COMBINING TO CURE®

Arcus is at the forefront of designing combination therapies, with best-in-class potential, in the relentless pursuit of cures for cancer.

CORPORATE PRESENTATION

Nov. 6, 2024

ARCUS BIOSCIENCES

Forward-looking Statements/Safe Harbor

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 regarding events or results to occur in the future contained in this presentation are forward-looking statements, including statements about: our strategy, advantages, and expectations, including regarding our productivity and competitiveness; expectation that our cash and investments are sufficient to fund operations into 2027; potential of our investigational products and portfolio, including our investigational products potential to be best or first in class; anticipated benefits of our collaborations with Gilead, Taiho and AstraZeneca; the ability of unconfirmed responses to become confirmed responses; achievement and expected timing of clinical and developmental milestones, including the initiation of clinical trials and the timing of completion of enrollment, availability or presentation of clinical data and launch of our investigational products; and possible first to market advantage for any of our investigational products.

These forward-looking statements are subject to a number of risks, uncertainties and assumptions that may cause actual results to differ materially from those contained in any forward-looking statements we may make, including, but not limited to: risks associated with preliminary or interim clinical data or preclinical data not being guarantees that future data will be similar; the unexpected emergence of adverse events or other undesirable side effects; difficulties or delays in initiating, conducting or completing our clinical trials due to difficulties or delays in the regulatory process, enrolling subjects or manufacturing or supplying product for such clinical trials, all of which may be exacerbated by unfavorable global economic, political and trade conditions; risks associated with our collaboration arrangement with Gilead including our dependence on Gilead for the successful development and commercialization of our investigational products; changes in the competitive landscape; our limited operating history and our ability to manage our growth; 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 and adversely 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 are described in our most recent periodic reports filed with the U.S. Securities and Exchange Commission filed with the U.S. Securities and Exchange Commission. 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 and completeness of the forward-looking statements. We undertake no obligation to update publicly 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 are investigational and Arcus (and Gilead for all of the molecules in each optioned program) has not received approval from any regulatory authority for any use globally, nor established the safety and efficacy of these investigational molecules.

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Arcus Has Created a Late-stage Portfolio of Differentiated Assets, Fueled by a Highly Productive R&D Engine

FUNDING INTO MID-2027

~$1.1B in cash, cash equivalents & marketable securities**

POTENTIAL BEST-IN-CLASS HIF-2a INHIBITOR, CASDATIFAN

Commercially validated mechanism

First Phase 3 initiation 1H25

PEAK-1

PHASE 3 STUDIES FOR DOM IN LUNG & UPPER GI PROGRESSING TO DATA

STAR-121 — Ongoing

STAR-221 — ✓ Fully enrolled

PACIFIC-8

MULTIPLE UPCOMING DATASETS

Casdatifan (HIF-2a)

- ✓ **2H24** ARC-20: ORR and safety
- **1Q25:** ARC-20: Mature ORR and PFS
- **2H25:** ARC-20: Safety data for cas + cabo; ORR from other cohorts

Domvanalimab* (TIGIT)

- ✓ **2H24** ARC 10: OS & PFS data from Part 1

TOP TIER PARTNERS

Provides funding and resources enabling a diversified pipeline

GILEAD

AstraZeneca

TAIHO PHARMA

WORLD CLASS DRUG DISCOVERY

1-2 new development candidates a year

AB801

Phase 1/1b dose escalation ongoing for potential best-in-class small molecule AXL inhibitor

2L: second-line; B: billion; ccRCC: clear cell renal cell carcinoma; GI: gastrointestinal; mg: milligram; OS: overall survival; PFS: progression-free survival; R&D: research and development; YE: year end

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*includes combination with zimberelimab (anti-PD1)

** as of September 30, 2024

ARCUS BIOSCIENCES

New Disclosures in Third Quarter 2024 Earnings

Casdatifan
(HIF-2a)

- ARC-20 results for the 50mg BID and 50mg QD were presented at EORTC-NCI-AACR; The 50mg BID cohort showed best-in-class potential:
  - **25% cORR (8/32) / 34% ORR (11/32)**
    - **2 PRs remain on treatment with the potential to confirm**
    - 1 PR will not confirm
    - 16% SDs remain on treatment – potential to increase the ORR over time
  - **19% primary progressive disease rate / 81% disease control rate**
  - **Median PFS had not been reached at the time of the data cutoff**
- Announced a clinical collaboration with AstraZeneca to evaluate cas + volrustomig (investigational PD-1/CTLA-4 bispecific) in IO-naïve ccRCC

Dom (+ Zim)
(Fc-silent anti-TIGIT + anti-PD-1)

- Results from ARC-10[2] for dom + zim vs. zim vs. chemo in PD-L1 high NSCLC to be presented at SITC:
  - Dom + zim demonstrated higher PFS, OS and ORR vs zim alone
  - **OS HR=0.64 for dom + zim vs zim**
  - **Zim reached a median OS of two years** in line with anti-PD-1 monotherapy in benchmark studies; the median OS for dom + zim was not reached
  - Treatment-related adverse events leading to treatment discontinuation were low (10.5%) for dom + zim

cabo: cabozantinib; cas: casdatifan, ccRCC: clear cell renal cell carcinoma; dom: domvanalimab; etruma: etrumadenant; GI: gastrointestinal; mg: milligram; NSCLC: non-small cell lung cancer; OS: overall survival; PFS: progression-free survival; quemli: quemliclustat; R&D: research and development; YE: year end; zim: zimberelimab

1. ARC-20 – Choueiri et al. ENA 2024, Oct. 24, 2024, data cut off of August 30, 2024
2. ARC-10 – Johnson et al. SITC 2024, Nov. 5 2024, data cut off of May 17, 2024

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ARC-20 Results Support Casdatifan's Potential Best-in-Class Profile, Despite Shorter 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[1]	**27%**	**11**	**18.8%**	**34.4%*** **25.0%**	**Not reached**	**81.3%**	**7.7%**	**36%**
LITESPARK-005[2] Belz (Phase 3)	**0%**	**18**	**33.7%**	**21.9%**	**5.6**	**61.2%**	**11.2%[3]**	**33%[3]**

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.ARC-20 – Choueiri et al. ENA 2024, Oct. 24, 2024, data cut off of August 30, 2024
2.Efficacy data for belzutifan from IA1 of LITESPARK-005. Source: Albiges L. et al. Abstract LBA88, ESMO 2023
3.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

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

EXPECTED TIMING	ARC-20 COHORT(S)	OUTCOME MEASURES
1Q 2025	50mg BID (100mg) and 50mg QD	More mature ORR & PFS
2H 2025	50mg BID (100mg) and 50mg QD	ORR & PFS for all monotherapy cohorts
	150mg and 100mg QD (tablet)	
	cas + cabo	Safety
Late 2025 / Early 2026	cas + cabo	ORR

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

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Targeting Huge Market Opportunities and Unmet Need

	PHASE 1/2 STUDIES	PHASE 3 STUDY	INDICATION	PH 3 STUDY DETAILS	ADDRESSABLE PATIENTS[1]	MARKET POTENTIAL[2]
DOM + ZIM Fc-silent anti-TIGIT MAb + anti-PD-1 MAb	EDGE-Gastric mPFS presented at ASCO '24	STAR-221 Fully Enrolled 2Q24	**1L Gastric/GEJ/EAC - all comers**	dom + zim + chemo vs nivo + chemo	**103K**	**~$3B**
	ARC-10 OS and PFS presented at SITC '24	STAR-121 Recruiting	**1L NSCLC – all comers**	dom + zim + chemo vs pembro + chemo	**303K**	**~$10B**
	EDGE-Lung Enrolling dose-optimization cohorts	PACIFIC-8 Recruiting	**Stage 3 NSCLC**	dom + durva vs durva + placebo	**48K**	**~$2B**
CAS HIF-2a small molecule inhibitor	ARC-20 100 mg expansion cohort presented at ENA '24	PEAK-1 Initiating 1H25	**Post-IO ccRCC**	cas + cabo vs cabo	**19K**	**~$2B+**
QUEMLI Small molecule CD73 inhibitor	ARC-8 OS data presented at ASCO GI '24	PRISM-1 Initiated 4Q24	**1L PDAC**	quemli + G/nP vs G/nP	**106K**	**~$4B**
ETRUMA Small molecule A2a & A2b receptor antagonist	ARC-9 OS data (3L cohort) presented at ASCO '24	**Next steps in planning**	**CRC**	Next steps to be determined	**82K**	**~$2B**

1. Drug Treatable Addressable Populations (G7, 2024); Decision Resources Group, Arcus analysis
2. G7 Markets (US, EU5, JP) - total projected 2034 PD-(L)1 + TIGIT opportunity, Q opportunity & Hif2α opportunity

1L: first line; 2L: second line; 3L: third line; B: billion; cabo: cabozantinib; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; chemo: chemotherapy; CRC: colorectal cancer; dom: domvanalimab; durva: durvalumab; EAC: esophageal adenocarcinoma; ENA: EORTC-NCI-AACR Symposium; etruma: etrumadenant; GEJ: gastroesophageal junction; GI: gastrointestinal; G/nP: gemcitabine/nab-paclitaxel; IO: immuno-oncology; mAb: monoclonal antibody; mPFS, progression-free survival; nivo: nivolumab; NSCLC: non-small cell lung cancer; OS: overall survival; PDAC: pancreatic ductal adenocarcinoma; PD: pharmacodynamic; pembro: pembrolizumab: Ph: phase; PK: pharmacokinetic; quemli: quemliclustat; zim: zimberelimab

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Our Partnerships Greatly Expand & Accelerate Our Opportunities

10-YEAR COLLABORATION

- Gilead has opted into 5 molecules to date -- shares costs for studies within the joint development plan
- Arcus retains U.S. co-commercialization rights

COLLABORATION FOR JAPAN AND OTHER TERRITORIES IN ASIA (EX-CHINA)

- Taiho has optioned dom, zim, etruma and, most recently, quemli
- Up to $275mm in development, regulatory and commercial milestones per program
- Tiered royalties from high-single digit to mid-teens on net sales

TWO CLINICAL COLLABORATIONS: DOMVANALIMAB AND CASDATIFAN

- PACIFIC-8, a Phase 3 registrational trial of dom plus durvalumab in unresectable Stage III NSCLC
- Phase 1/1b study of cas plus volrustomig, AstraZeneca's investigational PD-1/CTLA-4 bispecific antibody, in IO-naïve ccRCC
- Retained economics on respective molecules

ENABLES MULTIPLE "SHOTS ON GOAL" AND FUNDING INTO 2027

1L: first-line; 2L: second-line; b: billion; cas: casdatifan; dom: domvanalimab; etruma: etrumadenant; mm: million; NSCLC: non-small cell lung cancer; ccRCC: clear cell renal cell carcinoma; quemli: quemliclustat; zim: zimberelimab

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Casdatifan (HIF-2a) in ccRCC

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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. Comparative claims are not from head-to-head studies. Cross-trial comparisons should be considered with caution. Such comparisons are limited by differences in study population, sample size, inclusion and exclusion criteria and many other factors.

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

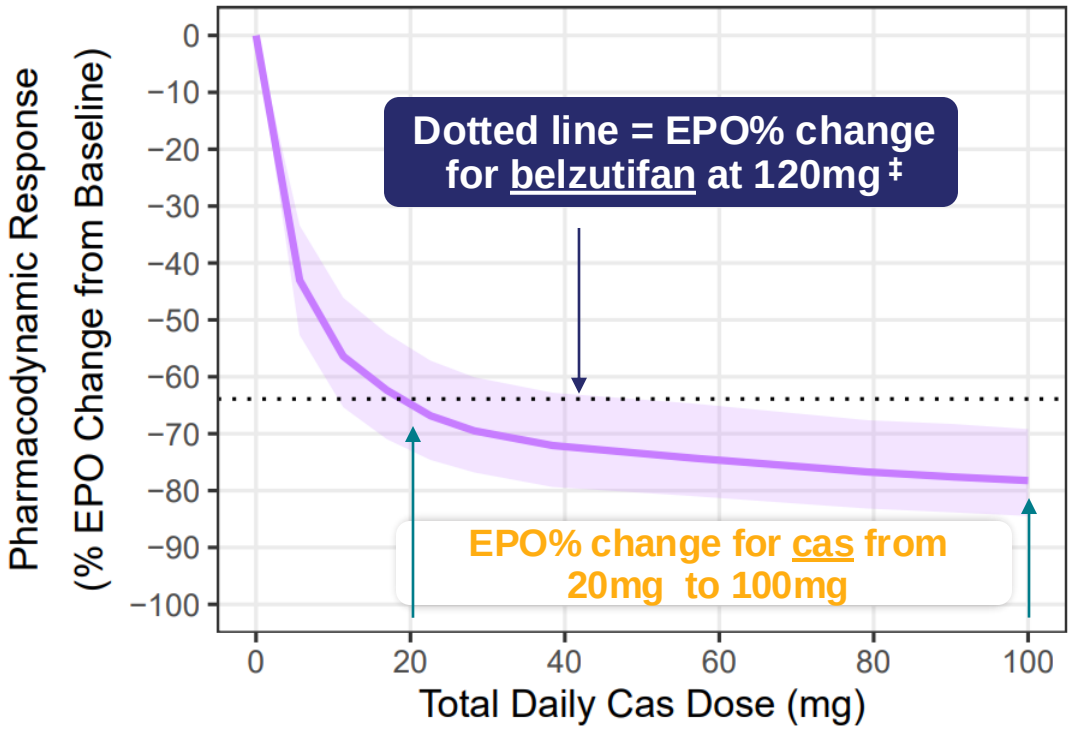
1L: first-line; AE: adverse event; BID: twice-daily; cabo: cabozantinib; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; cORR: confirmed objective response rate; CTLA-4: cytotoxic T-lymphocyte associated protein 4; IO: immuno-oncology; mg: milligram; ORR: objective response rate; PD: progressive 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

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Cas Has an Optimal PK / PD Profile

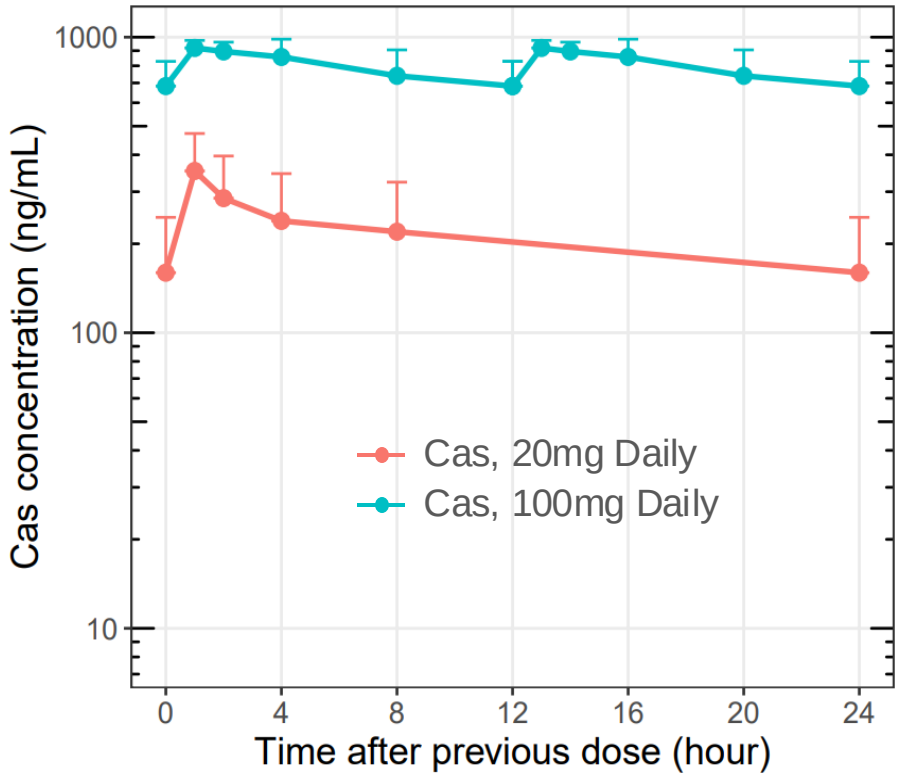
Pharmacodynamics

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



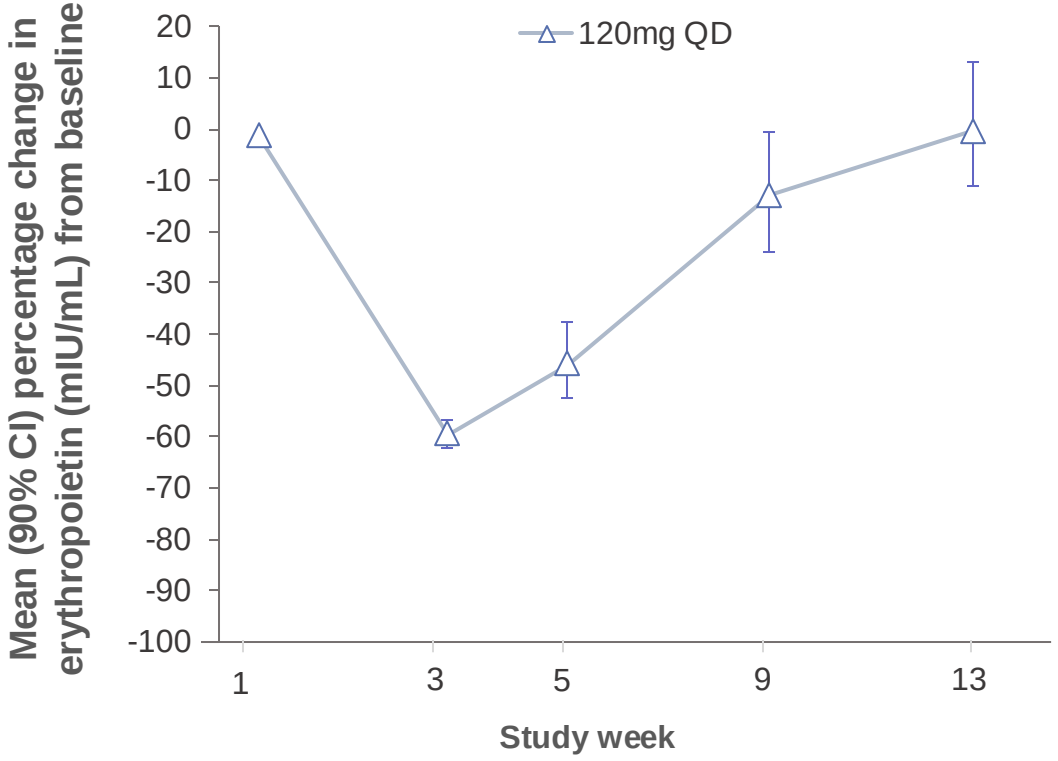
§ AB521: median (solid line) and inter-quartile range (shaded area) of population PK/PD simulations using model developed from data
‡ Source: belzutifan NDA - FDA review document. Comparison not based on head-to-head studies.
Casdatifan (AB521) is an investigational molecule and its safety and efficacy 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

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

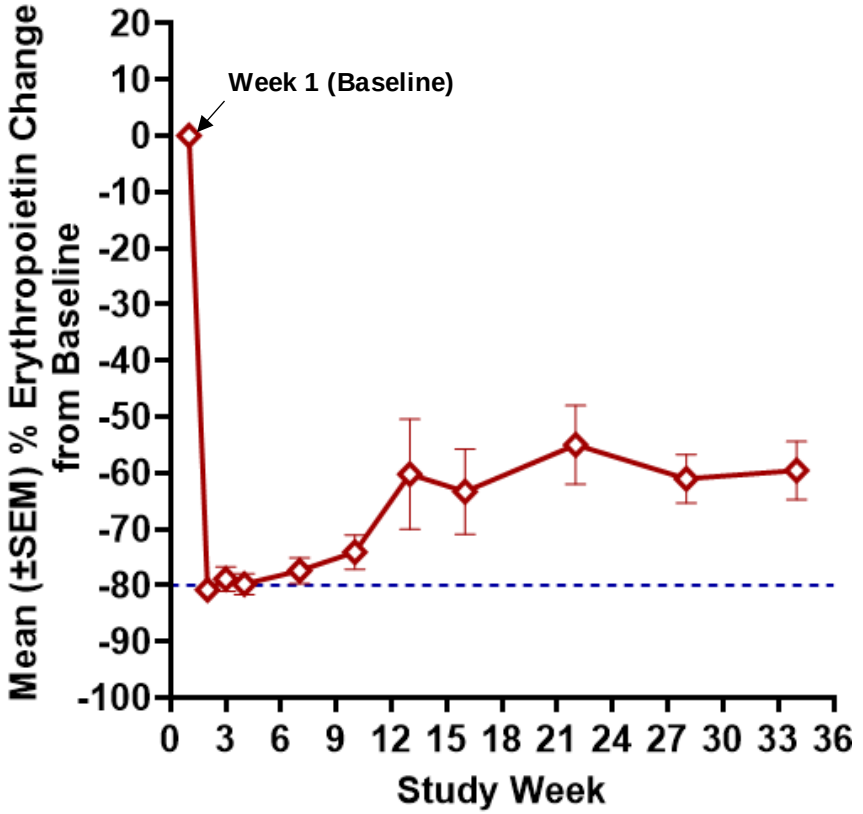
Belzutifan

Mean percentage change in erythropoietin from baseline over time



Casdatifan 100mg Daily

ccRCC patients in dose escalation + dose expansion



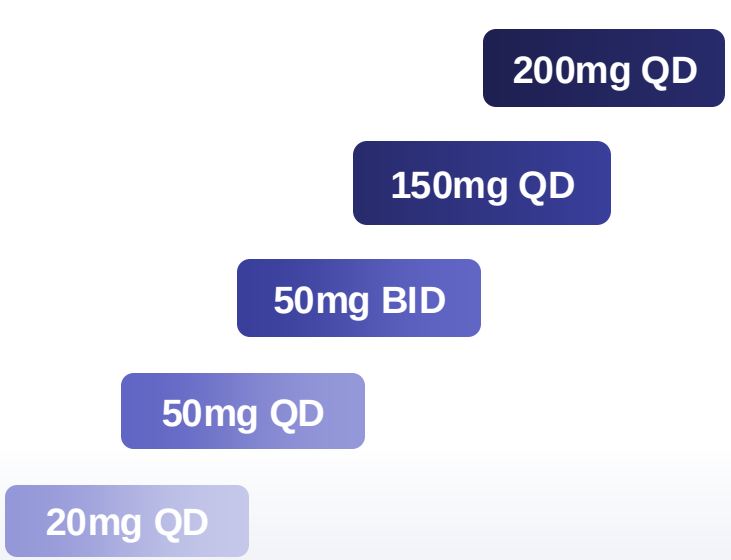
Source: Marathe DD, J Clin Pharm 2024, Fig S20
ccRCC: clear-cell renal cell carcinoma; EPO: erythropoietin; mIU/mL: milli-international units per milliliter; mg: milligram; QD: once-daily; SEM: standard error of the mean

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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:

- **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

ARC-20 – Choueiri et al. ENA 2024, Oct. 24, 2024, data cut off of August 30, 2024
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

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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)

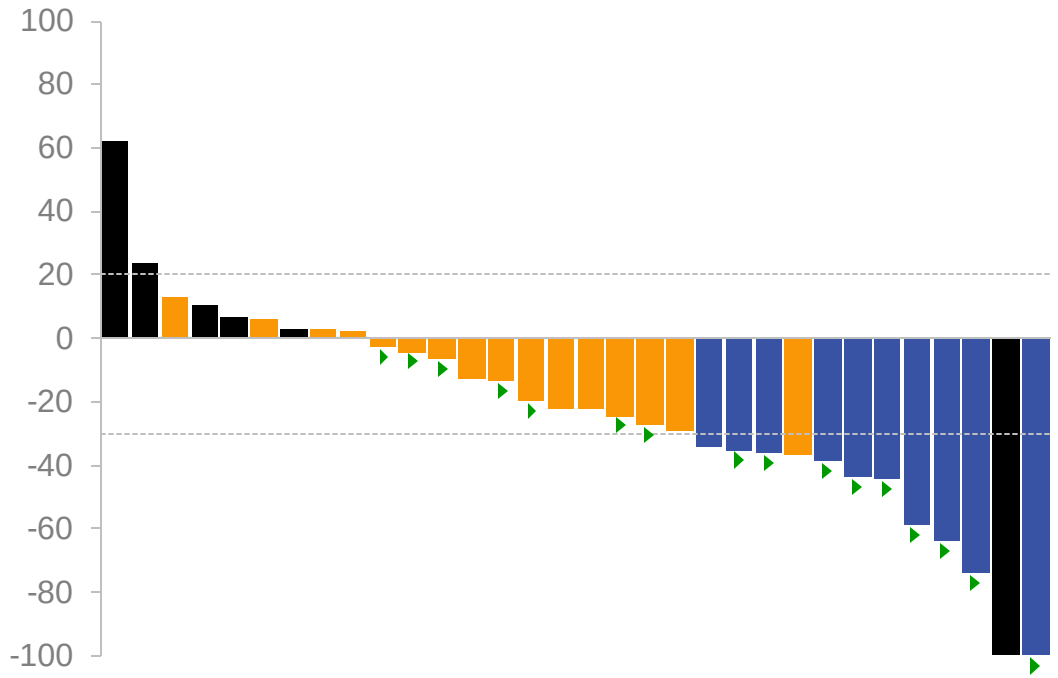
- **2 unconfirmed responders in the 100mg Daily and 1 in the 50 mg QD cohorts remain on study with the potential to achieve a confirmed response**
- Only 1 unconfirmed response (in the 100mg Daily cohort) does not have the potential to be confirmed

ARC-20 – Choueiri et al. ENA 2024, Oct. 24, 2024, data cut off of August 30, 2024
1. Across both cohorts, there were four ineligible patients, all of whom were on study for a short period of time. 3 patientsdeemed 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

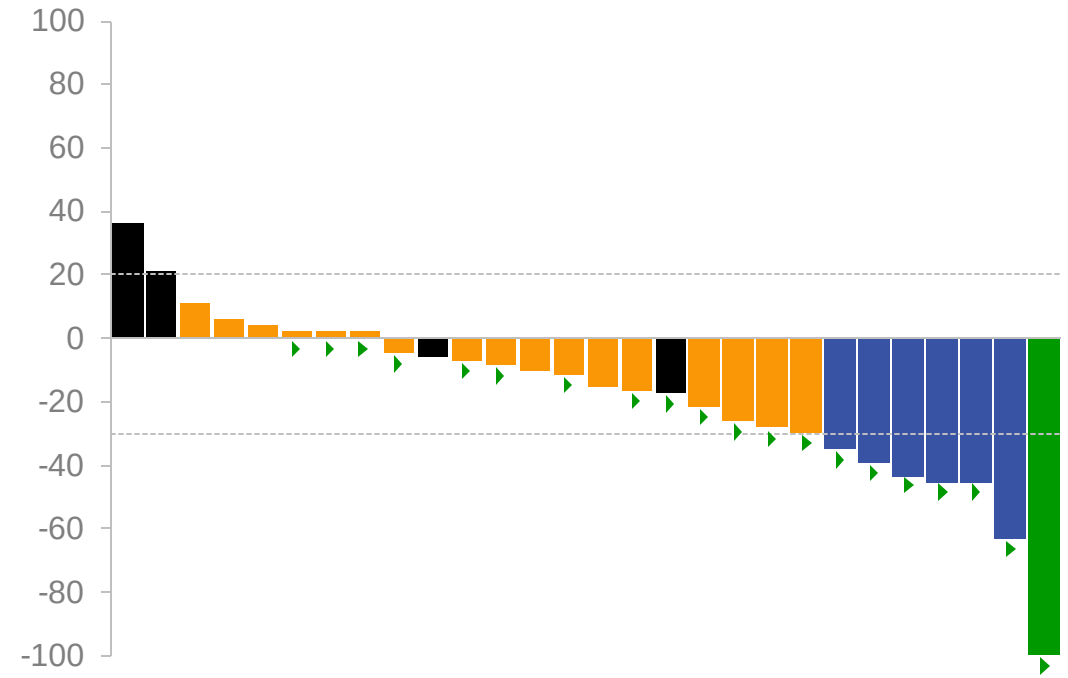
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Vast Majority of Patients Experienced Tumor Reduction in Both Cohorts

100mg Daily Cohort



50mg QD Cohort



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

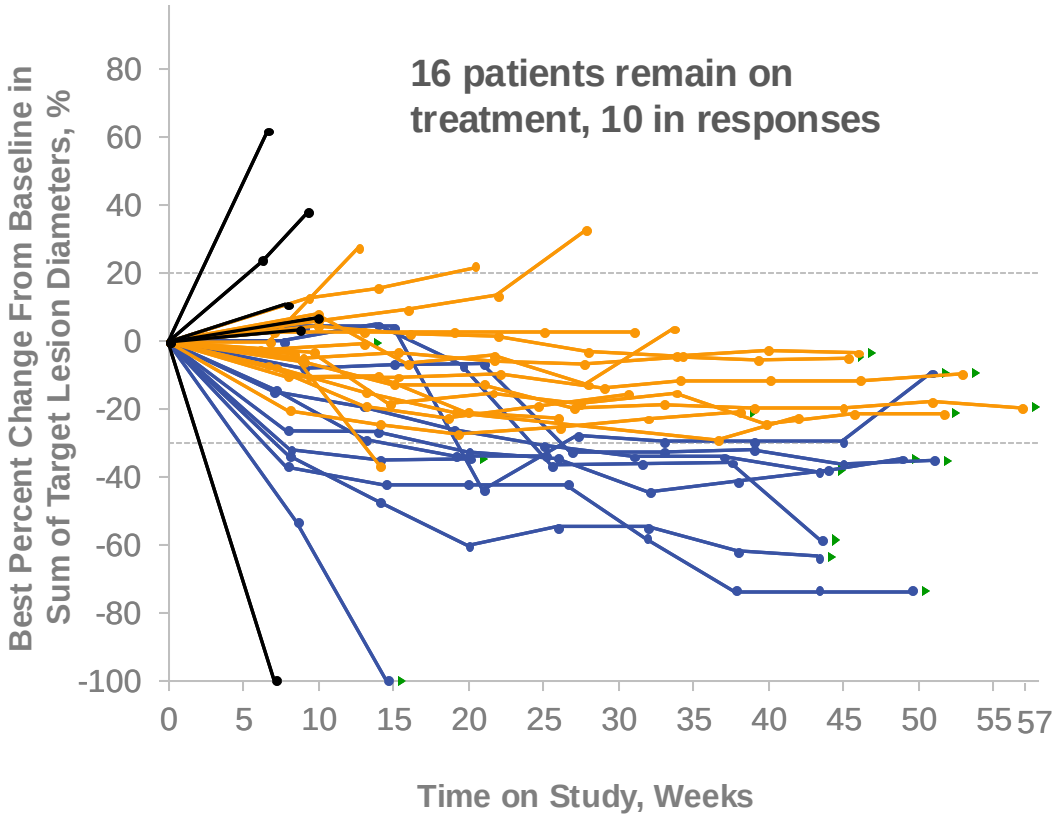
- **5 patients* in the 100mg Daily cohort and 11 patients** in the 50mg QD cohort with stable disease remain on treatment and could respond with longer follow-up**
- One patient in 100mg Daily cohort with best response of PD achieved 100% tumor reduction in their primary lesion
- Deep responses seen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

ARC-20 – Choueiri et al. ENA 2024, Oct. 24, 2024, data cut off of 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.
QD: once daily

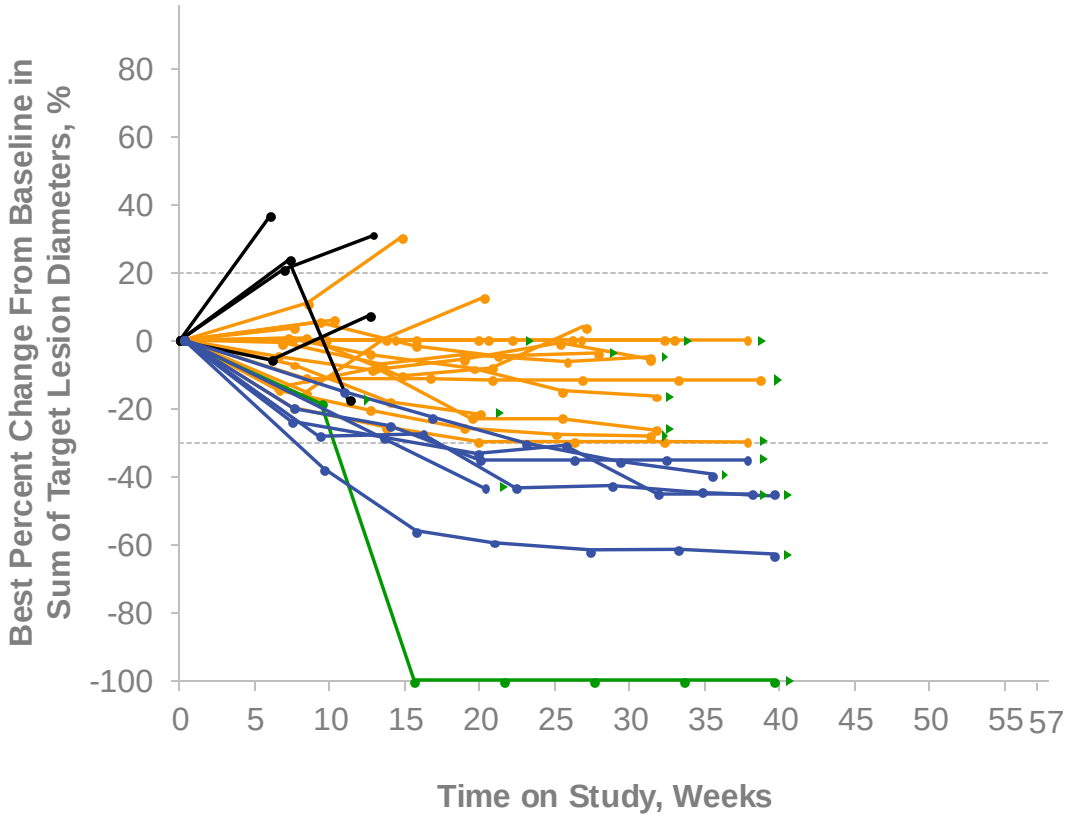
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Spider Plots Illustrate Durable Disease Control for Both Doses

100mg Daily Cohort



50mg QD Cohort



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

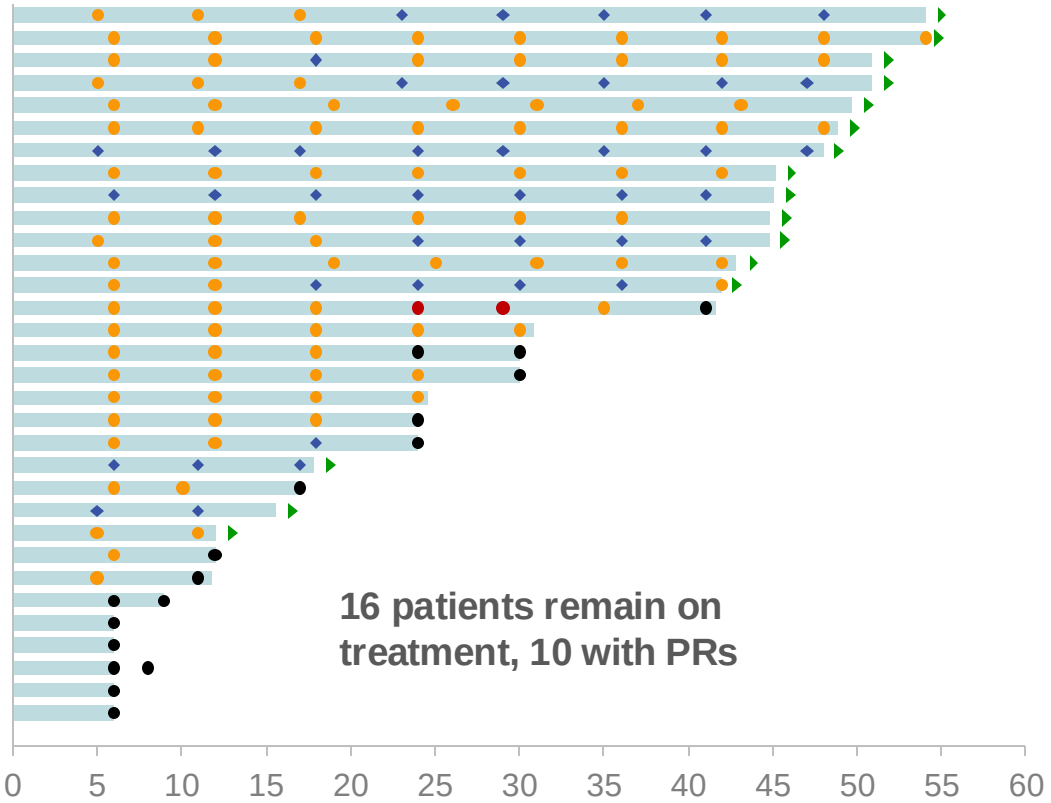
- **10 of 11 and 7 of 7 responders remain on study in the 100mg Daily and 50mg QD cohorts, respectively**

ARC-20 – Choueiri et al. ENA 2024, Oct. 24, 2024, data cut off of August 30, 2024
QD: once daily

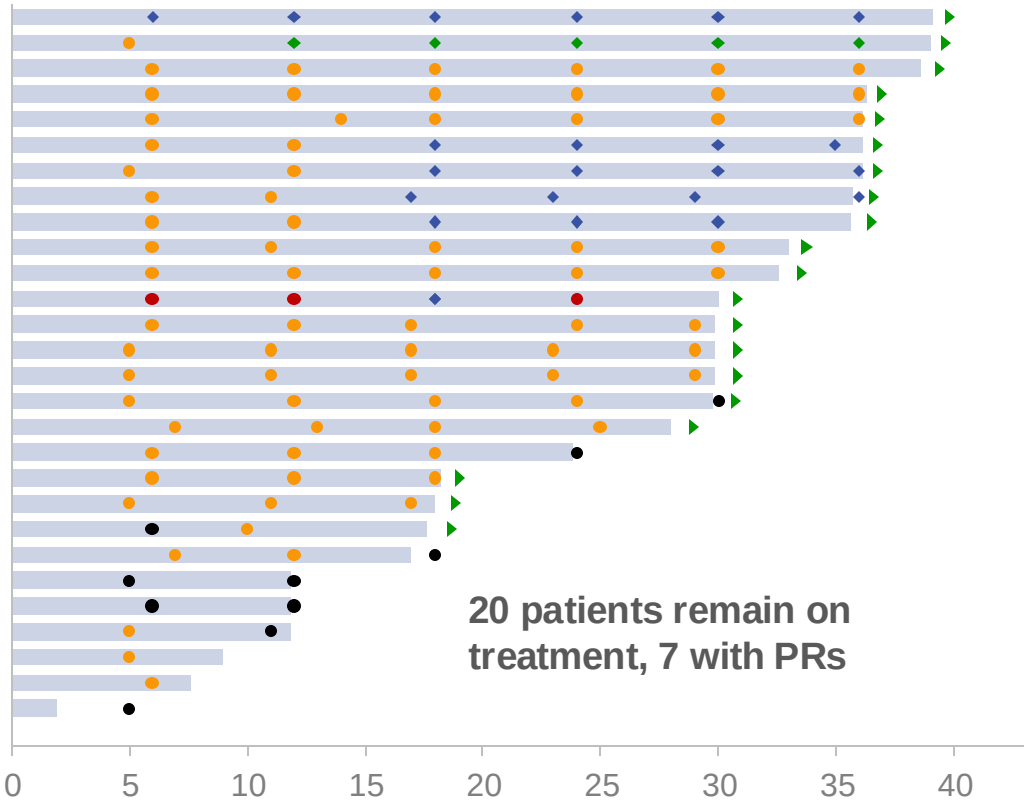
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Significant Portion of Patients Remain on Study for Both Cohorts

100mg Daily Cohort



50mg QD Cohort



Complete Response Partial Response Stable Disease Progressive Disease Ongoing Not Estimable

ARC-20 – Choueiri et al. ENA 2024, Oct. 24, 2024, data cut off of August 30, 2024
QD: once daily

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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.

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.

ARC-20 – Choueiri et al. ENA 2024, Oct. 24, 2024, data cut off of 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

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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[1]	**27%**	**11**	**18.8%**	**34.4%*** **25.0%**	**Not reached**	**81.3%**	**7.7%**	**36%**
LITESPARK-005[2] Belz (Phase 3)	**0%**	**18**	**33.7%**	**21.9%**	**5.6**	**61.2%**	**11.2%[3]**	**33%[3]**

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.ARC-20 – Choueiri et al. ENA 2024, Oct. 24, 2024, data cut off of August 30, 2024
2.Efficacy data for belzutifan from IA1 of LITESPARK-005. Source: Albiges L. et al. Abstract LBA88, ESMO 2023
3.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

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

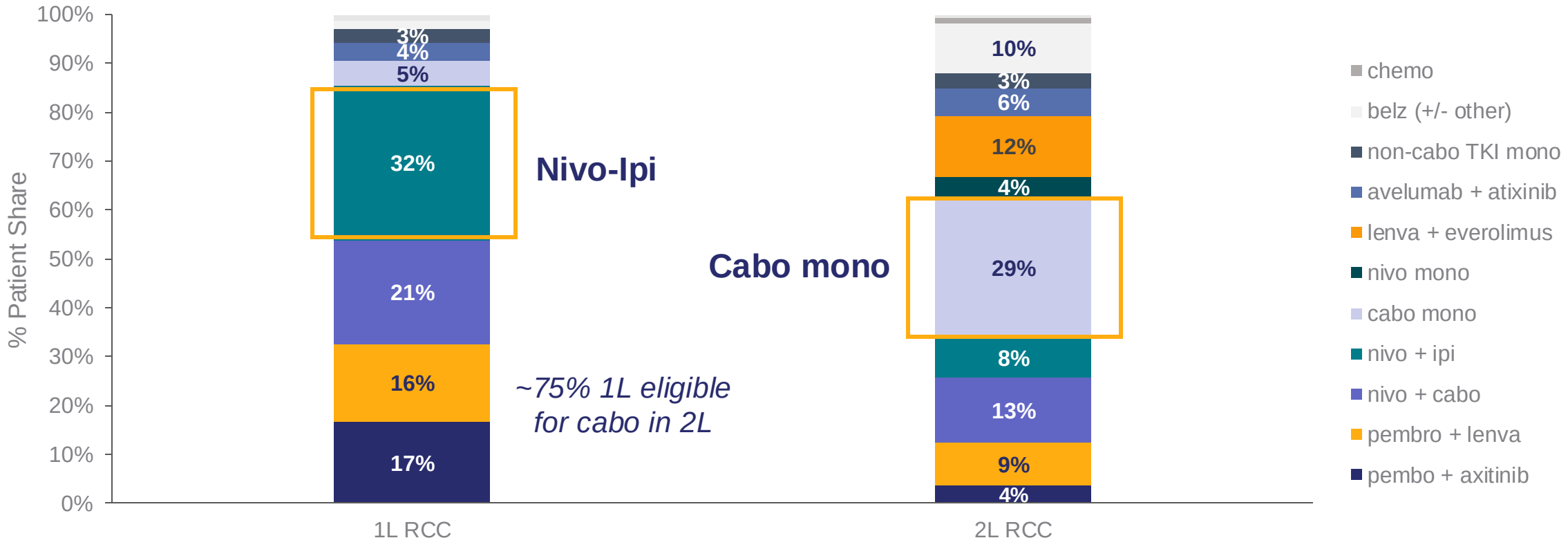
EXPECTED TIMING	ARC-20 COHORT(S)	OUTCOME MEASURES
1Q 2025	50mg BID (100mg) and 50mg QD	More mature ORR & PFS
2H 2025	50mg BID (100mg) and 50mg QD	ORR & PFS for all monotherapy cohorts
	150mg and 100mg QD (tablet)	
	cas + cabo	Safety
Late 2025 / Early 2026	cas + cabo	ORR

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

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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

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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

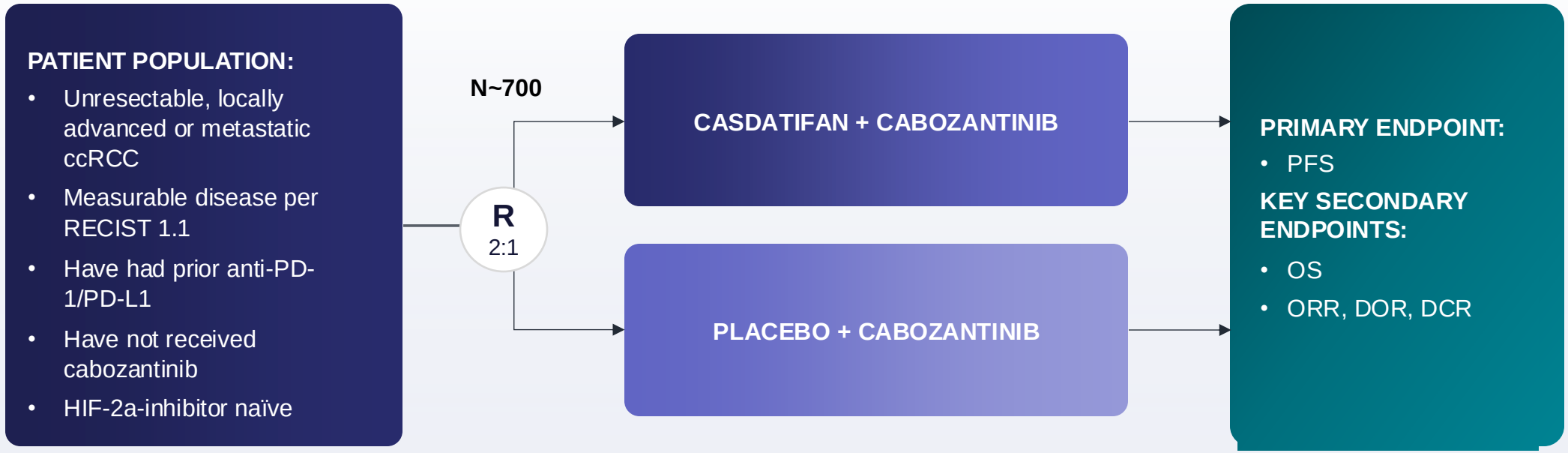
Expansion into new tumor types

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

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Proposed Phase 3 Study Evaluating Cas + Cabo in Advanced or Metastatic ccRCC, following prior PD-1 Tx



cabo: cabozantinib cas: casdatifan; ccRCC: clear-cell renal cell carcinoma; DCR: disease control rate; DOR: deration of response; IO: immuno-oncology; ORR: overall response rate; OS: overall survival; PFS: progression free survival; tx: treatment

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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	**11.3k patients**	**Arcus regimen builds on a preferred SOC (cabo) in the Post-IO setting** Potential DOT: 15+ months
		HIF-2α + TKI: belz + lenva		
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

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Domvanalimab in Non-Small Cell Lung Cancer and Upper GI Cancers

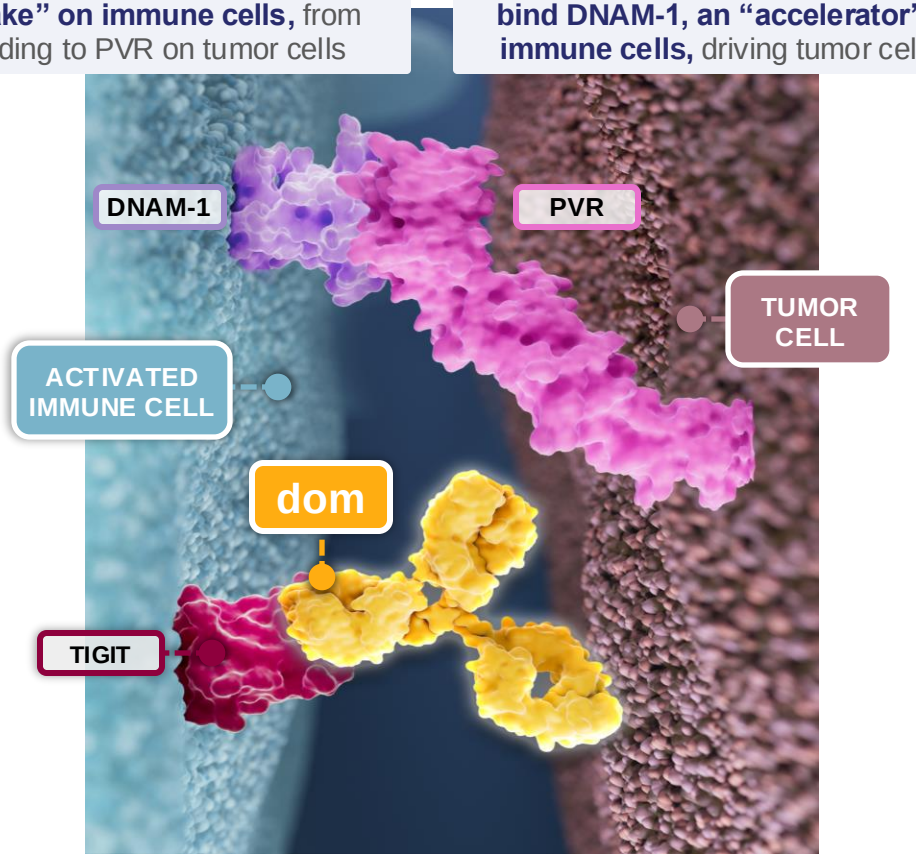
© Arcus Biosciences 2024

Dom is the Most Clinically Advanced Fc-Silent Anti-TIGIT Antibody in Development

TIGIT inhibition turns an immuno-suppressive "brake" into an accelerator of adaptive immunity

1 **Dom blocks TIGIT, an inhibitory "brake" on immune cells,** from binding to PVR on tumor cells

2 TIGIT blockade **enables PVR to bind DNAM-1, an "accelerator" on immune cells,** driving tumor cell kill



First-to-Market potential in Upper GI & the only Fc-silent anti-TIGIT in Ph3 NSCLC

Fc-silent — **Avoids peripheral T_{reg} depletion** that can lead to immune-related adverse events and treatment interruptions

Optimized dose — **1200 mg dose selected for maximum efficacy,** without the potential safety concerns of Fc effector function

Co-administered dosing — **Co-administered dom + zim** can reduce infusion times, without the constraints of fixed-dose co-formulation

DNAM-1: DNAX accessory molecule; dom: domvanalimab; GI: gastrointestinal; NSCLC: non-small cell lung cancer; Ph: phase; PVR: poliovirus receptor; TIGIT, T cell immunoreceptor with immunoglobulin and ITIM domain; Treg: regulatory T-cells; zim: zimberelimab
Note: co-administration of dom + zim was not part of STAR-121 Phase 3 study in 1L NSCLC

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Three De-Risking Phase 2 Datasets Have Been Presented for Domvanalimab Plus Zimberelimab Regimens

EDGE-Gastric

1L Gastric/EAC/GEJ

dom + zim + FOLFOX (n=40)

2024 ASCO ANNUAL MEETING

- mPFS well beyond historical benchmarks of 7 to 8 months[1-3]
  - PD-L1-high*: **13.8 months**
  - Overall: **12.9 months**
- Incidence of adverse events was similar to prior experience with anti-PD-1 + FOLFOX

ARC-7

1L PD-L1 high NSCLC

dom + **zim** *vs.* **zim** *vs.* **etruma** + **dom** + **zim** (n=150)

2023 ASCO ANNUAL MEETING

- PFS HRs:
  - **0.67** for DZ vs. Z
- ORRs for DZ and EDZ vs. Z
  - **Up to 14% improvement** in ORR
  - **Lower incidence** of progressive disease
- Similar rates of immune-related adverse events observed for DZ and Z – including rates of infusion-related reactions, rash and pruritus

ARC-10

1L PD-L1 high NSCLC

dom + **zim** *vs.* **zim** *or* **chemo** (n=95)

Society for Immunotherapy of Cancer SITC 2024 NOV. 6-10 | HOUSTON

- HRs, (mOS):
  - **0.64, (NR)** for DZ vs. Z (24.4mos)
  - **0.43** for DZ vs. C (11.9mos)
- PFS HRs:
  - **0.69** for DZ vs. Z
  - **0.69** for DZ vs. C
- cORRs:
  - **44.7%** for DZ **vs 35%** for Z
- Treatment-related adverse events leading to treatment discontinuation were low for DZ (10.5%)

*PD-L1 high population defined as TAP≥5

1L: first-line; D/dom: domvanalimab; EAC: esophageal adenocarcinoma; E/etruma: etrumadenant; GEJ: gastroesophageal junction; HR:hazard ratio; ORR: overall response rate; OS: overall survival; PFS: progression-free survival; TAP: tumor area positivity; Z/zim: zimberelimab

1. Phase 3: Janjigian, 2024. Shitara Nature 2022, Janjigian Lancet 2021, Moehler ASCO 2021 #4003 (36.2m, 24.0m, 12.1m, and 12.1m minimum follow up, respectively)
2. Phase 3: Rha, ESMO Virtual Plenary Feb 2023 and ASCO 2023 #4014 (31.0m median follow up)
3. Phase 3: Moehler, ASCO GI 2023 #286 (15.9m median follow up), and Xu, ESMO 2023 LBA80 (24.6m minimum follow up)

EDGE-Gastric - Janjigian et al. ASCO 2024, Jun. 1, 2022; data cut off of March 12,2024

ARC-7 Johnson et al. Abstract 397600, ASCO 2023; data cut-off of Feb. 7, 2023

ARC-10 – Johnson et al. SITC 2024, Nov. 5 2024, data cut off of May 17, 2024

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Summary of ARC-10 Results and Domvanalimab Plus Zimberelimab Clinical Program in Non-Small Cell Lung Cancer

Data presented at the 2024 Society for Immunotherapy of Cancer (SITC)
ASCO, based on data cut-off of Aug. 30, 2024.

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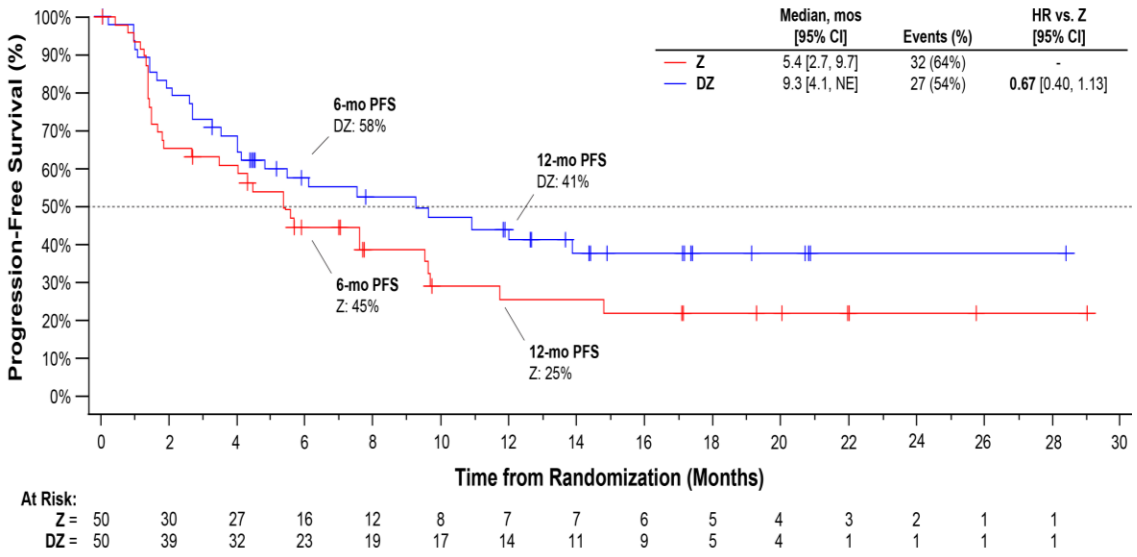
Two Different Datasets Demonstrate a Very Consistent Improvement for Dom + Zim in 1L PD-L1 High NSCLC

ARC-7

1L PD-L1 high NSCLC

dom + **zim** *vs.* **zim** *vs.* **etruma** + **dom** + **zim** (n=150)

2023 ASCO ANNUAL MEETING



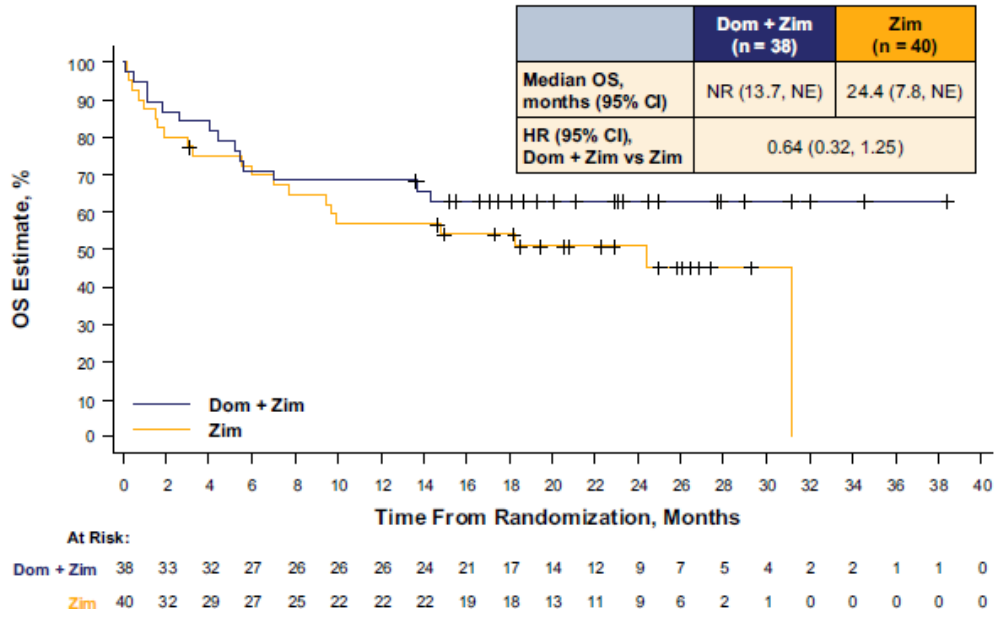
33% reduction in risk of progression or death (PFS) for DZ vs Z

ARC-10

1L PD-L1 high NSCLC

dom + **zim** *vs.* **zim** *or* **chemo** (n=95)

Society for Immunotherapy of Cancer SITC 2024 NOV. 6-10 | HOUSTON



36% reduction in risk of death (OS) for DZ vs Z

1L: first-line; D/dom: domvanalimab; E/etruma: etrumadenant; HR: hazard ratio; ORR: overall response rate; OS: overall survival; PFS: progression-free survival; Z/zim: zimberelimab

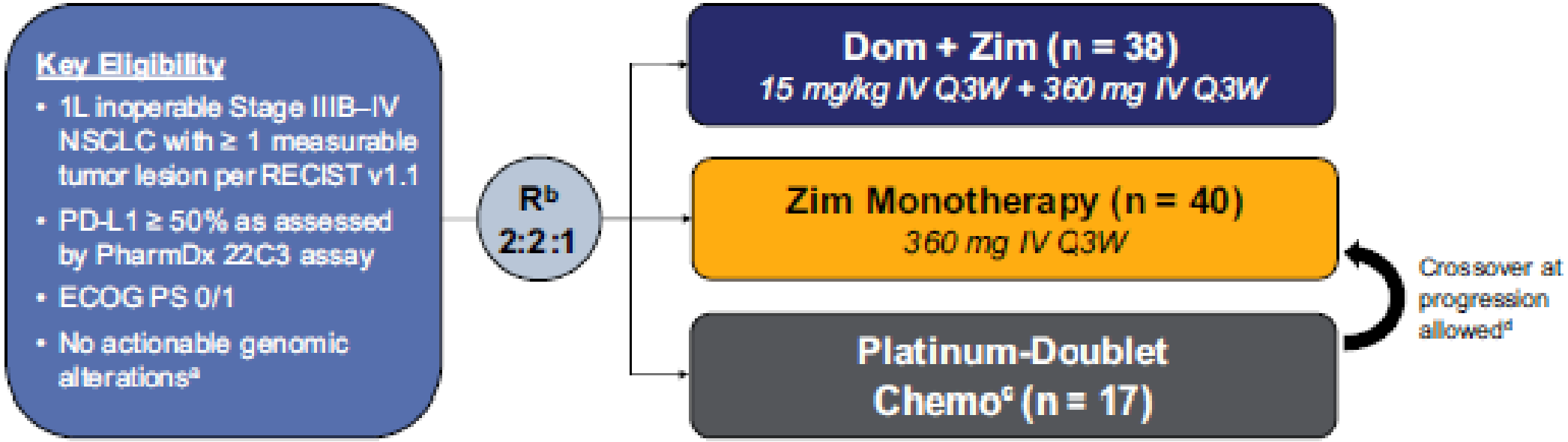
ARC-7 Johnson et al. Abstract 397600, ASCO 2023; data cut-off of Feb. 7, 2023

ARC-10 – Johnson et al. SITC 2024, Nov. 5 2024, data cut off of May 17, 2024

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Part 1: Global, Multi-Center, Randomized, Open-Label Trial in Front-Line, PD-L1-High, Stage IIIb-IV NSCLC



- At time of protocol development, platinum-doublet chemo was selected as the control arm in countries where anti–PD-(L)1 therapy was not yet the standard of care
- Tumor assessments were performed every 9 weeks

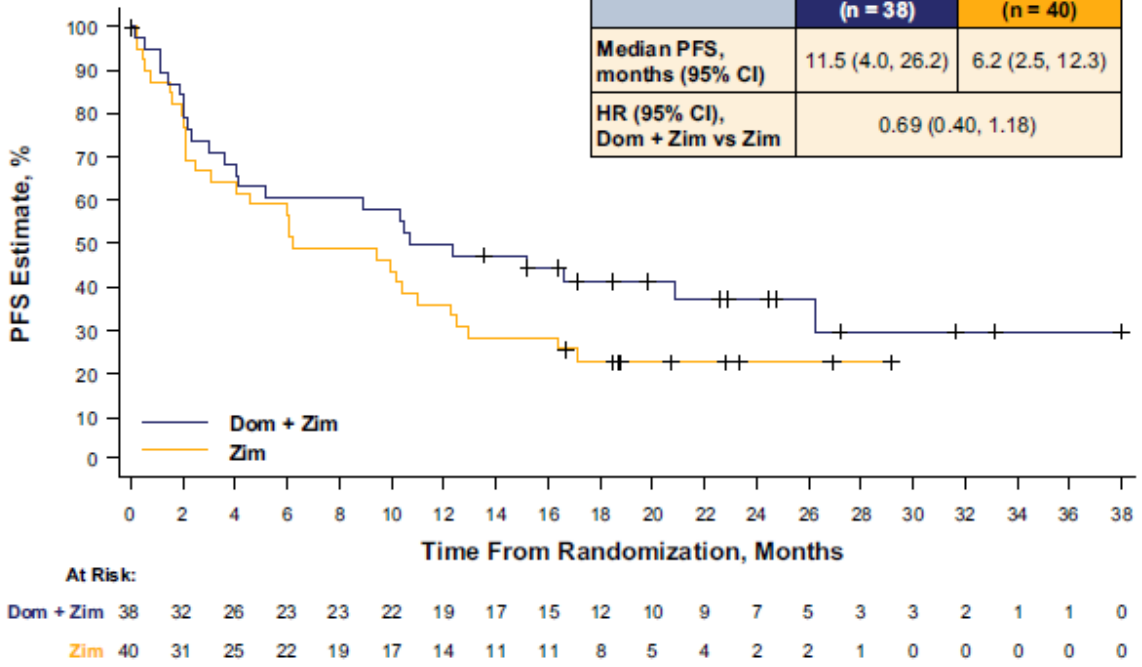
1L, first line; ALK, anaplastic lymphoma kinase; AUC, area under the concentration–time curve; chemo, chemotherapy; dom, domvanalimab; ECOG PS, Eastern Cooperative Oncology Group Performance Status; EGFR, epidermal growth factor receptor; IV, intravenous; NSCLC, non-small cell lung cancer; PD-(L)1, programmed cell death protein 1 or ligand 1; Q3W, every 3 weeks; R, randomized; RECIST, Response Evaluation Criteria in Solid Tumors; zim, zimberelimab.
[a]No EGFR or ALK mutations or other genomic tumor aberrations (eg, ROS proto-oncogene [ROS], v-raf murine sarcoma viral oncogene homolog B [BRAF], neurotrophic tropomyosin-related kinase [NTRK]) for which there is an available and approved targeted therapy. [b]Stratification factors: ECOG PS (0 vs 1), sex (male vs female), and geography (Asia vs non-Asia). [c]Patients received carboplatin (target AUC 5 or 6) IV Q3W plus either paclitaxel 200 mg/m^2 IV Q3W or pemetrexed 500 mg/m^2 IV Q3W (non-squamous histology only).
[d]Crossover at progression allowed before protocol version 5.0.

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(A) PFS and (B) OS Were Greater With Dom + Zim vs Zim

A

	Dom + Zim (n = 38)	Zim (n = 40)
Median PFS, months (95% CI)	11.5 (4.0, 26.2)	6.2 (2.5, 12.3)
HR (95% CI), Dom + Zim vs Zim	0.69 (0.40, 1.18)	

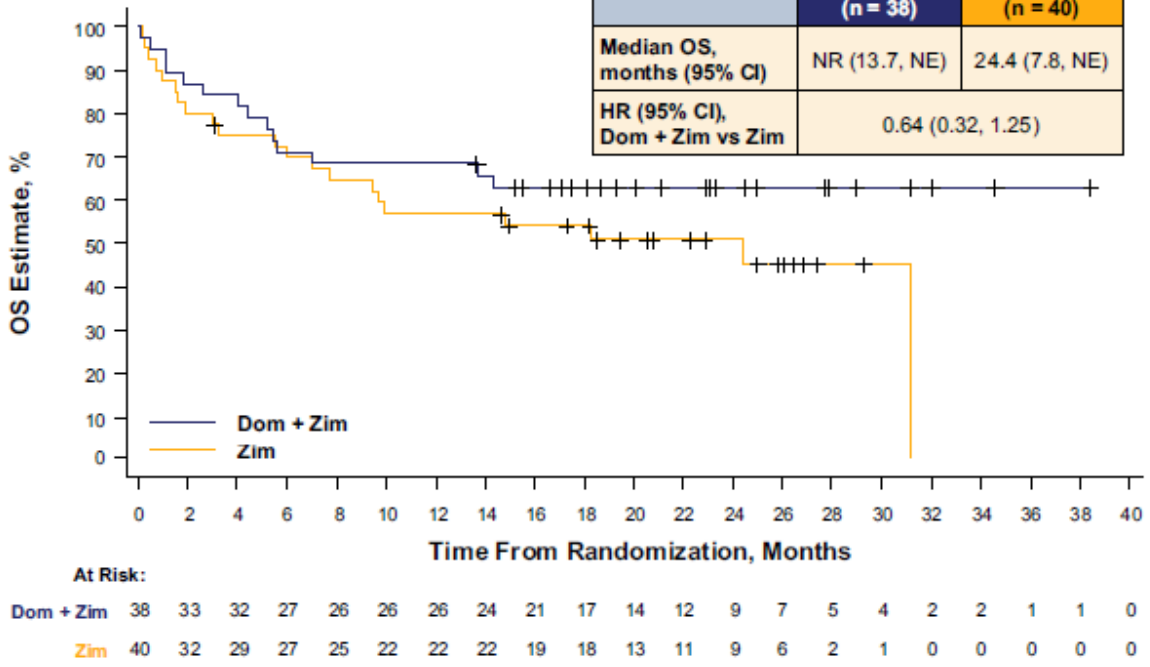


At Risk:

Dom + Zim	38	32	26	23	23	22	19	17	15	12	10	9	7	5	3	3	2	1	1	0
Zim	40	31	25	22	19	17	14	11	11	8	5	4	2	2	1	0	0	0	0	0

B

	Dom + Zim (n = 38)	Zim (n = 40)
Median OS, months (95% CI)	NR (13.7, NE)	24.4 (7.8, NE)
HR (95% CI), Dom + Zim vs Zim	0.64 (0.32, 1.25)	



At Risk:

Dom + Zim	38	33	32	27	26	26	26	24	21	17	14	12	9	7	5	4	2	2	1	1	0
Zim	40	32	29	27	25	22	22	22	19	18	13	11	9	6	2	1	0	0	0	0	0

Dom, domvanalimab; HR, hazard ratio; NE, not evaluable; NR, not reached; OS, overall survival; PFS, progression-free survival; zim, zimberelimab.
Tick marks indicate censored patients.

ARC-10 – Johnson et al. SITC 2024, Nov. 5 2024, data cut off of May 17, 2024, median follow-up of 24.5 months

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Treatment-Related Adverse Events (TRAEs) Leading to Treatment Discontinuation were Greater with Chemo

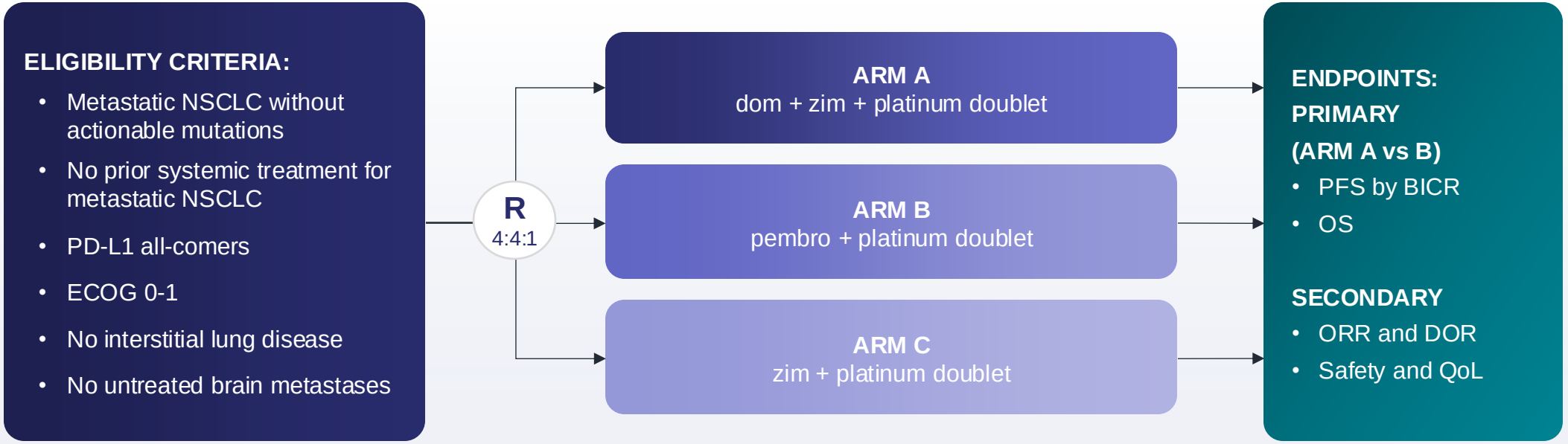
Parameter	Dom + Zim (n = 38)	Zim (n = 40)	Chemo (n = 17)
Treatment duration, months, median (range)	13.1 (0.7–38.6)	9.3 (0.7–29.9)	4.2 (0.7–23.5)
All-causality TEAE, n (%)			
Any	37 (97.4)	39 (97.5)	17 (100)
Serious	17 (44.7)	18 (45.0)	8 (47.1)
Grade 3 or higher	21 (55.3)	21 (52.5)	10 (58.8)
Leading to treatment discontinuation	8 (21.1)	7 (17.5)	5 (29.4)
Leading to death	5 (13.2)	7 (17.5)	3 (17.6)
Treatment-related TEAE, n (%)			
Any	31 (81.6)	23 (57.5)	14 (82.4)
Grade 3 or higher	8 (21.1)	6 (15.0)	8 (47.1)
Leading to treatment discontinuation	4 (10.5)	3 (7.5)	4 (23.5)
Leading to death	1 (2.6)[a]	4 (10.0)[b]	2 (11.8)[c]
Immune-mediated TEAE, n (%)			
Any	9 (23.7)	8 (20.0)	0
Grade 1	2 (5.3)	5 (12.5)	0
Grade 2	6 (15.8)	3 (7.5)	0
Grade 3	1 (2.6)[d]	0	0
Any infusion-related reactions, n (%)	3 (7.9)	1 (2.5)	0

ARC-10 – Johnson et al. SITC 2024, Nov. 5 2024, data cut off of May 17, 2024
dom: domvanalimab; TEAE: treatment emergent adverse event; zim: zimberelimab
a. sudden death
b. Event each of sudden death, acute kidney injury, acute myocardial infarction and intestinal perforation
c. Event each of febrile neutropenia and ischemic stroke

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Phase 3 Evaluating Dom + Zim + Chemo vs. Pembro + Chemo in 1L NSCLC (All PD-L1 Subgroups)

- Uses standard of care, pembrolizumab, in the comparator arm



Strat Factors:
- Baseline PDL1 PD-L1 status (<50% vs ≥50%)
- Geography (east Asia vs non-east Asia)
- Histology (Sq vs Non-sq)

★ ONGOING

1L: first-line; BICR: blinded independent central review; dom: domvanalimab; DOR: duration of response; ECOG: Eastern Clinical Oncology Group; NSCLC: non-small cell lung cancer; ORR: objective response rate; OS: overall survival; pembro: pembrolizumab; PFS: progression-free survival; QoL: quality of life; R: randomized; sq: squamous; zim: zimberelimab

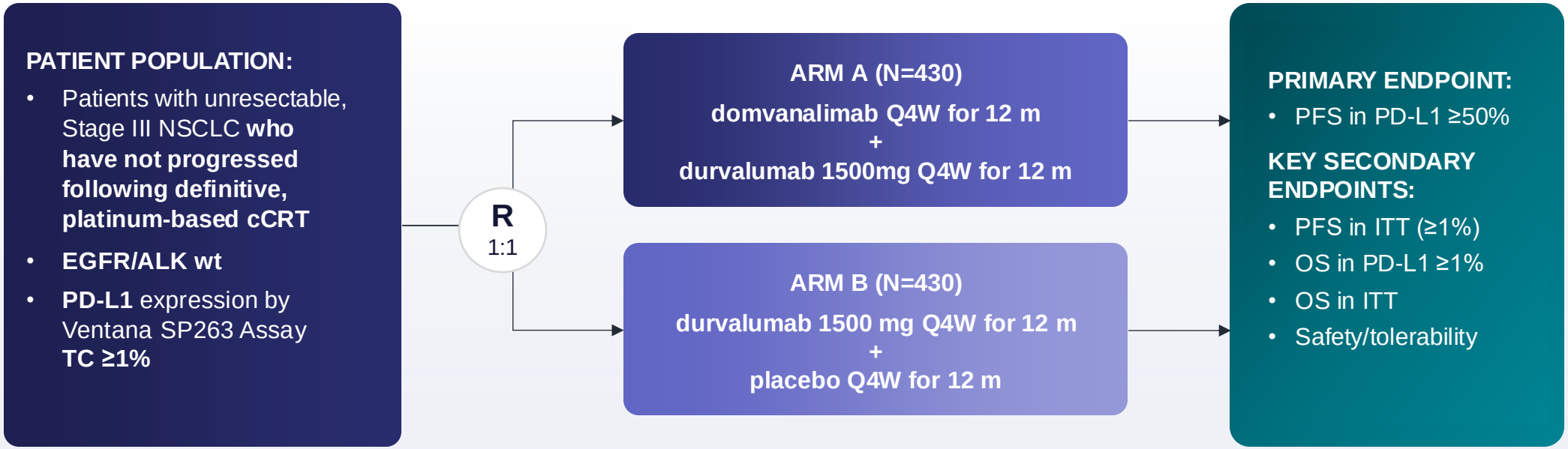
Gilead Sciences is operationalizing STAR-121

NCT #: NCT05502237

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Phase 3 Evaluating Dom + Durva vs Placebo + Durva in Unresectable, Stage III NSCLC

- Combines domvanalimab (dom) with durvalumab (durva) standard-of-care in Stage III NSCLC
- Potential to be first anti-TIGIT combination in this curative intent setting



Strat Factors:

- Disease stage prior to cCRT (IIIA vs. IIIB/IIIC)
- PD-L1 status (TC ≥ 50% vs. TC 1-49%), as assessed by a central reference laboratory using the VENTANA PD-L1 (SP263) IHC assay
- Histology (Sq vs Non-sq)

cCRT: concurrent chemoradiotherapy; IHC: immunohistochemistry; ITT: intent to treat; m: months; NSCLC: non-small cell lung cancer; OS: overall survival; PFS: progression free survival; Q4W: every 4 weeks; TC: tumor count

NCT #: NCT05211895

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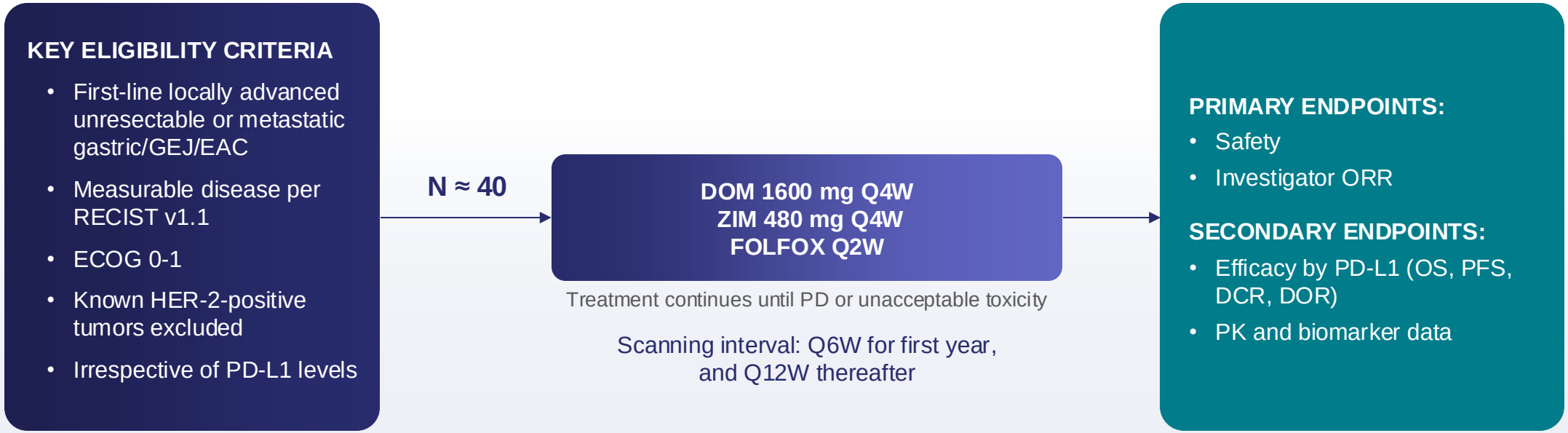
Summary of EDGE-Gastric Arm-A1 Results and Domvanalimab Plus Zimberelimab Clinical Program in Upper GI Cancers

Data presented at 2024 ASCO Annual Meeting, based on data cut off of March 12, 2024.

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Arm A1: 1L Metastatic Gastric/GEJ/EAC Cohort

EDGE-Gastric (NCT05329766) is a Phase 2 study evaluating the safety and efficacy of treatment combinations with and without chemotherapy in adults with advanced upper gastrointestinal tract malignancies



At the 12, March 2024 data cutoff, the median follow-up was 13.9 months

EDGE-Gastric - Janjigian et al. ASCO 2024, Jun. 1, 2022; data cut off of March 12,2024
1L: first line; DCR: disease control rate; dom: domvanalimab; DOR: duration of response; EAC: esophageal adenocarcinoma; GEJ: gastroesophageal junction; ORR: objective response rate; OS: overall survival; PD: progressive disease; PFS: progression-free survival; PK: pharmacokinetics; Q2W: every two weeks; Q4W: every four weeks; Q6W: every six weeks; Q12W: every twelve weeks; zim: zimberelimab

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Baseline Characteristics

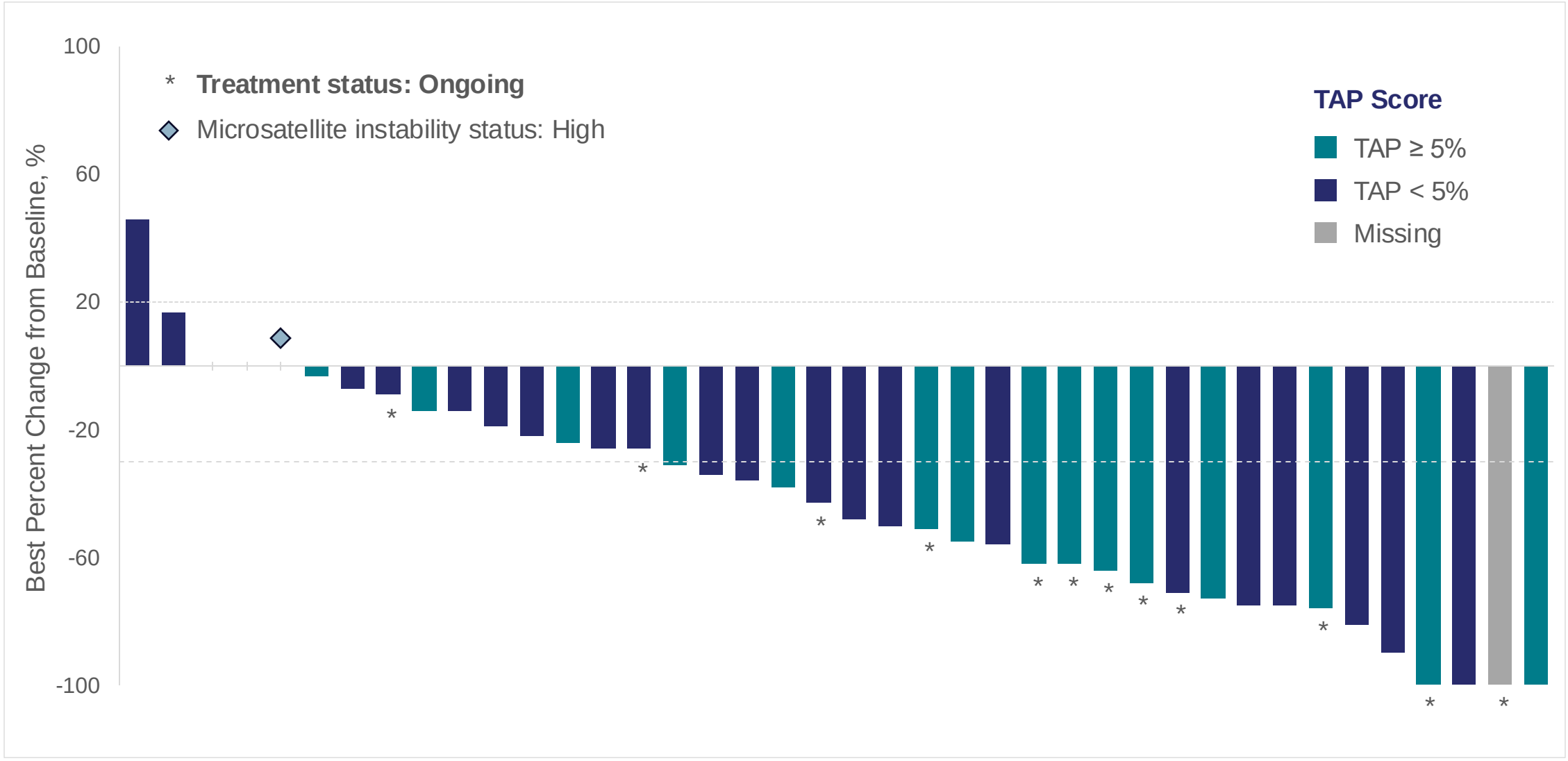
	Arm A1 N=41, n (%)
Mean age, years (range)	61 (30 to 82)
Female	17 (41)
Country	
United States/France	22 (54)
Korea	19 (46)
Baseline ECOG performance status 1	25 (61)
Histologically confirmed diagnosis	
Esophageal	10 (24)
Gastric	26 (63)
Gastroesophageal Junction (GEJ)	5 (12)

	Arm A1 N=41, n (%)
Current disease status	
Locally advanced unresectable disease	3 (7)
Metastatic disease	38 (93)
Liver metastases	13 (32)
Peritoneal metastases	15 (37)
TAP category (Central Lab)*	
TAP ≥ 5%	16 (39)
TAP < 5%	24 (59)
Unavailable†	1 (2)
Microsatellite instability status	
High	1 (2)
Low/Stable	35 (85)
Unknown	5 (12)

EDGE-Gastric - Janjigian et al. ASCO 2024, Jun. 1, 2022; data cut off of March 12,2024
* Ventana SP263 assay used for all TAP scores.
† 1 patient did not have tissue available for central testing.
ECOG: Eastern Cooperative Oncology Group; TAP: tumor area positivity

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Almost All Patients Experienced Meaningful Tumor Reduction, Regardless of PD-L1 Status



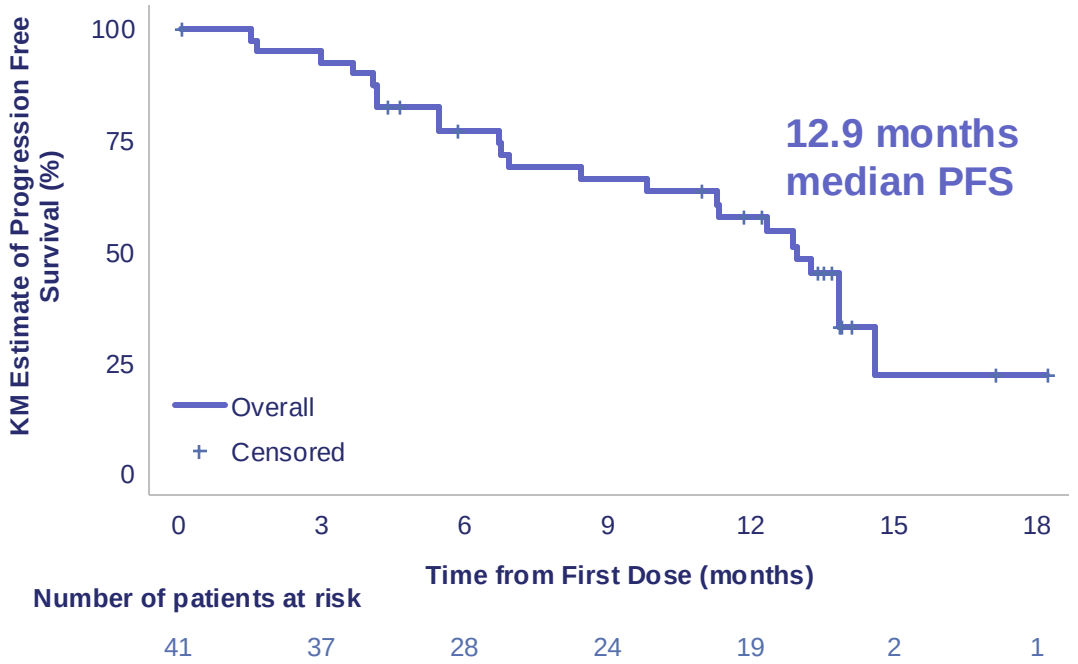
One patient had no tissue available for TAP central lab testing (grey bar). From local lab results, the patient was PD-L1 low via 22-C3 assay.
EDGE-Gastric - Janjigian et al. ASCO 2024, Jun. 1, 2022; data cut off of March 12,2024
TAP: tumor area positivity

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Unprecedented Median PFS of 12.9 months in the Overall Population

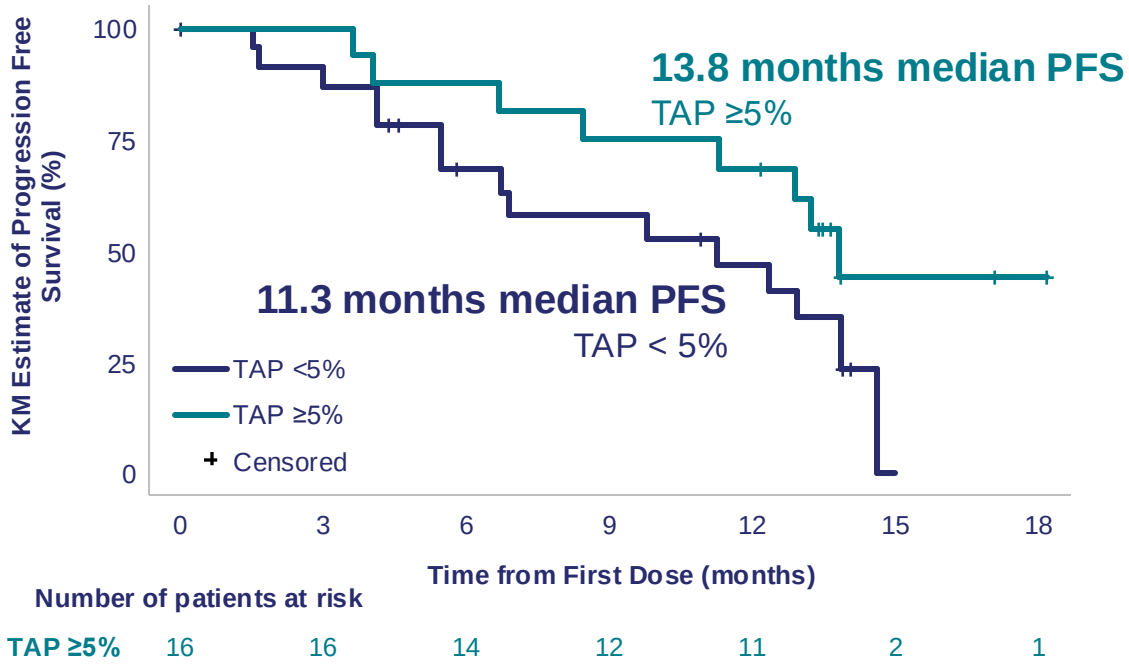
Efficacy-Evaluable (N=41)

	Median, months (95% CI)	Month 12 rate, % (95% CI)	Median PFS follow-up time, months (95% CI)	Events, n (%)
Overall (N=41)	12.9 (9.8, 13.8)	58 (42, 74)	13.9 (13.5, 14.1)	24 (59)



TAP ≥ 5% (n=16); TAP < 5% (n=24)

	Median, months (95% CI)	Month 12 rate, % (95% CI)	Median PFS follow-up time, months (95% CI)	Events, n (%)
TAP ≥ 5% (n=16)	13.8 (11.3, NE)	69 (46, 91)	13.8 (13.5, 17.1)	8 (50)
TAP < 5% (n=24)	11.3 (5.5, 13.8)	47 (25, 69)	13.9 (10.9, 14.1)	16 (67)



EDGE-Gastric - Janjigian et al. ASCO 2024, Jun. 1, 2022; data cut off of March 12,2024
CI: confidence interval; NE: not estimable; PFS: progression-free survival; TAP: tumor area positivity

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Dom + Zim + Chemo Has the Potential to Become the New SOC in 1L Gastric/GEJ/EAC

Data below 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

		EDGE-GASTRIC	CHECKMATE-649[1]	KEYNOTE-859[2]	RATIONALE-305[3]
mPFS	ITT	**12.9m**	7.7m	6.9m	6.9m
	PD-L-1 High	**13.8m**	7.7m[4] 8.3m[5]	8.1m	7.2m
mDOR	ITT	**12.4m**	8.5m	8.0m	8.6m
	PD-L1 High	**NE**	9.5m[4] 9.6m[5]	10.9m	9.0m
ORR	ITT	**59%**	58%[6]	51%	47%
	PD-L1 High	**69%**	60%	61%	50%

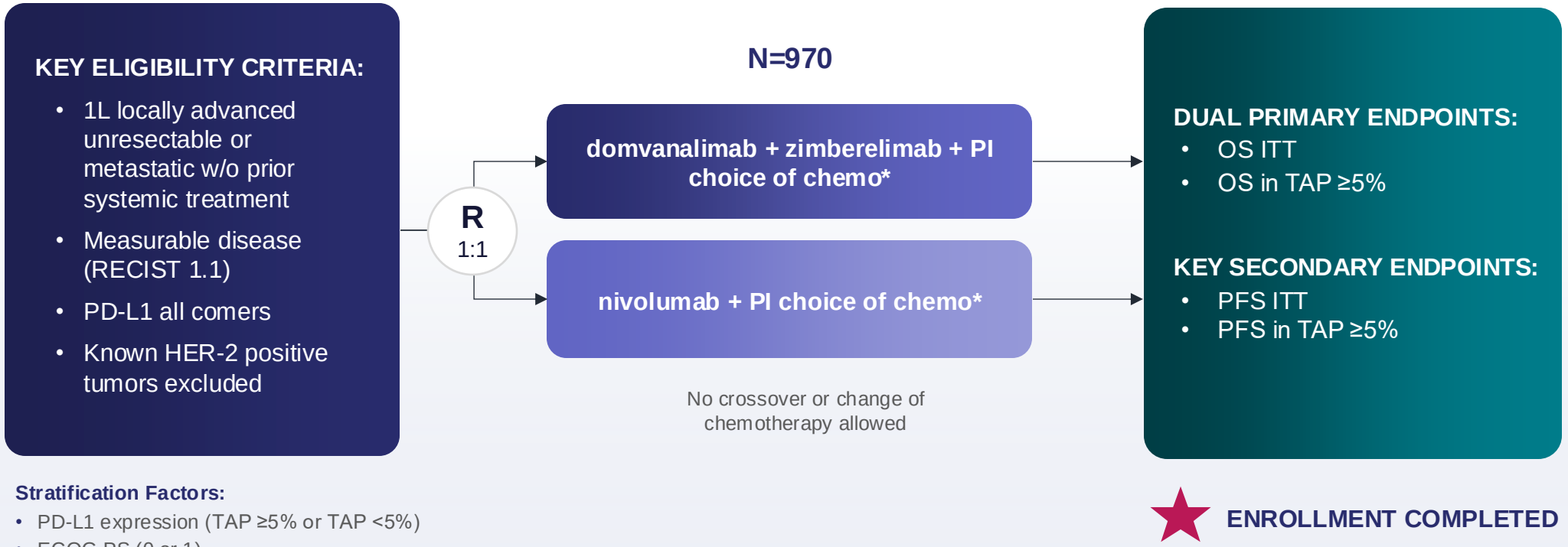
EDGE-Gastric - Janjigian et al. ASCO 2024, Jun. 1, 2022; data cut off of March 12,2024
1. Phase 3: Janjigian, 2024. Shitara Nature 2022, Janjigian Lancet 2021, Moehler ASCO 2021 #4003 (36.2m, 24.0m, 12.1m, and 12.1m minimum follow up, respectively)
2. Phase 3: Rha, ESMO Virtual Plenary Feb 2023 and ASCO 2023 #4014 (31.0m median follow up)
3. Phase 3: Moehler, ASCO GI 2023 #286 (15.9m median follow up), and Xu, ESMO 2023 LBA80 (24.6m minimum follow up)
4. With12.1 months minimum follow-up
5. With 36.2 months minimum follow-up
6. ITT population for Checkmate-649 included ~60% patients with PD-L1 high status at baseline. Note that EDGE-Gastric overall population included only 39% PD-L1 high at baseline.

CPS: combined positive score; EAC: esophageal adenocarcinoma; GEJ: gastroesophageal junction; IO: immuno-oncology; ITT: intent-to-treat; mOS: median overall survival; mPFS: median progression-free survival; NE: not estimable; nivo: nivolumab; ORR: overall response rate; pembro: pembrolizumab; TAP: tumor area positivity

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Phase 3 Evaluating Dom + Zim + Chemo vs Nivo + Chemo in 1L Gastric/GEJ/EAC

STAR-221 is evaluating the same regimen in the same setting as EDGE-Gastric – and dom + zim has the potential to be the first anti-TIGIT combination approved for 1L Gastric/GEJ/EAC



Stratification Factors:
- PD-L1 expression (TAP ≥5% or TAP <5%)
- ECOG PS (0 or 1)
- Region (US/Canada/EU5 vs. Asia vs. rest of world)

*PI choice of chemo: FOLFOX or CAPOX.
NCT #: NCT05568095
1L: first-line; chemo: chemotherapy; dom: domvanalimab; EAC: esophageal adenocarcinoma; ECOG: Eastern Cooperative Oncology Group; GEJ: gastroesophageal junction; nivo: nivolumab; ITT: intent to treat; OS: overall survival; PFS: progression-free survival; PI: principal investigator; RECIST: Response Evaluation Criteria in Solid Tumors; TAP: tumor area positivity; R: randomized; zim: zimberelimab

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CD73-Adenosine Axis Programs

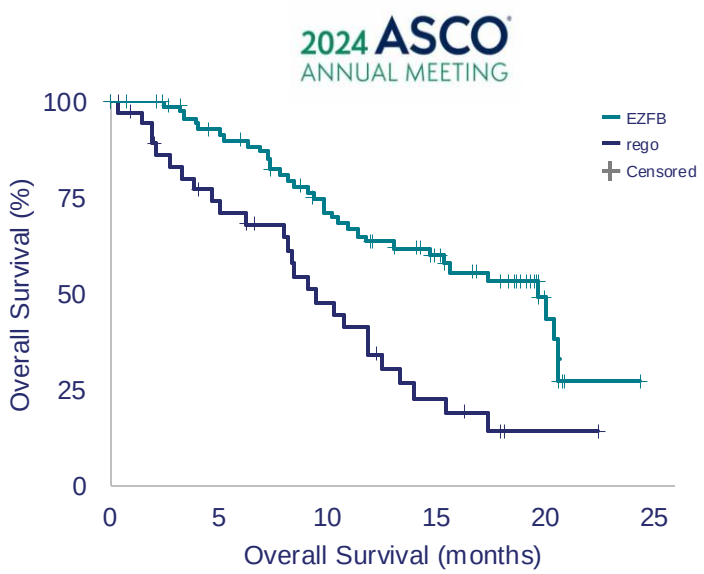
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Three Datasets in Six Months Demonstrate the Potential Benefits of Combining Adenosine Blockade with Chemotherapy

3L Colorectal Cancer

etruma + zim + FOLFOX/bev vs. rego (n=112)

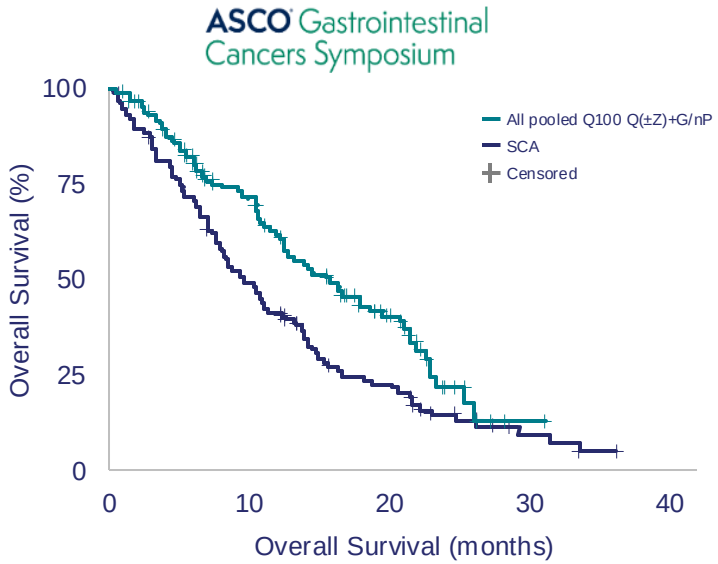
ARC-9



1L Metastatic PDAC

quemli ± zim + G/nP (n=122)

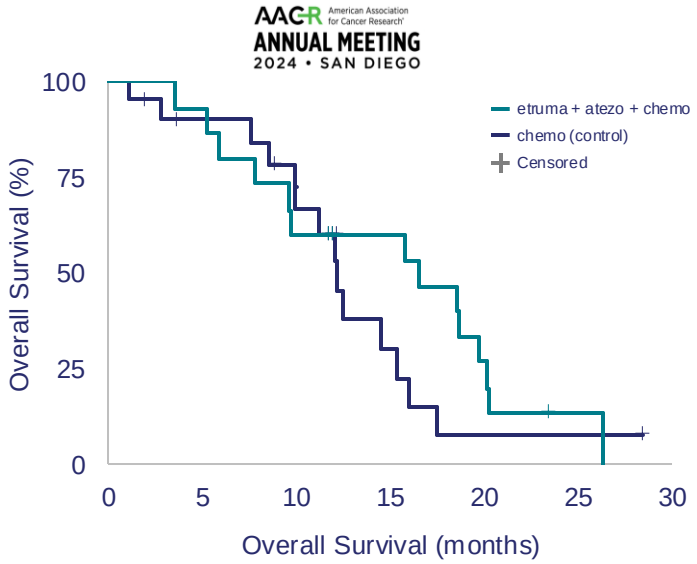
ARC-8



1L Metastatic PDAC

etruma + atezo + G/nP (n=35)

MORPHEUS COMBINATIONS PLATFORM



	EZFB	Rego	HR (95% CI)	Q(±Z)+G/nP	SCA	HR (95% CI)	etruma + atezo + chemo	Chemo	HR (95% CI)
mOS (mos)	19.68	9.13	0.36 (0.2. - 0.66)	15.7	9.8	0.63 (0.47 – 0.85)	16.5	12.1	0.67 (0.3-1.5)

⬇ 63% reduction in risk of death
⬆ 10.2 month increase in mOS
vs. standard of care (rego)

⬇ 37% reduction in risk of death
⬆ 5.9 month increase in mOS
vs. matched synthetic control arm

⬇ 33% reduction in risk of death
⬆ 4.4 month increase in mOS
vs. standard of care (chemo)

1L: first line; 3L: third line; atezo: atezolizumab; bev: bevacizumab; chemo: chemotherapy; E/etruma: etrumadenant; EZFB, etrumadenant + zimberelimab + mFOLFOX6 + bevacizumab; FOLFOX: oxaliplatin 85 mg/m2 IV; G/nP: gemcitabine/nab-paclitaxel; HR: hazard ratio; mOS: median overall survival; PDAC: pancreatic ductal adenocarcinoma; Q/quemli: quemliclustat; rego: regorafenib; SCA: Synthetic Control Arm; Z/zim: zimberelimab

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Etrumadenant Represents a Potentially Best-in-Class Adenosine Receptor Antagonist

ETRUMADENANT

- Highly potent small molecule that inhibits both the A_{2a} and A_{2b} receptors
- Excellent penetration of tumor tissue and drug properties (PK, etc.)
- MORPHEUS-PDAC (operationalized by Roche) data presented at AACR 2024 (Abstract CT212)
- Data from ARC-9 evaluating etruma + zim + chemo* vs. regorafenib in 3L CRC; mature PFS and OS were presented at ASCO 2024 (Abstract 3508)

Etrumadenant has an ideal profile

- ✓ Retains potency in physiologically relevant conditions
  - IC_{50} = 87 nM
- ✓ High tumor penetration
  - Tumor: Plasma ratio: >60%
- ✓ Low CNS permeability (in mouse model)
  - ~1% of the concentration found in blood
- ✓ Full engagement of target across dosing time period in humans
  - ≥90% target inhibition at trough

1H: first half; 3L third-line; CNS: central nervous system; CRC: colorectal cancer; etruma: etrumadenant; PFS: progression-free survival; PK: pharmacokinetics; OS: overall survival; zim: zimberelimab

Etrumadenant is an investigational molecule and its safety and efficacy have not been established.

*+/- biologic, e.g. bevacizumab or biosimilar, will be included for all patients in whom it is not contraindicated

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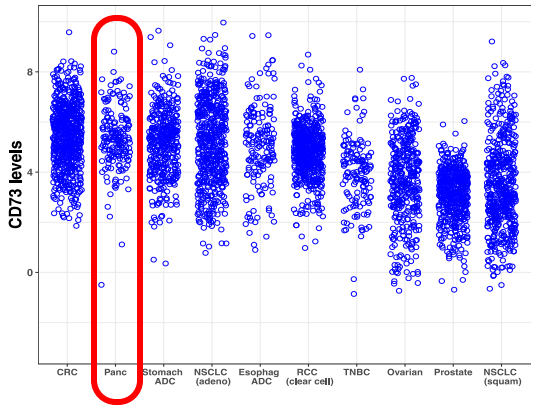
Quemliclustat (quemli): A Small Molecule CD73 Inhibitor with Several Key Attributes

QUEMLICLUSTAT

- Highly potent small molecule
- Target coverage achieved at doses as low as 25 mg every two weeks
- Extremely long (4+ days) half-life, enabling Q2W dosing by IV infusion

Biological rationale for CD73 inhibition in pancreatic cancer

Pancreatic cancer exhibits very high expression levels of CD73



mRNA Levels from analysis of The Cancer Genome Atlas (TCGA)

Potential advantages over CD73 antibodies[1]

- ✓ Highly potent and selective inhibition of both tumor cell-bound and soluble CD73
- ✓ Greater inhibition of enzymatic production of adenosine
- ✓ Orders of magnitude more potent
- ✓ Greater permeability of tumor tissue

Q2W: every 2 weeks

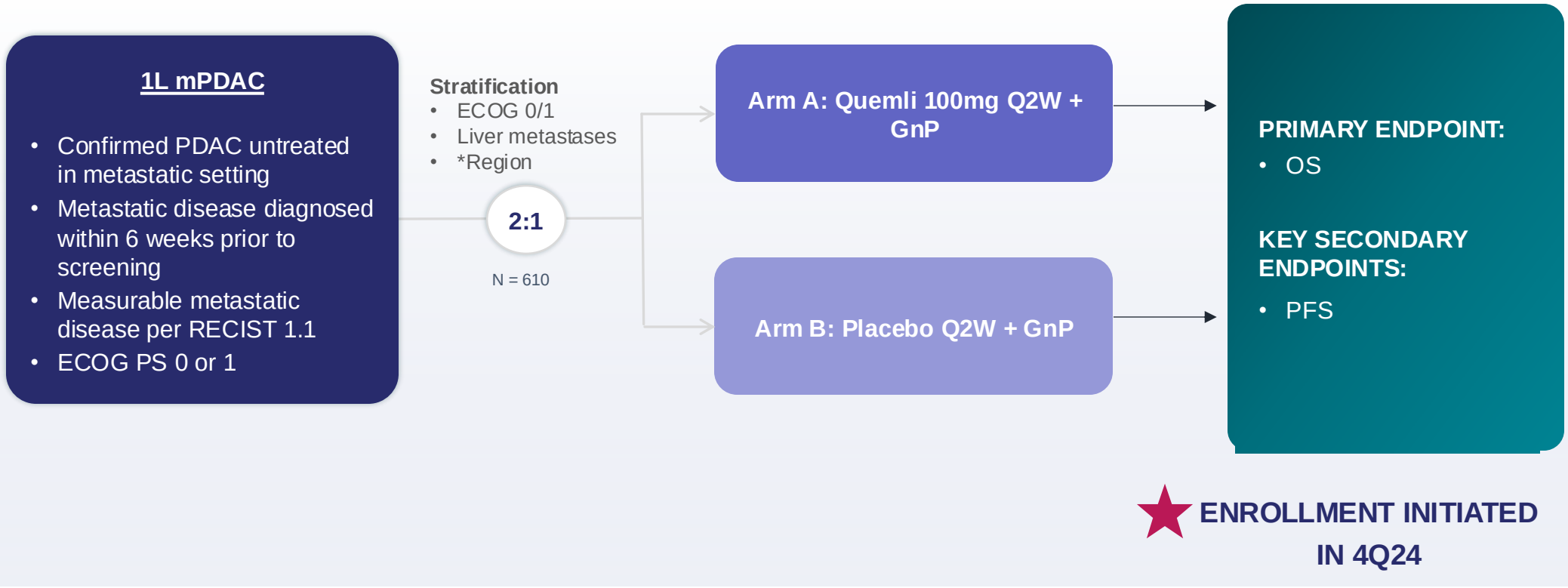
quemliclustat is an investigational molecule and its safety and efficacy have not been established.

1) Arcus Biosciences data on file; based on preclinical studies

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PRISM-1

Phase 3 Study of Quemli + Chemo in 1L Metastatic PDAC



1L: first-line; GnP: gemcitabine/nab-paclitaxel; PDAC: pancreatic ductal adenocarcinoma; OS: overall survival; PFS: progression-free survival; Q2w: every two weeks; quemli: quemliclustat

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AXL Program

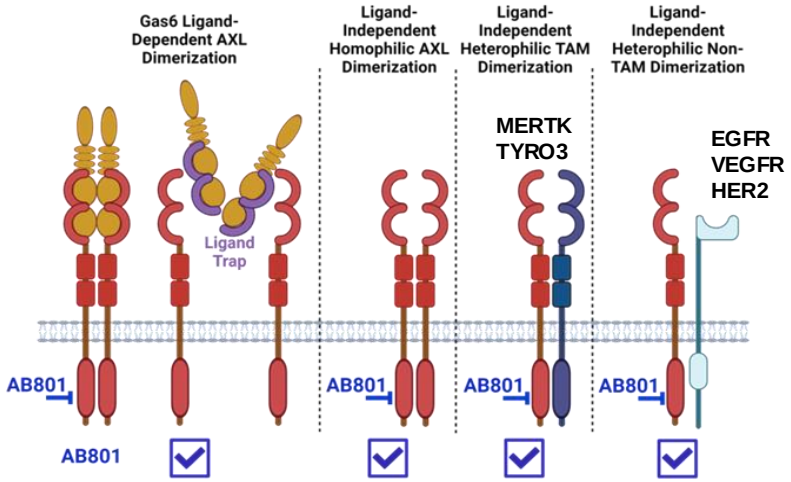
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AB801 is a Potent, Selective AXL Inhibitor

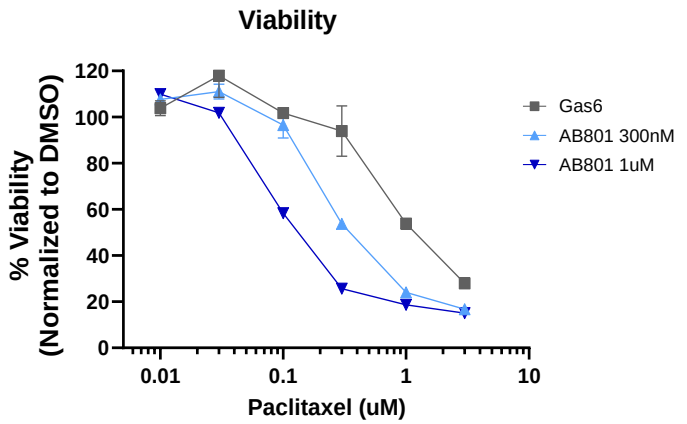
AB801 is a highly potent and selective AXL inhibitor

	Assay	AB801
BIOCHEMICAL	AXL K_i	**0.024 nM**
	Fold selectivity over hMERTK/ hTYRO3 (enzyme K_i over AXL K_i)	**860x / 1400x**
	Kinome Selectivity against 403 kinases at 100x IC_{50} for AXL	**Only one kinase with less that 200-fold selectivity**
CELLULAR	pAXL ELISA IC_{50} (serum-free media)	**17 nM**
	pAXL ELISA IC_{50} (100% serum)	**68 nM**

AXL signals via Ligand-dependent and Ligand-independent mechanisms



AB801 sensitizes cancer cells to chemotherapy



*Syngeneic mouse MC38 tumor model; data on file at Arcus.
AB801 is an investigational molecule and its safety and efficacy have not been established.

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AB801 is Potentially the Most Potent & Selective AXL Inhibitor in Clinical Development

THERAPEUTIC HYPOTHESIS: Inhibiting AXL will overcome resistance against chemotherapy and immunotherapy in human tumors

- AB801 was designed to potently and selectively inhibit AXL signaling in tumors, resulting in enhanced responses to chemotherapy and immunotherapy
  - Other “AXL inhibitors” may not be potent enough or lack selectivity (leading to toxicity) that may limit their use at doses suitable for efficient AXL inhibition
- Phase 1 study in healthy volunteers is completed:
  - No safety issues have been observed to date in the first 3 dose-escalation cohorts
  - Pharmacokinetics were dose-proportional and appear to support once-daily dosing
- Phase 1 study (ARC-27) in patients with advanced solid tumors is ongoing; **expansion cohort planned in 2L+ NSCLC early 2025**

2L: second-line; NSCLC: non-small cell lung cancer

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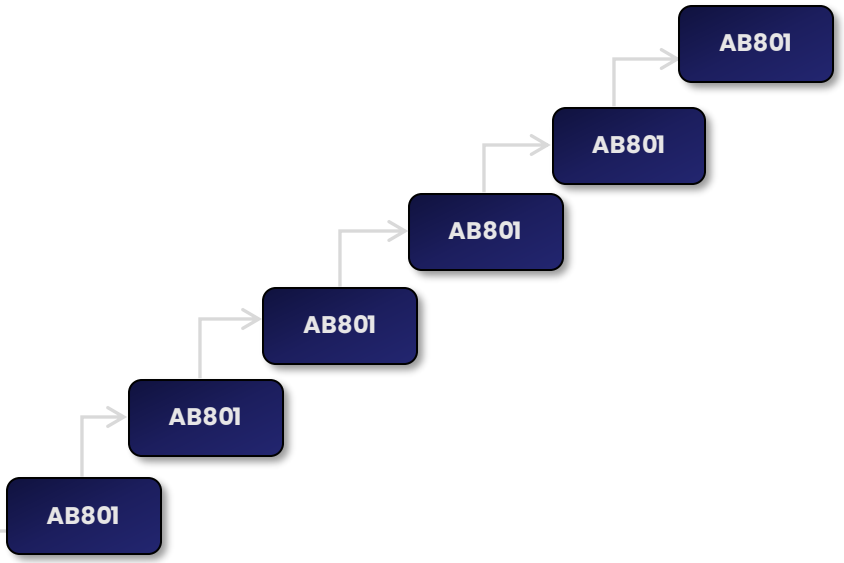
Phase 1 Dose-Finding Study in Patients with Advanced Solid Tumors

ARC-27

PRE-SCREENING / SCREENING | DOSE ESCALATION STAGE | EXPANSION STAGE

Advanced Solid Tumors

NSCLC, CRC, Breast, RCC, Ovarian, HNSCC, Bladder



Cohort 1: NSCLC adenocarcinoma

AB801 + docetaxel

Safety run-in n=6

n=40
Prior α-PD-(L)-1 and chemo

DOSE ESCALATION

PRIMARY ENDPOINT
- Safety / DLT

SECONDARY ENDPOINT
- PK
- ORR

EXPLORATORY ENDPOINTS
- Biomarkers / PD
- PFS, OS

DOSE EXPANSION

PRIMARY ENDPOINT
- Safety

SECONDARY ENDPOINT
- PK
- ORR

EXPLORATORY ENDPOINTS
- Biomarkers / PD
- PFS, OS

- Evaluate AB801 single agent tolerability and activity to inform dose in expansion stage
- Expansion cohort: all comers NSCLC adenocarcinoma designed to generate preliminary safety, PK, and activity signal (ORR), to support randomized POC Phase 2 study

CRC: colorectal cancer; DLT: dose-limiting toxicity; mg: milligram; NSCLC: non-small cell lung cancer; ORR: objective response rate; PD: pharmacodynamics; PFS: progression-free survival; PK: pharmacokinetics; OS: overall survival; RCC: renal cell carcinoma

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APPENDIX

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Expansive Development Plan with Multiple Phase 3 Studies Ongoing or Planned in 2024

Program	Disease	Study	Line & Regimen	Ph 1/1b	Ph 2	Ph 3	Upcoming Milestones
Dom + Zim (Fc-silent anti-TIGIT + anti-PD-1)	NSCLC	STAR-121	**1L, PD-L1 all-comers, metastatic** **dom** + **zim** + chemo vs pembro + chemo				
		PACIFIC-8	**Stage 3:** durva ± **dom**				
		ARC-10	**1L, PD-L1-high: dom+zim vs zim (p1) or pembro (p2)**				✓ OS results for part 1 presented at SITC
		EDGE-Lung	**1L / 2L, all-comers: dom** ± **zim** ± **quemli** ± chemo				
		VELOCITY-Lung	**1L/2L NSCLC: dom** ± **zim** ± **etruma** ± SG				
	Upper GI	STAR-221	**1L Upper GI Malignancies** **dom + zim +** chemo vs. nivo + chemo				✓ 2024: Enrollment completed
		EDGE-Gastric	**1L / 2L Upper GI Malignancies** **dom** ± **zim** ± **quemli** ± FOLFOX				✓ 1H24: ASCO presentation
Cas (HIF-2α inhibitor)	ccRCC	PEAK-1	**2L ccRCC: cas** + cabo vs cabo	IN PLANNING			
		ARC-20	**all-comer cancer; 2L+ ccRCC** **cas** monotherapy and **cas** + cabo				✓ Early 2024: Dose escalation data ✓ 2H24: Dose expansion data (30 pts, 7m+ follow-up)
ADENOSINE **Quemli (CD73 inhib.)**	PDAC	PRISM-1	**1L quemli +** G/nP vs. GnP				✓ Ph 3 initiated 4Q24
		ARC-8	**1L: quemli** + **zim** + G/nP vs **quemli** + G/nP				✓ Jan 2024: ASCO GI poster; mature OS
ADENOSINE **Etruma (A2R antag.)**	CRC	ARC-9	**2L: etruma** + **zim** + FOLFOX* vs FOLFOX* **3L: etruma** + **zim** + FOLFOX* vs rego				✓ 1H24: MORPHEUS-PDAC (etruma); mature PFS/OS ✓ 1H24: ASCO presentation; PFS/OS data in 3L
AB801 (Axl inhibitor)	NSCLC	ARC-27	**2L+: AB801** ± chemo				
AB598 (anti-CD39)	GI	ARC-25	**1L: AB598** ± zim + chemo				

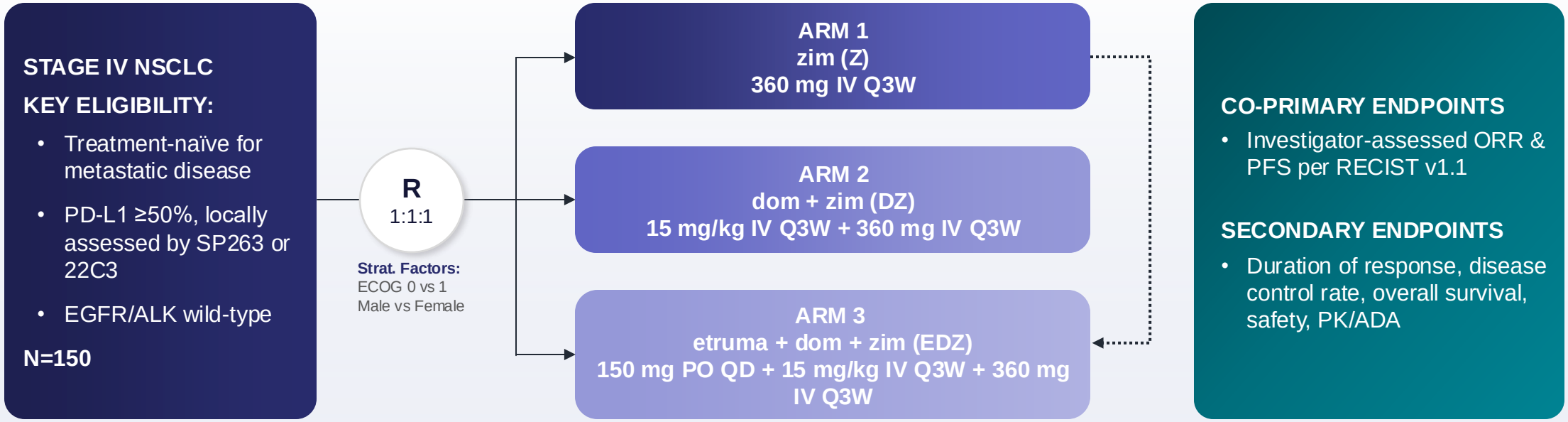
1L: first line; 2L: second line; 3L: third line; cabo: cabozantimib; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; dom: domvanalimab; durva: durvalumab; etruma: etrumadenant; GI: gastrointestinal; G/nP: gemcitabine/nab-paclitaxel; NSCLC: non-small cell lung cancer; P1/P2: part 1, part 2 PD: pharmacodynamic; pembro: pembrolizumab; PFS; progression-free survival; Ph: phase; PK: pharmacokinetic; OS: overall survival; rego: regorafenib; SG:Sacituzumab govitecan-hziy; quemli: quemliclustat; zim: zimberelimab

*+/- biologic, e.g. bevacizumab or biosimilar, will be included for all patients in whom it is not contraindicated

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Randomized, Open-label, Ph2 Study in First-Line, Metastatic, PD-L1-High NSCLC



Participants randomized to Arm 1 had the option to crossover to separate, 2L EDZ cohort upon radiographically confirmed disease progression (PD)

- As of the clinical cut-off date (Feb. 7, 2023), a total of 150 patients were randomized, with a median follow-up of 18.5 months

ADA: anti-drug antibody; D/dom: domvanalimab; ECOG: Eastern Cooperative Oncology Group; E/etruma: etrumadenant; IV: intravenous; NSCLC: non-small cell lung cancer; ORR: overall response rate; Ph: phase; PFS: progression-free survival; PK: pharmacokinetics; PO: orally; R: randomized; RECIST: Response Evaluation Criteria in Solid Tumors; Z/zim: zimberelimab; Q3W: every 3 weeks; QD: once-daily

Johnson et al. Abstract 397600, ASCO 2023; data cut-off of Feb. 7, 2023

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Final Overall Survival Analysis for Quemliclustat and Zimberelimab in Pancreatic Cancer (ARC-8)

Data presented at ASCO GI, January 19, 2024, based on a data cutoff of June 19, 2023.

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Highlights from the ARC-8, a Phase 1b Study in 1L PDAC

Median overall survival (mOS) was 15.7 months for patients treated with a quemliclustat-based regimen, which exceeds the historical benchmark data for chemotherapy alone (8.5 – 11.7 months)[1,2]

A 37% reduction in risk of death and a 5.9-month improvement in mOS was observed for patients treated with the quemli-based regimen when compared to a synthetic control arm of patients treated with G/nP alone[1] in a post-hoc analysis

The quemli-based regimen was well-tolerated, with no new safety signals or significant added toxicity compared to chemotherapy alone[1]

Phase 3 study initiation expected by early 2025

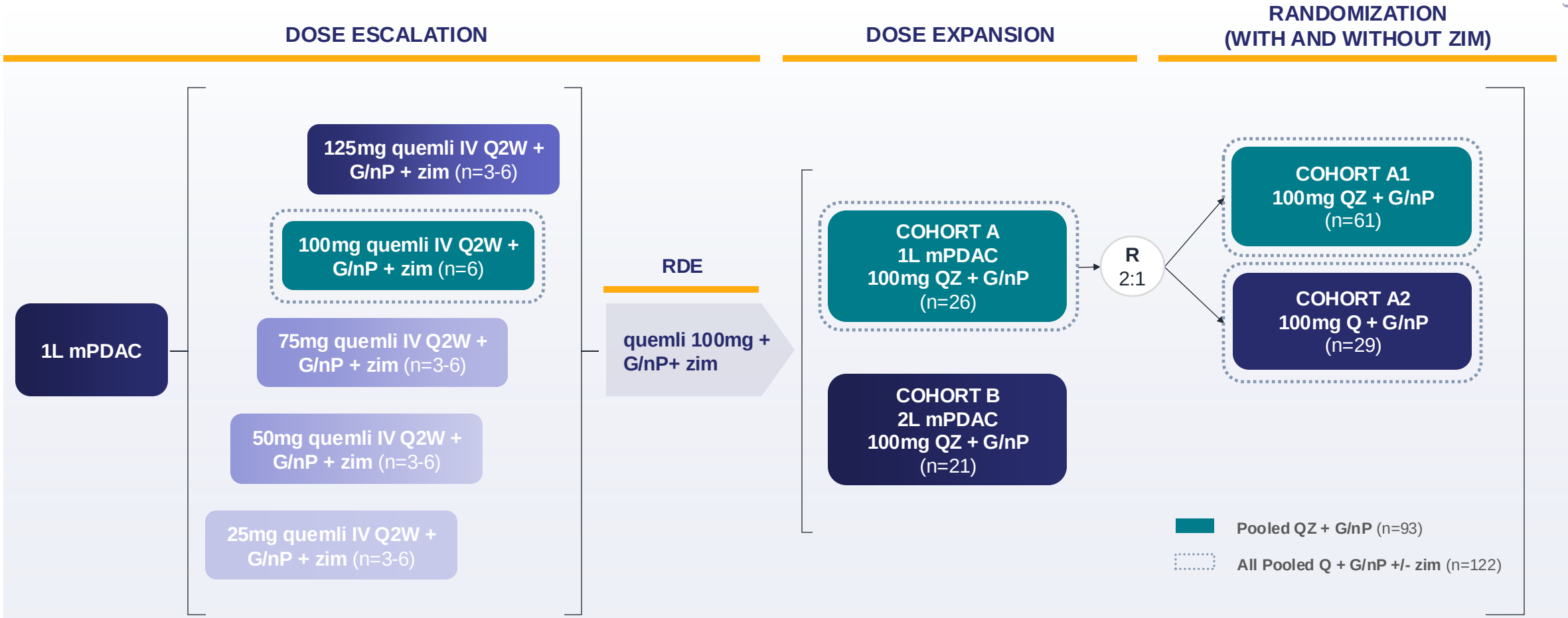
1L first-line; G/nP: gemcitabine/nab-paclitaxel; PDAC: pancreatic ductal adenocarcinoma; quemli: quemliclustat

1. Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023

2. Abraxane USPI, 2020 and Wainberg ZA, Melisi D, Macarulla T, et al. NALIRIFOX versus nab-paclitaxel and gemcitabine in treatment-naive patients with metastatic pancreatic ductal adenocarcinoma (NAPOLI 3): a randomised, open-label, phase 3 trial. Lancet. 2023;402(10409):1272-1281. doi:10.1016/S0140-6736(23)01366-1

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ARC-8 Study Design Included Dose Escalation, Expansion and Randomized Portions



Safety monitoring throughout treatment period; radiographic disease evaluation every 8 weeks. Study treatment continued to disease progression, unacceptable toxicity, consent withdrawal, or investigator decision.

1L: first-line; 2L: second-line; IV: intravenously; G/nP: gemcitabine/nab-paclitaxel; mPDAC: metastatic pancreatic ductal adenocarcinoma; PDAC: pancreatic ductal adenocarcinoma; Q2W: every 2 weeks; Q/quemli: quemliclustat; R: randomization; RDE: recommended dose for expansion; Z/zim: zimberelimab

NCT #: NCT04104672

Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023

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Dataset Includes Four Groups of Patients Treated with 100 mg of Quemli

Cohort	Quemli Dose	Combination	Participants Dosed			>18m OS f/u?	Population
Dose escalation	25mg	Q + Z + G/nP (quad)	4			Yes	1L mPDAC
Dose escalation	50mg	Q + Z + G/nP (quad)	6			Yes	1L mPDAC
Dose escalation	75mg	Q + Z + G/nP (quad)	3			Yes	1L mPDAC
Dose escalation	**100mg**	**Q + Z + G/nP (quad)**	6	**93** Pooled Q100 quad	**122** Pooled Q100 All	Yes	1L mPDAC
Cohort A	**100mg**	**Q + Z + G/nP (quad)**	26*			Yes (except for 3)*	1L mPDAC
Cohort A1 (randomized)	**100mg**	**Q + Z + G/nP (quad)**	**61**			Yes	1L mPDAC
Cohort A2 (randomized)	**100mg**	**Q + G/nP (triplet)**	**29**			Yes	1L mPDAC
Dose escalation	125mg	Q + Z + G/nP (quad)	3			Yes	1L mPDAC

1L: first-line; f/u: follow up; G/nP: gemcitabine/nab-paclitaxel; mPDAC: metastatic pancreatic ductal adenocarcinoma; OS: overall survival; Q/quemli: quemliclustat; Z/zim: zimberelimab

3 additional patients enrolled as contemporaneous control for Cohort C

Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023

© Arcus Biosciences 2024

Demographics And Baseline Characteristics Are Well Balanced Across Arms & Efficacy-evaluated Populations

% ECOG 1 (65%-69%) Was Higher than Historical G/nP Studies (42-57%); % Liver Mets (59%-69%) Was Slightly Lower than Historical G/nP Studies (78-85%)

% (n)		A2: Q + G/nP (n=29)	A1: QZ + G/nP (n=61)	Pooled Q100 QZ + G/nP (n=93)	All Pooled Q100 Q (±Z) +G/nP (n=122)
Median Age (IQR)		65.0 (61, 70)	66.0 (58, 72)	66.0 (58, 72)	65.5 (59, 72)
Age ≥65		55 (16)	59 (36)	58.1 (54)	57.4 (70)
Female		48 (14)	49 (30)	47 (44)	48 (58)
Race	White	83 (24)	74 (45)	74 (69)	76 (93)
	Asian	6.9 (2)	8.2 (5)	8.6 (8)	8.2 (10)
	Black	3.4 (1)	6.6 (4)	5.4 (5)	4.9 (6)
	Other/NR	6.9 (2)	11 (7)	12 (11)	11 (13)
ECOG 0		31 (9)	30 (18)	34 (32)	34 (41)
ECOG 1		**69** (20)	**69** (42)	**65** (60)	**66** (80)
ECOG Missing		-	1.6 (1)	1.1 (1)	0.8 (1)
Liver Metastasis at Baseline[1]		**58.6** (17)	**68.9** (42)	**66.7** (62)	**64.8** (79)

ECOG: Eastern Cooperative Oncology Group; G/nP: gemcitabine/nab-paclitaxel; IQR: interquartile range; NR: not reported; Q: quemliclustat; Z: zimberelimab

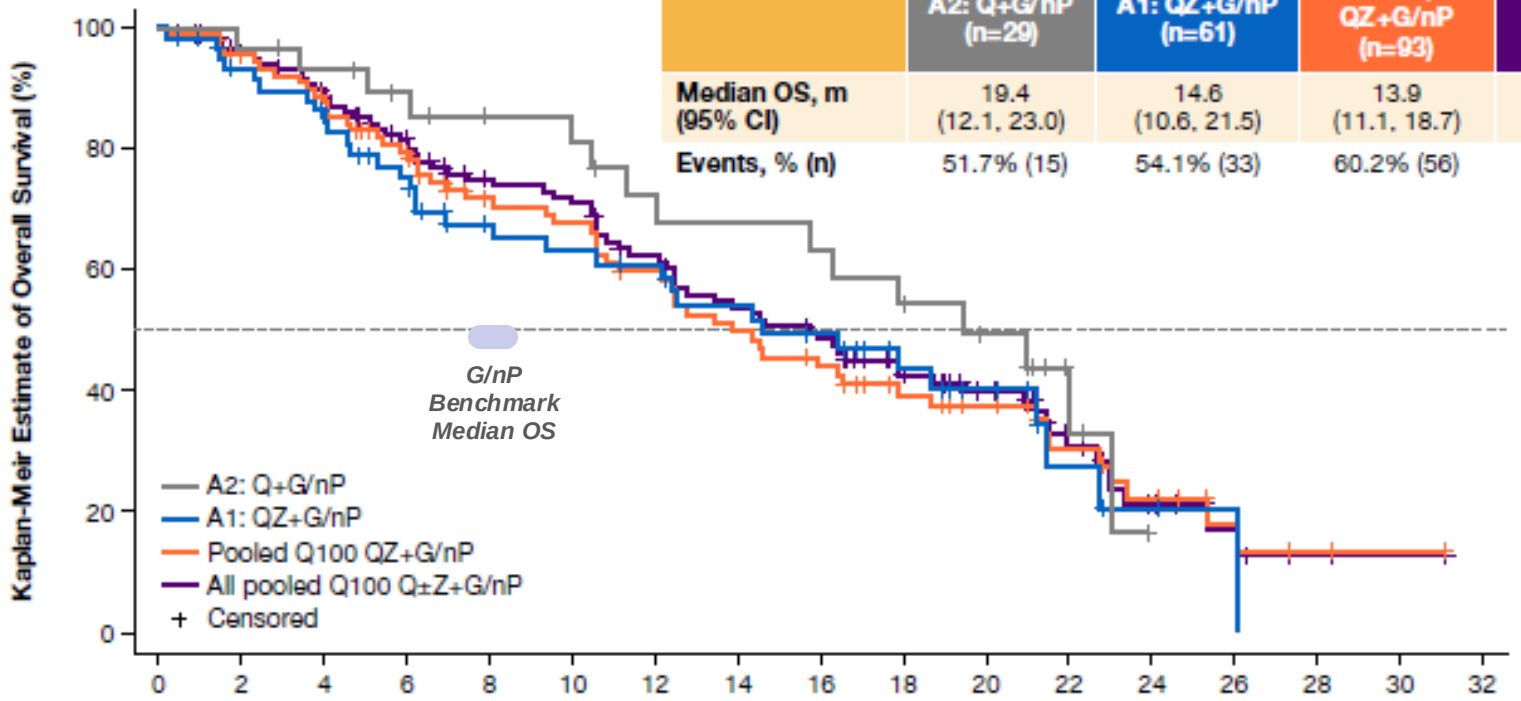
1. Derived from baseline tumor assessment data

Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023

© Arcus Biosciences 2024

With 21-month Median Follow-up, OS Results Exceed Ph3 Benchmarks for G/nP

	A2: Q+G/nP (n=29)	A1: QZ+G/nP (n=61)	Pooled Q100 QZ+G/nP (n=93)	All pooled Q100 Q(±Z)+G/nP (n=122)
Median OS, m (95% CI)	19.4 (12.1, 23.0)	14.6 (10.6, 21.5)	13.9 (11.1, 18.7)	15.7 (12.4, 20.9)
Events, % (n)	51.7% (15)	54.1% (33)	60.2% (56)	58.2% (71)



Number of patients at risk

A2: Q+G/nP	29	28	26	23	20	19	16	15	14	12	9	3	0	0	0	0	0
A1: QZ+G/nP	61	53	48	40	31	29	27	23	20	13	9	4	2	1	0	0	0
Pooled Q100 QZ+G/nP	93	84	77	66	53	50	43	35	30	22	18	12	8	4	2	1	0
All pooled Q100 Q(±Z)+G/nP	122	112	103	89	73	69	59	50	44	34	27	15	8	4	2	1	0

NE, not estimable; OS, overall survival; Q, quemliclustat; Z, zimberelimab.

Phase 3 G/nP median OS Benchmarks[1,2]

8.5 – 11.1 months

CI: confidence interval; G/nP: gemcitabine/nab-paclitaxel; Ph3: Phase 3

1. Abraxane USPI, 2020 and Wainberg ZA, Melisi D, Macarulla T, et al. NALIRIFOX versus nab-paclitaxel and gemcitabine in treatment-naive patients with metastatic pancreatic ductal adenocarcinoma (NAPOLI 3): a randomised, open-label, phase 3 trial. Lancet. 2023;402(10409):1272-1281. doi:10.1016/S0140-6736(23)01366-1

2. Von Hoff et al. N Engl J Med 2013;369:1691-703.

Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023

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Favorable OS for Patients With & Without Liver Metastasis

- Because ARC-8 had a lower incidence of liver mets than historical studies, we analyzed the OS for ARC-8 patients with and without liver mets as shown below
- When adjusting for the lower incidence of liver mets in the triplet arm, mOS for the triplet and quad arms looked almost identical at approx. 12 months
- **When evaluating just those patients *with* liver mets, median OS still exceeded historical benchmarks AND meaningfully outperformed the OS for patients with liver mets treated with G/nP in NAPOLI-3 (the most contemporary phase 3 in 1L pancreatic) -- 12.1 mos for ARC-8 vs. 8.6 mos for NAPOLI-3**

Liver Mets at Baseline	A2: Q + G/nP (n=17)	A1: QZ + G/nP (n=42)	Pooled Q100 QZ + G/nP (n=62)	All Pooled Q100 Q(±Z) + G/nP (n=79)	NAPOLI-3 (n=309)
Events (%)	11 (64.7)	26 (61.9)	40 (64.5)	51 (64.6)	242 (78.3)
Median OS, months	**12.1**	**12.2**	**11.1**	**12.1**	**8.6**
95% CI	10.0, 20.9	6.2, 17.9	8.1, 14.5	10.0, 15.7	

No Liver Mets at Baseline	A2: Q + G/nP (n=12)	A1: QZ + G/nP (n=19)	Pooled Q100 QZ + G/nP (n=31)	All Pooled Q100 Q(±Z) + G/nP (n=43)	NAPOLI-3 (n=78)
Events (%)	4 (33.3)	7 (36.8)	16 (51.6)	20 (46.5)	43 (55.1)
Median OS, months	**22.0**	**21.2**	**21.2**	**21.5**	**13.8**
95% CI	17.9, NE	14.6, NE	13.9, 25.4	17.9, 25.4	

BL: Baseline; CI: confidence interval; G/nP: gemcitabine/nab-paclitaxel; mets: metastasis; mOS: median overall survival; mos: months; NE: not estimable; OS: overall survival; Q: quemliclustat

NAPOLI-3: Wainberg, et al. *The Lancet*. Sept 2023. https://doi.org/10.1016/S0140-6736(23)01366-1. Data shown is for the G/nP arm only

Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023

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Safety Profile Similar to G/nP with Regards to Overall TEAEs

%	A2: Q + G/nP (n=29)	Pooled Q100 QZ + G/nP (n=93)	All Pooled Q100 Q (±Z)+G/nP (n=122)	NAPOLI-3 G/nP Benchmark[4] (n=379)
Any TEAE	100	100	100	99
Any TRAE	100	98.9	99.2	93
Grade 3-5 TEAE	89.7	83.9	85.2	86
Grade 3-5 TRAE	75.9	72.0	73.0	68
Serious TEAE	51.7	53.8	53.3	52
Serious TRAE	34.5	25.8	27.9	19
Grade 5 TEAE	0	5.4	4.1	6
Grade 5 TRAE	0	0	0	2
AE leading to mod[1]	58.6	51.6	53.3	54
AE leading to dose delay	75.9	75.3	75.4	NR
AE leading to discon[2]	24.1	22.6	23.0	23
IRR[2]	10.3	6.5	7.4	N/A
Immune related AE[3]	6.9	10.8	9.8	N/A

AE: adverse event; G/nP: gemcitabine/nab-paclitaxel; IRR: infusion-related reaction; NA: not applicable; NR: not reported; TEAE: treatment-emergent adverse event; TRAE: treatment-related adverse event

1. AE leading to dose reduction; 2. Discontinuation of any study drug; 3. As reported by investigator;
4. Wainberg, et al. The Lancet. Sept 2023. https://doi.org/10.1016/S0140-6736(23)01366-1

Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023

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Arcus & Medidata AI Synthetic Control Arm (SCA) Project

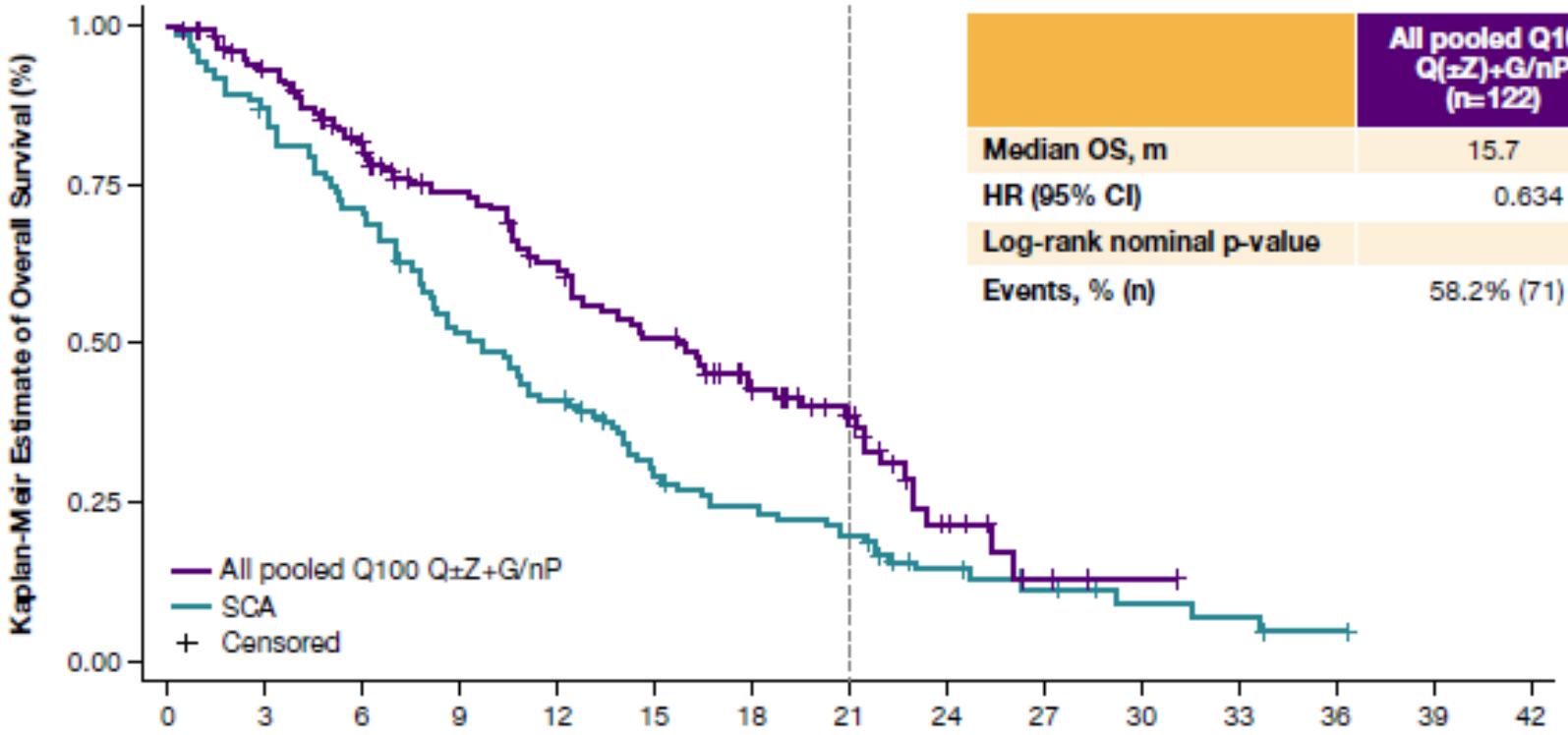
- Developed in collaboration with Medidata, the industry's leading provider of electronic data capture for clinical trials
- Constructed SCA using historical data from patients treated with G/nP alone and balanced to the patient baseline characteristics of ARC-8
  - Contemporaneous global randomized Phase 2 and 3 clinical trials that meet key ARC-8 entry criteria
  - 515 eligible external patients identified for further matching
  - SCA matched to All Pooled Q100 Q±Z+G/nP (n=122) using propensity score statistical method including exact matching on baseline liver metastasis
- Assessed the treatment effects on OS, PFS, and objective response rate in the SCA patients and compared these to the matched ARC-8 patients
- **SCA analyses were conducted versus all four analysis groups and showed consistent results**; for simplicity, only the SCA for the All Pooled Q100 group was reported

AI: artificial intelligence; G/nP: gemcitabine/nab-paclitaxel; OS: overall survival; PFS: progression-free survival; Q: quemliclustat; Z: zimberelimab

Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023

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Quemli-based Regimen Reduced Risk of Death by 37% and increased mOS by 5.9 months Compared to SCA



	All pooled Q100 Q(±Z)+G/nP (n=122)	SCA (n=122)
Median OS, m	15.7	9.8
HR (95% CI)	0.634 (0.471-0.854)	
Log-rank nominal p-value	0.0030	
Events, % (n)	58.2% (71)	86.1% (105)

Number of patients at risk

All pooled Q100 Q±Z+G/nP	122	108	89	72	59	47	34	23	8	3	1	0		
SCA	122	104	85	61	49	32	26	21	12	7	4	3	1	0

G/nP, gemcitabine/nab-paclitaxel; OS, overall survival; Q, quemliclustat; SCA, synthetic control arm; Z, zimberelimab.

CI: confidence interval; mOS: median overall survival; quemli: quemliclustat; SCA: Synthetic Control Arm

Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023

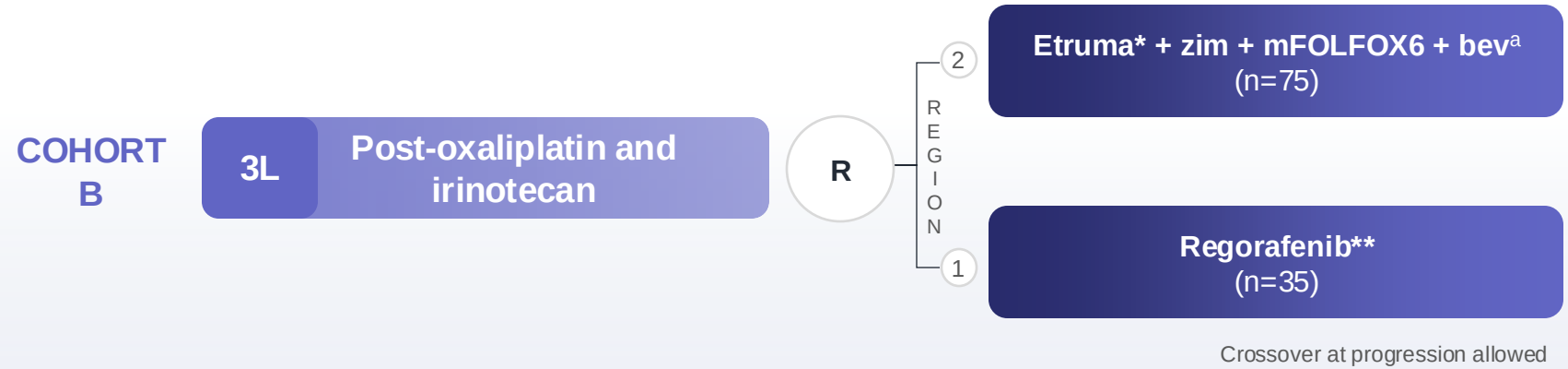
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Summary of ARC-9 Results

Data presented at 2024 ASCO Annual Meeting, based on data cut off of November 13, 2023.

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ARC-9 Cohort B: Etruma + Zim + mFOLFOX6 + Bev[a] (EZFB) vs Regorafenib (Rego) in 3L mCRC



PRIMARY ENDPOINTS:

- PFS (investigator assessed)

KEY SECONDARY ENDPOINTS:

- OS
- ORR (investigator assessed)
- Safety

Sample size of approximately 105 participants was estimated in a 2:1 ratio randomization to detect an improvement of HR of 0.5 in PFS using a log-rank test in order to achieve 80% power at a two-sided significance level of 0.05

KEY INCLUSION CRITERIA

- Histologically confirmed unresectable mCRC
- Measurable disease per RECIST v1.1
- ECOG PS of 0 or 1
- Disease progression on or after treatment with oxaliplatin and irinotecan containing chemotherapy in combination with anti-VEGF(R) or anti-EGFR

KEY EXCLUSION CRITERIA

- Prior treatment with immune checkpoint blockade therapies
- Mutation in the BRAF oncogene; patients with unknown BRAF status will be required to undergo testing at a local laboratory and provide results at screening

ARC-9 - Wainberg et al. ASCO 2024, Jun. 2, 2022; data cut off of November 13, 2023
a bev will be included for all patients in whom it is not contraindicated
*100 mg, IV, every 2 weeks (Days 1 and 15 of 28-day cycle)
**Dose ramp up starting at 80mg PO QD week 1, 120mg PO QD Week 2 and 160mg PO QD week 3 for the first cycle, followed by 160mg QD for 21 days out of 28-day cycle thereafter
3L: third line; bev: bevacizumab; CRC: colorectal cancer; etruma: etrumadenant; irino: irinotecan; mCRC: metastatic CRC; ORR: objective response rate; OS: overall survival; oxali: oxaliplatin; R: randomized; zim: zimberelimab.

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Prior Performance on FOLFOX Is Consistent With Historical 1L Data

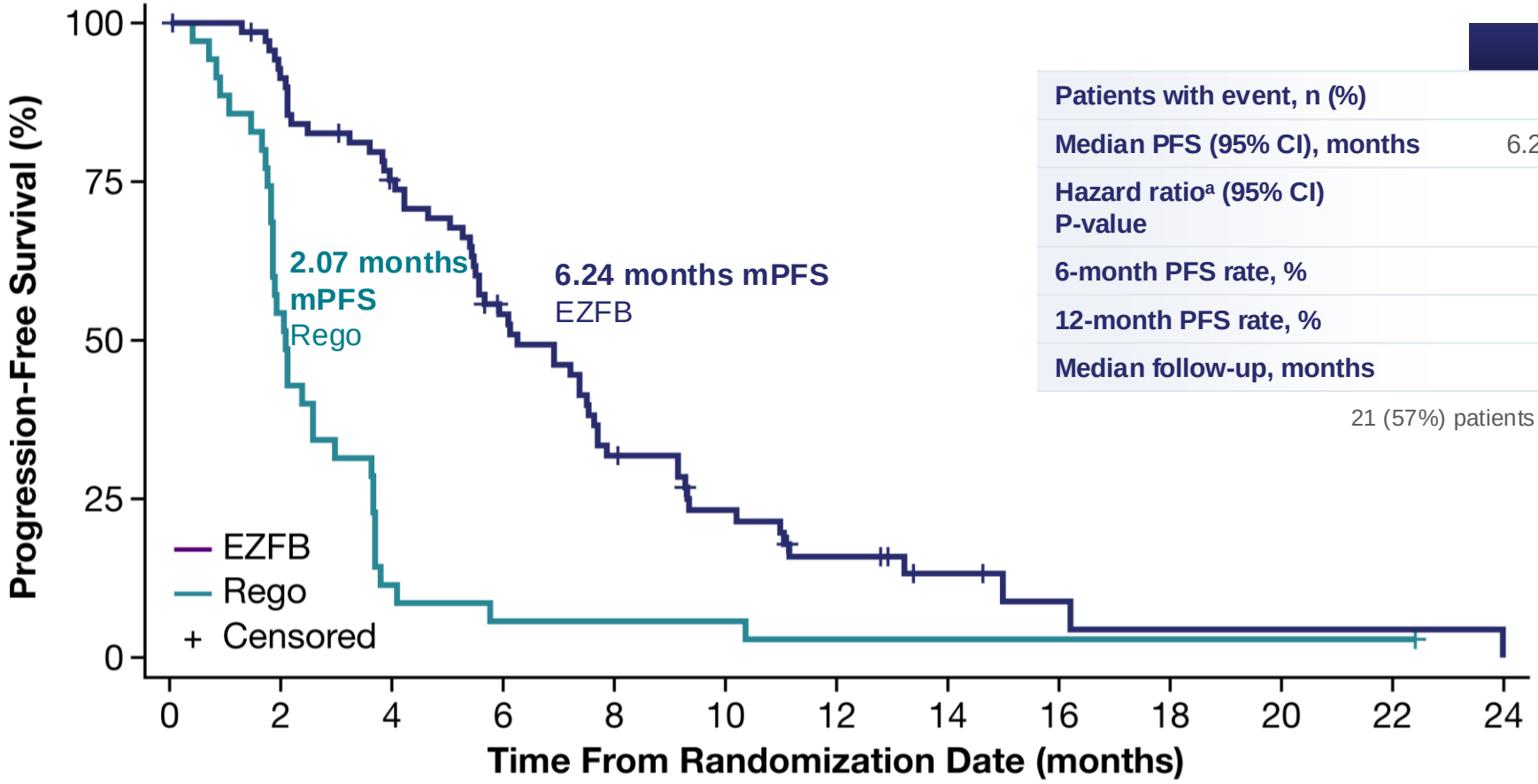
- Patients previously performed in-line with expectations for FOLFOX + bev in prior lines
- Prior performance in FOLFOX was well-balanced between arms

	EZFB (N=75)	REGO (N=37)
Time from first oxaliplatin dose date to progression/discontinuation date of the last prior oxali-containing regimen, n (%)	74 (98.7)	36 (97.3)
Median, months	9.0	9.8
Min, Max, months	0.7, 57.2	0.9, 33.7
Prior BOR of last oxaliplatin regimen under metastatic setting, n (%)	63 (84.0)	31 (83.8)
CR	2 (3.2)	2 (6.5)
PR	29 (46.0)	12 (38.7)
SD	15 (23.8)	9 (29.0)
PD	10 (15.9)	2 (6.5)
Unknown/Missing	7 (11.1)	6 (19.4)

ARC-9 - Wainberg et al. ASCO 2024, Jun. 2, 2022; data cut off of November 13, 2023
Efficacy-evaluable population.
BOR: best overall response; CR: complete response; EZFB: etrumadenant + zimberelimab + mFOLFOX6 + bevacizumab; mets: metastasis; oxali: oxaliplatin; PD: progressive disease; PR: partial response; rego: regorafenib; SD: stable disease

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EZFB Demonstrated Statistically Significant Improvement in PFS vs Rego



	EZFB	Rego
Patients with event, n (%)	58 (77)	34 (92)
Median PFS (95% CI), months	6.24 (5.49, 7.52)	2.07 (1.84, 2.96)
Hazard ratio[a] (95% CI)	0.27 (0.17, 0.43)	
P-value	<0.001	
6-month PFS rate, %	54	6
12-month PFS rate, %	16	3
Median follow-up, months	20.4	

21 (57%) patients randomized to rego crossed over to EZFB

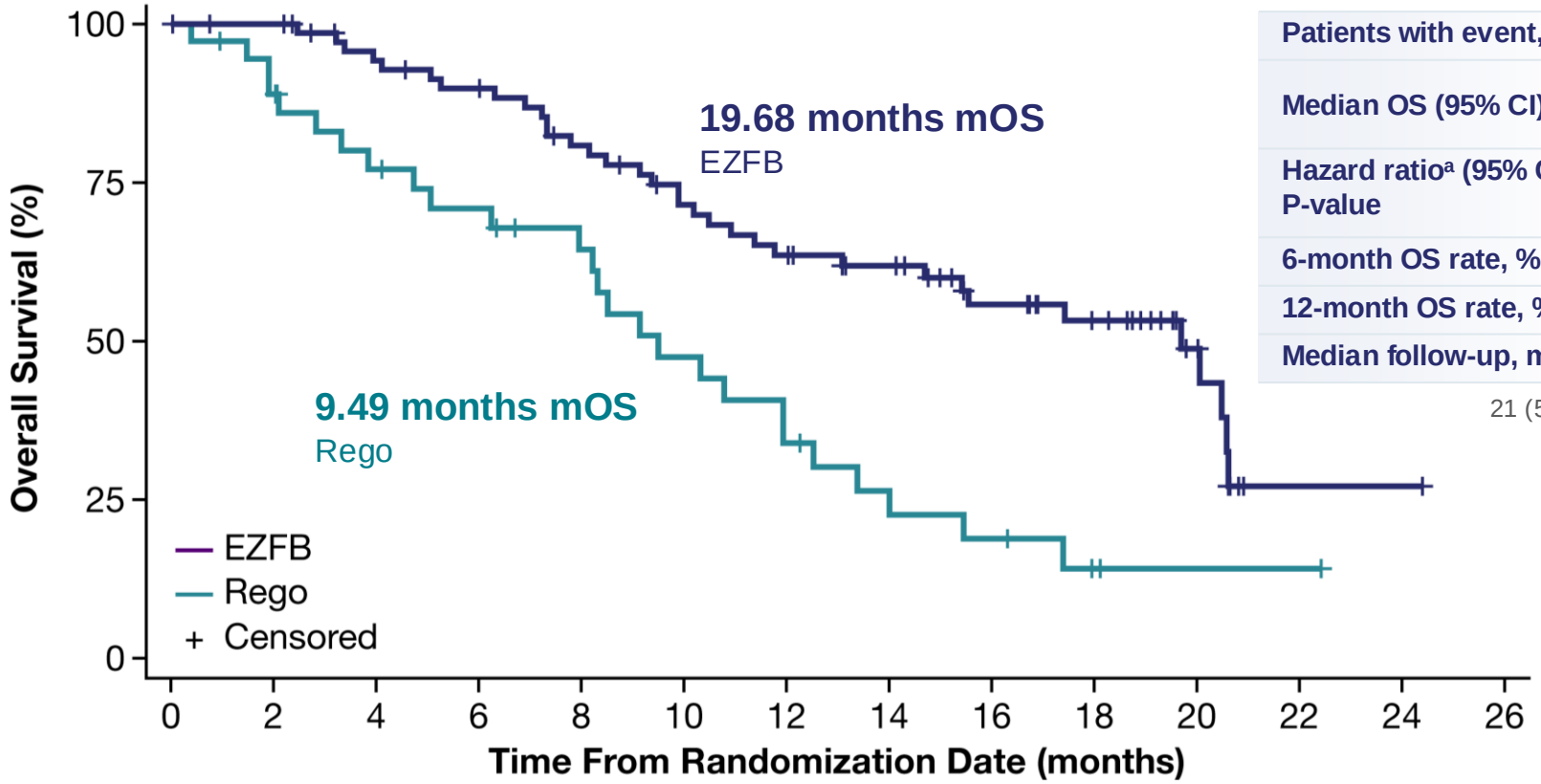
Number of patients at risk

EZFB	75	63	50	34	20	13	8	4	2	1	1	1
Rego	37	19	4	2	2	2	1	1	1	1	1	1

ARC-9 - Wainberg et al. ASCO 2024, Jun. 2, 2022; data cut off of November 13, 2023
Progression free survival is defined as the first occurrence of progressive disease per RECIST v1.1 or death, whichever occurs first. Patients without documented disease progression at the time of analysis were censored on the date of their last adequate tumor assessment. If no tumor assessment was performed after the start of study treatment, PFS will be censored on the date of first dose of study treatment with duration of 1 day.
a Hazard ratio and 95% confidence interval based on stratified (geographic region) Cox model. Study was not designed as a powered study to control for alpha in multiplicity testing.
EZFB, etrumadenant + zimberelimab + mFOLFOX6 + bevacizumab; PFS, progression-free survival; rego, regorafenib.

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EZFB Demonstrated Significant Improvement in OS vs Rego



Number of patients at risk

EZFB	75	73	65	61	53	45	40	35	26	20	10	1	1
Rego	37	32	26	23	19	14	10	6	5	2	1	1	0

	EZFB	Rego
Patients with event, n (%)	34 (45)	26 (70)
Median OS (95% CI), months	19.68 (14.69, 20.60)	9.49 (7.95, 12.52)
Hazard ratio[a] (95% CI)	0.37 (0.22, 0.63)	
P-value	<0.001	
6-month OS rate, %	90	71
12-month OS rate, %	64	34
Median follow-up, months	20.4	

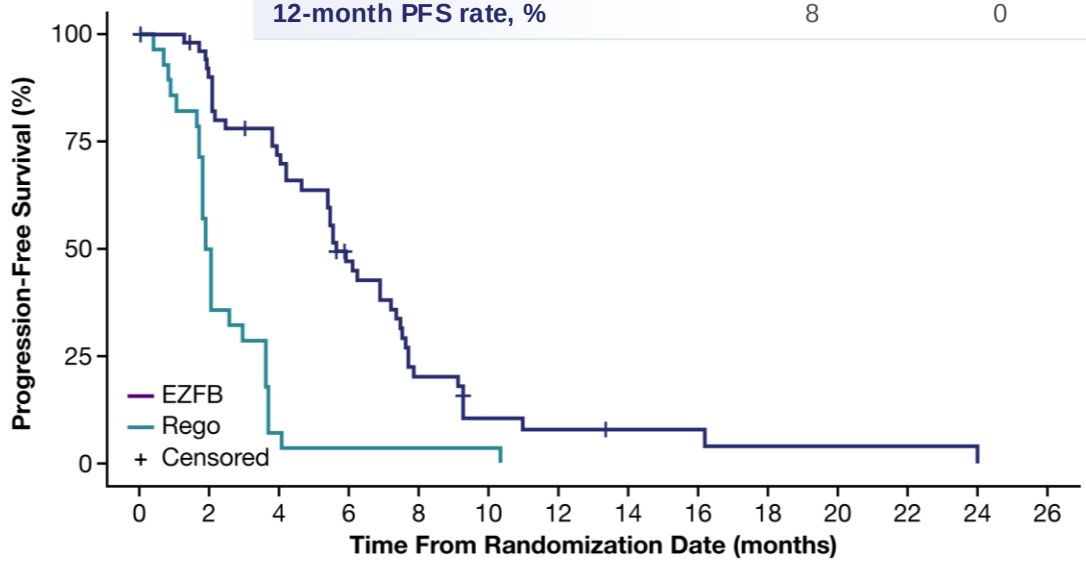
21 (57%) patients randomized to rego crossed over to EZFB

ARC-9 - Wainberg et al. ASCO 2024, Jun. 2, 2022; data cut off of November 13, 2023.
Overall survival is defined as time (months) from randomization until death from any cause. Patients who did not die while on study are censored at the last known date they were alive.
a Hazard ratio and 95% confidence interval based on stratified (geographic region) Cox model. Study was not designed as a powered study to control for alpha in multiplicity testing.
EZFB: etrumadenant + zimberelimab + mFOLFOX6 + bevacizumab; OS: overall survival; rego: regorafenib

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5.7 Month Median PFS and 20 Month Median OS for EZFB in Patients With Liver Metastasis

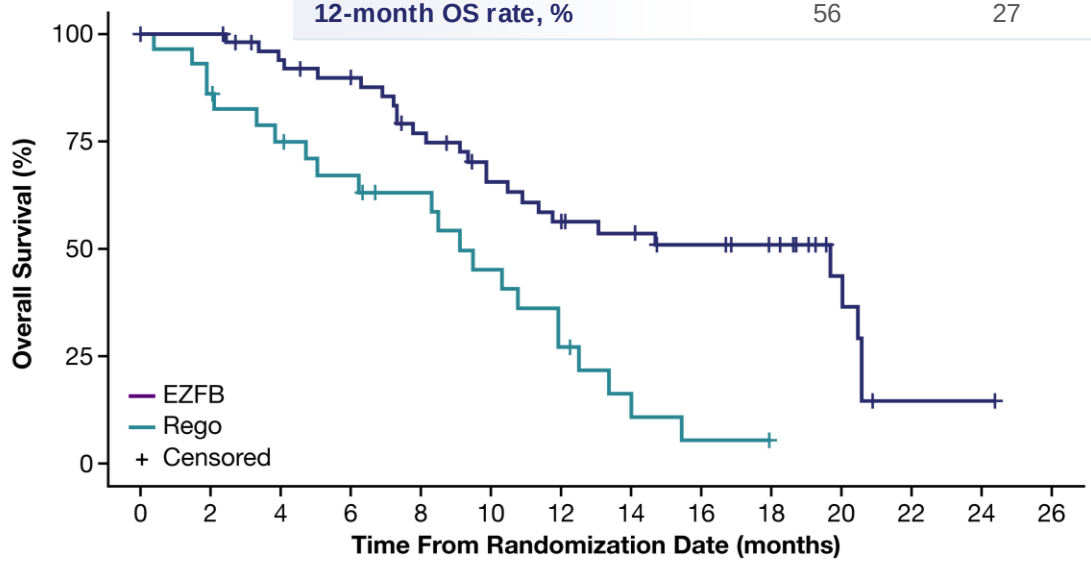
	EZFB	Rego
Patients with events , n (%)	45 (85)	28 (97)
Median PFS, months	5.65	1.97
Hazard ratio (95% CI)	0.19 (0.10, 0.35)	
6-month PFS rate, %	47	4
12-month PFS rate, %	8	0



Number of patients at risk

EZFB	53	45	35	21	9	4	3	2	2	1	1	1	0
Rego	29	14	2	1	1	1	0						

	EZFB	Rego
Patients with events , n (%)	27 (51)	22 (76)
Median OS, months	19.68	9.13
Hazard ratio (95% CI)	0.36 (0.2. 0.66)	
6-month OS rate, %	90	67
12-month OS rate, %	56	27



Number of patients at risk

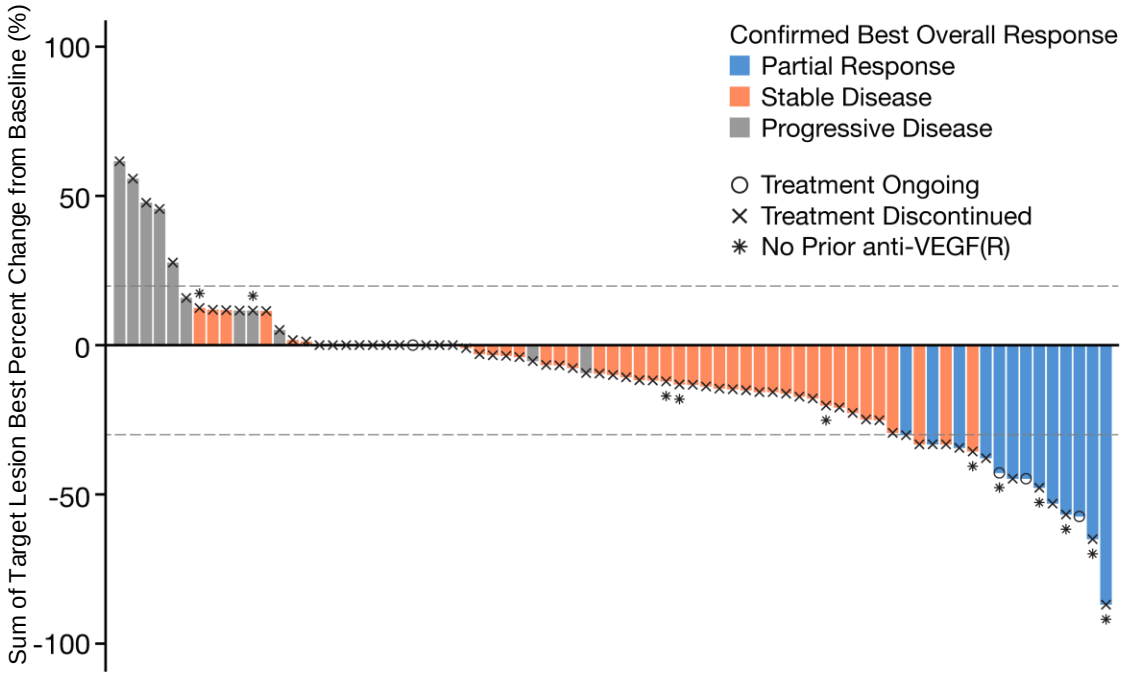
EZFB	53	52	46	43	35	28	24	21	18	13	6	1	1	0
Rego	29	25	20	17	14	10	6	2	1	0				

ARC-9 - Wainberg et al. ASCO 2024, Jun. 2, 2022; data cut off of November 13, 2023
Progression free survival is defined as the first occurrence of progressive disease per RECIST v1.1 or death, whichever occurs first. Patients without documented disease progression at the time of analysis were censored on the date of their last adequate tumor assessment. If no tumor assessment was performed after the start of study treatment, PFS will be censored on the date of first dose of study treatment with duration of 1 day. Overall survival is defined as time (months) from randomization until death from any cause. Patients who did not die while on study are censored at the last known date they were alive.
CI: confidence interval; EZFB: etrumadenant + zimberelimab + mFOLFOX6 + bevacizumab; OS: overall survival; PFS: progression-free survival; rego: regorafenib

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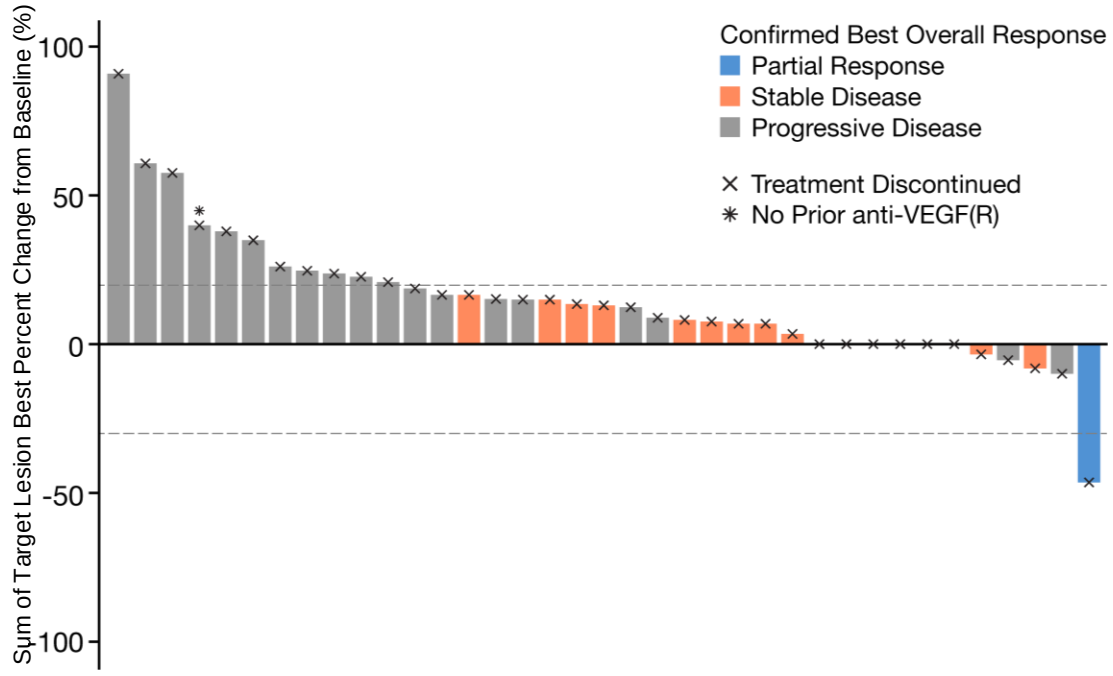
Two-Thirds (66%) of Patients on EZFB Experienced Tumor Reduction

EZFB



- Confirmed ORR for EZFB: 17.3%
- Median DOR for EZFB: 11.5 months

REGO



- Confirmed ORR for rego: 2.7%
- Median DOR for rego: N/A

ARC-9 - Wainberg et al. ASCO 2024, Jun. 2, 2022; data cut off of November 13, 2023
DOR was defined as the time from first documentation of confirmed disease response (CR or PR) until first documentation of progressive disease per RECIST v1.1.
DOR: duration of response; EZFB: etrumadenant + zimberelimab + mFOLFOX6 + bevacizumab; ORR: objective response rate; rego: regorafenib.

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EZFB Had an Acceptable Safety Profile, Consistent With Known Toxicity Profile of FOLFOX/bev in Combination With Anti-PD-1

n (%)	EZFB (N=74)	Rego (N=35)
Median treatment duration, weeks	26	7
Any TEAEs	73 (99)	31 (89)
Serious TEAEs	37 (50)	9 (26)
Grade ≥3 TEAEs	61 (82)	17 (49)
Any TEAEs leading to discontinuation of study drug	44 (59)	7 (20)
Leading to oxaliplatin discontinuation[a]	39 (53)[a]	-
Any TEAE leading to discontinuation of all study drugs	4 (5)	6 (17)
Any TEAEs leading to death	0	0
Any TEAEs that are immune-mediated reactions (per sponsor)[b]	12 (16)	2 (6)
≥3 event	4 (5)	0

Note: All-cause Grade 3+ AE rate for mFOLFOX6 + bev alone in 1L CRC of 67%; Serious AE rate for mFOLFOX6 +bev alone of 33%[1]. Grade 3+ TEAE rate for TAS-102 (Lonsurf) + bev was 72.4% in the SUNLIGHT Trial[2].

ARC-9 - Wainberg et al. ASCO 2024, Jun. 2, 2022; data cut off of November 13, 2023
Safety-evaluable population includes all enrolled patients who received any amount of any study treatment. TEAEs are any AEs that start on or after the study treatment start date/time and within 90 days of the last dose date for all zim arms (30 days for non-zim arms), excluding any AEs occurring after initiation of new anti-cancer therapy. Treatment related corresponds to any adverse event marked as related to etruma or zim or FOLFOX or bev or rego on the case report form.
a AEs leading to oxaliplatin discontinuation included: neuropathy, neutropenia, thrombocytopenia, and infusion reactions.
b Immune-mediated reactions programmatically identified via sponsor-defined preferred terms.
1. Schmoll et al 2012., Ph2/3 HORIZON III; 2. SUNLIGHT Ph3 Prager et al, Lancet 2023
AE: adverse event; etruma: etrumadenant; EZFB: etruma + zimberelimab + mFOLFOX6 + bevacizumab; rego: regorafenib; TEAE: treatment-emergent AE; zim: zimberelimab.

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Conclusions

This is the first randomized, Phase 2, proof-of-concept study showing EZFB significantly improves PFS and OS compared with standard of care in microsatellite-stable 3L mCRC

- **Longest OS reported for a randomized clinical trial in 3L mCRC**
- Meaningful improvement shown across all subgroups, **including 20-month median OS in patients with liver metastasis**
- **Tumor reduction was observed in two-thirds of patients**, with a clinically meaningful ORR and DOR for this latter line of treatment

Safety was consistent with the individual study drugs and manageable with no treatment related deaths

- Immune-mediated AE profile was consistent with that of anti-PD-1 antibodies

These encouraging results support further development of EZFB in CRC, including both late-line and early line settings

ARC-9 - Wainberg et al. ASCO 2024, Jun. 2, 2022; data cut off of November 13, 2023
AE: adverse event; 3L: third line; DOR: duration of response; EZFB: etruma + zimberelimab + mFOLFOX6 + bevacizumab; mCRC: metastatic colorectal cancer; ORR: objective response rate; OS: overall survival; PFS: progression-free survival;

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