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

A CME/MOC- and NCPD-Accredited Event

Saturday, October 22, 2022
7:30 AM – 5:30 PM ET

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Agenda

Module 1 — Lung Cancer: *Drs Langer and Lovly*

Module 2 — Chronic Lymphocytic Leukemia and Lymphomas: *Drs LaCasce and Smith*

Module 3 — Prostate and Bladder Cancers: *Drs Morgans and Yu*

Module 4 — Renal Cell Carcinoma: *Prof Powles*

Module 5 — Multiple Myeloma: *Dr Usmani*

Module 6 — Hepatobiliary Cancers: *Dr Abou-Alfa*

Agenda

Module 7 — Breast Cancer: *Drs Goetz and Krop*

Module 8 — Endometrial Cancer: *Dr Westin*

Module 9 — Ovarian Cancer and PARP Inhibitors: *Dr O'Malley*

Module 10 — Gastrointestinal Cancers: *Drs Messersmith and Strickler*

Module 11 — Melanoma: *Prof Long*

Renal Cell Carcinoma Faculty

Thomas Powles, MBBS, MRCP, MD
Professor of Genitourinary Oncology
Barts Cancer Institute
Director of Barts Cancer Centre
Queen Mary University of London
London, United Kingdom

Renal Cell Carcinoma Agenda

MODULE 1: Optimal First-Line Therapy for Patients with Metastatic RCC

MODULE 2: Management of High-Risk Renal Cell Carcinoma (RCC) in the Adjuvant Setting

MODULE 3: Treatment Approaches for Relapsed/Refractory Metastatic RCC

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1ST LINE RENAL CANCER AND COSMIC-313

Thomas Powles

Director of Barts Cancer Centre.

The story so far: PD-1 based therapy with VEGF TKI or CTLA-4 depending on IMDC risk group.

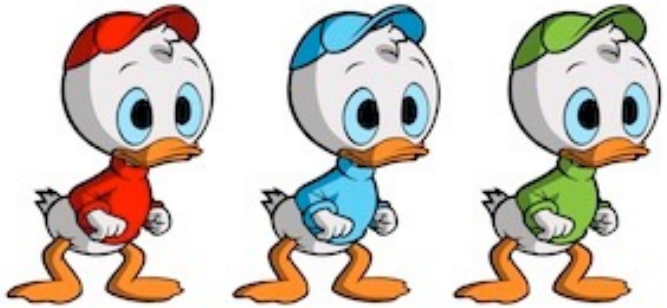
Good risk disease	Intermediate and poor risk disease
VEGF TKI and PD1 inhibition	VEGF TKI and PD1 inhibition
Sunitinib or pazopanib	CTLA4 and PD1 inhibition

ITT data

Subset data

VEGF TKI & PD1 combinations

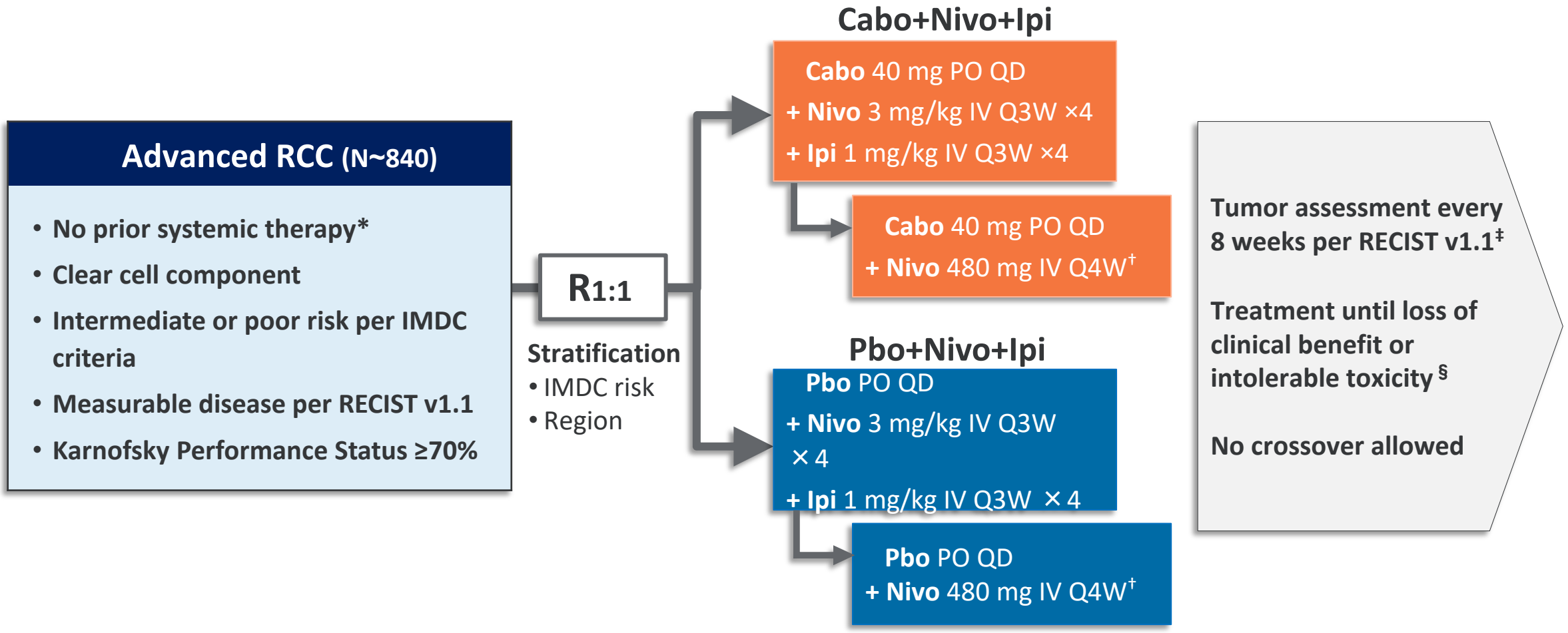
More similarities than differences



CTLA4 & PD1 combination

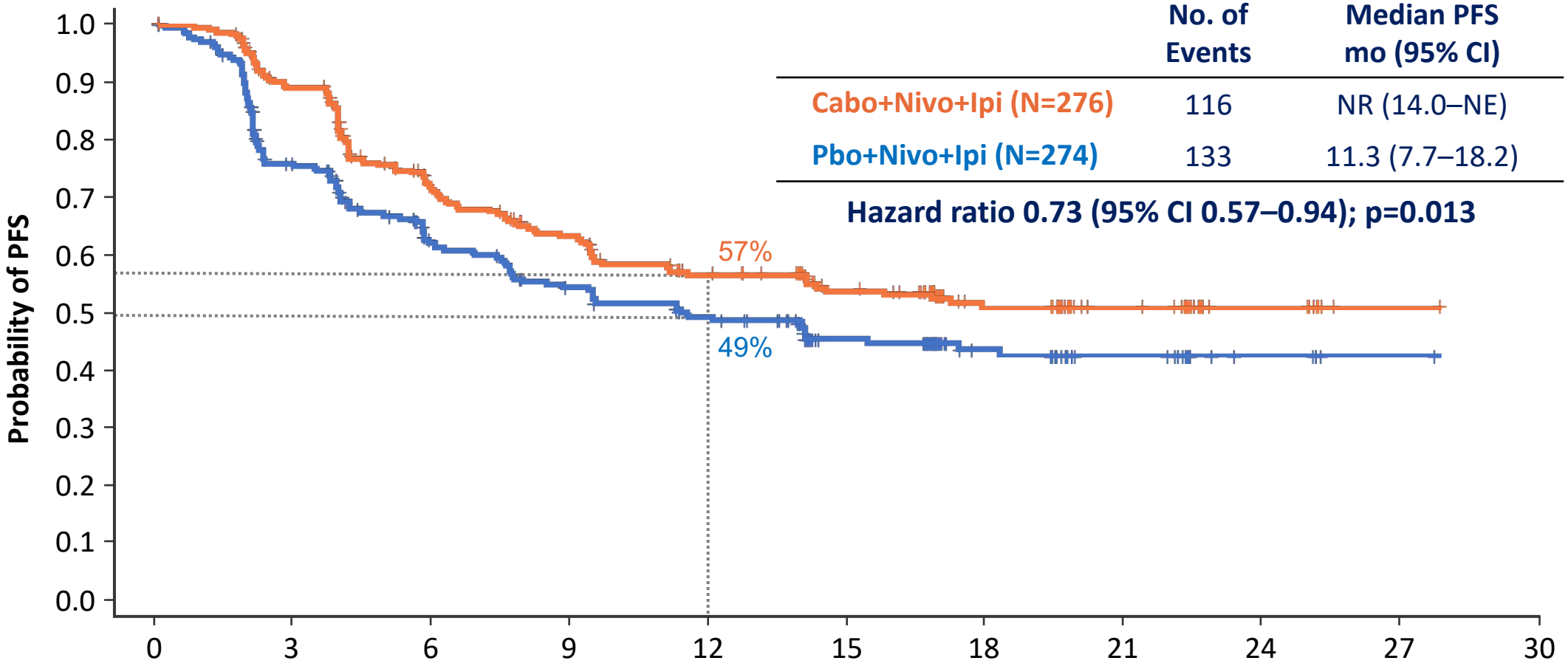
- Less good than VEGF/PD1 at getting initial control of disease
- Thought to be associated with more durable remissions
- Randomised data awaited

COSMIC-313 Study Design



*One prior systemic adjuvant therapy allowed for completely resected RCC and if recurrence occurred ≥6 months after the last dose of adjuvant therapy; adjuvant PD-1 or PD-L1 inhibitor in combination with a CTLA-4 inhibitor not permitted. †Nivolumab given for a maximum of 2 years. ‡Tumor assessment (RECIST v1.1) at week 10, then every 8 weeks through week 50, then every 12 weeks thereafter. §Discontinuation of one agent did not mandate discontinuation of all agents.

COSMIC-313: PFS Final Analysis (PITT Population)



	No. of Events	Median PFS mo (95% CI)
Cabo+Nivo+Ipi (N=276)	116	NR (14.0–NE)
Pbo+Nivo+Ipi (N=274)	133	11.3 (7.7–18.2)

Hazard ratio 0.73 (95% CI 0.57–0.94); p=0.013

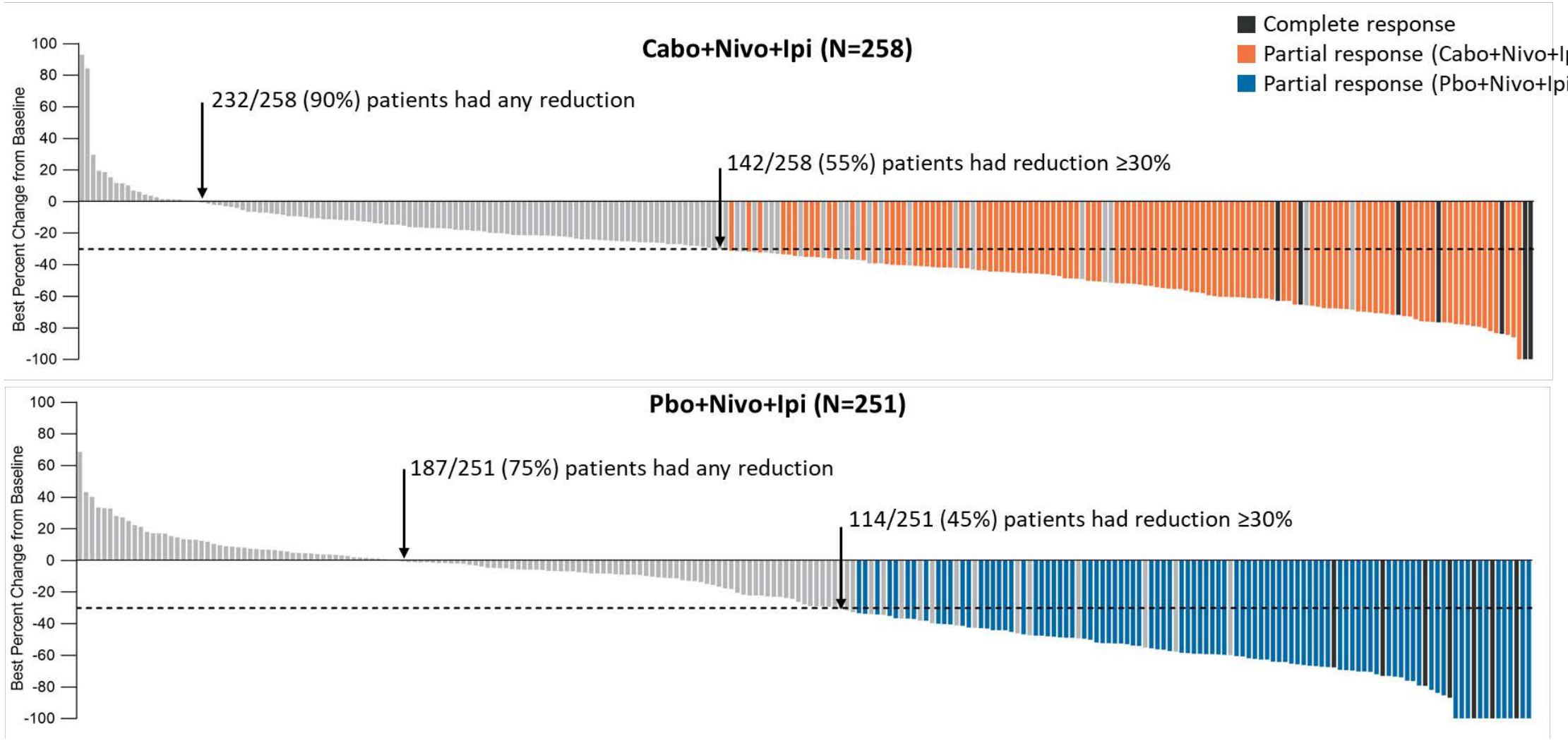
Number at Risk

Cabo+Nivo+Ipi	276	234	170	145	119	97	56	33	10	1	0
Pbo+Nivo+Ipi	274	185	136	115	98	69	37	19	5	1	0

PFS per RECIST v1.1 by BIRC.

Data cut-off: Aug 23, 2021

More shrinkage with triplet but less deep responses



Sumanta K. Pal, MD, FASCO

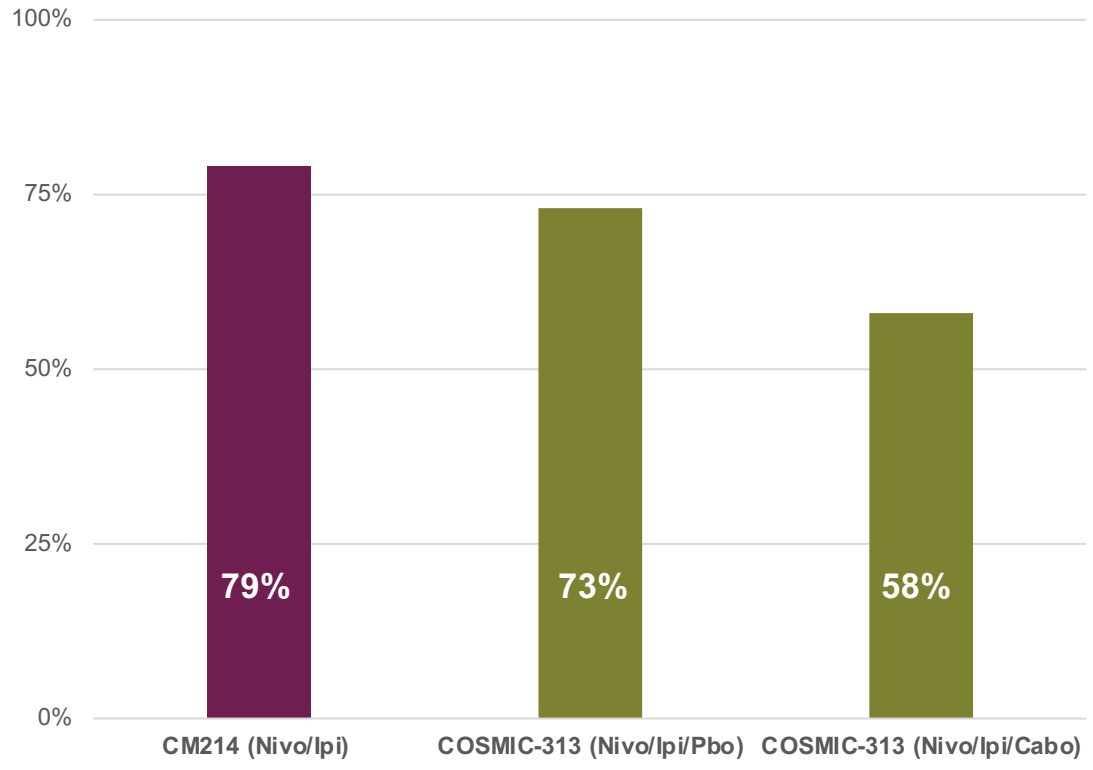
Treatment Exposure and Discontinuation (Safety Population)

	Cabo+Nivo+Ipi (N=426)	Pbo+Nivo+Ipi (N=424)
Median duration of exposure of study treatment (range), mo	10.9 (0.2–28.5)	10.3 (0.1–28.1)
Median average daily dose (range) of Cabo or Pbo, mg	23.2 (3.6–40.0)	36.1 (0.8–40.0)
Median Nivo infusions (range) received, no	10 (1–27)	9 (1–27)
Doses of Ipi received, %		
4	58	73
3	13	14
2	22	7
1	7	6
Any dose hold due to an AE, %	90	70
Any dose reduction of Cabo or Pbo due to an AE, %	54	20
Treatment-related AE leading to discontinuation, %		
Any study treatment	45	24
Cabo or Pbo	28	14
Nivo	26	18
Ipi	30	12
All treatment components (due to the same AE)	12	5

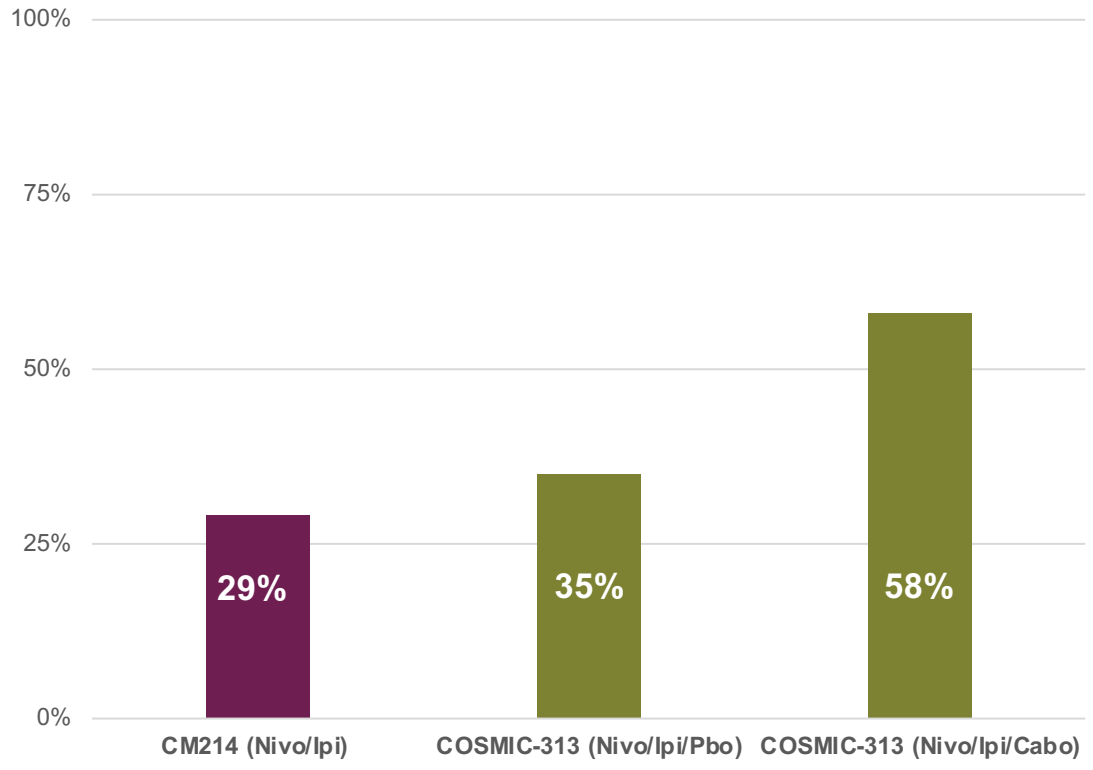
Data cut-off: Jan 31, 2022

Toxicity limited drug delivery

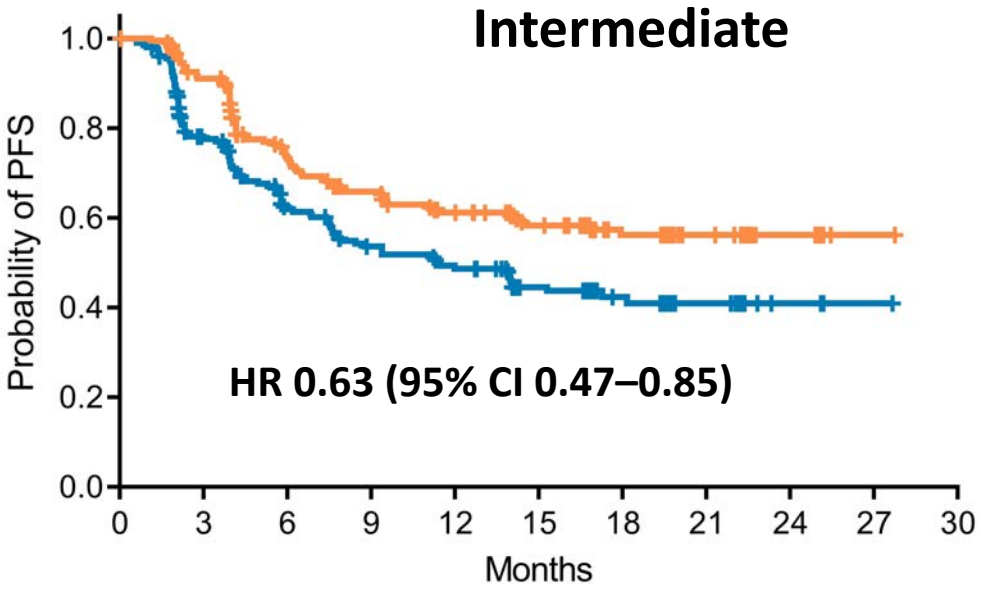
Proportion of patients receiving 4 doses of ipilimumab

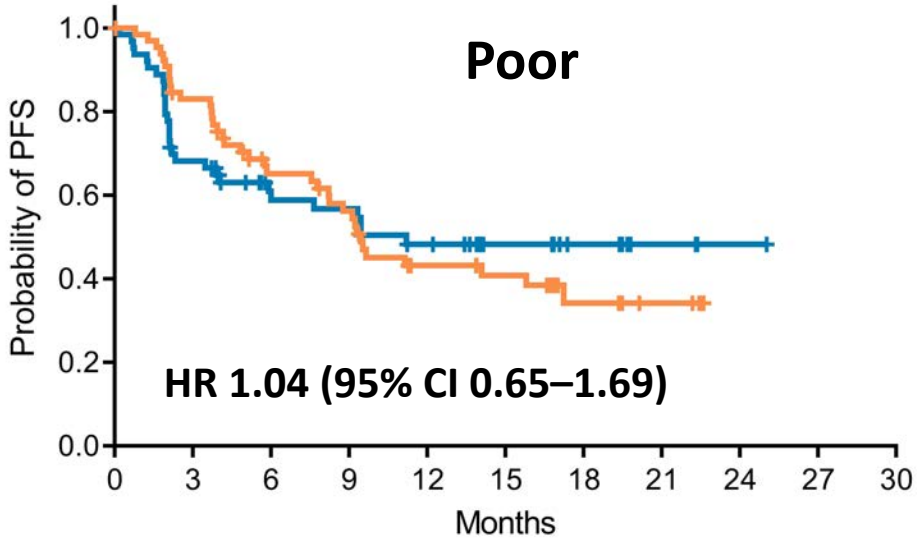


Proportion of patients receiving >40 mg of prednisone or equivalent



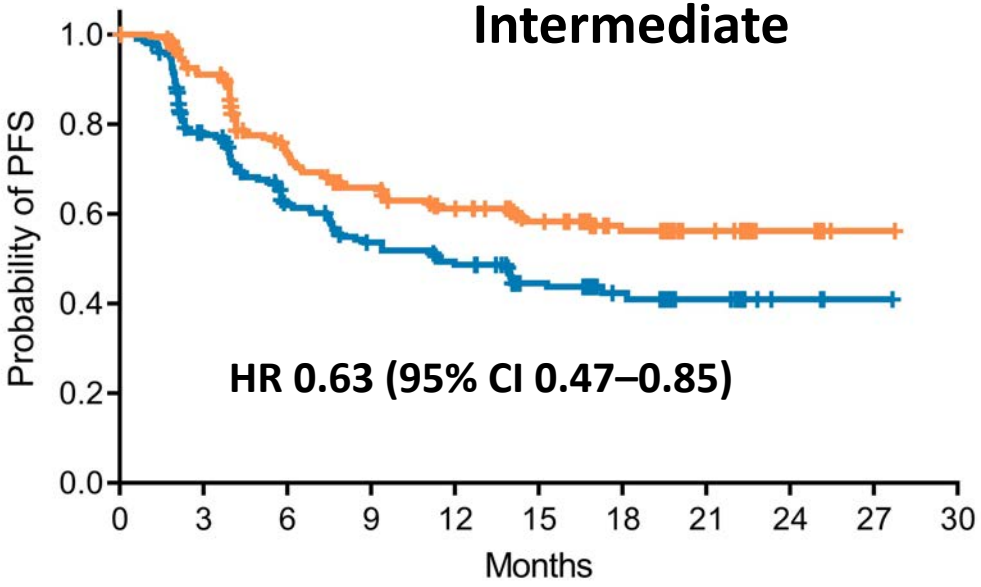
COSMIC-313: PFS by IMDC Risk Group (PITT Population)

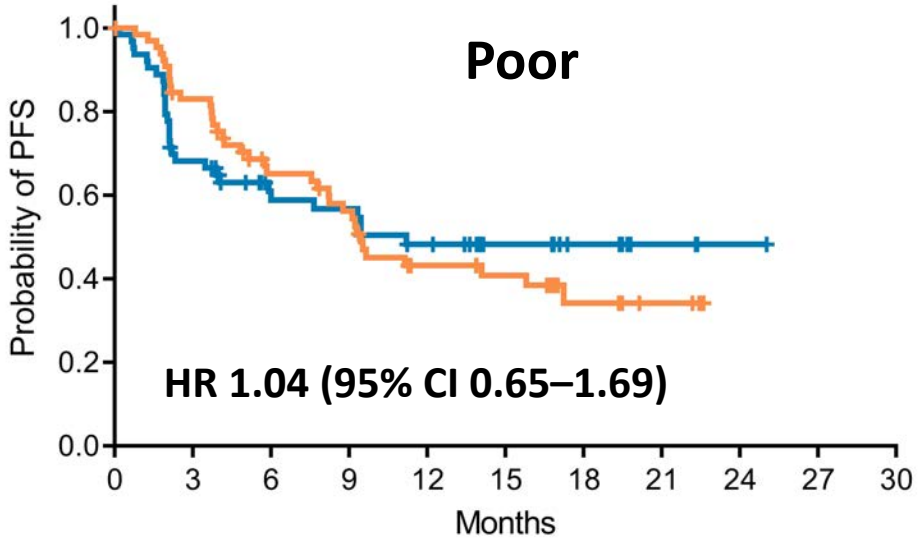


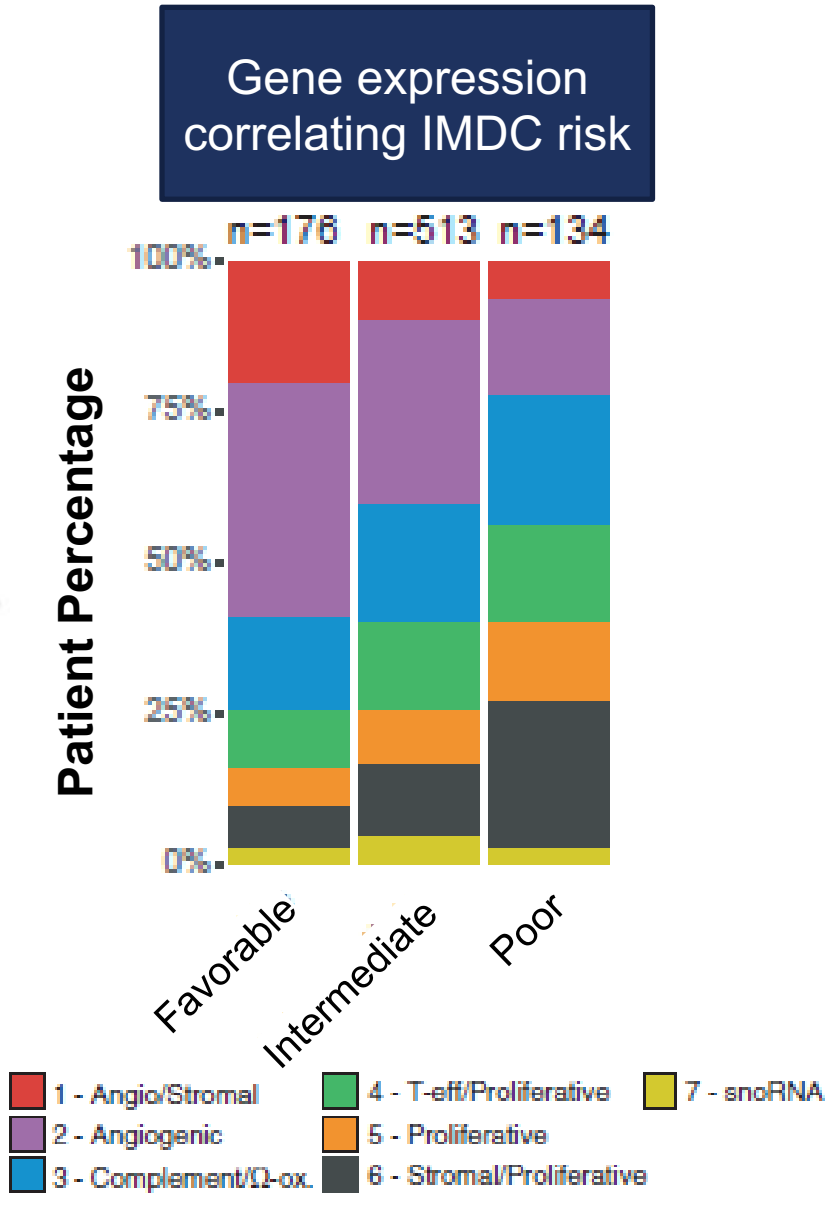


Data cut-off: Aug 23, 2021

COSMIC-313: PFS by IMDC Risk Group (PITT Population)







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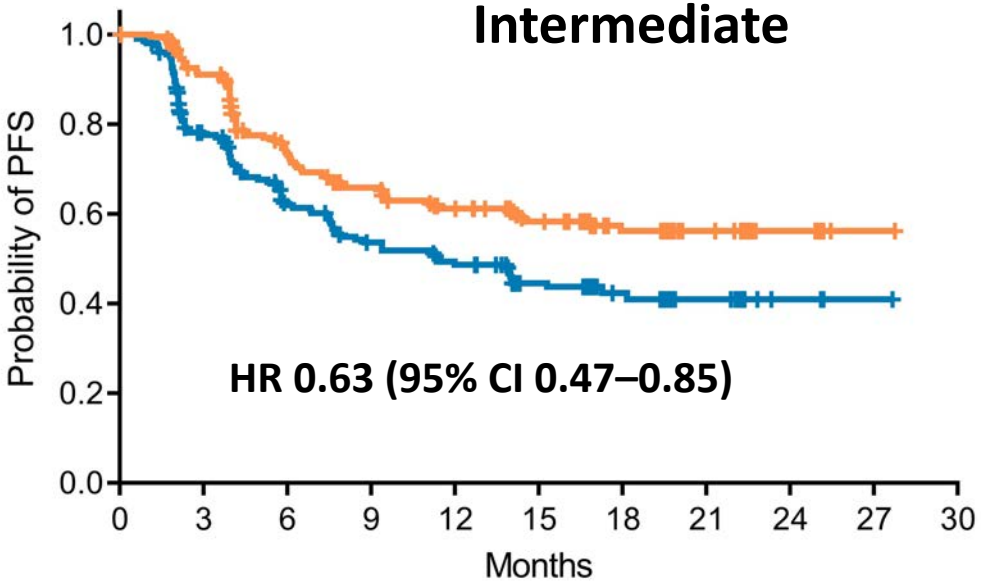
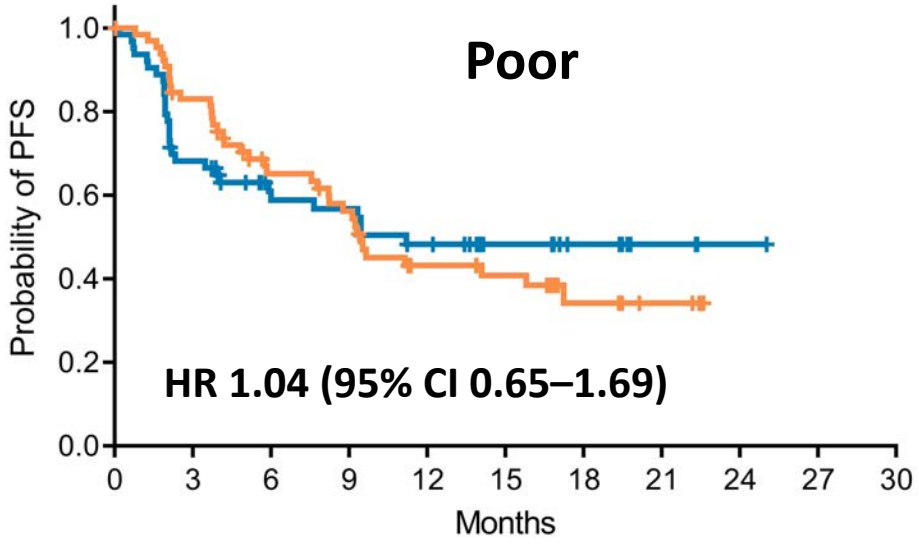
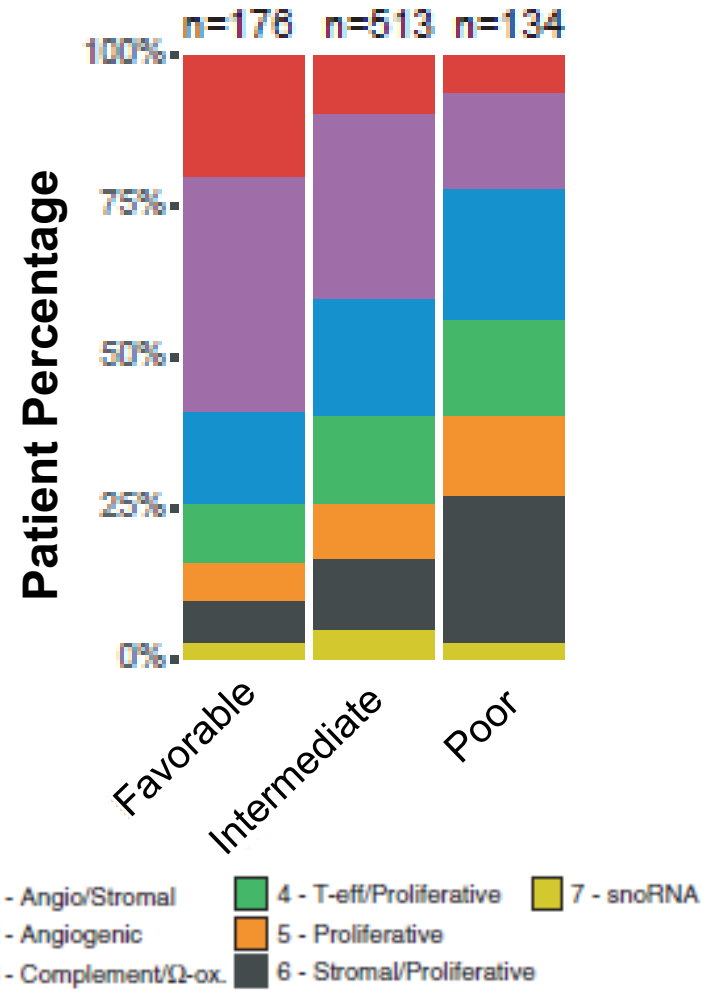
COSMIC-313: PFS by IMDC Risk Group (PITT Population)

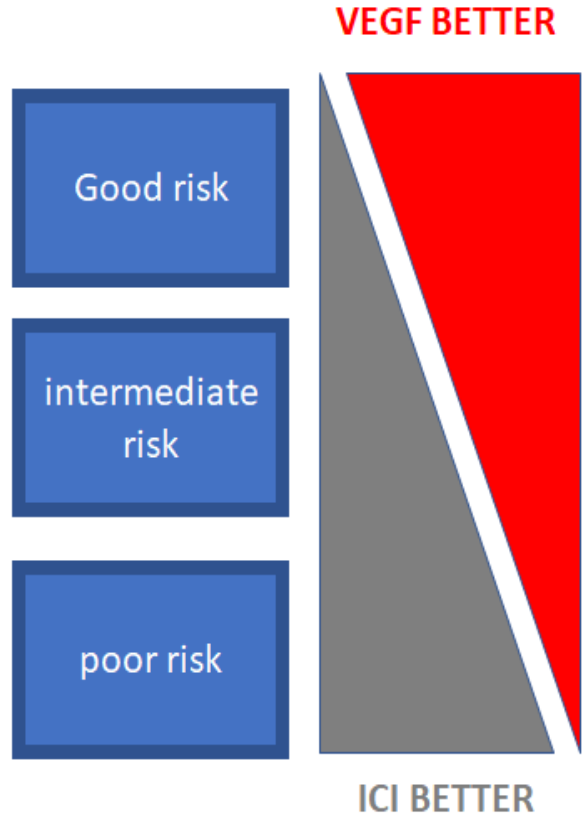




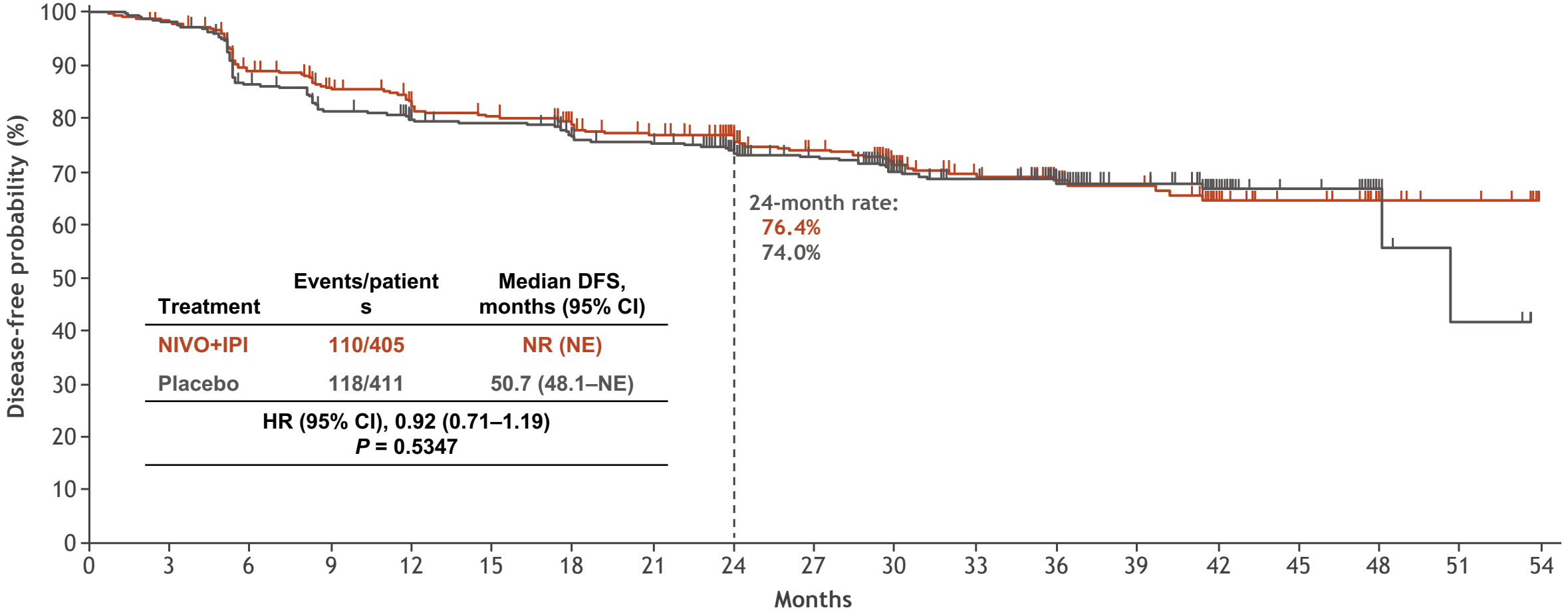
Gene expression correlating IMDC risk



A summary of efficacy and IMDC risk



Does a negative adjuvant trial for ipilimumab and nivolumab have any impact on how we think about 1st line?



Median (range) follow-up, 37.0 (15.4–58.0) months.
As the DFS endpoint was not met, no formal analysis of OS was performed (in total, there were 33 deaths in the NIVO+IPI arm and 28 deaths in the placebo arm).

What does all this mean?

- It's unlikely the triple of cabo/ipi/nivo will have a big impact on 1st line treatment without an OS advantage.
- It’s hard to identify a patient population to treat, we thought the IMDC poor risk to get control, but the data doesn’t support that.
- Triplet therapy looked difficult to give.
- Other triplet trials may be different and these results are awaited.

Discussion Questions

- Regulatory and reimbursement issues aside, what do you consider the optimal approach to first-line therapy for mRCC?

Renal Cell Carcinoma Agenda

MODULE 1: Optimal First-Line Therapy for Patients with Metastatic RCC

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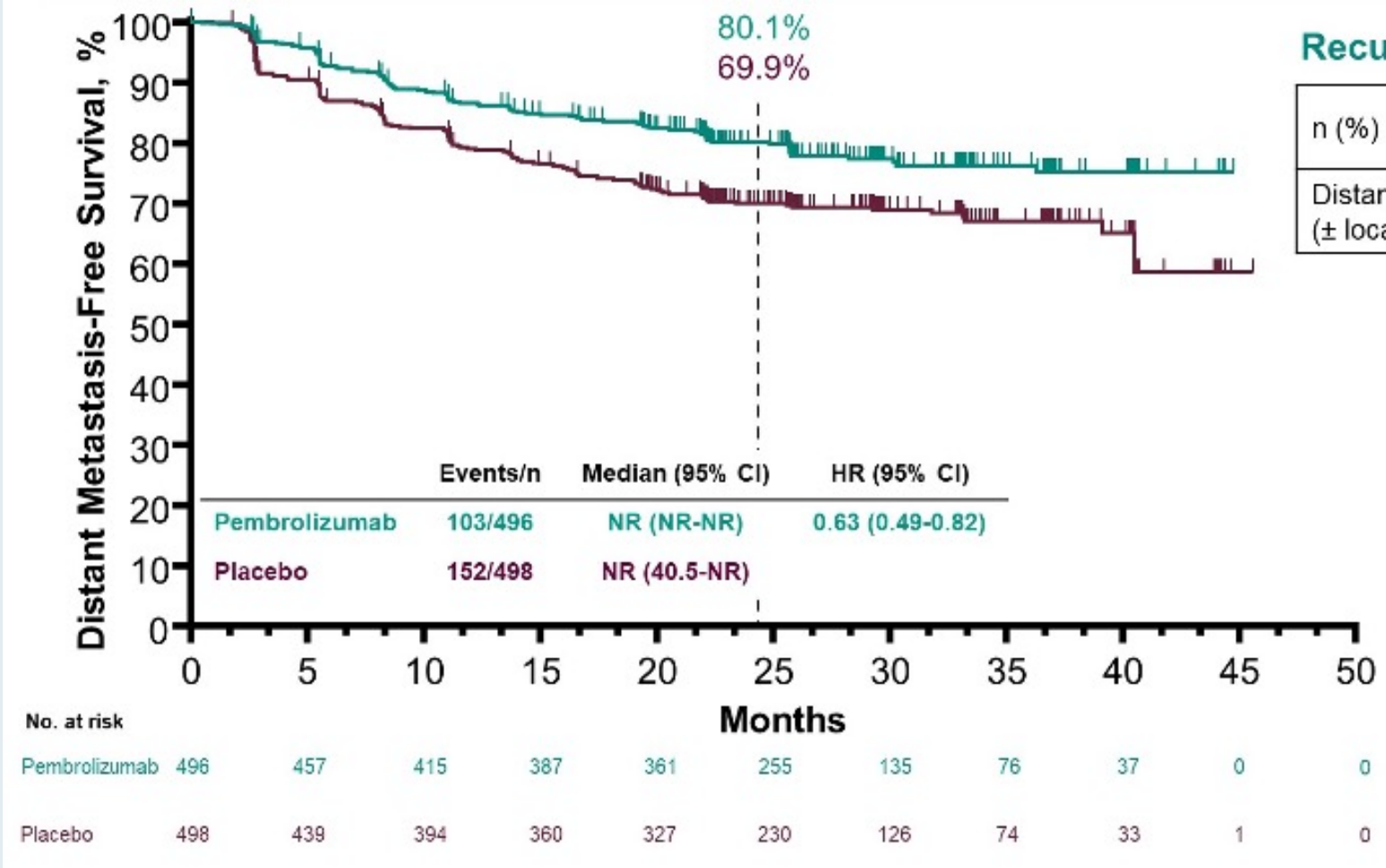
Adjuvant pembrolizumab for postnephrectomy renal cell carcinoma: Expanded efficacy analyses from KEYNOTE-564

T. K. Choueiri[1]; P. Tomczak[2]; S. H. Park[3]; B. Venugopal[4]; T. Ferguson[5]; S. N. Symeonides[6]; J. Hajek[7]; Y.-H. Chang[8]; J.-L. Lee[9]; N. Sarwar[10]; A. Thiery-Vuillemin[11]; M. Gross-Goupil[12]; M. Mahave[13]; N. B. Haas[14]; P. Sawrycki[15]; H. Gurney[16]; L. Xu[17]; K. Imai[17]; J. Burgents[17]; T. Powles[18]

[1]Dana-Farber Cancer Institute and Harvard Medical School, Boston, MA, USA; [2]Poznan University of Medical Sciences, Poznan, Poland; [3]Sungkyunkwan University, Samsung Medical Center, Seoul, South Korea; [4]Beatson West of Scotland Cancer Centre and University of Glasgow, Glasgow, United Kingdom; [5]Fiona Stanley Hospital, Perth, WA, Australia; [6]Edinburgh Cancer Centre and University of Edinburgh, Edinburgh, United Kingdom; [7]Fakultni Nemocnice Ostrava, Ostrava, Czech Republic; [8]Taipei Veterans General Hospital, Taipei, Taiwan; [9]Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea; [10]Imperial College Healthcare NHS Trust, London, United Kingdom; [11]University Hospital Jean Minjoz, Besançon, France; [12]University Hospital of Bordeaux, Bordeaux, France; [13]Fundacion Arturo Lopez Perez FALP, Santiago, Chile; [14]Abramson Cancer Center, Penn Medicine, Philadelphia, PA, USA; [15]Provincial Hospital in Torun, Torun, Poland; [16]Macquarie University, Sydney, NSW, Australia; [17]Merck & Co., Inc., Rahway, NJ, USA; [18]Barts Health NHS Trust and the Royal Free NHS Foundation Trust, Barts Cancer Institute, and Queen Mary University of London, London, United Kingdom

ASCO 2022;Abstract 4512

KEYNOTE-564: Pembrolizumab as Adjuvant Therapy for Patients with Renal Cell Carcinoma – Disease-Free Survival



Recurrence events

n (%)	Pembrolizumab n = 496	Placebo n = 498
Distant (± local)	95 (19.2)	140 (28.1)

Choueiri TK et al. ASCO 2022;Abstract 4512.

Select Ongoing Phase III Clinical Trials of Immune Checkpoint Inhibitors as Neoadjuvant or Adjuvant Therapy for High-Risk RCC

Trial identifier	N	Study arms	Estimated primary completion date
PROSPER (NCT03055013)	766	• Nivolumab → nephrectomy → nivolumab • Nephrectomy	November 2023
RAMPART (NCT03288532)	1,750	• Active monitoring • Durvalumab • Durvalumab + tremelimumab	July 2024
MK-6482-022 (NCT05239728)	1,600	• Pembrolizumab + belzutifan • Pembrolizumab + placebo	October 2027

www.clinicaltrials.gov. Accessed September 2022.

Renal Cell Carcinoma Agenda

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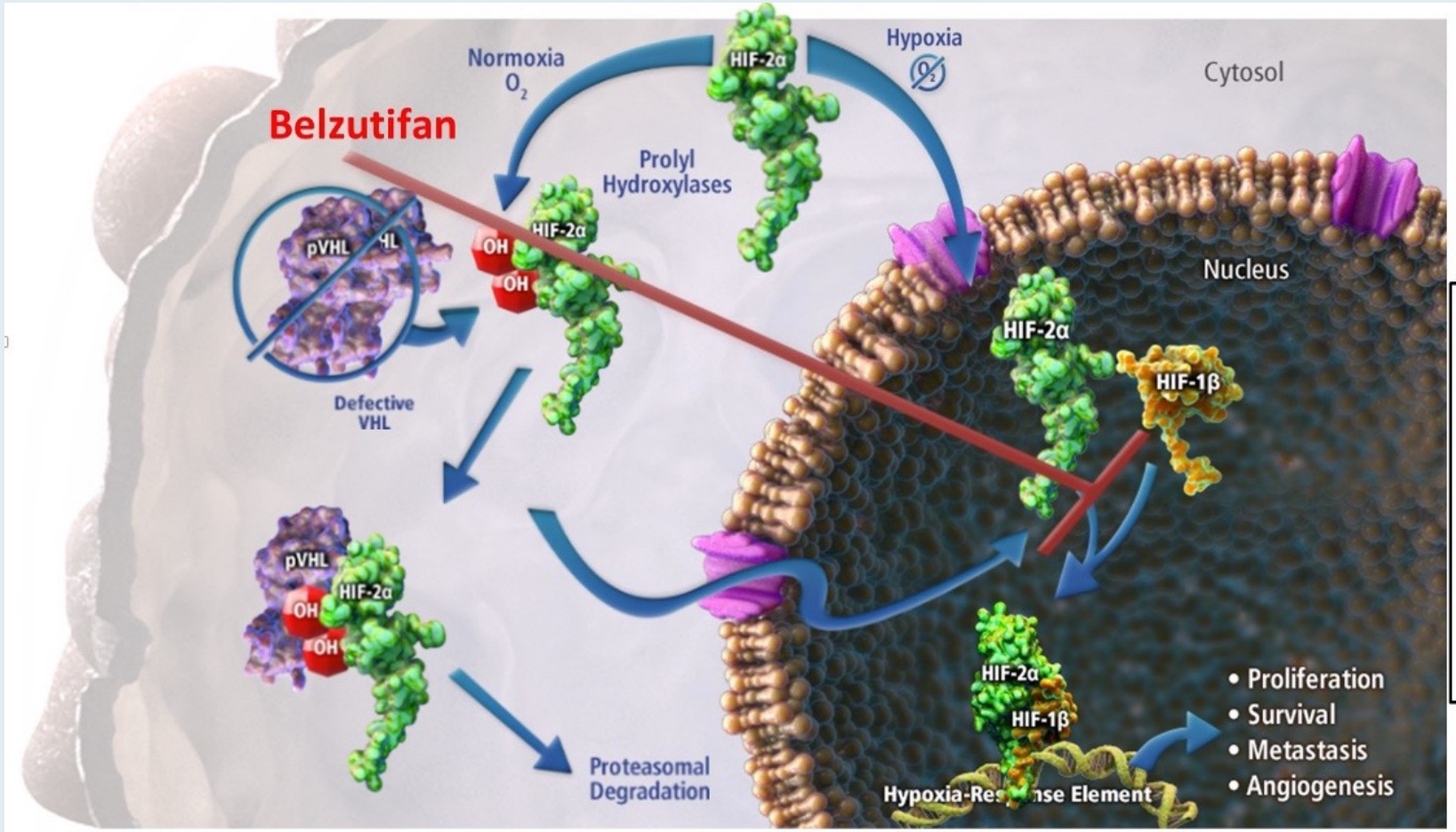
Belzutifan Is a Selective Small Molecule Inhibitor of HIF-2-alpha



- 90% of patients with sporadic ccRCC have defective pVHL function[1]
- Loss of pVHL function results in constitutive activation of HIF-2α[2]
- Belzutifan is a potent, selective, small molecule HIF-2α inhibitor

1. Linehan WM, Rickets CJ. *Nat Rev Urol.* 2019;16:539-552. 2. Couvé S et al. *Cancer Res.* 2014;74:6554-6564.

ccRCC = clear cell RCC

Bauer TD et al. Genitourinary Cancers Symposium 2021;Abstract 273.

The NEW ENGLAND JOURNAL of MEDICINE

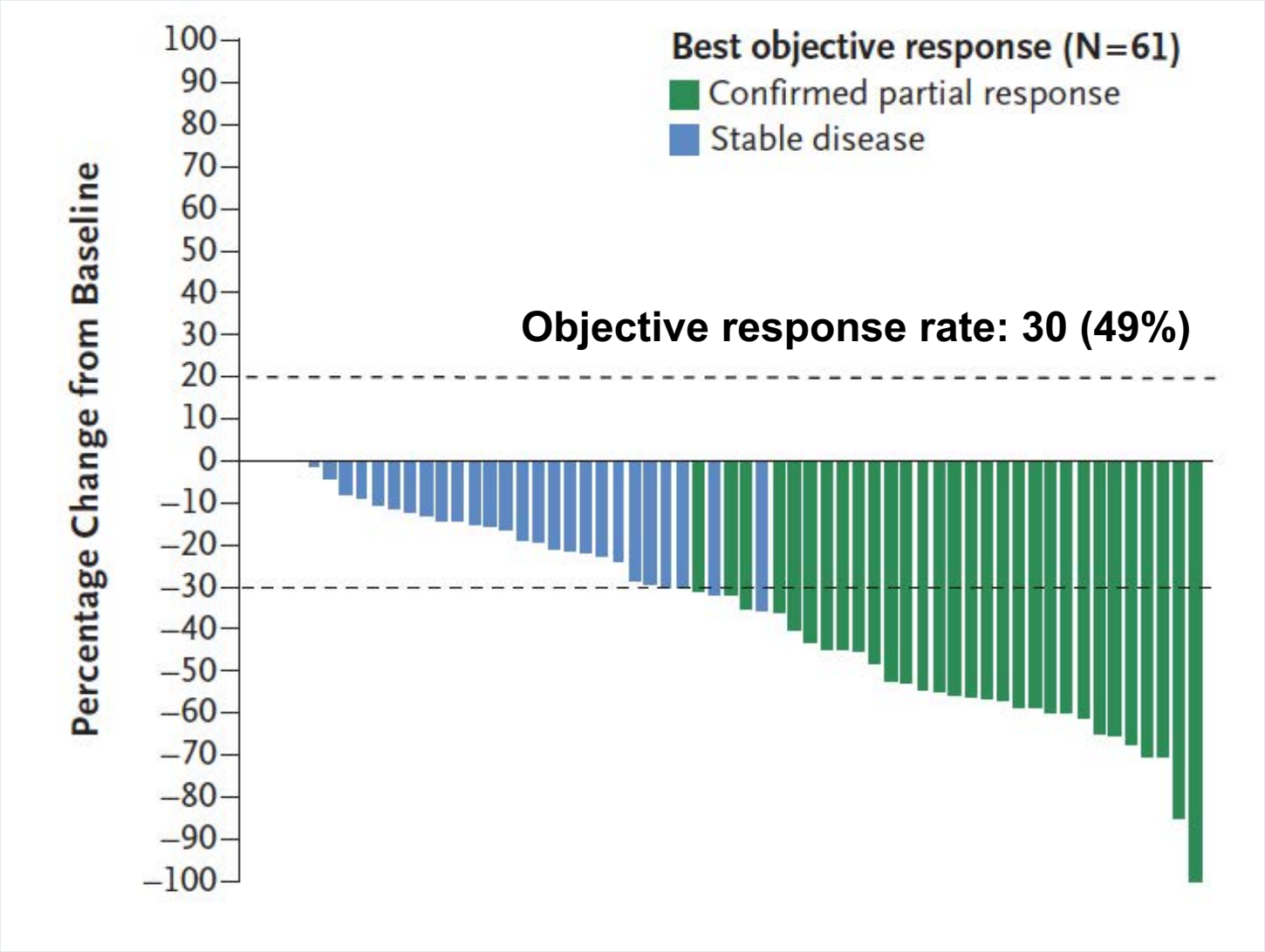
ORIGINAL ARTICLE

Belzutifan for Renal Cell Carcinoma in von Hippel–Lindau Disease

Eric Jonasch, M.D., Frede Donskov, M.D., Ph.D., Othon Iliopoulos, M.D., W. Kimryn Rathmell, M.D., Ph.D., Vivek K. Narayan, M.D., Benjamin L. Maughan, M.D., Stephane Oudard, M.D., Tobias Else, M.D., Jodi K. Maranchie, M.D., Sarah J. Welsh, M.D., Sanjay Thamake, Ph.D., Eric K. Park, M.D., Rodolfo F. Perini, M.D., W. Marston Linehan, M.D., and Ramaprasad Srinivasan, M.D., Ph.D., for the MK-6482-004 Investigators*

N Engl J Med 2021;385:2036-46.

Phase II Trial of Belzutifan: Maximum Change in Target Renal Tumors



Jonasch E et al. *N Engl J Med* 2021;385:2036-46.

Phase II Trial of Belzutifan: Select Adverse Events

Adverse event (n = 61)	Any grade	Grade 3
Anemia	55 (90%)	5 (8%)
Fatigue	40 (66%)	3 (5%)
Dyspnea	14 (23%)	1 (2%)
Myalgia	12 (20%)	1 (2%)
Hypertension	10 (16%)	5 (8%)
Diarrhea	8 (13%)	1 (2%)

Jonasch E et al. *N Engl J Med* 2021;385:2036-46.

Select Ongoing Phase III Clinical Trials of Belzutifan for Advanced RCC

Trial identifier	N	Study arms	Estimated primary completion date
MK-6482-012 (NCT04195750)	736	• Belzutifan • Everolimus	September 2025
MK-6482-012 (NCT04736706)	1,653	• Belzutifan + pembrolizumab + lenvatinib • Pembrolizumab/quavonlimab + lenvatinib • Pembrolizumab + lenvatinib	October 2026
NCT04586231	708	• Belzutifan + lenvatinib • Cabozantinib	December 2024

www.clinicaltrials.gov. Accessed September 2022.

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Thank you for joining us!

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

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