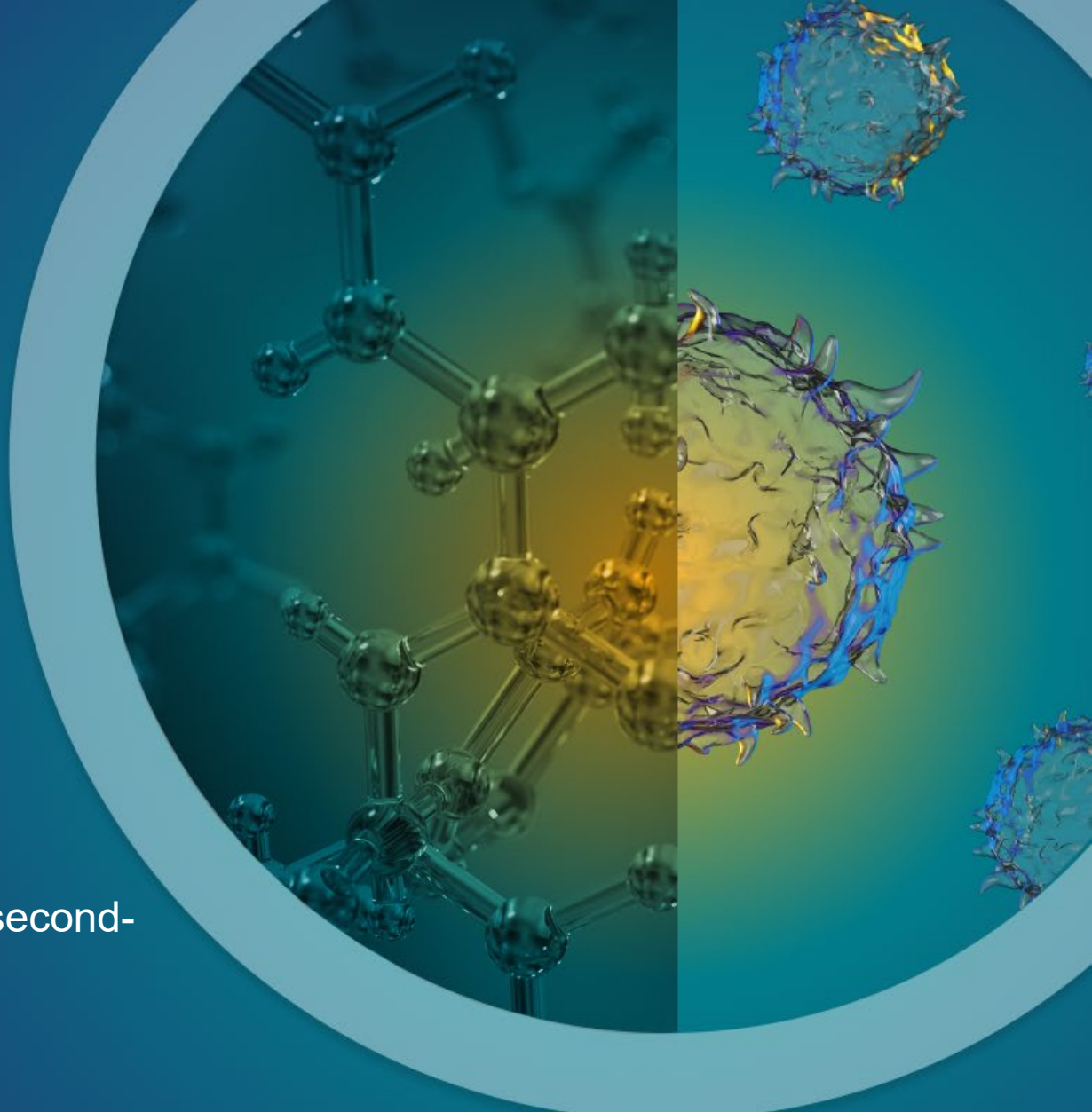


Casdatifan Investor Day

New monotherapy and combination data in first-line, second-line and late-line kidney cancer

October 20, 2026



ARCUS
BIOSCIENCES

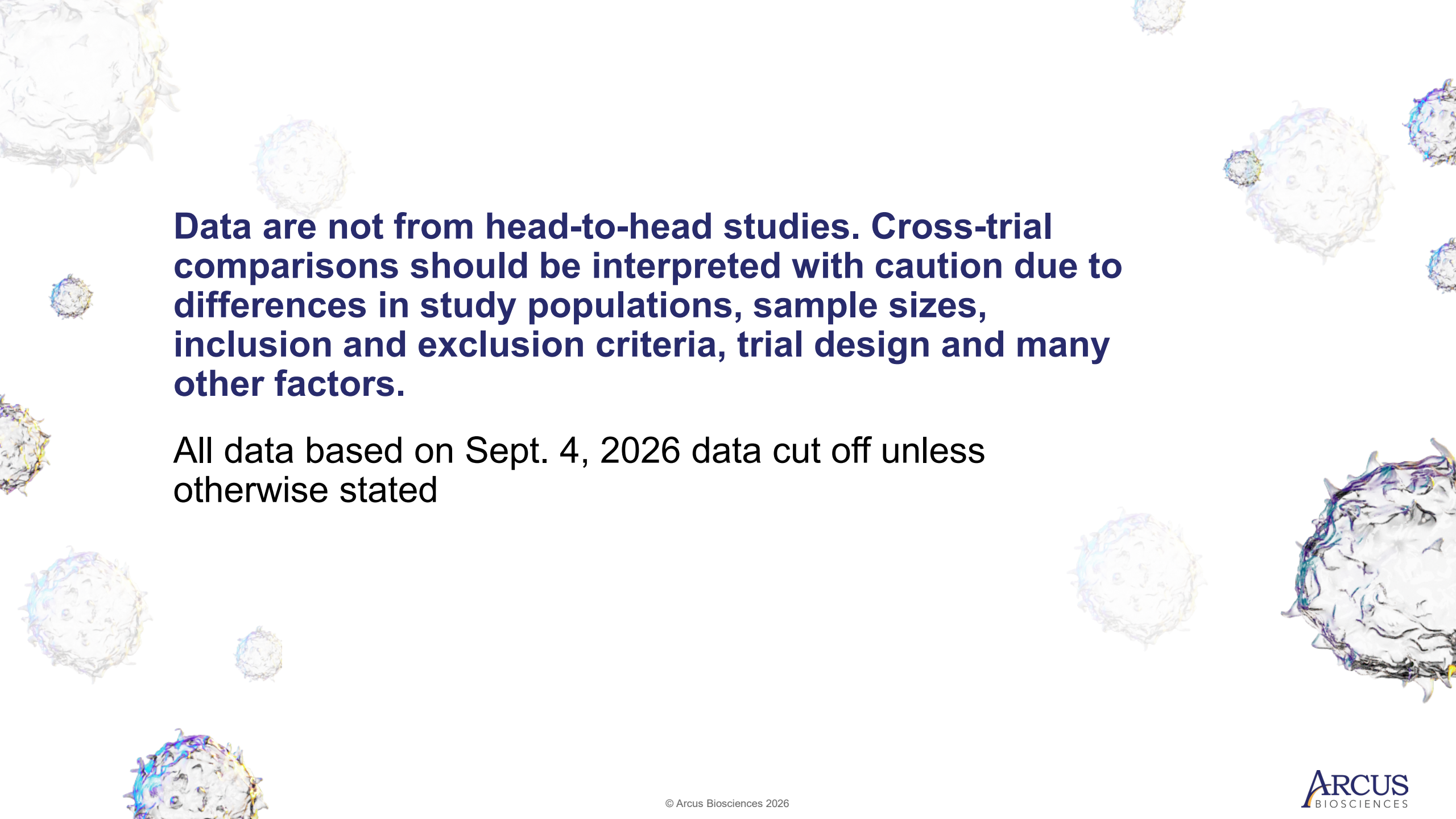
Forward-Looking Statements Safe Harbor: This presentation contains forward-looking statements about Arcus Biosciences, Inc. (“we,” “Arcus” or the “Company”) made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. All statements in this presentation that are not historical facts are forward-looking statements, including, without limitation, statements regarding: our anticipated cash runway; our strategies, goals, opportunities, and potential advantages for our programs, including casdatifan and its potential to become a backbone therapy for patients with clear cell renal cell carcinoma; the timing and achievement of milestones, including the expected timing for completion of enrollment for PEAK-1, the initiation of PEAK-20 and additional data readouts from ARC-20; the initiation, conduct and results of our clinical trials, including future practice-changing trials with casdatifan; estimates of market potential for our investigational products; and our productivity. Forward-looking statements are often identified by words such as “anticipate,” “believe,” “expect,” “intend,” “may,” “should,” “plan,” “project,” “target,” “will,” and similar expressions, although not all forward-looking statements contain these identifying words.

These forward-looking statements are subject to numerous risks, uncertainties and assumptions that may cause actual results to differ materially from those expressed or implied by any forward-looking statements, including, but not limited to: our ability to manage the breadth and pace of our development plans for casdatifan; interim, preliminary or exploratory data may not be predictive of final results and may not be replicated in ongoing or future studies evaluating casdatifan, including the Phase 3 PEAK-1 study and the upcoming Phase 3 PEAK-20 and PEAK-30 studies; the unexpected emergence of adverse events or other undesirable side effects with our investigational products, including casdatifan, alone or in combination with other agents; difficulties or delays in initiating, enrolling, conducting or completing our clinical trials due to regulatory review, site activation, patient identification or enrollment, or manufacturing and supply constraints of investigational or standard-of-care products for such clinical trials, all of which may be exacerbated by unfavorable global economic, political, public health and trade conditions; changes to our cash runway due to changes in our operating plans; changes in the competitive landscape; our ability to obtain and maintain intellectual property protection for our product candidates; and the inherent uncertainty associated with pharmaceutical product development and clinical trials. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those anticipated or implied in the forward-looking statements. Further information on these and other factors that could affect the forward-looking statements made herein is described in our most recent periodic reports filed with the U.S. Securities and Exchange Commission, including our most recent Annual Report on Form 10-K, and in other filings and reports we make with the SEC from time to time. You should not rely upon forward-looking statements as predictions of future events. Except as required by law, neither we nor any other person assumes responsibility for the accuracy or completeness of the forward-looking statements and we undertake no obligation to update any forward-looking statements for any reason after the date of this presentation to conform these statements to actual results or to changes in our expectations.

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No Regulatory Approval: All of Arcus’s molecules, including casdatifan, are investigational and Arcus has not received approval from any regulatory authority for any use globally, nor established the safety or efficacy of these investigational molecules.

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The background of the slide is white and features several stylized, 3D-rendered virus particles. These particles are spherical with a textured, spiky surface, colored in shades of blue, purple, and yellow. They are scattered across the slide, with some appearing larger and more detailed than others.

Data are not from head-to-head studies. Cross-trial comparisons should be interpreted with caution due to differences in study populations, sample sizes, inclusion and exclusion criteria, trial design and many other factors.

All data based on Sept. 4, 2026 data cut off unless otherwise stated

Agenda

TOPIC	PRESENTER(S)	TIME (ET)
Casdatifan Strategy & Takeaways from Today	Terry Rosen, Ph.D.	8:30-9:00
Opportunities for Improving the Treatment Paradigm in ccRCC <i>with Q&A</i>	Dr. Rana McKay	9:00-9:30
Translational Science Supports the Best-in-Class Profile of Casdatifan	Juan Jaen, Ph.D.	9:30-9:40
Review of Casdatifan Development Plan	Dr. Richard Markus	9:40-9:50
Market Opportunity	Bob Goeltz	9:50-9:55
Closing Remarks	Terry Rosen, Ph.D.	9:55-10:00
Q&A	Arcus Management	10:00-10:30



Casdatifan Strategy & Takeaways from Today

Terry Rosen, Ph.D., Chief Executive Officer

Arcus Has a Robust Portfolio of Potential Best-in-Class Medicines

FOUNDED 2015

R&D ENGINE

- World class medicinal chemistry
- Goal of 1-2 new molecules advancing to the clinic each year

CAPITAL EFFICIENCY & RISK SHARING
HAVE BEEN GROWTH ENABLING



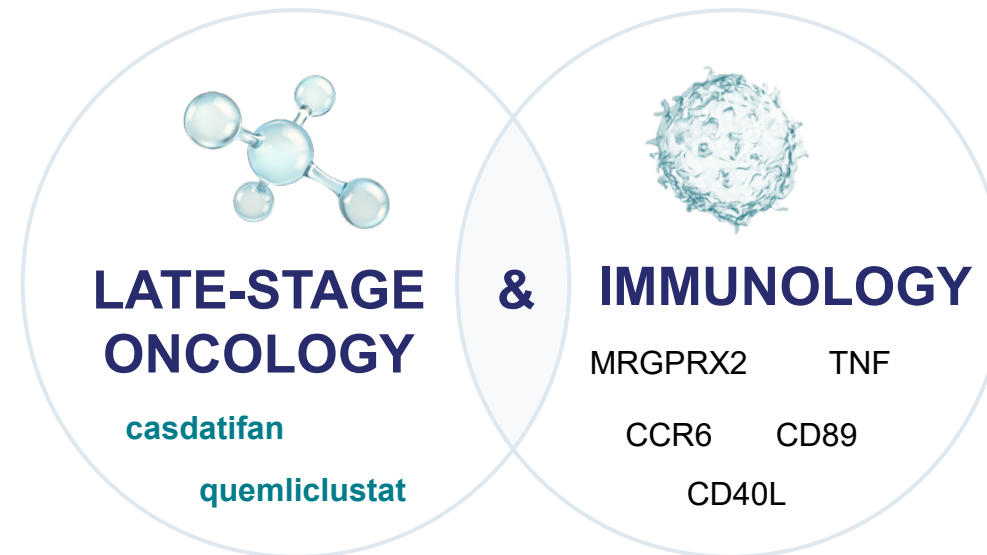
~\$775M IN CASH*

- Funded until at least 2H:28**

*Cash, cash equivalents and marketable securities as of June 30, 2026

**Runway estimate based on cash, cash equivalents, marketable securities, and current planned operations

References and acronyms on slide 91



1st immunology molecule entered the clinic in Q3,
addressing **multi-billion-dollar** market opportunities

Cancers with Large Patient Populations

Kidney

Pancreatic

Inflammation & Autoimmune Diseases

IBD

RA

Psoriasis

Urticaria

AD

Emerging Casdatifan Franchise Has all the Pieces to Transform the Treatment Paradigm for Kidney Cancer

Our development plan provides every ccRCC patient the opportunity to benefit from casdatifan
\$5B – \$10B

1L

\$4B+
cas + ipi + nivo

2L

\$2B+
cas + cabo

Late Line

\$1B+
cas + tivo

Molecular Design



Cas delivers uniquely robust and durable HIF-2 α inhibition

This deep and sustained inhibition drives profound OS benefit, not previously seen for the class

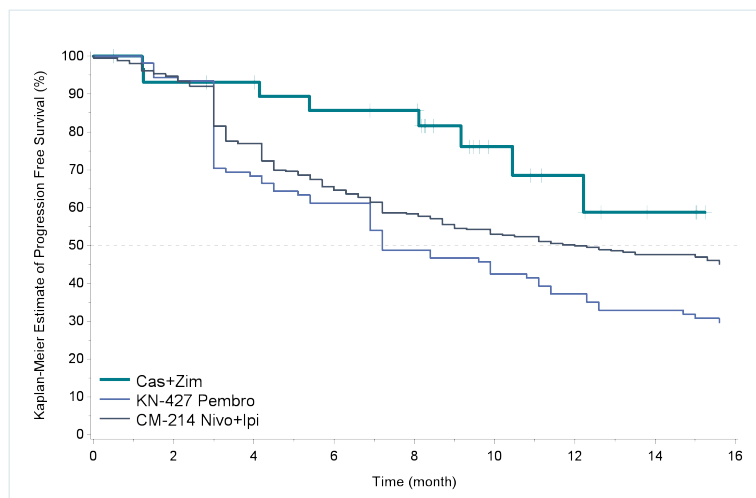
Casdatifan Addresses Clinical Need in Every Line of Therapy

1L

Early efficacy
(PD, ORR, PFS) vs IO
benchmarks

Potential for best 1L treatment

PFS: cas + zim vs. IO benchmarks^{1,2}

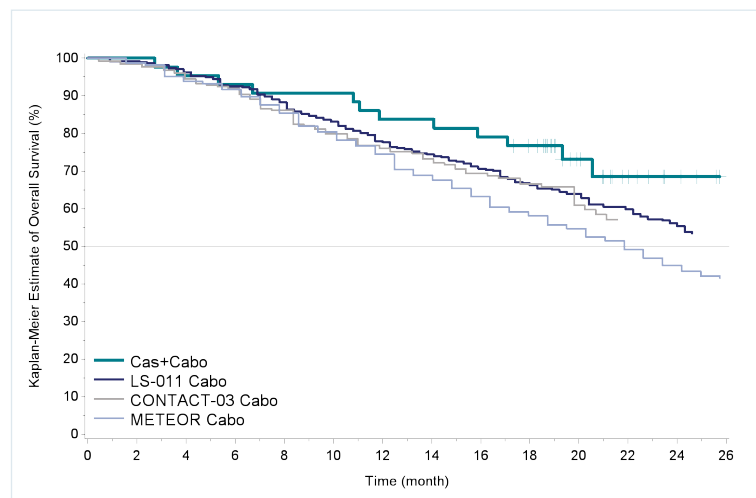


2L

Profound benefit
for all patients (including post TKI
progression, ~60% of 2L)

Strong OS signal
vs benchmarks

OS: cas + cabo vs. cabo³⁻⁶

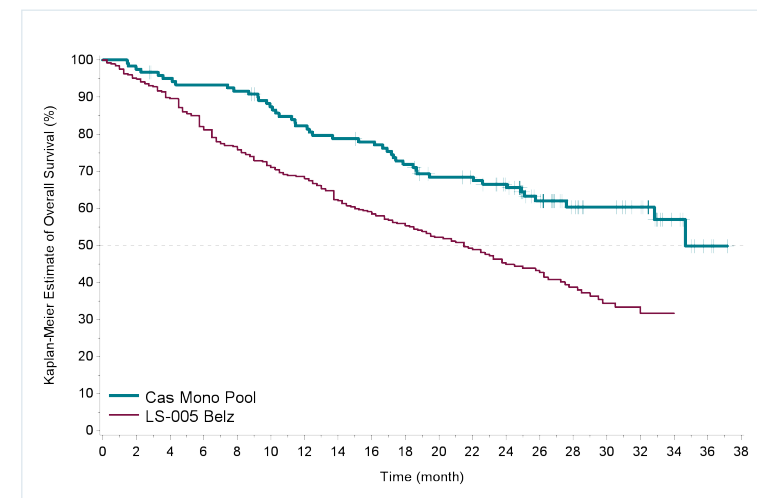


Late
line

Unprecedented 35-month OS
(cas mono)

>12-month benefit
vs benchmarks

OS: cas mono vs. belz mono (LS-005)⁷



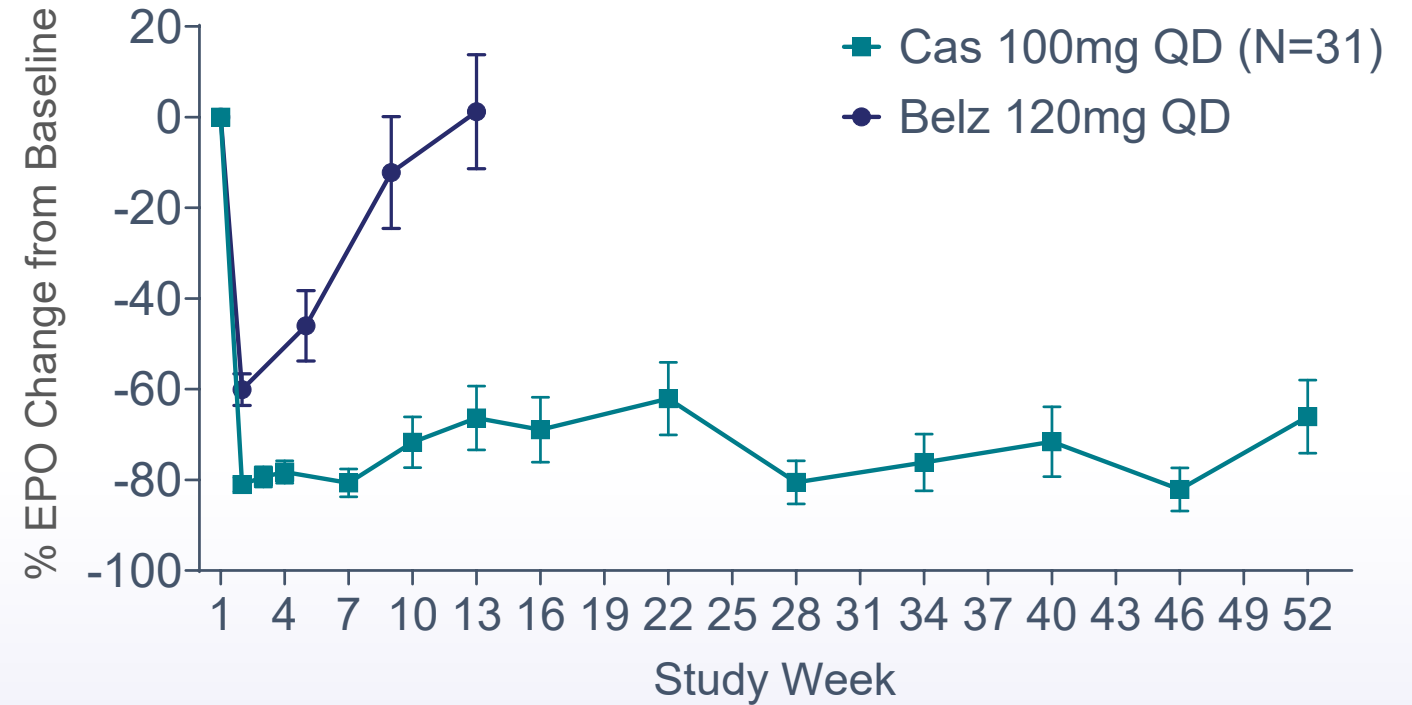
Profile of Casdatifan Reveals the True Potential of HIF-2 α Inhibition and Drives Dramatic Clinical Differentiation

Casdatifan is the only molecule to provide robust and sustained HIF-2 α inhibition

Casdatifan monotherapy has demonstrated clear differentiation:

- ✓ Lower PD rate
- ✓ Higher ORR
- ✓ Longer PFS
- ✓ Longer OS (first data to be presented today)

Published data from Arcus⁸ and Merck⁹



Casdatifan shows durable response linked to HIF-2 α biology in kidney cancer

<https://doi.org/10.1038/s41586-026-10718-x>

Received: 16 February 2026

Accepted: 27 May 2026

Published online: 1 July 2026

Toni K. Choueiri¹✉, Jaime Merchán², Amita Patnaik³, Alexandra Drakaki⁴, Brian I. Rini⁵, Sun Young Rha⁶, Jae Lyun Lee⁷, Moshe C. Ornstein⁸, Rohit Kumar⁹, Clara Hwang¹⁰, Yusra Shao¹¹, Se Hoon Park¹², Pedro C. Barata¹³, Bradley A. McGregor¹, Paul Foster¹⁴, Jianfen Chen¹⁴, Melissa Eisen¹⁴, Hunter Cole¹⁴, Ben Weeder¹⁴, Yinghui Guan¹⁴, Jaskirat Singh¹⁴, Angelo Kaplan¹⁴, Soonweng Cho¹⁴, Richard Markus¹⁴, Omar Kabbarah¹⁴ & Rana R. McKay¹⁵

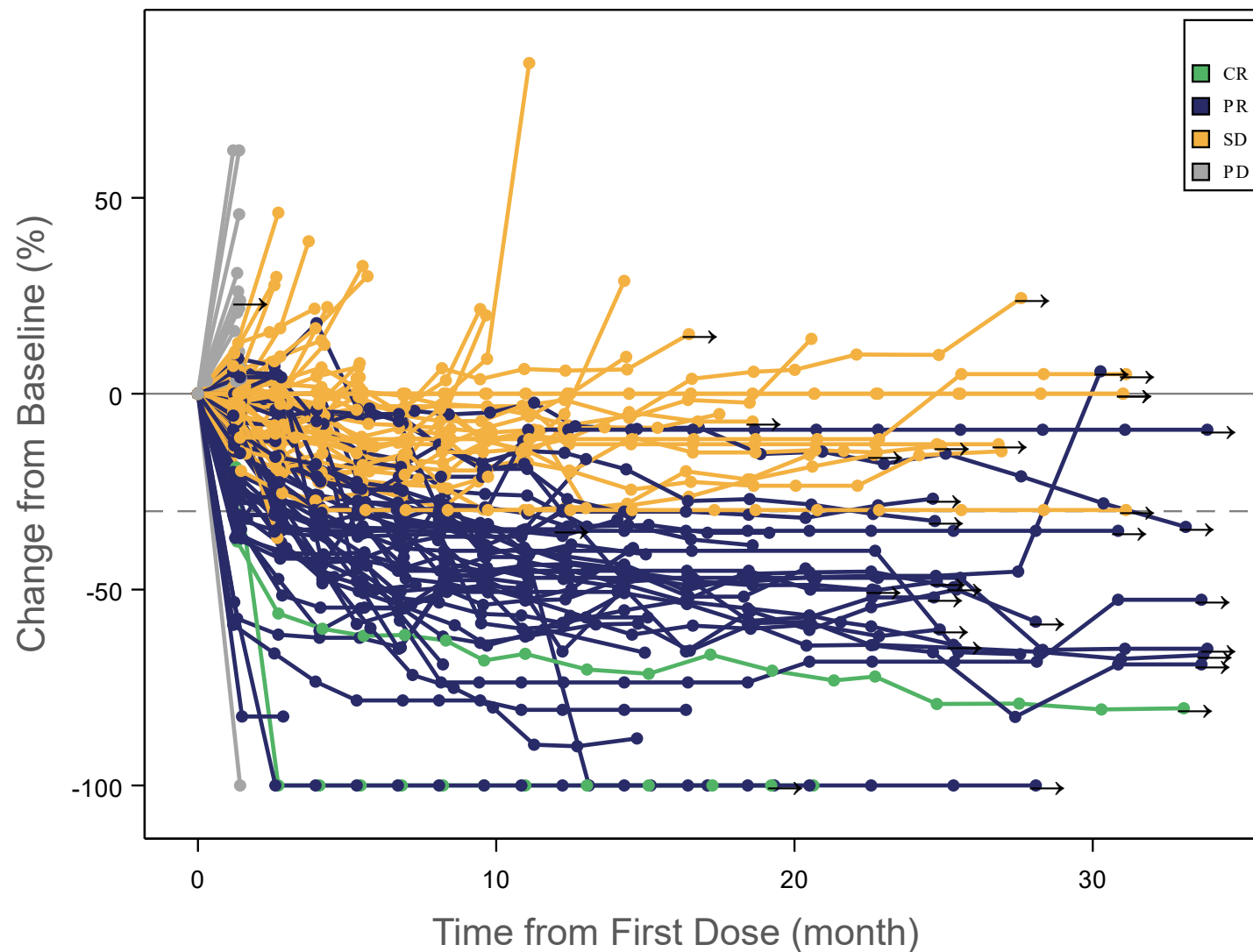


First study to comprehensively connect clinical outcomes from patients receiving a HIF-2 α inhibitor with peripheral biomarker changes and associated tumor biology

HIF-2 α inhibition with casdatifan resulted in deep and sustained suppression of the hormone erythropoietin in blood (serum EPO), which correlated with higher response rates and longer PFS

Robust HIF-2 α Inhibition Provides Remarkable and Enduring Clinical Benefit

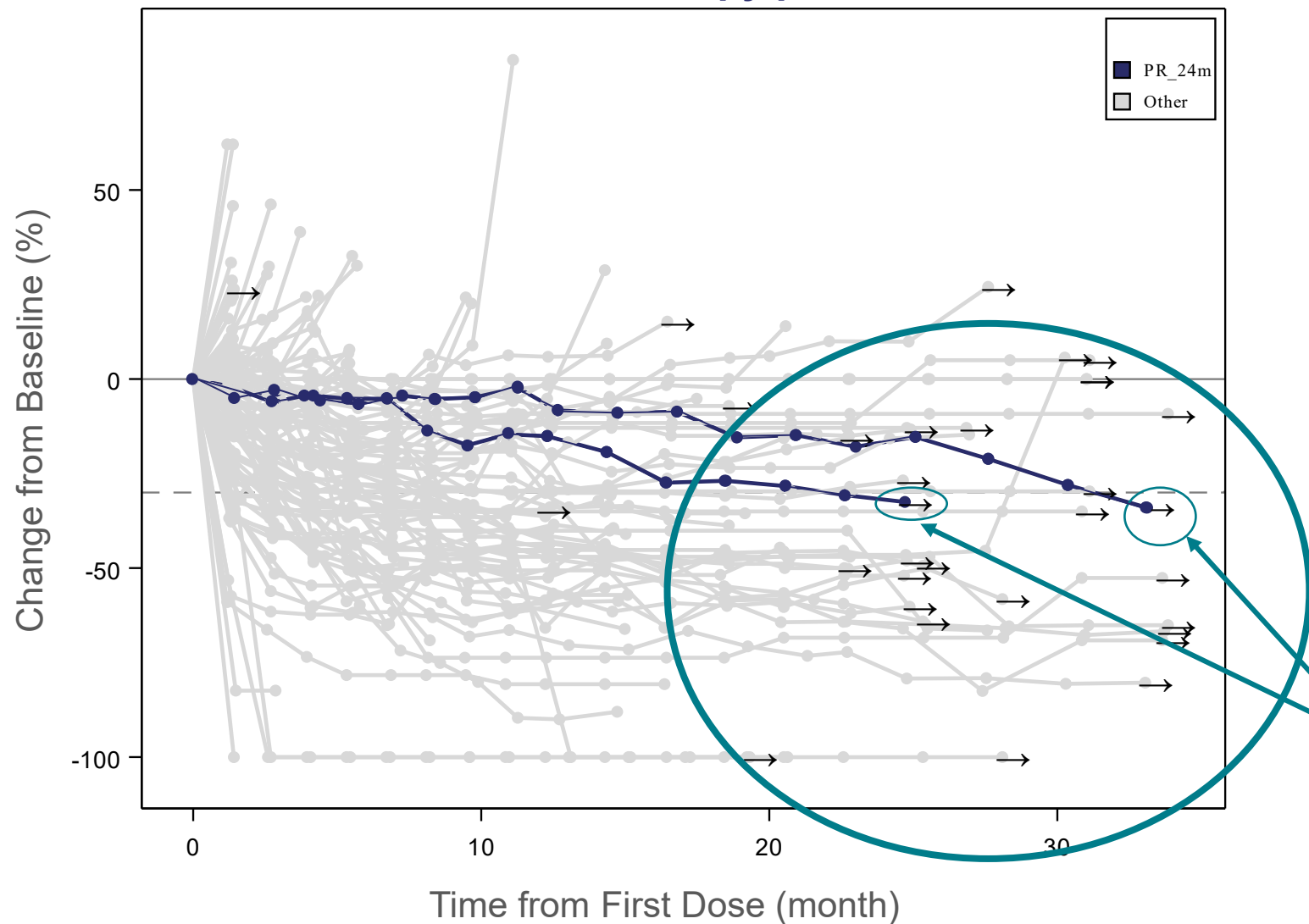
Cas monootherapy pooled



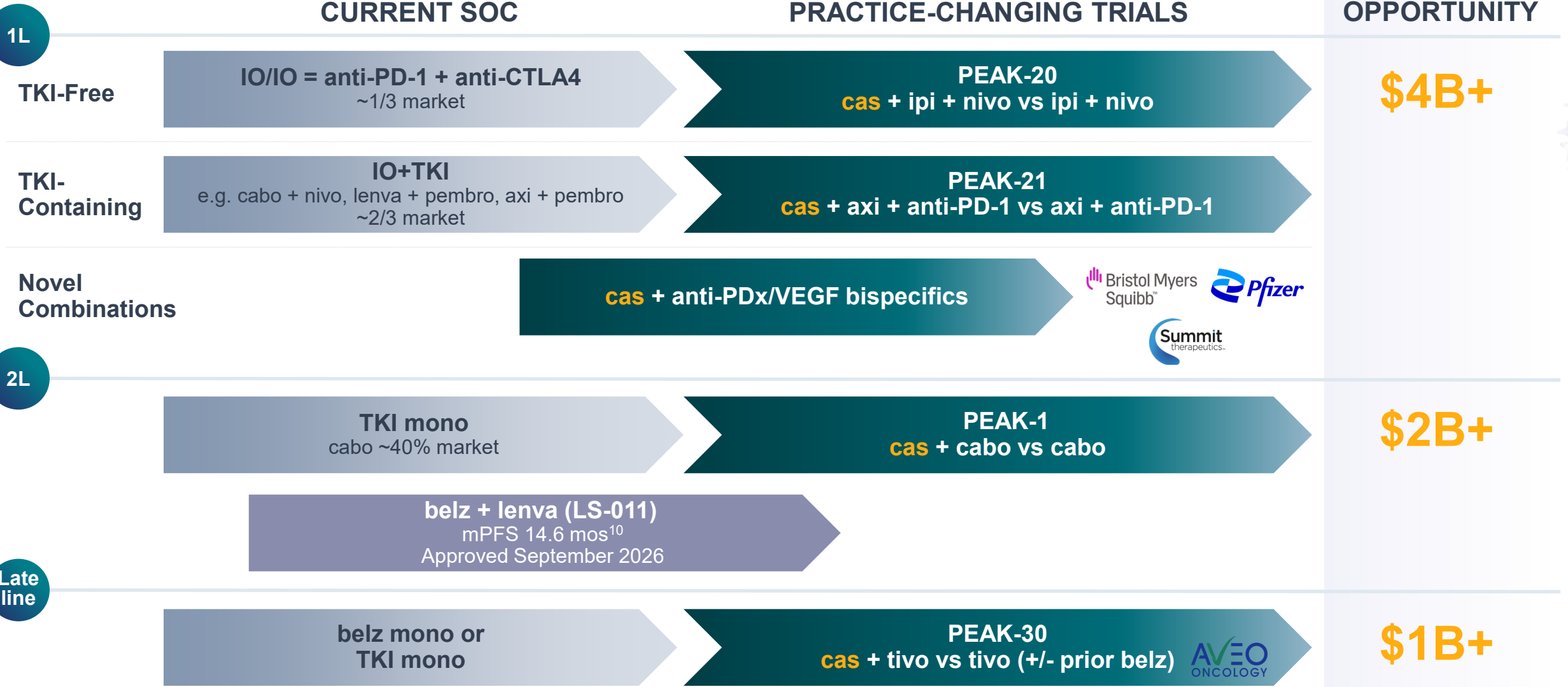
~25% of patients continue treatment beyond 24 months

Robust HIF-2 α Inhibition Provides Remarkable and Enduring Clinical Benefit

Cas monootherapy pooled



Our Development Plan Provides Every ccRCC Patient the Opportunity to Benefit from Casdatifan





Late Line: Unprecedented OS in Heavily Pretreated Patients

Data from the “Pooled” Casdatifan Cohorts Continue to Improve and Exceed Benchmarks for Belzutifan

Efficacy-evaluable population ^a	casdatifan pooled monotherapy (n = 121)		belzutifan ⁷ 120mg QD (n = 374)
	 ASCO Genitourinary Cancers Symposium February 26–28, 2026 Moscone West San Francisco, CA & Online gu.asco.org		TODAY'S DATA
Median Follow-Up, mos (range)	20.8 (11.8, 31.5)	27.9 (19.0, 38.7)	25.7 (16.8–39.1)
Confirmed ORR (95% CI)	35% (26, 44)	36% (26, 45)	23% (19, 27)
Complete Response, % (n)	1% (1)	2% (2)	4% (13)
Partial Response, % (n)	34% (41)	34% (41)	19% (72)
Stable Disease, % (n)	46% (56)	46% (55)	38% (143)
Progressive Disease, % (n)	17% (21)*	17% (21)*	34% (127)
mPFS, mos (95% CI)	12.2 (9.4, 16.5)	13.0 (9.4, 16.4)	5.6 (4.6-7.4)

Casdatifan showed substantially lower rate of PD, higher ORR and longer PFS than belzutifan benchmarks

DCO date for ASCO GU: Jan. 30, 2026

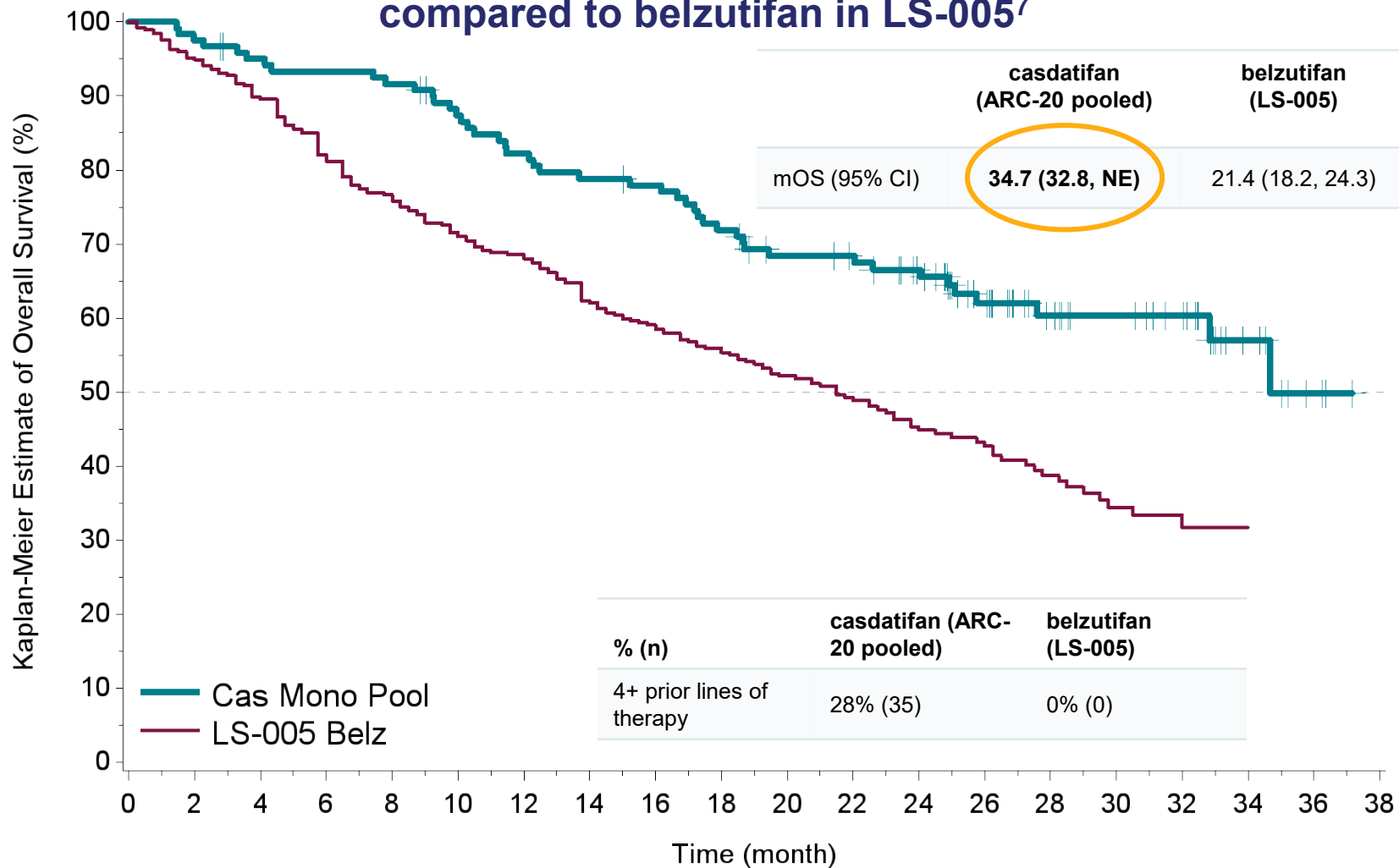
*Two patients were considered non-evaluable; they had clinical progression before the first scan and did not meet criteria for progressive disease per RECIST.

a. Efficacy-evaluable population for this expansion cohort is defined as all eligible participants who received any study treatment and have at least one post-baseline efficacy assessment, or who discontinued study treatment due to progressive disease or death, regardless of whether they had a scan.

References and acronyms on slide 91

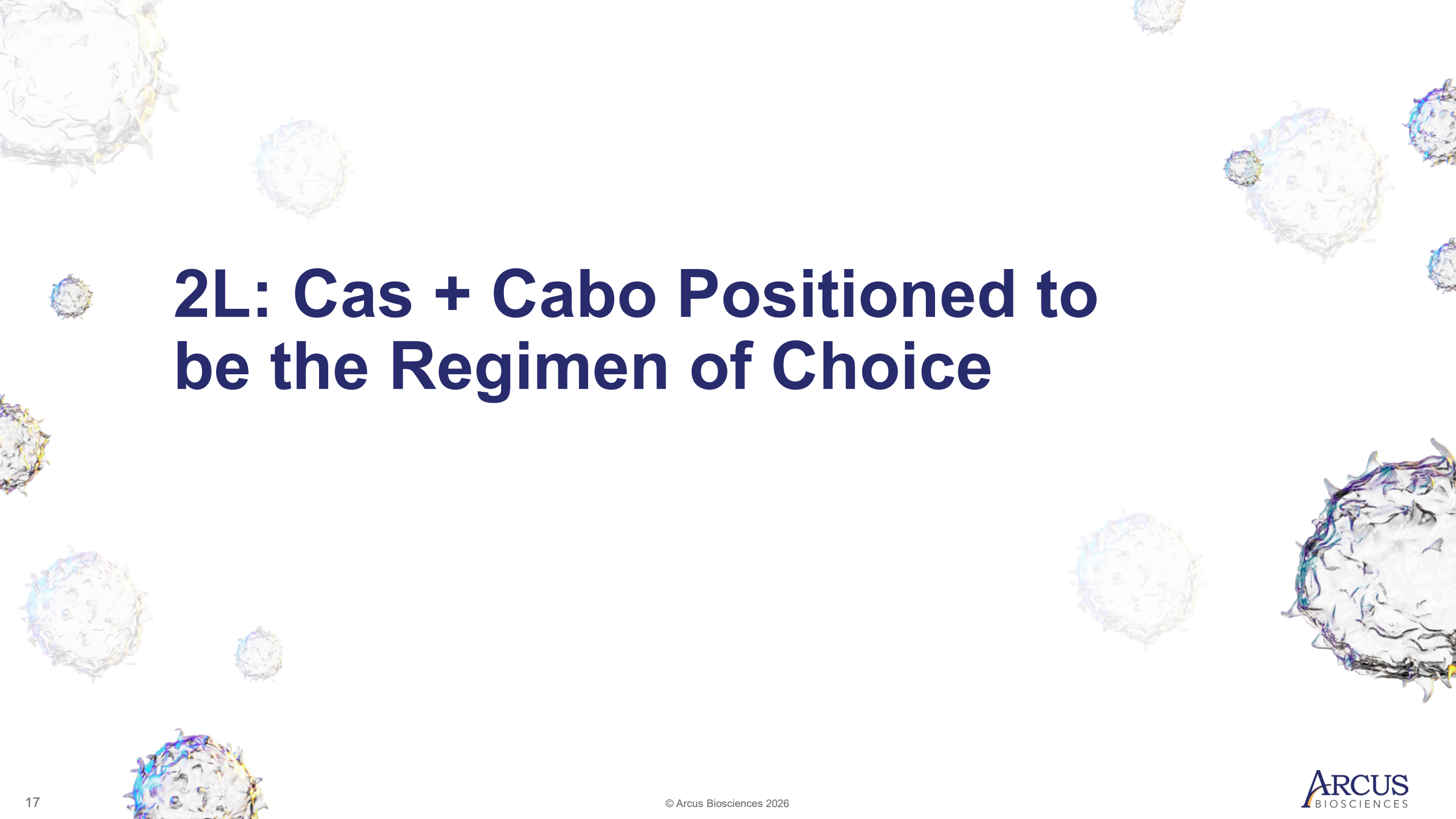
Casdatifan Monotherapy Shows an Exceptional OS Trend With Potential to Drive Survival Across Lines of Therapy

OS of pooled casdatifan monotherapy compared to belzutifan in LS-005⁷



- mOS of 35 months, with median follow-up of 28 months
- OS curve substantially improved relative to that of belzutifan, despite more heavily pre-treated patient population in ARC-20
- OS benefit is correlated with pharmacodynamic markers of HIF-2 α inhibition (discussed later today)

These data demonstrate the potential for casdatifan to be the **only** HIF-2 α inhibitor to achieve OS benefit **in any setting**



2L: Cas + Cabo Positioned to be the Regimen of Choice

LS-011 Underrepresented the Patients Previously Treated with 2nd-Generation TKIs, Who Respond Poorly to Cabo

Prior Therapy Agent	ARC-20		LITESPARK-011 ¹¹			
	cas + cabo (n = 44)		belz + lenva (n = 371)		cabo (n = 376)	
	N	%	N	%	N	%
Adjuvant[‡]	11	25%	23	6%	25	7%
First Line	36	82%	356	96%	358	95%
IO + axi	6	14%	107	29%	103	27%
Pembro + lenva	7	16%	0	0%	0	0%
IO only [§]	17	39%	136	37%	143	38%
Pazopanib or sunitinib	3	7%	93	25%	101	27%
Other*	3	7%	0	0%	0	0%
Second Line	5	11%	104	28%	107	28%
Nivo	2	5%	84	23%	98	26%
IO/IO; IO + axi	3	7%	0	0%	0	0%
Third Line	0	0%	4	1%	0	0%

Patients with prior lenva expected to perform much worse on cabo mono in 2L (ORR ~5%, PFS 4.1-5.8 months, OS 8.1 months^{12,13**})

1st-generation TKIs that are no longer commonly prescribed as 1L agents

Median follow-up 21.3 months

[‡]Includes axitinib/pembrolizumab, Bacillus Calmette-Guérin plus interferon, dendritic cells cytokine induced killer cells, everolimus, ipilimumab/nivolumab, nivolumab, pazopanib, pembrolizumab, placebo, sunitinib, and sunitinib malate.

[§]Includes ipilimumab + nivolumab and nivolumab.

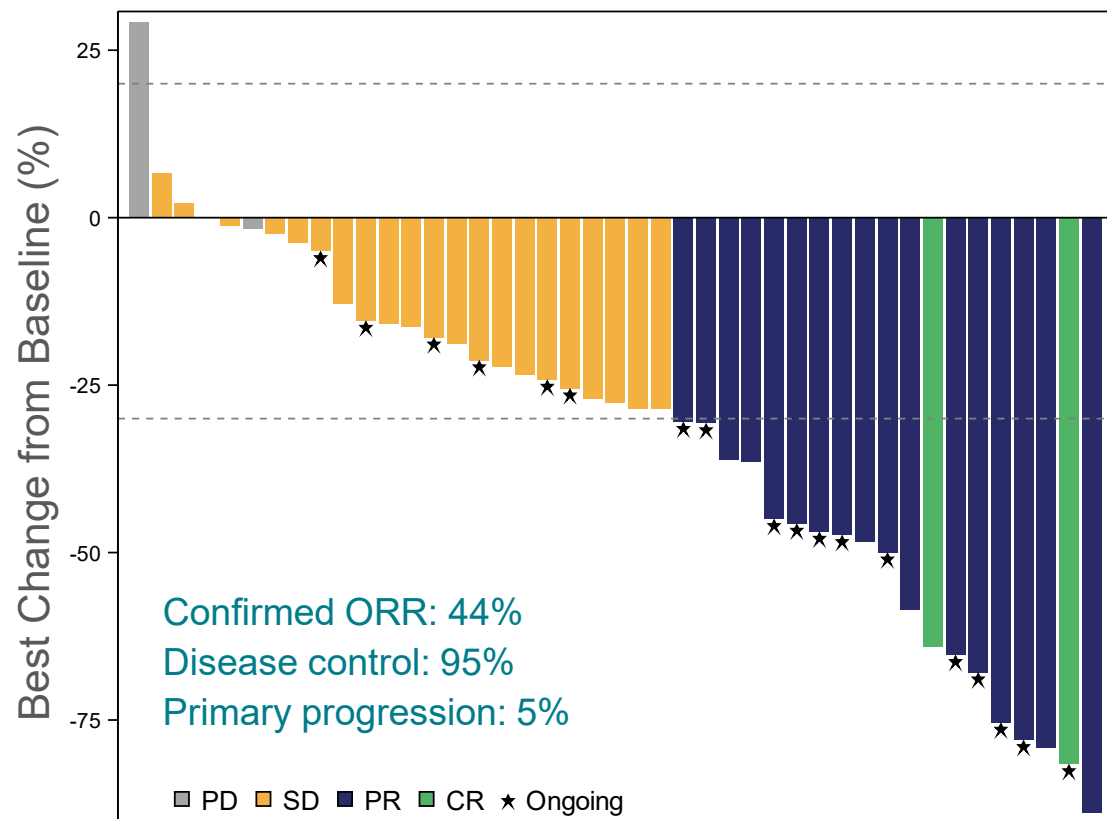
*Includes one patient with IO + zanzalitinib and two with IO + bevacizumab.

**TOT and TTF used as proxy for PFS expectation.

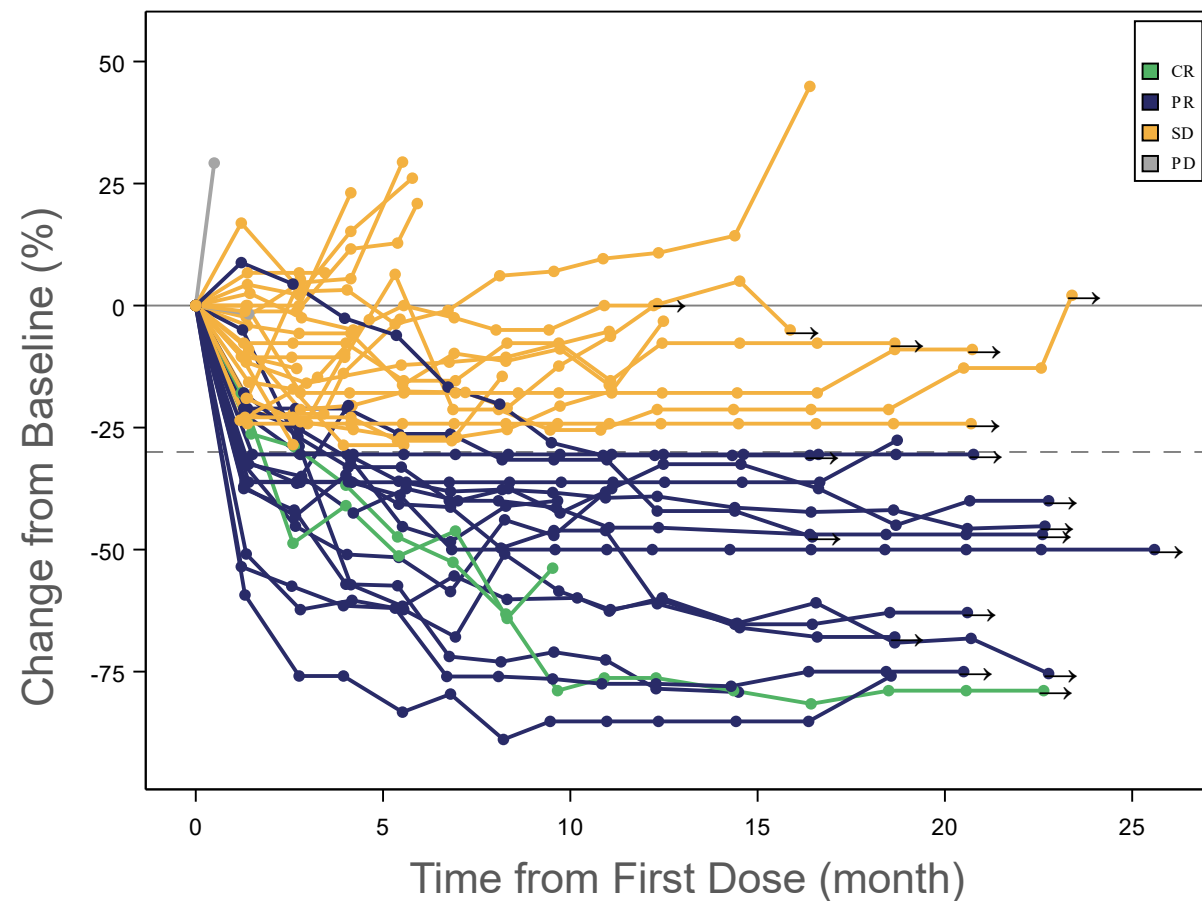
References and acronyms on slide 91

Cas + Cabo Provides Durable Clinical Benefit for the Vast Majority of Patients

Best percent change in target lesions

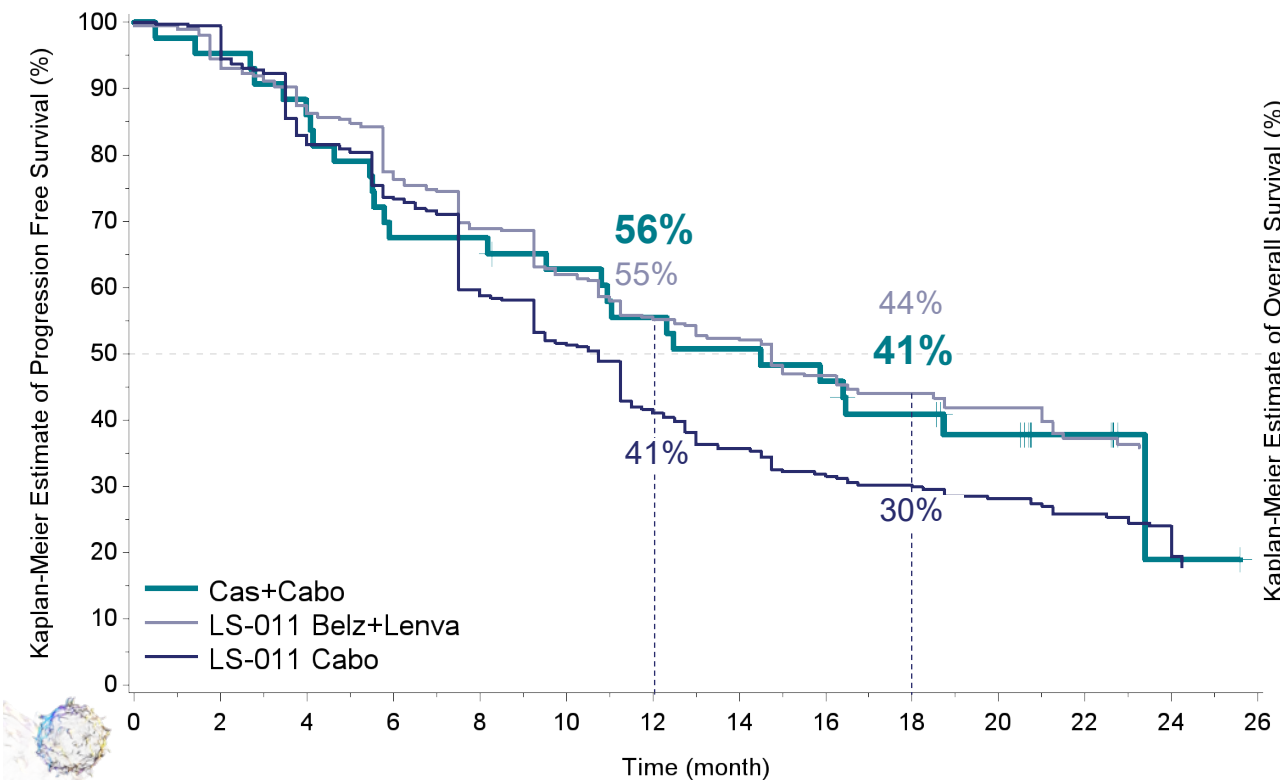


Change in target lesions over time

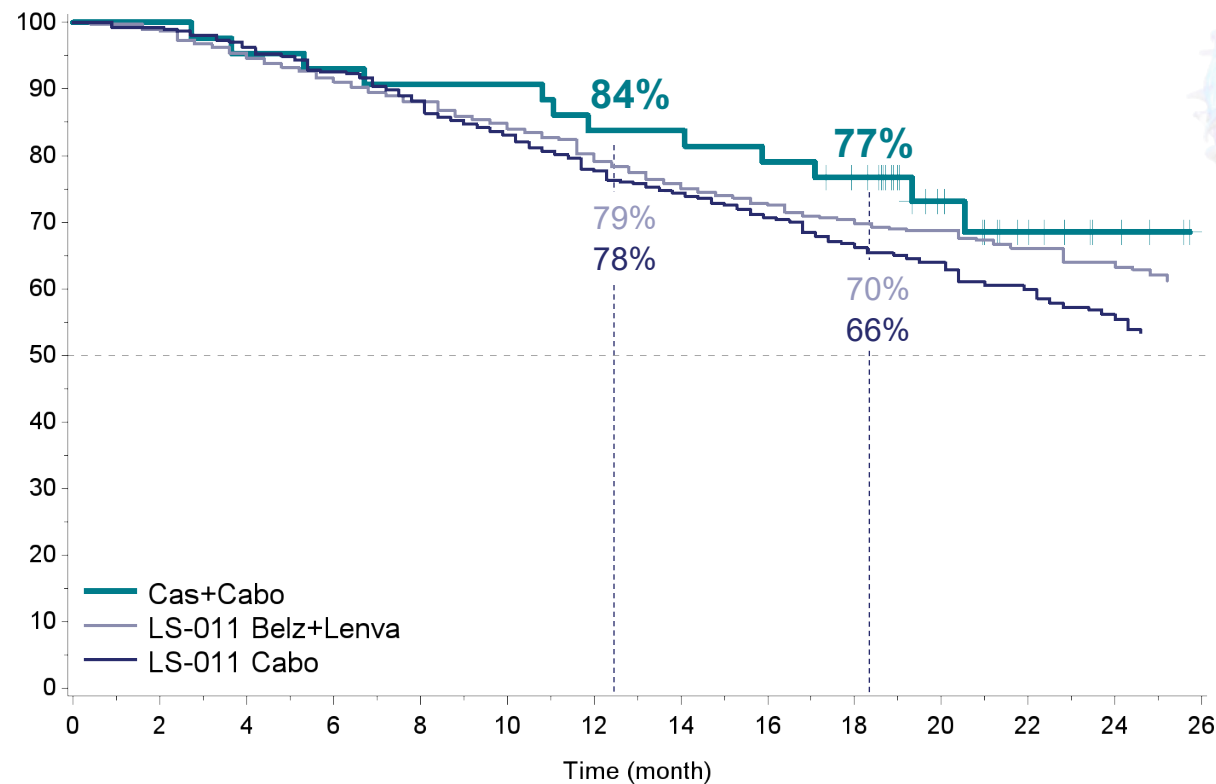


Despite Population Differences, Comparison to LS-011 Shows Similar PFS and Reveals Potential OS Benefit

PFS curves: cas + cabo vs LS-011^{3,11}



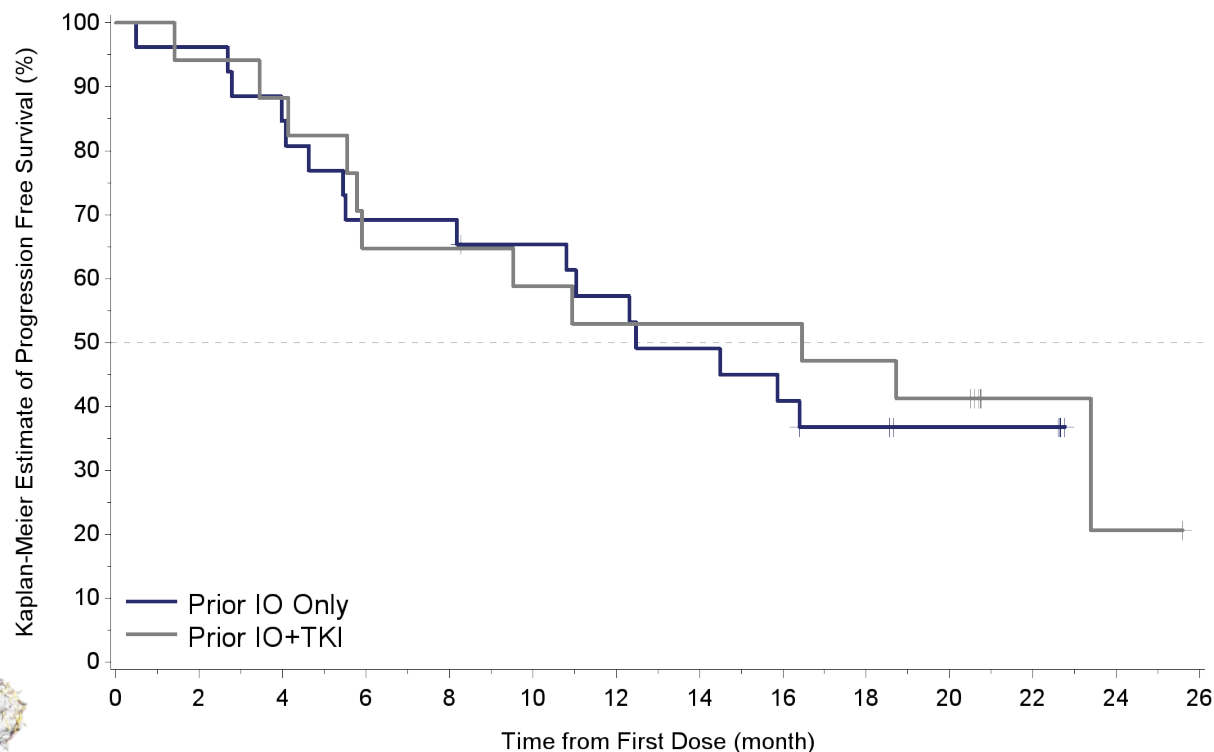
OS curves: cas + cabo vs LS-011^{3,11}



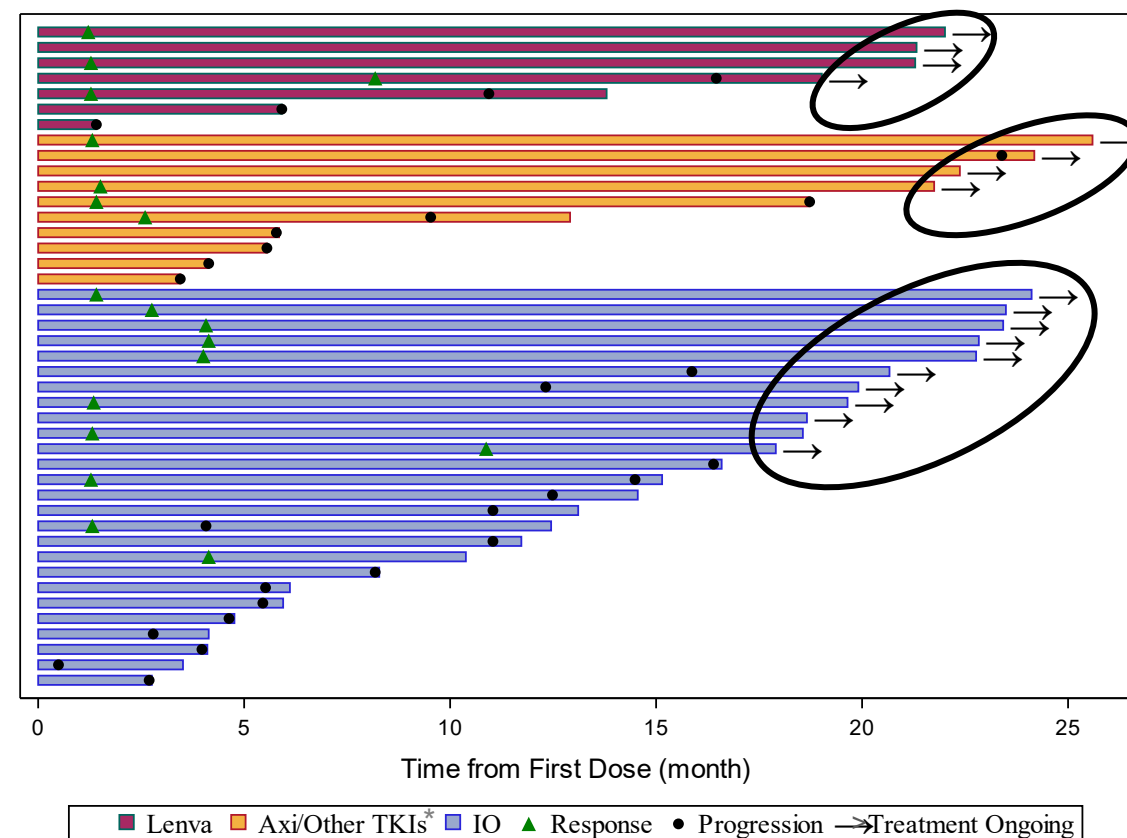
LS-011 HR was 0.90 at IA1 and 0.85 at IA2 for belz + lenva vs. cabo
More durable and robust inhibition from cas could lead to significant OS improvement

Cas + Cabo Demonstrated Similar Efficacy in Prior IO Only and Prior IO + TKI Patients, Including Lenva-Pretreated Patients

Cas + Cabo PFS by prior TKI exposure



Cas + cabo by prior TKI exposure



Median follow-up 21.3 months

Tick marks indicate censored patients

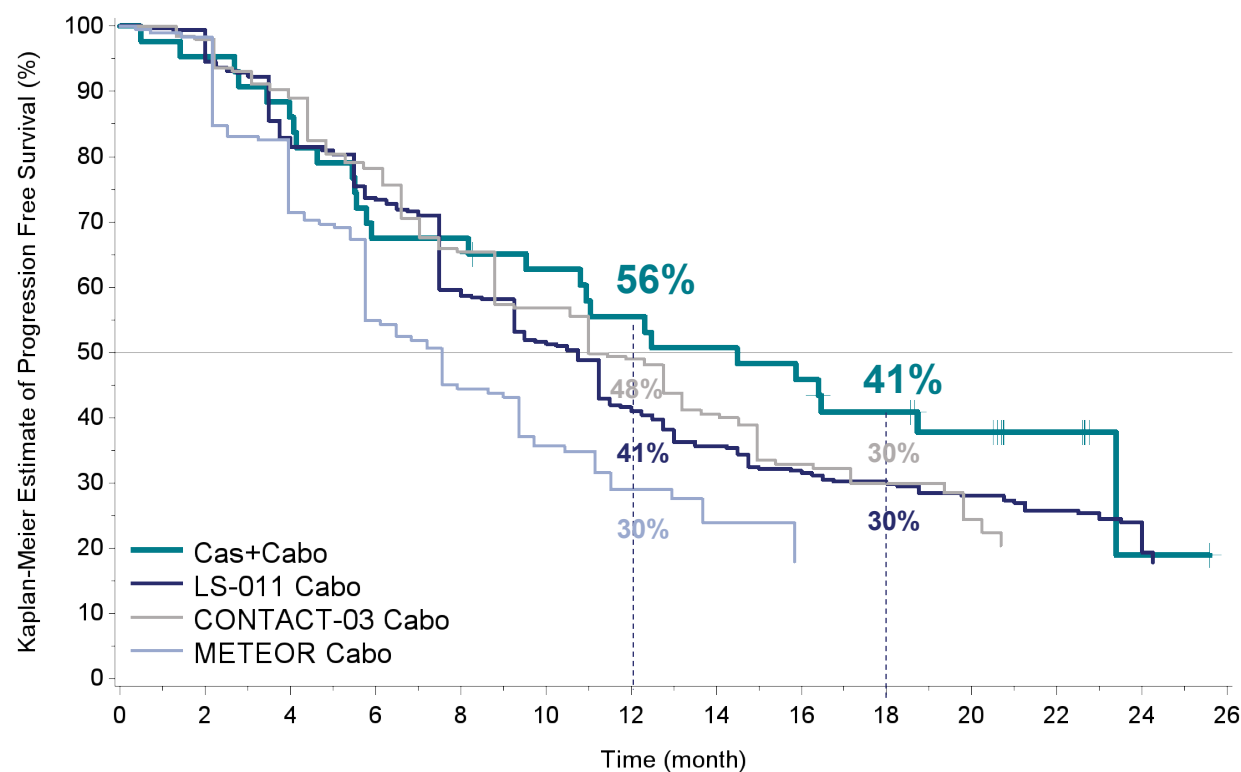
*Axi/Other TKIs are 6 with prior Axitinib/IO, 1 prior Zanzalintinib/IO, 1 prior Sunitinib, 2 prior Pazopanib

References and acronyms on slide 91

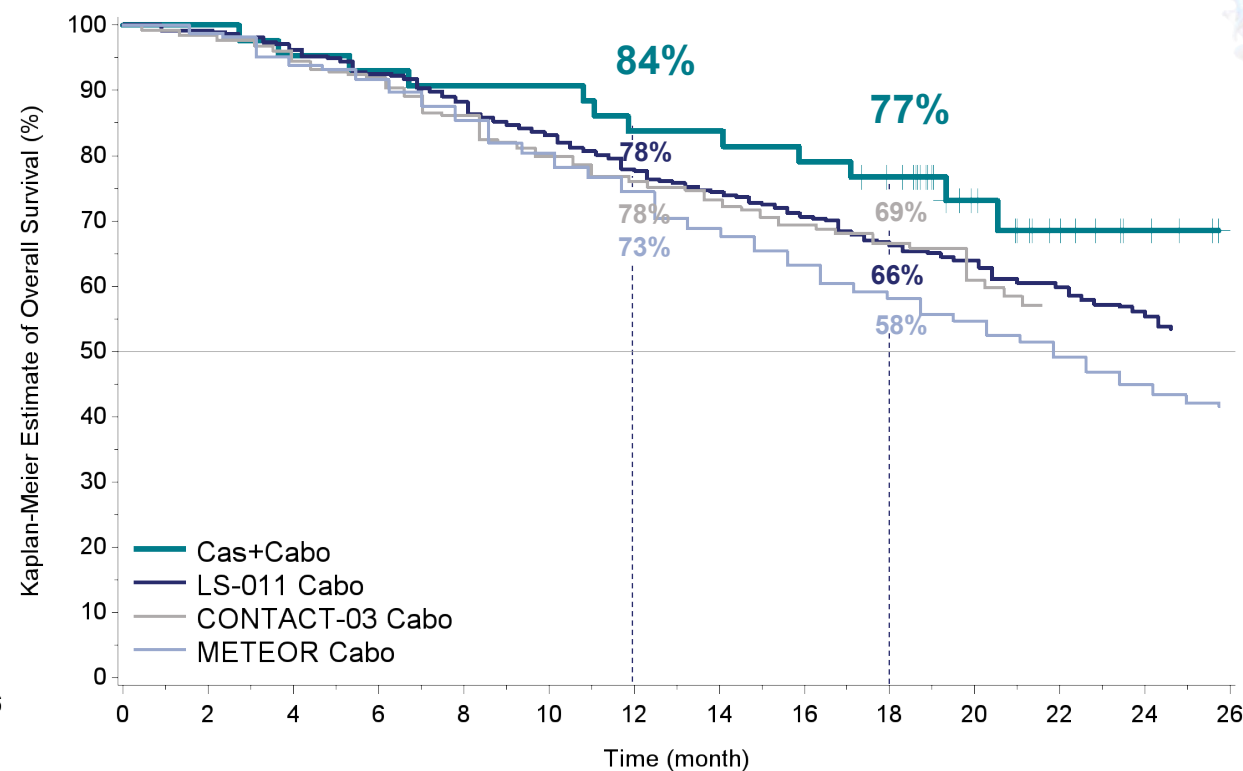
In 2L, Cas + Cabo PFS and OS Support High Likelihood of PEAK-1 Success

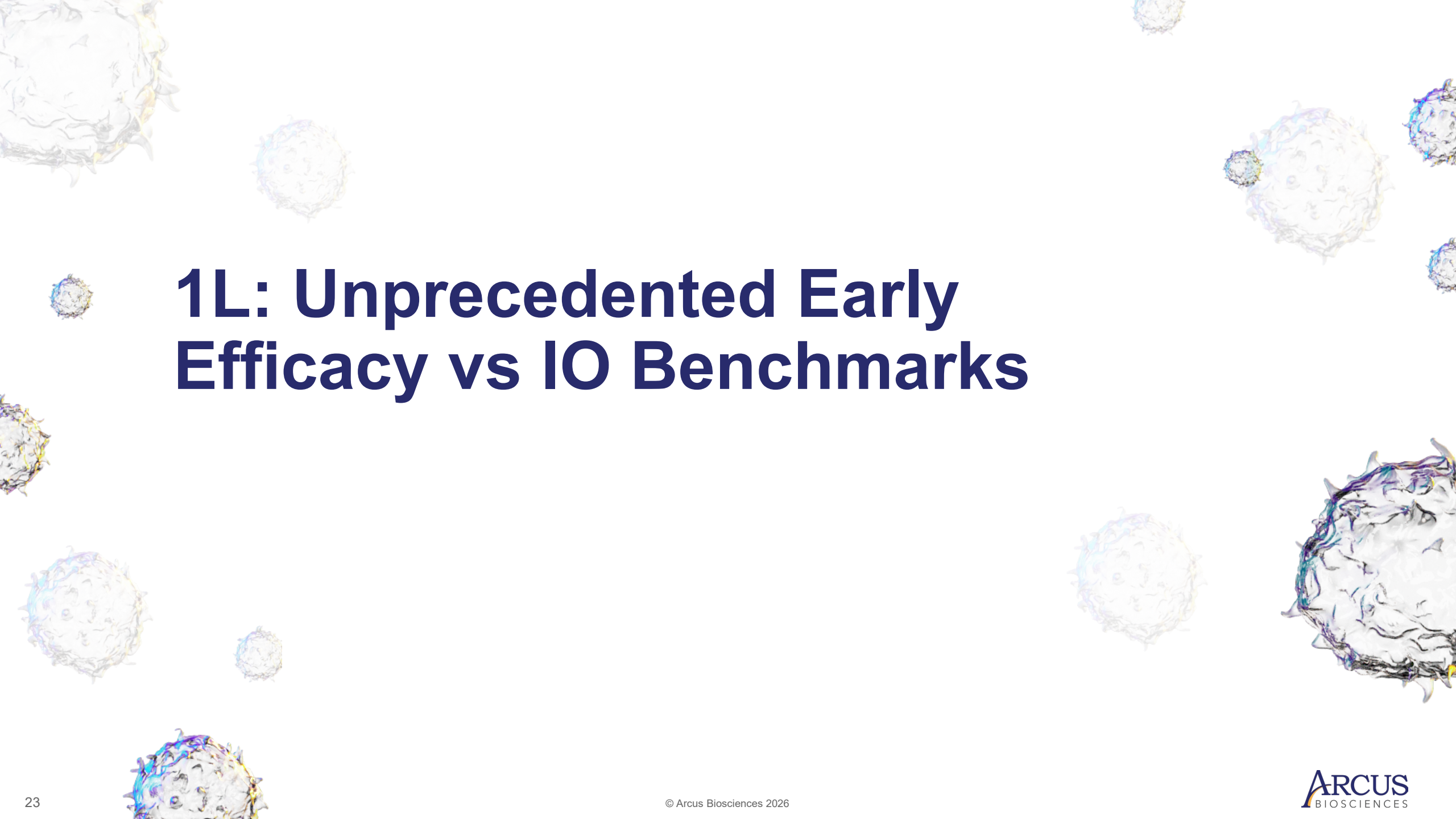
Both PFS and OS for cas + cabo are trending substantially better than those of Phase 3 cabo mono benchmarks^{3-6,11}

PFS: cas + cabo vs cabo benchmarks



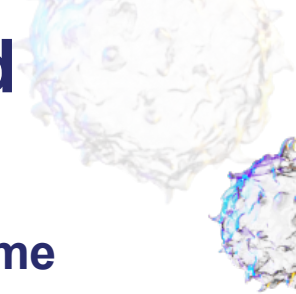
OS: cas + cabo vs cabo benchmarks



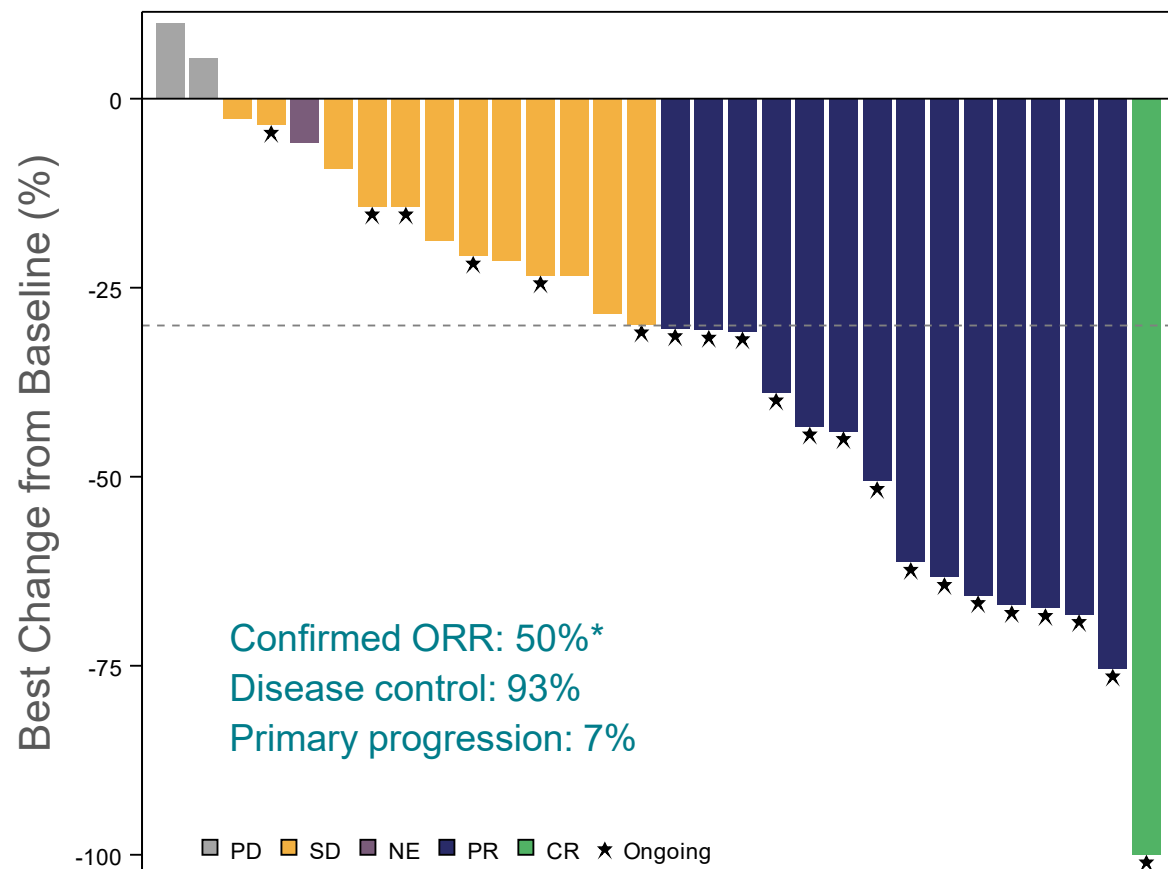


1L: Unprecedented Early Efficacy vs IO Benchmarks

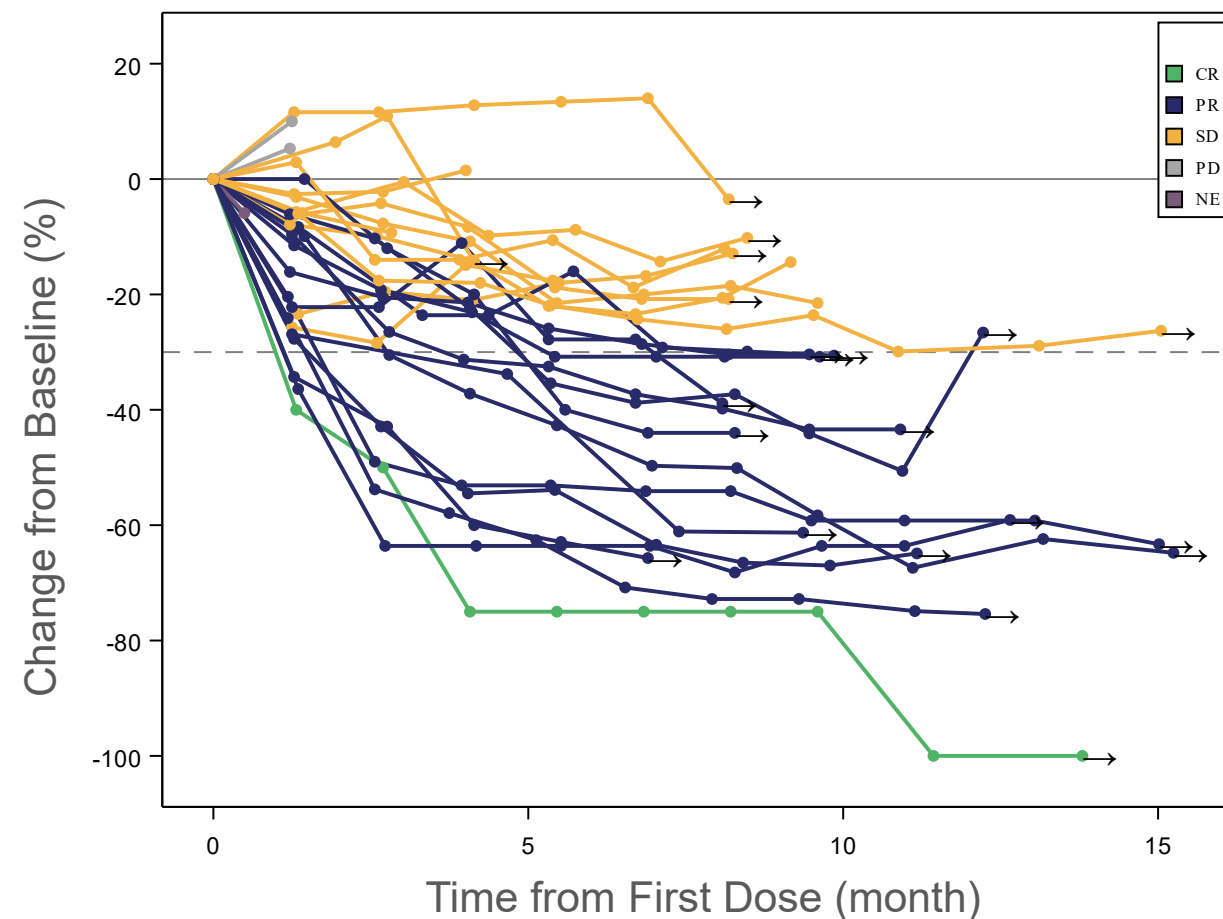
Cas + Zim in 1L Shows Deep Tumor Volume Reduction and Meaningful Disease Control



Best percent change in target lesions



Change in target lesions over time



Median follow-up 11.5 months

*Includes two patients whose responses confirmed after the data cut-off

References and acronyms on slide 91

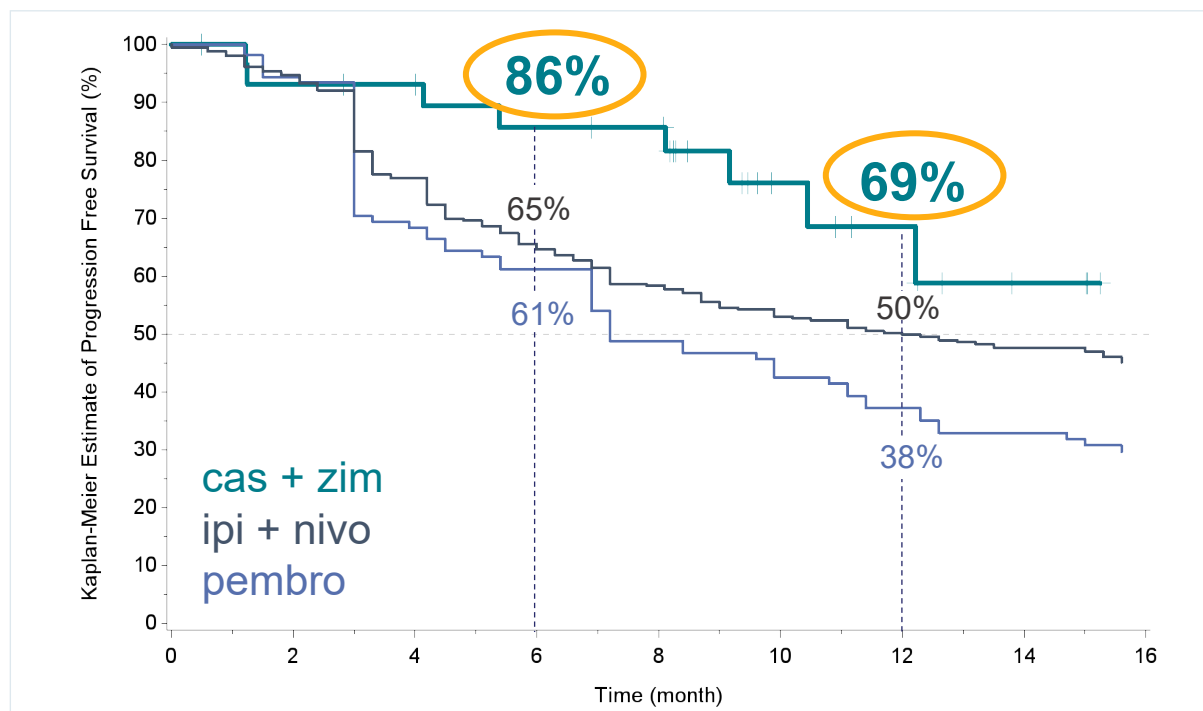
Casdatifan Enhances Disease Control Relative to Ipi + Nivo in 1L

Efficacy data are unprecedented for a TKI-sparing regimen

Rate of primary progression & ORR

	ARC-20		CM-214	KN-427
	cas + zim (n=30)	cas + zim + ipi (n=31)	ipi + nivo (n=550) ²	pembro (n=110) ¹
Primary Progression	6.7%	4.0%**	20%	30.0%
cORR	50.0%*	TBD	39%	36.4%
Median follow-up, months	11.5	3.0	25.2	35.9

Progression-free survival



Note: 12-month PFS landmark for cas + zim also exceeds those of anti-PD-1 + TKI combinations, including cabo + nivo (58% in CM-9ER¹⁴) and pembro + axi (60% in KN-426¹⁵)

*Includes two patients whose responses confirmed after the data cut-off

**Only one patient experienced primary progression (4%, n=24 with at least one scan)

Tick marks indicate censored patients

References and acronyms on slide 91

Emerging Casdatifan Franchise Has all the Pieces to Transform the Treatment Paradigm for Kidney Cancer

Our development plan provides every ccRCC patient the opportunity to benefit from casdatifan
\$5B – \$10B

1L

\$4B+
cas + ipi + nivo

2L

\$2B+
cas + cabo

Late Line

\$1B+
cas + tivo

Molecular Design



Cas delivers uniquely robust and durable HIF-2 α inhibition

This deep and sustained inhibition drives profound OS benefit, not previously seen for the class

Introducing Dr. Rana McKay



Rana McKay, MD, FASCO

Professor of Medicine, Urology and
Radiation Medicine

Associate Director, Clinical Science
Co-Lead of GU Oncology Program

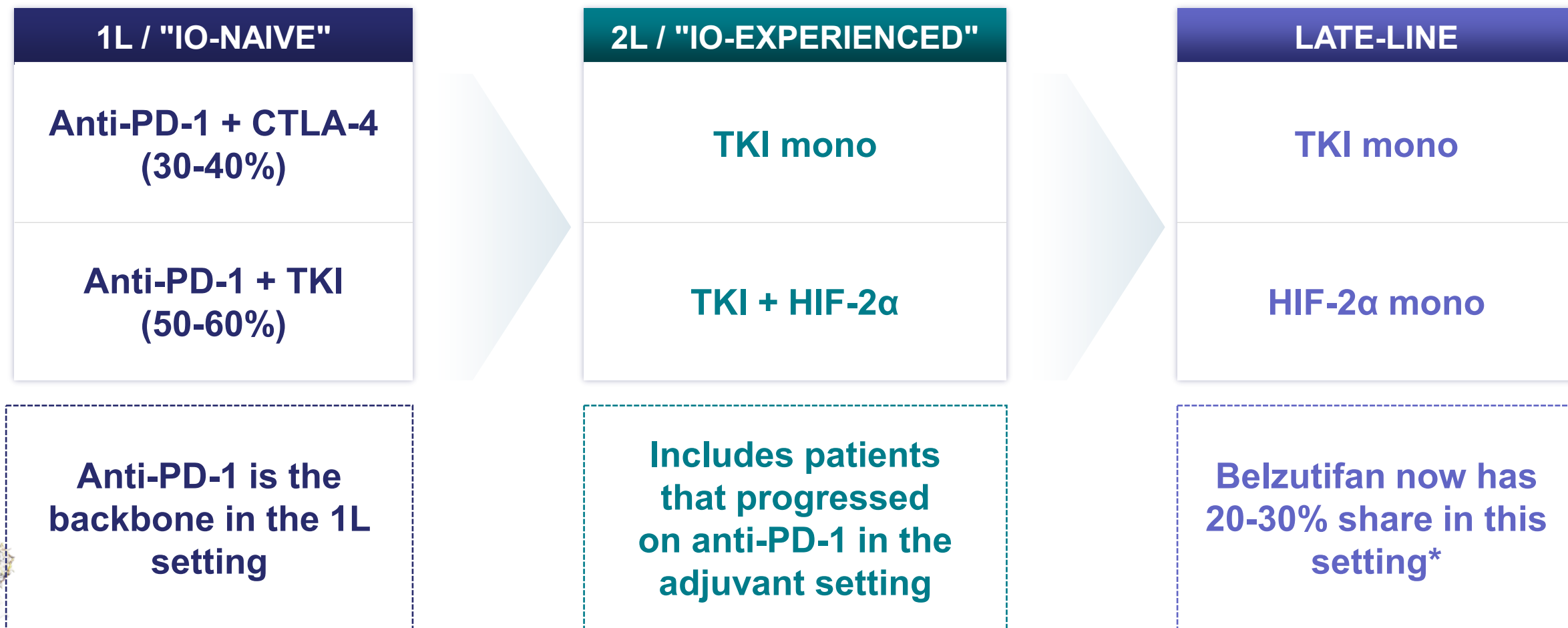
Moore's Cancer Center, UCSD

- Winner of the 2024 Christopher G. Wood Rising Star Award at IKCS Europe
- Winner of the 2023 KCA Trailblazer Award for research on “Dissecting predictors of response to immunotherapy in patients with renal cell carcinoma”
- Winner of the KidneyCan Catalyst Award at 2025 KCRS
- Member of the 2026-29 ASCO nominating committee and current member of the ESMO Congress Education Program Committee's Genitourinary Cancer – Kidney and Bladder Track

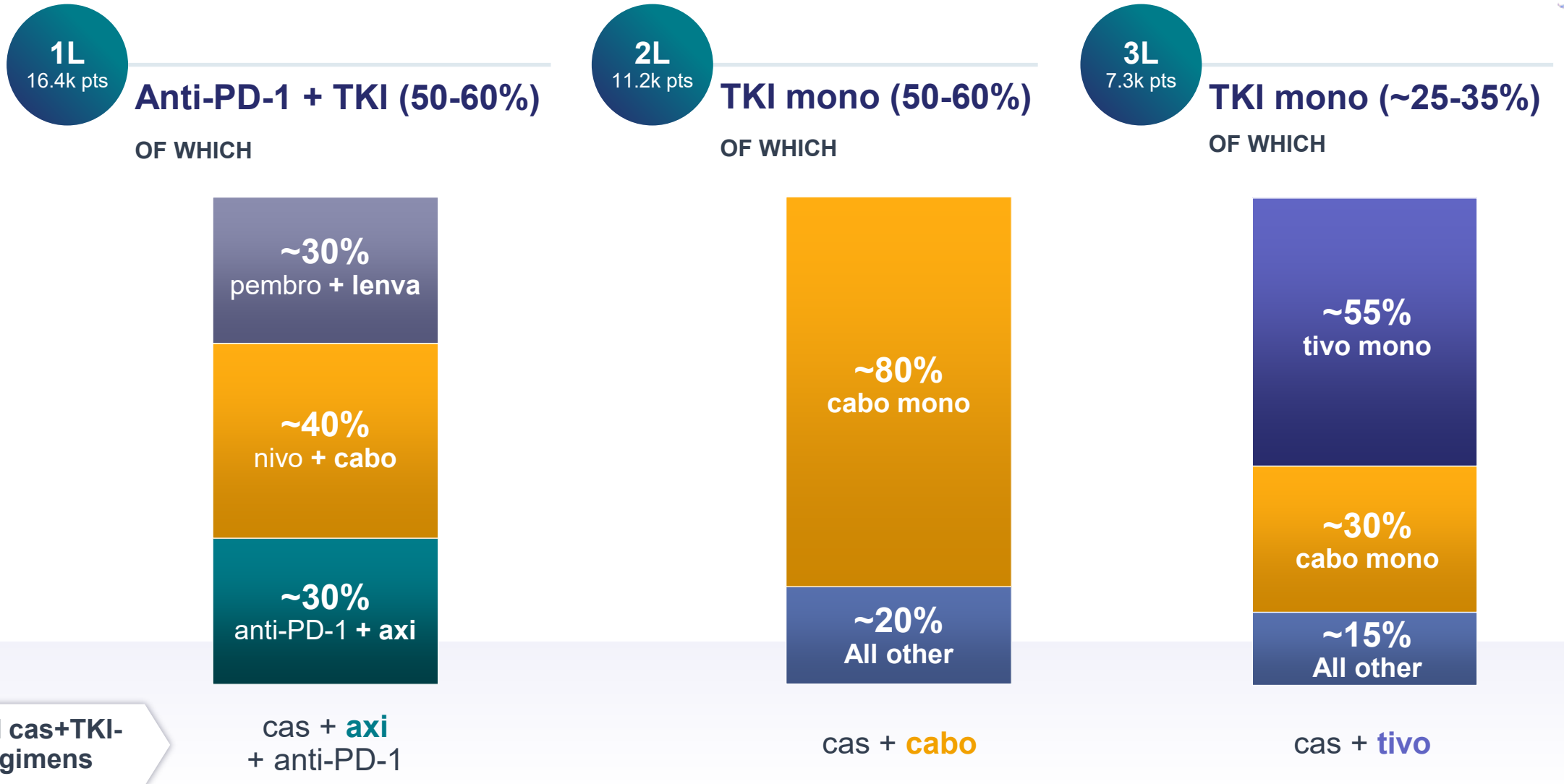
Opportunities for Improving the Treatment Paradigm in ccRCC

Dr. Rana McKay, University of California San Diego

The RCC Patient Journey Today



TKI Sequencing is an Important Consideration for Physicians



1L Opportunity: Durable Remission With a TKI-Free Regimen

Opportunity for cas + ipi + nivo

- ✓ Ipi + nivo is the most widely used regimen in 1L ccRCC, particularly in the academic setting
- ✓ Greatest liability of nivo-ipi is its **high rate of primary progression (~1 in 5 patients)** and shorter PFS relative to anti-PD-1 + TKI
- ✓ Best opportunity for patients to achieve durable remission, and enables patients to avoid TKIs in the 1L
- ✓ **Cas has the potential to reduce this high rate of PD and improve PFS with minimal added toxicity**

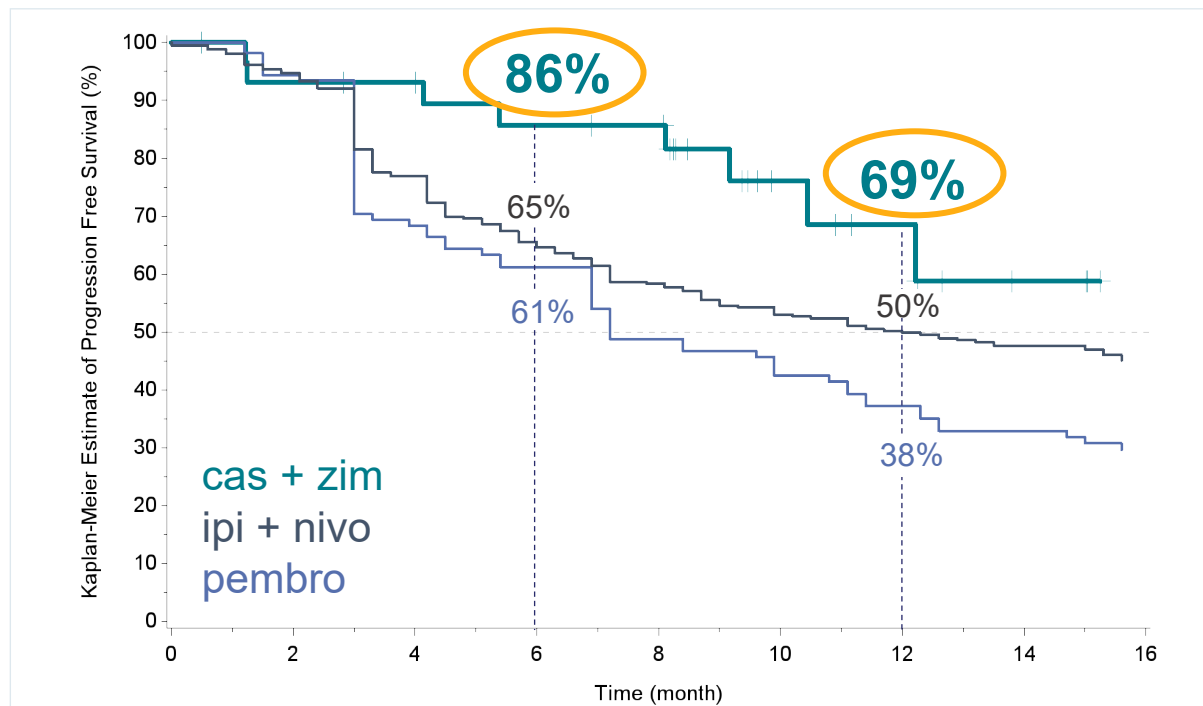
Median follow-up 11.5 months

*Includes two patients whose responses confirmed after the data cut-off date

Tick marks indicate censored patients

References and acronyms on slide 91

Early cas + zim data showing improvement in primary PD and PFS



	cas + zim (n=30)	ipi + nivo ² (n=550)	pembro ¹ (n=110)
mPFS, mos.	NR (>12)	11.6	7.1
cORR, %	50%*	39%	36%
Progressive disease, %	7%	20%	30%

2L Opportunity: Cas + Cabo Has the Potential to Improve PFS and OS and Provide Dramatic Benefit to TKI-Pretreated Patients

If approved, cas + cabo likely to be the preferred HIF-2 α - based combination

- ✓ Cabo is the most commonly prescribed TKI in 2L
- ✓ Significant comfort / experience with managing cabo-related toxicities
- ✓ Opportunity to dramatically benefit patients with prior TKI experience
- ✓ Opportunity to show an OS benefit over cabo where belz + lenva failed

Overall 2L cabo mono performance has been consistent...

Phase 3 Trial	Study Arms	N	Median PFS	Median OS
LITESPARK-011 ¹⁰	belz + lenva vs. cabo	371 vs. 376	10.6m	28.6m
CONTACT-03 ⁴	atezo + cabo vs. cabo	263 vs. 259	10.8m	NR

...However, cabo performs worse in patients who received prior TKI

Trial / Publication	Study Arms	N	Median PFS	Median OS
CABOPOINT ¹⁶	cabo: no prior TKI, with prior TKI	79, 40	10.9m, 8.3m	24.3m, 24.1m
 ^{13*} European Association of Urology	cabo post-pembro+lenva	20	5.8m*	NA
 ¹²	cabo post-pembro+lenva	22	4.1m	8.1m

*Median time to treatment failure is used as a proxy for mPFS
References and acronyms on slide 91

Late-line Opportunity: Improve Upon Existing Regimens, Including in HIF-2 α -Experienced Patients

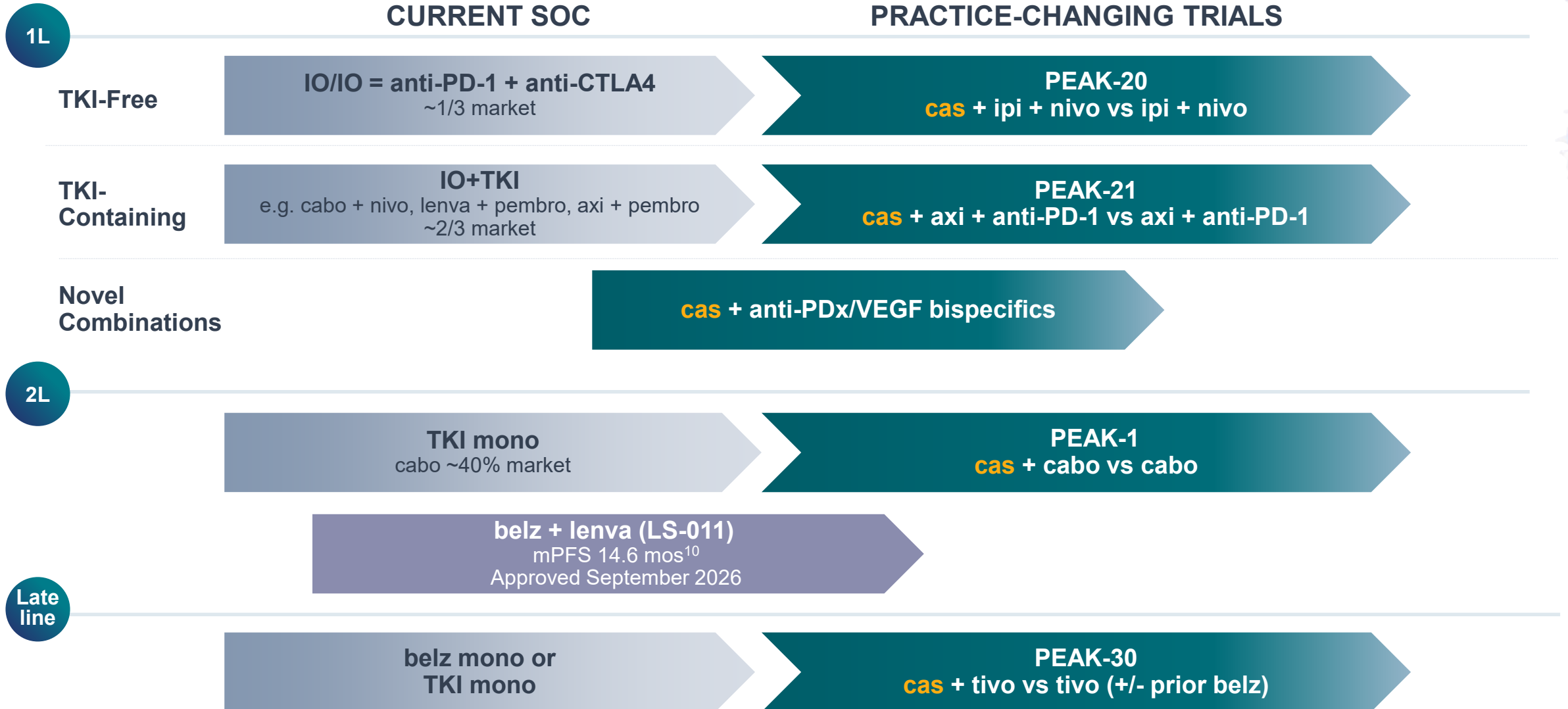
Cas + tivo could address the limitations of TKI and belz mono

- ✓ Reduce the high rate of primary progression
- ✓ Potential to substantially increase median PFS
- ✓ Opportunity to show an OS benefit over TKI mono
- ✓ Opportunity to demonstrate benefit in HIF-2 α -experienced patients

High rate of PD and short PFS for both tivo and belz monotherapy

PHASE 3 TRIAL	EXPERIMENTAL ARM	N	PRIMARY PROGRESSION	MEDIAN PFS	OS HR
TIVO-3^{17,18}	tivo	175	22%	5.6m	0.89
LITESPARK-005¹⁹	belz	374	34%	5.6m	0.92

Casdatifan Has the Potential to Benefit Every ccRCC Patient Throughout Their Treatment Journey

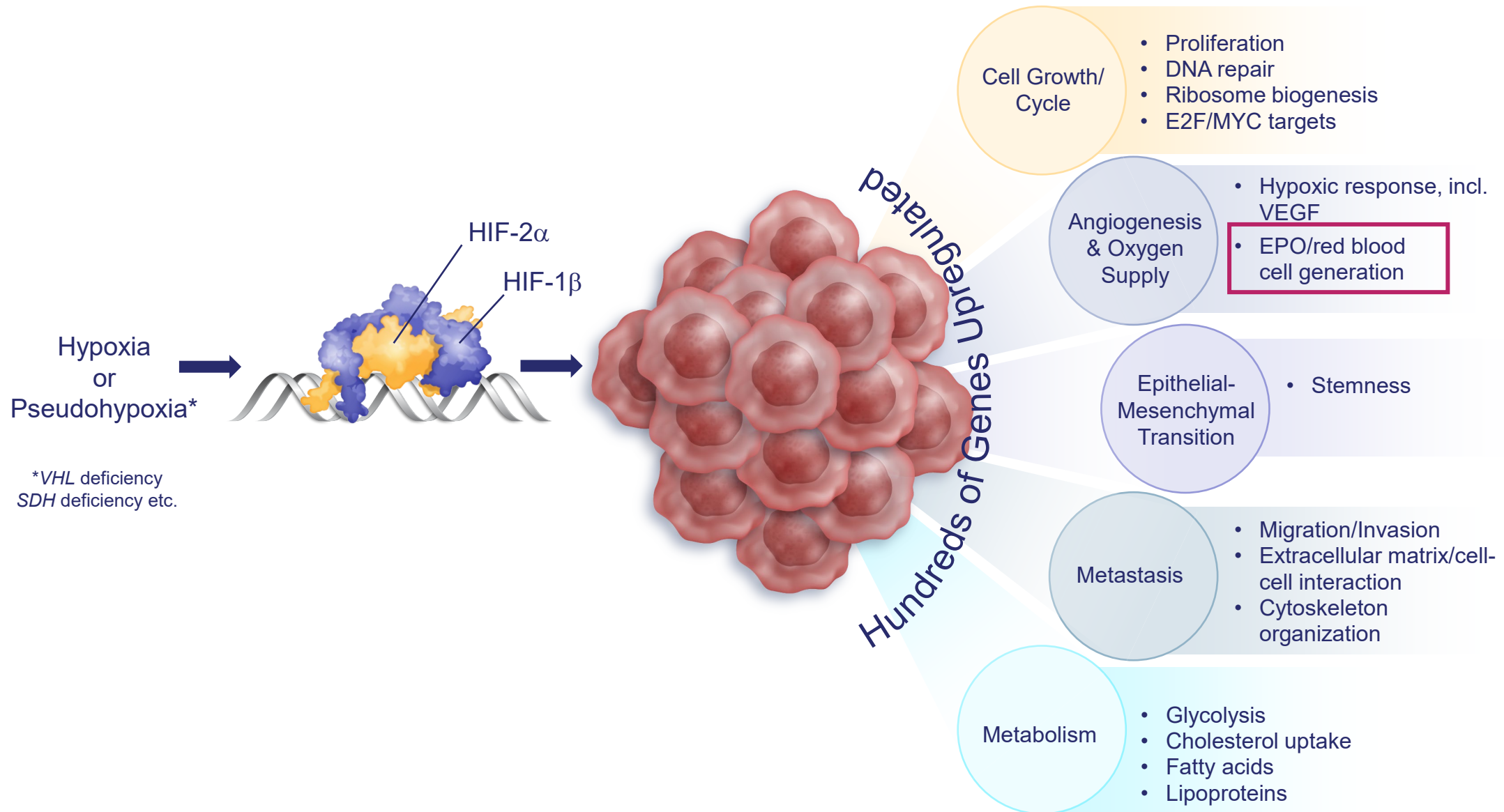




Translational Science Supports the Best-in-Class Profile of Casdatifan

Juan Jaen, Ph.D., President

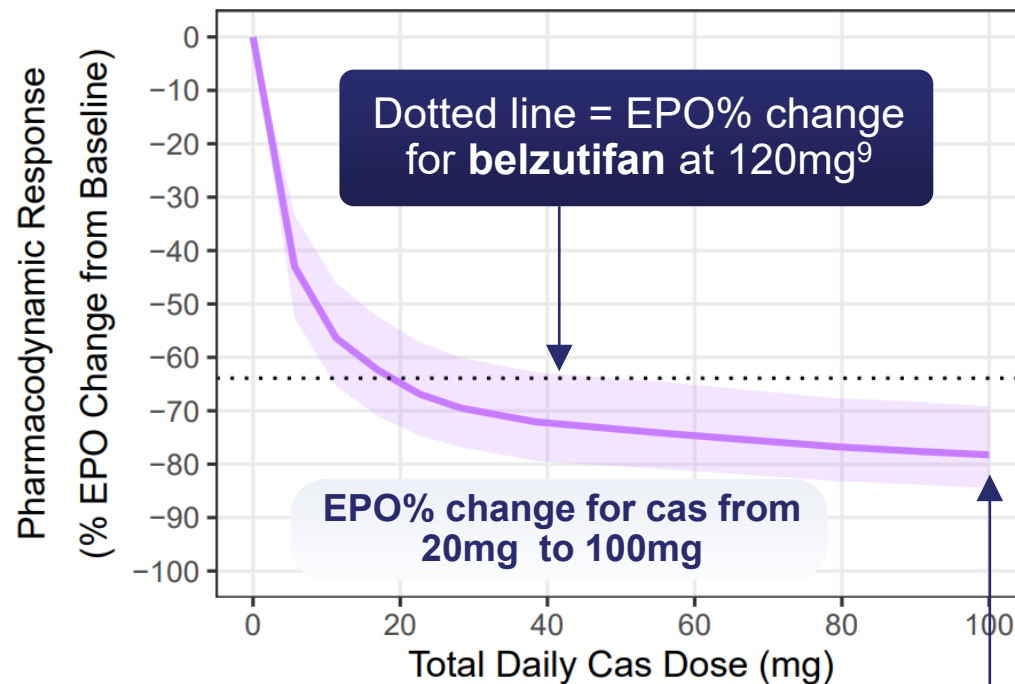
Increased HIF-2 α Activity Allows ccRCC Tumors to Survive and Metastasize



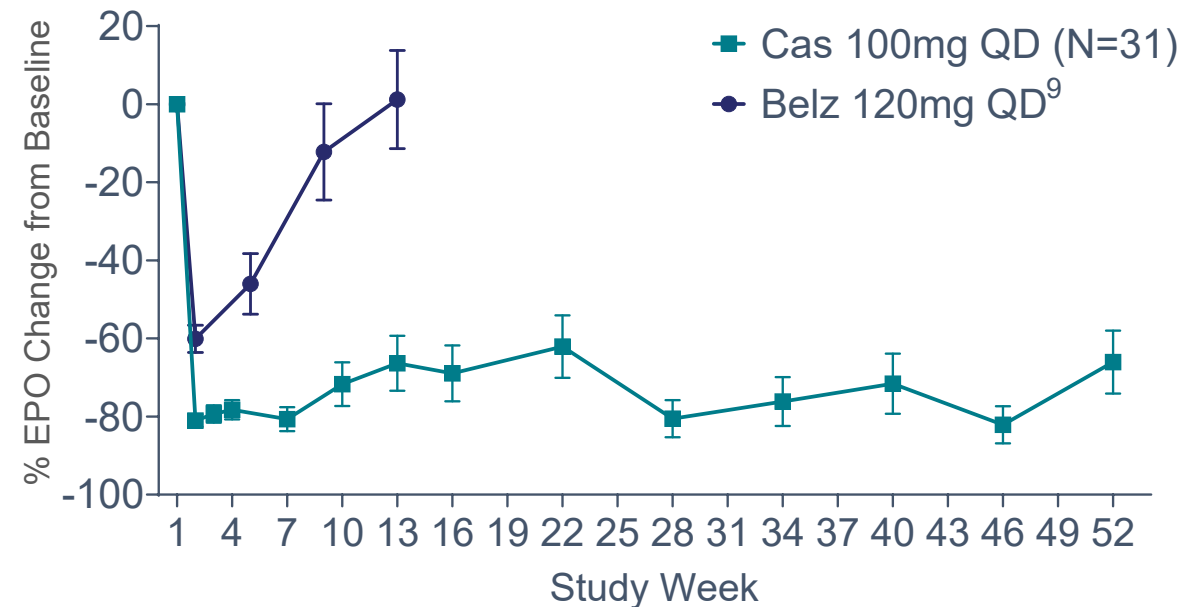
Casdatifan's Advantages Stem from an Improved PK / PD Profile, Enabling it to "Hit the Target Harder"

EPO suppression: PD biomarker for HIF-2 α inhibition

20mg of cas achieves the same EPO reduction as that of 120mg of belz, with significantly greater sustained suppression

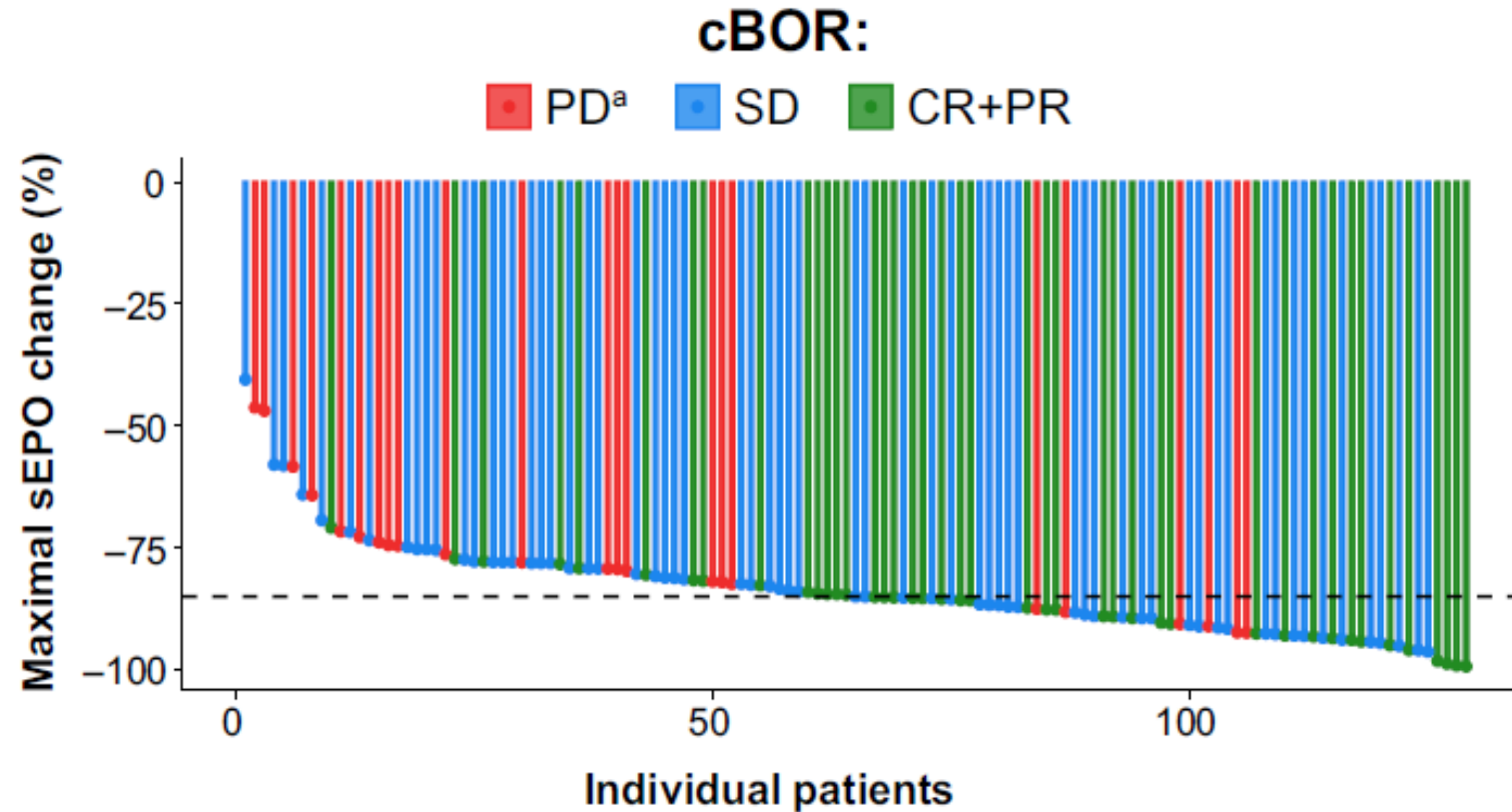


20mg of cas is **one-fifth** our Phase 3 dose of 100mg



100mg QD of cas results in substantial and **sustained** EPO suppression

Systemic Suppression of HIF-2 α –Regulated sEPO is Highly Correlated with Clinical Benefit from Casdatifan (ORR)



Across all doses, most patients (88/129 [68%]) experienced > 80% maximal sEPO reduction²⁰

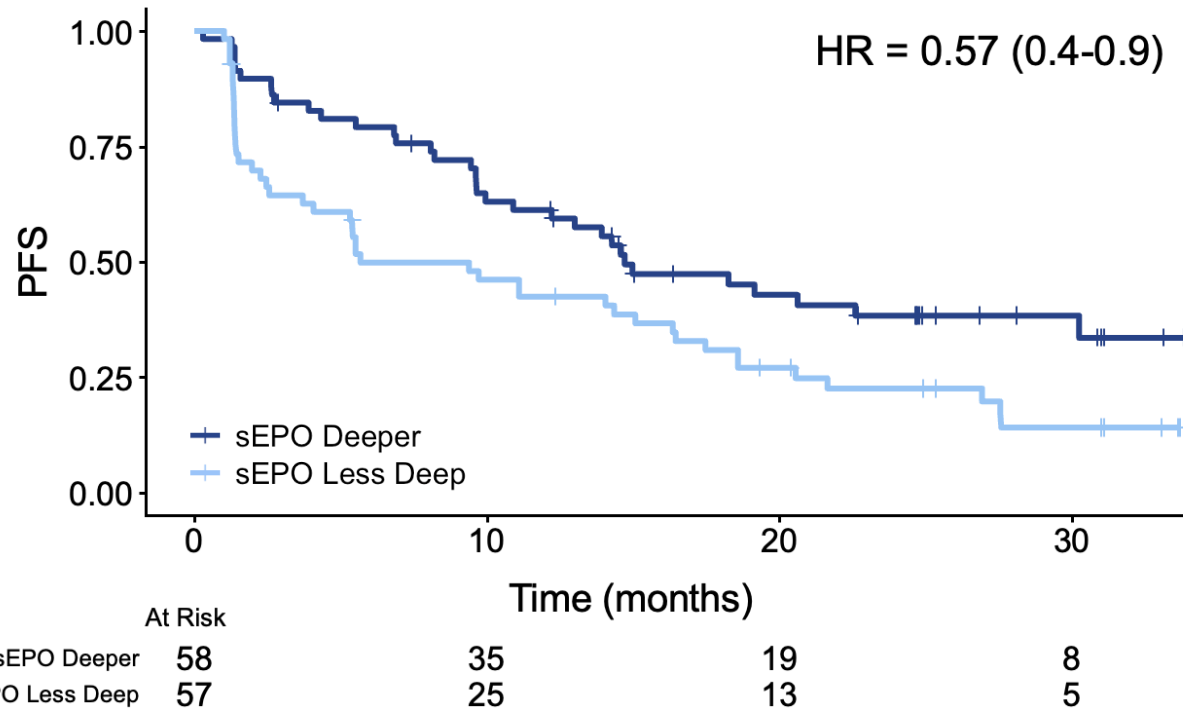
Deeper reductions in sEPO were highly correlated with clinical responses²⁰

a. PD was defined according to RECIST v1.1 as a $\geq 20\%$ increase in the sum of diameters of target lesions relative to the smallest sum on study (including baseline, if smallest), with an absolute increase of ≥ 5 mm. The appearance of 1 or more new lesions was also considered progression.

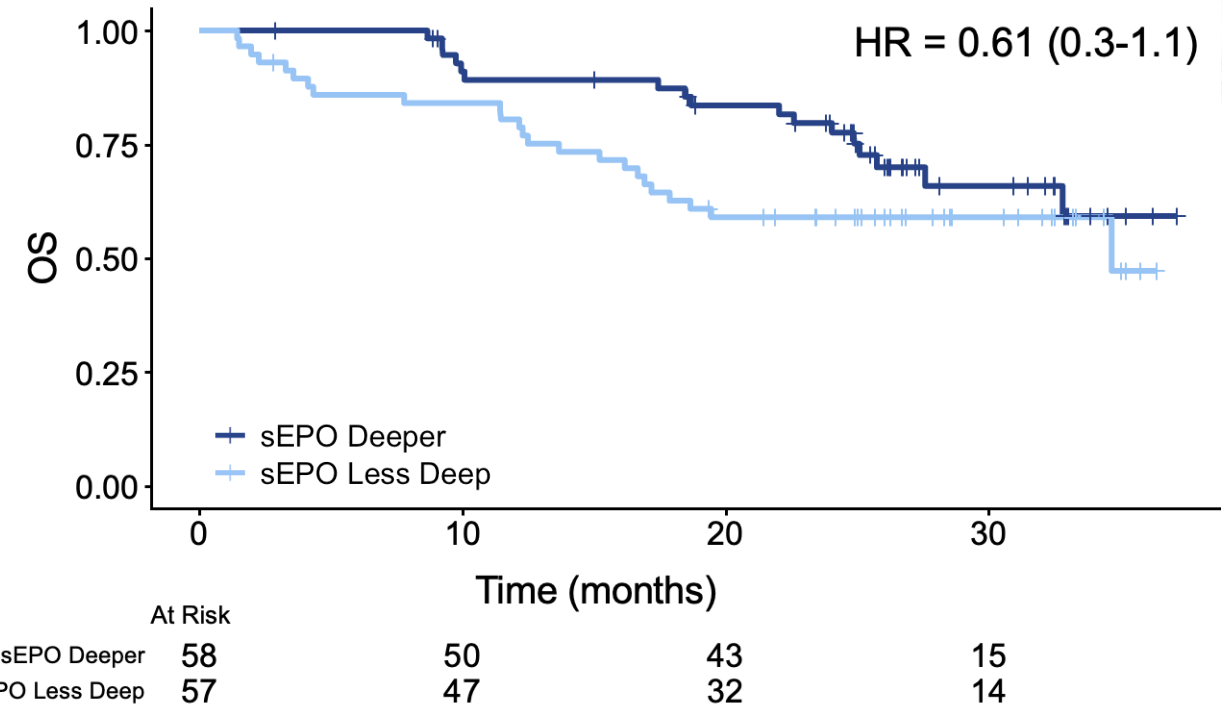
References and acronyms on slide 91

Deeper and Sustained HIF-2 α Inhibition by Casdatifan is Associated with Better PFS and OS

PFS – relationship with sEPO change



OS – relationship with sEPO change

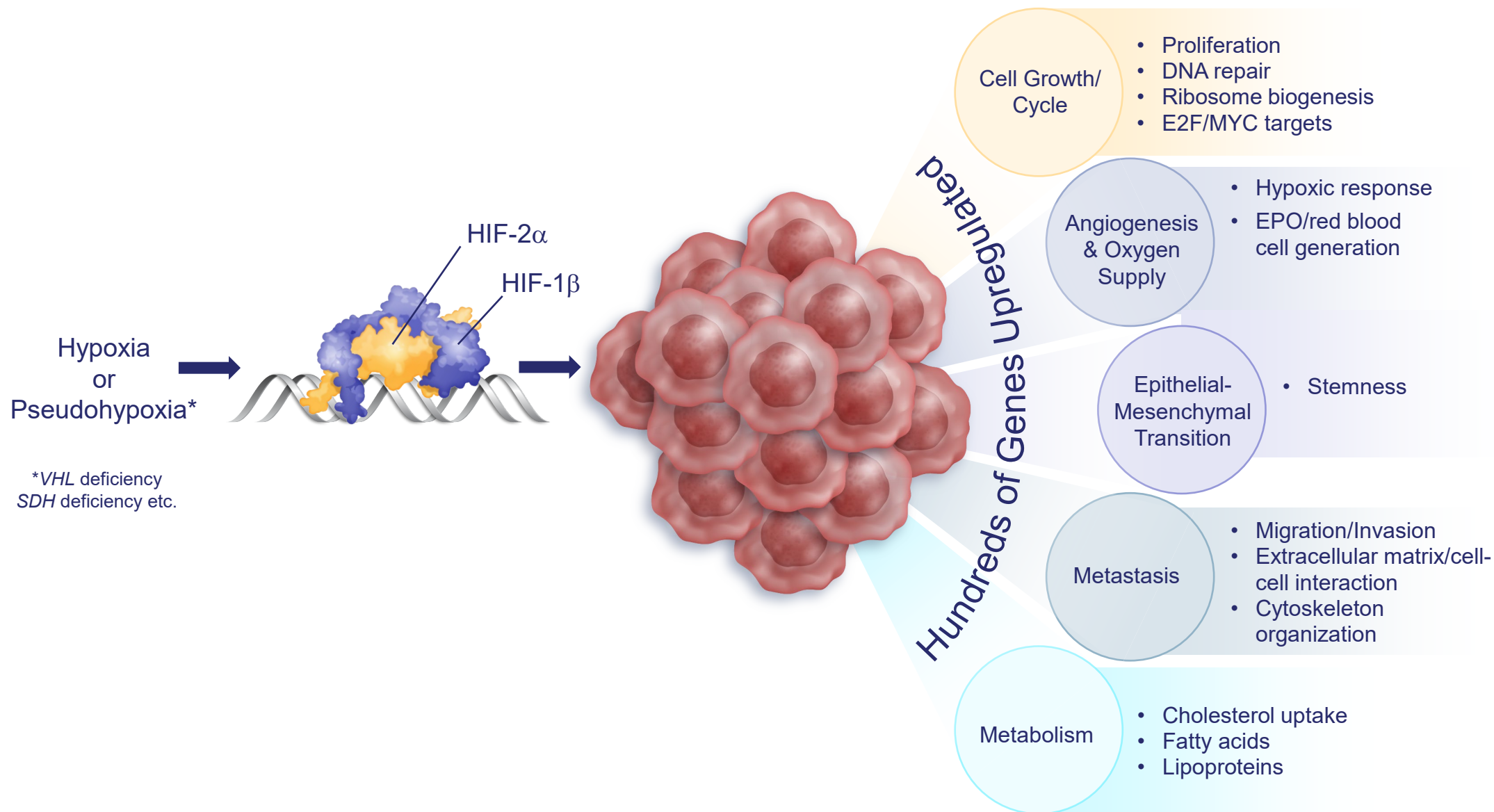


ARC-20 pooled monotherapy cohorts (50mg QD, 50mg BID, 100mg QD, 150mg QD)

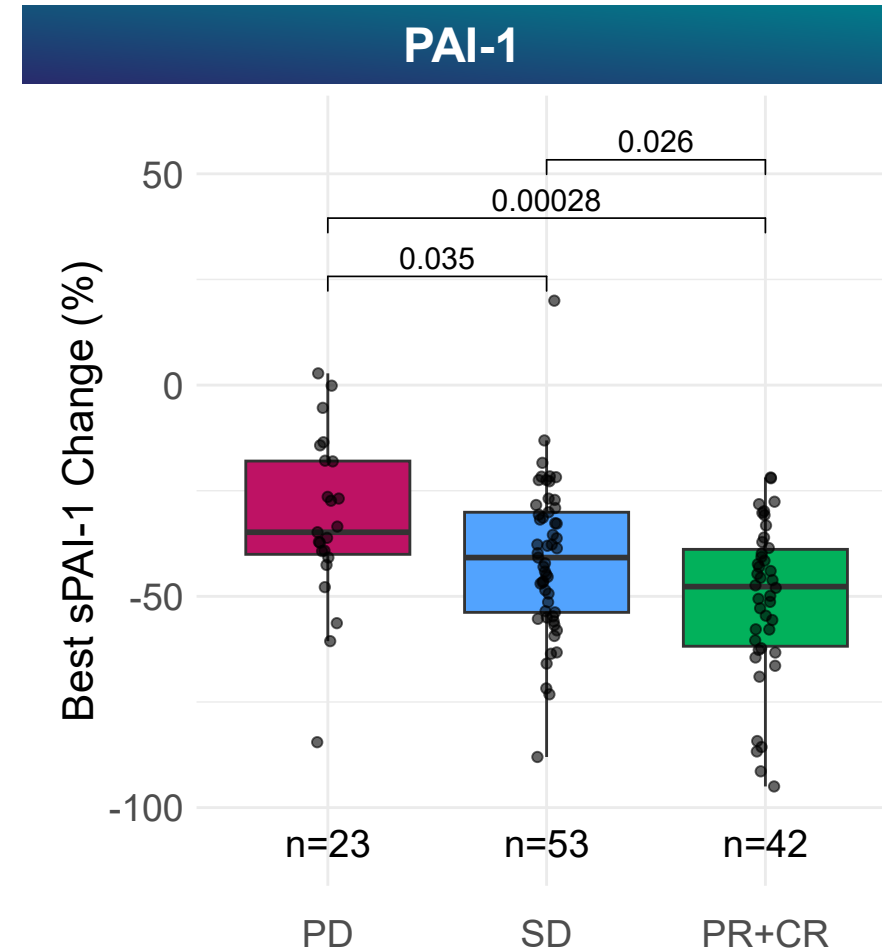
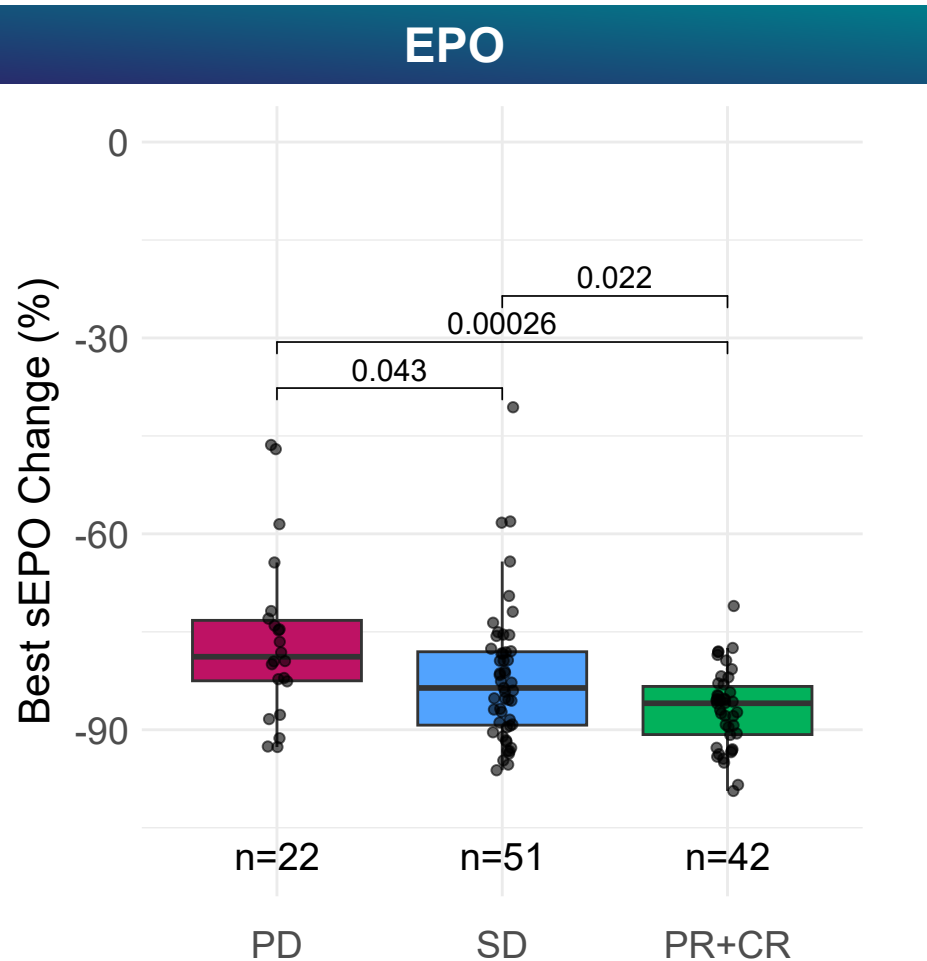
Tick marks indicate censored patients

References and acronyms on slide 91

HIF-2 α Regulates the Transcription of Many Genes²¹



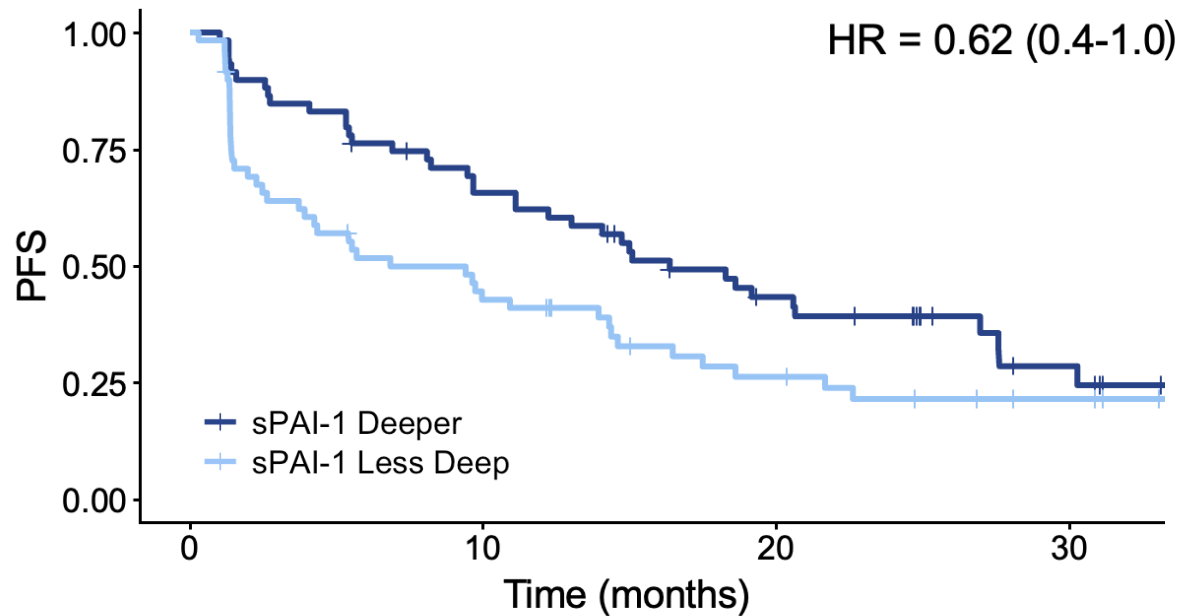
Patients with Tumor Responses Experience Deeper sEPO and sPAI-1 Decreases with Cas Monotherapy



Changes in New Biomarker (PAI-1) Correlate with Clinical Results: Better PFS and OS are Reflective of Biology

PAI-1 is also controlled by HIF-2 α , and deeper suppression is associated with longer PFS and OS

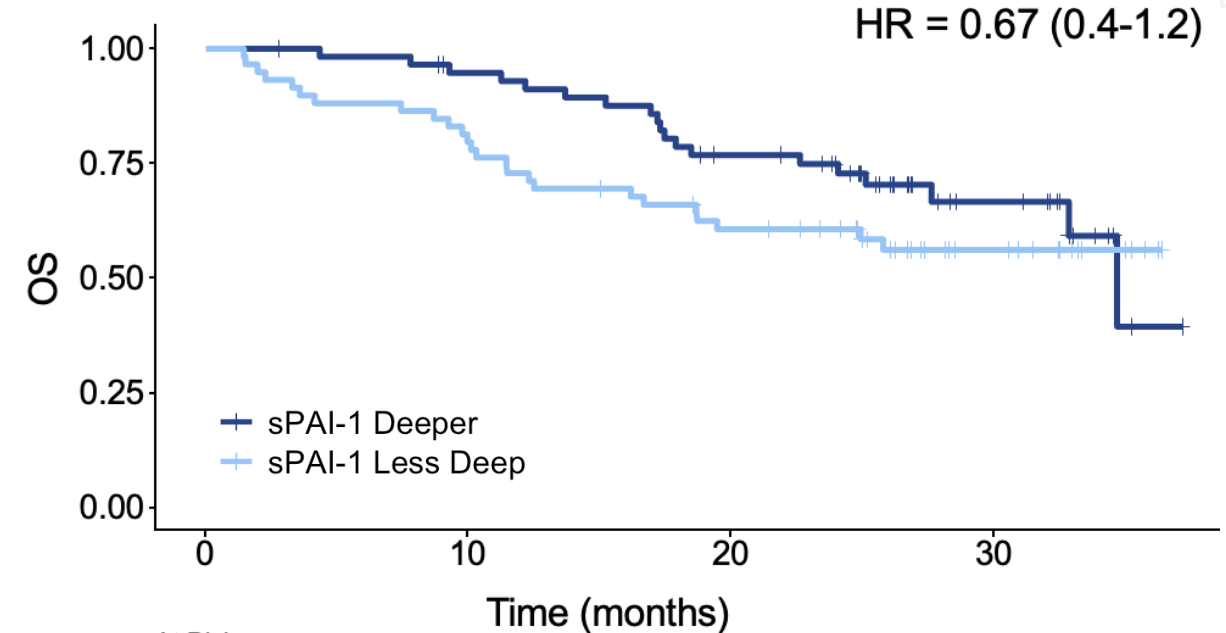
PFS – relationship with sPAI-1 change



At Risk

sPAI-1 Deeper	59	37	21	7
sPAI-1 Less Deep	59	24	12	6

OS – relationship with sPAI-1 change



At Risk

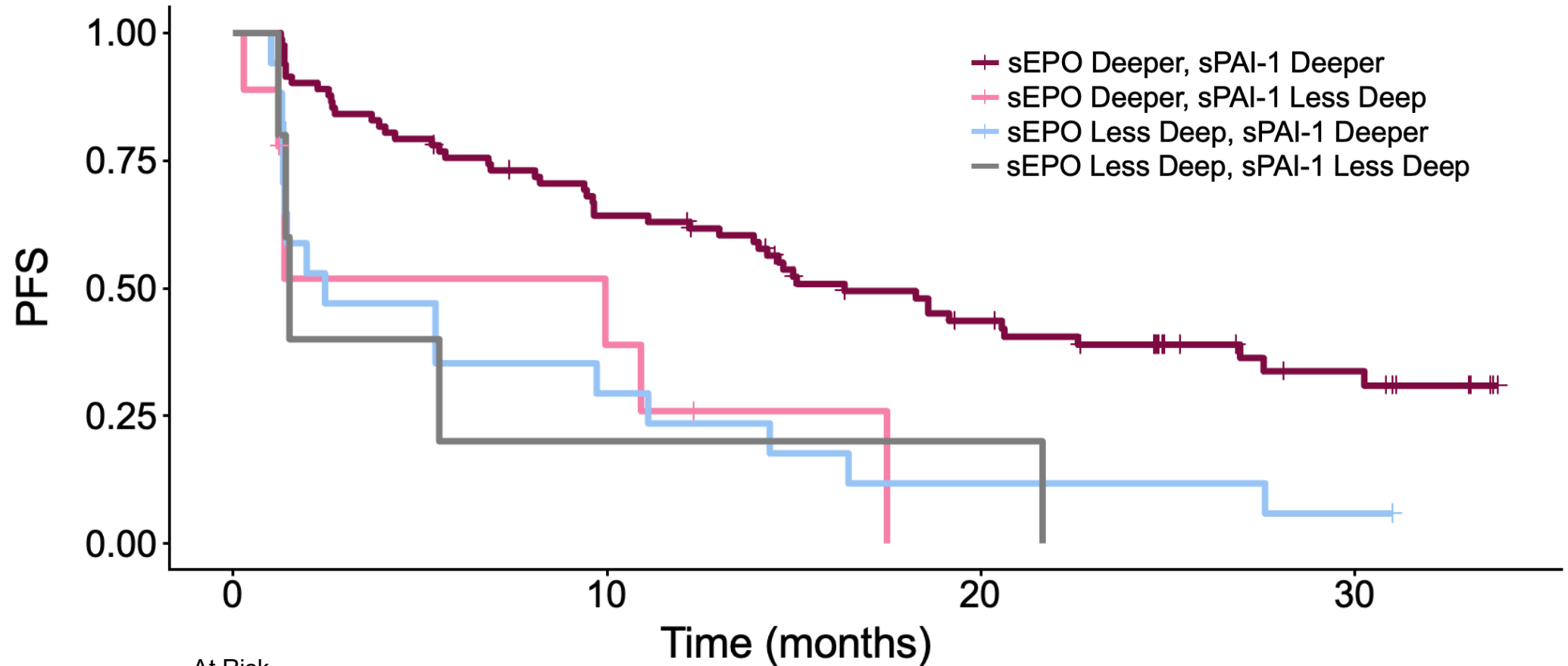
sPAI-1 Deeper	59	53	41	15
sPAI-1 Less Deep	59	47	34	14

ARC-20 pooled monotherapy cohorts (50mg QD, 50mg BID, 100mg QD, 150mg QD)

Tick marks indicate censored patients

References and acronyms on slide 91

Vast Majority of Patients Experience Pronounced Reduction in sEPO or sPAI-1 and Respond Well to Cas Monotherapy



At Risk

sEPO Deeper, sPAI-1 Deeper	84	52	30	12
sEPO Deeper, sPAI-1 Less Deep	9	3	0	0
sEPO Less Deep, sPAI-1 Deeper	17	5	2	1
sEPO Less Deep, sPAI-1 Less Deep	5	1	1	0

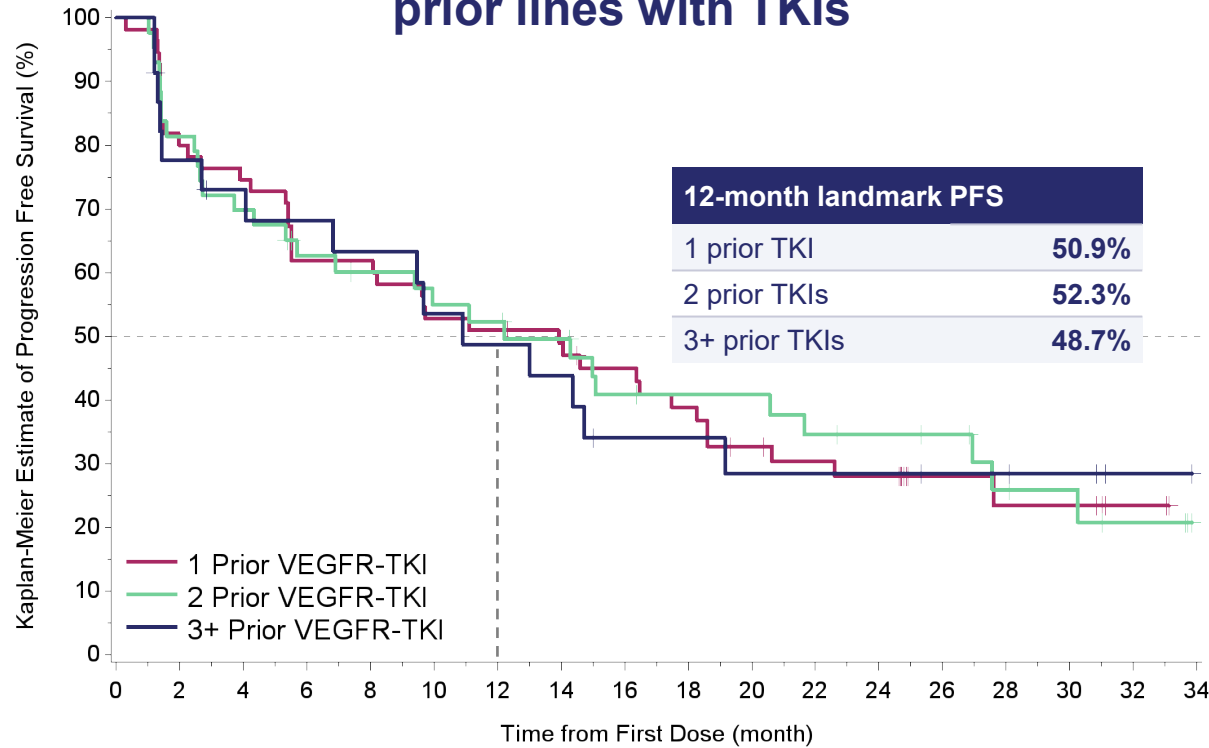
ARC-20 pooled monotherapy cohorts (50mg QD, 50mg BID, 100mg QD, 150mg QD)

Tick marks indicate censored patients

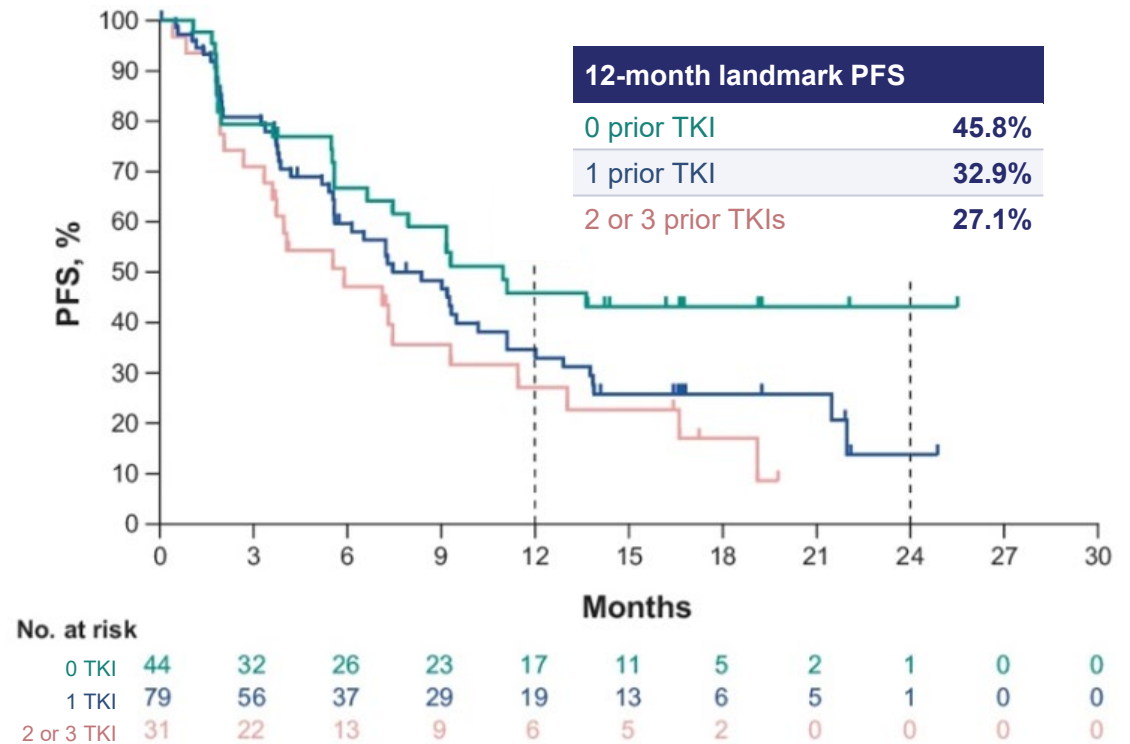
References and acronyms on slide 91

Casdatifan Can Overcome the Apparent Increase in HIF-2 α Activity Induced by TKI Therapies

PFS with casdatifan is not impacted by more prior lines with TKIs



PFS with belzutifan is diminished by more prior lines with TKIs (LS-013)²²



Tick marks indicate censored patients

References and acronyms on slide 91

Key Experimental Observations Following TKI Treatment Support **Adaptive HIF-2 α** Model

In the tumor

- Increased HIF-2 α protein (IHC)
- Increased HIF-2 α signature (mRNA)

In the periphery

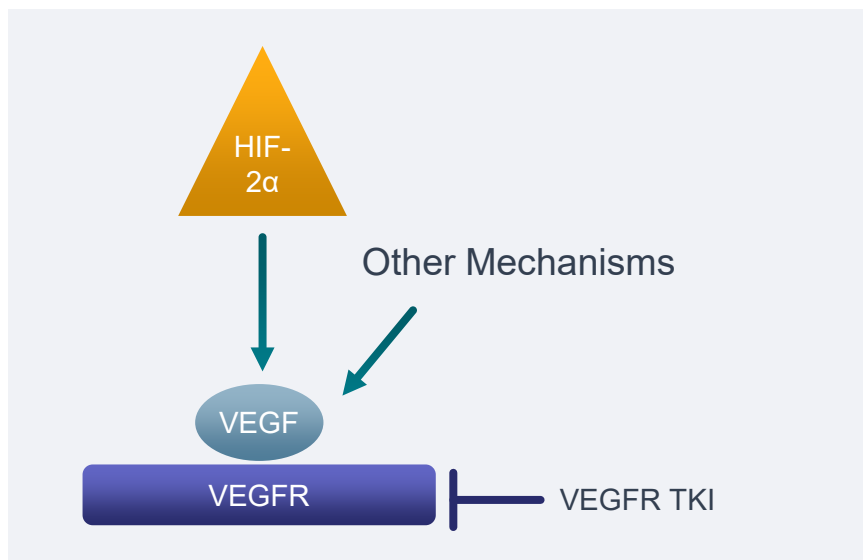
- Increased serum EPO
- Increased serum PAI-1

We believe TKI exposure leads to increased HIF-2 α activity and a more resilient tumor that requires stronger and sustained HIF-2 α inhibition

ccRCC Dependence on Innate and Adaptive HIF-2 α

Innate HIF-2 α

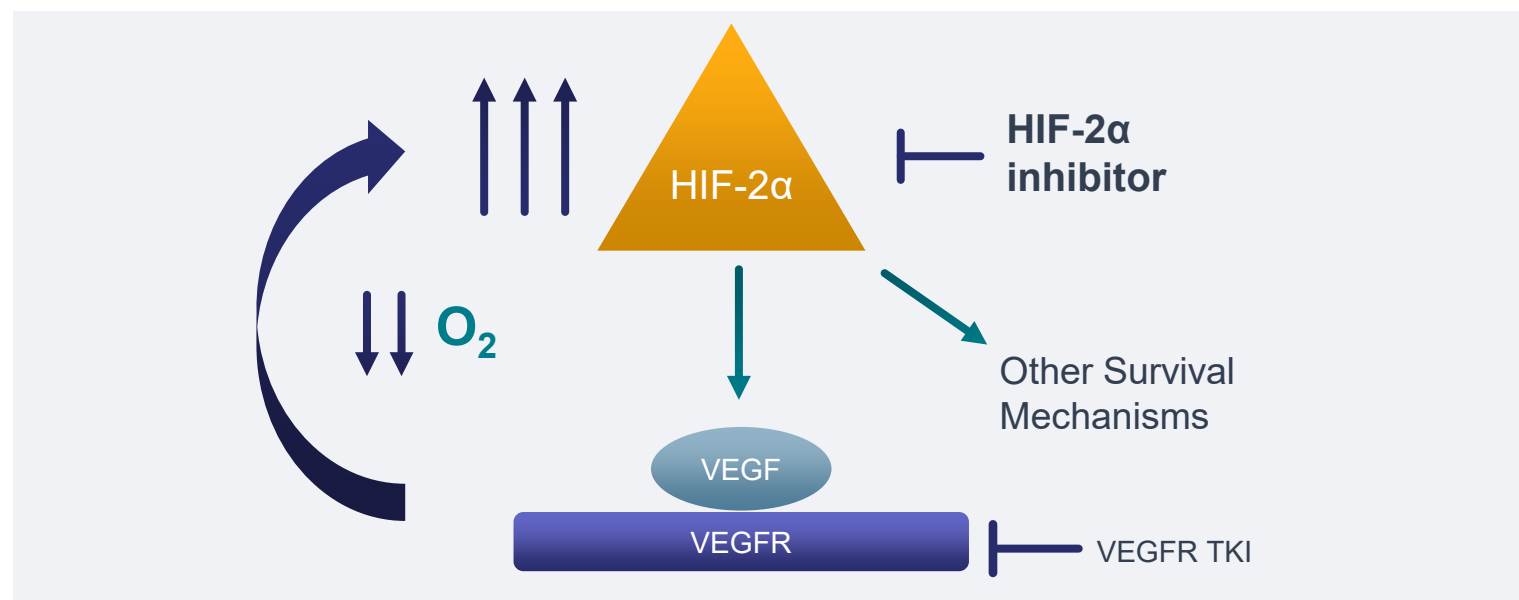
Tumors depend on VEGF to generate/maintain blood supply – production of VEGF may be controlled by HIF and other mechanisms



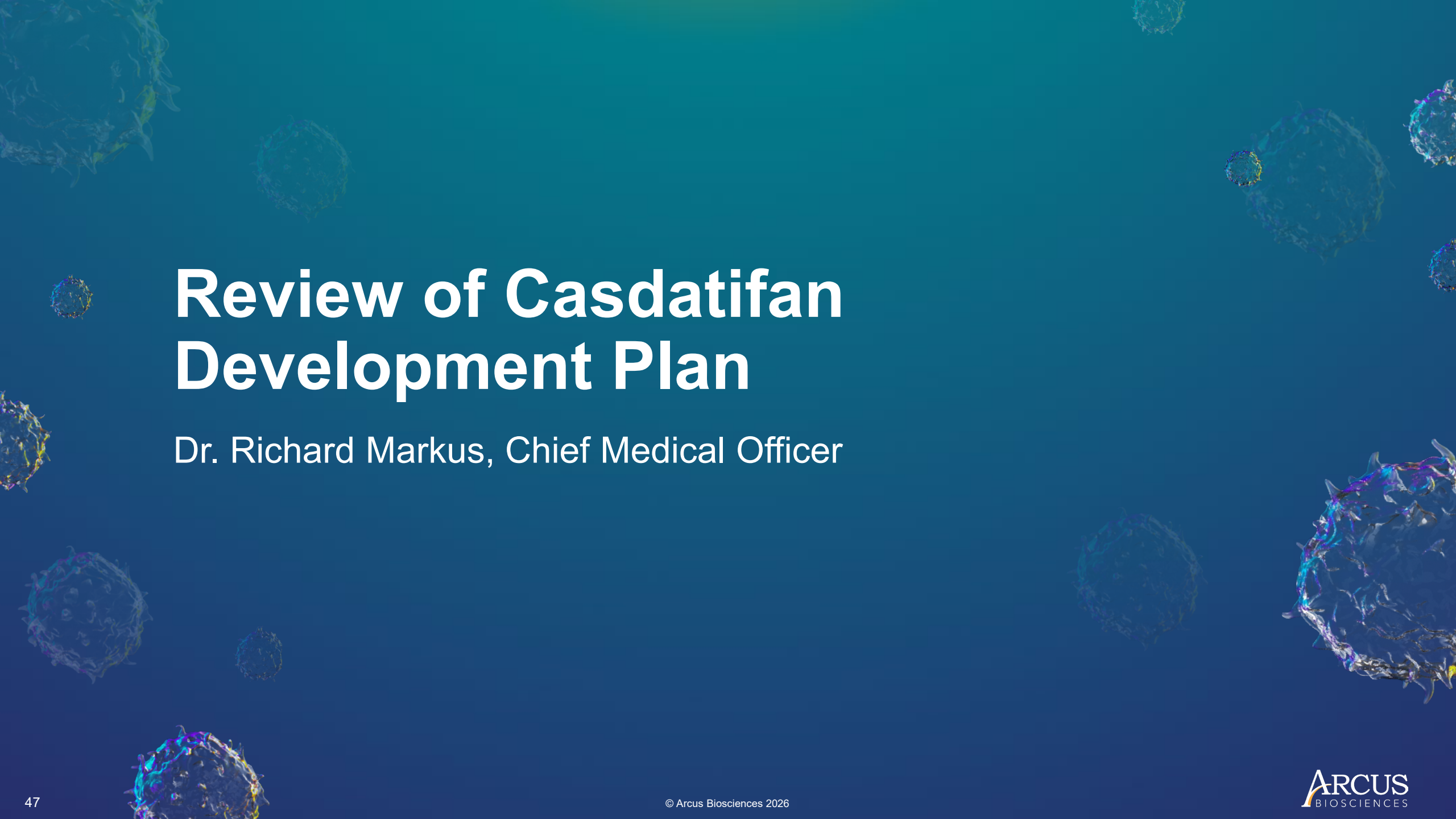
- Drives multiple survival mechanisms
- VHL deficiency
- **Well vascularized** tumors

Adaptive HIF-2 α

The hypoxia induced by anti-angiogenic agents leads to increased HIF activity



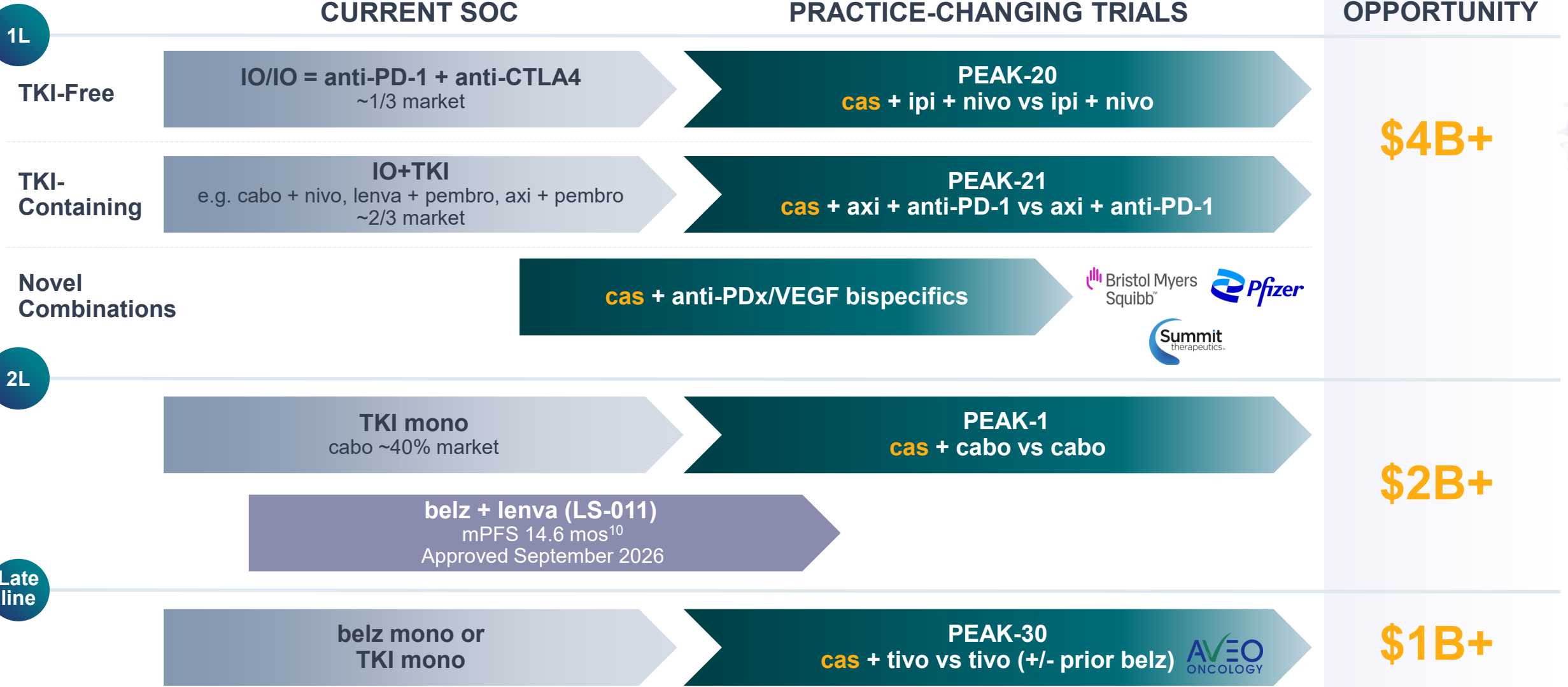
- Corresponds with **poorly vascularized** tumors, which drives HIF-2 α activity (EPO) in non-cancer cells
- Tumors less responsive to anti-angiogenic therapies (TKI)
- Survival advantage of clones with highest HIF-2 α activity/dependence
- Greater dependence on HIF-2 α makes tumors more sensitive to cas

The background is a solid dark blue color. Scattered across the slide are several stylized, glowing virus-like particles. These particles are spherical with a textured, almost crystalline surface, featuring hints of yellow, green, and purple. They vary in size and are positioned at different angles, giving a sense of depth and movement.

Review of Casdatifan Development Plan

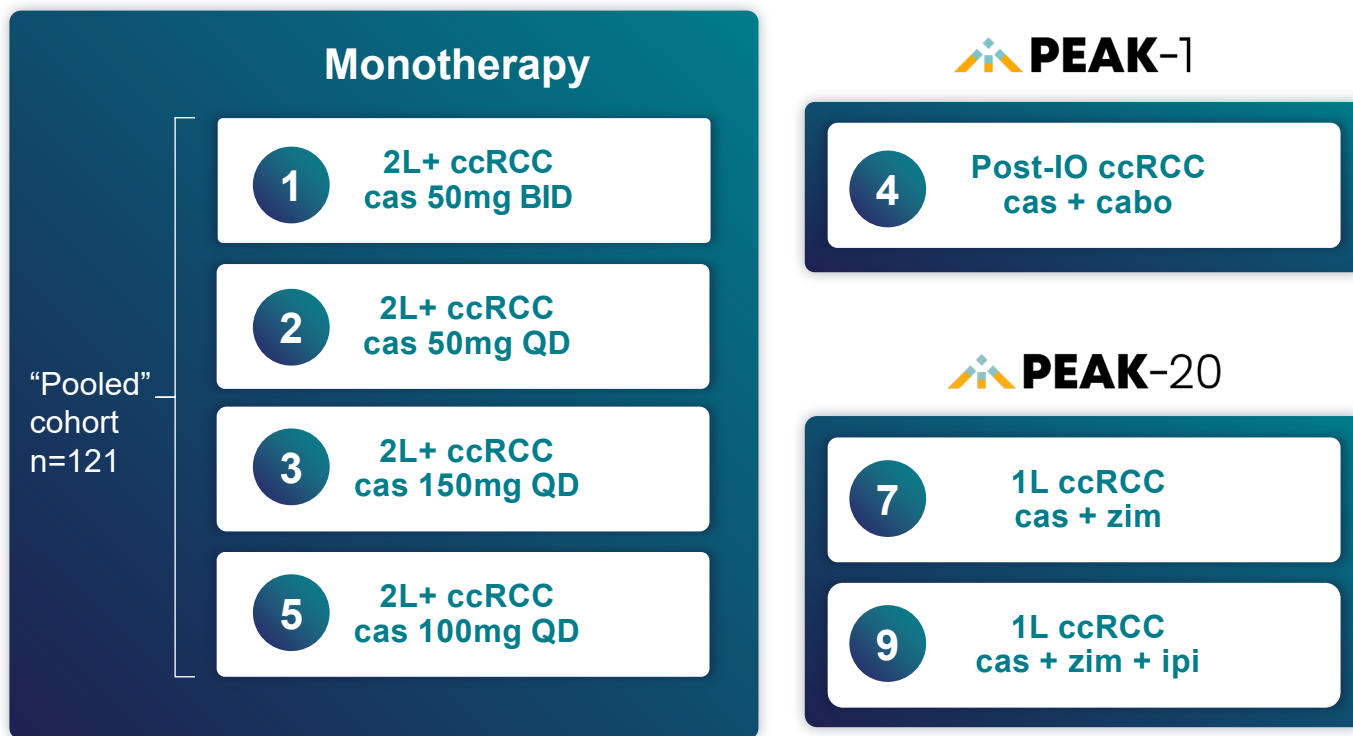
Dr. Richard Markus, Chief Medical Officer

Our Development Plan Provides Every ccRCC Patient the Opportunity to Benefit from Casdatifan



Platform Study Cohorts Provide Critical Enabling Data for Future Phase 3 Programs

Cohorts with data today



To date, over 300 patients have received casdatifan across all cohorts of ARC-20

New cohorts w/data in 2027+

Late-line randomized cohort

11 2L+ ccRCC (post HIF-2α)
cas + tivo vs tivo

1L Cohorts

12 1L ccRCC
cas + ivo

13 1L ccRCC
cas + zim + axi

Additional exploratory cohorts

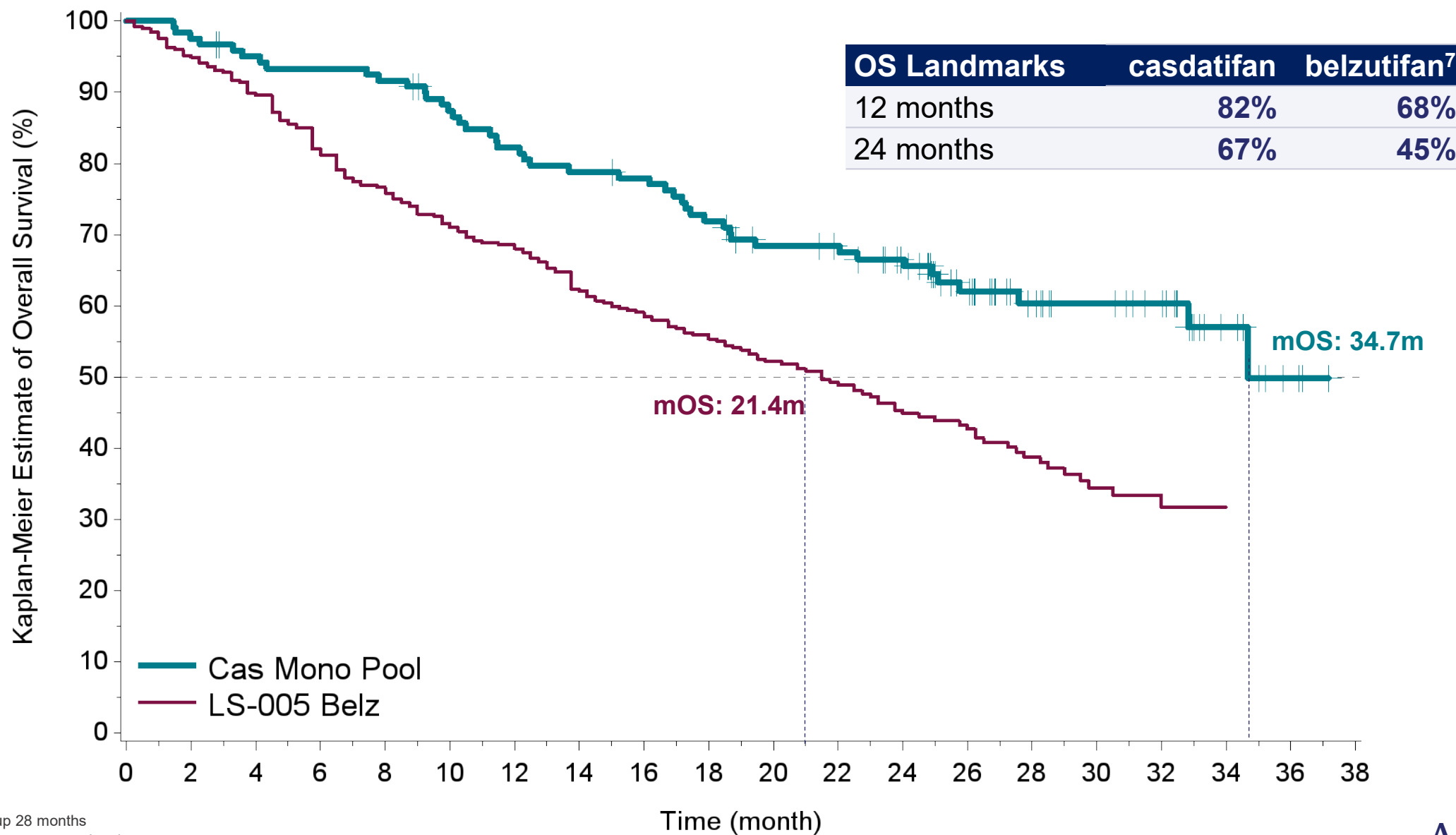
6 1L Favorable-risk ccRCC
monotherapy
cas 100mg QD

8 Post-IO ccRCC
monotherapy
cas 100mg QD



Late Line: Unprecedented OS in Heavily Pretreated Patients

Casdatifan Provides Unprecedented OS in Late-line Setting



Median follow-up 28 months
Tick marks indicate censored patients
References and acronyms on slide 91

Casdatifan Was Well Tolerated in All Cohorts, With a Comparable Safety Profile to That of Belzutifan

Safety-Evaluable Population*	100mg QD (n=32)	Pooled (n=127)	belzutifan (LITESPARK-005) ⁷
Median follow-up, months (range)	25.0 (19.0, 26.2)	28.1 (19.0, 38.7)	
Any TEAEs, n (%)	31 (97)	125 (98)	
Related to casdatifan	29 (91)	120 (95)	
Any Grade ≥3 TEAEs, n (%)	21 (66)	90 (71)	Serious AEs: All-cause: 43% TRAEs: 13%
Related to casdatifan	15 (47)	70 (55)	
Any Serious TEAEs, n (%)	14 (44)	50 (39)	
Related to casdatifan	3 (9)	11 (9)	

*The safety-evaluable population included all dose expansion enrolled patients who received any amount of any study treatment.
References and acronyms on slide 91

Casdatifan + Tivozanib Has the Potential to be the Dominant Regimen in Late-line ccRCC

Combination strategy has the potential to delay monotherapy to very late-line use and consolidate the fragmented landscape

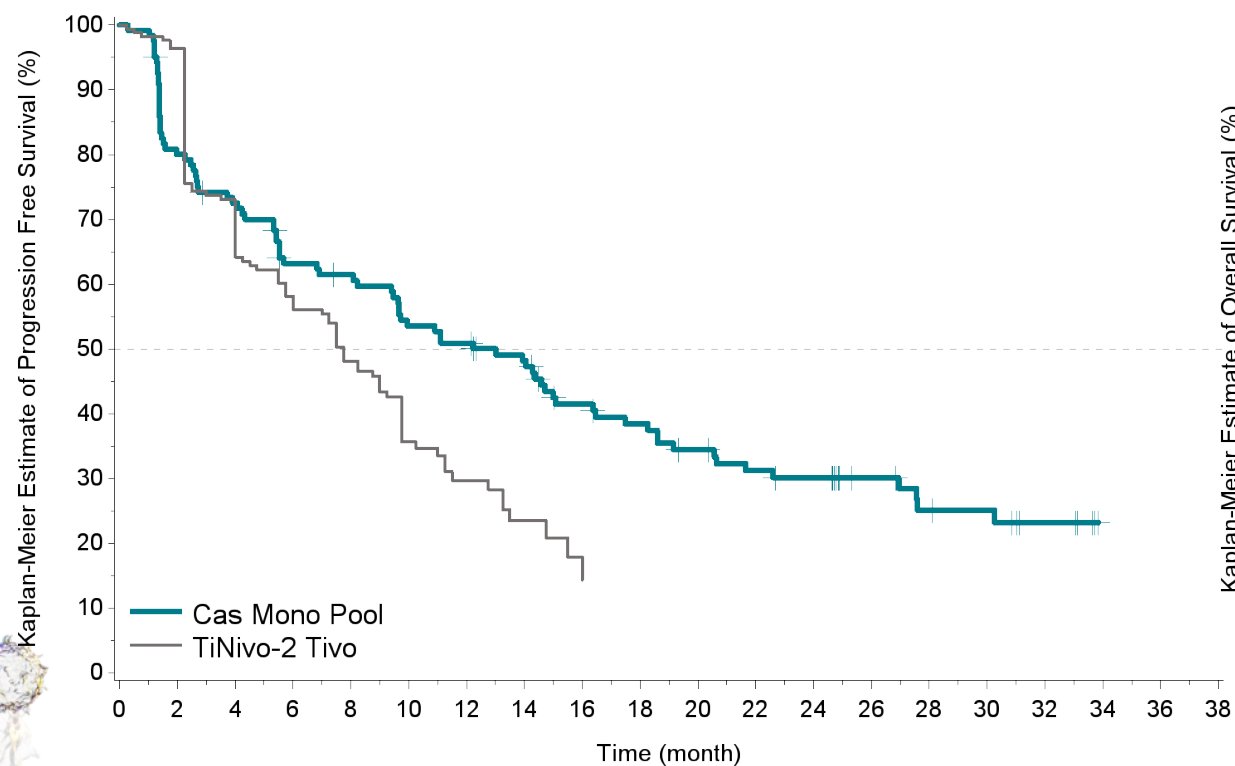
	Current 3rd-line options in metastatic ccRCC		
	belzutifan ⁴	tivozanib ¹⁷	everolimus ²³
Mechanism	HIF-2α inhibitor	Pan-VEGFR TKI	mTORC1 inhibitor
PFS (mo)	5.6	5.6	4.9
ORR	23%	18%	<5%
OS benefit	Not demonstrated	Not demonstrated	Not demonstrated
Market share in 3L*	20-30%	20-25%	5%

Potential future regimen
casdatifan + tivozanib
HIF-2α inhibitor + VEGFR TKI
Improved PFS
Improved ORR
OS benefit
Potential to supplant monotherapy options

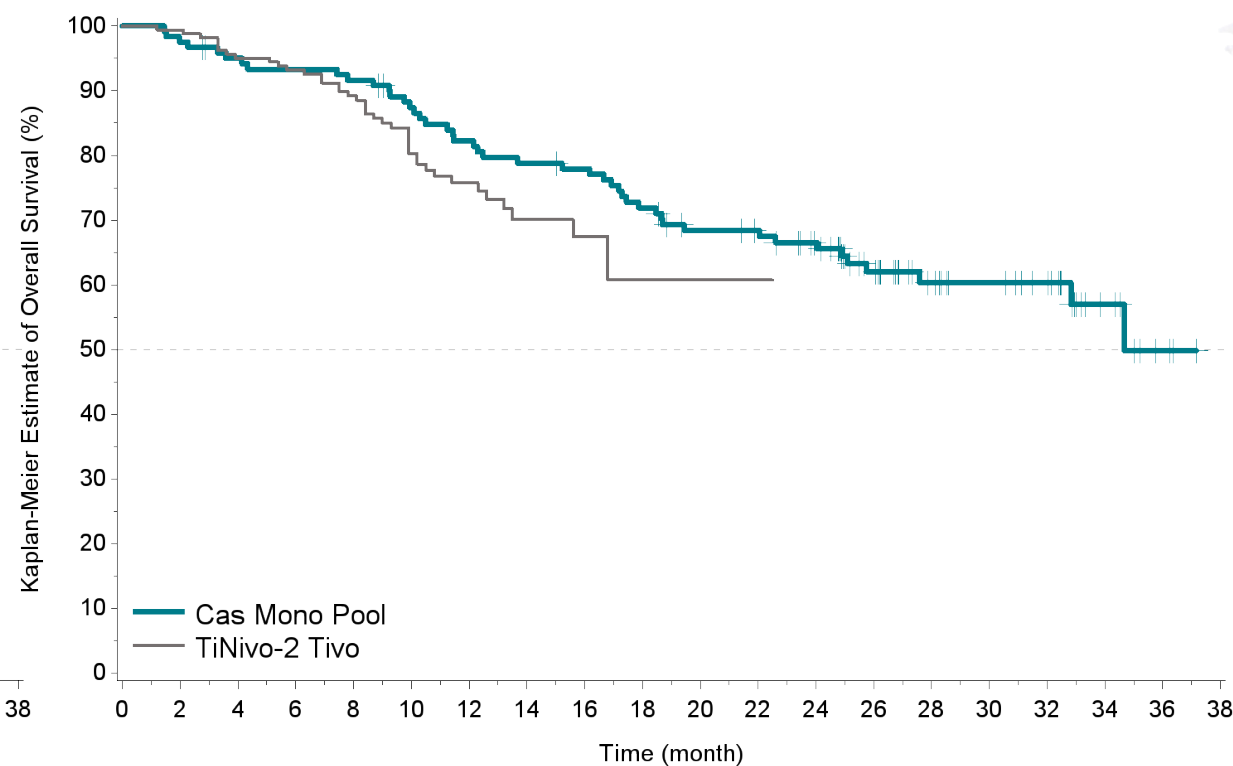
*Arcus primary research
References and acronyms on slide 91

Casdatifan Monotherapy Demonstrates Substantially Improved PFS and OS Relative to Tivozanib in Late-Line ccRCC

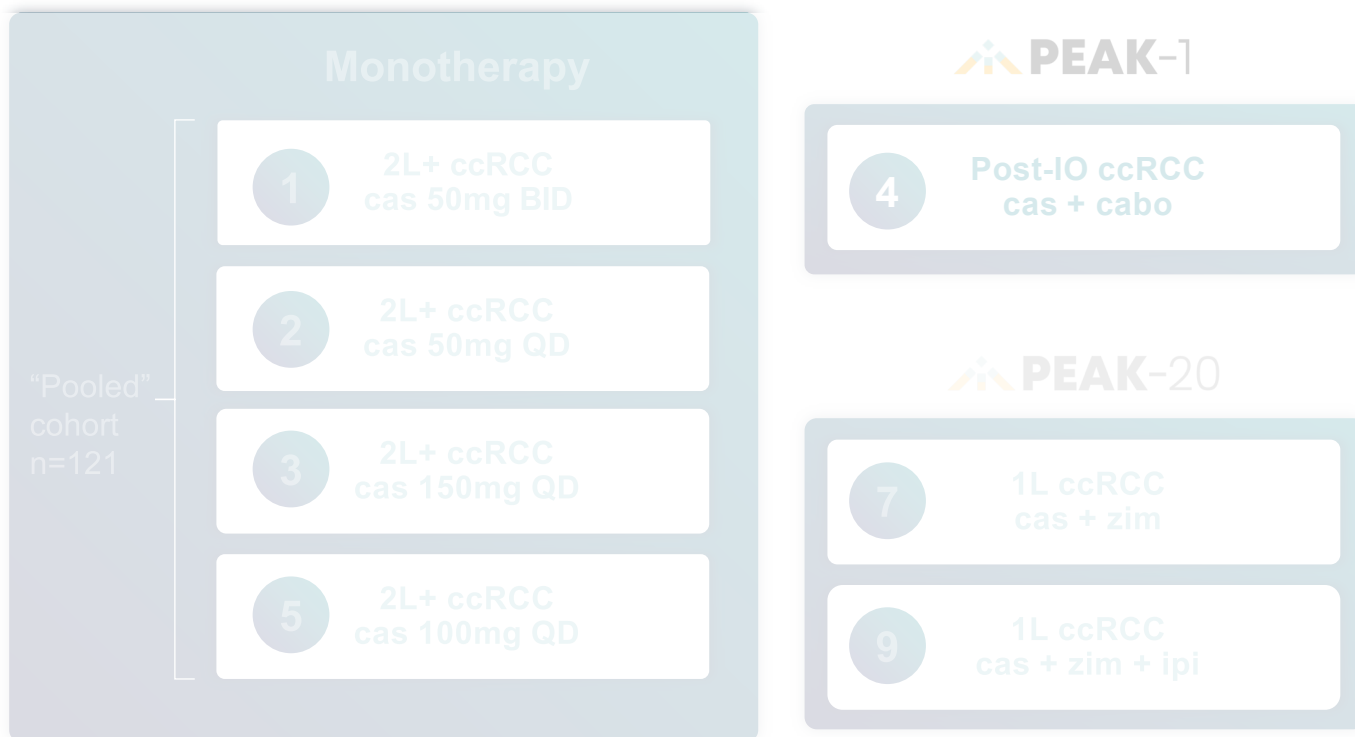
PFS: cas mono pooled (n=121) vs. tivo mono²⁴



OS: cas mono pooled (n=121) vs. tivo mono²⁴



Cohorts with data today



New cohorts w/data in 2027+

Late-line randomized cohort

11 2L+ ccRCC (post HIF-2α)
cas + tivo vs tivo

1L Cohorts

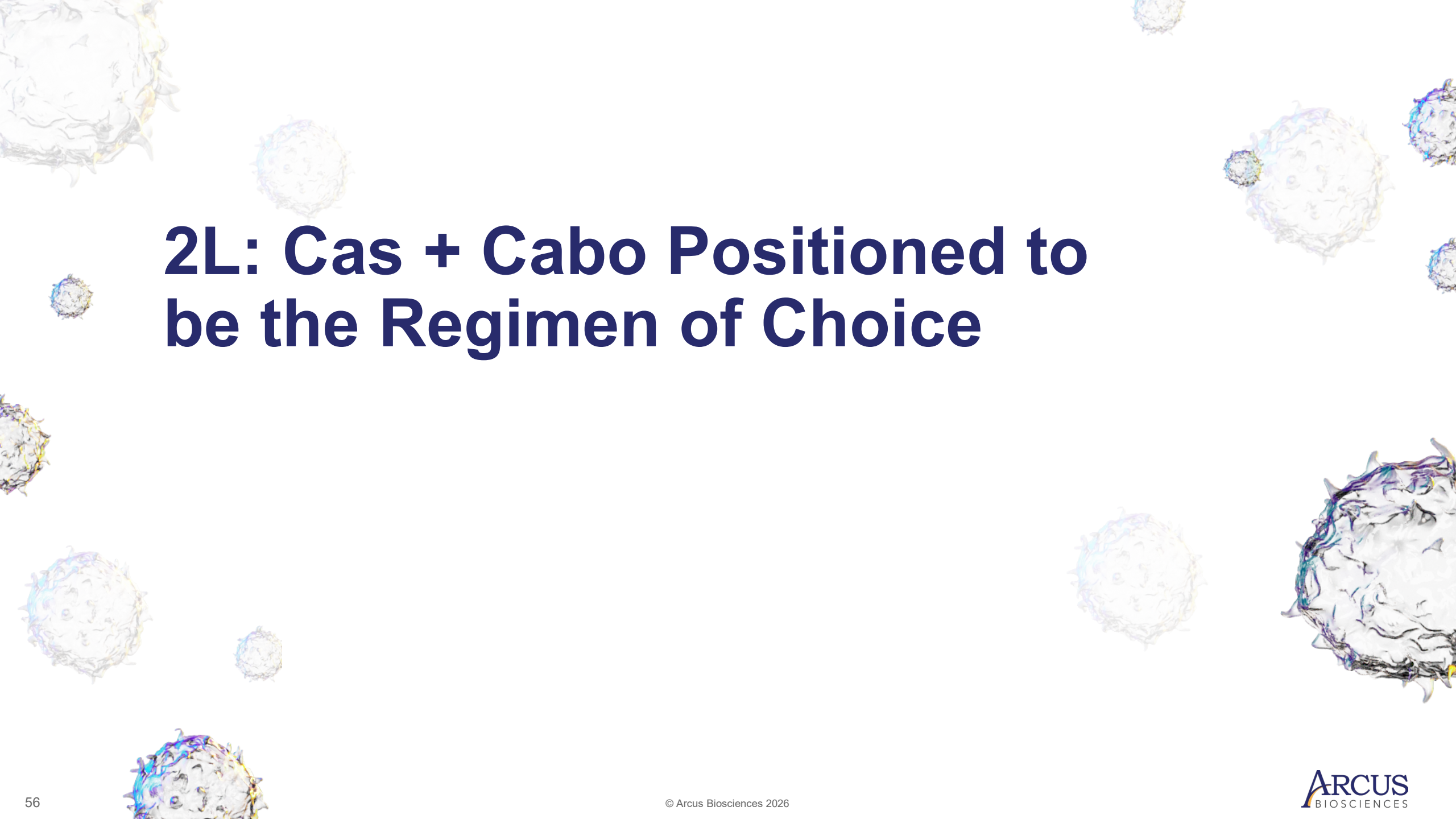
12 1L ccRCC
cas + ivo

13 1L ccRCC
cas + zim + axi

Additional Exploratory Cohorts

6 1L Favorable-risk ccRCC
monotherapy
cas 100mg QD

8 Post-IO ccRCC
monotherapy
cas 100mg QD

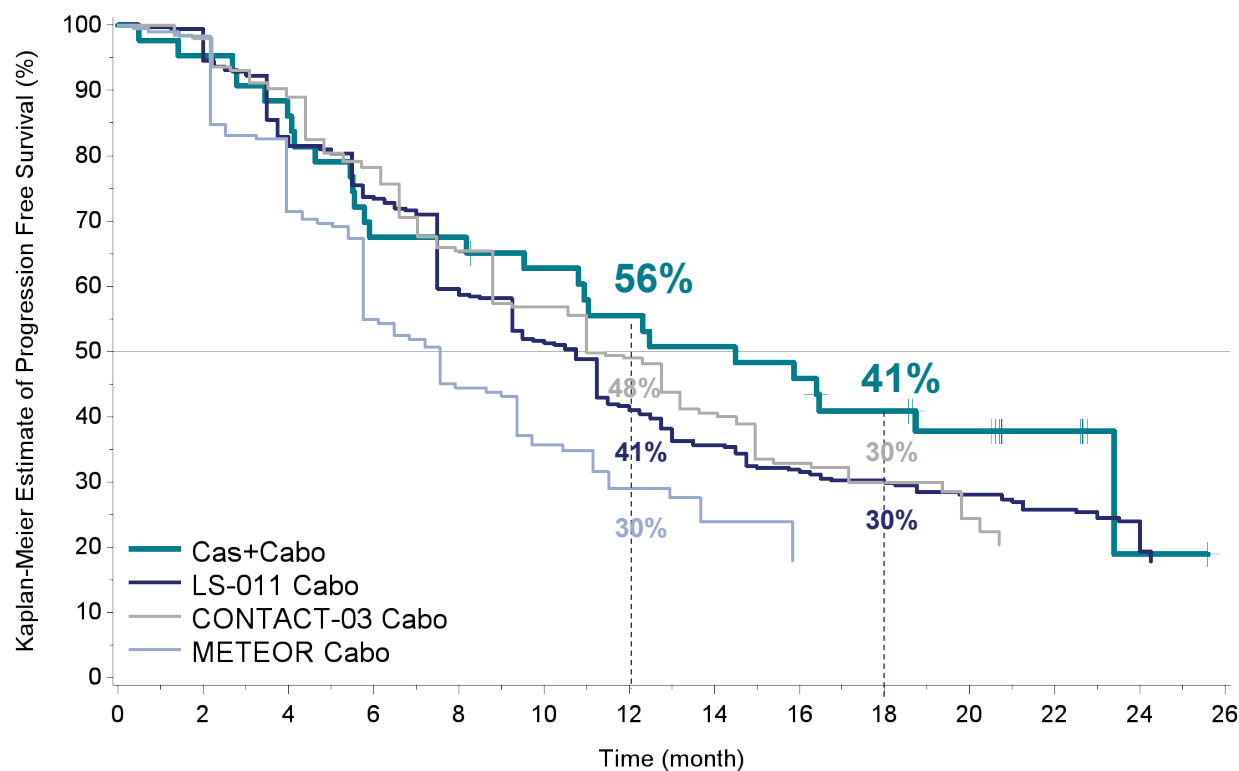


2L: Cas + Cabo Positioned to be the Regimen of Choice

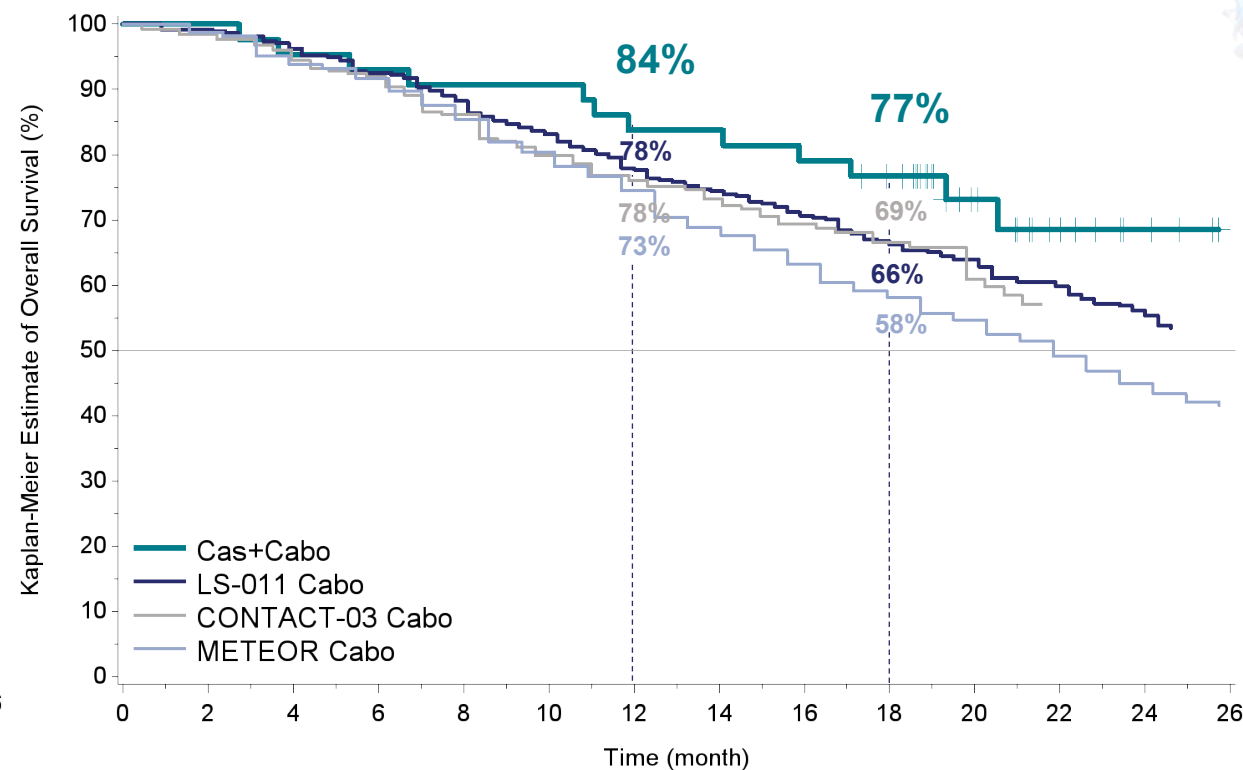
Cas + Cabo Demonstrates Clear Improvement Relative to Cabo Benchmarks; High Probability for PEAK-1 Success

Both PFS and OS for cas + cabo are trending substantially better than that of Phase 3 cabo mono benchmarks^{3-6,11}

PFS: cas + cabo vs cabo benchmarks



OS: cas + cabo vs cabo benchmarks



Other than Anemia, Very Few Grade 3 or Higher AEs Related to Casdatifan

SAFETY POPULATION,^a n (%) (N = 44)

GRADE 3 OR HIGHER AE RELATED TO:

	casdatifan	cabozantinib	any study drug
Patients with any treatment-related $\geq$ grade 3 AE^b	28 (64%)	27 (61%)	34 (77%)
Anemia	23 (52%)	13 (30%)	23 (52%)
Hypertension	1 (2%)	8 (18%)	8 (18%)
Hypoxia	6 (14%)	0	6 (14%)
Fatigue	3 (7%)	3 (7%)	3 (7%)
Hyponatraemia	0	3 (7%)	3 (7%)
Neutrophil count decreased	1 (2%)	3 (7%)	3 (7%)
Diarrhoea	1 (2%)	2 (5%)	2 (5%)
Nausea	0	2 (5%)	2 (5%)
Vomiting	0	2 (5%)	2 (5%)

- No casdatifan-related Grade 4 or 5 AEs were observed
- A total of four patients (9.1%) discontinued casdatifan due to TEAEs.

Median follow-up 21.3 months

a. Safety population included patients who received any amount of study drug and had at least 1 month of safety follow-up at the data cutoff date.

b. Treatment-emergent adverse events (grade 3 or higher) related to casdatifan, cabozantinib, or any study drug reported in $\geq$ 3% of patients in any treatment arm.

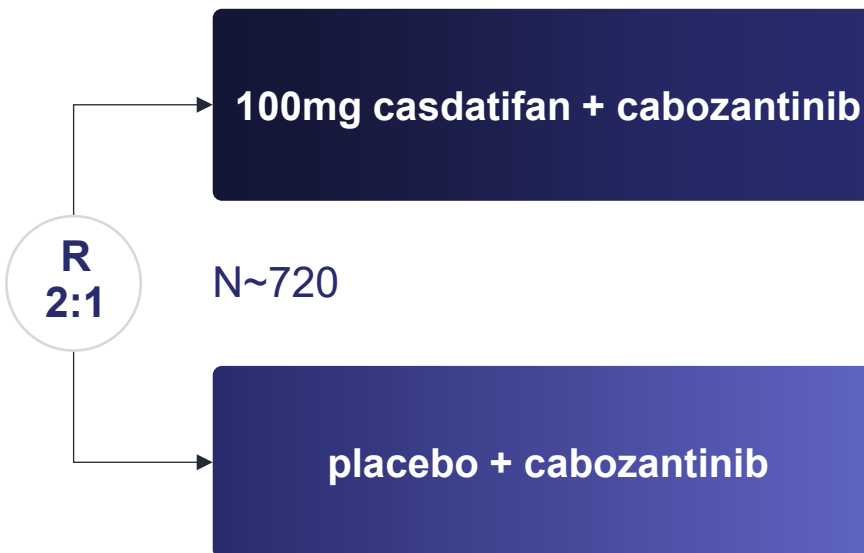
References and acronyms on slide 91

Phase 3 Registrational Study Evaluating Casdatifan in 2L ccRCC

Only Phase 3 study evaluating casdatifan with cabozantinib, the most widely used TKI in ccRCC

PATIENT POPULATION:

- Unresectable, locally advanced or metastatic ccRCC
- Have had prior anti-PD-1/ PD-L1 (either in adjuvant or 1L metastatic setting with/without TKI)
- Have not received cabozantinib

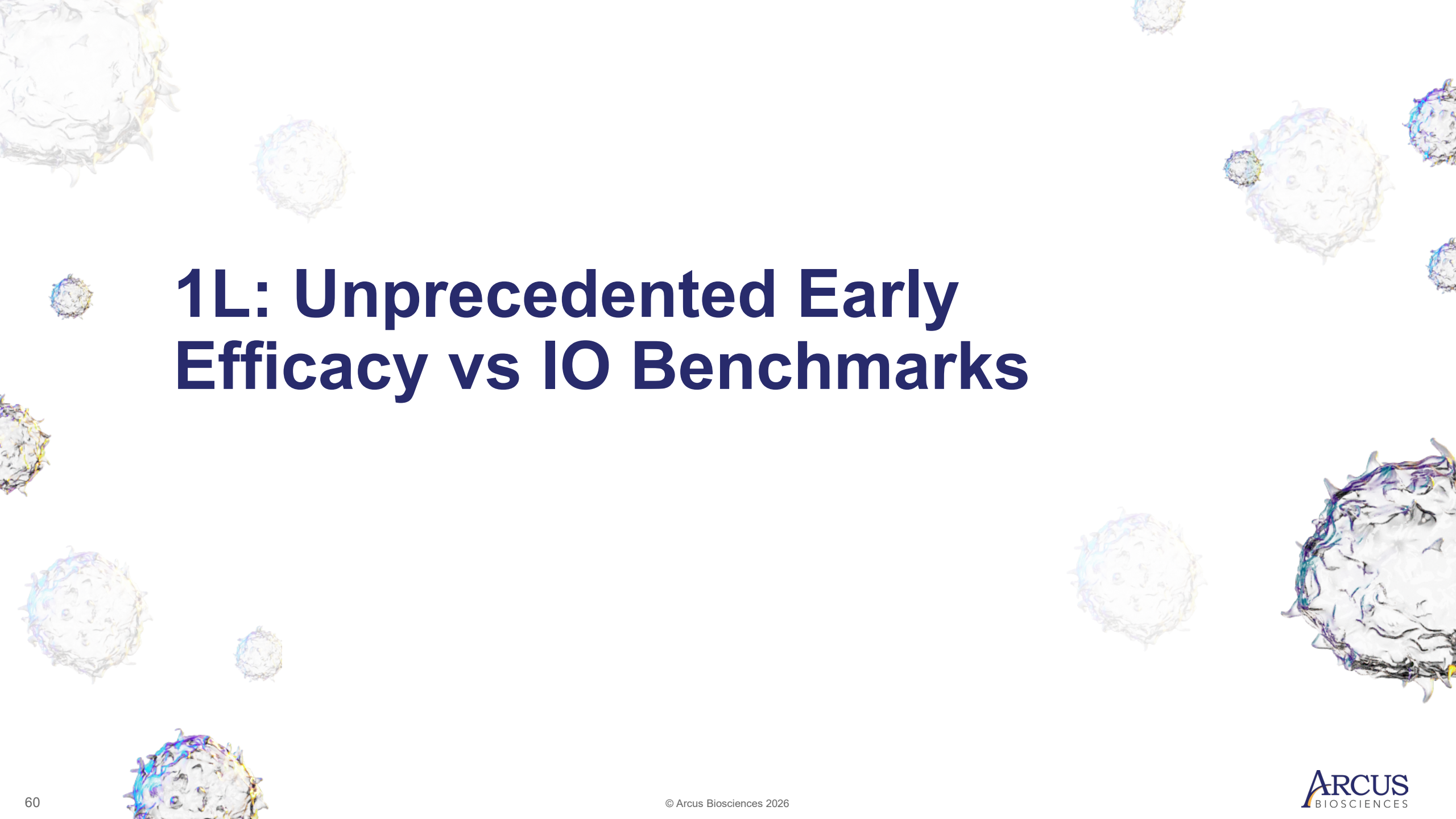


PRIMARY ENDPOINT

- PFS

KEY SECONDARY ENDPOINTS

- OS
- ORR, DOR, DCR



1L: Unprecedented Early Efficacy vs IO Benchmarks

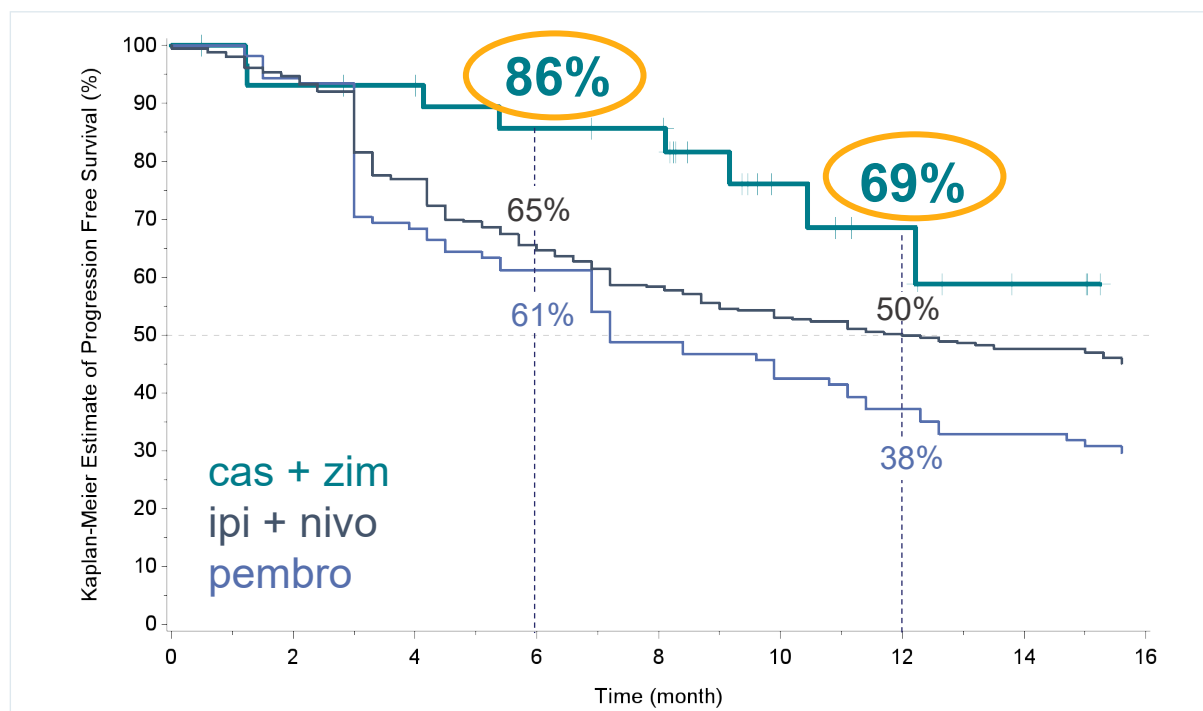
Casdatifan Enhances Disease Control Relative to Ipi + Nivo in 1L

Efficacy data are unprecedented for a TKI-sparing regimen

Rate of primary progression & ORR

	ARC-20		CM-214	KN-427
	cas + zim (n=30)	cas + zim + ipi (n=31)	ipi + nivo (n=550) ²	pembro (n=110) ¹
Primary Progression	6.7%	4.0%**	20%	30.0%
cORR	50.0%*	TBD	39%	36.4%
Median follow-up, months	11.5	3.0	25.2	35.9

Progression-free survival



Note: 12-month PFS landmark for cas + zim also exceeds those of anti-PD-1 + TKI combinations, including cabo + nivo (58% in CM-9ER¹⁴) and pembro + axi (60% in KN-426¹⁵)

*Includes two patients whose responses confirmed after the data cut-off

**Only one patient experienced primary progression (4%, n=24 with at least one scan)

Tick marks indicate censored patients

References and acronyms on slide 91

ARC-20 Cas + Zim + Ipi (Cohort 9) Safety Summary

cas + zim + ipi safety data are consistent with expectations for cas + nivo + ipi

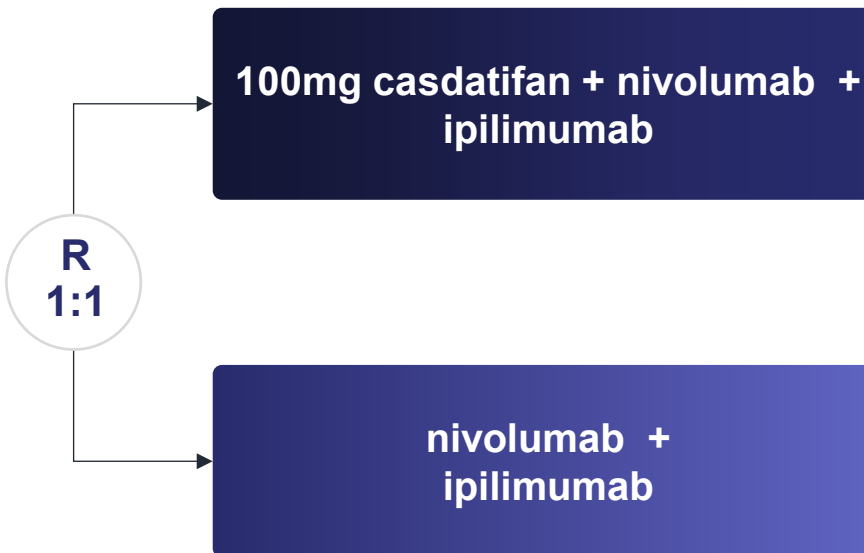
- 31 patients, median follow-up 3.0 months
- 18 patients completed induction phase (first 4 cycles or 12 weeks)
 - 9 (50%) pts. received all 4 doses of zim + ipi and 5 (28%) pts. received 3 of 4 doses of zim + ipi
- Casdatifan-related Grade ≥ 3 events of anemia and hypoxia similar to cas monotherapy
 - 1 casdatifan discontinuation (patient had hepatitis and decided to withdraw from study)
- Grade ≥ 3 immune-mediated events are generally consistent with ipi + nivo frequency, severity, and timing:
 - Hepatitis in 3 patients
 - Colitis in 2 patients
 - Myositis, myocarditis, myasthenia gravis in 1 patient
 - No patient with Grade 5 TEAEs

1L Phase 3 Study to Evaluate Cas with TKI-Free SOC

Potential for novel treatment to combine low PD rates with survival benefit

PATIENT POPULATION:

- 1L advanced or metastatic ccRCC
- No prior systemic therapy in the metastatic setting
- All IDMC risk groups



PRIMARY ENDPOINT

- PFS

SECONDARY ENDPOINTS

- OS (Key Secondary)
- ORR, DOR, DCR
- Safety

Expected to be initiated by year-end

TREATMENT CYCLES:





Market Opportunity

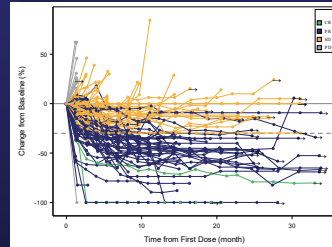
Bob Goeltz, Chief Financial Officer

Casdatifan is Positioned to be the Backbone Therapy for All Patients with ccRCC

Attribute

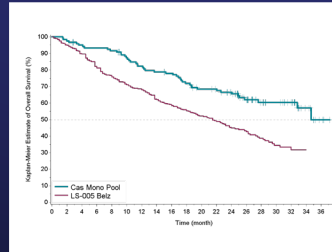
Casdatifan profile

Disease control



- ✓ Extremely low rate of primary progression in every setting to date
- ✓ Tumor reduction seen in the vast majority of patients
- ✓ Durable disease control drives long duration of therapy

Survival



- ✓ Strong progression free survival in every line of therapy
- ✓ Unprecedented overall survival in late-line monotherapy cohorts
- ✓ Early OS signal in 2L cas + cabo

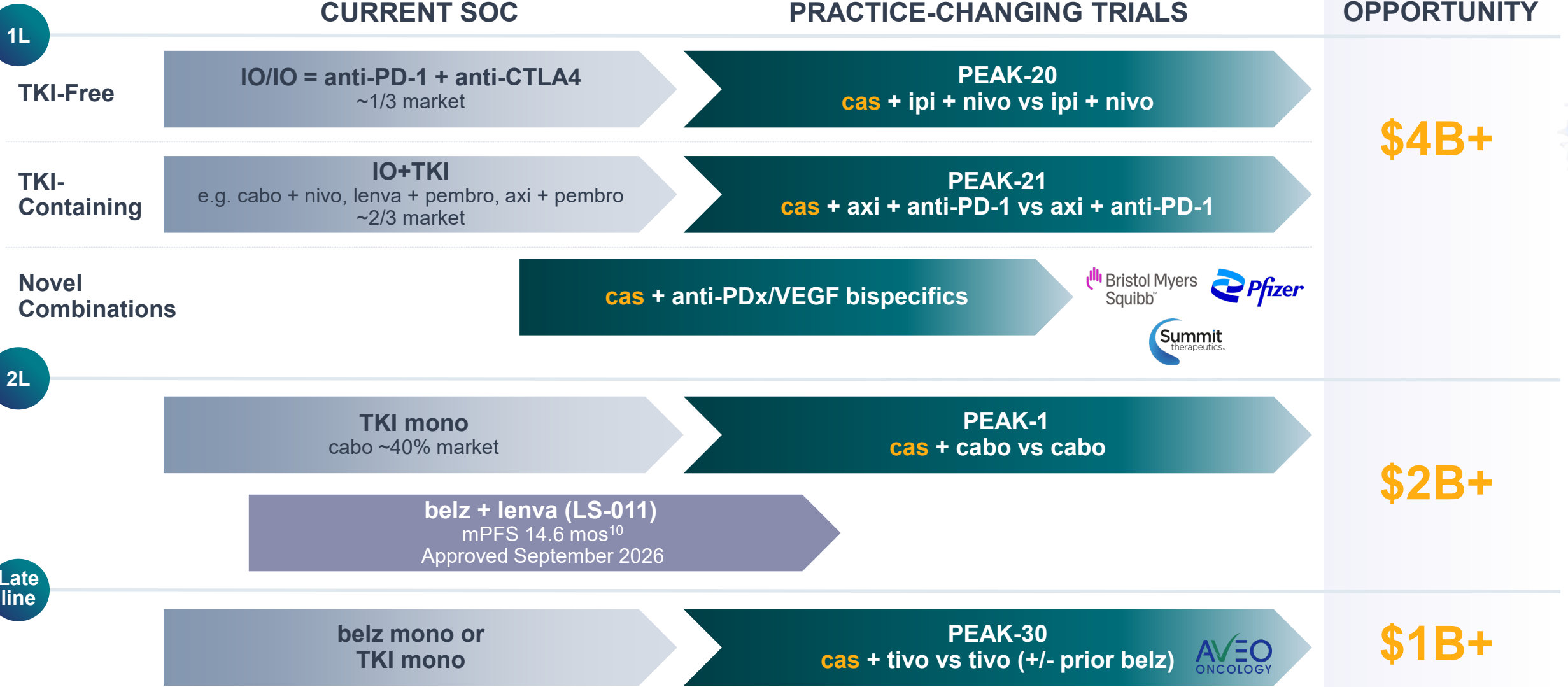
Tolerability



- ✓ Established safety data that are combinable with multiple agents across settings
- ✓ Low rate of treatment discontinuation

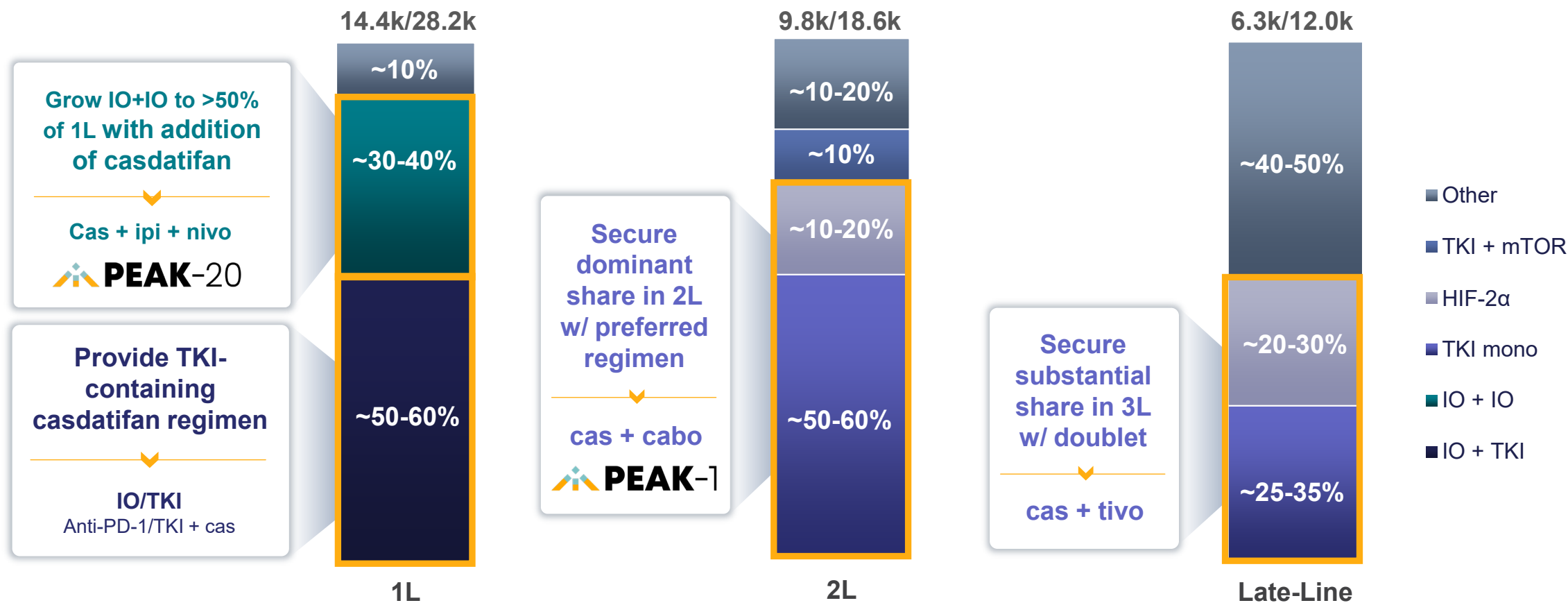
As the **only** HIF-2 α inhibitor with robust, durable effect, casdatifan is positioned to be the **therapeutic agent of choice** for ccRCC in **every setting**

Our Development Plan Provides Every ccRCC Patient the Opportunity to Benefit from Casdatifan



Substantial Opportunity for Casdatifan in 1L, 2L & 3L ccRCC

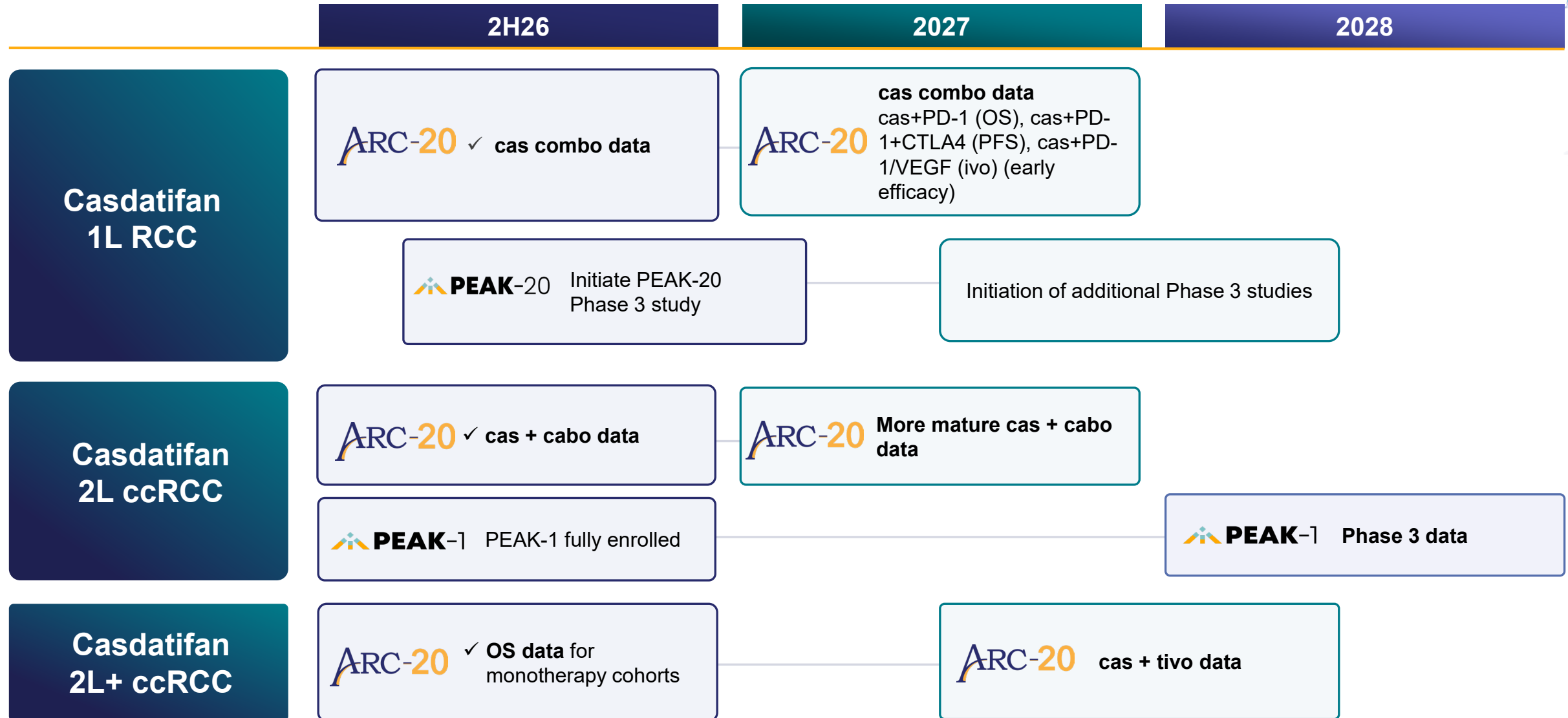
2026 ccRCC drug treatable incidence (US/MM) and US market share



Closing Summary

Terry Rosen, Ph.D., Chief Executive Officer

Arcus Milestones Will Generate Additional Data To Solidify Kidney Cancer Franchise



Emerging Casdatifan Franchise Has all the Pieces to Transform the Treatment Paradigm for Kidney Cancer

Our development plan provides every ccRCC patient the opportunity to benefit from casdatifan
\$5B – \$10B

1L

\$4B+
cas + ipi + nivo

2L

\$2B+
cas + cabo

Late Line

\$1B+
cas + tivo

Molecular Design



Cas delivers uniquely robust and durable HIF-2 α inhibition

This deep and sustained inhibition drives profound OS benefit, not previously seen for the class

Appendix

Late-Line: Cas monotherapy

Patients in ARC-20 Monotherapy Cohorts Had Greater Number of Prior Therapies Relative to the Patients in LITESPARK-005

Safety-Evaluable Population ^a	Dose Expansion: 2L+ ccRCC					Belzutifan ^{7,25*}
	50mg BID (n = 33)	50mg QD (n = 31)	100mg QD (n = 32)	150mg QD (n = 31)	Pooled (n = 127)	120mg QD (n = 374)
Age, years, median (range)	62 (41–79)	65 (43–82)	60 (45–77)	65 (53–78)	63 (41–82)	66 (49–78)
Sex, Female/Male, n (%)	8 (24) / 25 (76)	10 (32) / 21 (68)	5 (16) / 27 (84)	8 (26) / 23 (74)	31 (24) / 96 (76)	77 (21) / 297 (79)
ECOG PS 0/1, n (%)	16 (48) / 17 (52)	18 (58) / 13 (42)	15 (47) / 17 (53)	13 (42) / 18 (58)	62 (49) / 65 (51)	NA
IMDC Risk Score, n (%) ^b						
Favorable	10 (30)	8 (26)	7 (22)	9 (29)	34 (27)	79 (21)
Intermediate	21 (64)	17 (55)	21 (66)	19 (61)	78 (61)	249 (67)
Poor	2 (6)	5 (16)	3 (9)	3 (10)	13 (10)	46 (12)
Prior lines of therapy, n (%)						
1	2 (6)	5 (16)	6 (19)	7 (23)	20 (16)	46 (12)
2	14 (42)	9 (29)	8 (25)	6 (19)	37 (29)	157 (42)
3	8 (24)	8 (26)	10 (34)	7 (23)	33 (26)	171 (46)
4 or more	9 (27)	9 (29)	8 (25)	11 (36)	37 (29)	0 (0)

a. The safety-evaluable population included all dose expansion enrolled patients who received any amount of study treatment.

b. One patient in the 50 mg QD group had an unknown IMDC risk score and one patient in the 100 mg QD group had a missing IMDC risk score.

*2 or 3 prior VEGF-R TKI regimens; DCO date: August 30, 2024.; Baseline was defined as the last non-missing assessment prior to the first dosing of treatment.

References and acronyms on slide 91

ORR, PFS and OS for Each Cohort Compare Favorably to LS-005

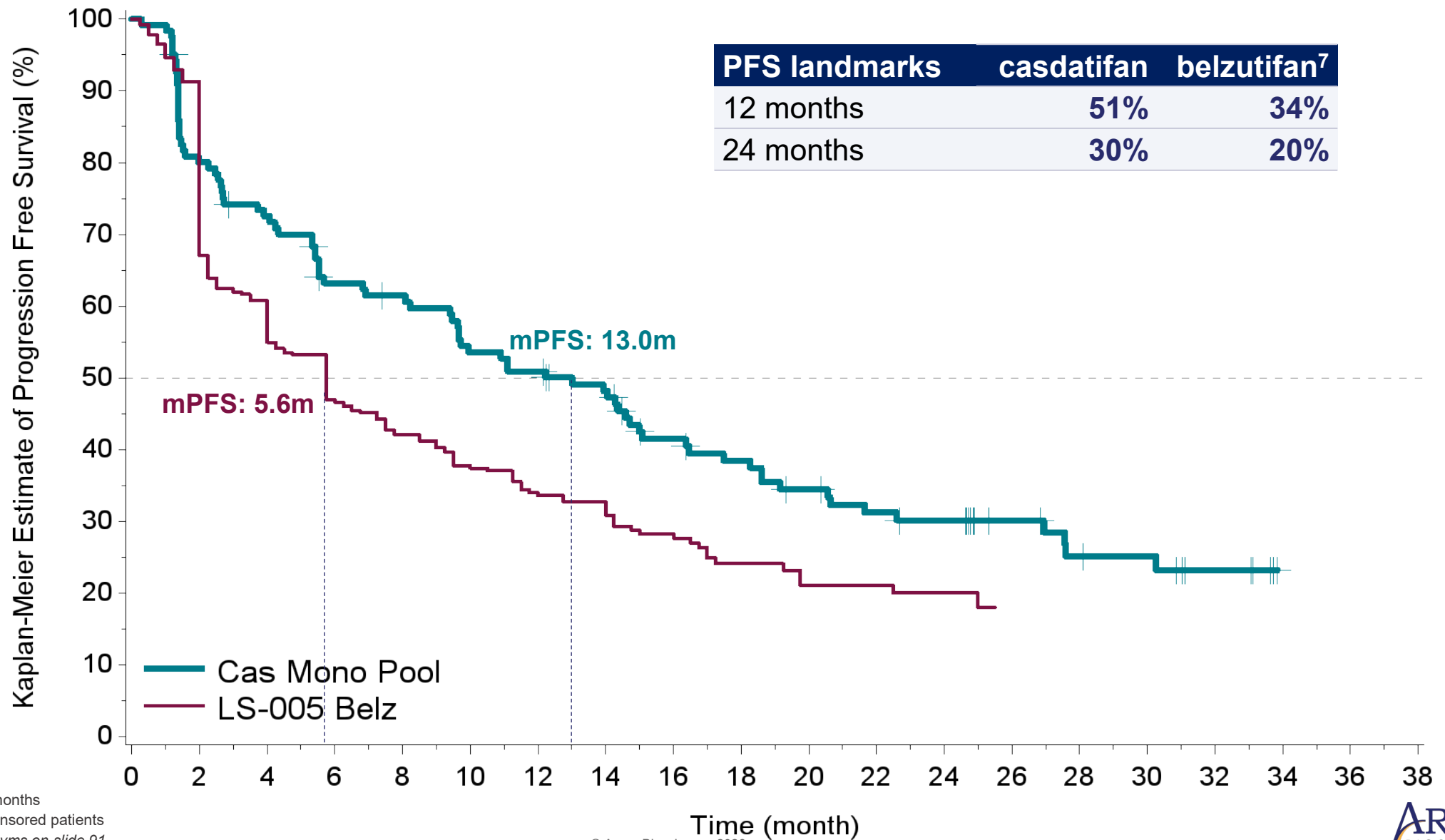
Efficacy-Evaluable Population ^a	Dose Expansion: 2L+ ccRCC					Belzutifan ⁷
	50mg BID (n = 31)	50mg QD (n = 28)	100mg QD (n=31)	150mg QD (n = 31)	All Pooled (n = 121)	120mg QD (n = 374)
Median Follow-Up, mos (range)	22.8 (14.4, 26.0)	19.7 (15.9, 21.3)	25.0 (19.0, 26.2)	14.4 (12.5, 15.5)	27.9 (19.0, 38.7)	25.7 (16.8–39.1)
Confirmed ORR (95% CI)	26% (12, 45)	36% (19, 56)	45% (27, 64)	36% (19, 55)	36% (27, 45)	23% (19, 27)
Complete Response, % (n)	0% (0)	7% (2)	0% (0)	0% (0)	2% (2)	4% (13)
Partial Response, % (n)	26% (8)	29% (8)	45% (14)	36% (11)	34% (41)	19% (72)
Stable Disease, % (n)	55% (17)	50% (14)	39% (12)	39% (12)	45% (55)	38% (143)
Progressive Disease, % (n)	19% (6)	14% (4)	16% (5) ^b	26% (8)	17% (21) ^b	34% (127)
Median PFS (95% CI)	9.7 (5.3, 27.6)	17.5 (5.3, 22.6)	15.0 (5.7, 18.6)	9.7 (2.7, 14.4)	13.0 (9.4, 16.4)	5.6 (3.8, 6.5)
Median OS (95% CI)	32.8 (16.7, NE)	NE (27.6, NE)	NE (24.0, NE)	NE (17.2, NE)	34.7 (32.8, NE)	21.4 (18.2, 24.3)

a. Efficacy-evaluable population for this expansion cohort is defined as all eligible participants who received any study treatment and have at least one post-baseline efficacy assessment, or who discontinued study treatment due to progressive disease or death, regardless of whether they had a scan.

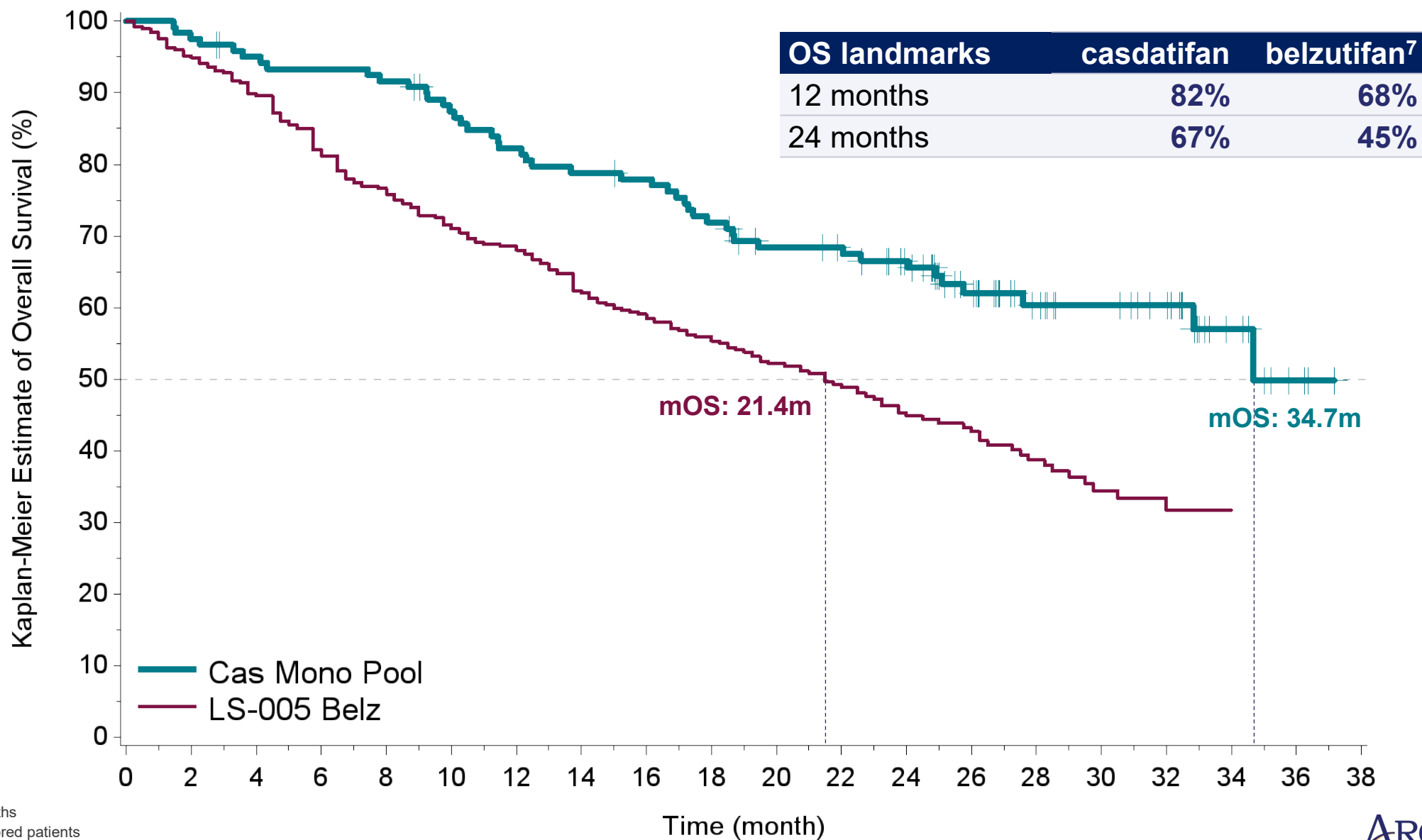
b. Includes three patients with radiological progressive disease and two patients who had clinical progression before the first scan, which have been included but do not meet criteria for progressive disease per RECIST.

References and acronyms on slide 91

Casdatifan Monotherapy Demonstrates Strong PFS Despite a More Heavily Pre-Treated Population than that of LS-005



Casdatifan Provides Unprecedented OS in Late-line Setting



Casdatifan Was Well Tolerated in All Cohorts, With a Comparable Safety Profile to That of Belzutifan

Safety-Evaluable Population ^a	50mg BID (n=33)	50mg QD (n=31)	100mg QD (n=32)	150mg QD (n=31)	Pooled (n=127)	belzutifan ^{7*} (LITESPARK-005)
Median follow-up, months (range)	35.5 (27.1, 38.7)	32.3 (28.6, 33.9)	25.0 (19.0, 26.2)	27.0 (25.1, 28.2)	28.1 (19.0, 38.7)	
Any TEAEs, n (%)	33 (100)	30 (97)	31 (97)	31 (100)	125 (98)	
Related to casdatifan	31 (94)	29 (94)	29 (91)	31 (100)	120 (95)	
Any Grade ≥3 TEAEs, n (%)	22 (67)	23 (74)	21 (66)	24 (77)	90 (71)	
Related to casdatifan	18 (55)	15 (48)	15 (47)	22 (71)	70 (55)	Serious AEs:
Any Serious TEAEs, n (%)	7 (21)	15 (48)	14 (44)	14 (45)	50 (39)	All-cause: 43%
Related to casdatifan	1 (3)	3 (10)	3 (9)	4 (13)	11 (9)	TRAEs: 13%

a. The safety-evaluable population included all dose expansion enrolled patients who received any amount of any study treatment.

*Belzutifan safety details not reported at IA1

References and acronyms on slide 91

Casdatifan Was Well Tolerated in All Cohorts, With a Comparable Safety Data to That of Belzutifan

Safety-Evaluable Population ^a	50mg BID (n=33)	50mg QD (n=31)	100mg QD (n=32)	150mg QD (n=31)	Pooled (n=127)	belzutifan ⁷ (LITESPARK-005)
Anemia, n (%)						Anemia:
All grades	31 (94)	29 (94)	29 (91)	31 (100)	120 (95)	All grade: 83%
Grade ≥3 related to casdatifan	17 (52)	15 (48)	10 (31)	17 (55)	59 (47)	Grade 3+: 33%
Related to casdatifan leading to interruptions	12 (36)	12 (39)	11 (34)	17 (55)	52 (41)	
Leading to dose reductions	5 (15)	5 (16)	3 (9)	5 (16)	18 (14)	
Leading to discontin.	0	0	0	0	0	
Hypoxia, n (%)						Hypoxia:
All grades	6 (18)	6 (19)	6 (19)	9 (29)	27 (21)	All Grade: 15%
Grade ≥3 related to casdatifan	3 (9)	2 (7)	3 (9)	6 (19)	14 (11)	Grade 3+: 11%
Related to casdatifan leading to interruptions	5 (15)	4 (13)	2 (6)	7 (23)	18 (14)	
Leading to dose reductions	3 (9)	2 (6)	1 (3)	5 (16)	11 (9)	
Leading to discontin.	0	1 (3)	1 (3)	1 (3)	3 (2)	

a. The safety-evaluable population included all dose expansion enrolled patients who received any amount of study treatment.

2L: Cas + Cabo

Baseline Patient Demographics are Consistent with LS-011

CHARACTERISTIC	cas + cabo ^a (n = 44)	belz + lenva ¹¹ (n = 371)	cabo mono ¹¹ (n = 376)
Age, years, median (range)	63 (43–81)	63 (55–70)	62.5 (55–68)
Sex, female/male, n (%)	9 (21%) / 33 (79%)	98 (26%) / 273 (74%)	84 (22%) / 292 (78%)
Karnofsky PSS 90 or 100 / 70 or 80, n (%)	29 (69%) / 13 (31%)	276 (74%) / 95 (26%)	277 (74%) / 99 (26%)
IMDC risk score, n (%)			
Favorable	9 (21%)	84 (23%)	95 (25%)
Intermediate	30 (70%)	226 (61%)	215 (57%)
Poor	4 (9%)	61 (16%)	66 (18%)
Number of prior regimens, n (%)			
Adjuvant Only	8 (18%)	15 (4%)	18 (5%)
1	31 (71%)	252 (68%)	251 (67%)
2+	5 (11%)	104 (28%)	107 (28%)
Median follow-up (range)	21.3 (18.1–26.8)	29.0 (23.7–34.9)	

a. The safety-evaluable population included all patients who received any amount of any study treatment.

References and acronyms on slide 91

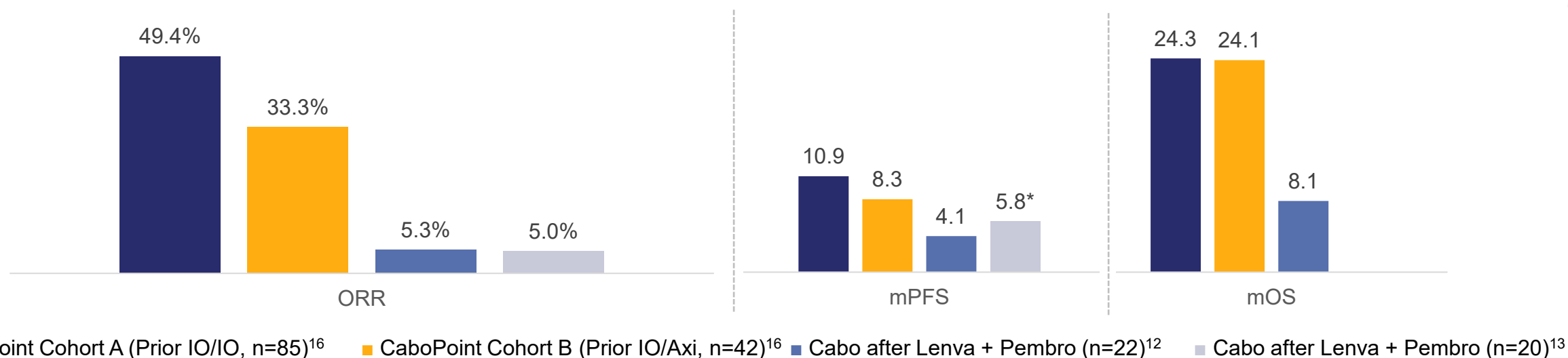
LS-011 Underrepresented the Patients Previously Treated with 2nd-Generation TKIs, Who Respond Poorly to Cabo

	ARC-20		LITESPARK-011 ¹¹		CONTACT-03 ⁴			METEOR ⁵			
Prior Therapy Agent	cas + cabo (n = 44)		cabo (n = 376)		cabo (n = 259)			PFS Population cabo (n = 187) <i>All TKI-Pretreated</i>		OS Population cabo (n = 330) <i>All TKI-Pretreated</i>	
	N	%	N	%	N	%		N	%	N	%
Adjuvant ^a	11	25%	25	7%	4	2%					
First Line	36	82%	358	95%	258	100%	All Lines ^g	187	100%	330	100%
axi ± IO	6	14%	103	27%	34	13%	axi ± IO	28	15%	52	16%
Pembro + lenva	7	16%	0	0%	4 ^c	2%	Pembro + lenva	0	0%	0	0%
IO only ^b	17	39%	143	38%	81	31%	IO only ^b	9	5%	17	5%
Pazopanib, sunitinib and/or sorafenib ^d	3	7%	101	27%	120	46%	Pazopanib, sunitinib and/or sorafenib ^d	212	113%	375	114%
Other ^e	3	7%	0	0%	19	7%	Other ^e	18	10%	44	13%
Second Line	5	11%	107	28%	125	48%					
Nivo	2	5%	98	26%	116	45%					
IO/IO ^f	0	0%	0	0%	4	2%					
axi ± IO	3	7%	0	0%	4	2%					
Other ^g	0	0%	0	0%	1	0%					

a. Includes axitinib/pembrolizumab, atezolizumab, Bacillus Calmette-Guérin plus interferon, dendritic cells cytokine induced killer cells, everolimus, ipilimumab/nivolumab, nivolumab, pazopanib, pembrolizumab, placebo, sunitinib, and sunitinib malate. b. Includes ipilimumab+nivolumab, nivolumab and pembrolizumab. c. Includes one patient with everolimus + lenvatinib. d. Includes pazopanib, sunitinib, nivolumab + sunitinib, pazopanib + sunitinib, pazopanib + sorafenib, and sorafenib. e. For ARC-20, includes one patient with IO + zanzalintinib and two with IO + bevacizumab. For CONTACT-03, includes bempegaldesleukin + nivo (9 patients), cemiplimab (2 patients), interleukin-2 (2 patients), tivozanib (2 patients), aldesleukin + pembro (1 patient), and atezolizumab + bevacizumab (1 patient), interferon alfa (1 patient), and retifanlimab (1 patient). For METEOR, includes interleukin-2, interferon alfa, and bevacizumab f. Includes ipilimumab+nivolumab and durvalumab+ tremelimumab g. Includes nivolumab + pazopanib g. Previous systemic therapy was not split by line of therapy in the METEOR publication.

Prior TKI Exposure Impacts Cabo Performance in 2L

- CaboPoint demonstrated that patients who received prior IO + axitinib had numerically lower mPFS on cabo in 2L than those with prior IO-only
- There are at least two retrospective studies demonstrating that prior exposure to lenvatinib specifically resulted in *drastically worse clinical outcomes* when treated with cabo mono



In the ARC-20 cas + cabo cohort, 7 of 17 patients with prior TKI exposure received lenvatinib
These patients would have been excluded from LITESPARK-011 (but included in PEAK-1)

Confirmed ORR of 44% Numerically Exceeds Cabo Monotherapy Benchmark from LS-011

	cas + cabo efficacy-evaluable (n = 43) ^a	LS-011 cabo mono (n = 376) ¹¹
Follow-up, months, median (range)	21 (18–27)	29 (24–35)
Confirmed ORR, % (n)	44% (19)	40% (151)
(95% CI)	(29%, 60%)	(35%, 45%)
Best Overall Response, n (%)		
CR	1 (2%)	4 (1%)
PR	18 (42%)	147 (39%)
SD	22 (51%)	186 (49%)
PD	2 (5%)	22 (6%)

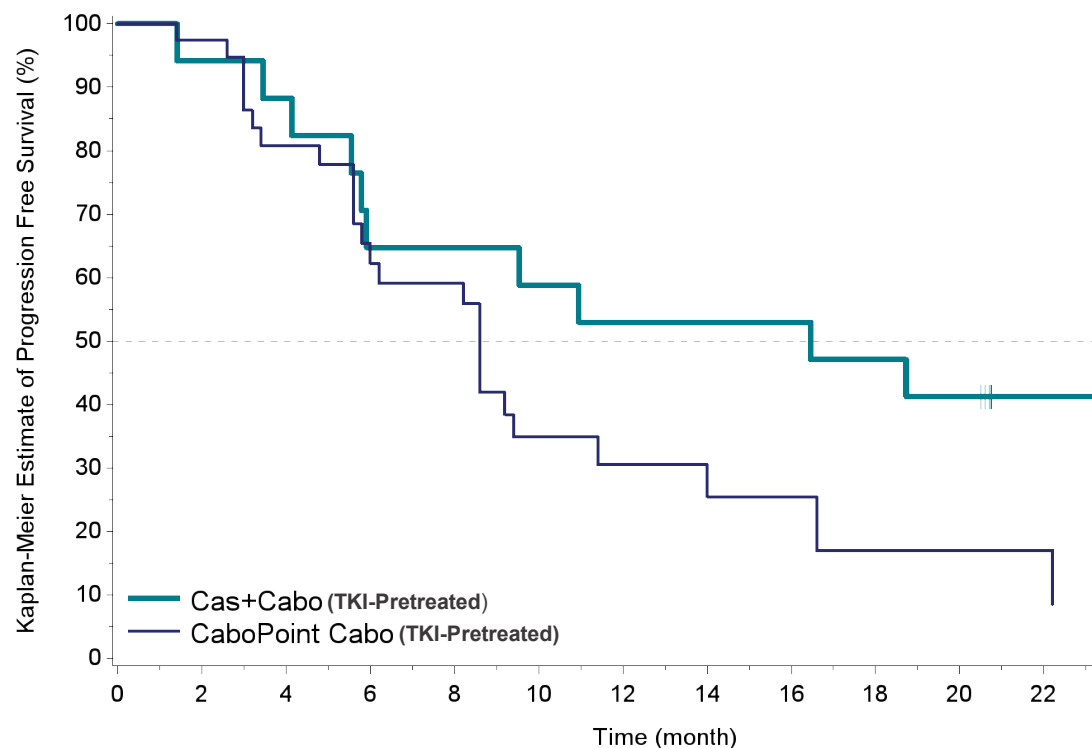
All eligible patients who had at least one post-baseline tumor assessment or discontinued from study treatment due to progressive disease or death.

References and acronyms on slide 91

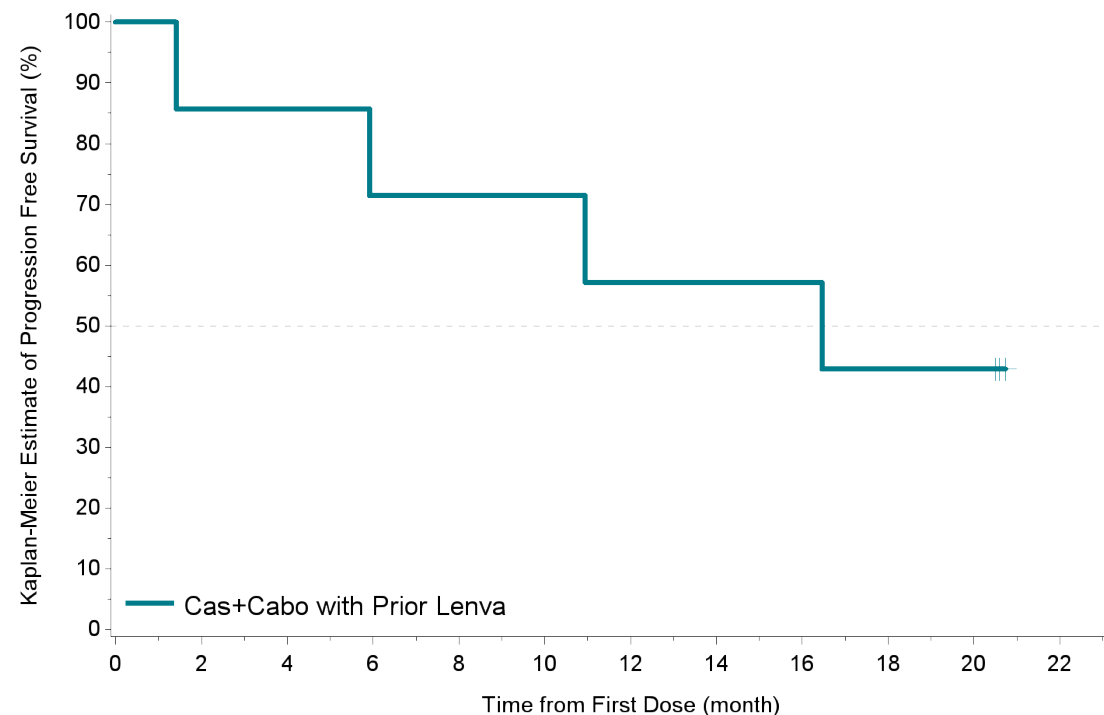
60% of 2L Patients Receive a TKI in 1L and Have a Very Poor Prognosis; Casdatifan Has the Potential to Drive a Paradigm Shift

Opportunity to greatly improve PFS for patients with prior TKI (especially lenva) exposure

With prior TKI: cas + cabo (n=17) vs CaboPoint prior TKI (n=40)



With prior lenva: cas + cabo (n=7)



Casdatifan Dose Intensity was Consistently High, Driving Efficacy and Durability

	cas 100mg QD + cabo 60mg QD n=44	cas 100mg QD N=32	cas mono pooled n=127
Median duration of follow-up, months	21.3	25.0	28.1
Median Tx duration, months	15	14	11
Cas relative dose intensity, median	88.9%	91.2%	96.6%
Cabo relative dose intensity, median	71.8%	NA	NA

Other than Anemia, Very Few Grade 3 or Higher AEs Related to Casdatifan

SAFETY POPULATION,^a n (%) (N = 44)

GRADE 3 OR HIGHER AE RELATED TO:

	casdatifan	cabozantinib	any study drug
Patients with any treatment-related $\geq$ grade 3 AE^b	28 (64%)	27 (61%)	34 (77%)
Anemia	23 (52%)	13 (30%)	23 (52%)
Hypertension	1 (2%)	8 (18%)	8 (18%)
Hypoxia	6 (14%)	0	6 (14%)
Fatigue	3 (7%)	3 (7%)	3 (7%)
Hyponatraemia	0	3 (7%)	3 (7%)
Neutrophil count decreased	1 (2%)	3 (7%)	3 (7%)
Diarrhoea	1 (2%)	2 (5%)	2 (5%)
Nausea	0	2 (5%)	2 (5%)
Vomiting	0	2 (5%)	2 (5%)

- No casdatifan-related Grade 4 or 5 AEs were observed
- A total of four patients (9.1%) discontinued casdatifan due to TEAEs.

Median follow-up 21.3 months

a. Safety population included patients who received any amount of study drug.

b. Treatment-emergent adverse events (grade 3 or higher) related to casdatifan, cabozantinib, or any study drug reported in $\geq$ 3% of patients in any treatment arm.

References and acronyms on slide 91

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AEs Were Manageable with Dose Reductions

SAFETY POPULATION,^a n (%) (N = 44)

LEADING TO REDUCTION IN:

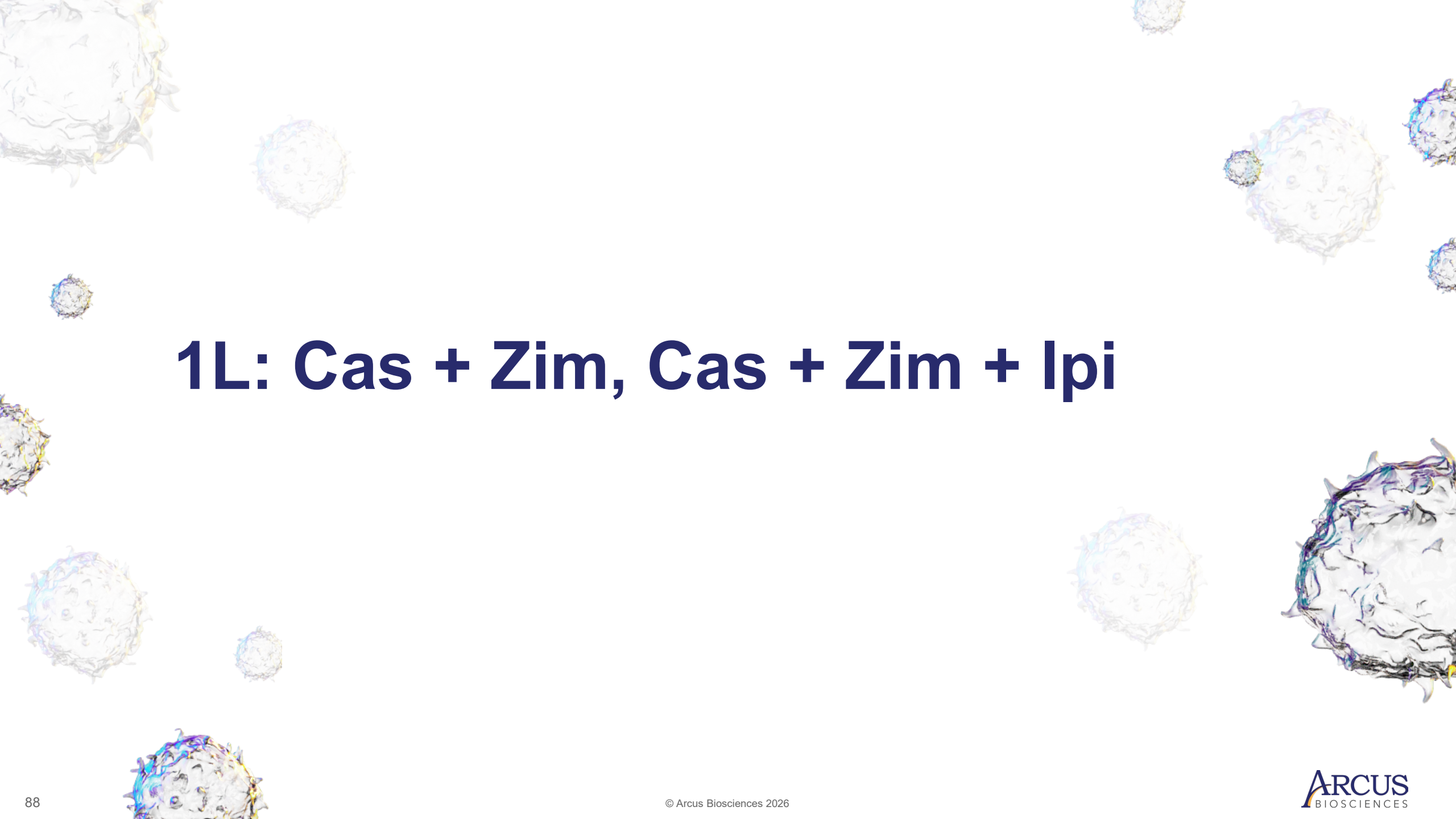
	casdatifan	cabozantinib	any study drug
Patients with any AE leading to dose reduction^b	17 (39%)	28 (64%)	32 (73%)
Fatigue	1 (2%)	9 (20%)	9 (20%)
Anemia	8 (18%)	2 (5%)	8 (18%)
Hypoxia	7 (16%)	1 (2%)	7 (16%)
Diarrhea	0	4 (9%)	4 (9%)
Ejection fraction decreased	1 (2%)	4 (9%)	4 (9%)
Palmar-plantar erythrodysesthesia	0	4 (9%)	4 (9%)
Alanine aminotransferase increased	0	3 (7%)	3 (7%)
Cognitive disorder	2 (5%)	0	2 (5%)
Stomatitis	0	2 (5%)	2 (5%)

Median follow-up 21.3 months

a. Safety population included patients who received any amount of study drug.

b. Treatment-emergent adverse events (any grade) leading to dose reduction in casdatifan, cabozantinib, or any study drug reported in ≥ 3% of patients in any treatment arm.

References and acronyms on slide 91



1L: Cas + Zim, Cas + Zim + Ipi

Baseline Characteristics for 1L Cohorts in ARC-20

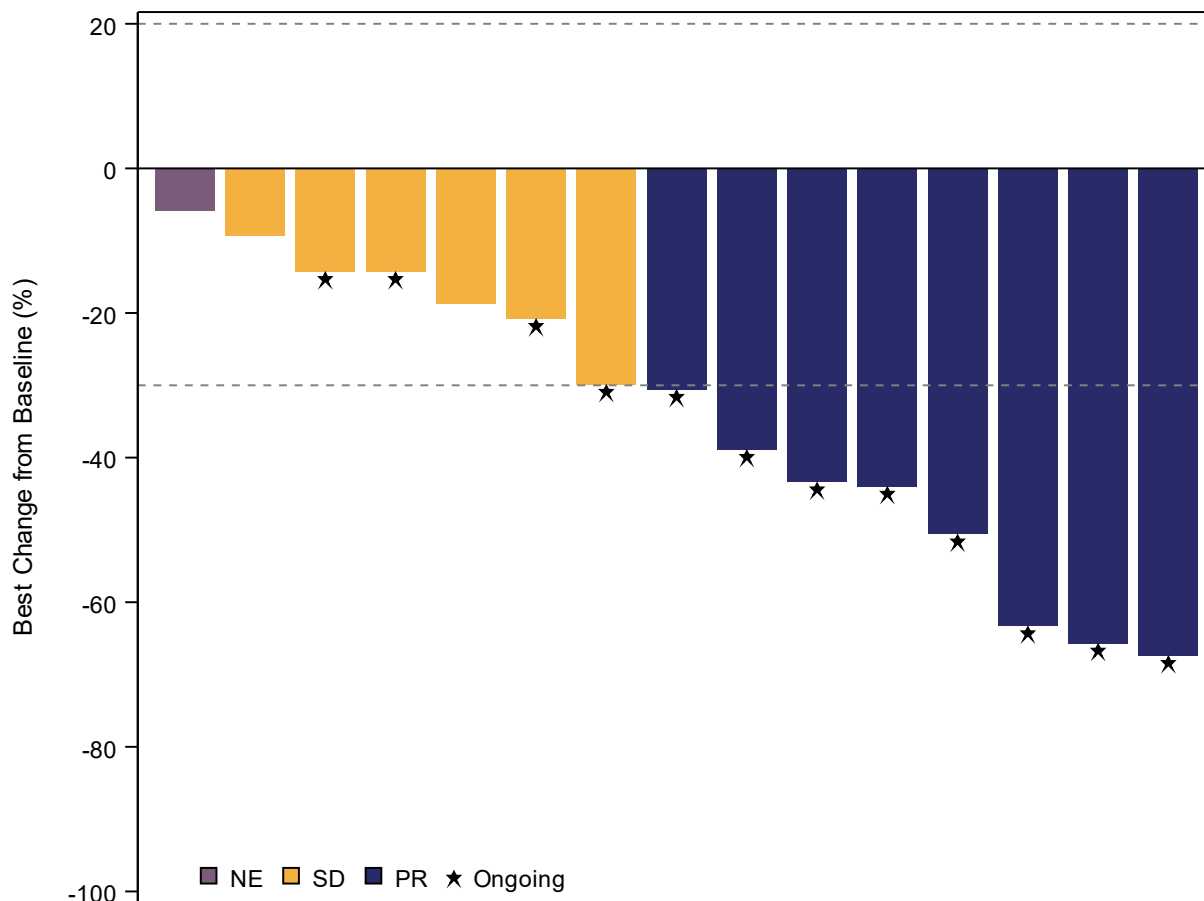
CHARACTERISTIC	cas + zim (n = 30)	cas + zim + ipi (n = 31)	ipi + nivo ² (n = 550)	pembro ¹ (n = 110)
Age, years, median (range)	63 (38, 89)	65 (47, 82)	62 (26-85)	64 (29-87)
Sex, female/male, n (%)	8 / 22 (27% / 73%)	5 / 26 (16% / 84%)	137 / 413 (25% / 75%)	24 / 86 (22% / 78%)
ECOG 0 / 1, n (%)	19 / 11 (63% / 37%)	22 / 9 (71% / 29%)	NA	88 / 22 (80% / 20%)*
IMDC risk score, n (%)				
Favorable	15 (50%)	15 (48%)	125 (23%)	42 (38%)
Intermediate	13 (43%)	12 (39%)	334 (61%)	68 (62%)
Poor	1 (3%)	4 (13%)	91 (17%)	

*Karnofsky Performance Score 90-100 / 70-80

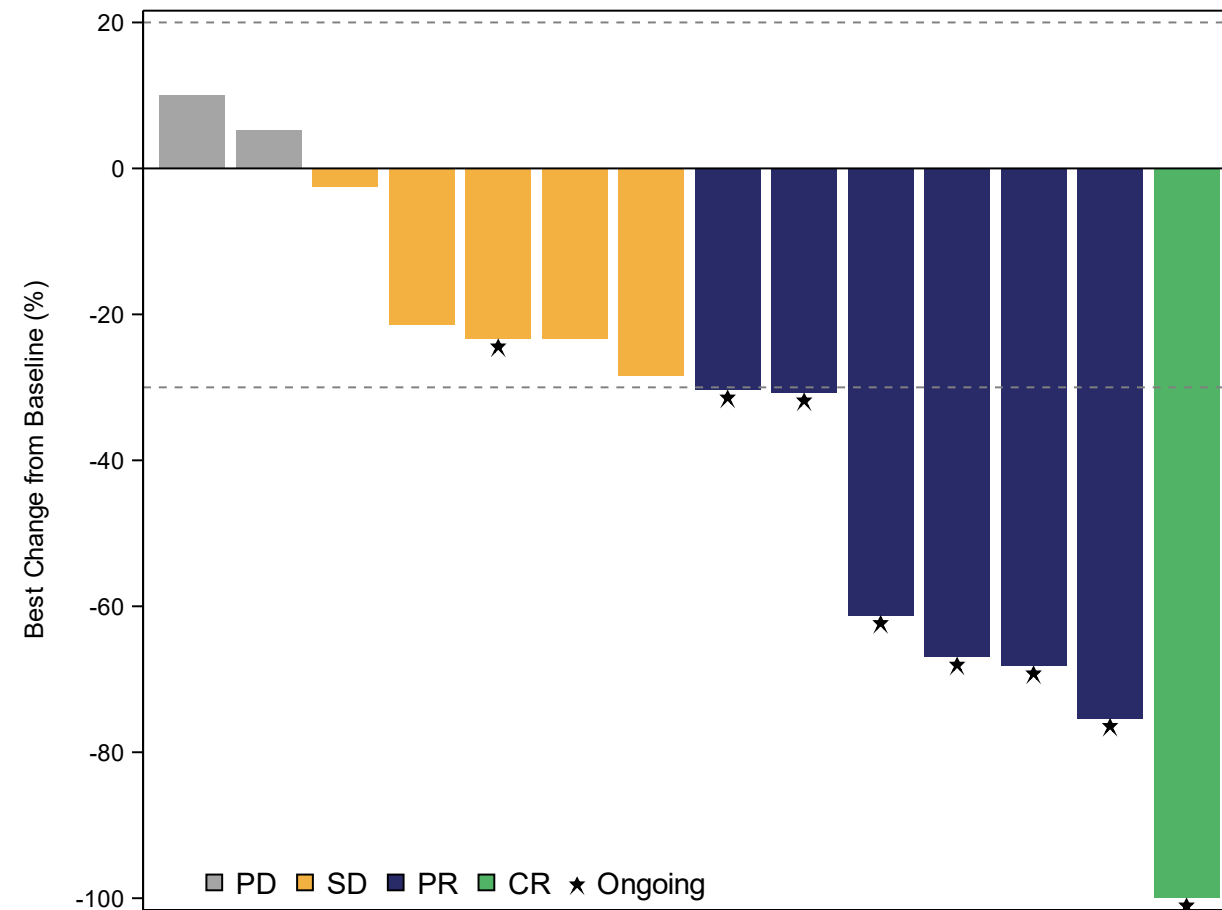
References and acronyms on slide 91

Cas + Zim Showed Strong Efficacy for Both Favorable and Intermediate/Poor IMDC Risk Patients

Favorable IMDC risk



Intermediate / poor IMDC risk



Early PFS observations for cas + zim by IMDC risk group compare favorably to the corresponding subgroups for ipi + nivo in CheckMate-214 (12-month PFS landmark rates for ipi + nivo were ~53% for Fav Risk and ~50% for I/P Risk²⁶)

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1L first-line	CI confidence interval	Ipi ipilimumab	NR not reached	RECIST Response Evaluation Criteria in Solid Tumors
2H second-half	cORR confirmed overall response rate	Ivo ivonescimab	ORR objective response rate	sEPO serum erythropoietin
2L second-line	CR complete response	k thousand	OS overall survival	SD stable disease
3L third-line	DCO data cutoff	KCA Kidney Cancer Association	PD pharmacodynamic	SOC standard of care
ASCO American Society of Clinical Oncology	DCR disease control rate	Lenva lenvatinib	PD progressive disease	TEAE treatment-emergent adverse event
AD atopic dermatitis	DOR duration of response	m months	pembro pembrolizumab	Tivo tivozanib
AE adverse event	ECOG Eastern Cooperative Oncology Group	mg milligrams	PFS progression-free survival	Tx treatment
Axi axitinib	EPO erythropoietin	MM = Major Markets = US, EU5, Japan	PK pharmacokinetics	Z/zim zimberelimab
B billion	ESMO European Society for Medical Oncology	Mono monotherapy	PR partial response	
belz belzutifan	HR hazard ratio	mos months	QD once daily	
BID twice daily	IBD inflammatory bowel disease	mOS median overall survival	R randomized	
Cabo cabozantinib	IDMC International Metastatic Renal Cell Carcinoma Database Consortium	mPFS median progression-free survival	R&D research & development	
Cas casdatifan	IKCS International Kidney Cancer Symposium	NE not estimable	RA rheumatoid arthritis	
ccRCC clear cell renal cell carcinoma	IO immunotherapy	Nivo nivolumab	RCC renal cell carcinoma	