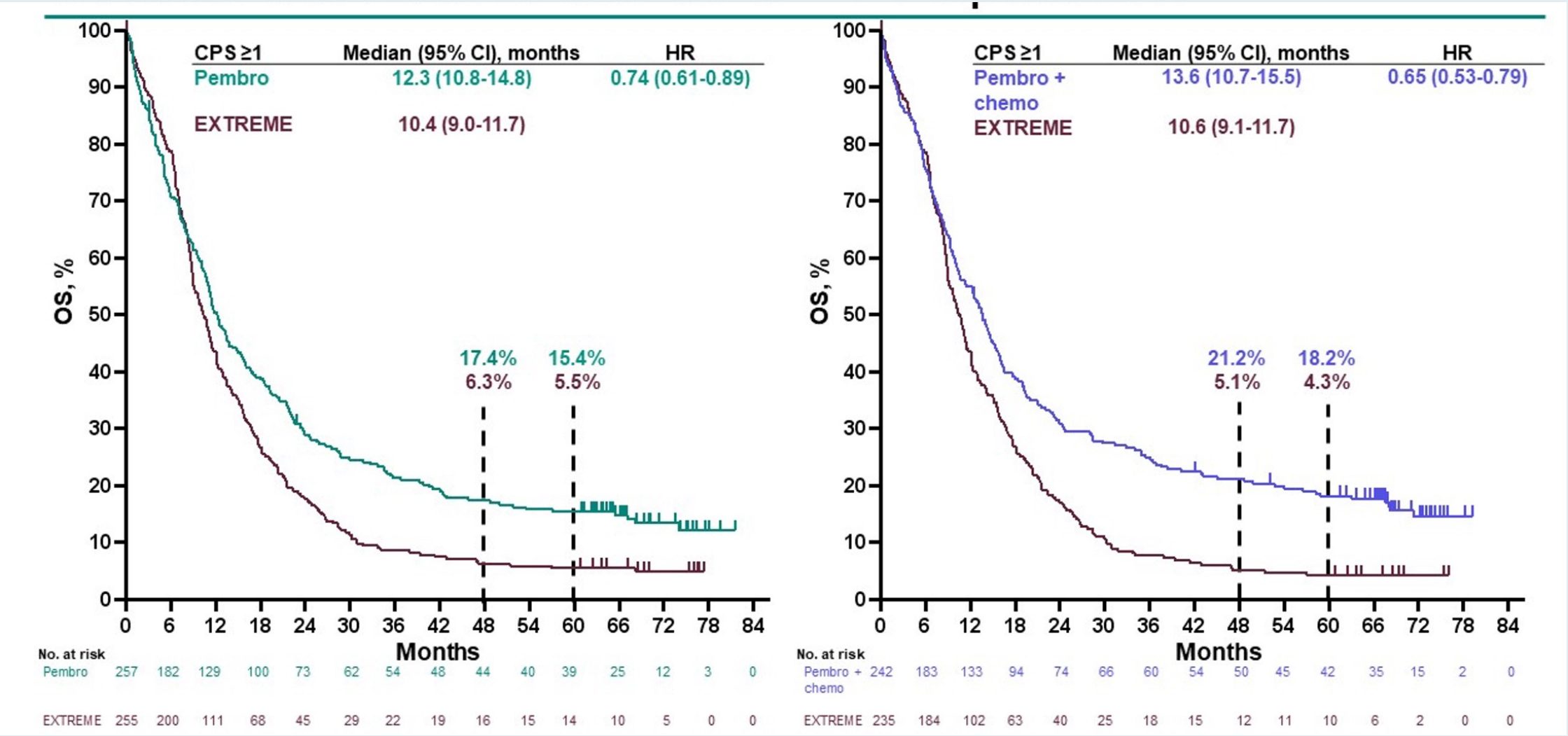


ITT = intent-to-treat

Tahara M et al. ESMO 2022;Abstract 659MO.

RTP RESEARCH TO PRACTICE

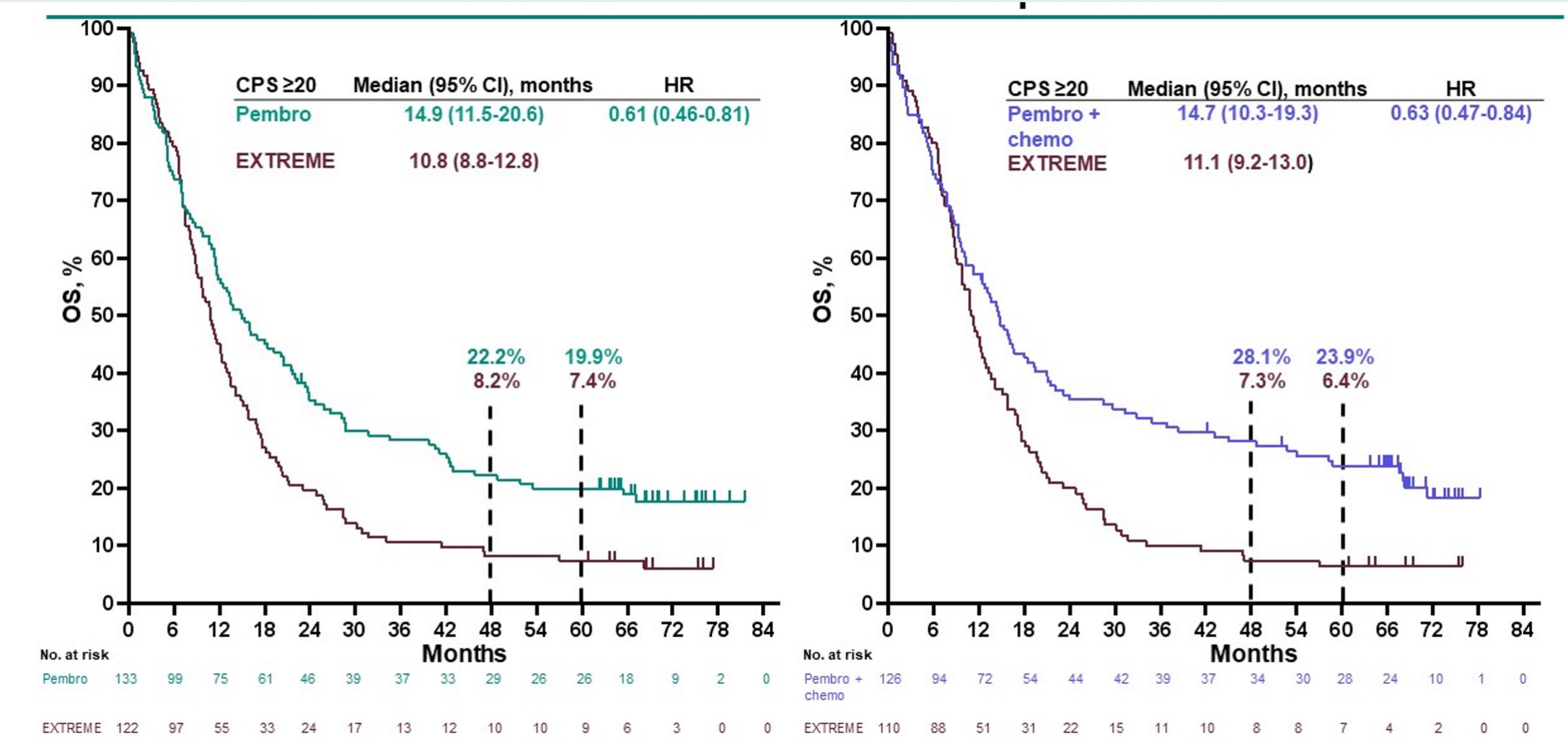
KEYNOTE-048: Overall Survival in the CPS ≥1 Population



Tahara M et al. ESMO 2022;Abstract 659MO.

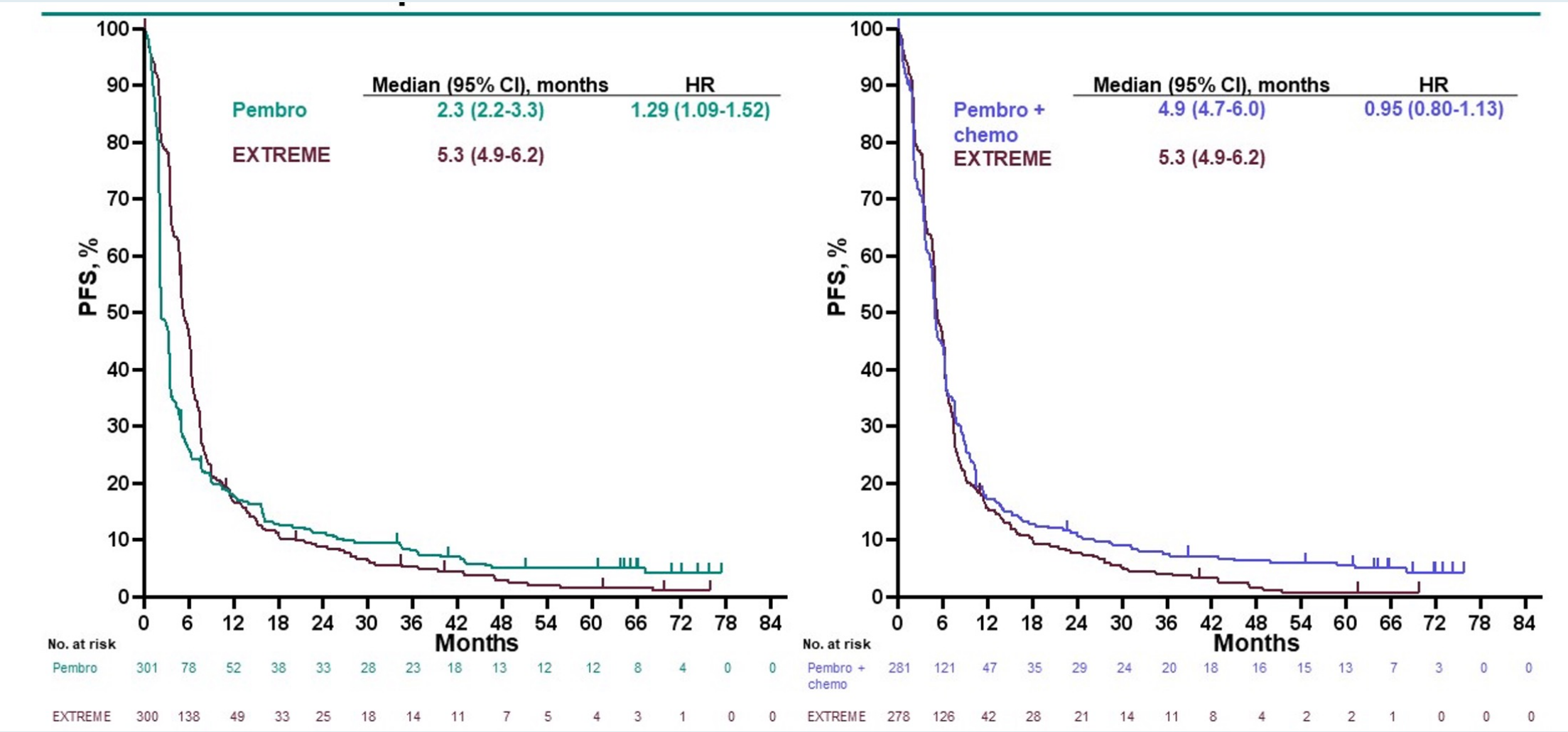
RTP RESEARCH TO PRACTICE

KEYNOTE-048: Overall Survival in the CPS ≥20 Population



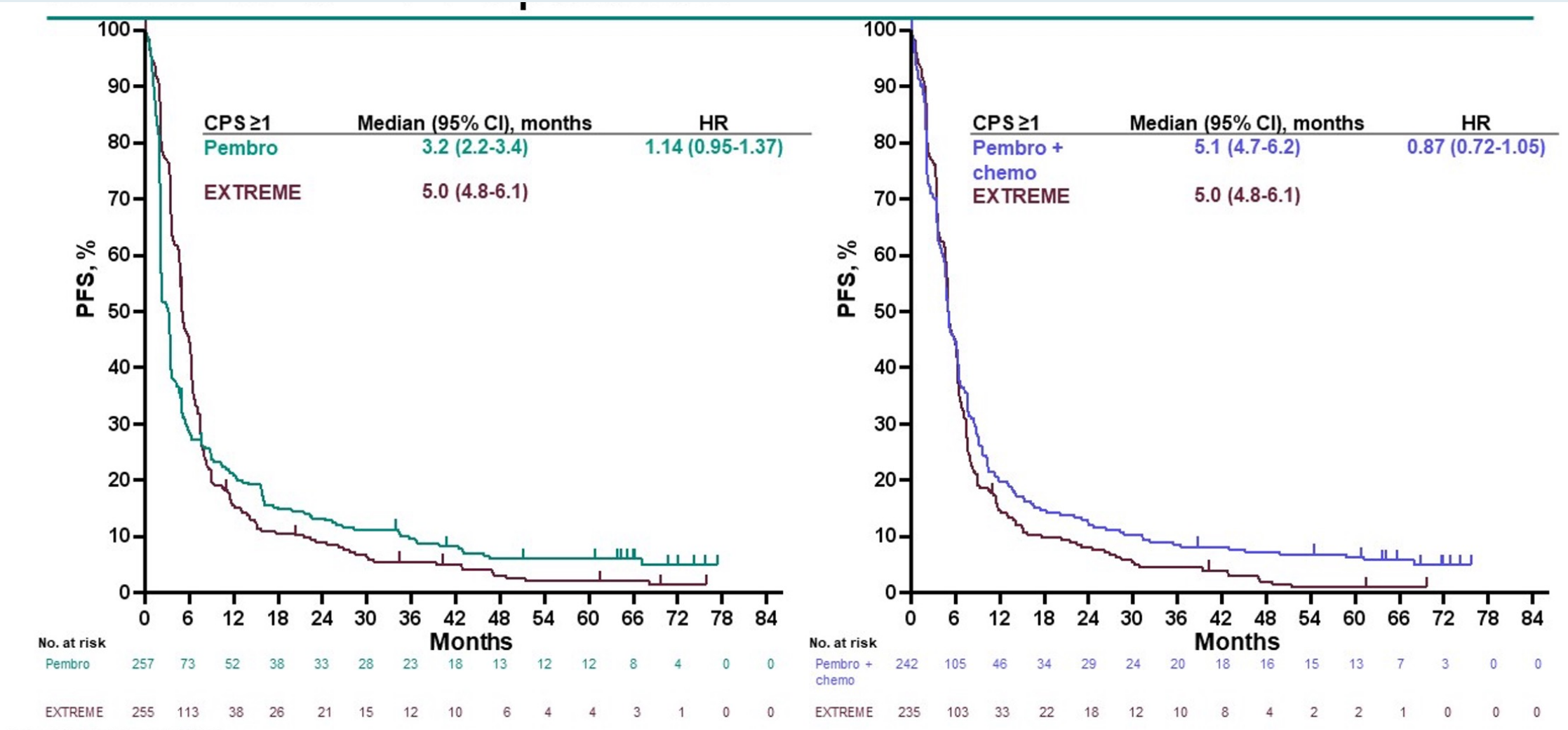
Tahara M et al. ESMO 2022;Abstract 659MO.

KEYNOTE-048: PFS in the ITT Population



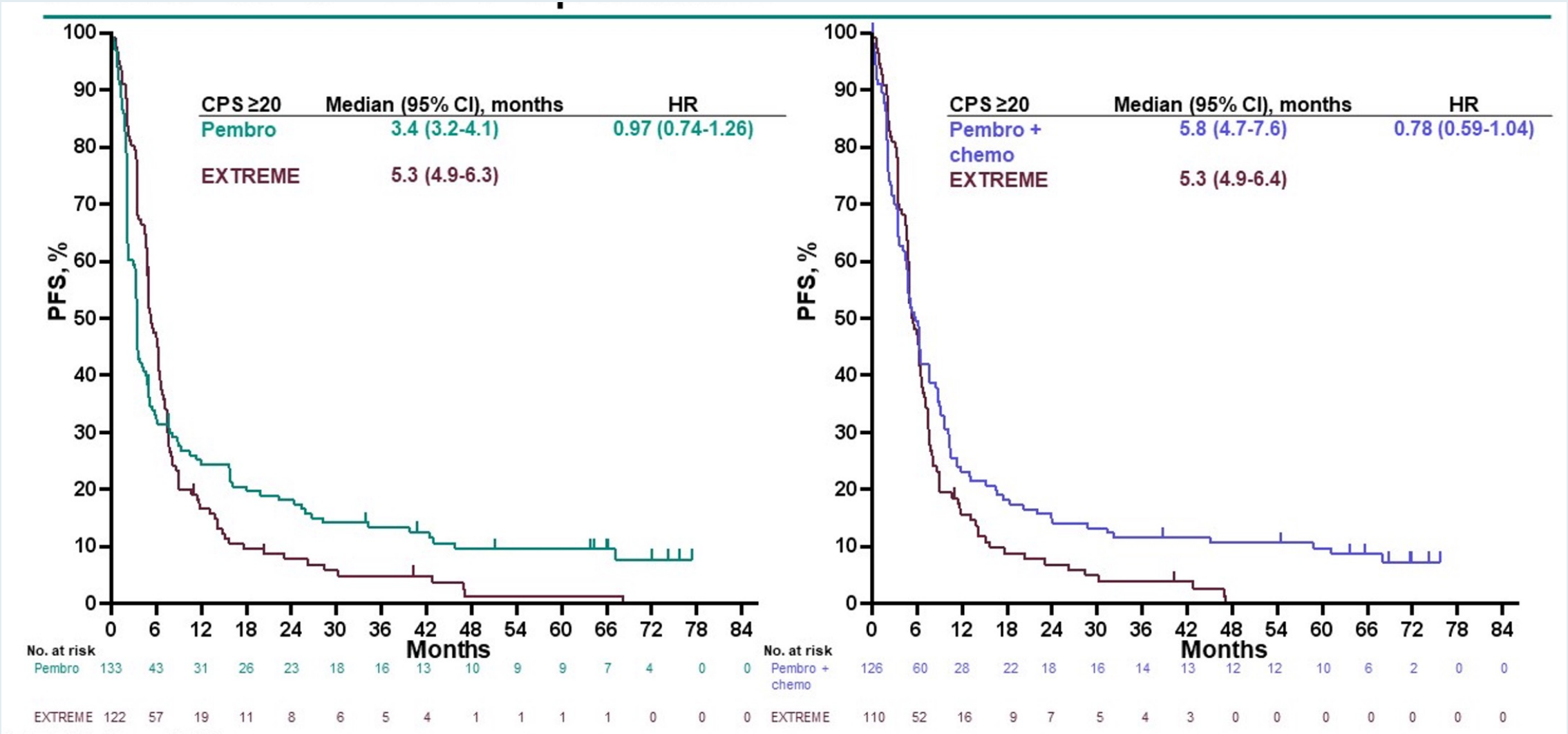
Tahara M et al. ESMO 2022;Abstract 659MO.

KEYNOTE-048: PFS in the CPS ≥1 Population



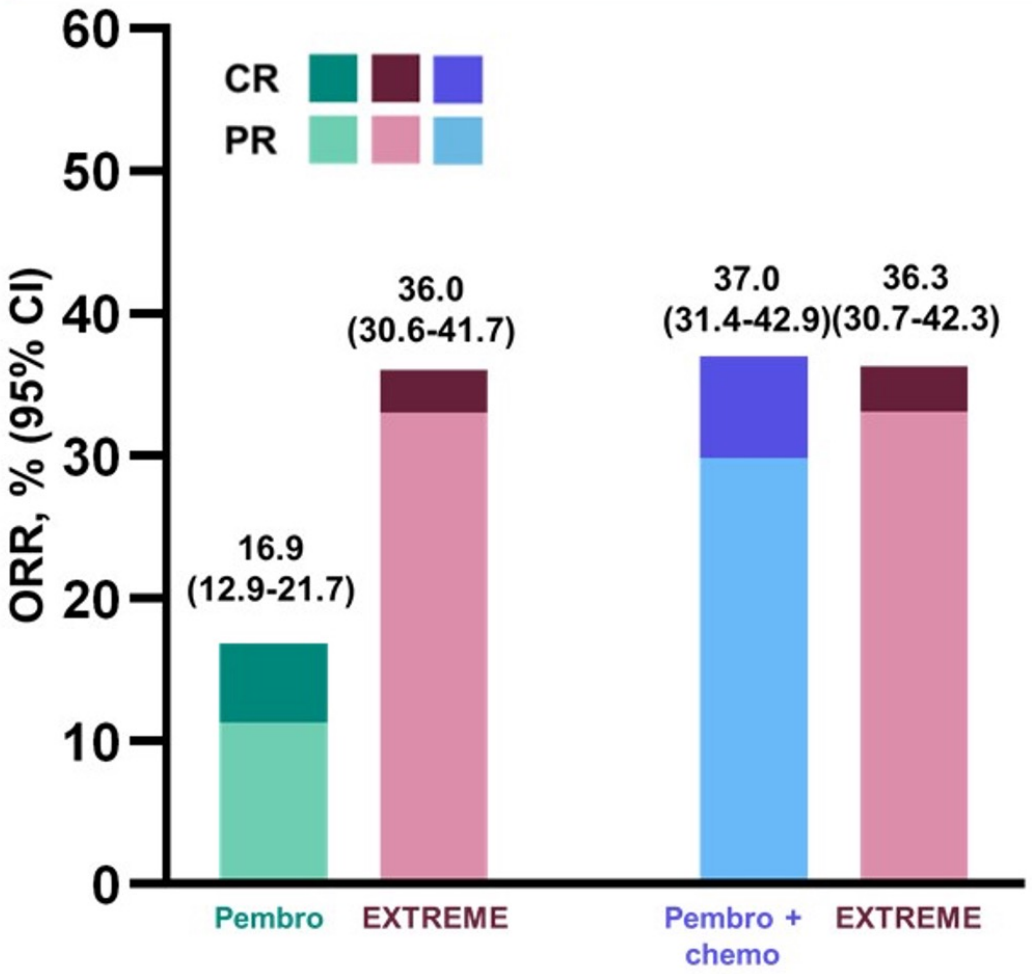
Tahara M et al. ESMO 2022;Abstract 659MO.

KEYNOTE-048: PFS in the CPS ≥20 Population



Tahara M et al. ESMO 2022;Abstract 659MO.

KEYNOTE-048: Objective Response Rate and Duration of Response by BICR in the ITT Population



	Pembro vs EXTREME		Pembro + chemo vs EXTREME	
	Pembro n = 301	EXTREME n = 300	Pembro + chemo n = 281	EXTREME n = 278
DOR, median (range), mo	22.6 (1.5+ to 75.5+)	4.5 (1.2+ to 73.9+)	6.7 (1.6+ to 73.8+)	4.3 (1.2+ to 66.5+)

BICR = blinded independent central review; CR = complete response; PR = partial response; ORR = objective response rate; DOR = duration of response

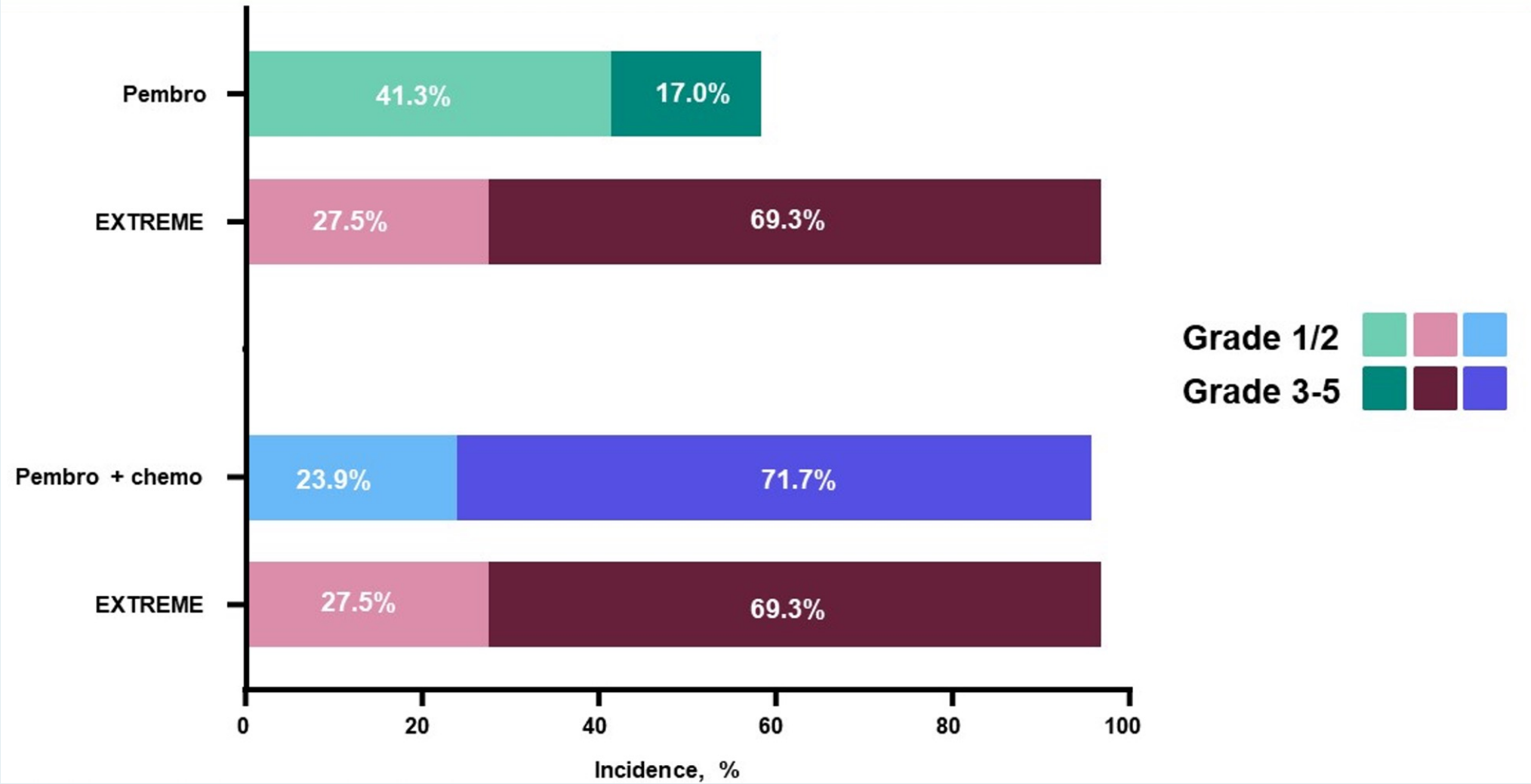
Tahara M et al. ESMO 2022;Abstract 659MO.

KEYNOTE-048: Objective Response Rate and Duration of Response by PD-L1 Status

	Pembro vs EXTREME		Pembro + chemo vs EXTREME	
	Pembro	EXTREME	Pembro + chemo	EXTREME
CPS ≥1, n	257	255	242	235
ORR, % (95% CI)	19.1 (14.5-24.4)	34.9 (29.1-41.1)	38.0 (31.9-44.5)	35.7 (29.6-42.2)
DOR, median, (range) mo	23.4 (1.5+ to 75.5+)	4.5 (1.2+ to 73.9+)	6.7 (1.6+ to 73.8+)	4.3 (1.2+ to 66.5+)
CPS ≥20, n	133	122	126	110
ORR, % (95% CI)	23.3 (16.4-31.4)	36.1 (27.6-45.3)	45.2 (36.4-54.3)	38.2 (29.1-47.9)
DOR, median, (range) mo	23.4 (2.7 to 75.5+)	4.3 (1.2+ to 38.2+)	7.1 (2.1+ to 73.8+)	4.2 (1.2+ to 38.2+)

Tahara M et al. ESMO 2022;Abstract 659MO.

KEYNOTE-048: Treatment-Related Adverse Events Summary



Tahara M et al. ESMO 2022;Abstract 659MO.

KEYNOTE-048 Conclusions

- With an extended follow-up of 5 years, first-line pembrolizumab monotherapy and pembrolizumab + chemotherapy continue to suggest clinical benefit in R/M HNSCC regardless of PD-L1 status
  - 5-year OS rate for overall ITT population
    - 14.4% versus 6.5% for pembrolizumab monotherapy versus EXTREME
    - 16.0% versus 5.2% for pembrolizumab + chemotherapy versus EXTREME
  - DOR remained longer with pembrolizumab or pembrolizumab + chemotherapy than with EXTREME
  - Safety was consistent with that of previous reports[1]
- Results from this study further support treatment with pembrolizumab and pembrolizumab + chemotherapy as first-line standard of care in R/M HNSCC

Tahara M et al. ESMO 2022;Abstract 659MO.

2021 ASCO ANNUAL MEETING **Abstract LBA2.**

JUPITER-02:
The randomized, double-blind, phase 3 study of toripalimab or placebo plus cisplatin and gemcitabine as first-line treatment for recurrent or metastatic nasopharyngeal carcinoma (NPC)

Rui-Hua Xu[1, *], Hai-Qiang Mai[2], Qiu-Yan Chen[2] Dongping Chen[3], Chaosu Hu[4], Kunyu Yang[5], Jiyu Wen[6], Jingao Li[7], Ying-Rui Shi[8], Feng Jin[9], Ruilian Xu[10], Jianji Pan[11], Shenhong Qu[12], Ping Li[13], Chunhong Hu[14], Yi-Chun Liu[15], Yi Jiang[16], Xia He[17], Hung-Ming Wang[18] and Wan-Teck Lim[19], Coherus Biosciences and Shanghai Junshi Biosciences.

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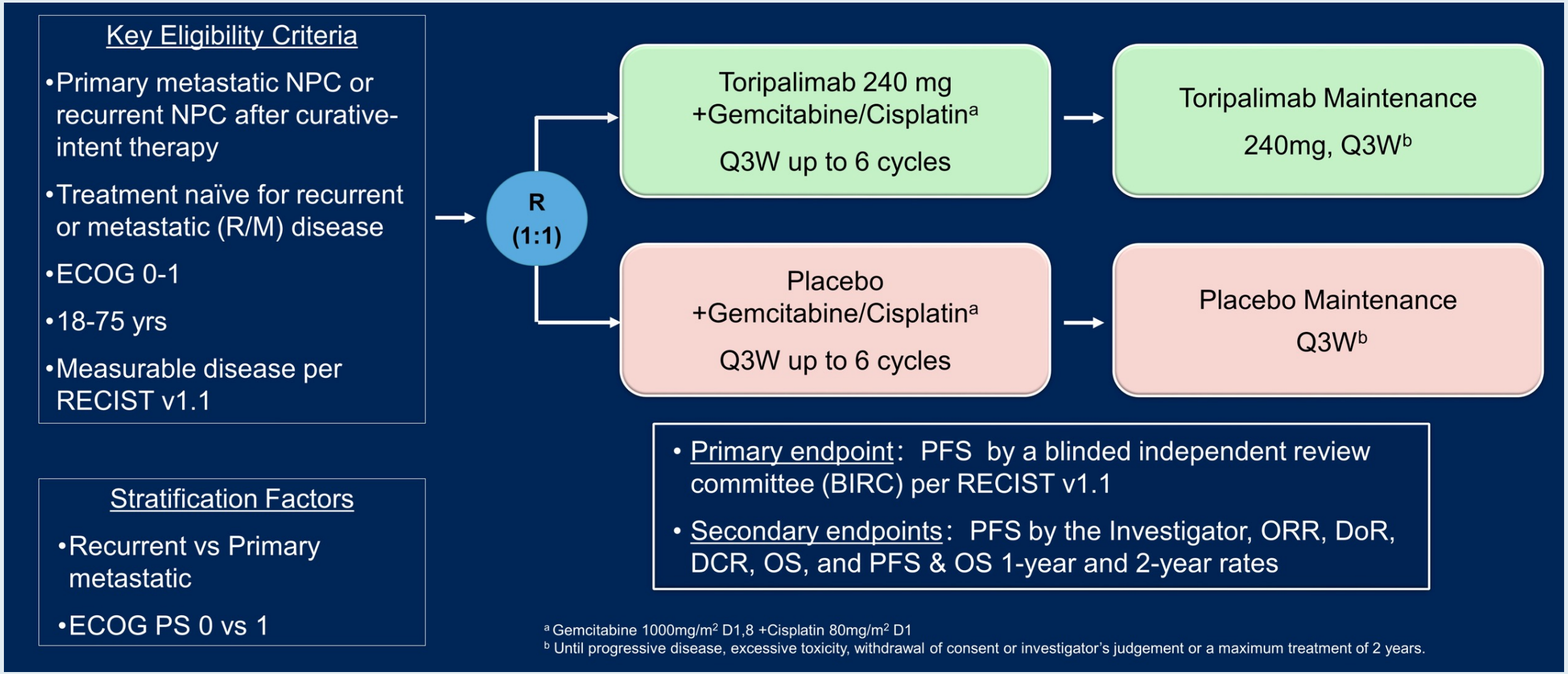
Toripalimab or placebo plus chemotherapy as first-line treatment in advanced nasopharyngeal carcinoma: a multicenter randomized phase 3 trial

Hai-Qiang Mai[1,37], Qiu-Yan Chen[1,37], Dongping Chen[2], Chaosu Hu[3], Kunyu Yang[4], Jiyu Wen[5], Jingao Li[6], Ying-Rui Shi[7], Feng Jin[8], Ruilian Xu[9], Jianji Pan[10], Shenhong Qu[11], Ping Li[12], Chunhong Hu[13], Yi-Chun Liu[14], Yi Jiang[15], Xia He[16], Hung-Ming Wang[17], Wan-Teck Lim[18], Wangjun Liao[19], Xiaohui He[20], Xiaozhong Chen[21], Zhigang Liu[22], Xianglin Yuan[23], Qi Li[24], Xiaoyan Lin[25], Shanghua Jing[26], Yanju Chen[27], Yin Lu[28], Ching-Yun Hsieh[29], Muh-Hwa Yang[30], Chia-Jui Yen[31], Jens Samol[32,33], Hui Feng[34,35], Sheng Yao[34,35], Patricia Keegan[35] and Rui-Hua Xu[36]✉

RTP RESEARCH TO PRACTICE

JUPITER-02 Phase III Study

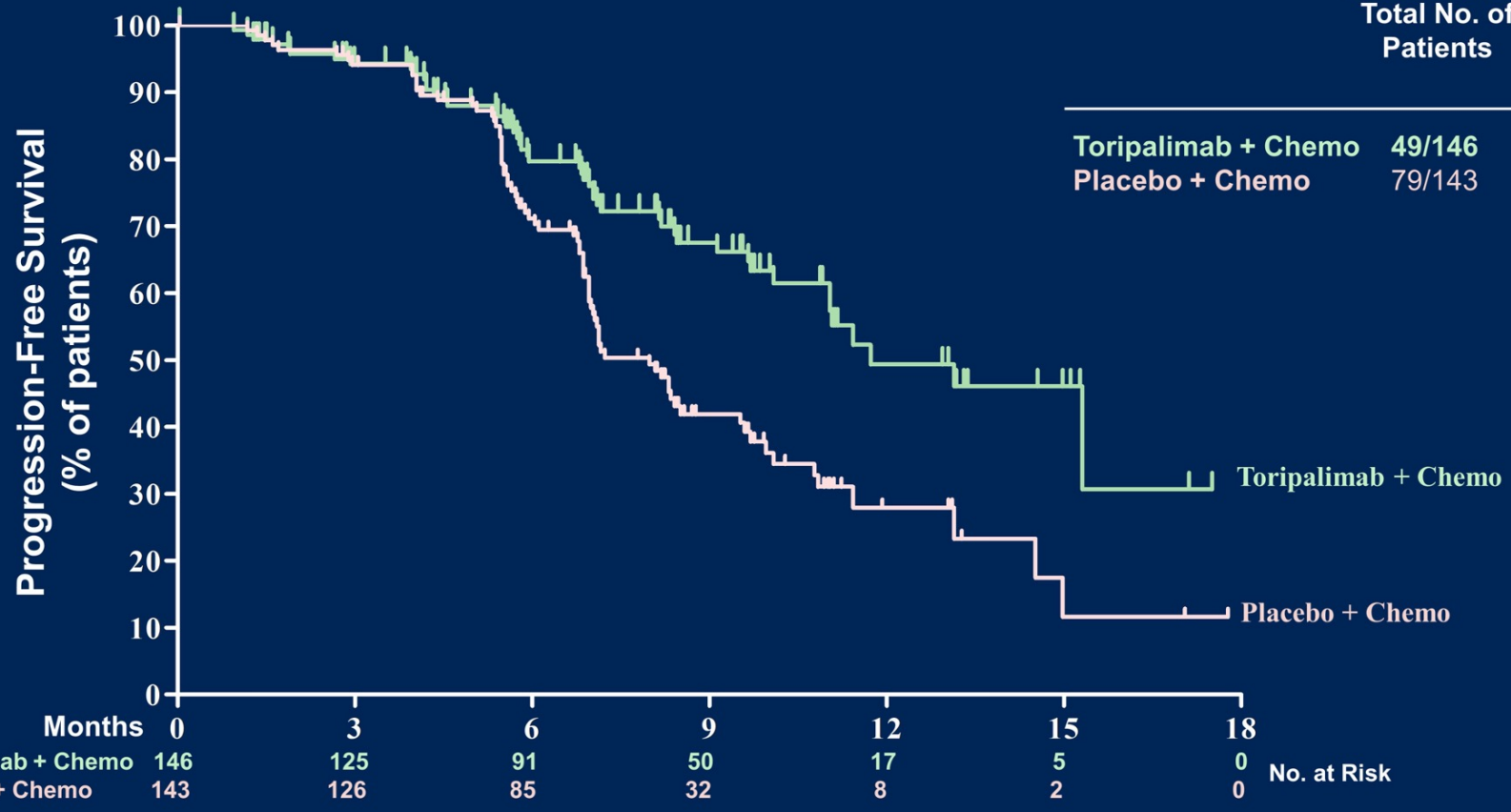


NPC = nasopharyngeal carcinoma; PFS = progression-free survival; ORR = overall response rate; DoR = duration of response; DCR = disease control rate; OS = overall survival

Xu R-H et al. ASCO 2021;Abstract LBA2.

JUPITER-02: Progression-Free Survival by BIRC

Interim Analysis Data cut-off Date: May 30, 2020



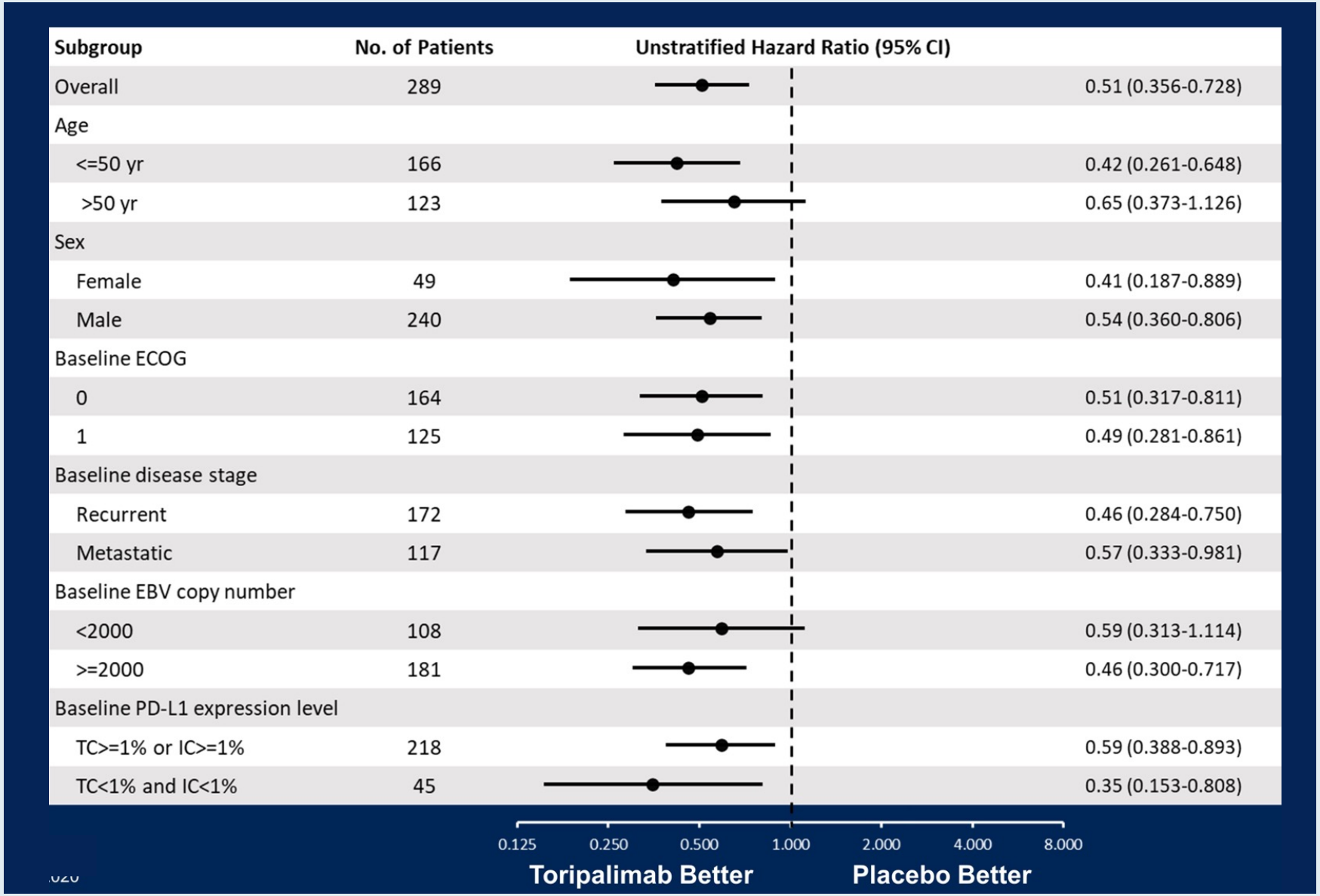
	No. of Events/ Total No. of Patients	Median Progression-free Survival, months (95% CI)	1-Yr Progression-free Survival Rate, % (95% CI)
Toripalimab + Chemo	49/146	11.7 (11.0, NE)	49.4 (36.4, 61.1)
Placebo + Chemo	79/143	8.0 (7.0, 9.5)	27.9 (18.0, 38.8)

Stratified HR for disease progression or death,

0.52 (95% CI 0.36-0.74); P=0.0003

Xu R-H et al. ASCO 2021;Abstract LBA2.

JUPITER-02: Progression-Free Survival by BIRC in Key Subgroups



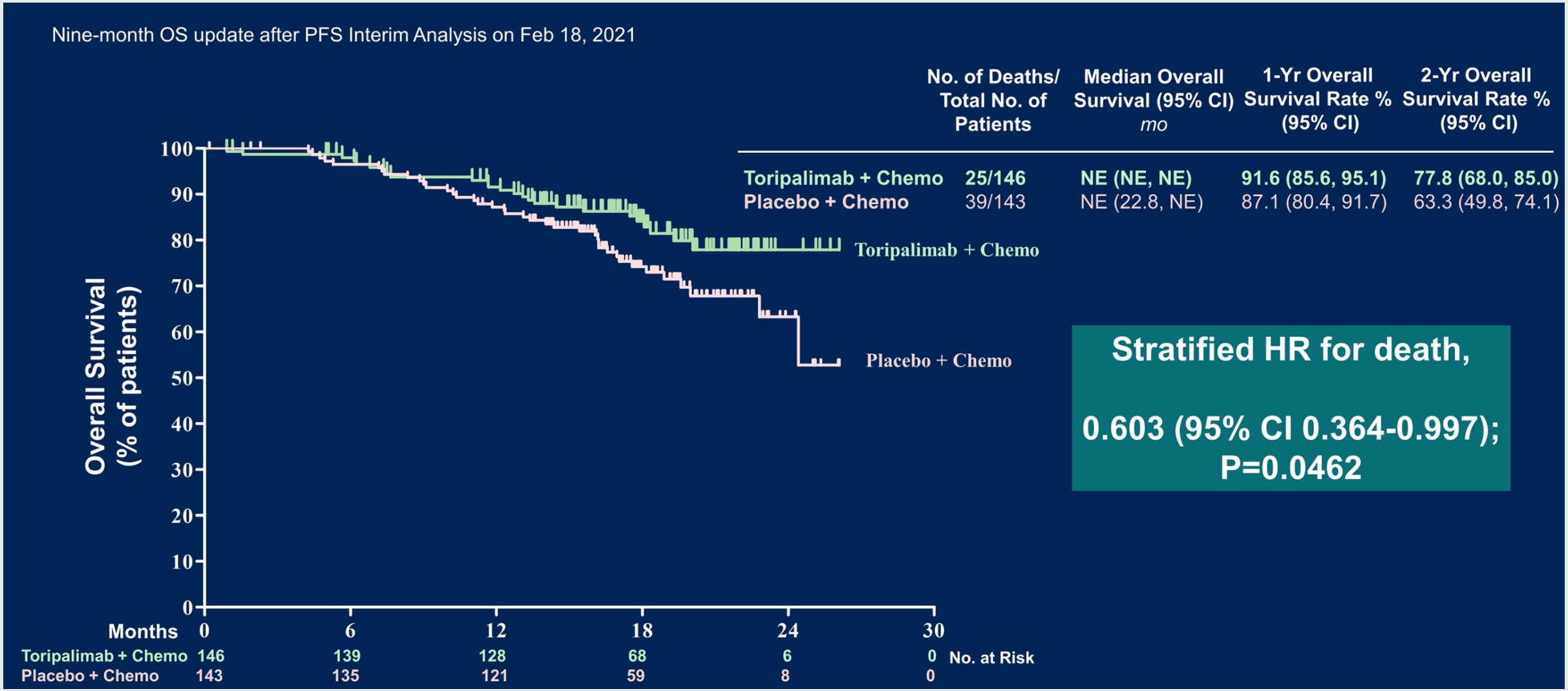
Xu R-H et al. ASCO 2021;Abstract LBA2.

RTP RESEARCH TO PRACTICE

JUPITER-02: Overall Survival Update

Nine-month OS update after PFS Interim Analysis on Feb 18, 2021

	No. of Deaths/ Total No. of Patients	Median Overall Survival (95% CI) *mo*	1-Yr Overall Survival Rate % (95% CI)	2-Yr Overall Survival Rate % (95% CI)
Toripalimab + Chemo	25/146	NE (NE, NE)	91.6 (85.6, 95.1)	77.8 (68.0, 85.0)
Placebo + Chemo	39/143	NE (22.8, NE)	87.1 (80.4, 91.7)	63.3 (49.8, 74.1)



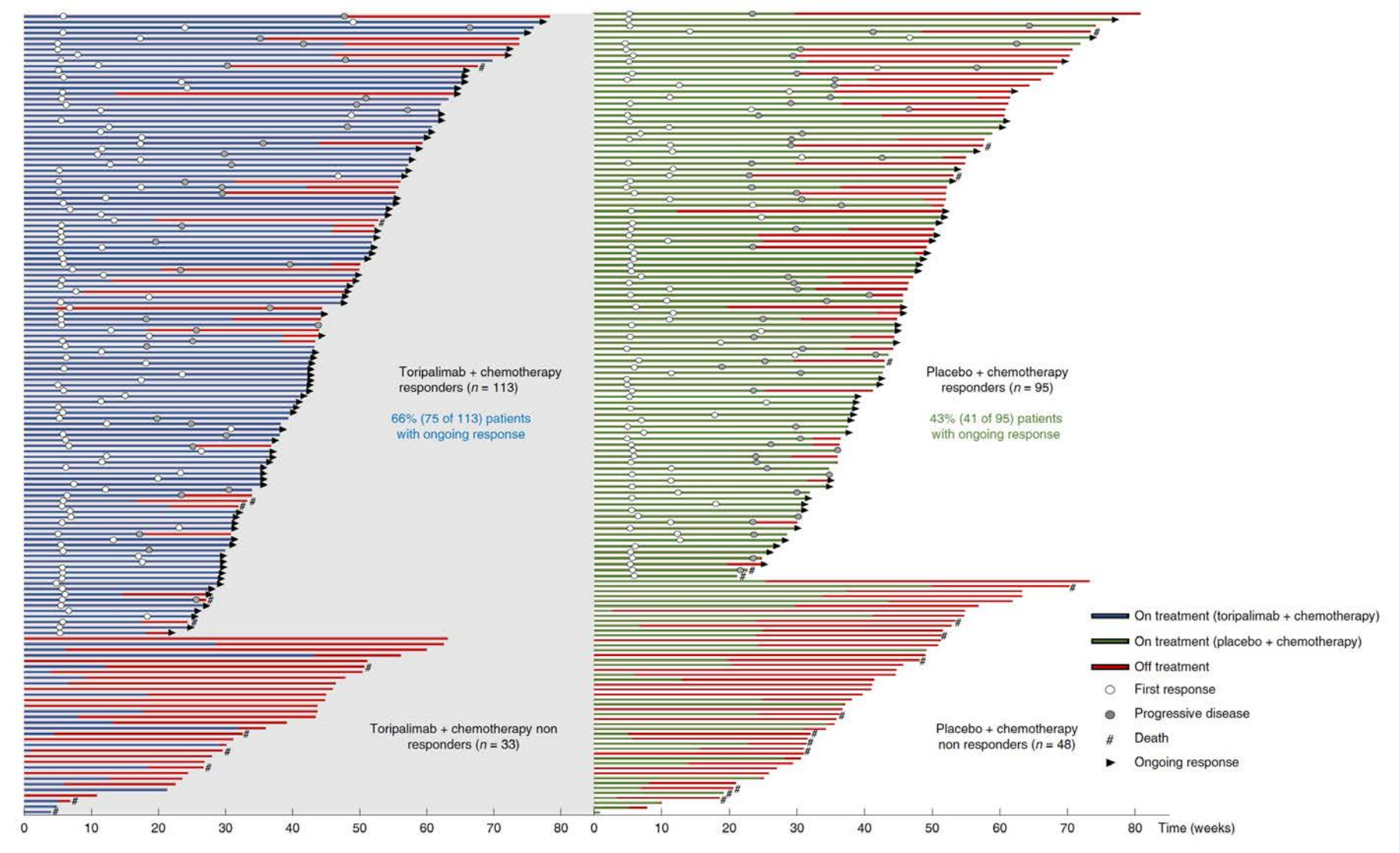
Stratified HR for death,

0.603 (95% CI 0.364-0.997); P=0.0462

Xu R-H et al. ASCO 2021;Abstract LBA2.

RTP RESEARCH TO PRACTICE

JUPITER-02: Exposure and Clinical Events in the ITT Population and DoR in Patients with Confirmed Objective Response



Mai HQ et al. *Nat Med* 2021 September;27(9):1536-43.

JUPITER-02: Response and Duration or Response

Characteristic (%)	Toripalimab + GP (N=146)	Placebo + GP (N=143)
Objective Response Rate [a]	77.4	66.4
95% CI	(69.8, 83.9)	(58.1, 74.1)
P value	0.0335	
Best Overall Response [a]		
Complete Response	19.2	11.2
Partial Response	58.2	55.2
Stable Disease	10.3	13.3
Progressive Disease	3.4	5.6
Not evaluable	6.2	5.6
Non-CR/non-PD [b]	2.7	8.4
No evidence of disease [c]	0	0.7
Median DoR, (95%CI), months	10.0 (8.8, NE)	5.7 (5.4, 6.8)
HR (95%CI)	0.50 (0.33-0.78)	
P value	0.0014	

GP = gemcitabine/cisplatin

Xu R-H et al. ASCO 2021;Abstract LBA2.

JUPITER-02: Safety Overview

Patients, n (%)	Toripalimab + GP (N=146)		Placebo + GP (N=143)	
	Any grade	Grade≥3	Any grade	Grade≥3
All Treatment Emergent AEs	146 (100.0)	130 (89.0)	143 (100.0)	128 (89.5)
AEs related to study drug [b,c]	139 (95.2)	118 (80.8)	139 (97.2)	119 (83.2)
Immune-related AEs [c]	58 (39.7)	11 (7.5)	27 (18.9)	1 (0.7)
AEs leading to discontinuation	11 (7.5)	/	7 (4.9)	/
Infusion reactions	6 (4.1)	0	6 (4.2)	0
Fatal AEs	4 (2.7)	4 (2.7)	4 (2.8)	4 (2.8)

AEs = adverse events

Xu R-H et al. ASCO 2021;Abstract LBA2.

JUPITER-02: Common Treatment-Emergent Adverse Events

Patients, n (%)	Toripalimab + GP (N=146)		Placebo + GP (N=143)	
	Any grade	Grade≥3	Any grade	Grade≥3
Leukopenia	133 (91.1)	90 (61.6)	135 (94.4)	83 (58.0)
Anemia	129 (88.4)	69 (47.3)	135 (94.4)	57 (39.9)
Neutropenia	125 (85.6)	84 (57.5)	133 (93.0)	91 (63.6)
Nausea	101 (69.2)	2 (1.4)	119 (83.2)	4 (2.8)
Vomiting	98 (67.1)	3 (2.1)	94 (65.7)	3 (2.1)
Thrombocytopenia	93 (63.0)	48 (32.9)	89 (62.2)	41 (28.7)
Decreased appetite	78 (53.4)	1 (0.7)	84 (58.7)	0 (0)
Constipation	57 (39.0)	0 (0)	64 (44.8)	0 (0)
Aspartate aminotransferase increased	55 (37.7)	2 (1.4)	44 (30.8)	2 (1.4)
Alanine aminotransferase increased	53 (36.3)	1 (0.7)	57 (39.9)	0 (0)
Fatigue	52 (35.6)	2 (1.4)	51 (35.7)	3 (2.1)
Pyrexia	45 (30.8)	2 (1.4)	31 (21.7)	1 (0.7)
Hypothyroidism	45 (30.8)	0 (0)	24 (16.8)	0 (0)
Neuropathy peripheral	44 (30.1)	0 (0)	41 (28.7)	1 (0.7)
Diarrhea	44 (30.1)	3 (2.1)	33 (23.1)	0 (0)
Hyponatremia	37 (25.3)	13 (8.9)	52 (36.4)	6 (4.2)

Xu R-H et al. ASCO 2021;Abstract LBA2.

JUPITER-02 Summary and Conclusions

- The addition of toripalimab to GP as a first-line treatment for R/M NPC patients provided superior PFS, OS, ORR and DoR than GP alone.
  - Significant improvement in PFS： mPFS 11.7 vs. 8.0 months, HR=0.52 (95%CI: 0.36-0.74), p=0.0003
  - Although mOS was not mature in either arm, a 40% reduction in risk of death was observed in the toripalimab arm over the placebo arm.
  - A second interim OS analysis will be performed at pre-specified final PFS analysis followed by the final OS analysis
- No new safety signals were identified with toripalimab added to GP.
- Toripalimab plus GP represents a new standard of care as 1st line therapy for patients with R/M NPC.

Xu R-H et al. ASCO 2021;Abstract LBA2.

RTP RESEARCH TO PRACTICE

2022 ASCO® ANNUAL MEETING

Presentation 384950.

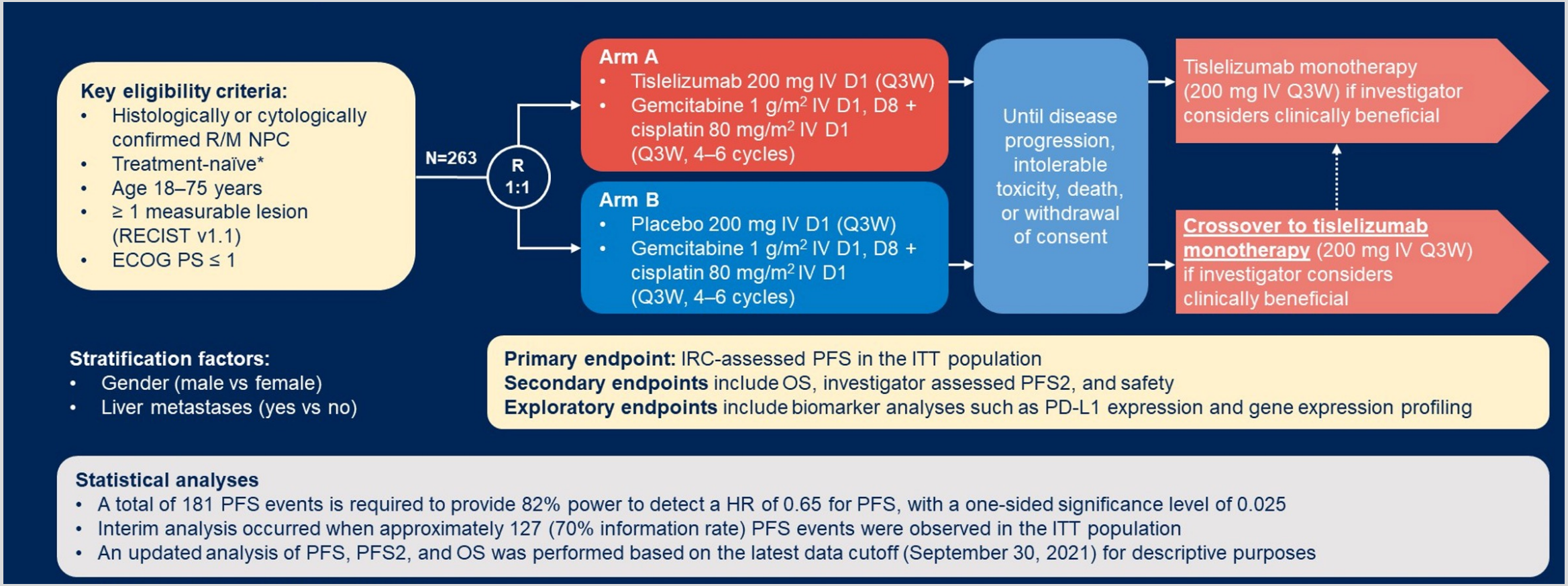
RATIONALE-309: Updated PFS, PFS2, and OS from a Phase 3 double-blind trial of tislelizumab versus placebo, plus chemotherapy, as first-line treatment for recurrent/metastatic nasopharyngeal cancer

Li Zhang, MD[1]

on behalf of Yunpeng Yang,[1] Jianji Pan,[2] Xiaozhong Chen,[3] Yan Sun,[4] Hui Wang,[5] Shenhong Qu,[6] Nianyong Chen,[7] Lizhu Lin,[8] Siyang Wang,[9] Qitao Yu,[10] Guihua Wang,[11] Feng Lei,[12] Jiyu Wen,[13] Chenqi Chen,[14] Yanjie Wu,[14] Shiangjiin Leaw,[14] Wenfeng Fang[1]

[1]Sun Yat-sen University Cancer Center, Guangzhou, China; [2]Fujian Cancer Hospital, Fuzhou, China; [3]Zhejiang Cancer Hospital, Hangzhou, China; [4]Beijing Cancer Hospital, Beijing, China; [5]Hunan Cancer Hospital, Changsha, China; [6]The People's Hospital of Guangxi Zhuang Autonomous Region, Otolaryngology Department, Nanning, China; [7]West China Hospital of Sichuan University, Chengdu, China; [8]The First Affiliated Hospital of Guangzhou Traditional Chinese Medicine University, Guangzhou, China; [9]The Fifth Affiliated Hospital Sun Yat-sen University, Zhuhai, China; [10]The Affiliated Cancer Hospital of Guangxi Medical University, Nanning, China; [11]Changsha Central Hospital, Changsha, China; [12]The People's Hospital of Zhongshan City, Zhongshan, China; [13]Affiliated Hospital of Guangdong Medical University, Zhanjiang, China; [14]BeiGene (Shanghai) Co., Ltd., Shanghai, China

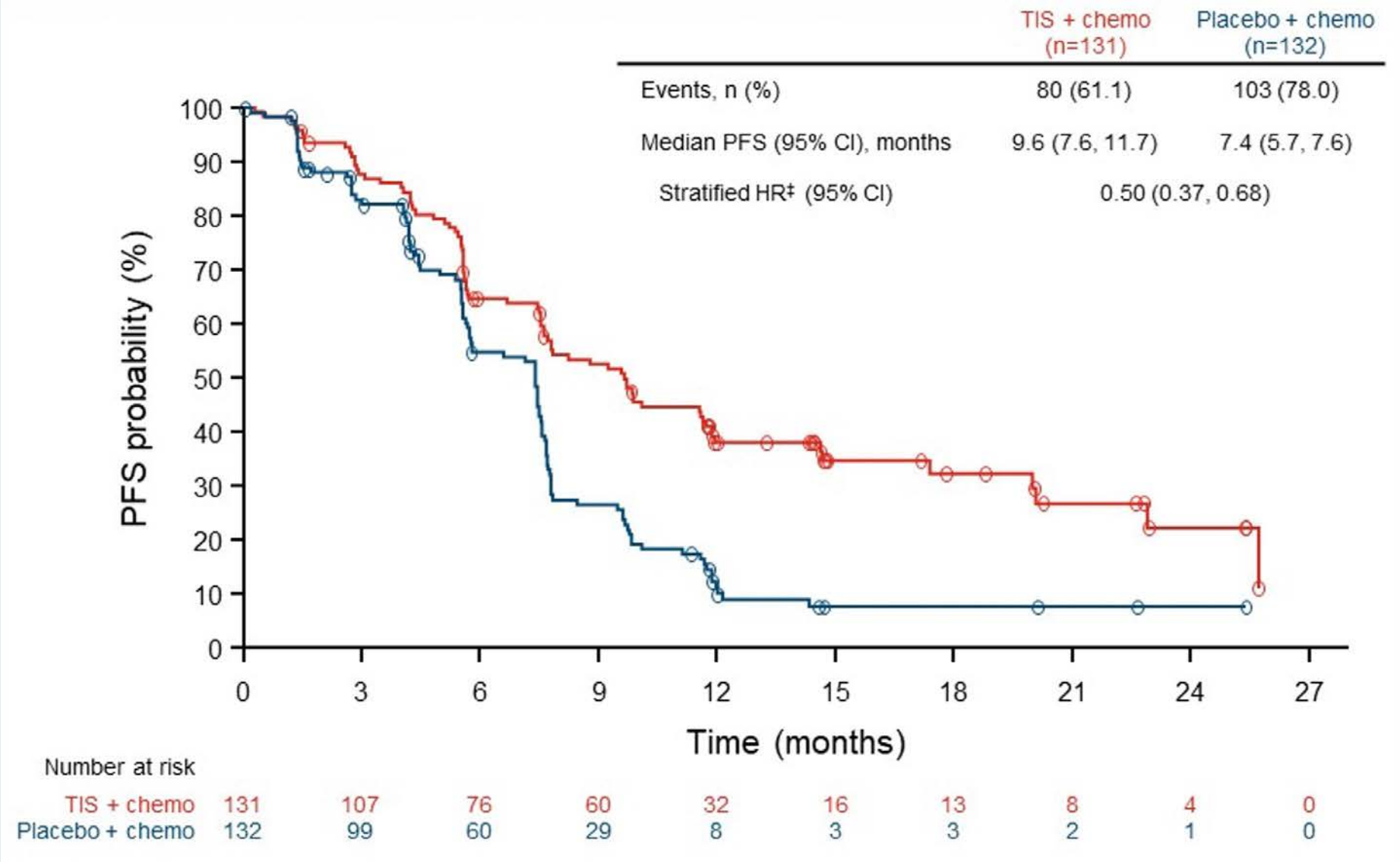
RATIONALE-309 Phase III Study Design



Zhang L et al. ASCO 2022;Presentation 384950.

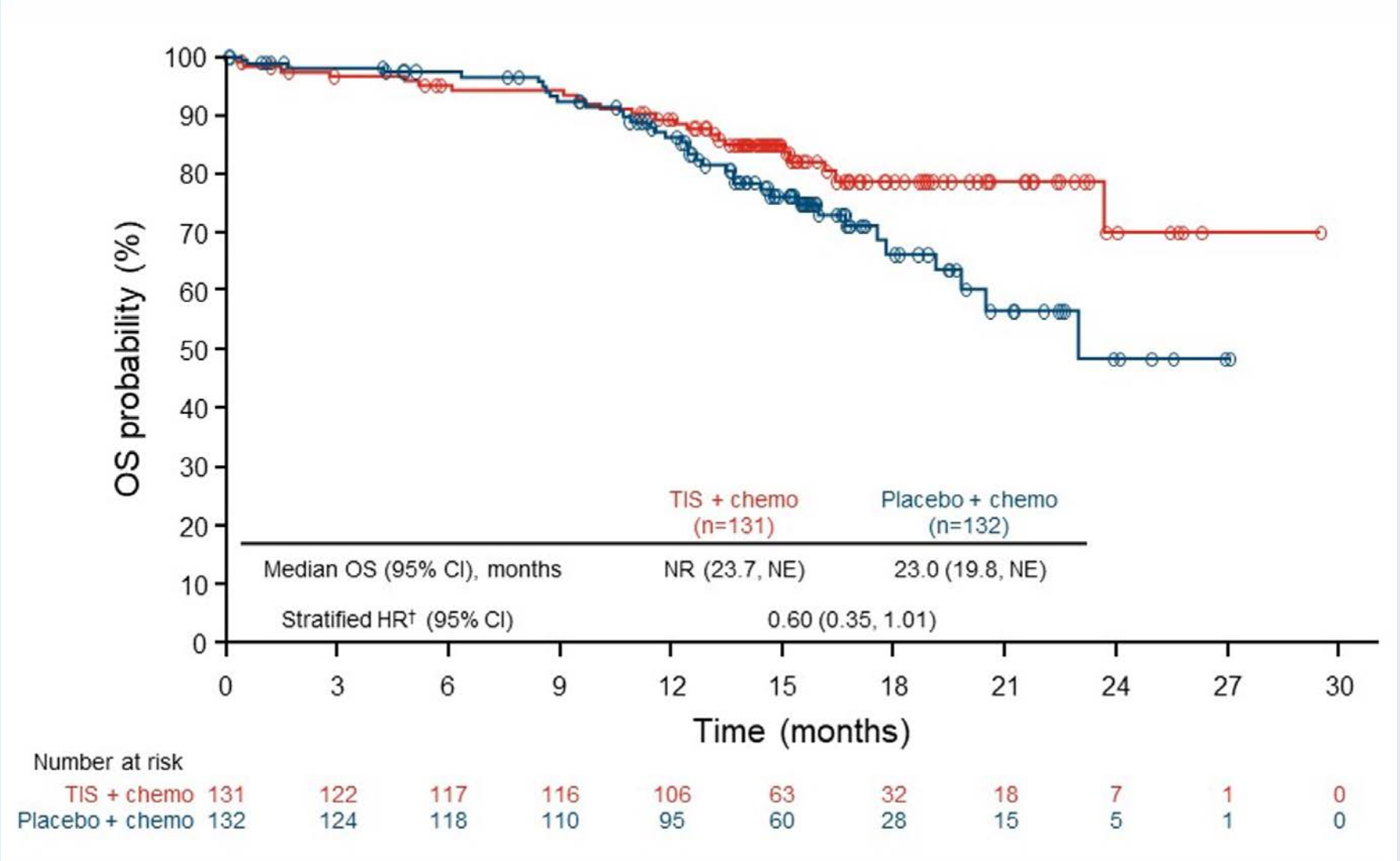
RTP RESEARCH TO PRACTICE

RATIONALE-309: Updated PFS (Median Follow-Up 15.5 Months)



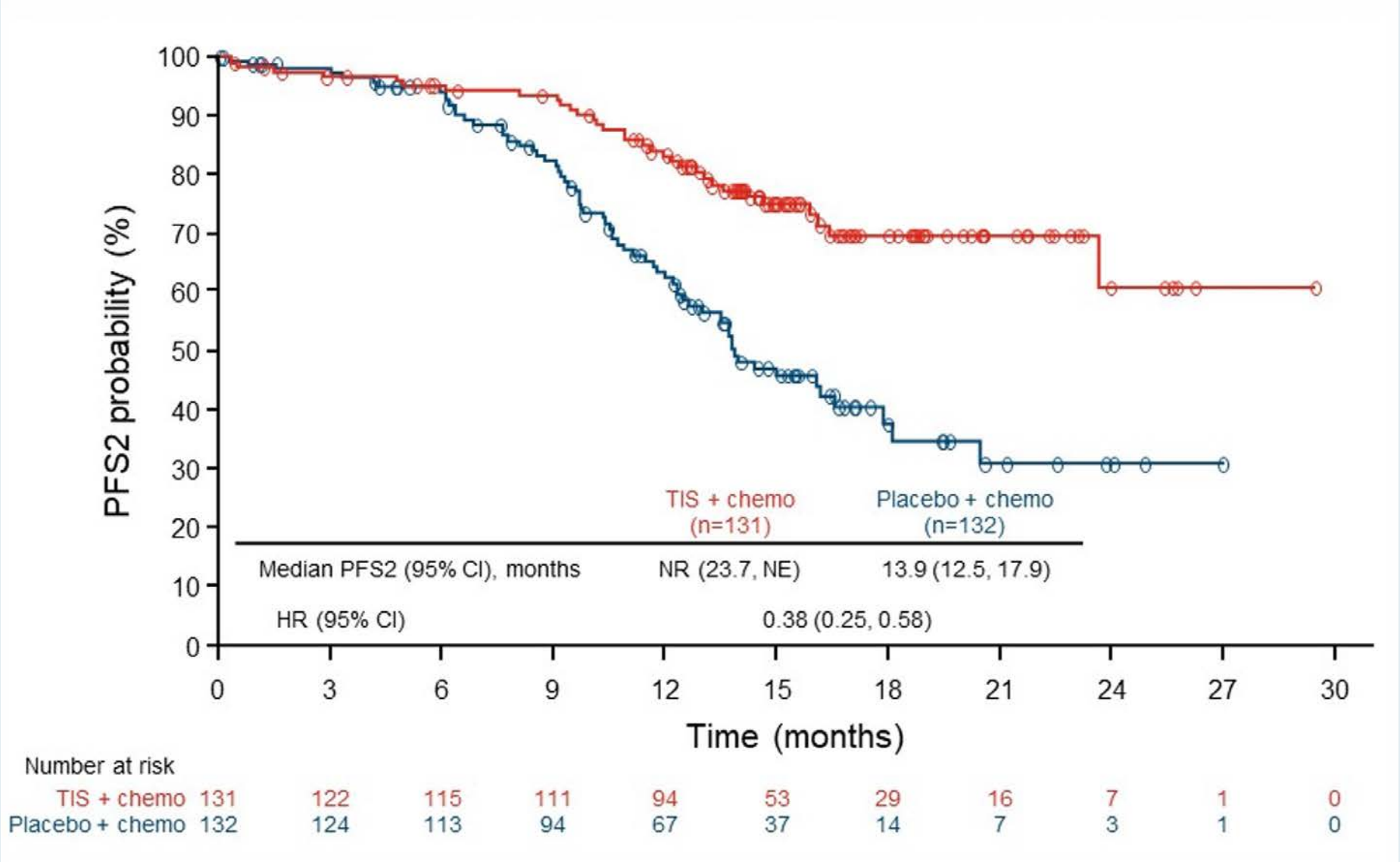
Zhang L et al. ASCO 2022;Presentation 384950.

RATIONALE-309: Updated Overall Survival



Zhang L et al. ASCO 2022;Presentation 384950.

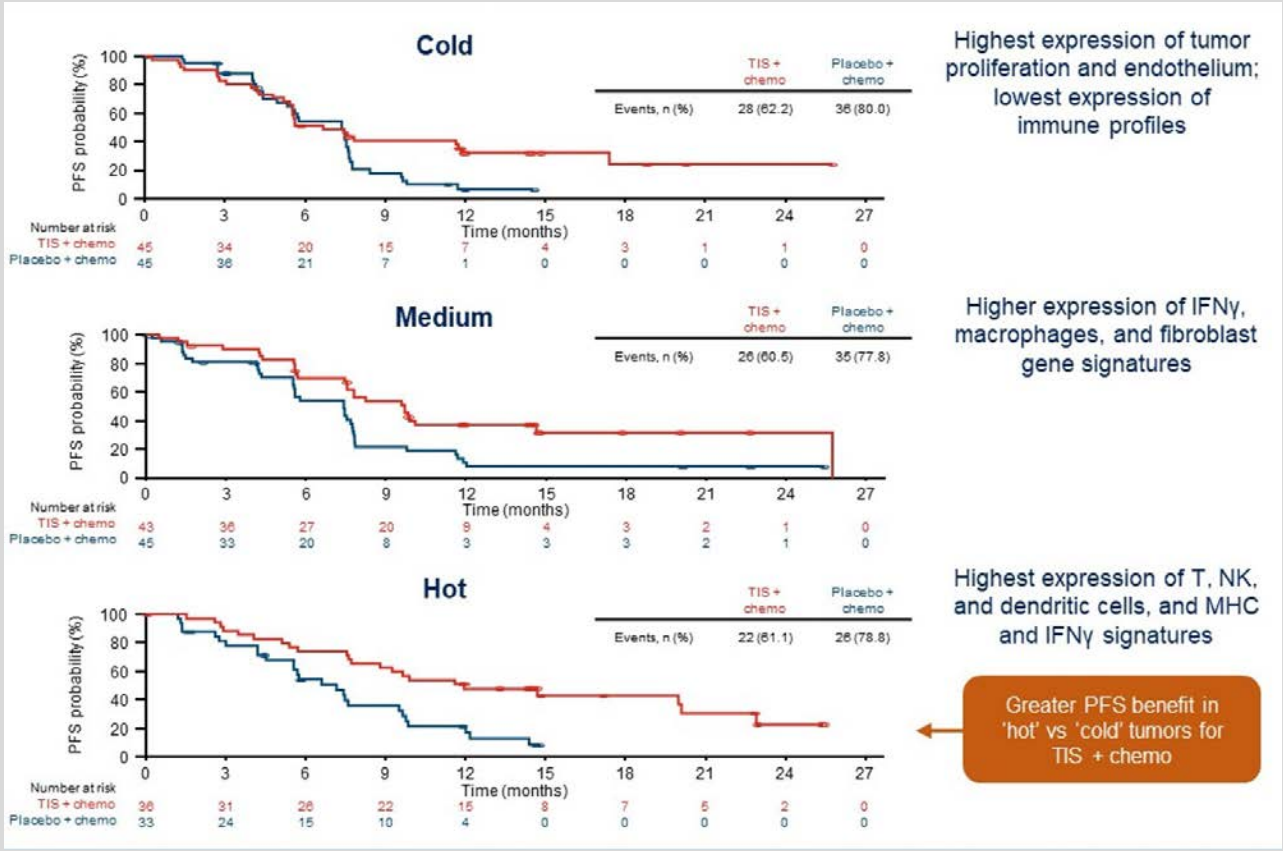
RATIONALE-309: Updated PFS2



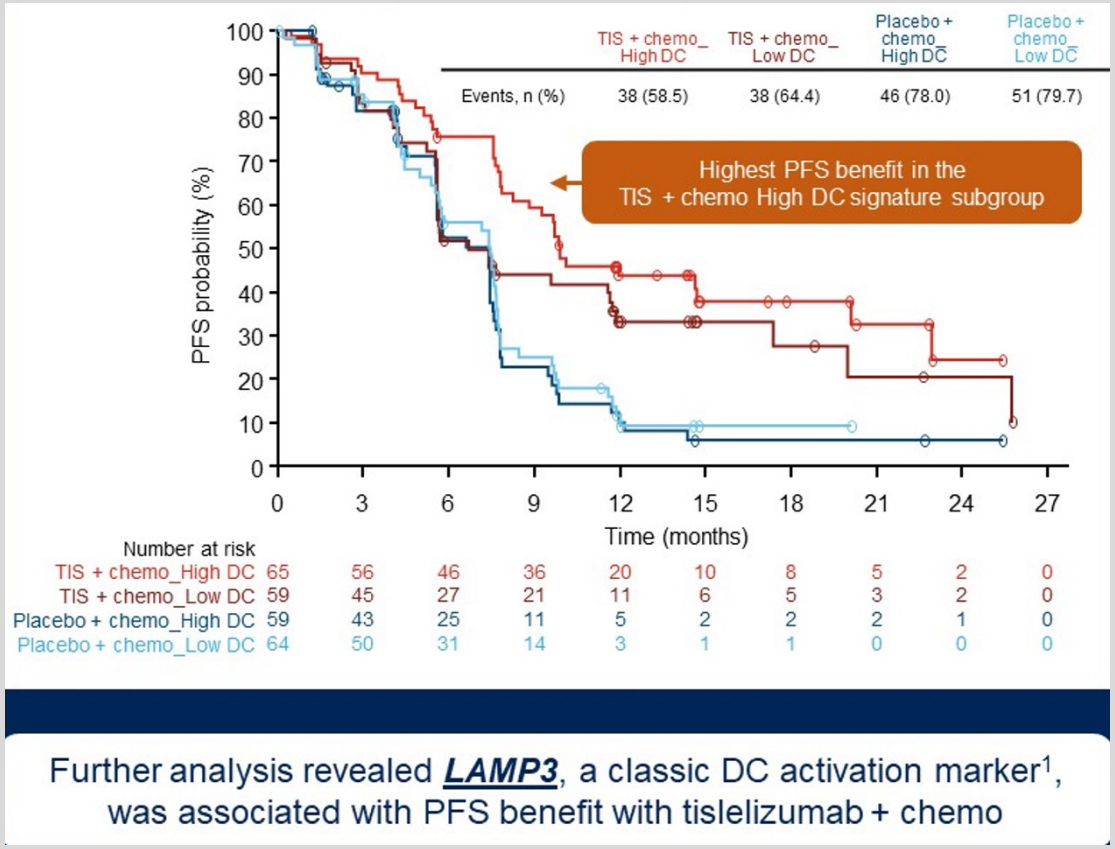
Zhang L et al. ASCO 2022;Presentation 384950.

RATIONALE-309: Gene Expression Profiling Identified 3 Gene Expression Clusters and Activated DC Signature as Potential Biomarkers of Efficacy

PFS by Gene Expression Cluster



PFS by Levels of DC Signature



Further analysis revealed ***LAMP3***, a classic DC activation marker[1], was associated with PFS benefit with tislelizumab + chemo

Zhang L et al. ASCO 2022;Presentation 384950.

RTP RESEARCH TO PRACTICE

Clinical Implications of RATIONALE-309

- RATIONALE-309 met its primary endpoint at the interim analysis
- The results of RATIONALE-309 are consistent with other Phase 3 RCTs in R/M NPC*[1,2]
  - Combined, these three studies provide robust support for the use of a PD-1 inhibitor + chemo for 1L R/M NPC
- This is the first analysis of PFS2 in 1L R/M NPC and the observed PFS2 benefit supports the use of tislelizumab + chemo first in the treatment sequence
- Biomarker analyses identified three unique gene expression clusters representing hot and cold tumors. Further analysis identified an activated DC signature as a potential biomarker for efficacy‡
  - In addition, the DC activation marker *LAMP3*[3] was found to be most associated with tislelizumab + chemo PFS benefit‡
- The safety profile of tislelizumab + chemo was manageable in the interim analysis and consistent with prior reports (presented previously)[4,5]

PFS and OS in Phase 3 RCTs in R/M NPC*

	RATIONALE-309†		JUPITER-02[1]		CAPTAIN-1st[2]	
	TIS + chemo (n=131)	Placebo + chemo (n=132)	Tori + chemo (n=146)	Placebo + chemo (n=143)	Cam + chemo (n=134)	Placebo + chemo (n=129)
PFS events, n (%)	80 (61.1)	103 (78.0)	49 (33.6)	79 (55.2)	78 (58.2)	100 (77.5)
Median PFS (95% CI), months	9.6 (7.6, 11.7)	7.4 (5.7, 7.6)	11.7 (11.0, NE)	8.0 (7.0, 9.5)	10.8 (8.5, 13.6)	6.9 (5.9, 7.9)
HR (95% CI)	0.50 (0.37, 0.68)		0.52 (0.36, 0.74)		0.51 (0.37, 0.69)	
Median OS (95% CI), months	NR (23.7, NE)	23.0 (19.8, NR)	NE (NE, NE)	NE (22.8, NE)	NR	22.6 (19.2, NR)
HR (95% CI)	0.60 (0.35, 1.01)		0.60 (0.36, 1.00)		0.67 (0.41, 1.11)	

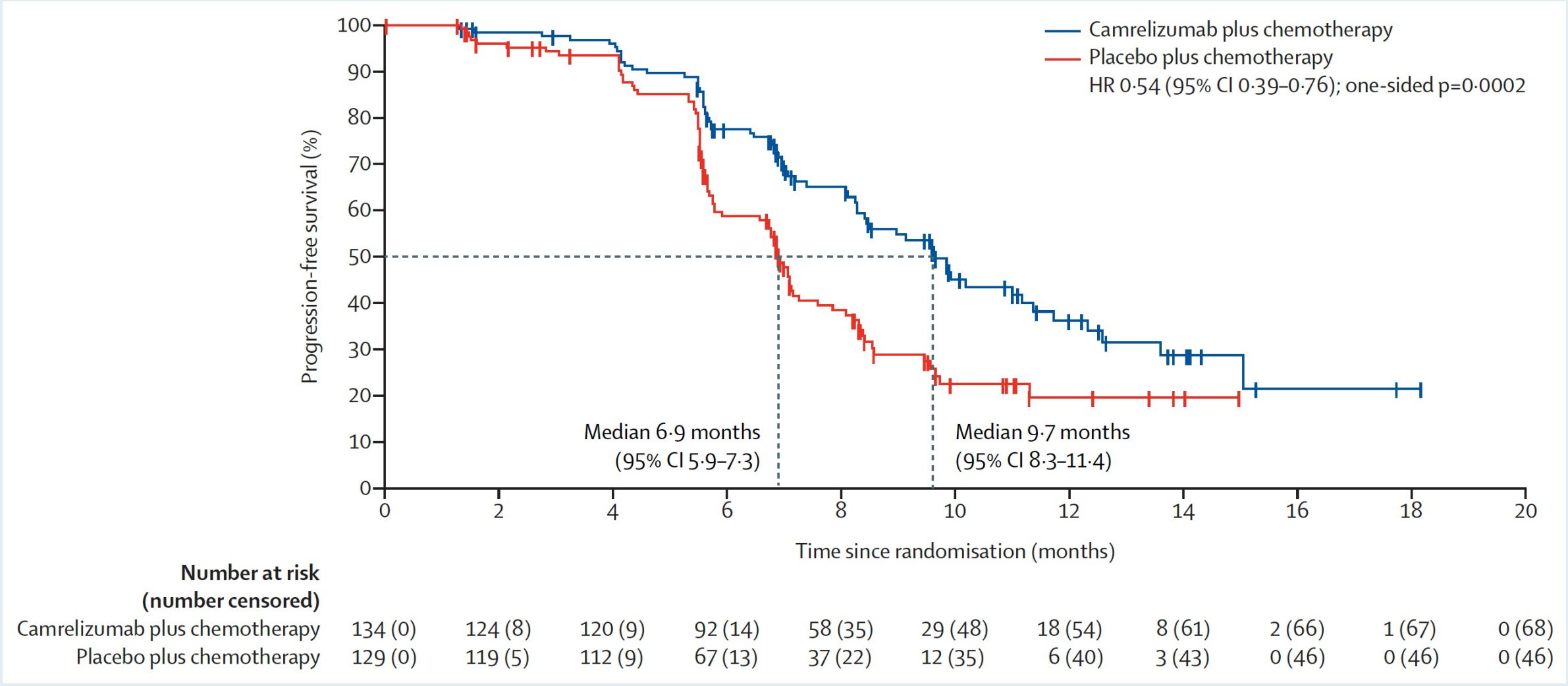
RTP RESEARCH TO PRACTICE

Lancet Oncol 2021August;22(8):1162-74.

Camrelizumab versus placebo in combination with gemcitabine and cisplatin as first-line treatment for recurrent or metastatic nasopharyngeal carcinoma (CAPTAIN-1st): a multicentre, randomised, double-blind, phase 3 trial

Yunpeng Yang, Song Qu*, Jingao Li*, Chaosu Hu*, Mingjun Xu*, Weidong Li*, Ting Zhou*, Liangfang Shen, Hui Wu, Jinyi Lang, Guangyuan Hu, Zhanxiong Luo, Zhichao Fu, Shenhong Qu, Weineng Feng, Xiaozhong Chen, Shaojun Lin, Weimin Zhang, Xiaojiang Li, Yan Sun, Zhixiong Lin, Qin Lin, Feng Lei, Jianting Long, Jinsheng Hong, Xiaoming Huang, Lingzhi Zeng, Peiguo Wang, Xiaohui He, Ben Zhang, Qing Yang, Xiaojing Zhang, Jianjun Zou, Wenfeng Fang†, Li Zhang†*

CAPTAIN-1st Primary Endpoint: Progression-Free Survival



Number at risk (number censored)											
Camrelizumab plus chemotherapy	134 (0)	124 (8)	120 (9)	92 (14)	58 (35)	29 (48)	18 (54)	8 (61)	2 (66)	1 (67)	0 (68)
Placebo plus chemotherapy	129 (0)	119 (5)	112 (9)	67 (13)	37 (22)	12 (35)	6 (40)	3 (43)	0 (46)	0 (46)	0 (46)

Yang Y et al. *Lancet Oncol* 2021;22(8):1162-74.

CAPTAIN-1st: Tumor Response per Independent Review Committee

	Camrelizumab plus gemcitabine and cisplatin (n=134)	Placebo plus gemcitabine and cisplatin (n=129)
Best overall response		
Complete response	7 (5%)	4 (3%)
Partial response	110 (82%)	100 (78%)
Stable disease	12 (9%)	18 (14%)
Progressive disease	2 (1%)	4 (3%)
Not assessable	3 (2%)	3 (2%)
Objective response	87·3% (80·5–92·4)	80·6% (72·7–87·1)
Disease control rate	96·3% (91·5–98·8)	94·6% (89·1–97·8)
Duration of response, months	8·5 (6·9–11·1)	5·6 (5·2–6·9)

Data are n (%), % (95% CI), or median (95% CI).

Yang Y et al. *Lancet Oncol* 2021;22(8):1162-74.

RTP RESEARCH TO PRACTICE

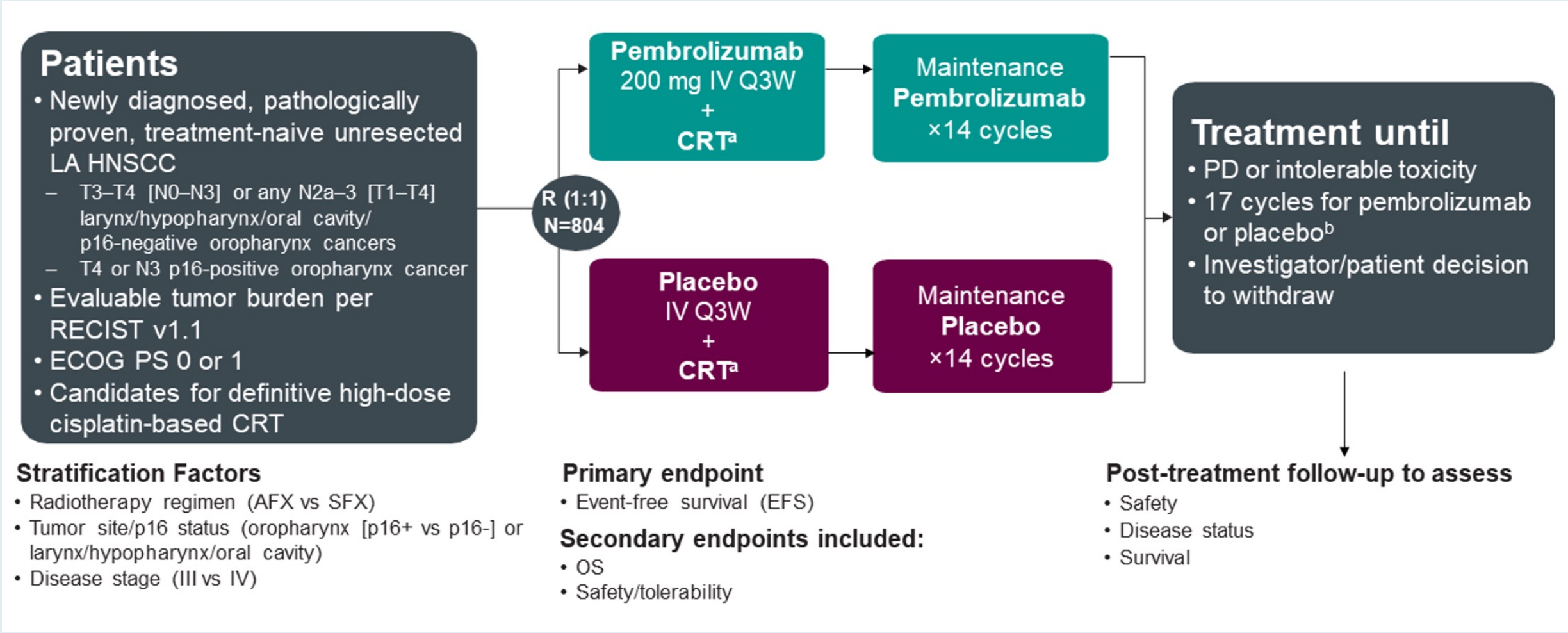
ESMO 2022;Abstract LBA5.

Primary Results of the Phase 3 KEYNOTE-412 Study: Pembrolizumab Plus Chemoradiation Therapy (CRT) vs Placebo Plus CRT for Locally Advanced Head and Neck Squamous Cell Carcinoma

Jean-Pascal Machiels[1], Yungan Tao[2], Barbara Burtness[3], Makoto Tahara[4], Danny Rischin[5], Gustavo V. Alves[6], Iane Pinto Figueiredo Lima[7], Brett G.M. Hughes[8], Yoann Pointreau[9], Sercan Aksoy[10], Simon Laban[11], Richard Greil[12], Martin Burian[13], Marcin Hetnal[14], Lisa Licitra[15], Ramona Swaby[16], Yayan Zhang[17], Burak Gumuscu[17], Behzad Bidadi[17], Lillian L. Siu[18]

[1]Cliniques universitaires Saint-Luc and Institut de Recherche Clinique et Expérimentale (Pole MIRO), UCLouvain, Brussels, Belgium; [2]Institut Gustave Roussy, Villejuif, France; [3]Yale University School of Medicine and Yale Cancer Center, New Haven, CT, USA; [4]National Cancer Center Hospital East, Kashiwa, Japan; [5]Peter MacCallum Cancer Centre and the University of Melbourne, Melbourne, Australia; [6]Centro Integrado de Pesquisa em Oncologia, Hospital Nossa Senhora da Conceição, Porto Alegre, Brazil; [7]CRIO Centro Regional Integrado de Oncologia, Fortaleza-CE, Brazil; [8]Royal Brisbane and Women's Hospital and University of Queensland, Brisbane, Queensland, Australia; [9]Centre Jean Bernard, Le Mans, France; [10]Hacettepe University, Cancer Institute, Ankara, Turkey; [11]Ulm University Medical Center, Head & Neck Cancer Center of the Comprehensive Cancer Center Ulm, Department of Otorhinolaryngology, Head & Neck Surgery, Ulm, Germany; [12]Paracelsus Medical University, Salzburg Cancer Research Institute, and Cancer Cluster Salzburg, Salzburg, Austria; [13]Krankenhaus der Barmherzigen Schwestern Linz, Linz, Austria; [14]Andrzej Frycz Modrzewski Krakow University, Amethyst Radiotherapy Centre, Rydygier Hospital, Krakow, Poland; [15]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; University of Milan, Milan, Italy.; [16]Merck & Co., Inc., Rahway, NJ, USA (currently at Carisma Therapeutics, Philadelphia, PA, USA); [17]Merck & Co., Inc., Rahway, NJ, USA; [18]Princess Margaret Cancer Centre, University of Toronto, Toronto, Canada.

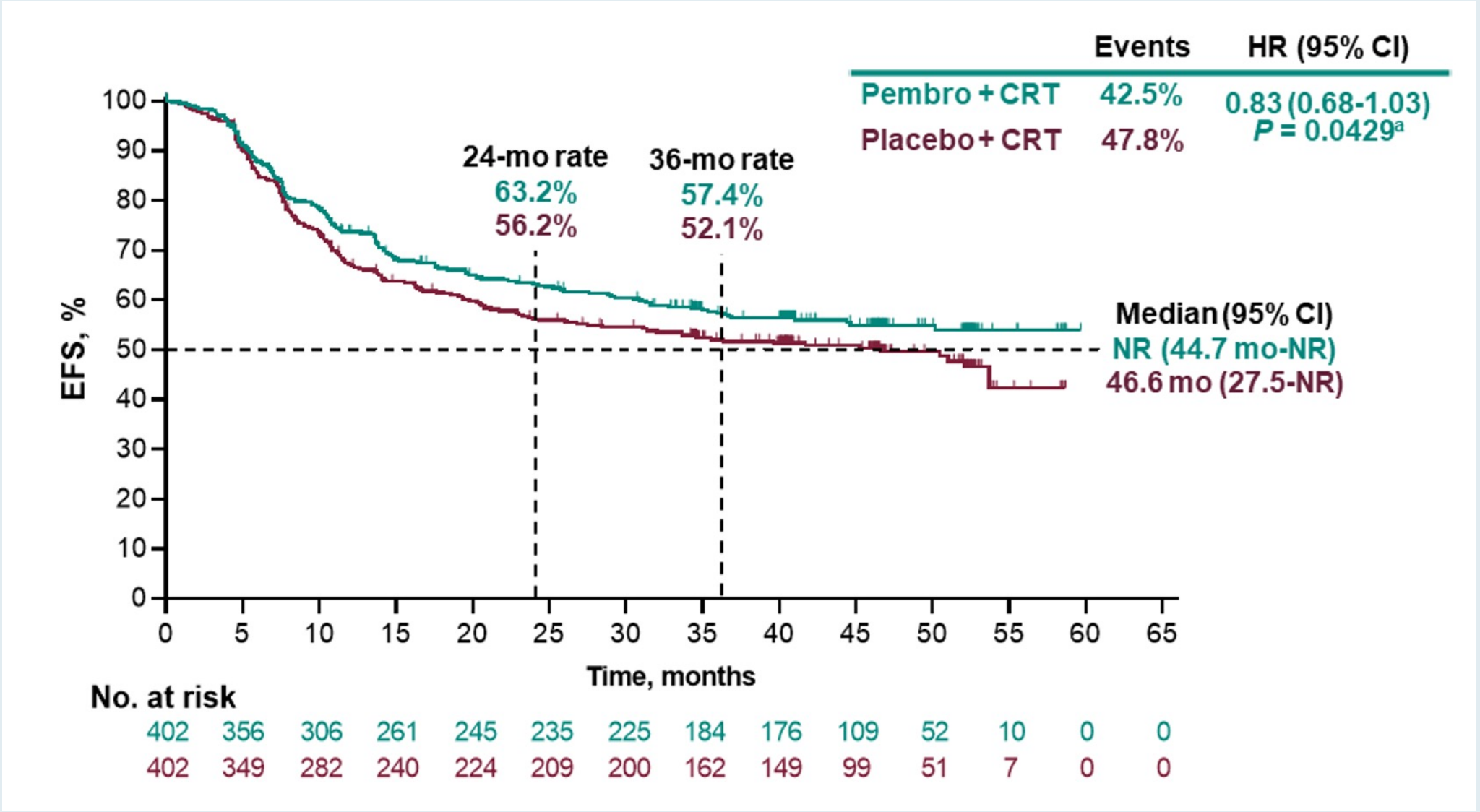
KEYNOTE-412 Phase III Study Design



LA HNSCC = locally advanced head and neck squamous cell carcinoma

Machiels JP et al. ESMO 2022;Abstract LBA5.

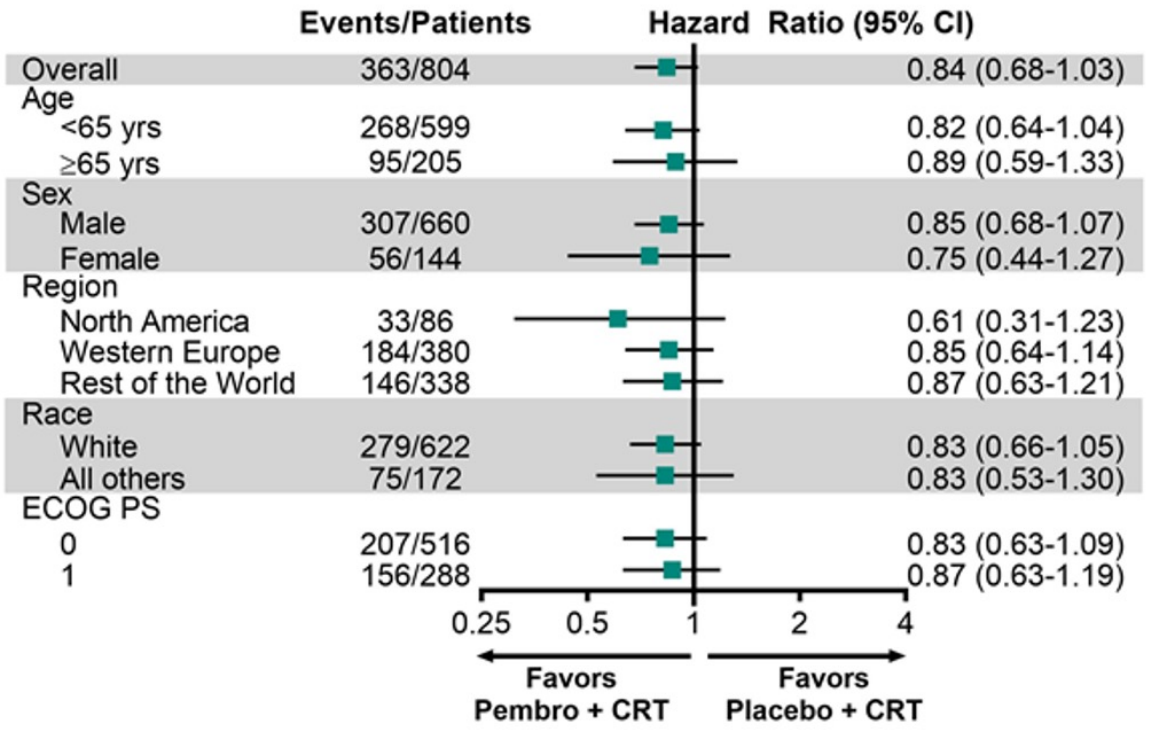
KEYNOTE-412: Event-Free Survival (EFS; ITT Population)

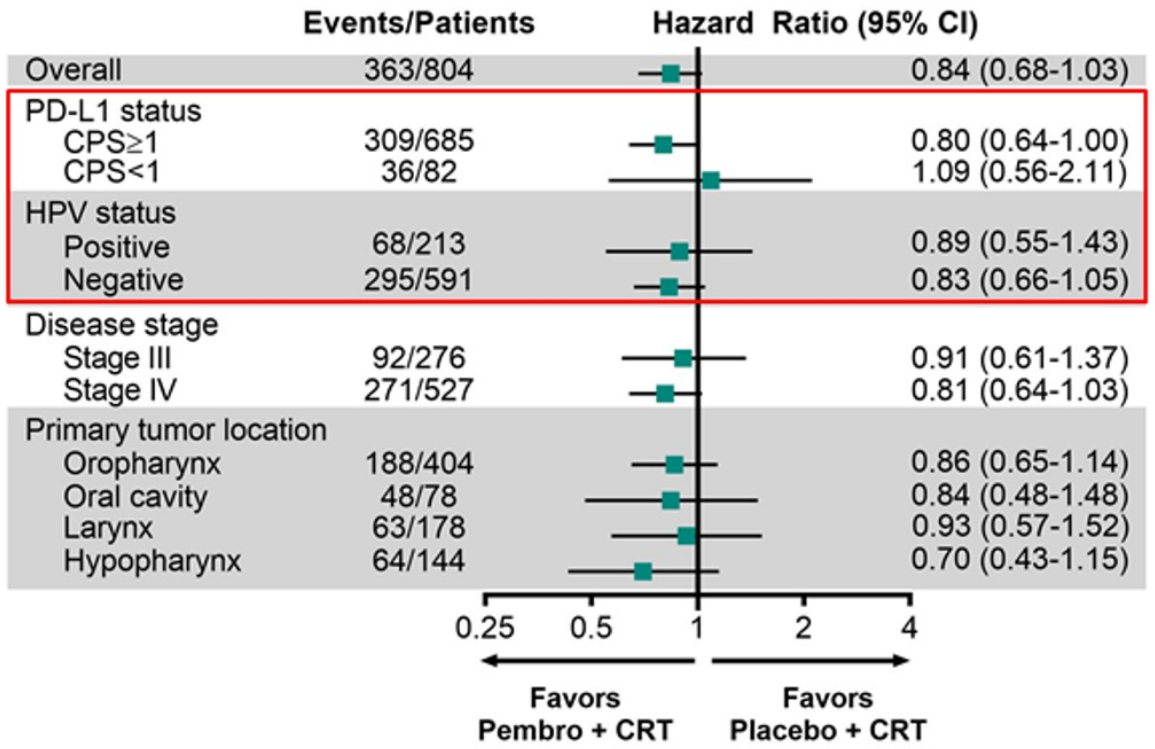


Machiels JP et al. ESMO 2022;Abstract LBA5.

RTP RESEARCH TO PRACTICE

KEYNOTE-412: EFS in Prespecified Subgroups (ITT)

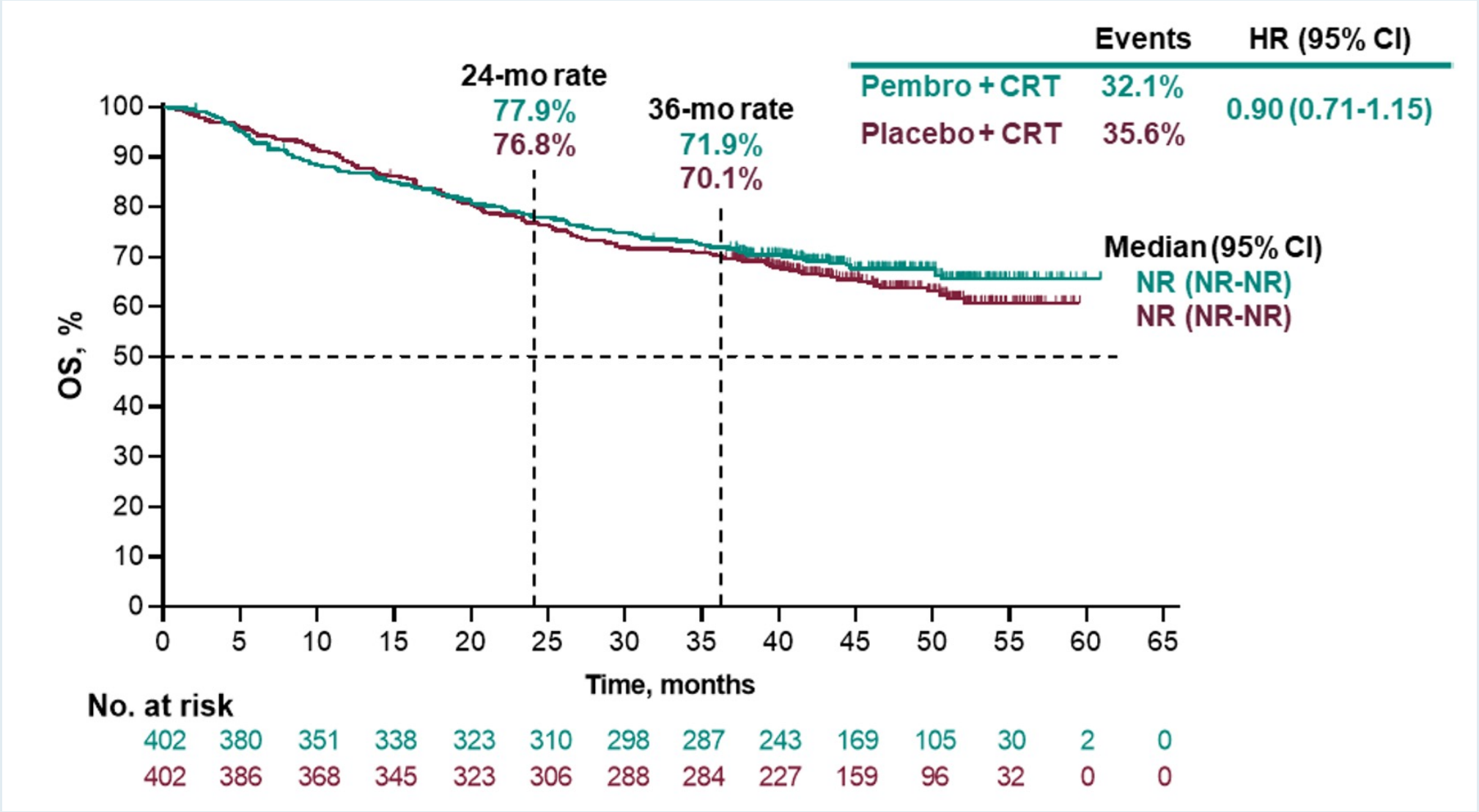




Machiels JP et al. ESMO 2022;Abstract LBA5.

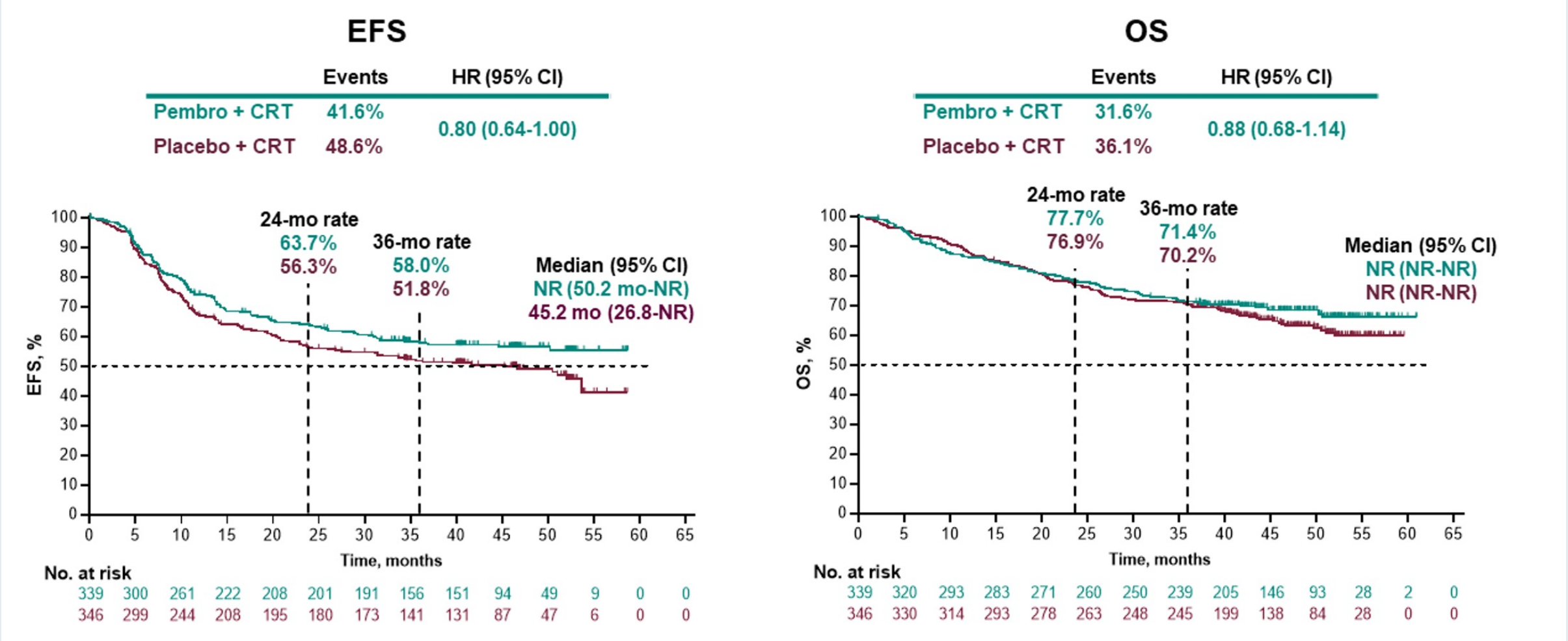
RTP RESEARCH TO PRACTICE

KEYNOTE-412: Overall Survival (ITT)



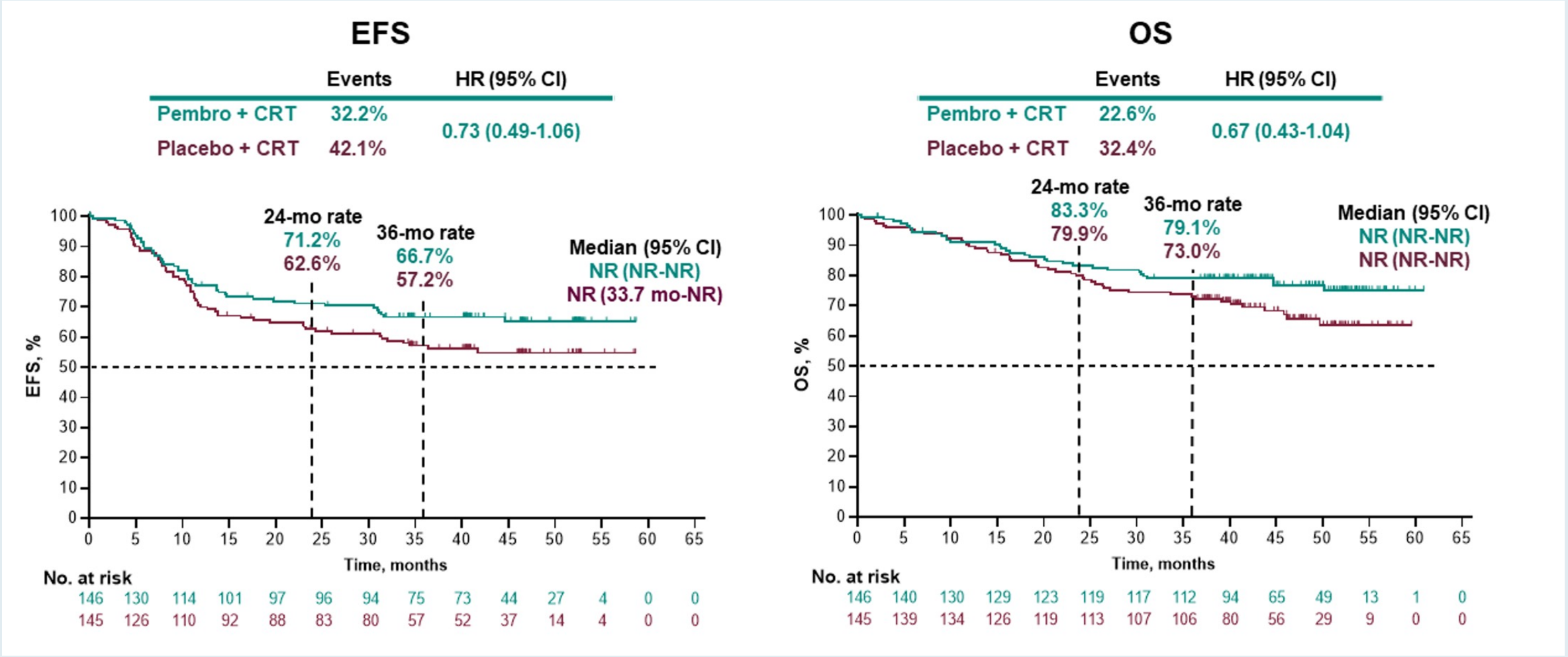
Machiels JP et al. ESMO 2022;Abstract LBA5.

KEYNOTE-412: EFS and OS in Patients with PD-L1 CPS ≥1 (Prespecified Subgroup Analysis)



Machiels JP et al. ESMO 2022;Abstract LBA5.

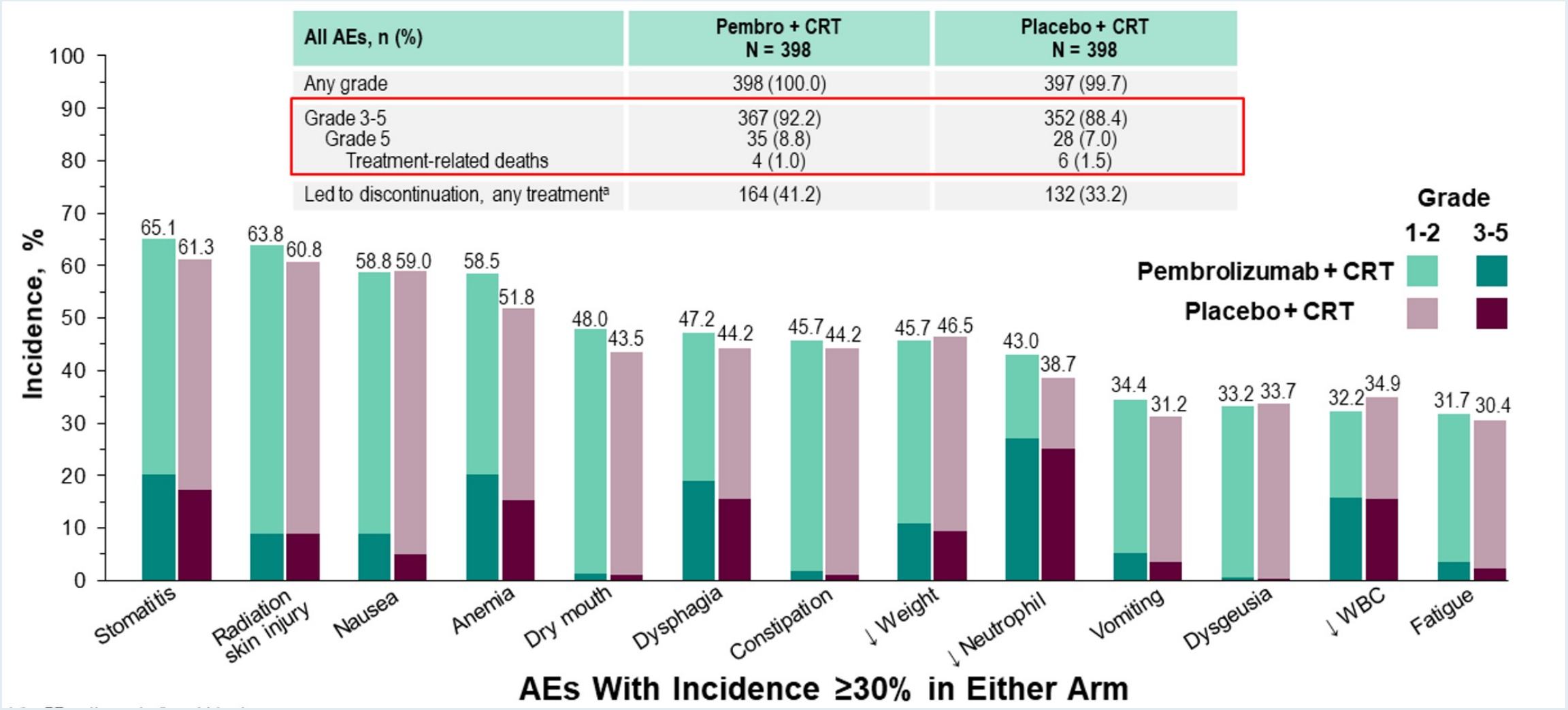
KEYNOTE-412: EFS and OS in Patients with PD-L1 CPS ≥20 (Post Hoc Analysis)



Machiels JP et al. ESMO 2022;Abstract LBA5.

KEYNOTE-412: All-Cause Adverse Events (AEs) Across Both Treatment Phases, as Treated

All AEs, n (%)	Pembro + CRT N = 398	Placebo + CRT N = 398
Any grade	398 (100.0)	397 (99.7)
Grade 3-5	367 (92.2)	352 (88.4)
Grade 5	35 (8.8)	28 (7.0)
Treatment-related deaths	4 (1.0)	6 (1.5)
Led to discontinuation, any treatment[a]	164 (41.2)	132 (33.2)

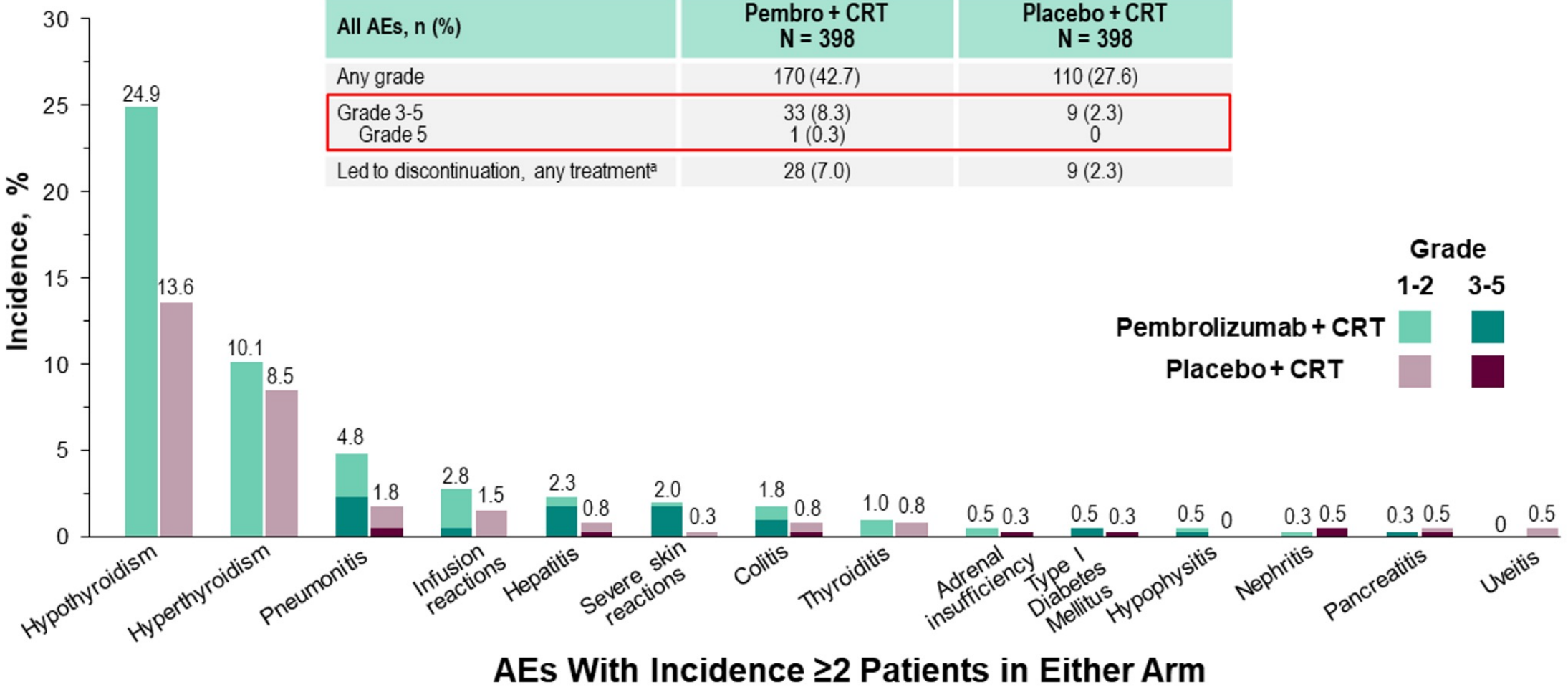


Machiels JP et al. ESMO 2022;Abstract LBA5.

RTP RESEARCH TO PRACTICE

KEYNOTE-412: Immune-Mediated AEs and Infusion Reactions, as Treated

All AEs, n (%)	Pembro + CRT N = 398	Placebo + CRT N = 398
Any grade	170 (42.7)	110 (27.6)
Grade 3-5	33 (8.3)	9 (2.3)
Grade 5	1 (0.3)	0
Led to discontinuation, any treatment[a]	28 (7.0)	9 (2.3)



AEs With Incidence ≥2 Patients in Either Arm

Machiels JP et al. ESMO 2022;Abstract LBA5.

KEYNOTE-412: Summary and Conclusions

- Pembrolizumab plus CRT was associated with a favorable trend toward improved EFS vs placebo plus CRT in patients with LA HNSCC (HR, 0.83; *P* = 0.0429)
  - The difference did not reach statistical significance (superiority threshold, one-sided *P* = 0.0242)
  - 24-mo EFS rate: 63.2% vs 56.2%
- PD-L1 expression may be an informative predictive biomarker
  - CPS ≥1: 24-mo EFS rate, 63.7% vs 56.3%; 36-mo OS rate, 71.4% vs 70.2%
  - CPS ≥20: 24-mo EFS rate, 71.2% vs 62.6%; 36-mo OS rate, 79.1% vs 73.0% (post hoc analysis)
- No new safety signals with the combination of pembrolizumab plus CRT
- LA HNSCC remains a challenging disease to treat

Machiels JP et al. ESMO 2022;Abstract LBA5.

Incorporation of Targeted Therapy for Advanced Head and Neck Cancer

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TO PRACTICE

Frequent Genomic Alterations Across Different Subtypes of Salivary Gland Cancers

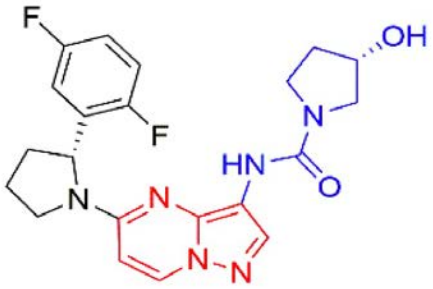
Subtype	Frequent genomic alterations Gene (%)	Overexpression on IHC Protein (%)
Adenoid cystic carcinoma	*MYB-NFIB/MYBL1-NFIB/5'-NFIB* (65-88), *NOTCH1* (11-29)	c-KIT (65-90), NICD (49-98), EGFR (24-85), VEGF (76)
Mucoepidermoid carcinoma	*CRTC1-MAML2/CTRC3-MAML2* (38-82), *PIK3CA* (20), *BRCA2* (17), *ERBB2* (13)	EGFR (46-100), HER2 (0-38)
Salivary duct carcinoma	*ERBB2* (32), *PIK3CA* (18-27), *HRAS* (16-23)	AR (78-96), HER2 (16-83), EGFR (53)
Mammary analogue secretory carcinoma	*ETV6-NTRK3* (95-98), *ETV6-nonNTRK3* (2-5)	NA
Acinic cell carcinoma	*HTN3-MSANTD3* (4-16)	NA
Polymorphous adenocarcinoma	*PRKD1/2/3* (50-80), *FGFR1* (20)	NA
Adenocarcinoma NOS	*PIK3CA* (20-24), *ERBB2* (17), *CDKN2A/B* (12-17), *HRAS* (14)	NA
Carcinoma ex pleomorphic adenoma	*FGFR1-PLAG* (9-86), *HMGA2* (29)	NA
Epithelial-myoepithelial carcinoma	*HRAS* (33), *KRAS* (18), *MYB* (18)	FGFR1 (86), c-KIT (69-83),
Myoepithelial carcinoma	*EWSR1* (39), *PIK3CA* (15)	NA
Intraductal carcinoma	*RET* (47)	NA
Poorly differentiated carcinoma	*PIK3CA* (20), *ERBB2* (15)	NA

Brose MS. ASCO 2022 Education Session.

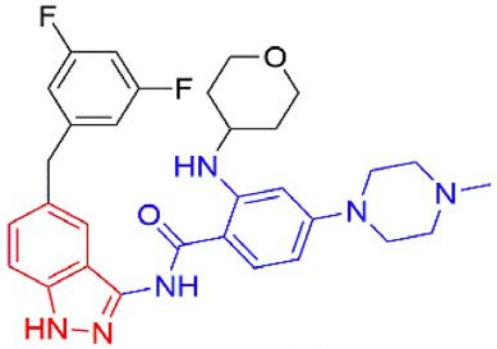
RTP RESEARCH TO PRACTICE

FDA Approved and Investigational TRK Inhibitors for Patients with Solid Tumors with NTRK Gene Fusions

FDA-approved first-generation NTRK gene fusion inhibitors

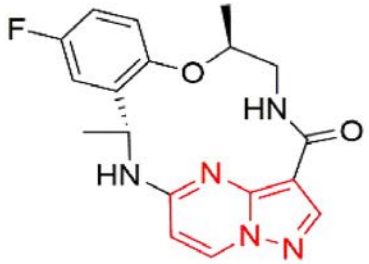


Larotrectinib
MW 428.44

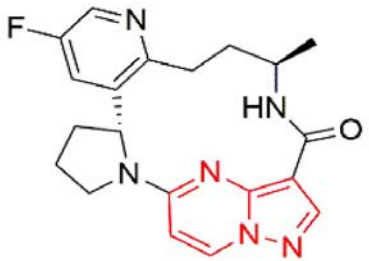


Entrectinib
MW 560.65

Second-generation investigational NTRK gene fusion inhibitors



Repotrectinib
MW 355.37



Selitrectinib
MW 380.43

Larotrectinib: FDA approval 11/26/2018

- Based on LOXO-TRK-14001, SCOUT and NAVIGATE

Entrectinib: FDA approval 8/15/2019

- Based on ALKA, STARTRK-1 and STARTRK-2

Repotrectinib* and selitrectinib

- Next-generation TRK tyrosine kinase inhibitors with a compact macrocyclic structure that binds completely inside the ATP binding pocket even in the presence of mutations

* Breakthrough therapy designation: 10/6/2021

Besse B et al. AACR-NCI-EORTIC Virtual International Conference 2021;Abstract LB6546.
Larotrectinib PI, rev 3/2021; Entrectinib PI, rev 7/2022; https://www.tptherapeutics.com/news-releases/news-release-details/turning-point-therapeutics-granted-breakthrough-therapy

TRK Inhibitor Activity in Solid Tumors with NTRK Gene Fusions – Data from the Registrational Studies

	Larotrectinib (LOXO-TRK-14001, SCOUT, NAVIGATE) (N = 244)	Entrectinib (ALKA, STARTRK-1, STARTRK-2) (N = 150)
Median age	38	58.5
NTRK fusion NTRK1 NTRK2 NTRK3	 46% 3% 51%	Not reported
Prior lines of systemic therapy 0 1 ≥2	 27% 28% 44%	 34% 29% 37%
ORR (CR)	69% (21%)	61% (17%)
Median DoR	33 mo	20 mo
Median PFS	29 mo	14 mo
Median OS	Not reached	37 mo

Drilon A et al. ASCO 2022;Abstract 3100. Krzakowski M et al. ASCO 2022;Abstract 3099.

Oncologist 2022 May 10;[Online ahead of print].

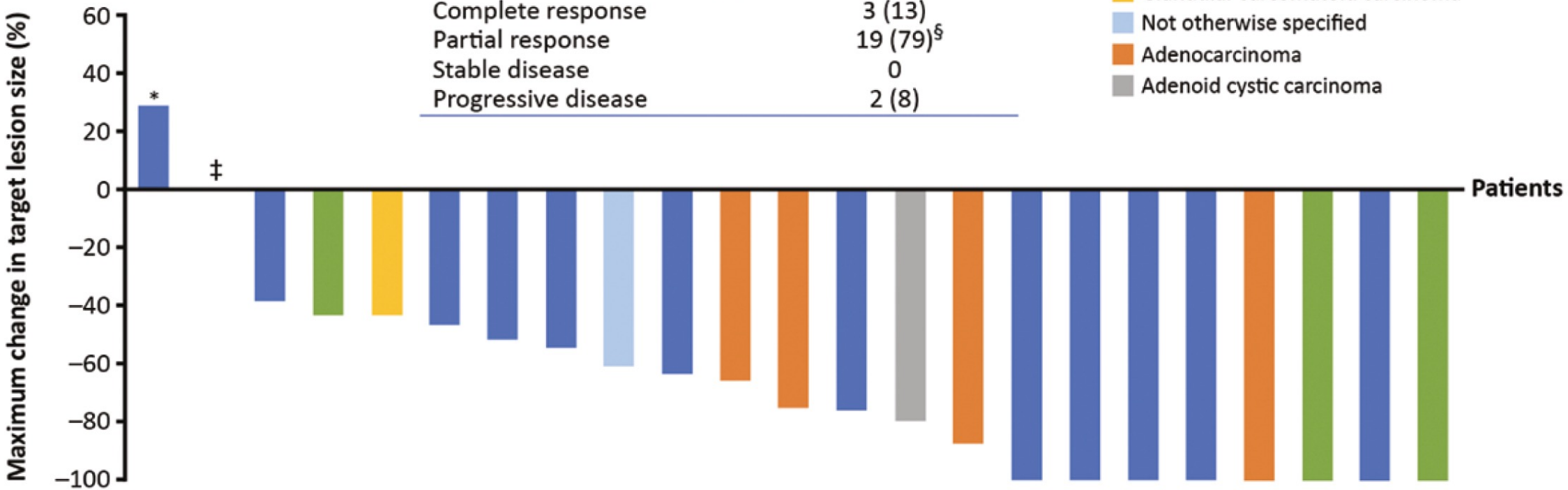
Original Article

Larotrectinib Treatment for Patients With TRK Fusion-Positive Salivary Gland Cancers

Xiuning Le[1,*], Christina Baik[2], Jessica Bauman[3], Jill Gilbert[4], Marcia S. Brose[5], Juneko E. Grilley-Olson[6], Tejas Patil[7], Ray McDermott[8,9], Luis E. Raez[10], Jennifer M. Johnson[5], Lin Shen[11], Makoto Tahara[12], Alan L. Ho[13,14], Ricarda Norenberg[15], Laura Dima[16], Nicoletta Brega[17], Alexander Drilon[13,14], David S. Hong[1]

Maximum Change in Target Lesion Size and Response After Treatment with Larotrectinib

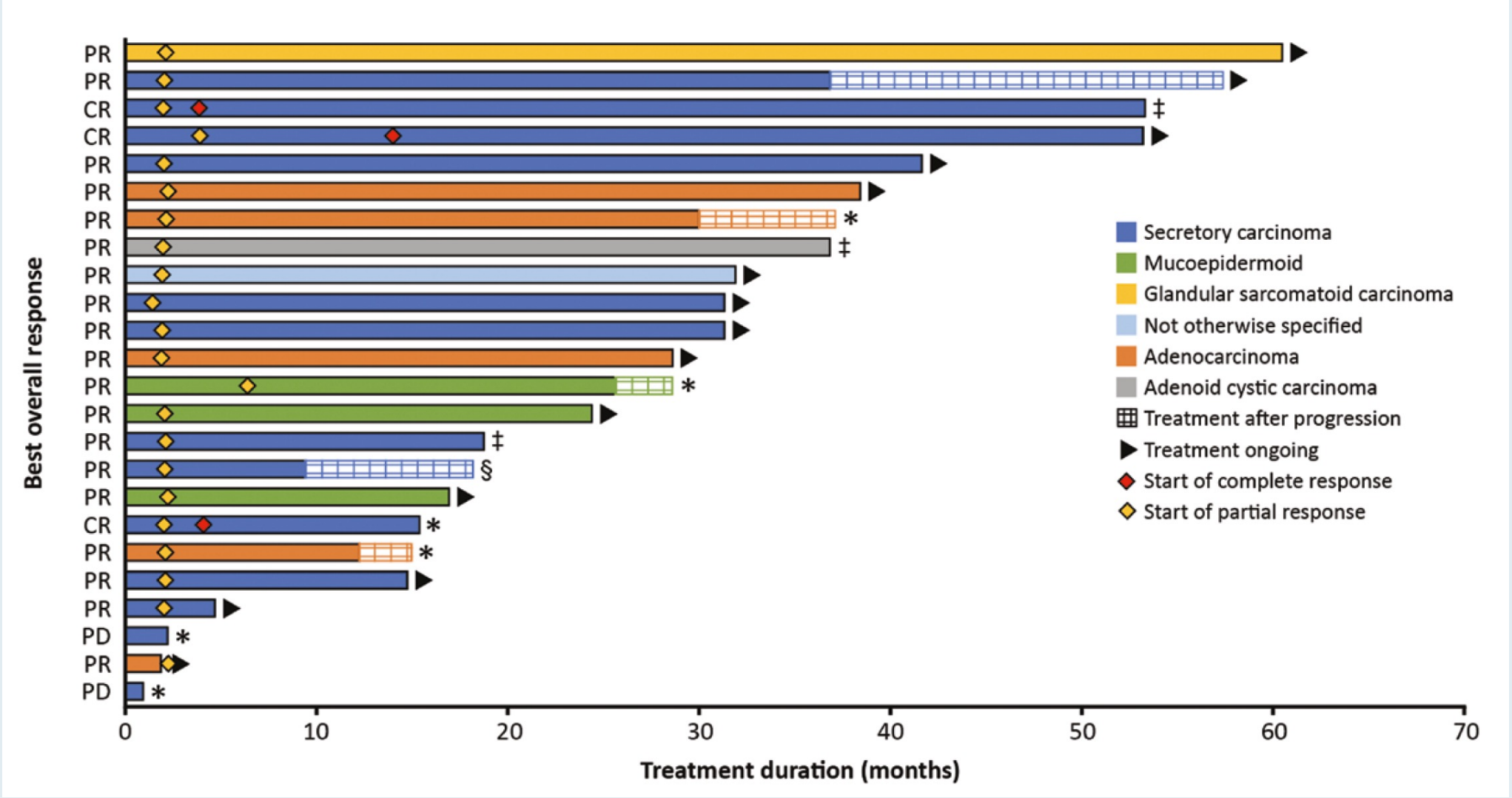
	N = 24
ORR, % (95% CI)	92 (73–99)
Best overall response, *n* (%)	
Complete response	3 (13)
Partial response	19 (79)[§]
Stable disease	0
Progressive disease	2 (8)



Le X et al. *Oncologist* 2022 May 10;[Online ahead of print].

RTP RESEARCH TO PRACTICE

Treatment Duration with Larotectinib for Patients with Salivary Gland Cancer with NTRK Fusions



Le X et al. *Oncologist* 2022 May 10;[Online ahead of print].

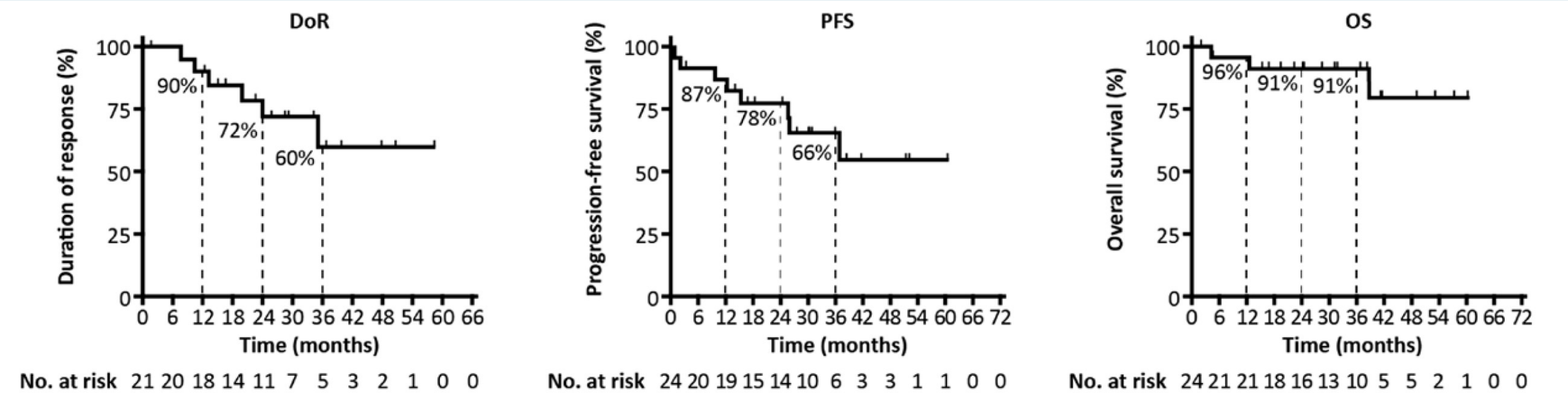
RTP RESEARCH TO PRACTICE

Larotrectinib Treatment-Related Adverse Events (TRAEs) in ≥20% of Patients

TRAE	Any grade	Grade ≥3
ALT increased	42%	13%
Dizziness	38%	4%
Constipation	25%	0
AST increased	38%	8%
Fatigue	33%	0
Myalgia	21%	0
Nausea	25%	0

Le X et al. *Oncologist* 2022 May 10;[Online ahead of print].

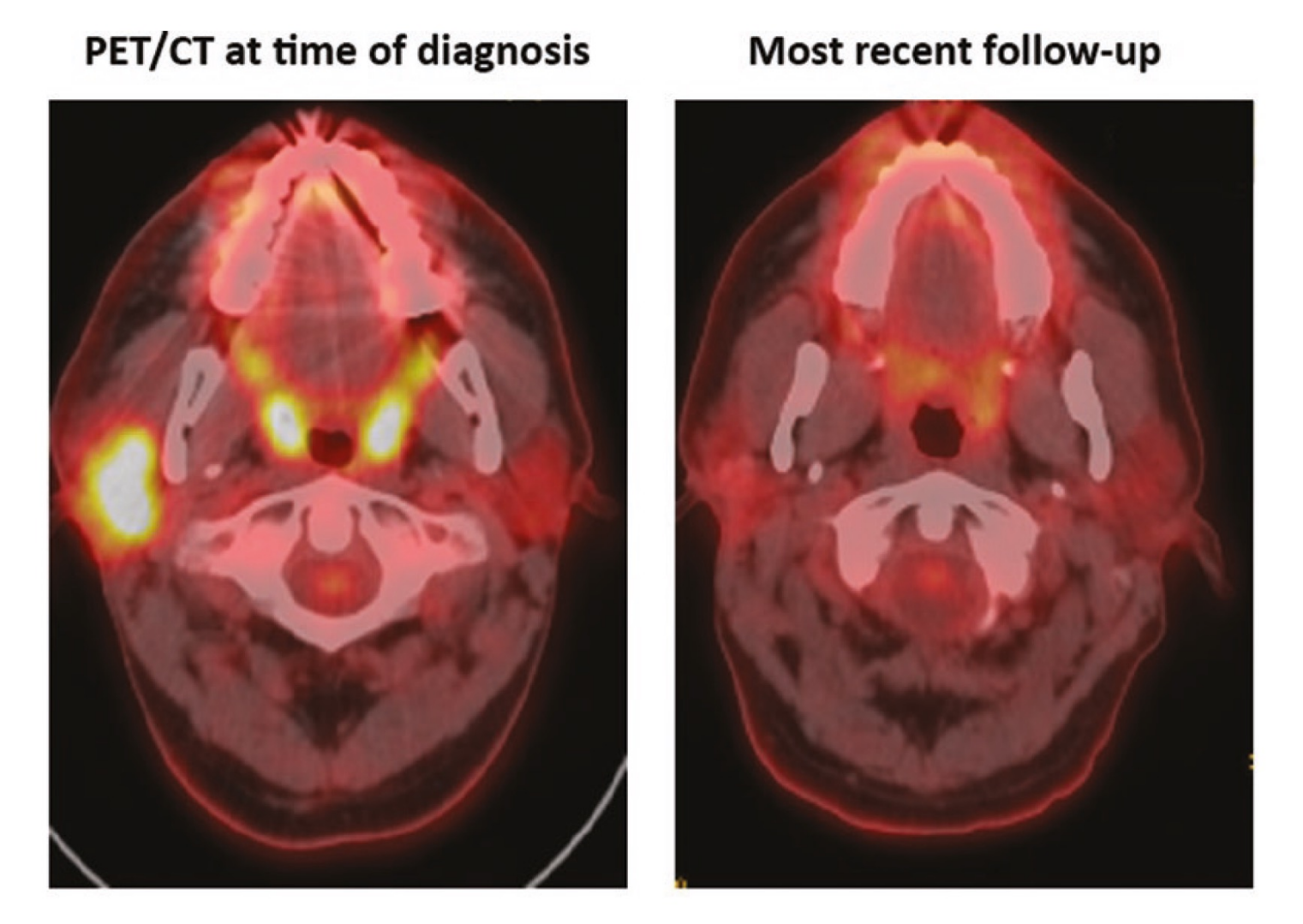
Duration of Response, PFS and OS with Larotrectinib



Le X et al. *Oncologist* 2022 May 10;[Online ahead of print].

RTP RESEARCH TO PRACTICE

Response to Larotrectinib in a Patient with Secretory Carcinoma of the Salivary Gland with ETV6-NTRK3 Fusion



Le X et al. *Oncologist* 2022 May 10;[Online ahead of print].

RTP RESEARCH TO PRACTICE

Lancet Oncol 2020;21(2):271-82.

Entrectinib in patients with advanced or metastatic *NTRK* fusion-positive solid tumours: integrated analysis of three phase 1–2 trials

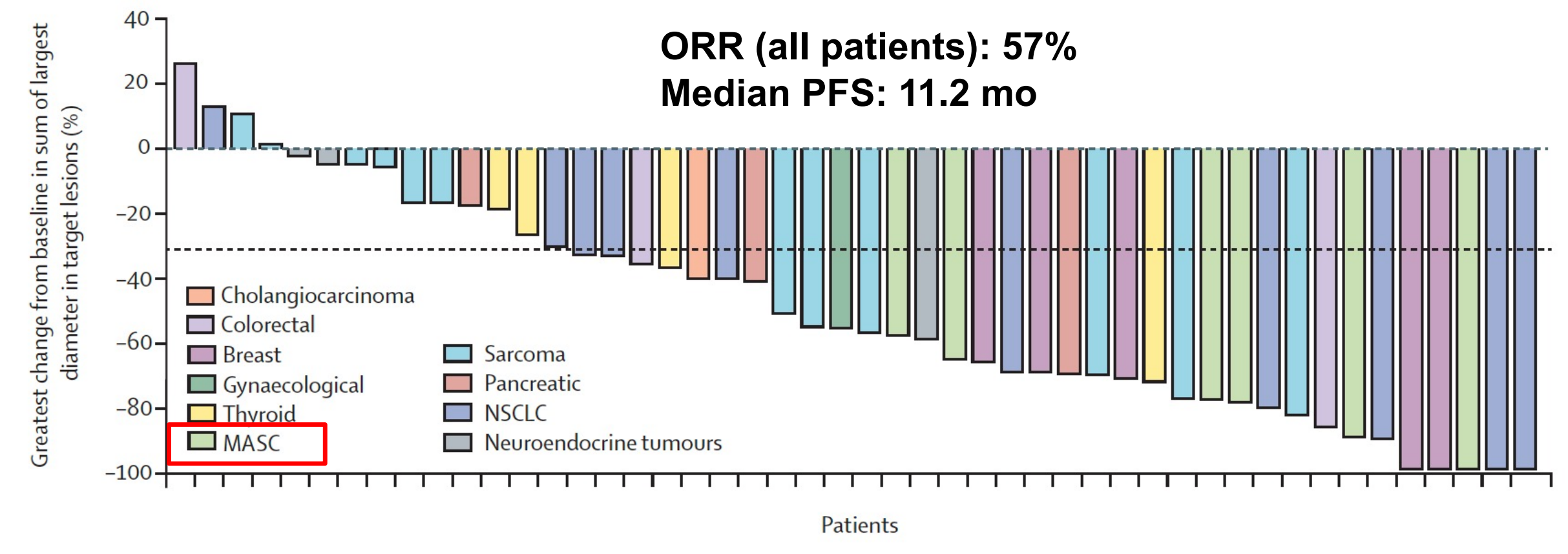
Robert C Doebele, Alexander Drilon*, Luis Paz-Ares, Salvatore Siena, Alice T Shaw, Anna F Farago, Collin M Blakely, Takashi Seto, Byung Chul Cho, Diego Tosi, Benjamin Besse, Sant P Chawla, Lyudmila Bazhenova, John C Krauss, Young Kwang Chae, Minal Barve, Ignacio Garrido-Laguna, Stephen V Liu, Paul Conkling, Thomas John, Marwan Fakih, Darren Sigal, Herbert H Loong, Gary L Buchschacher Jr, Pilar Garrido, Jorge Nieva, Conor Steuer, Tobias R Overbeck, Daniel W Bowles, Elizabeth Fox, Todd Riehl, Edna Chow-Maneval, Brian Simmons, Na Cui, Ann Johnson, Susan Eng, Timothy R Wilson, George D Demetri, on behalf of the trial investigators*

Entrectinib for Advanced or Metastatic Solid Tumors with NTRK Fusions (ALKA, STARTRK-1, STARTRK-2)

	All patients in *NTRK* gene fusion-positive efficacy-evaluable population (n=54)
Age, years	58 (48–67)
Tumour type	
Sarcoma‡	13 (24%)
NSCLC	10 (19%)
Mammary analogue secretory carcinoma (salivary)	7 (13%)
Breast	6 (11%)
Thyroid	5 (9%)
Colorectal	4 (7%)
Neuroendocrine	3 (6%)
Pancreatic	3 (6%)
Gynaecological	2 (4%)
Ovarian	1 (2%)
Endometrial	1 (2%)
Cholangiocarcinoma	1 (2%)

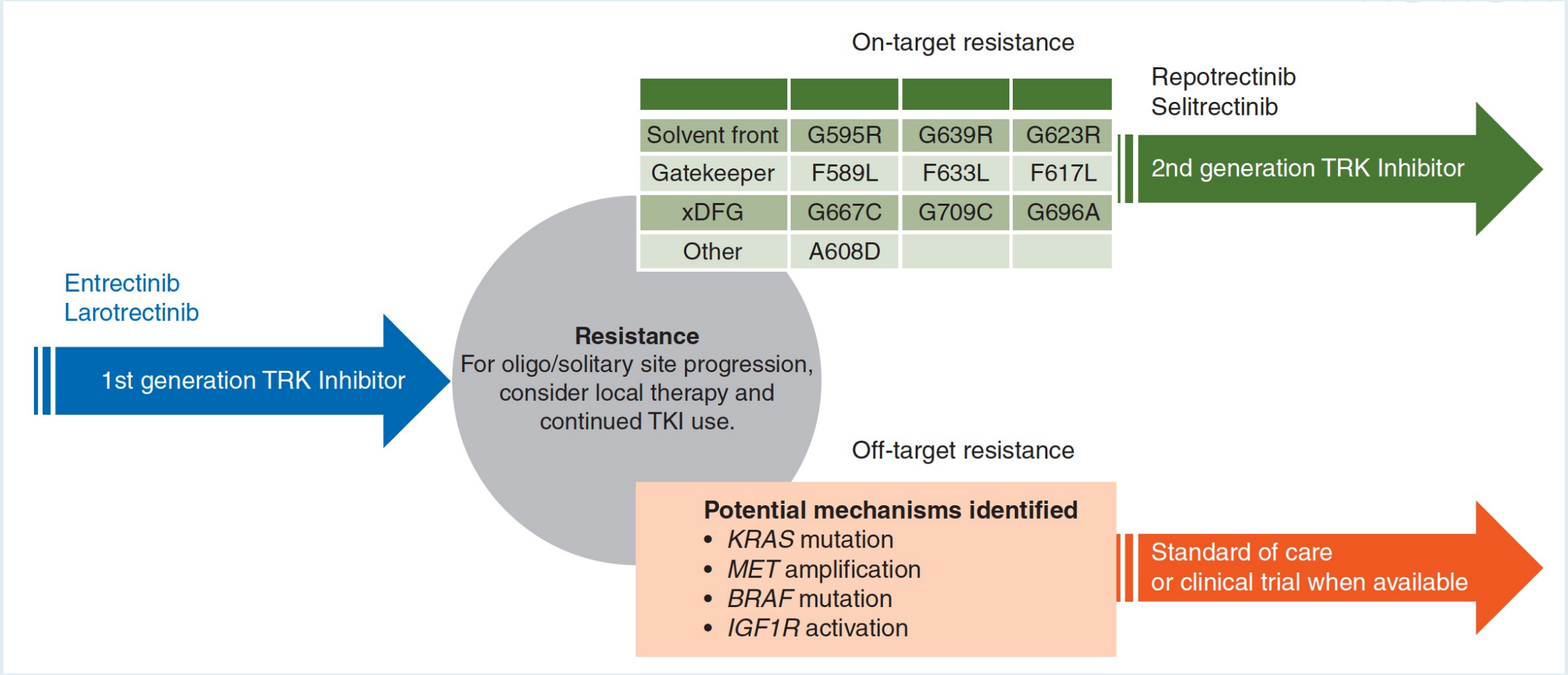
Doebele RC et al. *Lancet Oncol* 2020;21(2):271-82.

Entrectinib for Advanced or Metastatic Solid Tumors with NTRK Fusions (ALKA, STARTRK-1, STARTRK-2)



Doebele RC et al. *Lancet Oncol* 2020;21(2):271-82.

Mechanisms of Resistance to NTRK Inhibitors and Sequential Therapy



Drilon A. *Ann Oncol* 2019;30(Suppl 8):23-30.

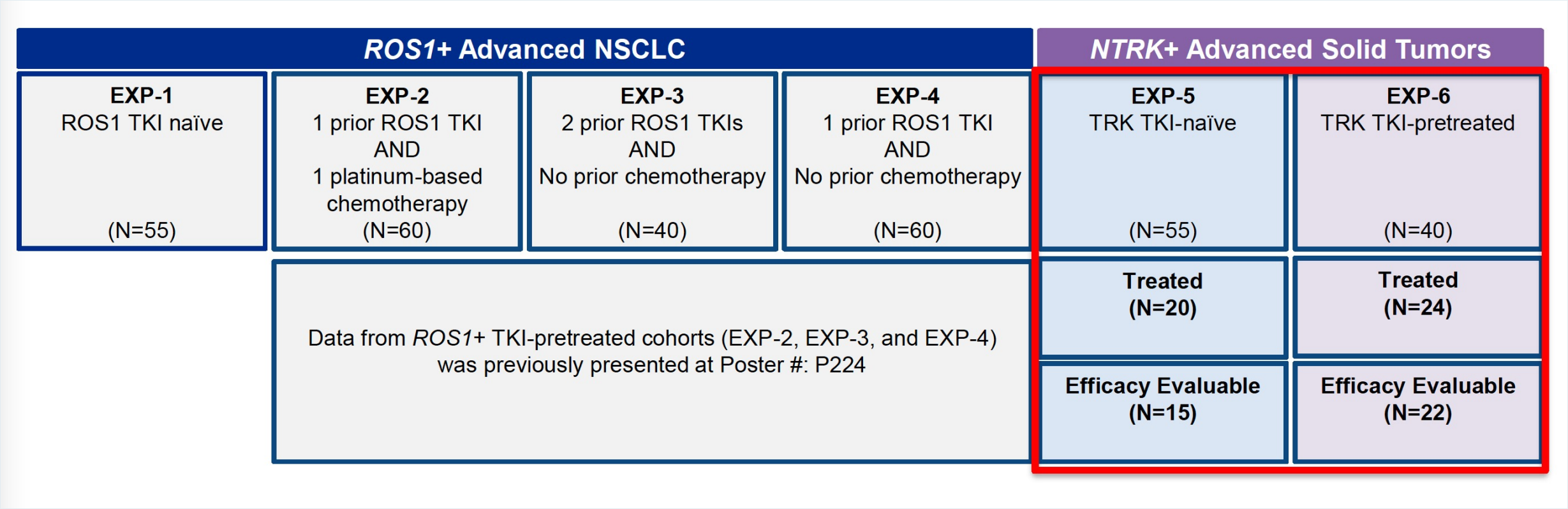
AACR-NCI-EORTC Virtual International Conference on
MOLECULAR TARGETS AND CANCER THERAPEUTICS
October 7-10, 2021

LB #6546

Repotrectinib in patients with *NTRK* fusion-positive advanced solid tumors: update from the registrational phase 2 TRIDENT-1 trial

Benjamin Besse,[1] Christina Baik,[2] Christoph Springfeld,[3] Alice Hervieu,[4] Victor Moreno,[5] Lyudmila Bazhenova,[6] Jessica J. Lin,[7] D. Ross Camidge,[8] Benjamin Solomon,[9] Vamsidhar Velcheti,[10] Young-Chul Kim,[11] Anthonie J. van der Wekken,[12] Enriqueta Felip,[13] Dipesh Uprety,[14] Denise Trone,[15] Shanna Stopatschinskaja,[15] Byoung Chul Cho,[16] Alexander Drilon[17]

TRIDENT-1 Phase II Study Design



Besse B et al. AACR-NCI-EORTC Virtual International Conference 2021;Abstract 6546.

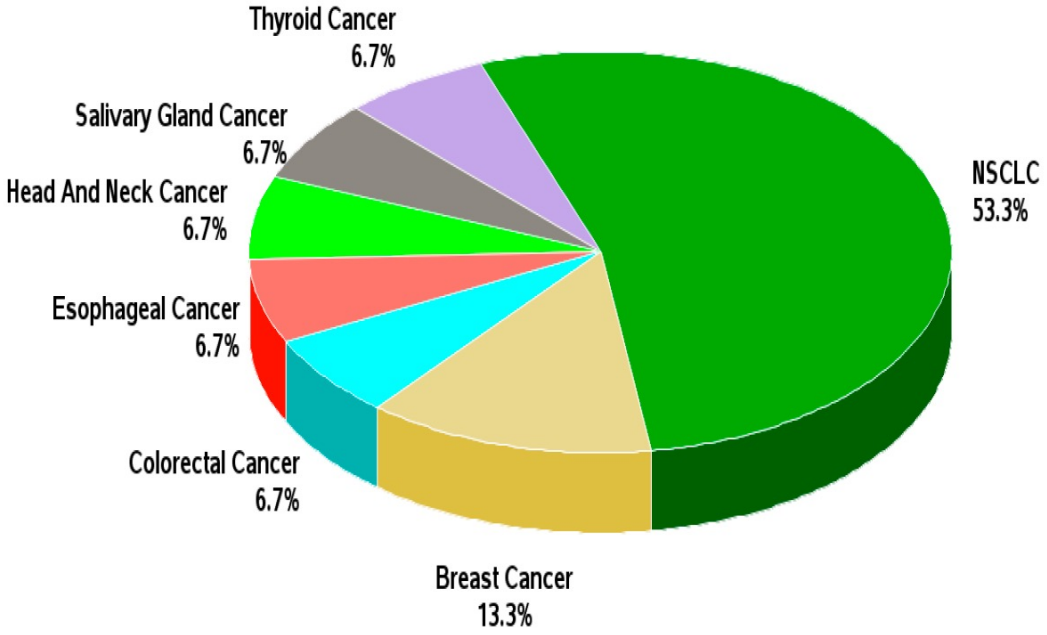
TRIDENT-1: Demographics and Baseline Characteristics

	EXP-5 (N=15)	EXP-6 (N=22)
Age (years)		
Median (range)	60.0 (33 – 80)	54.5 (23 – 81)
Age Group, n (%)		
≥ 18 to < 65	10 (66.7)	14 (63.6)
≥ 65	5 (33.3)	8 (36.4)
Sex, n (%)		
Male	9 (60.0)	10 (45.5)
ECOG Performance Status, n (%)		
0	8 (53.3)	11 (50.0)
1	7 (46.7)	11 (50.0)
CNS Metastasis, n (%)		
Yes	3 (20.0)	4 (18.2)
No	12 (80.0)	18 (81.8)
NTRK Resistance Mutation, n (%)		
Solvent Front	0	13 (59.1)
Other	0	0
None	15 (100.0)	9 (40.9)
# Prior Systemic Therapies		
Median (range)	1 (0, 4)	2 (1, 5)
# Prior TKIs	Not Applicable	
1		19 (86.4)
2		3 (13.6)
Prior TKIs, n (%)	Not Applicable	
Entrectinib		11 (50.0)
Larotrectinib		11 (50.0)
Selitrectinib		2 (9.1)
Cabozantinib		1 (4.5)

Besse B et al. AACR-NCI-EORTC Virtual International Conference 2021;Abstract 6546.

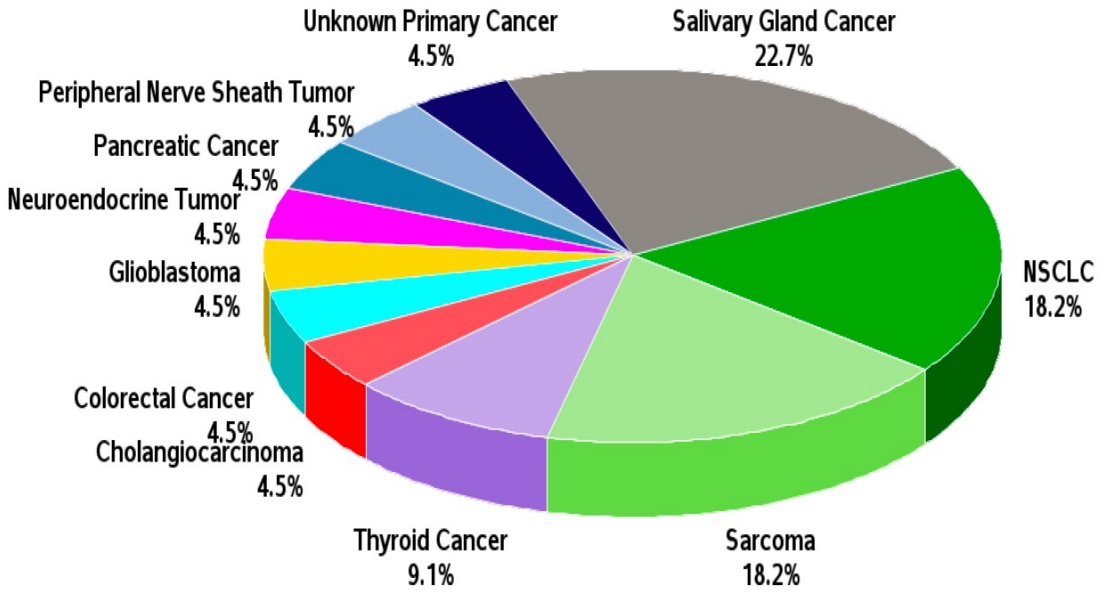
TRIDENT-1: Tumor Types

TRK TKI-Naive EXP-5
(N=15)



7 unique tumor types

TRK TKI-Pretreated EXP-6
(N=22)

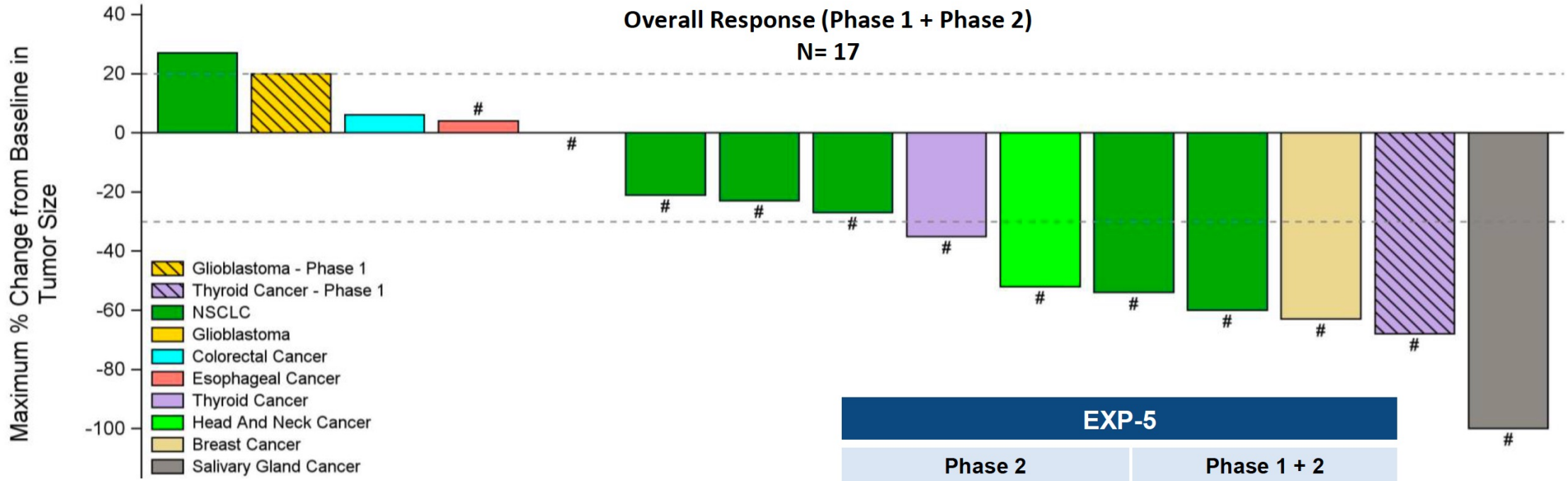


11 unique tumor types

TKI = tyrosine kinase inhibitor

Besse B et al. AACR-NCI-EORTC Virtual International Conference 2021;Abstract 6546.

TRIDENT-1: Preliminary Efficacy with Repotrectinib for TKI-Naïve Advanced Solid Tumors with NTRK Fusions



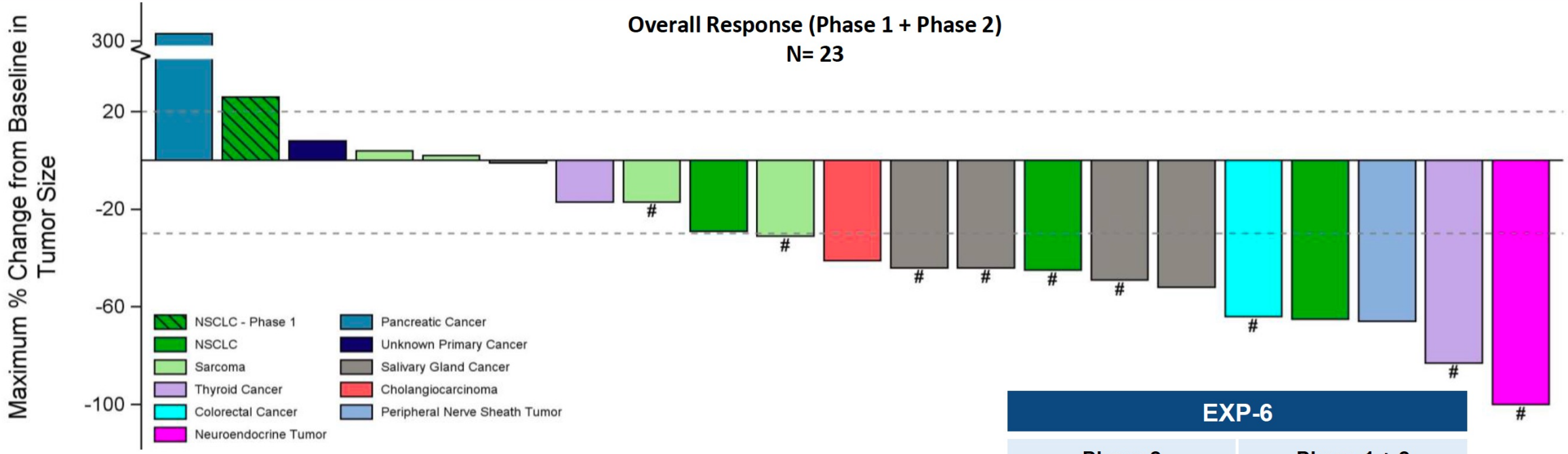
Patient remains on treatment.
2 patients not displayed due to discontinuing treatment prior to first post-baseline scan.

	EXP-5	
	Phase 2 (N=15)	**Phase 1 + 2 (N=17)**
Confirmed ORR (cORR) (95% CI)	**40%** (16 – 68)	**41%** (18 – 67)
Duration of Response (range in months)	1.9+ – 7.4+ n=6	1.9+ – 7.4+ n=7

Besse B et al. AACR-NCI-EORTC Virtual International Conference 2021;Abstract 6546.

RTP RESEARCH TO PRACTICE

TRIDENT-1: Preliminary Efficacy with Repotrectinib for TKI-Pretreated Advanced Solid Tumors with NTRK Fusions



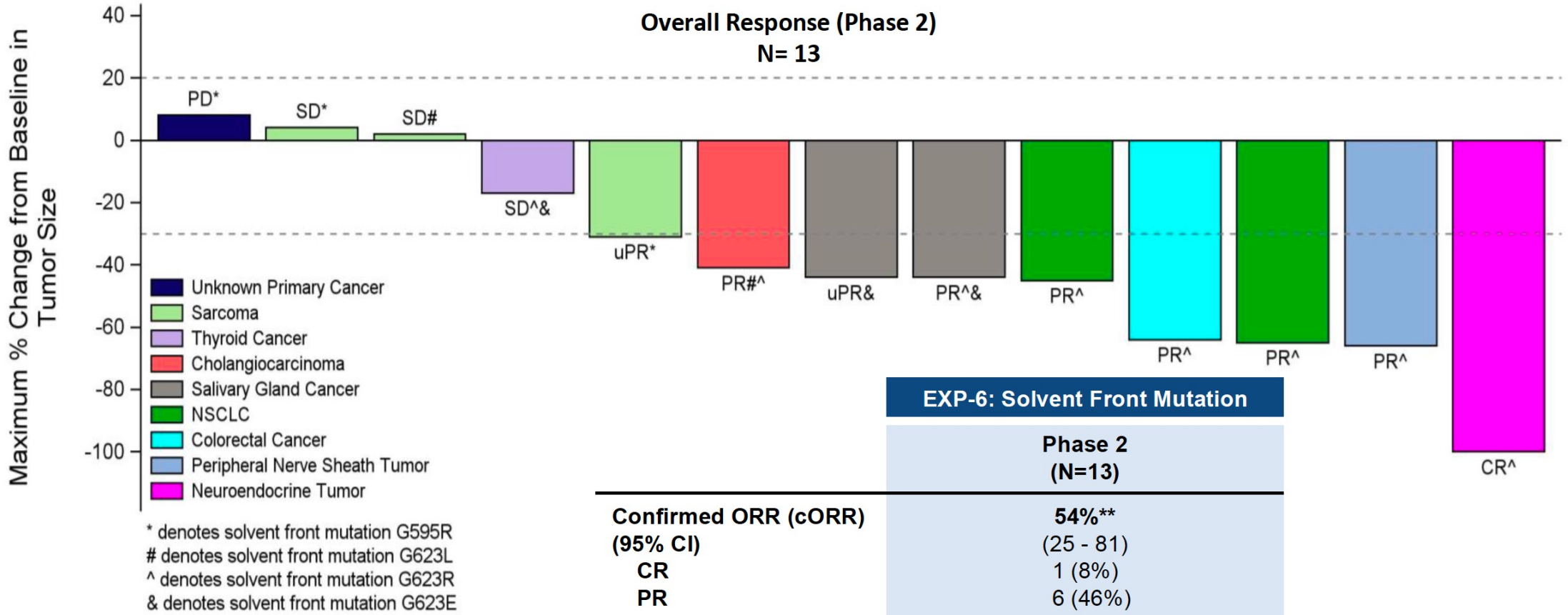
Patient remains on treatment.
1 patient not displayed due to discontinuing treatment prior to first post-baseline scan.
1 patient not displayed due target lesion measurement not performed at the post-baseline scan.

	EXP-6	
	Phase 2 (N=22)	**Phase 1 + 2 (N=23)**
Confirmed ORR (cORR) (95% CI)	**45%*** (24 – 68)	**43%*** (23 – 66)
Duration of Response (range in months)	1.9+– 15.1 n=10	1.9+– 15.1 n=10

Besse B et al. AACR-NCI-EORTC Virtual International Conference 2021;Abstract 6546.

RTP RESEARCH TO PRACTICE

TRIDENT-1: Preliminary Efficacy with Repotrectinib for Patients with TKI-Pretreated Advanced Solid Tumors and NTRK Resistance Mutations



EXP-6: Solvent Front Mutation	Phase 2 (N=13)
Confirmed ORR (cORR)	**54%****
(95% CI)	(25 - 81)
CR	1 (8%)
PR	6 (46%)
Duration of Response (range in months)	1.9+ - 13.7
	n=7

Besse B et al. AACR-NCI-EORTC Virtual International Conference 2021;Abstract 6546.

RTP RESEARCH TO PRACTICE

TRIDENT-1 Safety Summary with Repotrectinib for All Treated Patients

All Treated Patients (N=301)					
	TEAEs (≥15% of patients)			TRAEs	
Adverse Events	All Grades n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 3 n (%)	Grade 4 n (%)
Dizziness	181 (60.1)	7 (2.3)	0	7 (2.3)	0
Dysgeusia	132 (43.9)	1 (0.3)	0	1 (0.3)	0
Constipation	101 (33.6)	1 (0.3)	0	0	0
Paraesthesia	87 (28.9)	3 (1.0)	0	3 (1.0)	0
Dyspnea[a]	84 (27.9)	18 (6.0)	3 (1.0)	1 (0.3)	0
Anaemia	82 (27.2)	24 (8.0)	1 (0.3)	10 (3.3)	0
Fatigue	73 (24.3)	5 (1.7)	0	2 (0.7)	0
Nausea	62 (20.6)	3 (1.0)	0	0	0
Muscular weakness	57 (18.9)	5 (1.7)	0	3 (1.0)	0
Ataxia	51 (16.9)	0	0	0	0

- Repotrectinib was generally well tolerated
- Most TRAEs were Grade 1 or 2
- The most commonly-reported TEAE remains low-grade dizziness (60%)
  - 76% (138/181) were Grade 1
  - 11 (4%) patients reported ataxia in the absence of dizziness
  - No events of dizziness or ataxia led to treatment discontinuation
- Dose modifications due to TEAEs
  - 27% with TEAEs that led to dose reduction
  - 11% with TEAEs that led to drug discontinuation

TEAEs = treatment-emergent adverse events; TRAEs = treatment-related adverse events

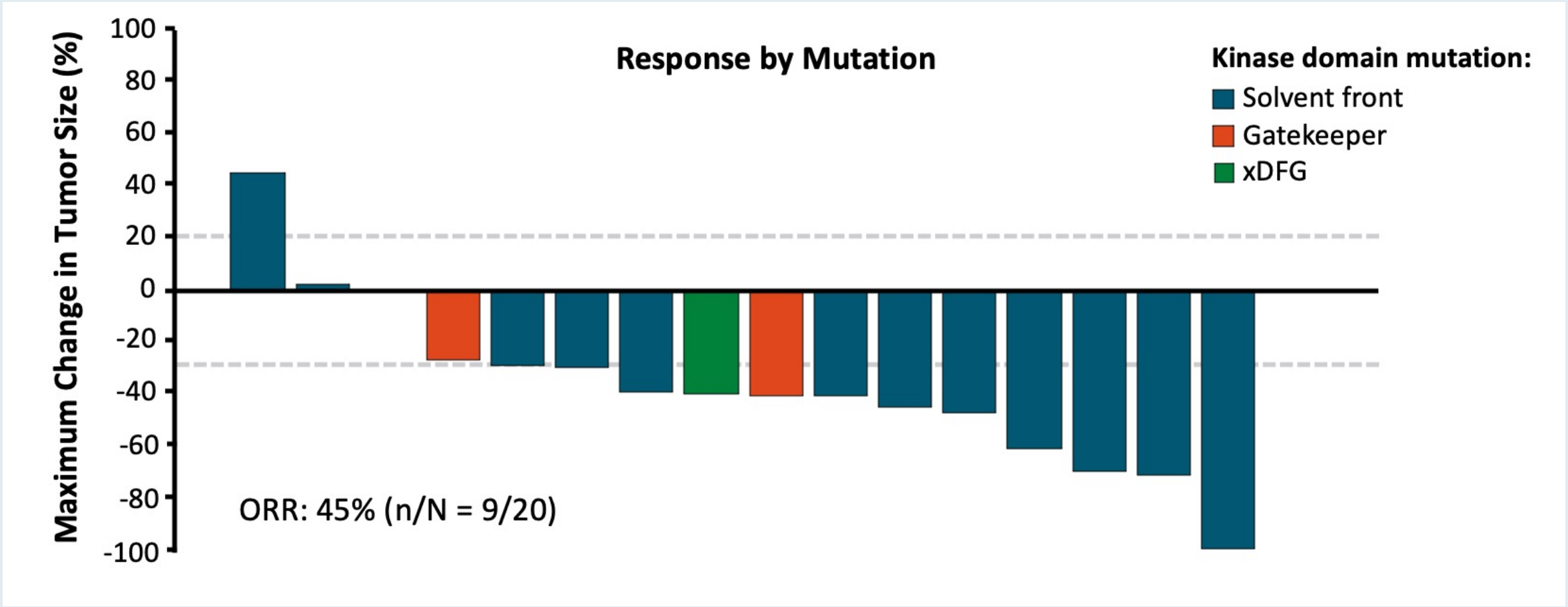
Besse B et al. AACR-NCI-EORTC Virtual International Conference 2021;Abstract 6546.

Phase I and Expanded Access Experience of LOXO-195 (BAY 2731954), a Selective Next-Generation TRK Inhibitor (TRKi)

Hyman D et al.

AACR 2019;Abstract CT127.

Activity of Selitrectinib (LOXO-195) in a Phase I/Expanded Access Study for Adults and Children with Progressive Disease or Intolerance to a Prior TRK Inhibitor



Hyman D et al. AACR 2019;Abstract CT127.

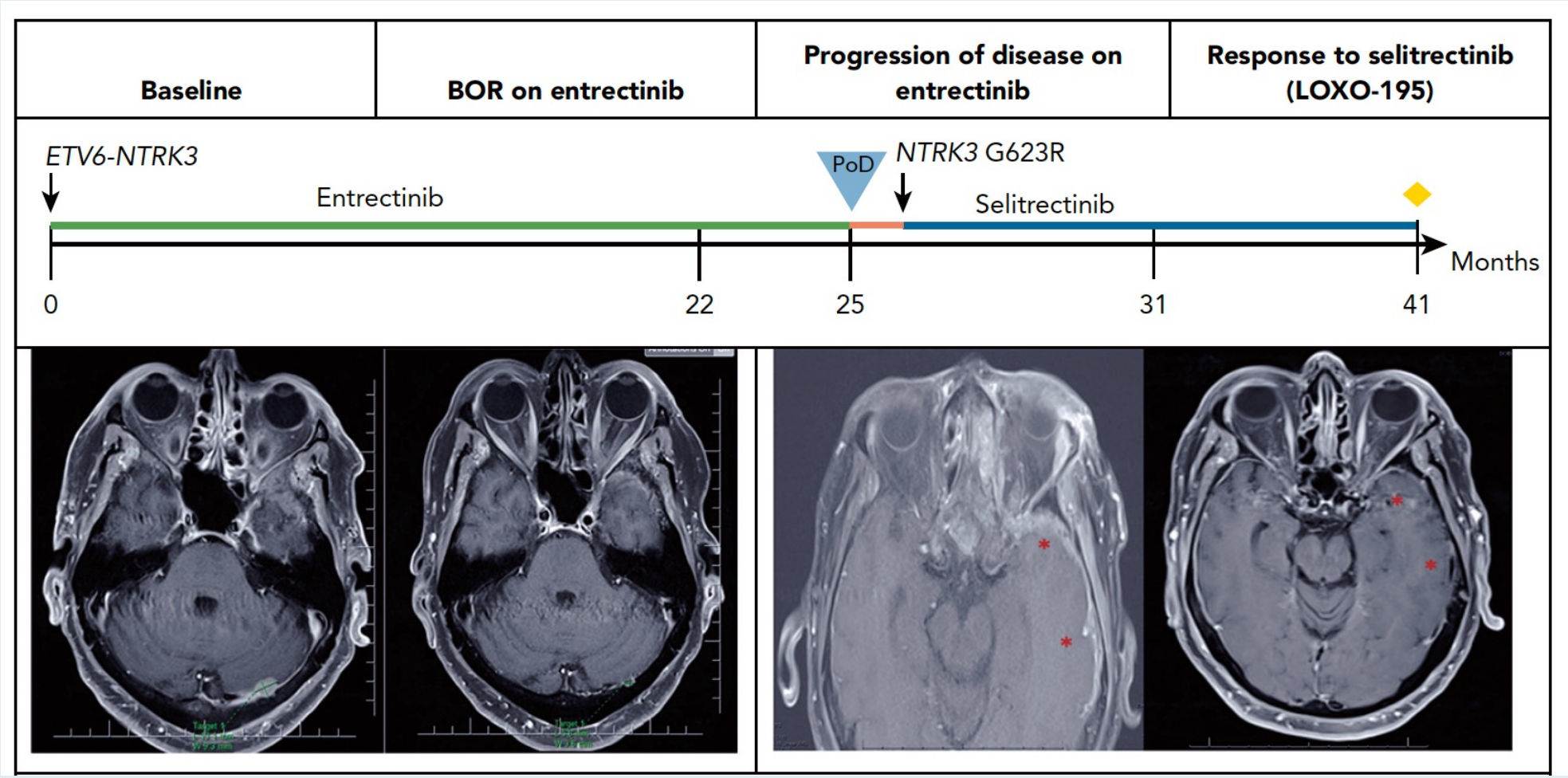
MOLECULAR INSIGHTS IN PATIENT CARE

Clinical Activity of Selitrectinib in a Patient With Mammary Analogue Secretory Carcinoma of the Parotid Gland With Secondary Resistance to Entrectinib

Vaia Florou, MD[1]; Christopher Nevala-Plagemann, MD[1]; Jonathan Whisenant, MD[1]; Patricia Maeda, MD[2]; Glynn W. Gilcrease, MD[1]; and Ignacio Garrido-Laguna, MD, PhD[1]

J Natl Compr Canc Netw 2021;19(5):478-82.

Most Characteristic Imaging Studies Showing Response to Selitrectinib After Disease Progression on Entrectinib



Florou V et al. *J Natl Compr Canc Netw* 2021;19(5):478-82.

RTP RESEARCH TO PRACTICE

Integration of Biomarker-Targeted Strategies for Advanced Thyroid Cancer

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Genetic Alterations Associated with Different Histotypes of Thyroid Cancer

	PTC	FTC	PDTC	ATC	MTC
AKT	1%	1%-2.6%	-	0%-3%	-
BRAF	**61.7%**	**1.7%**	**19%-33%**	**19%-45%**	-
DICER1	2.7%	5.1%	-	1.1%	-
EIF1AX	1.5%	5.1%	10%	9%	0.6%
HRAS	2%	7%	5%	6%	9.3%-15.8%
KRAS	1.3%	4%	2%	0%-5%	3.0%-6.2%
NRAS	6%	17%-57%	21%	18%	0.6%-1%
PAX8-PPARγ	0.8%	12%-53%	4%	0	-
PI3KCA	-	5.5%	2%	18%	-
PTEN	1%	7.1%	4%	15%	1%
RET	**-**	**-**	**-**	**-**	**55.8%**
RET/PTC	**6.8%**	**0**	**14%**	**0**	**Very rare**
SWI/SNF	-	-	6%	18%-36%	-
TERT promoter	9.4%	-	33%-40%	43%-73%	-
TP53	6%	5.1%-9.7%	0%-8%	43%-78%	1.2%
NTRK-Fusion	2-19%	-	-	-	-
TSHR	2%	10.3%	2%	6%	0.6%

Brose MS. ASCO 2022 Education Session. Prete A et al. *Front Endocrinol (Lausanne)* 2020;11:102.

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Considerations for RET and TRK Fusion Testing Methodologies

FISH	• Current standard for detection of gene fusions; break-apart probes preferred to fusion probes • Difficulties in FISH interpretation: pericentric fusions, close proximity of several possible partner genes to fusion gene (RET or TRK) • Limitation: not optimal for extensive and multiplex screening, or when recognition of fusion partner influences clinical decisions
RT-PCR	• Can detect fusion transcripts and identify fusion partner if primer for specific partner is present • Limitation: imbalance assay for unknown fusion partner is highly dependent on expression of partner and may not be reliable
DNA NGS	• NGS panel sequencing can identify fusions if specifically designed to examine introns • Limitations: limited sensitivity for detection of fusion genes and no information on effective transcription of rearranged *RET or TRK* genes
RNA NGS	• Targeted RNA-based assays are method of choice for *RET* and TRK fusion screening; allows detection of gene fusions with complex rearrangements • Limitation: assessment of RNA quality is crucial to ensure accuracy; poor preanalytical conditions may affect assay

Brose MS. ASCO 2022 Education Session. Bell C et al. *Ann Oncol* 2021:32(3):337-50.

Targeting RET Fusions in Advanced Medullary Thyroid Cancer

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N Engl J Med 2020;383(9):825-35.

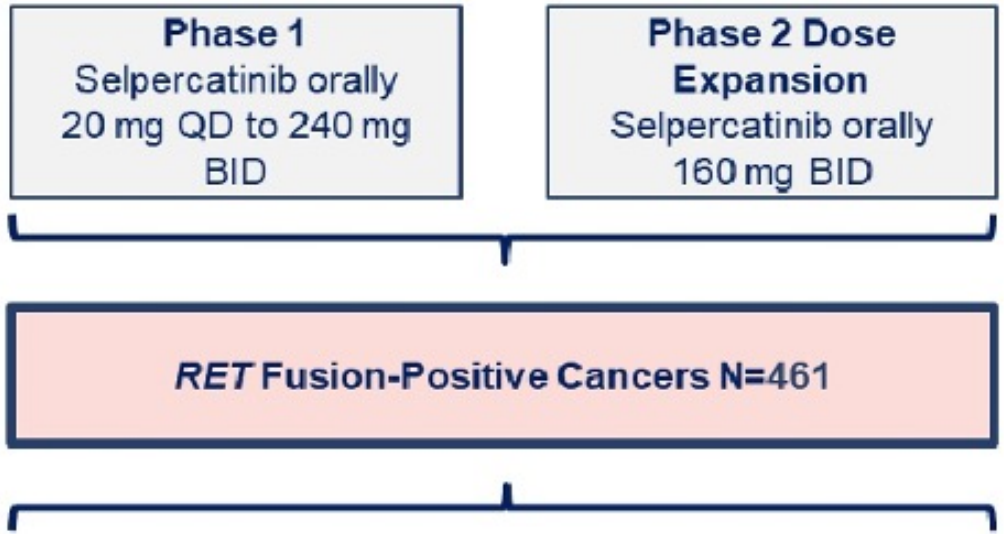
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Efficacy of Selpercatinib in *RET*-Altered Thyroid Cancers

L.J. Wirth, E. Sherman, B. Robinson, B. Solomon, H. Kang, J. Lorch, F. Worden, M. Brose, J. Patel, S. Leboulleux, Y. Godbert, F. Barlesi, J.C. Morris, T.K. Owonikoko, D.S.W. Tan, O. Gautschi, J. Weiss, C. de la Fouchardière, M.E. Burkard, J. Laskin, M.H. Taylor, M. Kroiss, J. Medioni, J.W. Goldman, T.M. Bauer, B. Levy, V.W. Zhu, N. Lakhani, V. Moreno, K. Ebata, M. Nguyen, D. Heirich, E.Y. Zhu, X. Huang, L. Yang, J. Kherani, S.M. Rothenberg, A. Drilon, V. Subbiah, M.H. Shah, and M.E. Cabanillas

LIBRETTO-001 Phase I/II Study Design



Study Design

- Ongoing, global, multicenter Phase 1/2 trial (NCT03157128)
- Patients enrolled based on locally identified *RET* alterations using NGS, FISH, or PCR
- Key inclusion criteria: Age of ≥12 years, diagnosis of advanced or metastatic solid tumor, ECOG PS 0 to 2

Primary Endpoint

- ORR (RECIST v 1.1) by Independent Review Committee (IRC)

Secondary Endpoints Included

- Duration of Response (DOR)
- Progression-Free Survival (PFS)
- Overall Survival (OS)
- Safety

Subbiah V et al. ASCO 2022;Abstract 3094.

LIBRETTO-001: Clinical Characteristics of Patients with Thyroid Cancer

Characteristic	*RET*-Mutant MTC Previously Treated (N=55)	*RET*-Mutant MTC Not Previously Treated (N=88)	Previously Treated *RET* Fusion–Positive Thyroid Cancer (N=19)
Median age (range) — yr	57 (17–84)	58 (15–82)	54 (25–88)
Histologic type of thyroid cancer			
Medullary	55 (100)	88 (100)	—
Papillary	—	—	13 (68)
Poorly differentiated	—	—	3 (16)
Hürthle cell	—	—	1 (5)
Anaplastic	—	—	2 (11)
Median no. of previous systemic regimens (range)	2 (1–8)	0 (0–2)	4 (1–7)
Previous regimen — no. (%)			
Cabozantinib, vandetanib, or both	55 (100)	0	—
Vandetanib only	18 (33)	0	—
Cabozantinib only	13 (24)	0	—
Cabozantinib and vandetanib	24 (44)	0	—
Radioiodine	—	—	16 (84)
Sorafenib, lenvatinib, or both	—	—	13 (68)
Multitargeted kinase inhibitor therapy	55 (100)	7 (8)	15 (79)
1	26 (47)	6 (7)	7 (37)
≥2	29 (53)	1 (1)	8 (42)
Therapy other than multitargeted kinase inhibitor therapy	17 (31)	9 (10)	14 (74)
Brain metastases — no. (%)	4 (7)	2 (2)	6 (32)

Wirth LJ et al. *N Engl J Med* 2020;383(9):825-35.

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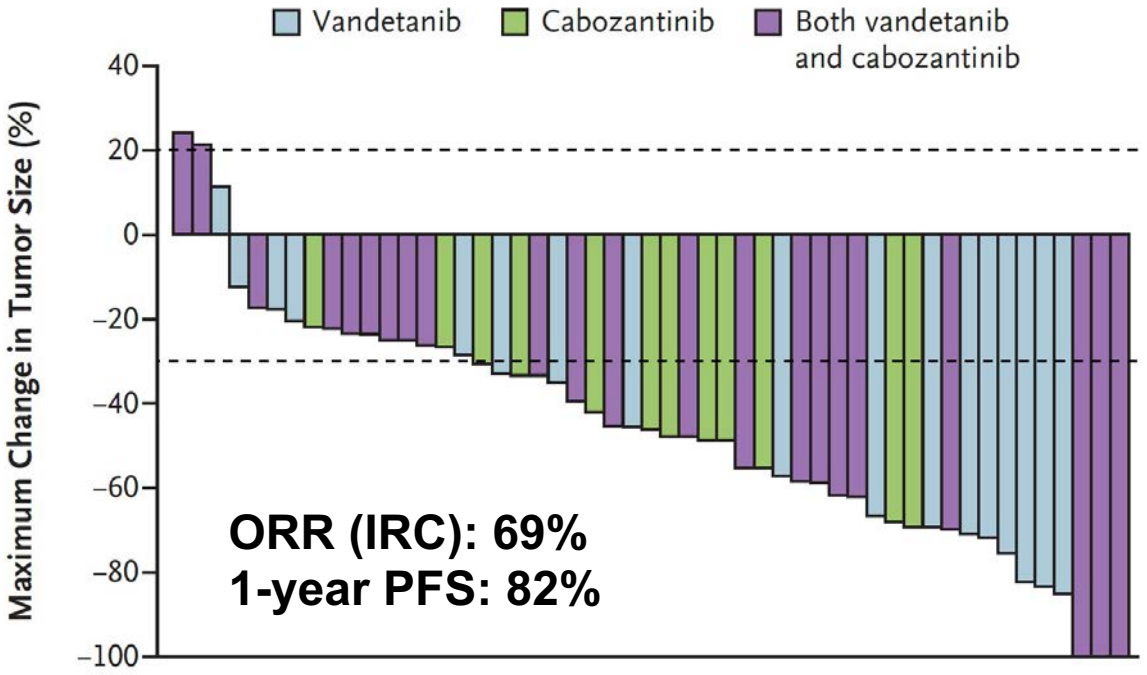
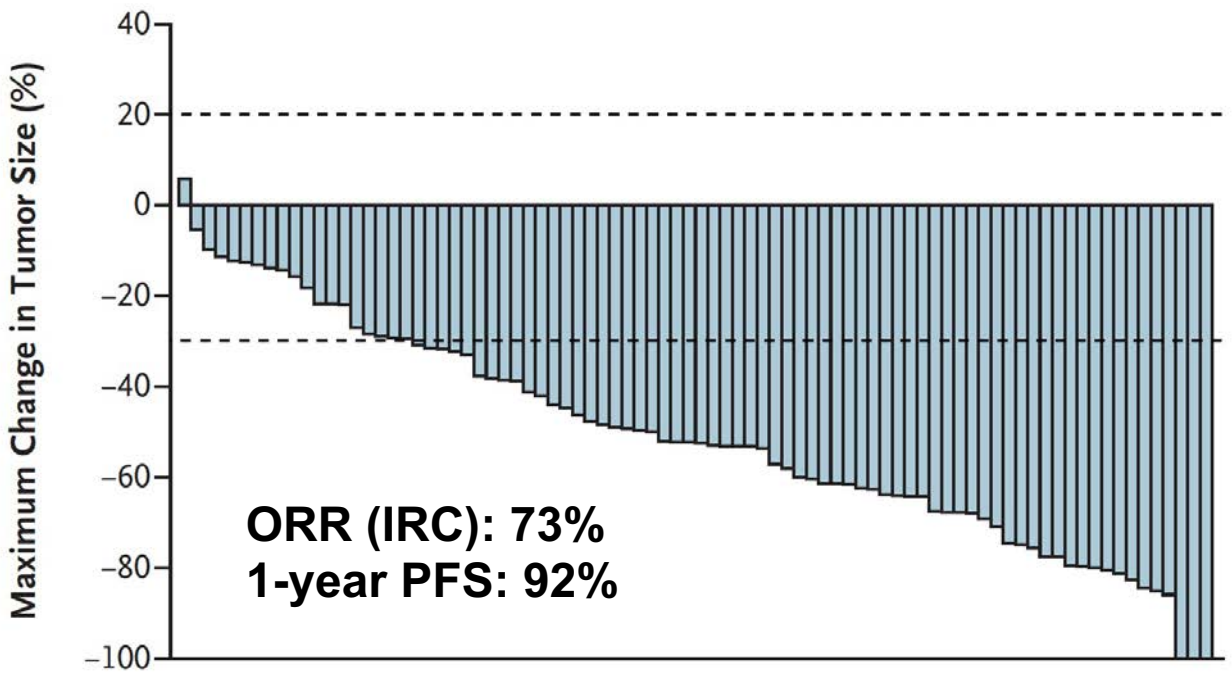
LIBRETTO-001: Response and PFS with Selpercatinib for Previously TKI-Treated and Untreated Medullary Thyroid Cancer (MTC) with a RET Mutation

MTC with a RET mutation previously treated with vandetanib, cabozantinib or both (n = 55)



MTC with a RET mutation not previously treated with vandetanib or cabozantinib (n = 88)



ORR = objective response rate

Wirth LJ et al. *N Engl J Med* 2020;383(9):825-35.

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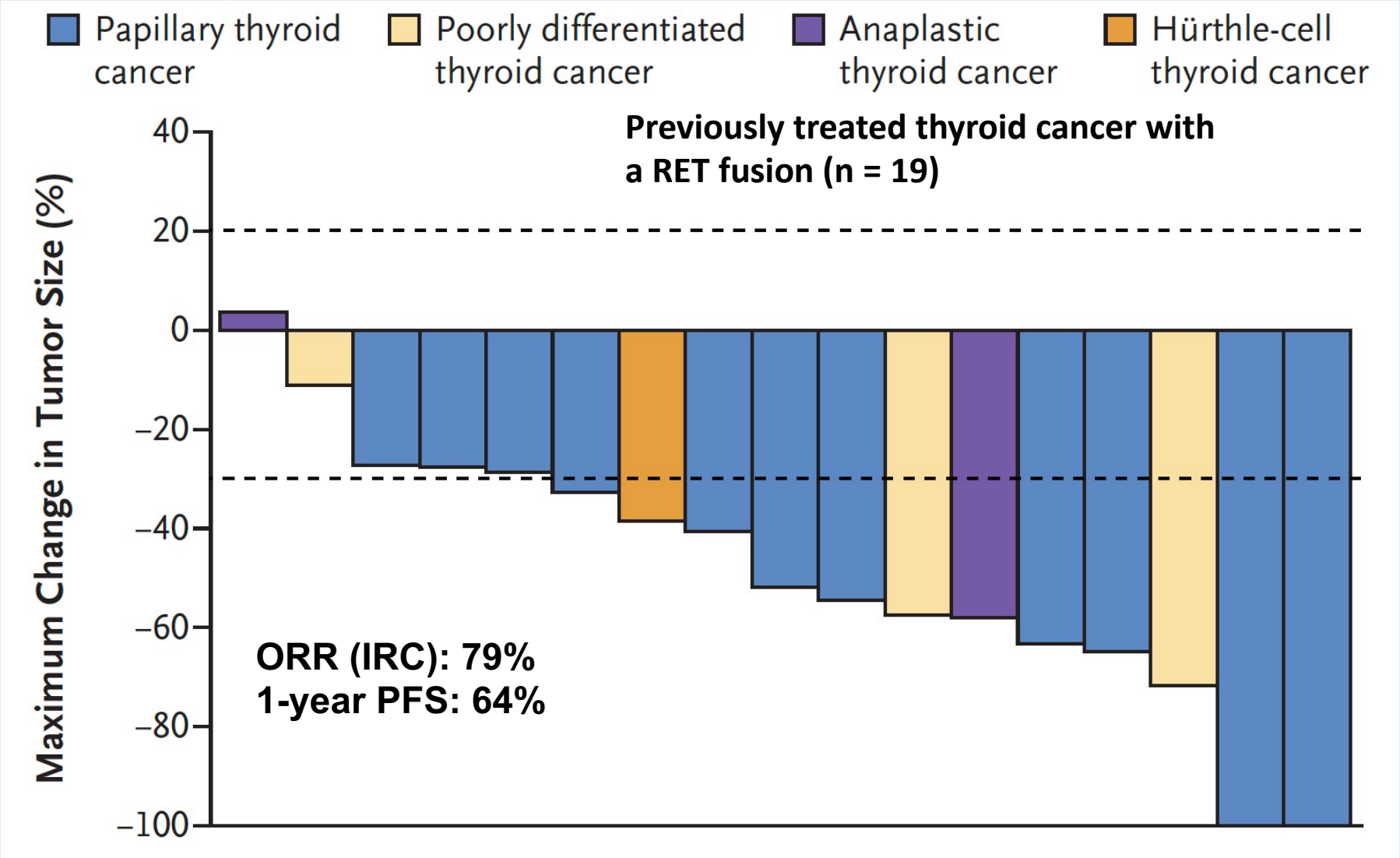
LIBRETTO-001: Response with Selpercatinib for Subtypes of Previously Treated Thyroid Cancer with a RET Fusion



Wirth LJ et al. *N Engl J Med* 2020;383(9):825-35.

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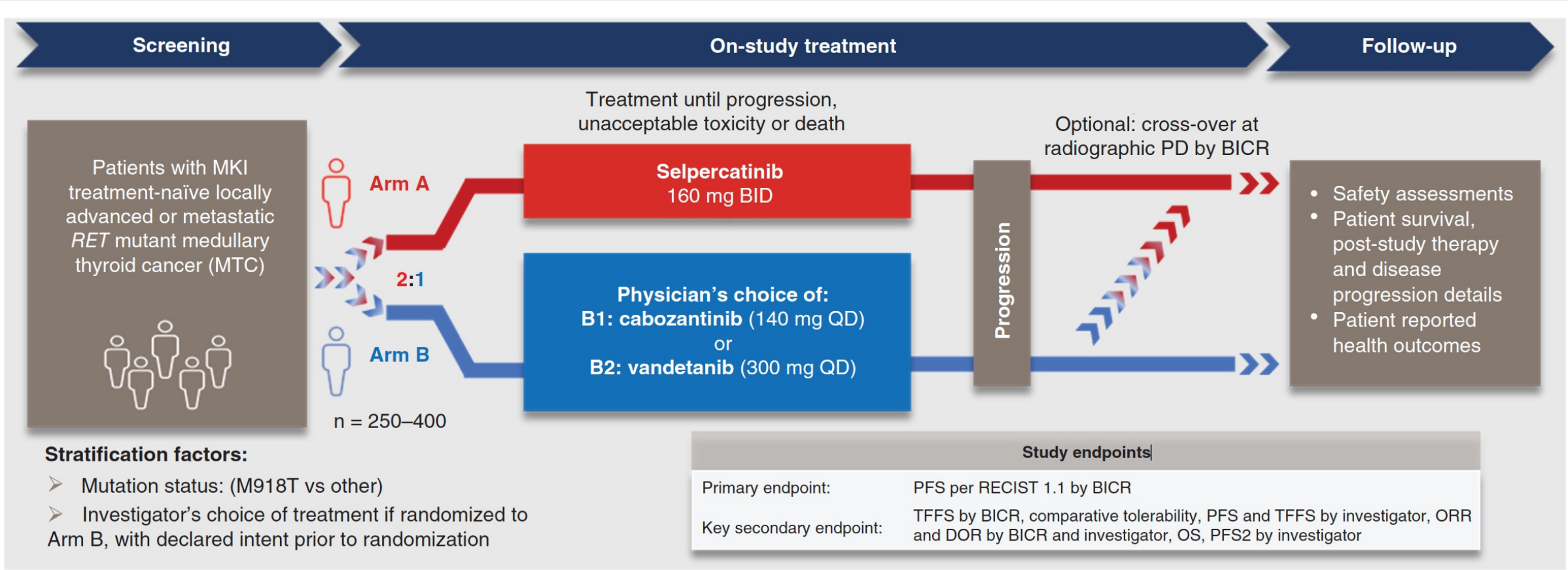
LIBRETTO-531: Phase III Trial of Selpercatinib for Multikinase Inhibitor (MKI) Treatment-Naïve MTC with a RET Mutation



Wirth LJ et al. *Future Oncol* 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

Lancet Diabetes Endocrinol 2021;9(8):491-501.

Pralsetinib for patients with advanced or metastatic *RET*-altered thyroid cancer (ARROW): a multi-cohort, open-label, registrational, phase 1/2 study

Vivek Subbiah, Mimi I Hu*, Lori J Wirth, Martin Schuler, Aaron S Mansfield, Giuseppe Curigliano, Marcia S Brose, Viola W Zhu, Sophie Leboulleux, Daniel W Bowles, Christina S Baik, Douglas Adkins, Bhumsuk Keam, Ignacio Matos, Elena Garralda, Justin F Gainor, Gilberto Lopes, Chia-Chi Lin, Yann Godbert, Debashis Sarker, Stephen G Miller, Corinne Clifford, Hui Zhang, Christopher D Turner, Matthew H Taylor*

2022 ASCO ANNUAL MEETING **Abstract 6080.**

PRALSETINIB IN PATIENTS WITH ADVANCED OR METASTATIC *RET*-ALTERED THYROID CANCER: UPDATED DATA FROM THE ARROW TRIAL

Aaron S. Mansfield[1], Vivek Subbiah[2], Martin Schuler[3], Viola W. Zhu[4], Julien Hadoux[5], Marcia S. Brose[6*], Giuseppe Curigliano[7], Lori Wirth[8], Elena Garralda[9], Douglas Adkins[10], Yann Godbert[11], Myung-Ju Ahn[12], Philippe Cassier[13], Byoung Chul Cho[14], Chia-Chi Lin[15], Hui Zhang[16], Alena Zalutskaya[16], Teresa Barata[17], Astrid Scalori[18], Matthew Taylor[19]

[1]Mayo Clinic, Rochester, MN, USA; [2]University of Texas MD Anderson Cancer Center, Houston, TX, USA; [3]West German Cancer Center, University Hospital Essen, Essen, Germany; [4]University of California Irvine, Orange, CA, USA; [5]Gustave Roussy, Villejuif, France; [6]Abramson Cancer Center at the University of Pennsylvania, Philadelphia, PA, USA; [7]European Institute of Oncology, IRCCS, and University of Milano, Milan, Italy; [8]Massachusetts General Hospital, Boston, MA, USA; [9]Vall d' Hebron Institute of Oncology, Barcelona, Spain; [10]Washington University School of Medicine, St. Louis, MO, USA; [11]Bergonié Institute Cancer Center, Bordeaux, France; [12]Samsung Medical Center Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [13]Centre Léon Bérard, Lyon, France; [14]Yonsei Cancer Center, Seoul, Republic of Korea; [15]National Taiwan University Hospital, Taipei, Taiwan; [16]Blueprint Medicines Corporation, Cambridge, MA, USA; [17]F. Hoffmann-La Roche Ltd, Basel, Switzerland; [18]F. Hoffmann-La Roche Ltd, Welwyn Garden City, UK; [19]Earle A. Chiles Research Institute, Providence Portland Medical Center, Portland, OR, USA.
**Currently at Sidney Kimmel Cancer Center, Jefferson University, Philadelphia, PA, USA*

2022 ASCO ANNUAL MEETING #ASCO22

PRESENTED BY: Aaron S. Mansfield M.D.

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

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ARROW: Patient Demographics

	RET-mutant medullary thyroid cancer		*RET* fusion-positive thyroid cancer
	Previous cabozantinib or vandetanib, or both, treatment group (n=61)	No previous systemic treatment group (n=23)	All (n=11)
Median age (rIQR), years	58 (49–64)	61 (54–70)	61 (54–70)
Age ≥65 years	15 (25%)	10 (43%)	4 (36%)
Number of previous therapies	2 (1–2)	0 (0–0)	2 (2–3)
Any previous systemic therapy	61 (100%)	0	11 (100%)
Radioactive iodine	..	..	11 (100%)
Multikinase inhibitor	61 (100%)	0	6 (55%)
Cabozantinib only	13 (21%)	0	0
Vandetanib only	26 (43%)	0	1 (9%)
Cabozantinib and vandetanib	22 (36%)	0	1 (9%)
Lenvatinib or sorafenib, or both	5 (8%)	0	6 (55%)
Chemotherapy	6 (10%)	0	0
Immunotherapy	3 (5%)	0	0
Other anticancer therapy	6 (10%)	0	11 (100%)
Primary *RET* mutation	61 (100%)	23 (100)	..

Subbiah V et al. *Lancet Diabetes Endocrinol* 2021;9(8):491-501.

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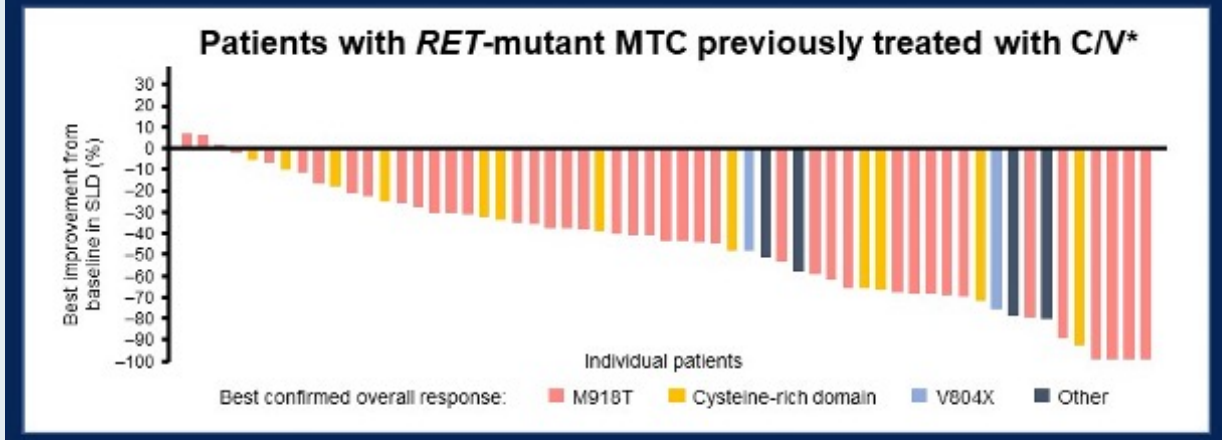
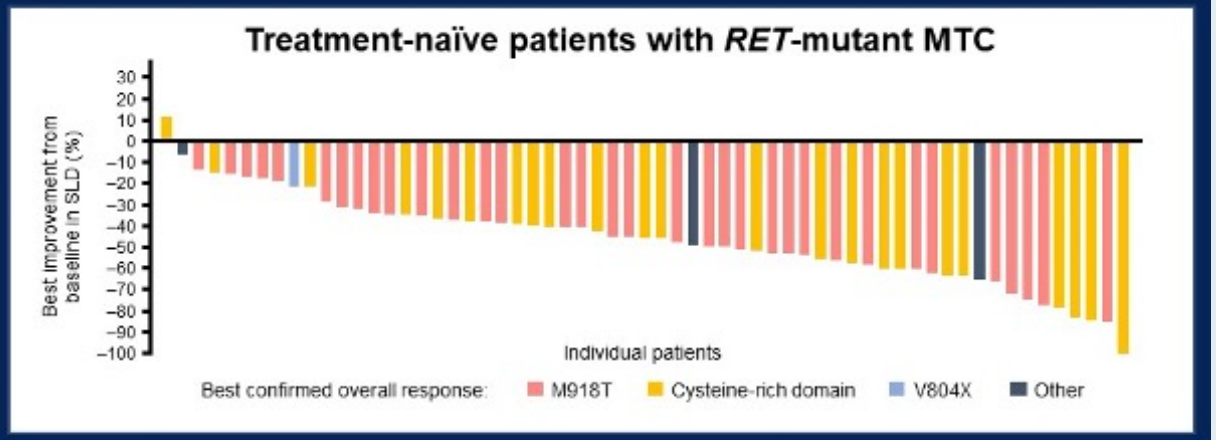
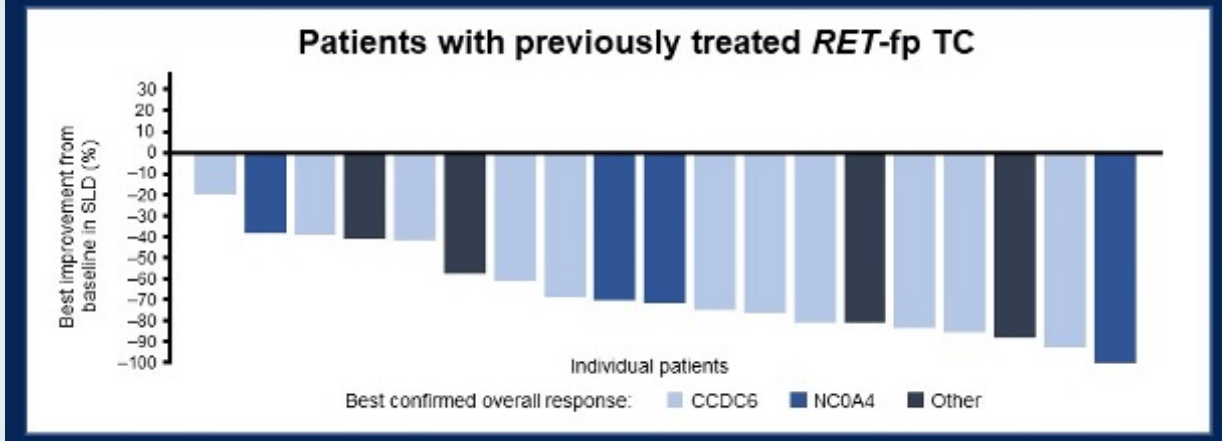
ARROW: Responses to Pralsetinib Observed Across All RET Mutation Genotypes and RET Fusion Partners







Median PFS:

- **24.9 months** (95% CI 19.7–31.2) in patients with *RET*-mutant MTC who had received prior C/V
- **Not reached** (95% CI 27.5–NE) in treatment-naïve patients with *RET*-mutant MTC
- **19.4 months** (95% CI 13.0–NE) in patients with previously treated *RET*-fp TC

Mansfield AS et al. ASCO 2022;Abstract 6080.

RTP RESEARCH TO PRACTICE

Targeting TRK Fusions for Advanced Thyroid Cancer

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Lancet Oncol 2020;21(4):531-40.

Larotrectinib in patients with TRK fusion-positive solid tumours: a pooled analysis of three phase 1/2 clinical trials

David S Hong, Steven G DuBois, Shivaani Kummar, Anna F Farago, Catherine M Albert, Kristoffer S Rohrberg, Cornelis M van Tilburg, Ramamoorthy Nagasubramanian, Jordan D Berlin, Noah Federman, Leo Mascarenhas, Birgit Geoerger, Afshin Dowlati, Alberto S Pappo, Stefan Bielack, François Doz, Ray McDermott, Jyoti D Patel, Russell J Schilder, Makoto Tahara, Stefan M Pfister, Olaf Witt, Marc Ladanyi, Erin R Rudzinski, Shivani Nanda, Barrett H Childs, Theodore W Laetsch, David M Hyman, Alexander Drilon**

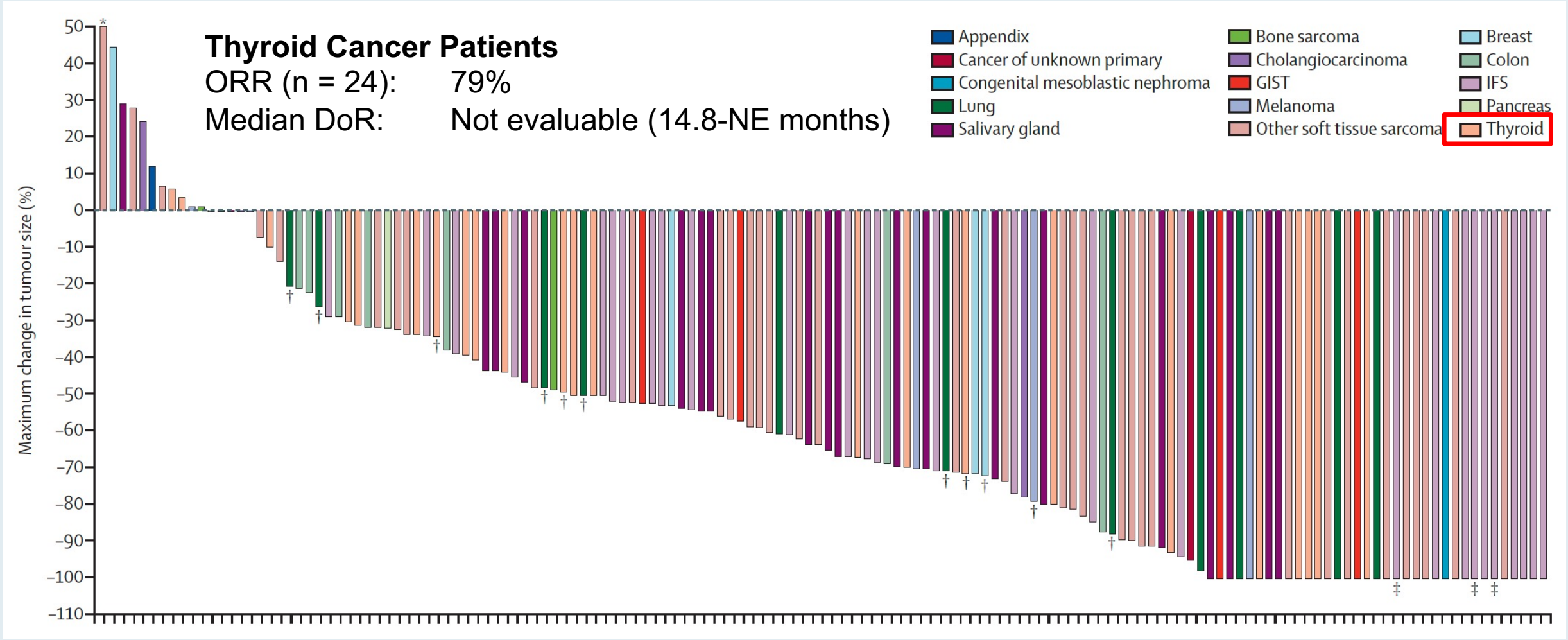
Clinical Characteristics of Patients in 3 Pooled Phase I/II Studies

	All patients (n=159)
Study*	
Adult phase 1	12 (8%)
Paediatric phase 1/2	50 (31%)
Adolescents and adult phase 2 basket study	97 (61%)
Sex	
Male	77 (48%)
Female	82 (52%)
Age	
Median, years	43·0 (6·5–61)
Range	<1 month to 84 years
Age group distribution, years	
<1	24 (15%)
1 to <18	28 (18%)
18 to <65	77 (48%)
≥65	30 (19%)

Tumour type	
Soft tissue sarcoma	
Infantile fibrosarcoma	29 (18%)
Gastrointestinal stromal tumour	4 (3%)
Other	36 (23%)
Thyroid	26 (16%)
Salivary gland	21 (13%)
Lung	12 (8%)
Colon	8 (5%)
Melanoma	7 (4%)
Breast	5 (3%)
Bone sarcoma	2 (1%)
Cholangiocarcinoma	2 (1%)
Pancreas	2 (1%)
Appendix	1 (<1%)
Congenital mesoblastic nephroma	1 (<1%)
Hepatocellular	1 (<1%)
Prostate	1 (<1%)
Unknown primary	1 (<1%)

Hong DS et al. *Lancet Oncol* 2020;21(4):531-40.

Waterfall Plot of Maximum Percent Change in Tumor Size with Larotrectinib in Patients with Solid Cancers with TRK Fusions



Hong DS et al. *Lancet Oncol* 2020;21(4):531-40.

Lancet Oncol 2020;21(2):271-82.

Entrectinib in patients with advanced or metastatic *NTRK* fusion-positive solid tumours: integrated analysis of three phase 1–2 trials

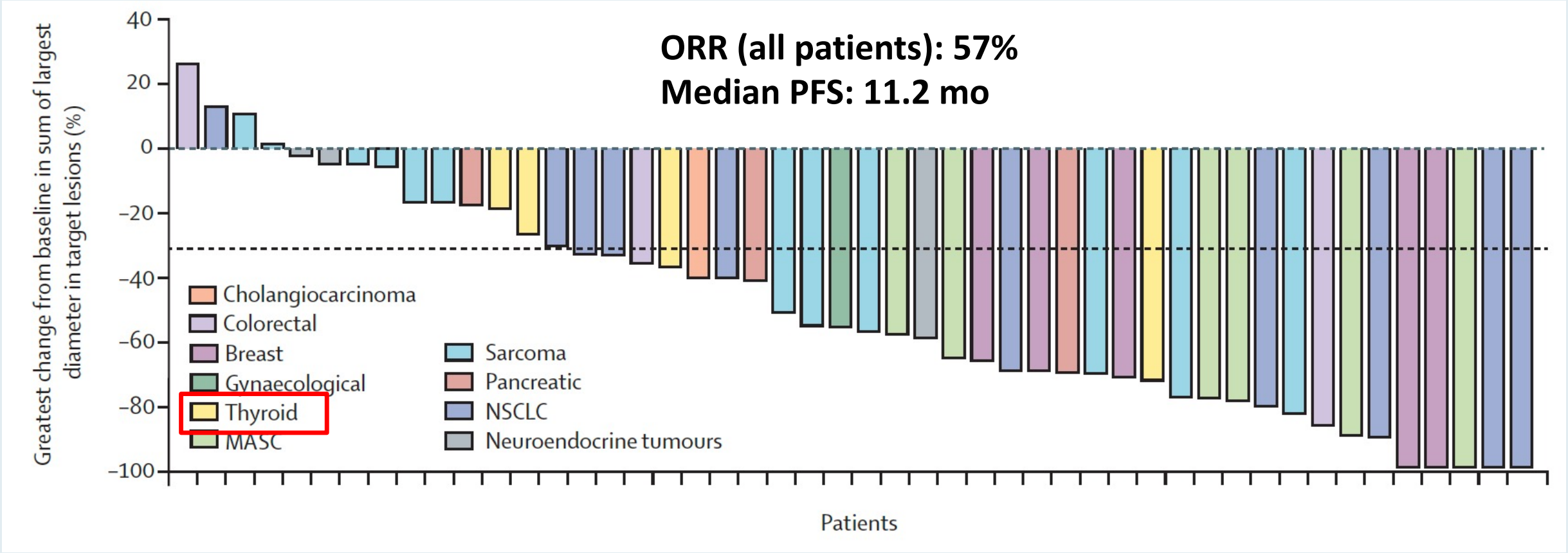
Robert C Doebele, Alexander Drilon*, Luis Paz-Ares, Salvatore Siena, Alice T Shaw, Anna F Farago, Collin M Blakely, Takashi Seto, Byung Chul Cho, Diego Tosi, Benjamin Besse, Sant P Chawla, Lyudmila Bazhenova, John C Krauss, Young Kwang Chae, Minal Barve, Ignacio Garrido-Laguna, Stephen V Liu, Paul Conkling, Thomas John, Marwan Fakih, Darren Sigal, Herbert H Loong, Gary L Buchschacher Jr, Pilar Garrido, Jorge Nieva, Conor Steuer, Tobias R Overbeck, Daniel W Bowles, Elizabeth Fox, Todd Riehl, Edna Chow-Maneval, Brian Simmons, Na Cui, Ann Johnson, Susan Eng, Timothy R Wilson, George D Demetri, on behalf of the trial investigators*

Entrectinib for Advanced or Metastatic Solid Tumors with NTRK Fusions (ALKA, STARTRK-1, STARTRK-2)

	All patients in *NTRK* gene fusion-positive efficacy-evaluable population (n=54)
Age, years	58 (48–67)
Tumour type	
Sarcoma‡	13 (24%)
NSCLC	10 (19%)
Mammary analogue secretory carcinoma (salivary)	7 (13%)
Breast	6 (11%)
Thyroid	5 (9%)
Colorectal	4 (7%)
Neuroendocrine	3 (6%)
Pancreatic	3 (6%)
Gynaecological	2 (4%)
Ovarian	1 (2%)
Endometrial	1 (2%)
Cholangiocarcinoma	1 (2%)

Doebele RC et al. *Lancet Oncol* 2020;21(2):271-82.

Entrectinib for Advanced or Metastatic Solid Tumors with NTRK Fusions (ALKA, STARTRK-1, STARTRK-2)



Doebele RC et al. *Lancet Oncol* 2020;21(2):271-82.

Optimal Selection and Sequencing of Multikinase Inhibitors for Thyroid Cancer

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Summary of FDA-Approved Multitargeted TKIs in Differentiated and Medullary Thyroid Cancer

Pivotal study — Agent	Study phase (N)	FDA approval year	Primary endpoint – PFS hazard ratio	Overall response rate
Medullary thyroid cancer				
ZETA[1] — vandetanib	Phase III (331)	2011	0.46	45% vs 13%
EXAM[2] — cabozantinib	Phase III (330)	2012	0.28	28% vs 0
Differentiated thyroid cancer				
DECISION[3] — sorafenib	Phase III (417)	2013	0.59	12.2% vs 0.5%
SELECT[4] — lenvatinib	Phase III (261)	2015	0.21	64.8% vs 1.5%

[1] Wells Jr SA et al. *J Clin Oncol* 2012;30(2):134-41. [2] Elisei R et al. *J Clin Oncol* 2013;31(29):3639-46. [3] Brose MS et al. *Lancet* 2014;384(9940):319-28. [4] Schlumberger M et al. *N Engl J Med* 2015;372(7):621-30.

Common Grade ≥3 Adverse Events with Approved Multitargeted TKIs for Differentiated and Medullary Thyroid Cancer

Grade ≥3 adverse events	Medullary thyroid cancer		Differentiated thyroid cancer	
	Vandetanib vs placebo ZETA[1] (N = 331)	Cabozantinib vs placebo EXAM[2] (N = 330)	Sorafenib vs placebo DECISION[3] (N = 417)	Lenvantinib vs placebo SELECT[4] (N = 261)
Hypertension	9% vs 0	8% vs 1%	10% vs 2%	42% vs 2%
Diarrhea	11% vs 2%	16% vs 2%	6% vs 1%	8% vs 0
Fatigue	6% vs 1%	9% vs 3%	6% vs 1%	9% vs 2%
Decreased appetite	4% vs 0	5% vs 1%	Not reported	5% vs 0
Stomatitis/mucositis	Not reported	2% vs 0	1% vs 0	4% vs 0
Hand-foot syndrome	Not reported	13% vs 0	20% vs 0	3% vs 0
Rash/pruritus	4% vs 0	1% vs 0	5% vs 0	<1% vs 0

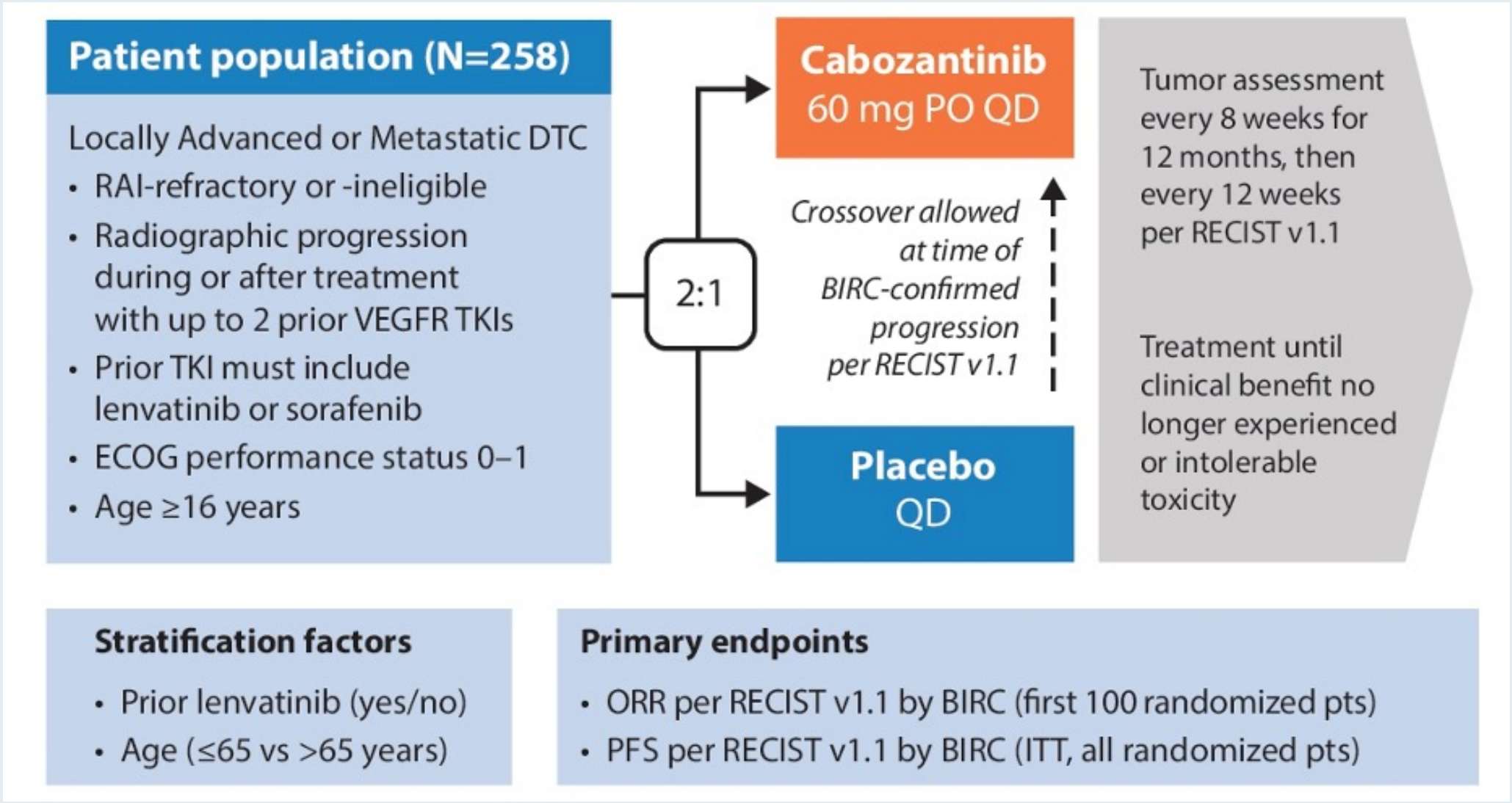
[1] Wells Jr SA et al. *J Clin Oncol* 2012;30(2):134-41. [2] Elisei R et al. *J Clin Oncol* 2013;31(29):3639-46. [3] Brose MS et al. *Lancet* 2014;384(9940):319-28. [4] Schlumberger M et al. *N Engl J Med* 2015;372(7):621-30.

Lancet Oncol 2021 August;22(8):1126-38.

Cabozantinib for radioiodine-refractory differentiated thyroid cancer (COSMIC-311): a randomised, double-blind, placebo-controlled, phase 3 trial

Marcia S Brose, Bruce Robinson, Steven I Sherman, Jolanta Krajewska, Chia-Chi Lin, Fernanda Vaisman, Ana O Hoff, Erika Hitre, Daniel W Bowles, Jorge Hernando, Leonardo Faoro, Kamalika Banerjee, Jennifer W Oliver, Bhumsuk Keam, Jaume Capdevila

COSMIC-311 Phase III Study Design



DTC = Differentiated thyroid cancer; RAI = radioactive iodine; TKI = tyrosine kinase inhibitor; ORR = objective response rate; BIRC = blinded independent central review; PFS = progression-free survival

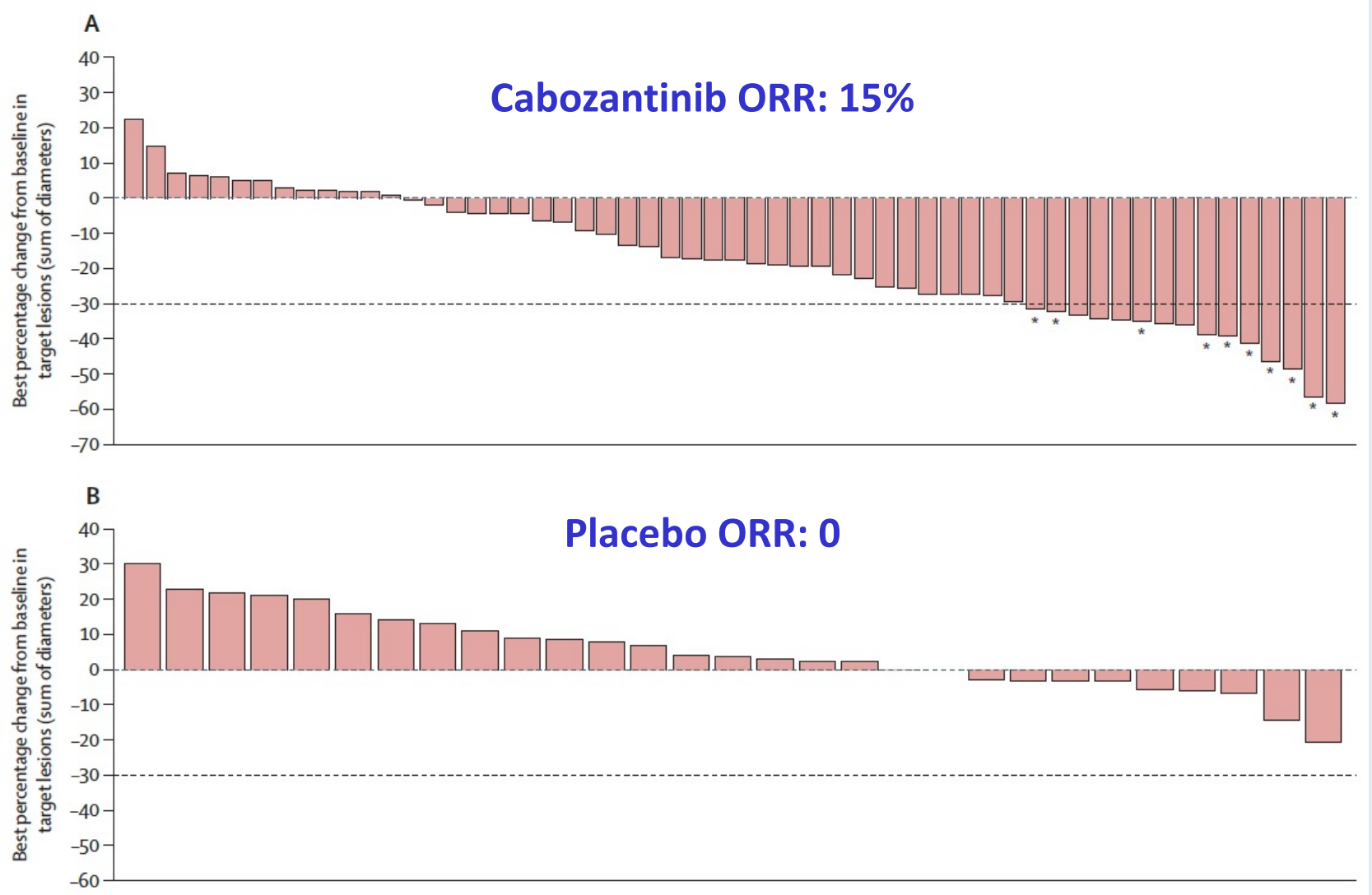
Capdevila J et al. ASCO 2022;Abstract 6081.

COSMIC-311: Baseline Clinical Characteristics

	Objective response rate intention-to-treat population		Intention-to-treat population	
	Cabozantinib group (n=67)	Placebo group (n=33)	Cabozantinib group (n=125)	Placebo group (n=62)
Age, years	62 (56–71)	63 (55–71)	65 (56–72)	66 (56–72)
≥65 years	32 (48%)	16 (48%)	63 (50%)	33 (53%)
Radioiodine therapy status†				
Refractory	65 (97%)	33 (100%)	121 (97%)	62 (100%)
Ineligible	3 (4%)	0	5 (4%)	0
Previous sorafenib or lenvatinib				
Sorafenib but no lenvatinib	26 (39%)	12 (36%)	46 (37%)	23 (37%)
Lenvatinib but no sorafenib	22 (33%)	13 (39%)	48 (38%)	26 (42%)
Sorafenib and lenvatinib	19 (28%)	8 (24%)	31 (25%)	13 (21%)
Number of previous vascular endothelial growth factor receptor tyrosine kinase inhibitors				
1	46 (69%)	24 (73%)	91 (73%)	48 (77%)
2	21 (31%)	9 (27%)	34 (27%)	14 (23%)
Thyroid stimulating hormone level, mIU/L	0·025 (0·01–0·06)	0·020 (0·01–0·06)	0·023 (0·01–0·06)	0·019 (0·01–0·04)
Histological subtype‡				
Papillary	39 (58%)	20 (61%)	67 (54%)	35 (56%)
Follicular	30 (45%)	13 (39%)	62 (50%)	28 (45%)

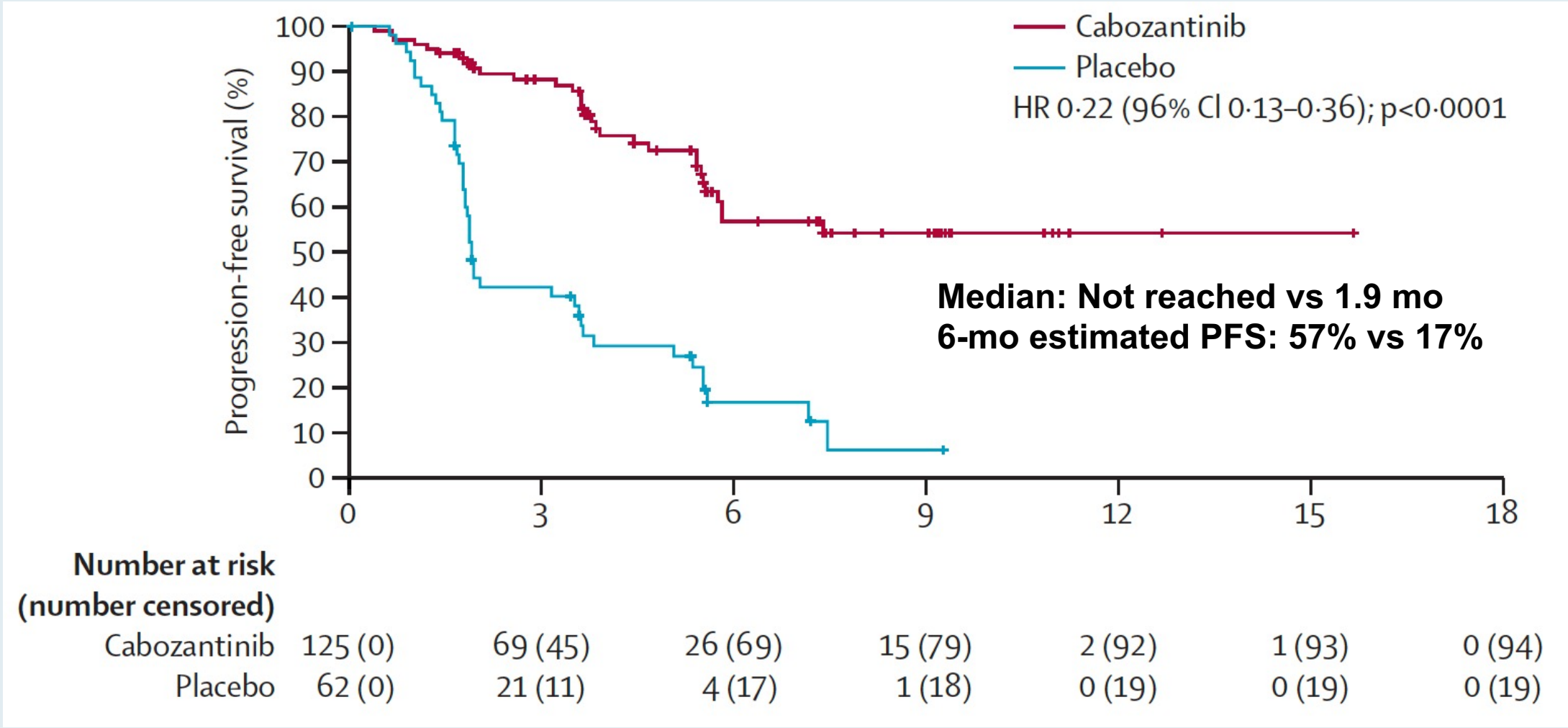
Brose MS et al. *Lancet Oncol* 2021 August;22(8):1126-38.

COSMIC-311: Response



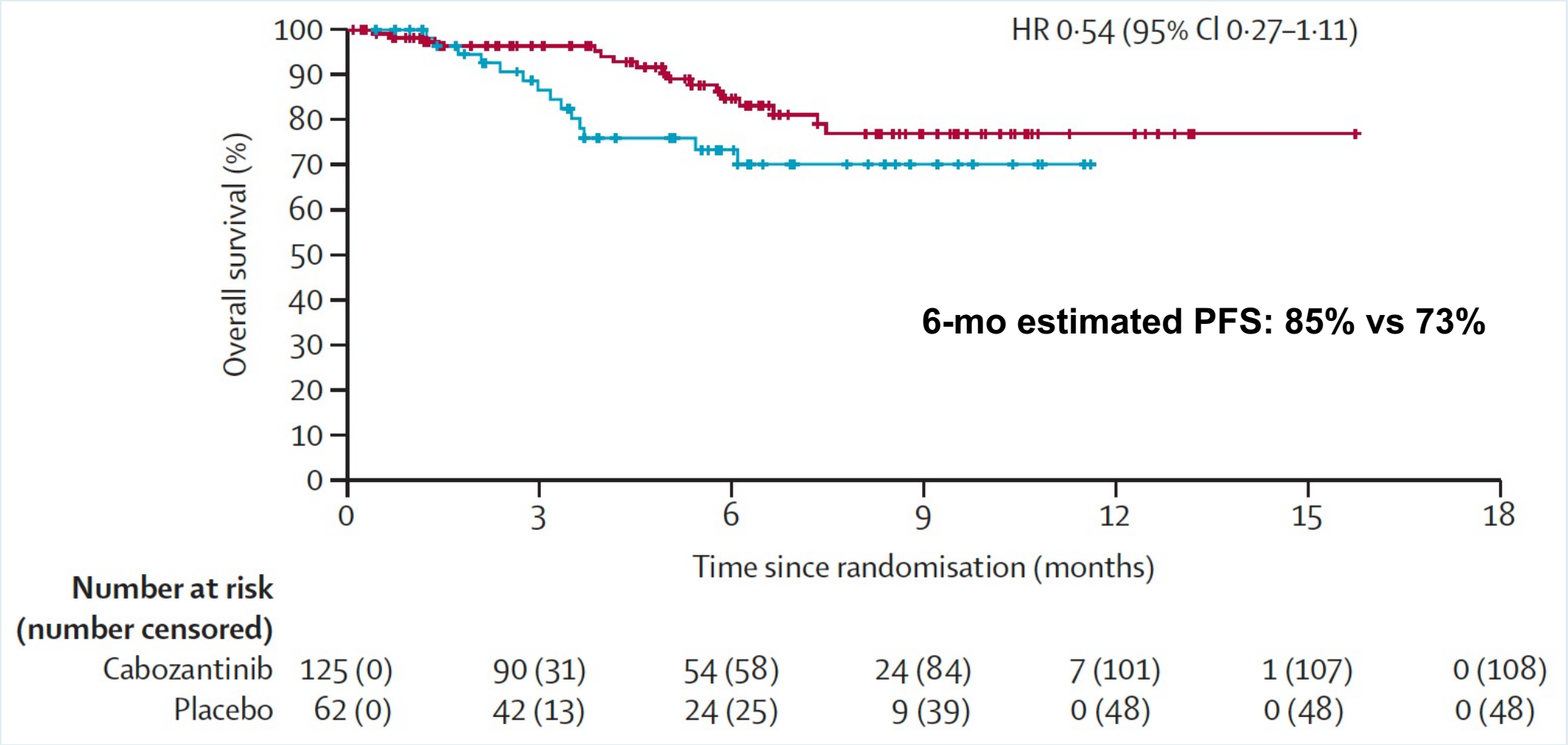
Brose MS et al. *Lancet Oncol* 2021 August;22(8):1126-38.

COSMIC-311: Progression-Free Survival (ITT, BIRC)



Brose MS et al. *Lancet Oncol* 2021 August;22(8):1126-38.

COSMIC-311: Overall Survival (ITT, BIRC)



Number at risk (number censored)							
Cabozantinib	125 (0)	90 (31)	54 (58)	24 (84)	7 (101)	1 (107)	0 (108)
Placebo	62 (0)	42 (13)	24 (25)	9 (39)	0 (48)	0 (48)	0 (48)

Brose MS et al. *Lancet Oncol* 2021 August;22(8):1126-38.

Meet The Professor

Optimizing the Management of Small Cell Lung Cancer

Wednesday, September 21, 2022
5:00 PM – 6:00 PM ET

Faculty

Carl M Gay, MD, PhD

Moderator

Neil Love, MD

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Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.

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