ARC-20 Presentation

Phase 1b Study of Casdatifan in ccRCC

Data presented at EORTC-NCI-AACR 2024, October 24, 2024, based on data cutoff of August 30, 2024.

ARCUS BIOSCIENCES

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Agenda

TOPIC	PRESENTER(S)
Introduction & Opportunity for Casdatifan	**Dr. Terry Rosen** CEO, Arcus Biosciences
ccRCC Treatment Landscape & Opportunity for HIF-2α Inhibition	**Dr. Rana McKay** University of California San Diego
ARC-20 Dose Expansion: Safety & Efficacy Data	**Dr. Dimitry S.A. Nuyten** CMO, Arcus Biosciences
Next Steps and Development Plan	**Dr. Dimitry S.A. Nuyten** CMO, Arcus Biosciences
Market Opportunity in Renal Cell Carcinoma	**Eric Matthews** CCO, Arcus Biosciences
Q&A	**All, including Dr. Juan Jaen (President, Arcus) and Jennifer Jarrett (COO, Arcus)**

ccRCC: clear cell renal cell carcinoma; HIF: hypoxia-inducible factor

Opportunity for Casdatifan

Dr. Terry Rosen
CEO, Arcus Biosciences

ARC-20 Results Support Casdatifan's Potential Best-in-Class Profile Despite Short Follow Up / Advanced Patient Population

Potential for Best-in-Class Efficacy with Comparable Safety*

100mg Daily Expansion Cohort**:

- ✓ Lower primary progression (primary PD) rate
- ✓ Higher confirmed ORR
- ✓ PFS trending meaningfully higher
- ✓ Comparable rates of grade 3+ hypoxia and anemia (both on-target AEs)

DIFFERENTIATED COMBINATIONS

PEAK-1 **Phase 3**

cas + cabo vs. cabo in post-IO ccRCC

- Cabo is the standard of care in the post-IO setting
- Simple 2-arm design
- Broadest post-IO and 2nd-line population

ccRCC **Phase 1b**

cas + volrustomig (anti-CTLA-4/anti-PD-1) in IO-naïve ccRCC

- Potential first-in-class, TKI-sparing combination
- Volru has demonstrated exciting preliminary data in 1L ccRCC (ESMO23)

*based on casdatifan in ARC-20, a Phase 1 study, and belzutifan in LITESPARK-005, a Phase 3 study; Source: Albiges L. et al. Abstract LBA88, ESMO 2023

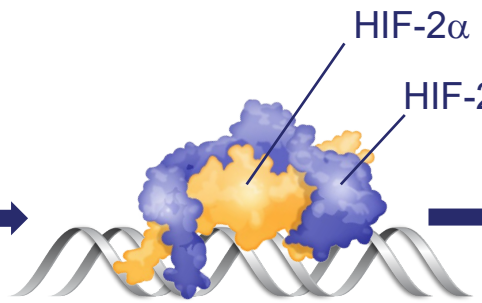
** throughout these materials, the 50mg BID expansion cohort is also referred to interchangeably as the 100mg Daily cohort

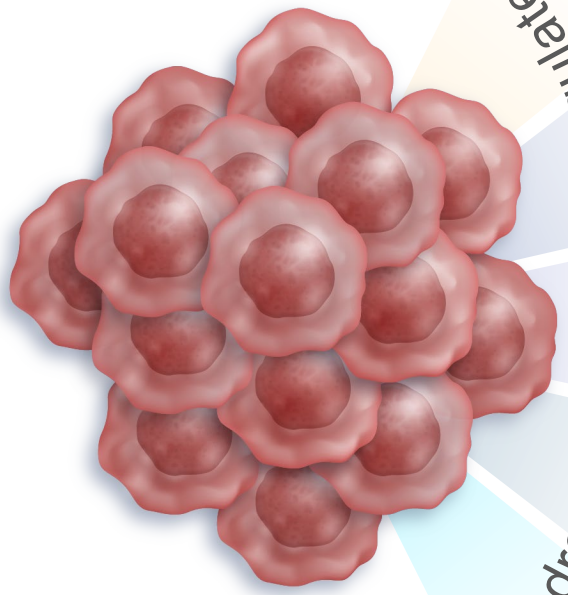
1L: first-line; AE: adverse event; BID: twice-daily; cabo: cabozantinib; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; cORR: confirmed objective response rate; CTLA-4: cytotoxic T-lymphocyte associated protein 4; IO: immuno-oncology; mg: milligram; ORR: objective response rate; PD: progressive disease; PD-L1: programmed death ligand 1; PFS: progression-free survival; PK: pharmacokinetics; RCC: renal cell carcinoma; SOC: standard of care; TKI: tyrosine kinase inhibitor; volru: volrustomig

Casdatifan Inhibits Transcription of HIF-2α-dependent Genes

Hypoxia
or
Pseudohypoxia*

**VHL* deficiency
SDH deficiency etc.





Hundreds of Genes Upregulated

- **Cell Growth/ Cycle**
  - Proliferation
  - DNA repair
  - Ribosome biogenesis
  - E2F/MYC targets
- **Angiogenesis & Oxygen Supply**
  - Hypoxic response
  - EPO/red blood cell generation
- **Epithelial-Mesenchymal Transition**
  - Stemness
- **Metastasis**
  - Migration/Invasion
  - Extracellular matrix/cell-cell interaction
  - Cytoskeleton organization
- **Metabolism**
  - Cholesterol uptake
  - Fatty Acids
  - Lipoproteins

DNA: deoxyribonucleic acid; E2F: early region 2 binding factor; EPO: erythropoietin; HIF: hypoxia-inducible factor; MYC: myelocytomatosis oncogene; SDH: succinate dehydrogenase; VHL: Von Hippel-Lindau disease

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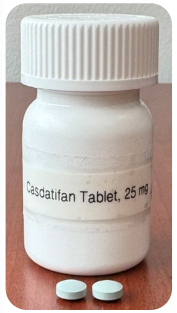
HIF-2α Is a Difficult Target for Drug Discovery, Significantly Limiting Potential Competition



casdatifan

- ~24-hour half-life in patients
- QD regimen
- Potential for improved efficacy relative to that of belzutifan
- ARC-20 showed a comparable safety profile to that of belzutifan

belzutifan

- 14-hour half-life
- Exposure limited by a sub-optimal PK profile
- QD regimen
- Good single-agent activity and safety profile
- Approved Dec 2023 in 3L+ ccRCC

2024 ASCO ANNUAL MEETING

Preliminary safety, pharmacokinetics and clinical activity of DFF332, an oral HIF-2α inhibitor, as monotherapy in a phase 1 dose escalation study in patients with advanced clear cell renal cell carcinoma

DFF322[1]

- 85-day half-life
- Only 5% ORR
- **Program appears to be terminated**

BARCELONA 2024 ESMO congress

NKT2152, a Novel Oral HIF-2α Inhibitor, in Participants with Previously Treated Advanced Clear Cell Renal Carcinoma (accRCC): Preliminary Results of a Phase 1/2 Study

NKT-2152[2]

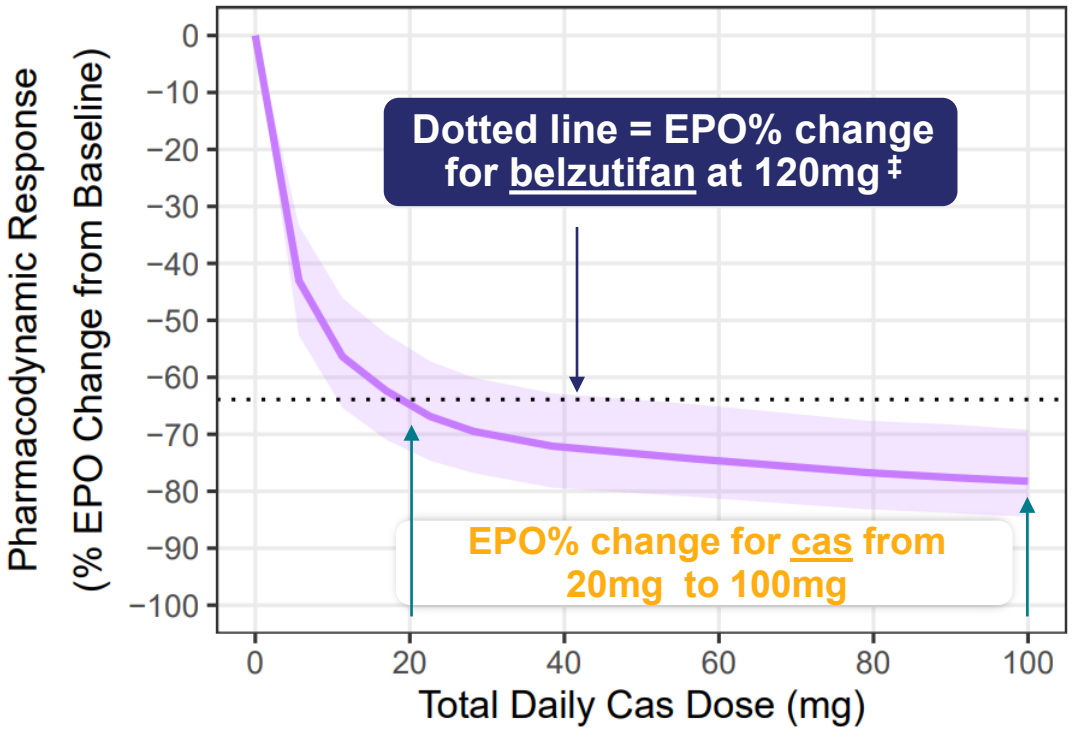
- 38-day half-life
- Higher levels of grade 3+ hypoxia
- Complicated dosing
- **Future plans unclear**

Sources: 1. ASCO 2024 4513; 2. ESMO 2024 1690O
3L: third-line; ccRCC: clear cell renal cell carcinoma; HIF: hypoxia-inducible factor; mg: milligram; ORR: objective response rate; PK: pharmacokinetic; QD: once daily

Cas Has an Optimal PK / PD Profile

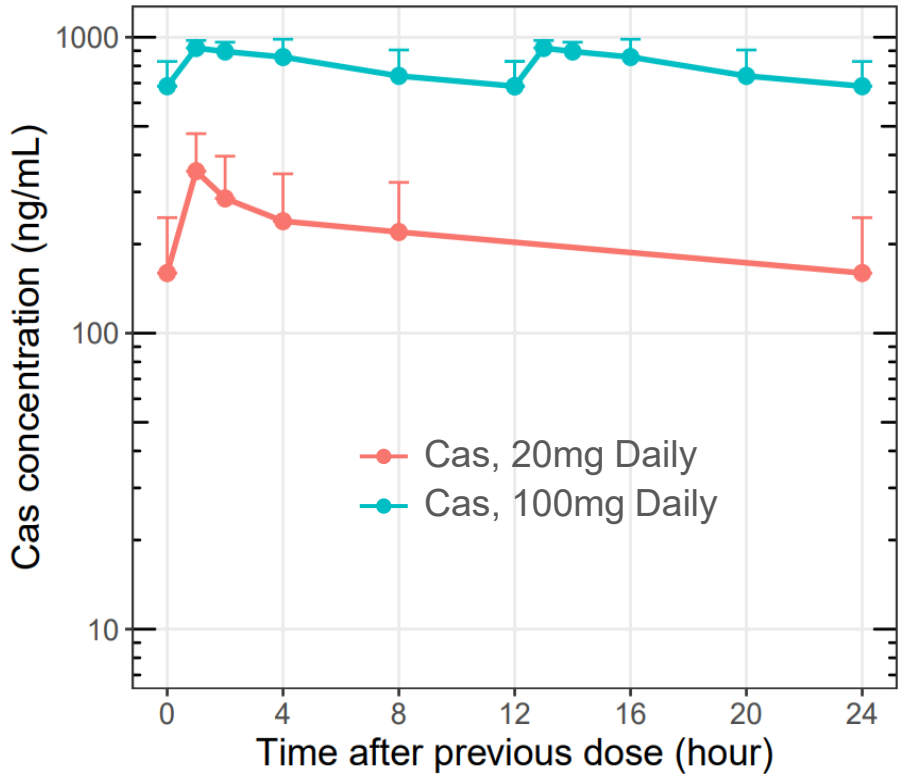
Pharmacodynamics

20mg of cas achieves the same EPO (peripheral PD biomarker) suppression as that of 120mg of belzutifan



Pharmacokinetics

Linear, dose-proportional PK and 24-hour half life

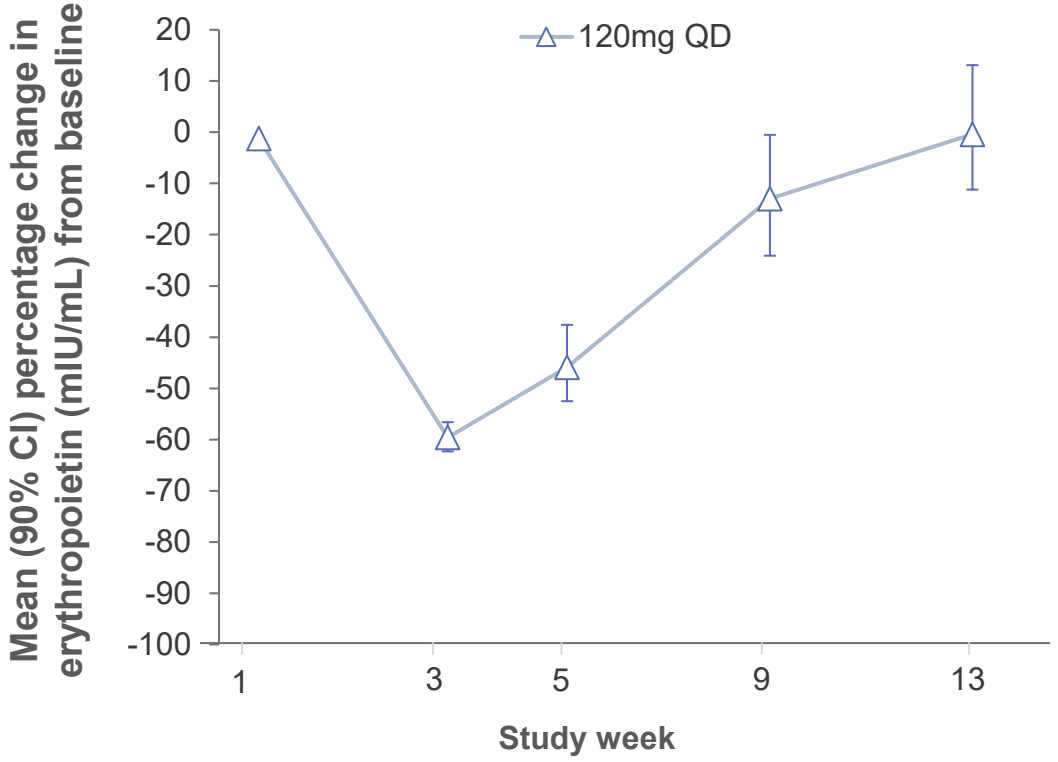


§ AB521: median (solid line) and inter-quartile range (shaded area) of population PK/PD simulations using model developed from data
‡ Source: belzutifan NDA - FDA review document. Comparison not based on head-to-head studies.
Casdatifan (AB521) is an investigational molecule and its safety and efficacy have not been established. PK/PD data are from both escalation and expansion cohorts
Cas: casdatifan; EPO: erythropoietin; mg: milligram; ng/mL: nanograms per milliliter; PD: pharmacodynamic; PK: pharmacokinetic

Cas Treatment Also Appears to Result in Greater and Longer-term Suppression of Erythropoietin

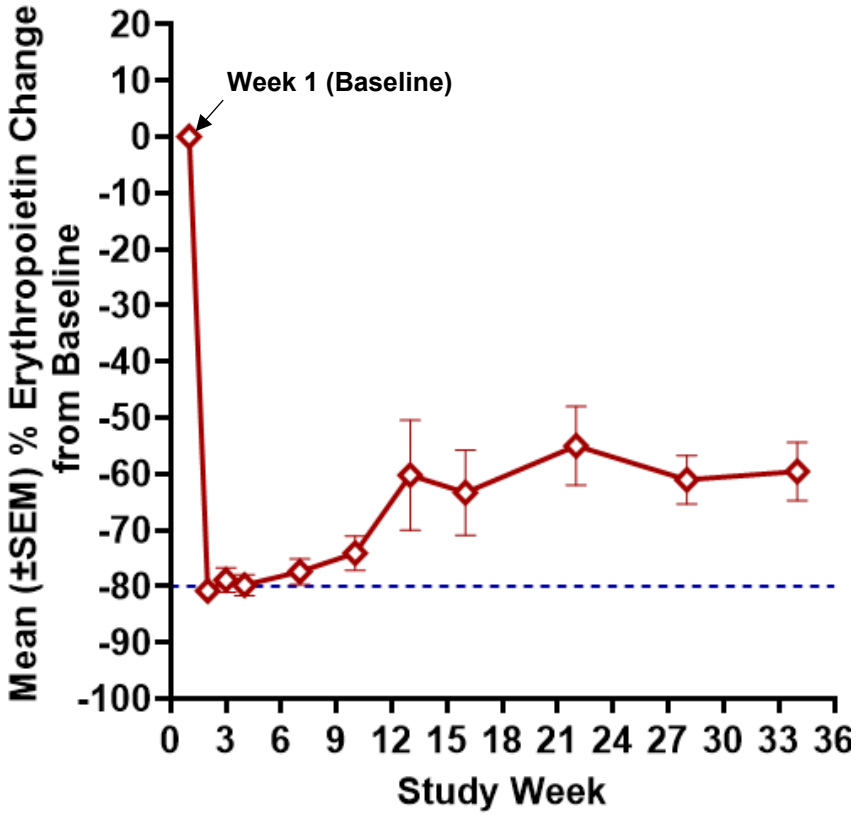
Belzutifan

Mean percentage change in erythropoietin from baseline over time



Casdatifan 100mg Daily

ccRCC patients in dose escalation + dose expansion



Source: Marathe DD, J Clin Pharm 2024, Fig S20
ccRCC: clear-cell renal cell carcinoma; EPO: erythropoietin; mIU/mL: milli-international units per milliliter; mg: milligram; QD: once-daily; SEM: standard error of the mean

ARC-20 Results Support Casdatifan's Potential Best-in-Class Profile, Despite Limited Follow-up

	MORE ADVANCED PATIENTS	SHORTER FOLLOW-UP	IMPROVED EFFICACY PROFILE				COMPARABLE SAFETY	
	% ≥4 prior LoT	Median months of follow-up	Primary progressive disease rate	ORR / cORR	mPFS (months)	DCR	Gr 3+ hypoxia	Gr 3+ anemia
ARC-20 (Phase 1/1b) Cas 100mg Daily	**27%**	**11**	**18.8%**	**34.4%*** **25.0%**	**Not reached**	**81.3%**	**7.7%**	**36%**
LITESPARK-005[1] Belz (Phase 3)	**0%**	**18**	**33.7%**	**21.9%**	**5.6**	**61.2%**	**11.2%[2]**	**33%[2]**

Data above are not from head-to-head studies. Cross-trial data interpretation should be considered with caution as it is limited by differences in study population, sample size, inclusion and exclusion criteria and many other factors.

*includes one patient who responded after data cut-off; 2 responses pending confirmation

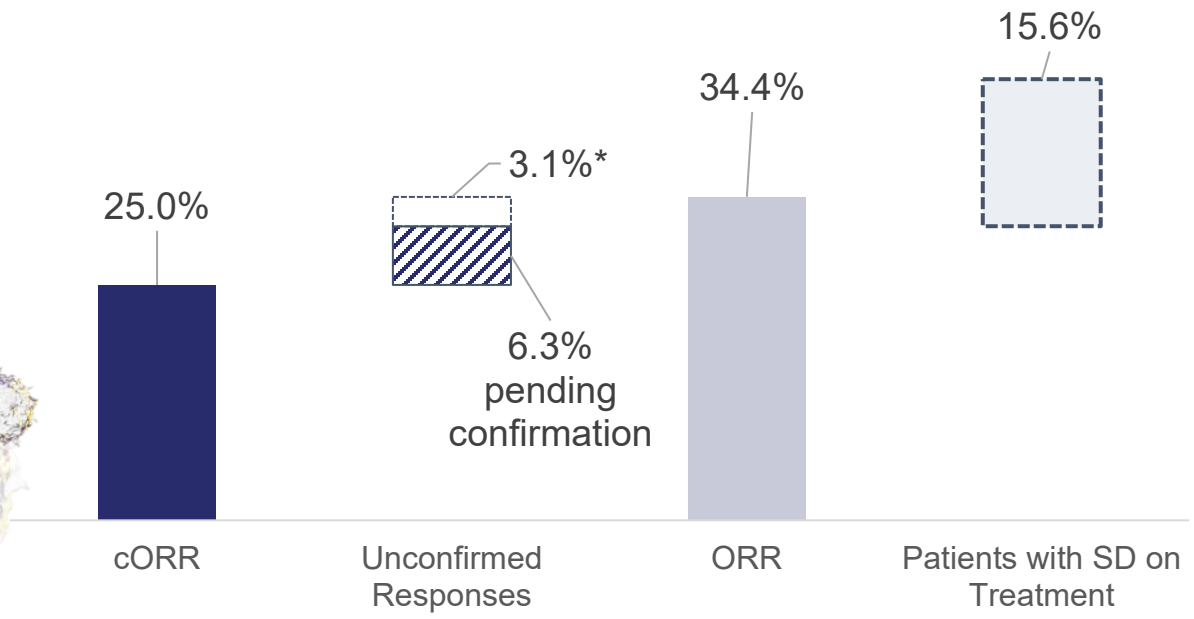
1.Efficacy data for belzutifan from IA1 of LITESPARK-005. Source: Albiges L. et al. Abstract LBA88, ESMO 2023
2.Safety details not reported at IA1. Data from IA2 of LITESPARK-005. Source: Choueiri et al. 2024
Belz: belzutifan; BID: twice daily; Cas: casdatifan; cORR: confirmed objective response rate; DCR: disease control rate; Gr: grade; IA1: first interim analysis; LoT: lines of therapy; mPFS: median progression free survival; N/A: not applicable; ORR: objective response rate; Pts: patients; SD: stable disease

cORR Should Continue to Improve as the Dataset Matures

100mg Daily Cohort (n=32)

Median follow-up: 11 months

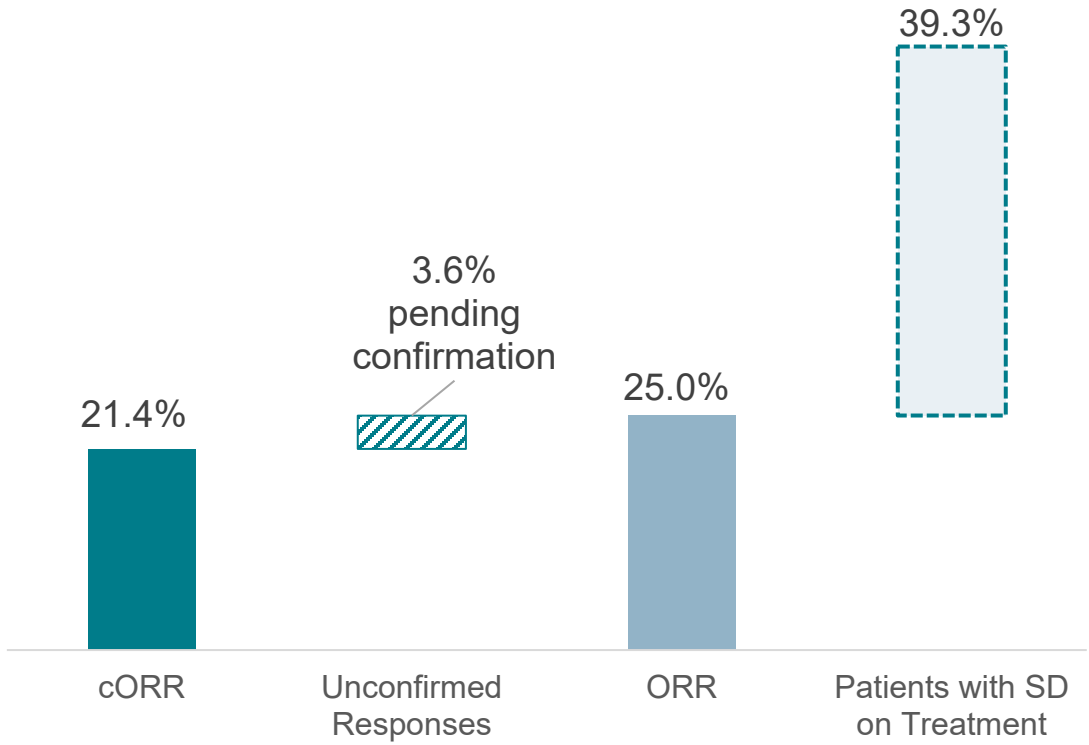
2 responses pending confirmation & 5 patients with SD have experienced tumor reduction and may respond with more follow-up



50mg QD Cohort (n=28)

Median follow-up: 8 months

1 response pending confirmation & 11 patients with SD have experienced tumor reduction and may respond with more follow-up



*1 response will not confirm due to progression
cORR: confirmed objective response rate; ORR: objective response rate; QD: once daily; SD: stable disease

ccRCC Treatment Landscape & Opportunity for HIF-2α Inhibition

Dr. Rana McKay
University of California, San Diego

1L and 2L+ RCC Treatment Landscape Today

1L RCC	
FAVORABLE RISK	POOR/INTERMEDIATE RISK
Anti-PD-1 + TKI	Anti-PD-1 + Anti-CTLA-4
TKI mono	Anti-PD-1 + TKI
Anti-PD-1 + Anti-CTLA-4*	

POST-IO
TKI mono
TKI + mTOR inhibitor
HIF-2α mono Post-progression on TKI

Following 1L, patients typically progress through different TKI regimens

Listed in order of preference by category
Source: Adapted from NCCN guidelines
*Not FDA approved, but used and recommended by physicians
1L: first-line; 2L: second-line; CTLA-4: cytotoxic T-lymphocyte associated protein 4; HIF: hypoxia-inducible factor; IO: immuno-oncology; mono: monotherapy; mTOR: mechanistic target of rapamycin; NCCN: National Comprehensive Cancer Network; PD-1: programmed cell death protein 1; RCC: renal cell carcinoma; TKI: tyrosine kinase inhibitor

There Remains a Significant Unmet Need in 2L ccRCC

Opportunity for Cas + Cabo

- Targeting meaningful extension in PFS for TKIs in the post-PD-1 setting
  - Contemporary studies for TKI monotherapy show ~7 to ~11 months median PFS
- Aim is to improve tolerability over lenva-based combinations
  - Lenva is associated with fatigue & hypertension among other AEs

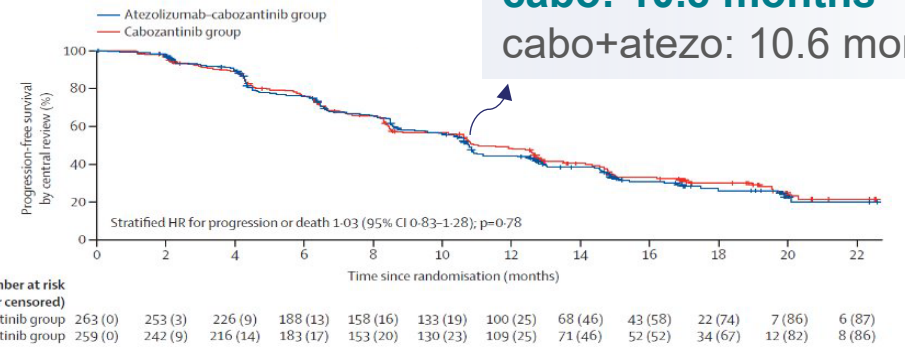
Limited PFS for TKI Monotherapy

CONTACT-03[1]

mPFS

cabo: 10.8 months

cabo+atezo: 10.6 months

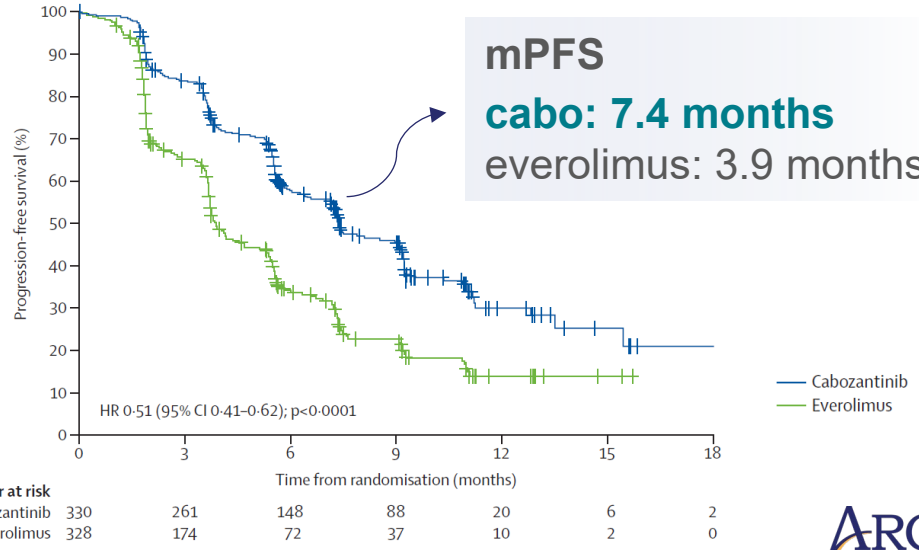


METEOR[2]

mPFS

cabo: 7.4 months

everolimus: 3.9 months



1. Pal et al 2023 2. Choueiri et al 2016

2L: second-line; AE: adverse events; atezo: atezolizumab; cabo: cabozantinib; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; lenva: lenvatinib; mPFS: median progression-free survival; nivo: nivolumab; PD-1: programmed cell death protein 1; PFS: progression-free survival; tivo: tivozanib; TKI: tyrosine kinase inhibitor

LITESPARK-005 Data Established Belz as a New SOC in 2L+ ccRCC, But Demonstrated Opportunity for Improvement

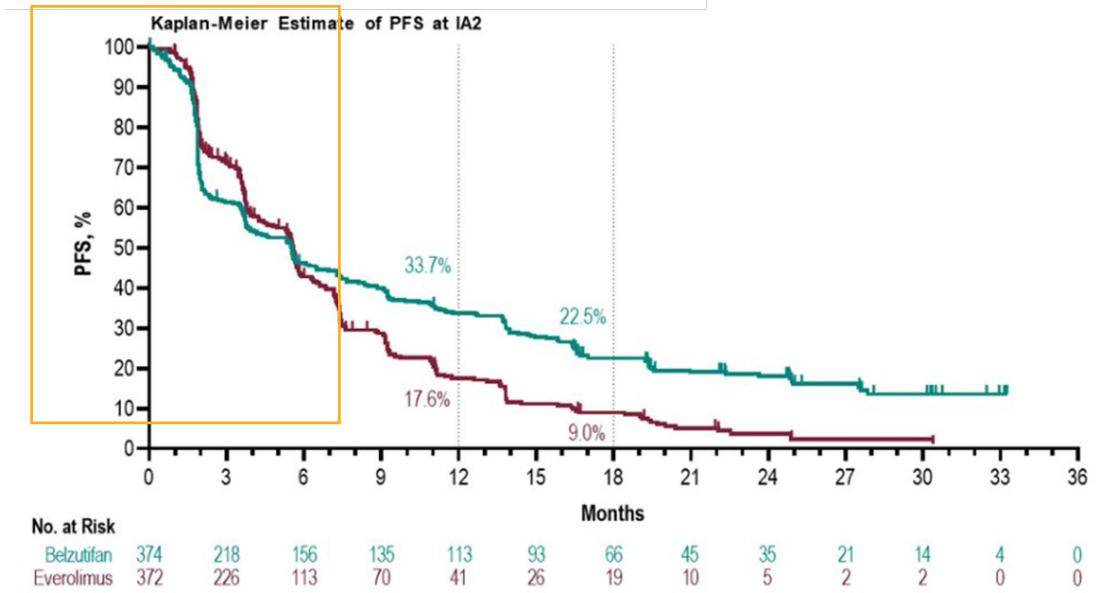
ORR / Primary Progressive Disease

	Belzutifan (N = 374)	Everolimus (N = 372)
	IA1	
ORR, % (95% CI)	**21.9% (17.8-26.5)**	**3.5% (1.9-5.9)**
Estimated difference in % (95% CI)	**18.4 (14.0-23.2); P<.00001***	
CR	2.7%	0
PR	19.3%	3.5%
SD	39.3%	65.9%
PD	**33.7%**	**21.5%**
Non-evaluable[a]	1.3%	2.2%
No assessment[b]	3.7%	7.0%

Data cut-off for IA1 of Nov 1, 2022; median follow-up of 18.4 months

Median PFS / Hazard Ratio

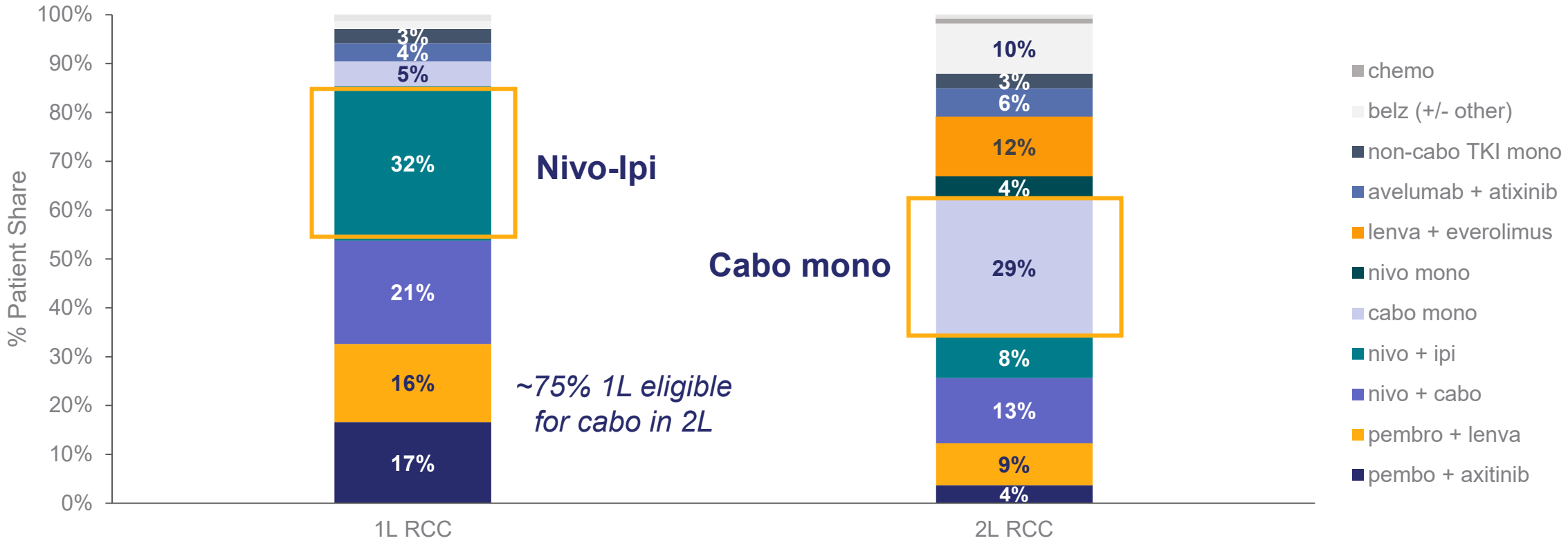
	IA1		IA2	
	Belzutifan	Everolimus	Belzutifan	Everolimus
Events	257 (68.7%)	262 (70.4%)	289 (77.3%)	276 (74.2%)
Median, mo (95% CI)	5.6 (3.9-7.0)	5.6 (4.8-5.8)	5.6 (3.8-6.5)	5.6 (4.8-5.8)
HR (95% CI)	0.75 (0.63-0.90); P <.001*		0.74 (0.63-0.88	



*denotes statistical significance.
Source: Albiges L. et al. Abstract LBA88, ESMO 2023
a. Insufficient data for response assessment per RECIST 1.1; b. No post-baseline assessment available.
2L: second-line; Belz: belzutifan; BICR: blinded independent central review; CI: confidence interval; CR: complete response; ccRCC: clear cell renal cell carcinoma; CI: confidence interval; HR: hazard ratio; IA1: first interim analysis; IA2: second interim analysis; mo: month; ORR: objective response rate; P: probability; PD: progressive disease; PFS: progression-free survival; PR: partial response; RECIST: Response Evaluation Criteria in Solid Tumors; SD: stable disease; SOC: standard of care

Cas Development Plan Targets the Largest Market Segments and Could Expand Share Within These Segments

2024 ccRCC • US Market Share



Sources - Epi: DRG, GlobalData | Share: Arcus primary research, US May 2024 (n=49)
1L: first-line; 2L: second-line; belz: belzutifan; cabo: cabozantinib; ccRCC: clear cell renal cell carcinoma; chemo: chemotherapy; ipi: ipilimumab; lenva: lenvatinib; mono: monotherapy; NCCN: National Comprehensive Cancer Network; nivo: nivolumab; pembro: pembrolizumab; TKI: tyrosine kinase inhibitor

ARC-20 Dose Expansion: Safety & Efficacy Data

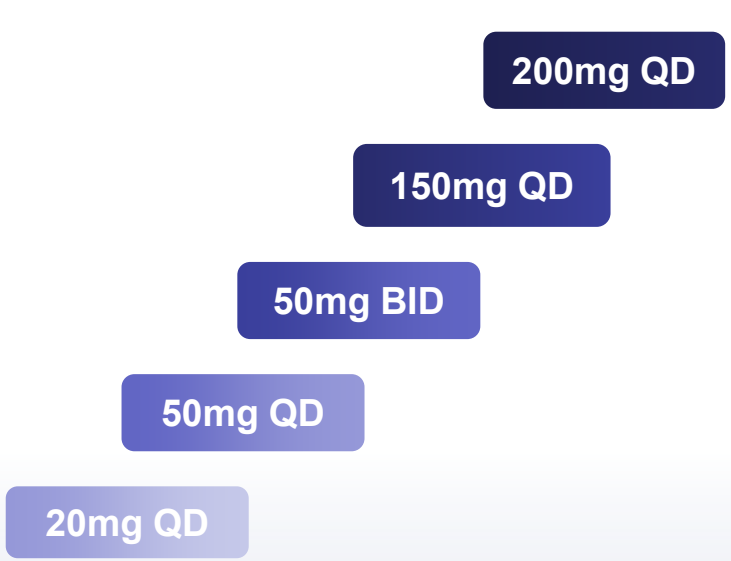
Data as of August 30, 2024. Results were presented at the EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics, 23–25 October 2024, Barcelona, Spain

Dr. Dimitry S.A. Nuyten
CMO, Arcus Biosciences

ARC-20 Is a Phase 1 Dose-Escalation and Dose-Expansion Study of Casdatifan

Dose Escalation[a]

3+3 design with 21-day DLT window
Patients with advanced solid-tumors



CASDATIFAN MONOTHERAPY

Dose Expansion

Patients with 2L+ ccRCC
N~30 per cohort

PRESENTED TODAY:

- **50mg BID (100mg Daily)**
- **50mg QD**
- 150mg QD
- 100mg QD tablet (enrolling)
- cas 100mg QD tablet + cabozantinib (enrolling)

KEY INCLUSION CRITERIA

- At least 1 measurable lesion per RECIST 1.1
- Adequate organ and marrow function

PRIMARY OUTCOMES:

- AEs
- DLTs

SECONDARY OUTCOMES:

- ORR[b]
- PK/PD

a. Dose escalation enrolled 22 patients at the 20mg QD, 50mg QD, 50mg BID, 150mg QD, and 200mg QD doses, 14 of whom had ccRCC (across all 5 doses) (August 30, 2024) b. Assessed by the investigator according to RECIST v1.1.
2L+: second-line treatment setting or greater; AE: adverse event; BID: twice daily; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; ECOG: Eastern Cooperative Oncology Group; DLT: dose-limiting toxicity; ORR: objective response rate; PD: pharmacodynamic; PD-1: programmed cell death protein-1; PK: pharmacokinetic; QD: once daily; RECIST: Response Evaluation Criteria in Solid Tumors

Baseline Characteristics Were Similar to Those in LITESPARK-005, Other than Prior Regimens

Characteristic	Dose Expansion: 2L+ ccRCC		Belzutifan[1]
	100mg Daily (n = 33)	50mg QD (n = 31)	120mg QD (n = 374)
Age, years, median (range)	62 (41–79)	65 (43–82)	66 (49–78)
Sex, Female/Male, n (%)	8 (24) / 25 (76)	10 (32) / 21 (68)	77 (21) / 297 (79)
ECOG PS 0/1, n (%)	16 (48) / 17 (52)	18 (58) / 13 (42)	NA
IMDC Risk Score, n (%)			
Favorable	9 (27)	8 (26)	79(21)
Intermediate	20 (61)	16 (52)	249 (67)
Poor	2 (6)	5 (16)	46 (12)
Unknown	2 (6)	2 (6)	0 (0)
Prior lines of therapy, all settings, n (%)			
1	**2 (6)**	**5 (16)**	**46 (12)**
2	**14 (42)**	**9 (29)**	**157 (42)**
3	**8 (24)**	**8 (26)**	**171 (46)**
4 or more	**9 (27)**	**9 (29)**	**0 (0)**
Prior VEGF-R TKI, n (%)			
1	13 (39)	15 (48)	187 (50)
2	12 (36)	8 (26)	187 (50)*
3	3 (9)	5 (16)	
4 or more	5(16)	3 (10)	0 (0)
Number of patients with prior mTOR treatment, n (%)	5 (15%)	7 (23%)	NA
Median follow-up, months (range)	**11 (3-15+)**	**8 (4-10+)**	**18.4 for IA1 (range NA)**

1. IA1 for LITESPARK-005. Source: Albiges L. et al. Abstract LBA88, ESMO 2023; *2 or 3 prior VEGF-R TKI regimens; Data cutoff date: August 30, 2024.; Baseline was defined as the last non-missing assessment prior to the first dosing of treatment.
BID: twice daily; ccRCC: clear cell renal cell carcinoma; ECOG PS: Eastern Cooperative Oncology Group performance status; IA1: first interim analysis; IMDC: International Metastatic Renal Cell Carcinoma Database Consortium; mTOR: mechanistic target of rapamycin; NA: not applicable; QD: once daily; TKI: tyrosine kinase inhibitor; VEGF-R: vascular endothelial growth factor receptors

Key Efficacy Measures All Compare Very Favorably to Contemporary Benchmark Studies Despite Shorter Follow-up

Efficacy Evaluable Population[1]	Casdatifan 100mg Daily (n = 32)
ORR (n) [90% CI]	**34.4%** (11*) [18.6%, 53.2%]
Responses pending confirmation, n	2*
Confirmed ORR (n) [90% CI]	**25.0% (8)** [11.5, 43.4]
Median time to response, months (range)	2.8 (1.2–5.5)
Primary progressive disease (n)	**18.8% (6)**
Disease control rate [90% CI]	**81.3%** [63.6, 92.8]
Median follow-up, months (range)	11 (3–15+)
Median progression free survival	**Not reached**

*Includes one patient in the 100mg Daily cohort who had a new response after data cut-off date (ORR of 31.3% as of DCO)

- **2 unconfirmed responders in the 100mg Daily and 1 in the 50 mg QD cohorts remain on study with the potential to achieve a confirmed response**
- Only 1 unconfirmed response (in the 100mg Daily cohort) does not have the potential to be confirmed

1. Across both cohorts, there were four ineligible patients, all of whom were on study for a short period of time. 3 patients deemed ineligible shortly after enrollment (2 patients due to kidney function, 1 patient due to hemoglobin levels). One patient discontinued treatment before the first scan due to an unrelated AE.
AE: adverse event; CI: confidence interval; DCO: data cut-off; ORR: objective response rate; QD: once daily

Key Efficacy Measures All Compare Very Favorably to Contemporary Benchmark Studies Despite Shorter Follow-up

Efficacy Evaluable Population[1]	Casdatifan 100mg Daily (n = 32)	Casdatifan 50mg QD (n = 28)
ORR (n) [90% CI]	**34.4%** (11*) [18.6%, 53.2%]	**25.0% (7)** [10.7, 44.9]
Responses pending confirmation, n	2*	1
Confirmed ORR (n) [90% CI]	**25.0% (8)** [11.5, 43.4]	**21.4% (6)** [8.3, 41.0]
Median time to response, months (range)	2.8 (1.2–5.5)	4 (1.3–4.1)
Primary progressive disease (n)	**18.8% (6)**	**14.3% (4)**
Disease control rate [90% CI]	**81.3%** [63.6, 92.8]	**85.7%** [67.3, 96.0]
Median follow-up, months (range)	11 (3–15+)	8 (4–10+)
Median progression free survival	**Not reached**	**Not reached**

*Includes one patient in the 100mg Daily cohort who had a new response after data cut-off date (ORR of 31.3% as of DCO)

- **2 unconfirmed responders in the 100mg Daily and 1 in the 50 mg QD cohorts remain on study with the potential to achieve a confirmed response**
- Only 1 unconfirmed response (in the 100mg Daily cohort) does not have the potential to be confirmed

1. Across both cohorts, there were four ineligible patients, all of whom were on study for a short period of time. 3 patients deemed ineligible shortly after enrollment (2 patients due to kidney function, 1 patient due to hemoglobin levels). One patient discontinued treatment before the first scan due to an unrelated AE.

AE: adverse event; CI: confidence interval; DCO: data cut-off; ORR: objective response rate; QD: once daily

100mg Cas Cohort ORR Exceeds the Belzutifan Benchmarks; 50mg Cohort Is Also Trending Better

STUDY DESCRIPTION	# OF LINES OF THERAPY	PRIOR TKI	PRIOR CPI	ORR (PRIOR CPI *AND* TKI PTS ONLY)	MEDIAN FOLLOW-UP
LITESPARK-001[1]	• Median 3 prior lines	• 91% had prior VEGF TKI	• 80% had prior CPI	• 20.5%	41 months
LITESPARK-005[2]	• 1-3 prior lines for inclusion • Mostly 2-3 prior lines	• 100% had prior TKI	• 100% had prior CPI	• 21.9%	18 months
LITESPARK-013[3]	• Mostly 1-2 prior lines	• 71.4% had prior TKI	• 100% had prior CPI	• 19.1%	20 months
ARC-20[4] **100mg Daily**	• **27% of patients had ≥4 prior lines** • **Median of 3 prior lines**	• **100% had prior TKI**	• **100% had prior CPI**	• **34.4% (2 pending confirmations*)** • **25.0% (confirmed as of DCO)**	**11 months**

Data above are not from head-to-head studies. Cross-trial data interpretation should be considered with caution as it is limited by differences in study population, sample size, inclusion and exclusion criteria and many other factors

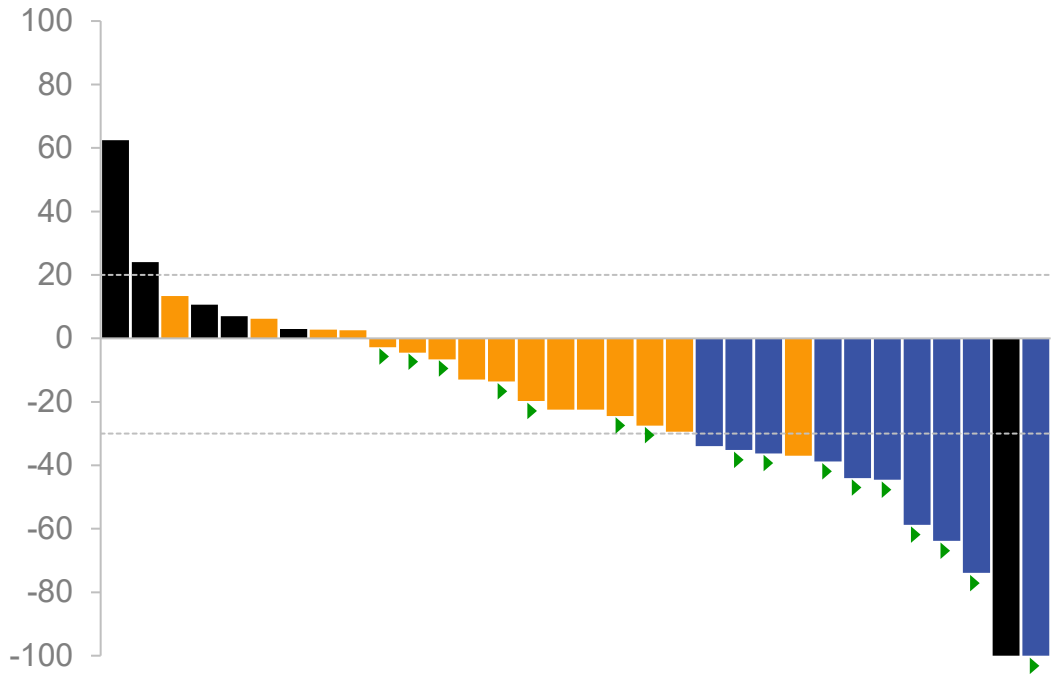
*includes one patient who had a new response after the data cut-off; 2 of 3 unconfirmed responders in the 100mg Daily cohort remain on study with potential to achieve a confirmed response

1. Phase 1; belzutifan in previously treated ccRCC (Dose Expansion Cohort) (NCT02974738); refs: Jonasch et al 2024; Choueiri et al 2021; ASCO GU 2021 273
2. Phase 3; belzutifan vs. everolimus in previously treated ccRCC (NCT04195750); ref: ESMO 2023 LBA88
3. Phase 2; belzutifan 120mg and 200mg (pooled) in previously treated ccRCC (NCT04489771); ref: ASCO 2024 4534
4. Phase 1/1b; casdatifan in previously treated ccRCC (NCT05536141); ref: ct.gov

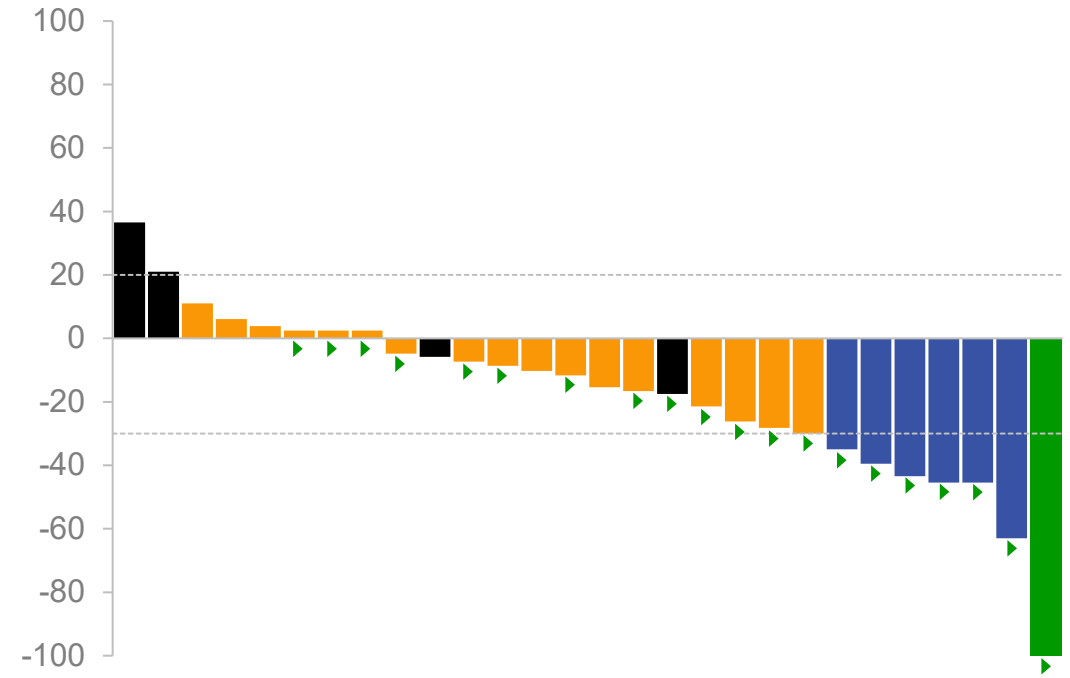
2L: second-line; ccRCC: clear cell renal cell carcinoma; CPI: checkpoint inhibitor; Pts: patients; RECIST: Response Evaluation Criteria in Solid Tumors; TKI: tyrosine kinase inhibitor

Vast Majority of Patients Experienced Tumor Reduction in Both Cohorts

100mg Daily Cohort



50mg QD Cohort



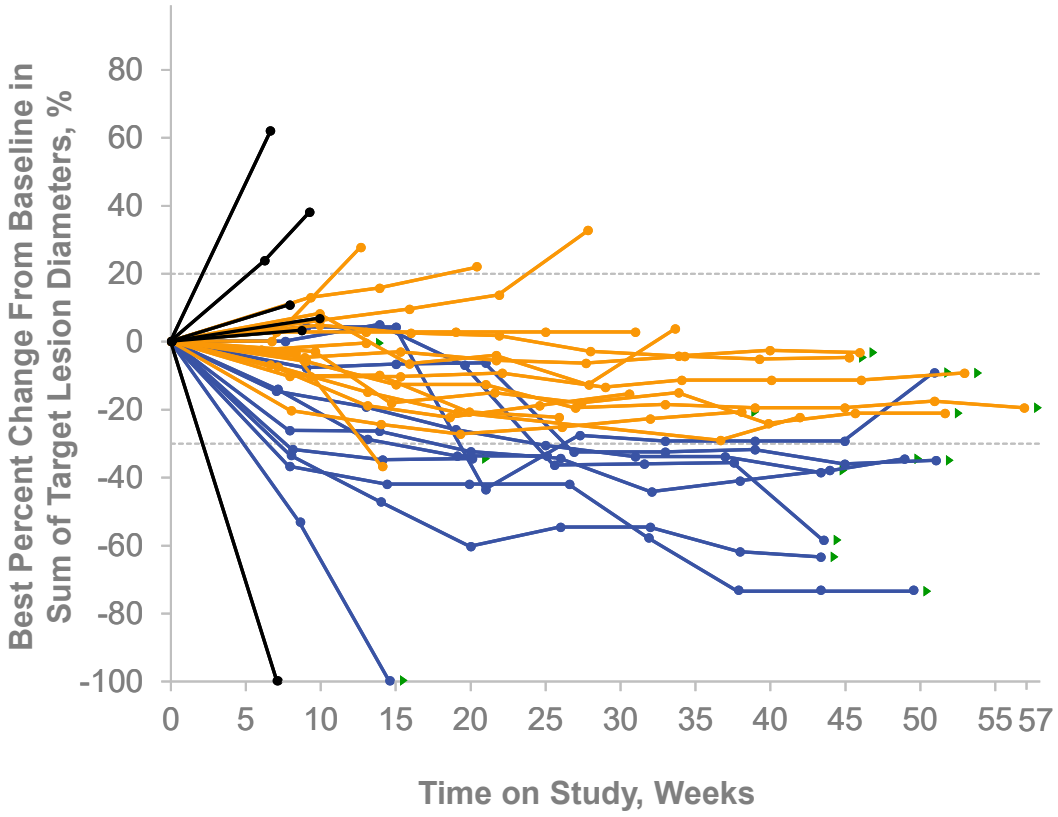
Best Response Type Complete Response Partial Response Stable Disease Progressive Disease Ongoing

- **5 patients* in the 100mg Daily cohort and 11 patients** in the 50mg QD cohort with stable disease remain on treatment and could respond with longer follow-up**
- One patient in 100mg Daily cohort with best response of PD achieved 100% tumor reduction in their primary lesion
- Deep responses seen regardless of # prior lines of therapy, including in patients with >3 prior lines

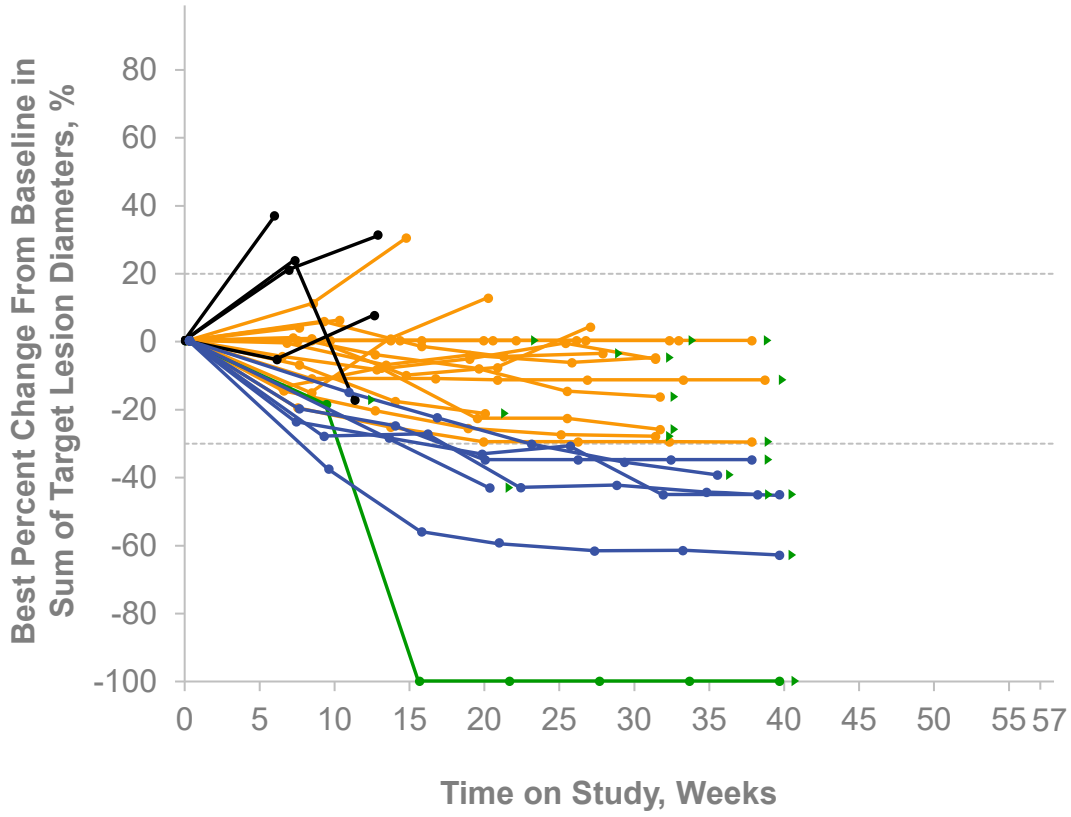
Data cutoff date: August 30, 2024.
*One patient in the 100mg Daily cohort converted to a response and one patient was recorded with progressive disease after the DCO.
**One patient in the 50mg QD cohort with best response of stable disease was recorded with progressive disease in a subsequent scan and will therefore not respond.
DCO: data cut-off; PD: progressive disease; QD: once daily

Spider Plots Illustrate Durable Disease Control for Both Doses

100mg Daily Cohort



50mg QD Cohort



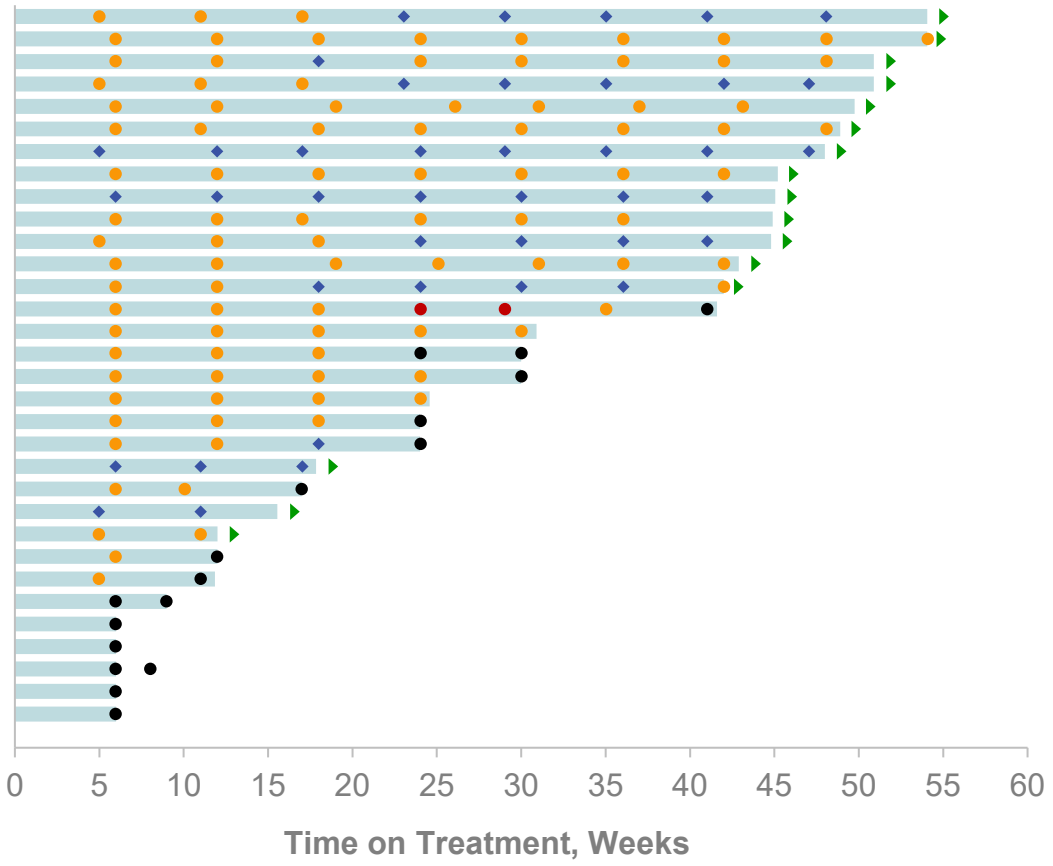
Best Response Type — Complete Response — Partial Response — Stable Disease — Progressive Disease — Ongoing

- **10 of 11 and 7 of 7 responders remain on study in the 100mg Daily and 50mg QD cohorts, respectively**

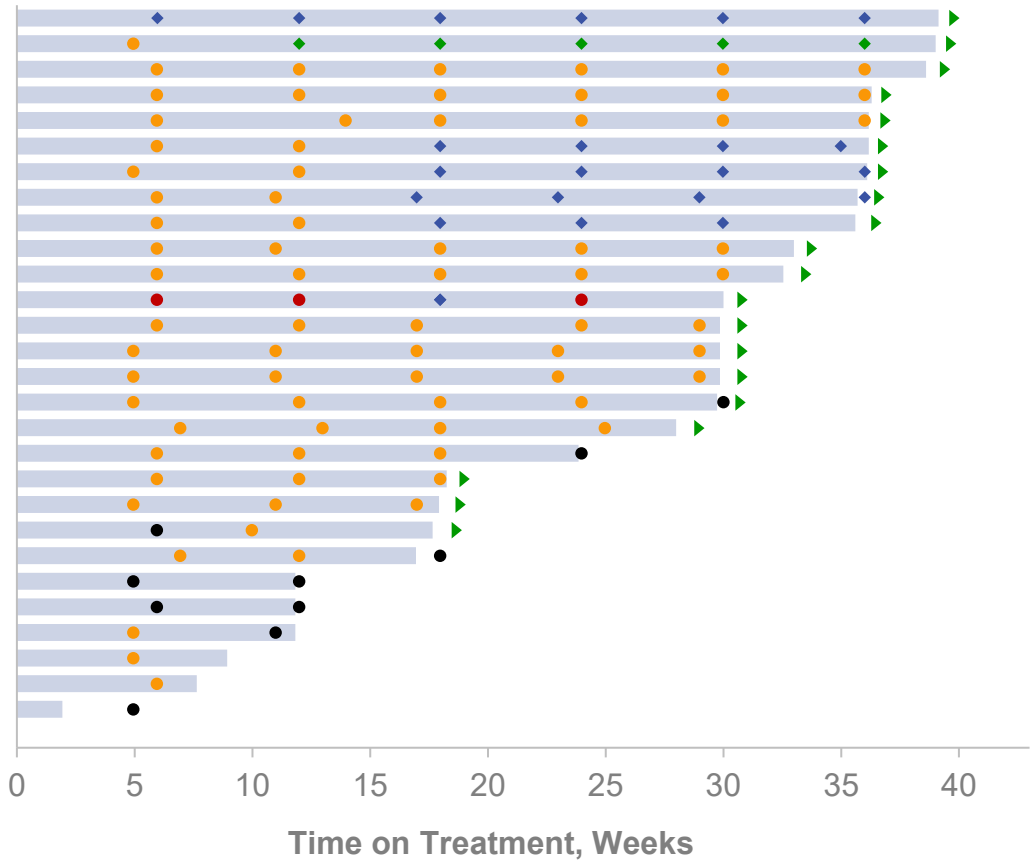
QD: once daily

Majority of Patients Remain on Study for Both Cohorts

100mg Daily Cohort



50mg QD Cohort



Complete Response Partial Response Stable Disease Progressive Disease Ongoing Not Estimable

Date cutoff date: August 30, 2024.
QD: once daily

Patient Case Study #1

PATIENT DETAILS: 65 Year-old Female

DIAGNOSIS (MAR 2023): Stage IV metastatic ccRCC, IMDC Risk: Intermediate

PRIOR TREATMENT:

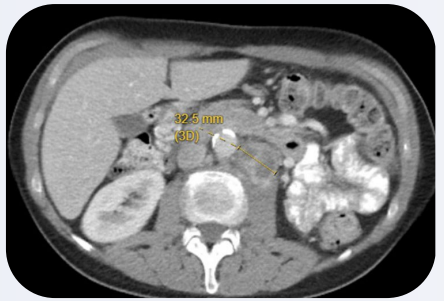
She underwent a left radical nephrectomy and splenectomy in March 2023.

In May 2023, she started lenvatinib + pembrolizumab (best overall response on treatment was stable disease). Progression occurred in October 2023.

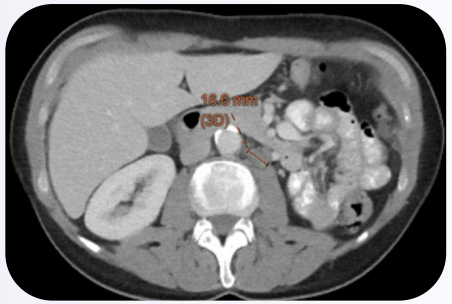
ARC-20 STUDY DETAILS:

- Patient enrolled in casdatifan 50mg daily cohort and was first dosed on 20 November 2023.
  - Tumor assessments demonstrated target lesions including retroperitoneal lymph nodes and a right paravertebral soft tissue lesion.
- Multiple non-target pulmonary nodules were also noted.
- A partial response was noted on the first post-baseline tumor assessment on 29 December 2023.
  - Continues to demonstrate a partial response through 6 September 2024.
- The patient has tolerated the regimen with no serious adverse events and no grade 3 or higher adverse events.
  - Grade 2 anemia is ongoing, with the most recent hemoglobin of 9.5 g/dl. The patient did not receive transfusions or ESAs while on study.
  - No hypoxia, with the most recent pulse oximetry of 98%.

TARGET LESION

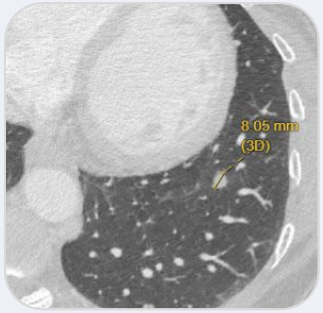


BEFORE | 3.2 cm LN

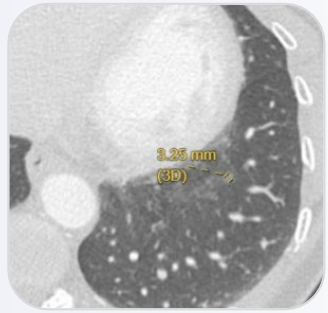


WEEK 6 | 1.7 cm LN

NON-TARGET LESION



BEFORE
8 mm LLL nodule



AFTER
3 mm LLL nodule

ccRCC: clear cell renal cell carcinoma; cm: centimeter; ESA: Erythropoietin Stimulating Agent; LLL: left lower lobe (in the lung); LN: lymph node; IMDC: International Metastatic RCC Database Consortium; mm: millimeter

TEAE Profile is Very Manageable

	DOSE EXPANSION	
Safety-evaluable population	**100mg Daily (n=33)**	**50mg QD (n=31)**
Any TEAEs, n (%)	32 (97)	30 (97)
Related to casdatifan	31 (94)	28 (90)
Any serious TEAEs, n (%)	4 (12)	7 (23)
Related to casdatifan	1 (3)	2 (7)
Any Grade 3 TEAEs, n (%)	15 (46)	16 (52)
Related to casdatifan	14 (42)	11 (36)
Anemia		
All grades	28 (85)	28 (90)
Grade 3 related	12 (36)	11 (36)
Leading to interruptions	11 (33)	8 (26)
Leading to dose reductions	2 (6)	4 (13)
Leading to discontinuation	0 (0)	0 (0)
Hypoxia		
All grades	5 (15)	3 (10)
Grade 3 related	3 (9)	2 (6)
Leading to interruptions	4 (12)	3 (10)
Leading to dose reductions	1 (3)	0 (0)
Leading to discontinuation	0 (0)	1 (3)

Belzutifan Anemia Rates

- All Grade: 83%
- Grade 3+: 33%

Belzutifan Hypoxia Rates

- All Grade: 15%
- Grade 3+ : 11%

Belzutifan demonstrated similar rates of All Gr / Gr3+ Anemia and Hypoxia in LITESPARK-005

Note: There were no Grade 4+ TRAEs or deaths related to casdatifan.

Date cutoff date: August 30, 2024.
Safety-evaluable population included all enrolled patients who received any amount of any study treatment.
Belzutifan safety details not reported at IA1. Data from IA2 of LITESPARK-005. Source: Choueiri et al. 2024.
Gr: grade; QD: once daily; TEAE: treatment-emergent adverse event; TRAE: treatment-related adverse event

ARC-20 Results Support Casdatifan's Potential Best-in-Class Profile, Despite Limited Follow-up

		MORE ADVANCED PATIENTS	SHORTER FOLLOW-UP		IMPROVED EFFICACY PROFILE				COMPARABLE SAFETY	
		% ≥4 prior LoT	Median months of follow-up	% SD Pts on treatment	Primary progressive disease rate	ORR / cORR	mPFS (months)	DCR	Gr 3+ hypoxia	Gr 3+ anemia
Cas ARC-20 (Phase 1/1b)	100mg Daily	**27%**	**11**	**16%**	**18.8%**	**34.4%*** / **25.0%**	**Not reached**	**81.3%**	**7.7%**	**36%**
	50mg QD	**29%**	**8**	**39%**	**14.3%**	**25.0%** / **21.4%**	**Not reached**	**85.7%**	**10%**	**36%**
Belz LITESPARK-005[1] (Phase 3)		0%	18	N/A	33.7%	21.9%	5.6	61.2%	11.2%[2]	33%[2]

Data above are not from head-to-head studies. Cross-trial data interpretation should be considered with caution as it is limited by differences in study population, sample size, inclusion and exclusion criteria and many other factors

*includes one patient who responded after data cut-off; 2 responses pending confirmation

1. Efficacy data from IA1 of LITESPARK-005. Source: Albiges L. et al. Abstract LBA88, ESMO 2023
2. Safety details not reported at IA1. Data from IA2 of LITESPARK-005. Source: Choueiri et al. 2024.
belz:belzutifan; casd: casdatifan; cORR: confirmed objective response rate; DCR: disease control rate; Gr: grade; LoT: lines of therapy; mPFS: progression-free survival; ORR: objective response rate; SD: stable disease; QD: once daily

Next Steps and Development Plan

Dr. Dimitry S.A. Nuyten
CMO, Arcus Biosciences

More ARC-20 Data are Expected Over the Next 12-18 Months

EXPECTED TIMING	ARC-20 COHORT(S)	OUTCOME MEASURES
1H 2025	Cohort 1: 100mg	More mature ORR, PFS
	Cohort 2: 50mg	More mature ORR, PFS
2H 2025	Cohort 1: 100mg	ORR & PFS for all monotherapy cohorts
	Cohort 2: 50mg	
	Cohort 3: 150mg	
	Cohort 5: 100mg (tablet)	
	Cohort 4: cas + cabo	Early safety
Late 2025/early 2026	Cohort 4: cas + cabo	Early efficacy

1H: first half; 2H: second half; cas: casdatifan; cabo: cabozantinib; mg: milligram; ORR: objective response rate; PFS: progression-free survival

Arcus is Pursuing Differentiated Combinations for Cas

Post-IO Setting

PEAK-1

Potential best-in-class HIF2α + TKI combination

- Phase 3 study of cas plus cabozantinib vs. cabo (current SOC)
- Target population: Following progression on IO-based treatment in either the adjuvant or first-line metastatic settings

Expected to Initiate 1H 2025

IO-Naïve Setting

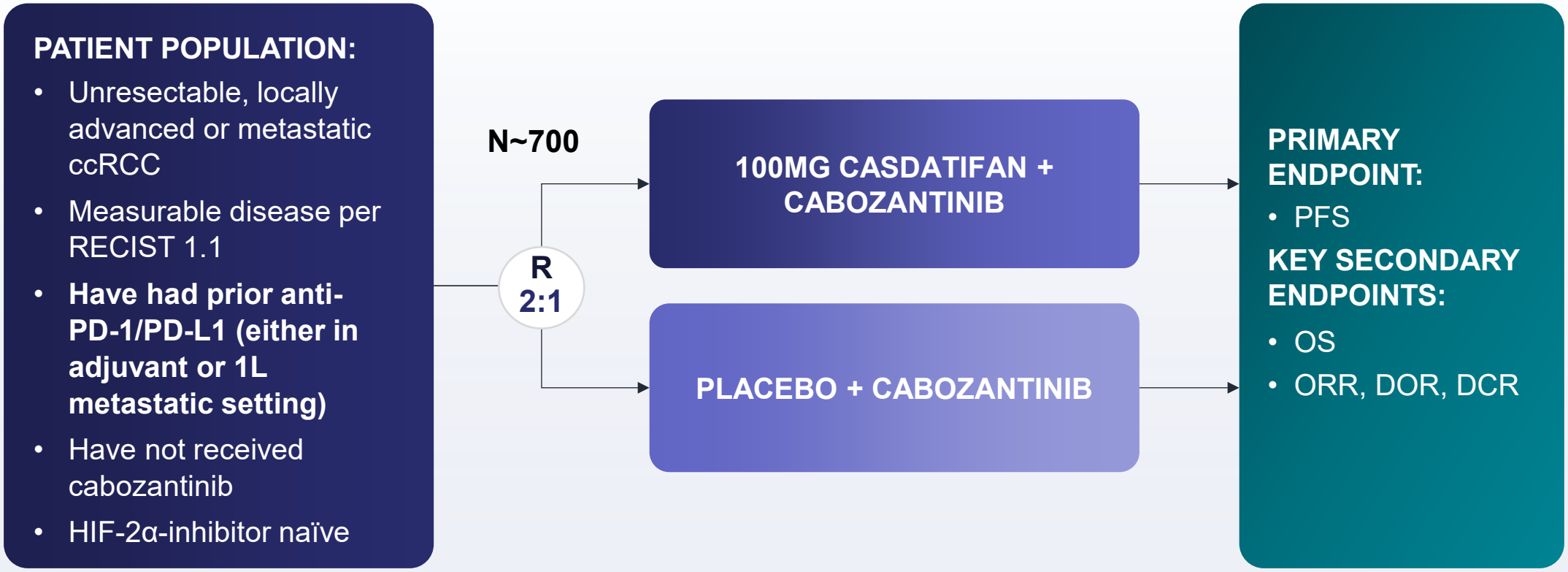
Casdatifan + Volrustomig

Potential first-in-class AND best-in-class combination

- Volru is AZ's anti-PD-1 / CTLA-4 bi-specific; Encouraging data in 1L RCC was presented at ESMO
- AstraZeneca is operationalizing evaluation of the combination
- First step will be to establish the safety and preliminary efficacy of the combination in IO-naïve ccRCC

1H: first half; AZ: AstraZeneca; cabo: cabozantinib; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; CTLA-4: cytotoxic T-lymphocyte associated protein 4; HIF: hypoxia-inducible factors; IO: immuno-oncology; PD-1: programmed cell death 1; PFS: progression-free survival; SOC: standard of care; TKI: tyrosine kinase inhibitor; volru: volrustomig

First Phase 3 for Cas Has a Simple Design that Utilizes the Preferred SOC in Post-IO RCC and Targets a Broad Population



1L: first-line; cabo: cabozantinib: cas: casdatifan; ccRCC: clear cell renal cell carcinoma; DCR: disease control rate; DOR: duration of response; HIF: hypoxia-induced factor; IO: immuno-oncology; mg: milligram; ORR: objective response rate; OS: overall survival; PD-1/PD-L1: programmed death protein 1/programmed death ligand 1; PFS: progression free survival; RCC: renal cell carcinoma; RECIST: Response Evaluation Criteria in Solid Tumors

HIF-2α Inhibition Has Shown a Benefit when Combined with TKI vs. TKI alone

LITESPARK-003

Cohort 2[1]:

belz + cabo

PHASE 2 (n=52)	
2L+ IO-Experienced ccRCC	
Median Follow-up	39.8 months
mPFS	13.8 months

KEYMAKER-U03B[2]:

belz + lenva

PHASE 2 (n=32)	
2L+ PDx and VEGF Experienced ccRCC	
Median Follow-up	6.9 months
mPFS	11.2 months

Sources: 1. ESMO 2023 LBA87 2. ASCO 2023 4553 3. METEOR Choueiri et al 2016 4. CONTACT-03. Pal et al 2023

2L: second-line; belz: belzutifan; cabo: cabozantinib; ccRCC: clear cell renal cell carcinoma; HIF: hypoxia induced factors; IO: immuno-oncology; lenva: lenvatinib; mPFS: median progression free survival; ORR: objective response rate; PDx: anti-PD-L1 or anti-PD-1; TKI: tyrosine kinase inhibitor; VEGF: vascular endothelial growth factor

ARCUS BIOSCIENCES

The Casdatifan Clinical Program Will Continue to Expand

CURRENT CAS DEVELOPMENT PROGRAM

TRIAL	GOAL(S)	STATUS
Phase 1a: ARC-14	Establish safety/ tolerability in healthy volunteers	**Completed** 56 healthy volunteers dosed with cas
Phase 1b: ARC-20	Establish safety / efficacy of cas monotherapy and cas + cabo Dose optimization	**Ongoing** >150 patients dosed with cas or cas + cabo to date
Phase 1b: AZ operationalizing	Safety / efficacy of cas + volru in ccRCC	**Planning activities underway**
Phase 3: PEAK-1	Registrational study evaluating cas + cabo vs. cabo in post-IO ccRCC	**Planning activities underway** Target initiation: 1H 2025

CAS FUTURE DEVELOPMENT

Other novel combinations

Expansion into ccRCC subpopulations

Expansion into new tumor types

1L: first-line; 1H: first half; cabo: cabozantinib; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; IO: immuno-oncology; mono: monotherapy; TKI: tyrosine kinase inhibitor; volru: volrustomig

ARCUS BIOSCIENCES

Market Opportunity in Renal Cell Carcinoma

Eric Matthews
CCO, Arcus Biosciences

Arcus is Targeting Substantial Markets with Potential Best-in-Class and First-in-Class Combinations

	CURRENT SOC	FUTURE TREATMENT	MARKET SIZE (US)[6]	DIFFERENTIATION
Adjuvant	**PD-1 mono:** mDFS NR, 4Y DFS ~65%[1]	**HIF-2α + PD-1** belz + pembro	 **17.5k patients[7]**	-
IO-naïve metastatic	**PD-1 + CTLA4:** ORR 39%, mPFS 12mo, mOS 53mo[3]	**HIF-2α + PD-1/CTLA4** cas + volrustomig	 **12.2k patients**	**Arcus regimen builds on a preferred SOC (PD-1 + CTLA4)** Potential DOT: 20+ months
	PD-1 + TKI: ORR 56-70%, mPFS 16-24mo, mOS 47-54mo[2]	**HIF-2α + PD-1 + TKI** belz + pembro + lenva		
Post-IO metastatic	**TKI mono:** ORR 20-40% mPFS 7-11mo mOS 22mo+[4]	**HIF-2α + TKI** cas + cabo **HIF-2α + TKI:** belz + lenva	 **11.3k patients**	**Arcus regimen builds on a preferred SOC (cabo) in the Post-IO setting** Potential DOT: 15+ months
Post-IO & Post-TKI	**mTOR, TKI, HIF-2α:** everolimus, belz ORR 4-23%, mPFS 5.6mo, mOS 18-21mo[5]		 **7.4k patients**	-

1.Choueiri et al 2024 (KN-564), 2. Motzer et al 2024 (CLEAR), ASCO 2023 LBA4501 (KN-426), ASCO GU 2024 362 (CM-9ER), 3. ASCO GU 2024 363 (CM-214), 4. Pal et al 2023 (CONTACT-03), Choueiri et al 2024 (TiNivo-2), 5. Choueiri et al 2024 (LITESPARK-005), 6. 2034 DRG epi, Arcus Primary Research, 7. Post-nephrectomy at high risk of recurrence.
belz: belzutifan; cabo: cabozantinib; cas: casdatifan; CTLA4: cytotoxic T-lymphocyte associated protein 4; DFS: disease-free survival; DOT: duration of treatment; HIF: hypoxia-inducible factor; IO: immuno-oncology; lenva: lenvatinib; mDFS: modified disease-free survival; mPFS: median progression-free survival; mo: months; mOS: median overall survival; ORR: objective response rate; pembro: pembrolizumab; SOC: standard of care; TKI: tyrosine kinase inhibitor

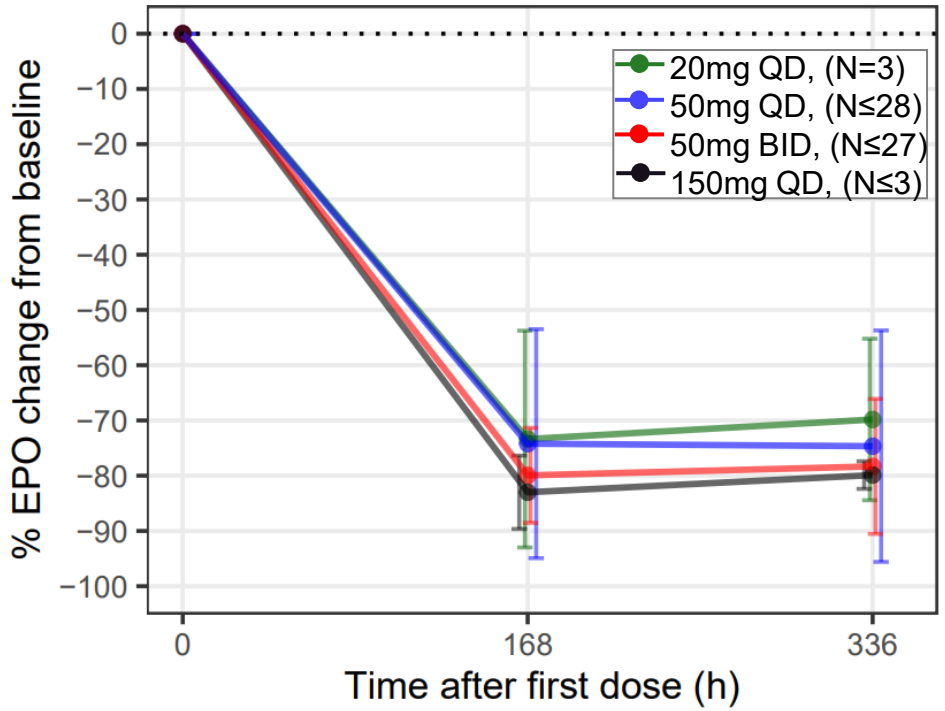
Closing Remarks

Appendix

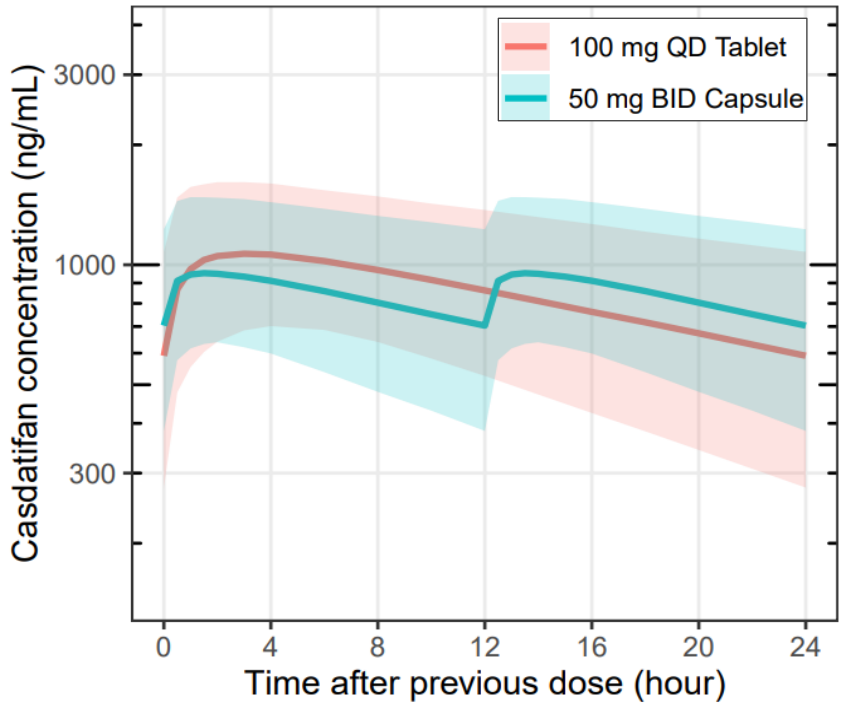
Casdatifan's Pharmacokinetic and Pharmacodynamic Profile Demonstrates Best-in-Class Properties[1]

- The PK/PD profile of casdatifan shows dose-proportional exposure increase with mean terminal half-life of ~18 to 24 hours, supporting QD dosing[1]

ARC-20 Change in EPO (Mean ± SD) vs Time in Patients with ccRCC and other Solid Tumors



PopPK Simulations of Casdatifan Steady-State PK Profile after 50mg BID Capsule and 100mg QD Tablet*[2]



*Solid line: Median of simulated concentrations Shaded area: 5th and 95th percentiles of simulated concentrations;

1. Ghasemi M et al. Oncologist, 2024;29: Abstract 56. 2. Ghasemi M et al. Presented at the Kidney Cancer Research Summit, Boston, Massachusetts, July 11–12, 2024.

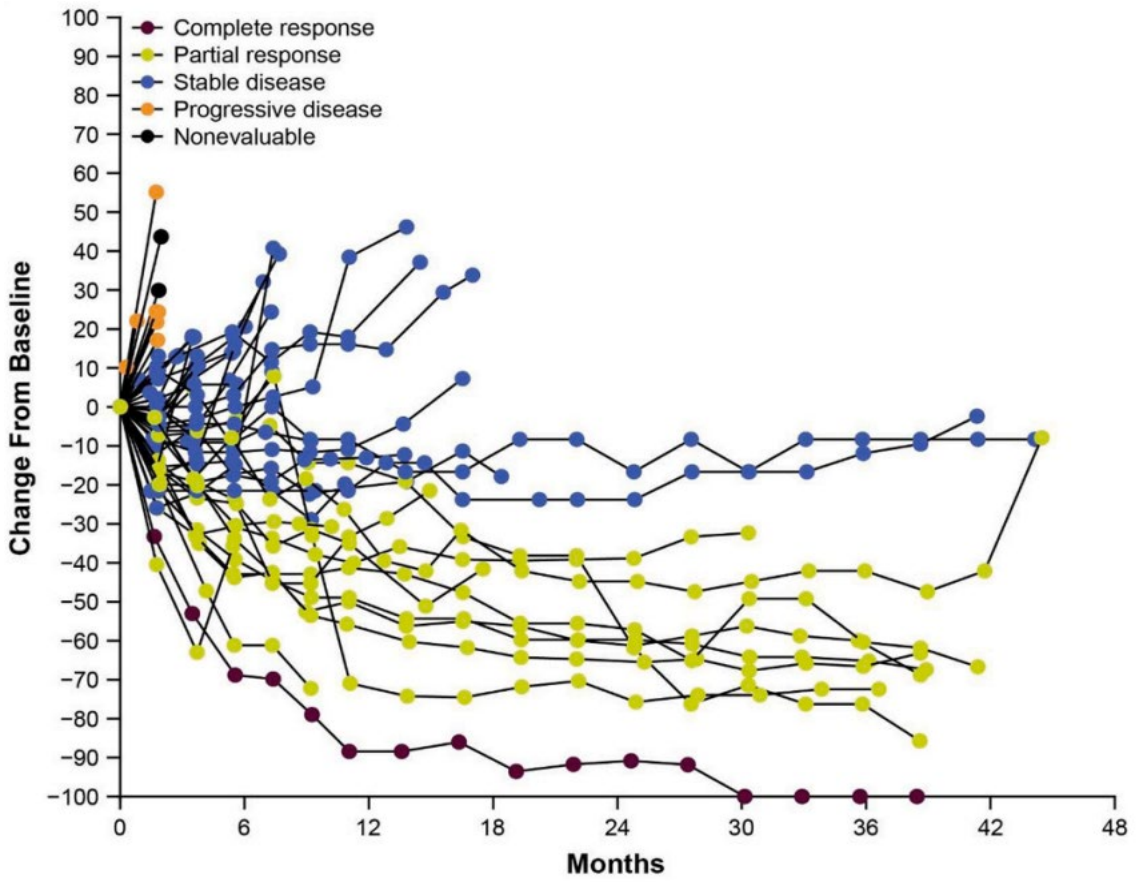
BID: twice daily; EPO: erythropoietin; PD: pharmacodynamics; PK: pharmacokinetics; QD: once daily; SD: standard deviation

HIF-2α Inhibition Kinetics Are "IO-Like", With Highly Durable, and "Later" Responses and Disease Control

LITESPARK-001

(Phase 1 for Belzutifan in Late-line ccRCC)

- 20%+ of patients have responses that extend beyond 2 years
- "IO-like kinetics": Reponses can take time to materialize and deepen over time
  - 60% of responses achieved by 6 months
  - 40% of responses achieved between months 6 and 18
- SD patients can have durable disease control



ccRCC: clear cell renal cell carcinoma; IO: immuno-oncology; SD: stable disease

Patient Case Study #2

PATIENT DETAILS: 59 Year-old Male

DIAGNOSIS (JAN 2022): Stage IV metastatic ccRCC, IMDC Risk: Intermediate

PRIOR TREATMENT:

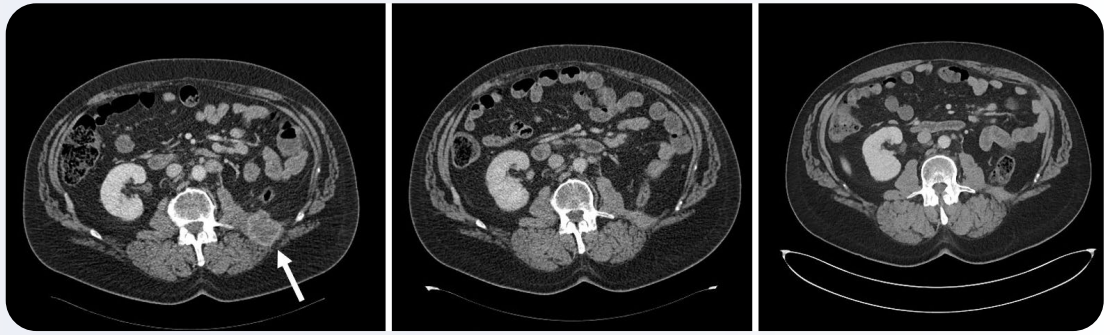
He was treated with nivolumab + ipilimumab between Feb 2022 and April 2023. The best overall response on treatment was a partial response.

Progression occurred in April 2023, after which the patient started treatment with cabozantinib + nivolumab between August 2023 and April 2024. The best overall response on treatment was stable disease.

ARC-20 STUDY DETAILS:

- The patient enrolled in a 150mg QD cohort and was first dosed on 23 May 2024.
  - Target lesions were recorded in the lung, peritoneum and a para-aortic lymph node.
- A partial response was noted on 27 June 2024, on the patient's first post-baseline scan.
  - Tumor assessments continue to demonstrate a partial response
- The patient has tolerated the regimen with no serious adverse events and no grade 3 or higher adverse events.
  - Patient has experienced grade 2 anemia, which is ongoing, and the most recent hemoglobin value is 9.8 g/dL. The patient received ESA in July and August 2024, but no blood transfusions.

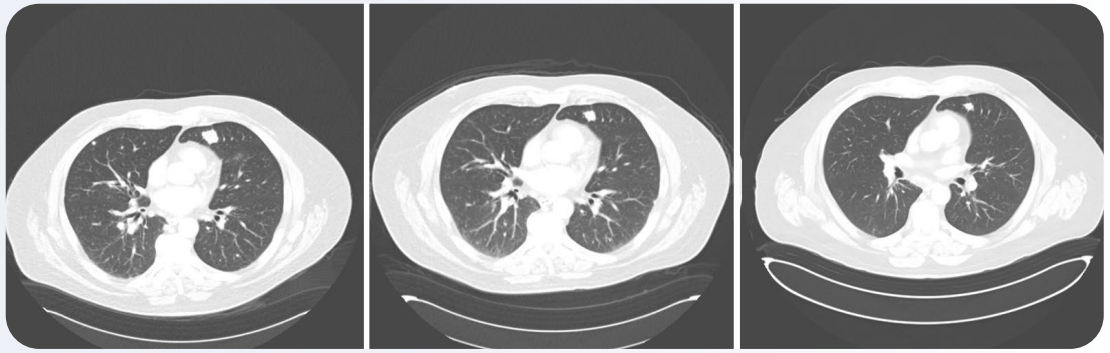
TARGET LESION: LYMPH NODE



BASELINE: 5/06/24 **6/27/24** **8/08/24**

Lymph node initially measured 22 mm, then decreased to 13mm.

TARGET LESION: LUNG



BASELINE: 5/06/24 **6/27/24** **8/08/24**

Lung nodule initially measured 16mm, then decreased to 9mm.

ccRCC: clear cell renal cell carcinoma; ESA: Erythropoietin Stimulating Agent; g/dL: grams per deciliter; IMDC: International Metastatic RCC Database Consortium; mg: milligram; mm: millimeter; QD: once daily

Patient Case Study #3

PATIENT DETAILS: 48 Year-old Male

DIAGNOSIS (2016): Stage Ib ccRCC, presented with metastatic disease (lung) in Jan 2019

PRIOR TREATMENT:

- Between June 2019 and Feb 2023, the patient was treated with atezolizumab + cabozantinib (in a clinical trial) with a best overall response of partial response.
  - Tumor assessments demonstrated progression in Feb 2023.
- The patient was then treated with lenvatinib + everolimus between March 2023 and September 2023.
  - Tumor assessments demonstrated a best overall response of partial response with progression noted in September 2023.

ARC-20 STUDY DETAILS:

- The patient enrolled in the 100mg Daily cohort and was first dosed on 29 September 2023.
  - Target lesions were present in the lung and in a mediastinal lymph node. One additional non-target lesion was present as a mediastinal lymph node.
- Tumor assessments demonstrated a partial response on the first baseline scan on 7 November 2023. Of note, there was a complete response in the non-target lesion.
  - Tumor assessments continue to demonstrate a partial response through 27 August 2024.
- The patient has tolerated the regimen with no serious adverse events and no grade 3 or higher adverse events.
  - The patient has ongoing grade 2 anemia, with the most recent hemoglobin 9.3 g/dL. The patient has not received any ESAs or blood transfusions on trial.

ccRCC: clear cell renal cell carcinoma; ESA: Erythropoietin Stimulating Agent; g/dL: grams per deciliter; IMDC: International Metastatic RCC Database Consortium; mg: milligram

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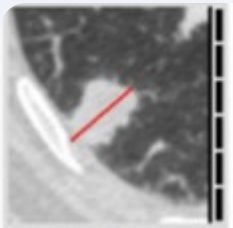
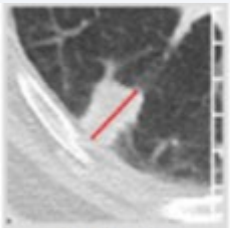
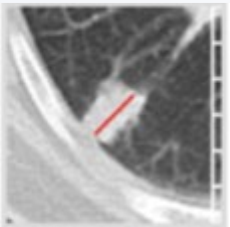
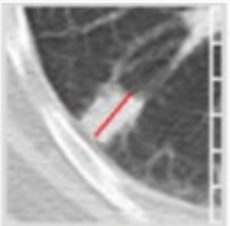
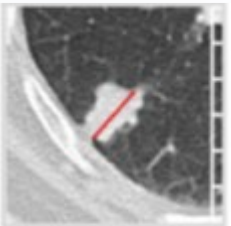
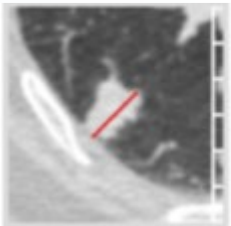
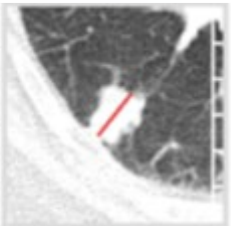
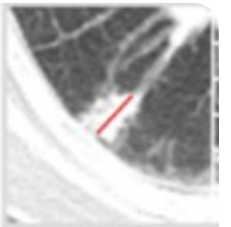
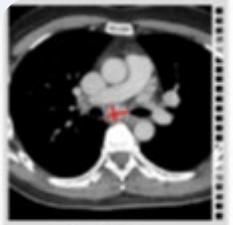
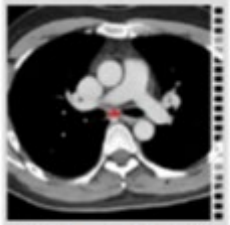
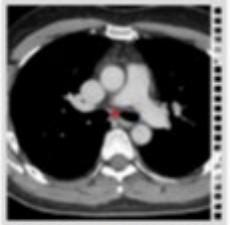
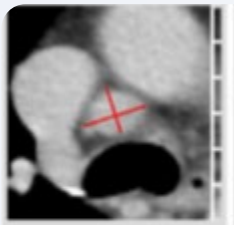
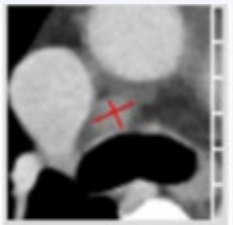
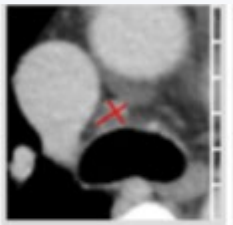
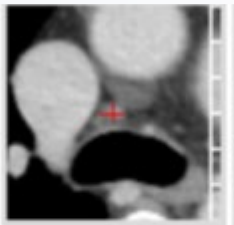
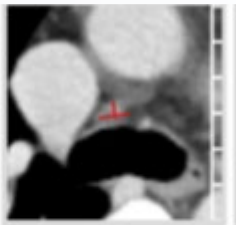
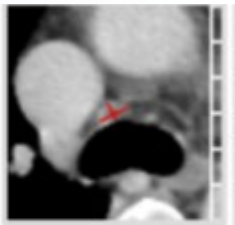
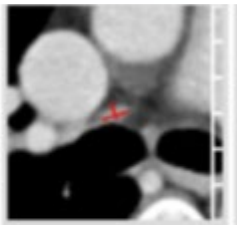
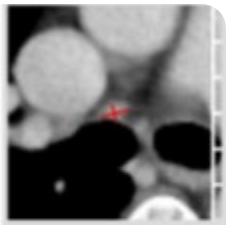
Patient Case Study #3 (continued)

LESION SNAPSHOTS

	BASELINE: (09/12/2023 (CT))	FOLLOW-UP 1: (11/07/2023 (CT))	FOLLOW-UP 2: (12/19/2023 (CT))	FOLLOW-UP 3: (01/30/2024 (CT))	FOLLOW-UP 4: (03/12/2024 (CT))	FOLLOW-UP 5: (04/23/2024 (CT))	FOLLOW-UP 6: (06/04/2024 (CT))	FOLLOW-UP 7: (07/12/2024 (CT))
TARGET LESIONS								
T01 Lung lower lobe right								
size	LA: 22.4 mm CT: SE 7 / IN 301 / TP -257.5	LA: 18.2 mm (-18.8% ΔP) CT: SE 15 / IN 64 / TP 108.5	LA: 15.4 mm (-15.4% ΔP) CT: SE 7 / IN 41 / TP -245	LA: 15.3 mm (-0.6% ΔP) CT: SE 7 / IN 41 / TP -243	LA: 17.5 mm (+14.4% ΔP) CT: SE 5 / IN 63 / TP 216	LA: 17.5 mm (0.0% ΔP) CT: SE 7 / IN 314 / TP -256.125	LA: 14.7 mm (-16.0% ΔP) CT: SE 9 / IN 66 / TP 69.6	LA: 14.1 mm (-4.1% ΔP) CT: SE 7 / IN 42 / TP -223.5
T02 Lymph node mediastinal								
size	SA: 16.3 mm CT: SE 3 / IN 52 / TP -197.5	SA: 7.5 mm (-54.0% ΔP) CT: SE 6 / IN 42 / TP 42.8	SA: 5.0 mm (-33.3% ΔP) CT: SE 3 / IN 51 / TP -170	SA: 0.0 mm (-100.0% ΔP) Disappeared	SA: 0.0 mm (-- ΔP) Disappeared	SA: 0.0 mm (-- ΔP) Disappeared	SA: 0.0 mm (-- ΔP) Disappeared	SA: 0.0 mm (-- ΔP) Disappeared
NON-TARGET LESIONS								
NT01 Lymph node mediastinal								
size	SA: 13.2 mm CT: SE 3 / IN 42 / TP -172.5 Present	SA: 8.4 mm (-36.4% ΔP) CT: SE 6 / IN 37 / TP 27.8 Disappeared	SA: 7.4 mm (-11.9% ΔP) CT: SE 3 / IN 45 / TP -155 Disappeared	SA: 4.7 mm (-36.5% ΔP) CT: SE 3 / IN 47 / TP -158 Disappeared	SA: 4.4 mm (-6.4% ΔP) CT: SE 4 / IN 37 / TP 138 Disappeared	SA: 4.8 mm (+9.1% ΔP) CT: SE 3 / IN 45 / TP -170.5 Disappeared	SA: 5.0 mm (+4.2% ΔP) CT: SE 5 / IN 40 / TP -8.4 Disappeared	SA: 4.7 mm (-6.0% ΔP) CT: SE 3 / IN 51 / TP -143.5 Disappeared

Clinical Collaboration with AstraZeneca

Potential Best-in-Class, First-in-Class Combination

- Combining cas with volrustomig, an anti-PD-1 / anti-CTLA-4 bi-specific antibody
- Anti-PD-1 + anti-CTLA-4 is a widely used standard of care in ccRCC
- Volru has demonstrated exciting preliminary data in 1L ccRCC (ESMO23)
- Opportunity to expand cas into IO-naïve ccRCC with a TKI-sparing
- Second clinical collaboration for Arcus with AstraZeneca

VOLRU PHASE 1 RESULTS IN CCRCC[1]

	V750 (N=32)		V500 (N=33)	
Response-evaluable, N	**31***		**33**	
Median follow-up, months (range)	22.7 (2.2-27.4)		14.9 (1.6-21.7)	
ORR, n (%)	15 (48.4)		15 (45.5)	
CR, n (%)	3 (9.7)		2 (6.1)	
PD, n (%)	3 (9.7)		8 (24.2)	
Disease control rate, n (%)	28 (90.3)		23 (69.7)	
Median duration of response, months (95% CI)[†]	17.0 (9.8-NE)		11.5 (5.8-NE)	
IMDC risk group	**I/P**	**F**	**I/P**	**F**
ORR, n/N (%)	13/23 (56.5)	2/8 (25.0)	8/21 (38.1)	7/12 (58.3)
Median duration of response, months (95% CI)	15.4 (8.4-NE)	NR (NE-NE)	8.4 (2.9-NE)	NR (2.8-NE)

*One ineligible subject is excluded.

[†]Median DOR in subjects who discontinued due to AE: NR at both doses

1L, first-line; CI, confidence interval; CR, complete response; F, favorable; I/P, intermediate/poor; IMDC, International Metastatic RCC Database Consortium; NE, not estimable; NR, not reached; ORR, objective response rate; PD, progressive disease; TTR, time to response; V500/750, volrustomig 500/750mg

Source: 1. Voss et al 2023

1L: first-line; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; CTLA-4 ORR: objective response rate; PD-1: programmed cell death 1; TKI: tyrosine kinase inhibitors; volru: volrustomig

Combination Therapy Benchmarks in 1L ccRCC

REGIMEN	PATIENT DETAILS	APPROVAL	ORR (CR)	mPFS	mOS	SAFETY OF INTEREST (G3/4)
nivolumab + ipilimumab[1,2,a]	1L intermediate-/ poor-risk	U.S. (Apr. 2018) E.U. (Jan. 2019)	42% (9%)	**11.6m**	**47.0m**	Lipase incr. 10% Diarrhea 4% Fatigue 4%
pembrolizumab + axitinib[3,b]	1L	U.S. (Apr. 2019) E.U. (Sep. 2019)	61% (12%)	**15.7m**	**47.2m**	Hypertension 22% PPES 5% ALT incr. 13%
avelumab + axitinib[4,c]	1L	U.S. (May 2019) E.U. (Oct. 2019) Jp (Mar. 2020)	51% (3%)	**13.8m**	**NYR**	Hypertension 24% PPES 6% ALT incr. 5%
nivolumab + cabozantinib[5,d]	1L	U.S. (Jan. 2021) E.U. (Mar. 2021) Jp (Aug. 2021)	56% (12%)	**16.6m**	**49.5m**	Hypertension 13% PPES 8% Diarrhea 7%
pembrolizumab + lenvatinib[6,7,e]	1L	U.S. (Aug. 2021) E.U. (Nov. 2021) Jp (Feb. 2022)	71% (18%)	**23.9m**	**53.7m**	Hypertension 25% PPES 4% AST incr. 3%
bevacizumab + IFN-α[8,f]	1L	U.S. (Aug. 2009) E.U. (Dec. 2007)	31% (NR)	**10.4m**	**23.3m**	Hypertension 6% Bleeding 3% Protein in urine 7%
toripalimab + axitinib[g]	1L intermediate-/ high-risk	China (Apr. 2024)	57% (5%)	**18.0m**	**NYR**	Hypertension 15% AST incr. 6% ALT incr. 7%

1L: first-line; ccRCC: clear cell renal cell carcinoma; CR: complete response; Jp: Japan; mOS: median overall survival; mPFS: median progression-free survival; NR: no response; ORR: objective response rate
a. Phase III CheckMate 214; favorable-risk favored sunitinib. b. Phase III KEYNOTE-426; Q6W pembro dosing approved for mono/combo indications (US 4/2020, Japan 8/2020). c. Phase III JAVELIN Renal 101. d. Phase III CheckMate 9ER. e. Phase III CLEAR. f. Phase III AVOREN; removed from NCCN guidelines 6/2019 (v1.2019). g. Phase III RENOTORCH; first immunotherapy approved for RCC in China.

1. Motzer et al. NEJM. 2018;378:1277-1290. 2. ESMO 2021 (abs. 661P). 3. ASCO 2023 (abs. LBA4501). 4. Motzer et al. NEJM. 2019; 380(12):1103-1115. 5. ASCO GU 2023 (abs. 603). 6. Motzer et al. NEJM. 2021;384:1289-1300. 7. ASCO 2023 (abs. 4502). 8. Escudier et al. JCO. 2010;28(13).

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RCC Is Now a $5B+ Market for TKIs Alone, Even With Generic TKI Entrants

TKI	GLOBAL 2023 SALES ($M)[1]	REGIMEN	PATIENT POPULATION	APPROVAL
cabozantinib	**$2,254**	monotherapy	1L intermediate-/poor-risk	U.S. (Dec. 2017) E.U. (May 2018) Jp (Mar. 2020)
		nivolumab + cabozantinib	1L	U.S. (Jan. 2021) E.U. (Mar. 2021) Jp (Aug. 2021)
lenvatinib	**$2,199**	pembrolizumab + lenvatinib	1L	U.S. (Aug. 2021) E.U. (Nov. 2021) Jp (Feb. 2022)
axitinib	**$1,036**	pembrolizumab + axitinib	1L	U.S. (Apr. 2019) E.U. (Sep. 2019)
		avelumab + axitinib	1L	U.S. (May 2019) E.U. (Oct. 2019) Jp (Mar. 2020)
sunitinib	**$180**	monotherapy	1L	U.S. (Feb. 2007) E.U. (Jan. 2007)
pazopanib	**$390**	monotherapy	1L/2L	U.S. (Oct. 2009) E.U. (Jun. 2010)
tivozanib	**~$105[2]**	monotherapy	1L/2L	E.U. (Aug. 2017)

1. $M USD, Globaldata 2. 2022, Aveo guidance per Fierce Pharma, https://www.fiercepharma.com/pharma/lg-chem-picks-aveo-and-kidney-cancer-drug-fotivda-566m
1L: first-line; 2L: second-line; E.U.: European Union; Jp: Japan; TKI: tyrosine kinase inhibitor; U.S.: United States