# COMBINING TO CURE®

ASCO 2024 Investor Presentation

**June 2, 2024**

ARCUS BIOSCIENCES

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# Today's Speakers

- **Dr. Terry Rosen**
  Chief Executive Officer
- **Dr. Dimitry S.A. Nuyten**
  Chief Medical Officer
- **Jennifer Jarrett**
  Chief Operations Officer
- **Eric Matthews**
  Chief Commercial Officer

- **Dr. Zev Wainberg**
  Professor of Medicine

  Co-Director of GI Oncology Program

  University of California, Los Angeles

Available for Q&A

- **Dr. Juan Jaen**
  President
- **Bob Goeltz**
  Chief Financial Officer


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# Agenda

| | TOPIC | PRESENTER(S) | TIME |
|---|---|---|---|
| **Introduction** | • Arcus's Late-Stage Portfolio | Dr. Terry Rosen | 7:05PM |
| **Domvanalimab + Zimberelimab in Upper GI Cancers** | • GI Treatment Landscape<br>• EDGE-Gastric Updated Data | Dr. Dimitry S.A. Nuyten | 7:20PM |
| | • Line-of-Sight to Upcoming Launches | Eric Matthews | |
| **Casdatifan in ccRCC** | • RCC Treatment Landscape & Potential of Casdatifan | Dr. Dimitry S.A. Nuyten | 7:40PM |
| | • Upcoming Data & Commercial Opportunity | Eric Matthews | |
| **Etrumadenant in Colorectal Cancer** | • CRC Treatment Landscape<br>• ARC-9 Results | Dr. Zev Wainberg, UCLA | 8:05PM |
| | • Commercial Opportunity | Eric Matthews | |
| **Q&A** | | All | |


ccRCC: clear cell renal cell carcinoma; GI: gastrointestinal
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# Introduction





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# Multiple Late-Stage Programs and Opportunities to "Win"

**Dom (+ Zim)**
(anti-TIGIT + anti-PD-1)

**THREE*** PHASE 3 STUDIES UNDERWAY

- Potential to be first-in-class in upper GI cancer ($3B market opportunity) and best-in-class in NSCLC ($10B+ market opportunity)
- 12.9 - 13.8 months PFS in EDGE-Gastric is meaningfully higher than benchmark studies

**Casdatifan**
(HIF-2α)

AT LEAST **ONE** PHASE 3 STUDY IN PLANNING

- Mechanism validated through belzutifan approval
- Data from 30-patient 100 mg expansion cohort planned for 2H:24; Multiple datasets from additional expansion cohorts expected to follow
- Cas has potential for a best-in-class efficacy profile – and a differentiated development / combination strategy vs. belzutifan

**Quemli / Etruma**
(CD73 inhibitor / A2R antagonist)

**ONE** PHASE 3 STUDY IN PLANNING (PDAC)

- Three recent datasets support the potential of adenosine blockade to prolong survival when combined with chemotherapy
- ~20 months overall survival in ARC-9 data is unprecedented in all-comer 3L CRC, meaningfully above benchmark studies for this population

*includes STAR-121, STAR-221 and PACIFIC-8

2H: second half; 3L: third line; cas: casdatifan; CRC: colorectal cancer; dom: domvanalimab; etruma: etrumadenant; GI: gastrointestinal; NSCLC: non-small cell lung cancer; PDAC: pancreatic ductal adenocarcinoma; PFS: progression-free survival; quemli: quemliclustat; zim: zimberelimab


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# Multiple Late-Stage Programs, Addressing High Unmet Need

| | PHASE 1/2 STUDIES | PHASE 3 STUDY | INDICATION | PH 3 STUDY DETAILS | ADDRESSABLE PATIENTS[1] | MARKET POTENTIAL[2] |
|---|---|---|---|---|---|---|
| **DOM + ZIM**<br>Fc-silent anti-TIGIT MAb + anti-PD-1 MAb | EDGE-Gastric<br>mPFS presented at ASCO '24 | STAR-221 | **1L Gastric/GEJ/EAC - all comers** | dom + zim + chemo vs nivo + chemo | **103K** | **~$3B** |
| | ARC-7<br>Final PFS presented at ASCO '23 | STAR-121<br>Recruiting | **1L NSCLC – all comers** | dom + zim + chemo vs pembro + chemo | **303K** | **~$10B** |
| | EDGE-Lung<br>Enrolling dose-optimization cohorts | PACIFIC-8<br>Recruiting | **Stage 3 NSCLC** | dom + durva vs durva + placebo | **48K** | **~$2B** |
| **CAS**<br>HIF-2α small molecule inhibitor | ARC-20<br>100 mg expansion cohort data: 2H '24 | PEAK-1<br>Initiating 1H '25 | **Post-IO ccRCC** | To be announced | **20K** | **~$2B** |
| **QUEMLI**<br>Small molecule CD73 inhibitor | ARC-8<br>OS data presented Q1 '24 | PRISM-1<br>Initiating early '25 | **1L PDAC** | quemli + G/nP vs. G/nP | **106K** | **~$4B** |
| **ETRUMA**<br>Small molecule A2a & A2b receptor antagonist | ARC-9<br>OS data (3L cohort) presented ASCO '24 | **Next steps in planning** | **mCRC** | Next steps to be determined | **82K** | **~$2B** |

1. Drug Treatable Addressable Populations (G7, 2023); Decision Resources Group
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; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; chemo: chemotherapy; CRC: colorectal cancer; dom: domvanalimab; durva: durvalumab; EAC: esophageal adenocarcinoma; 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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# Arcus Broad Development is Enabled by Funding from our Partnerships and Clinical Collaborations

## GILEAD

- ✓ $1.7B invested to date
- ✓ Cost sharing on joint studies
- ✓ Opt-in fees, milestones and option continuation payments

STAR-221
STAR-121
EDGE-Gastric
ARC-9
EDGE-Lung
VELOCITY-Lung

## TAIHO PHARMA

- ✓ Cost sharing for patients enrolled in their region
- ✓ Opt-in fees and milestones

STAR-221
STAR-121

## AstraZeneca

- ✓ Cost sharing

PACIFIC-8

## EXELIXIS

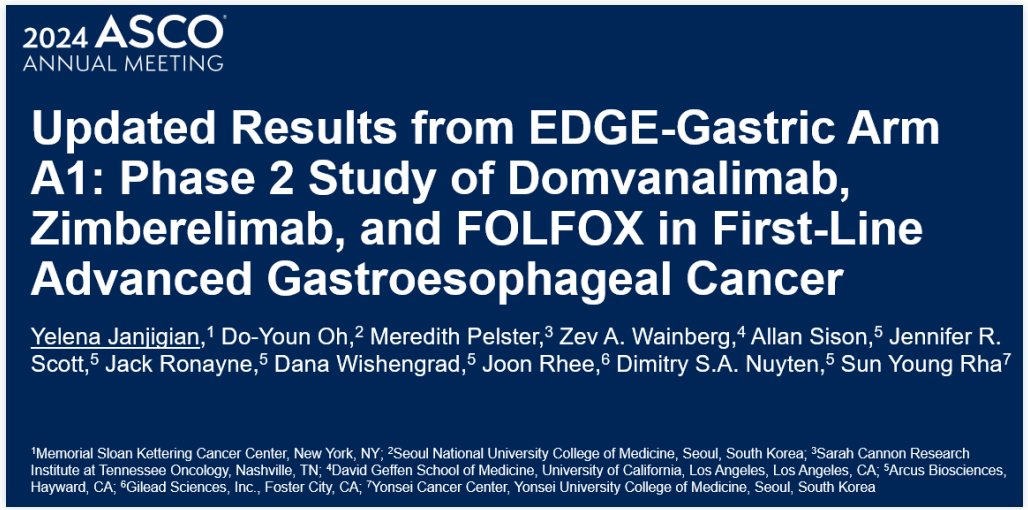
- ✓ Cost sharing

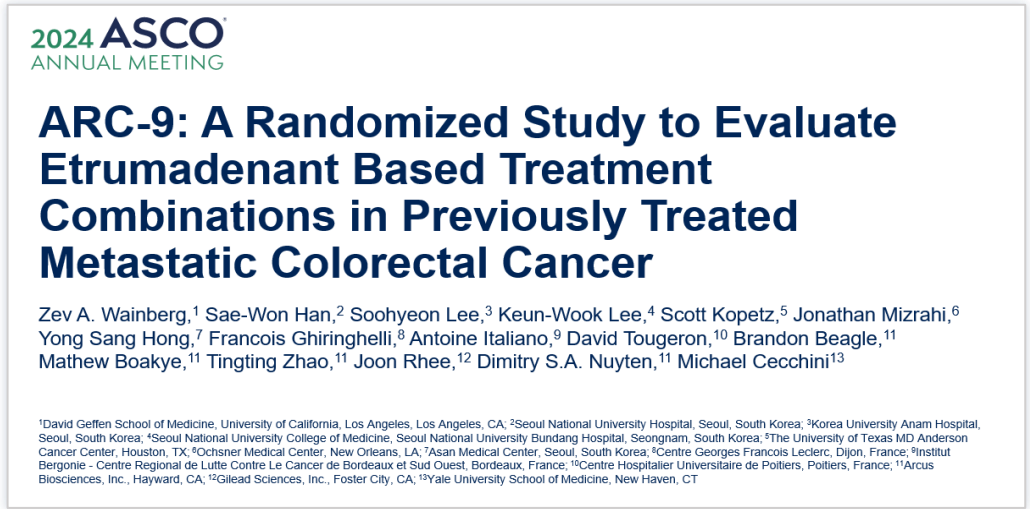
STELLAR 009

**$1.1B IN CASH AND EQUIVALENTS AS OF 3/31/24**


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# Two Datasets Presented Targeting GI Malignancies Will Be Discussed Today




## mPFS well beyond historical benchmarks of 7 to 8 months

- PD-L1-high*: **13.8 months**
- Overall: **12.9 months**

## Significant improvement in PFS and OS vs. rego

- mPFS: **6.2 months for EZFB vs 2.1 months for rego** (HR = 0.27)
- mOS: **19.7 months for EZFB vs 9.5 months for rego** (HR=.37)

EDGE-Gastric - Janjigian et al. ASCO 2024, Jun. 1, 2022; data cut off of March 12,2024
ARC-9 Wainberg et al., ASCO 2024; data cut-off of November 13,2023.
*PD-L1 high population population defined as TAP≥5
EZFB: etrumadenant + zimberelimab + mFOLFOX-6 + bevacizumab; GI: gastrointestinal; HR: hazard ratio; ITT: intent-to-treat; mOS: median overall survival; mPFS: median progression-free survival; rego: regorafenib ; TAP: tumor area positivity

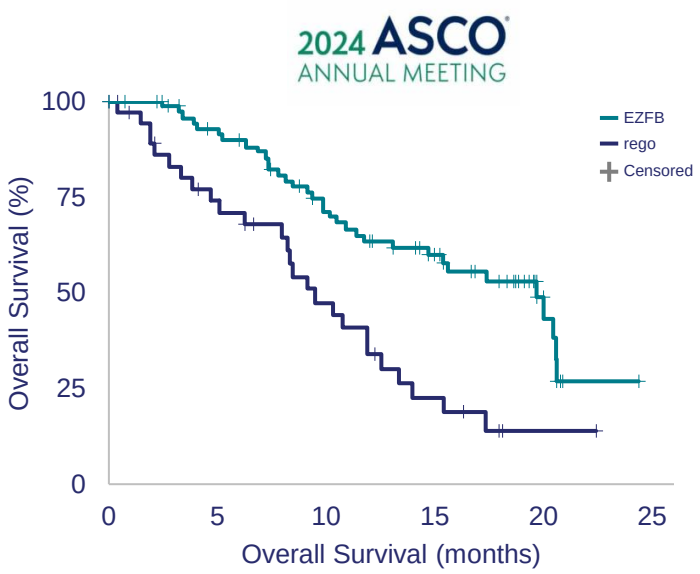

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# Three Datasets in Six Months Demonstrate the Potential Benefits of Combining Adenosine Blockade with Chemotherapy

## 3L Colorectal Cancer

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

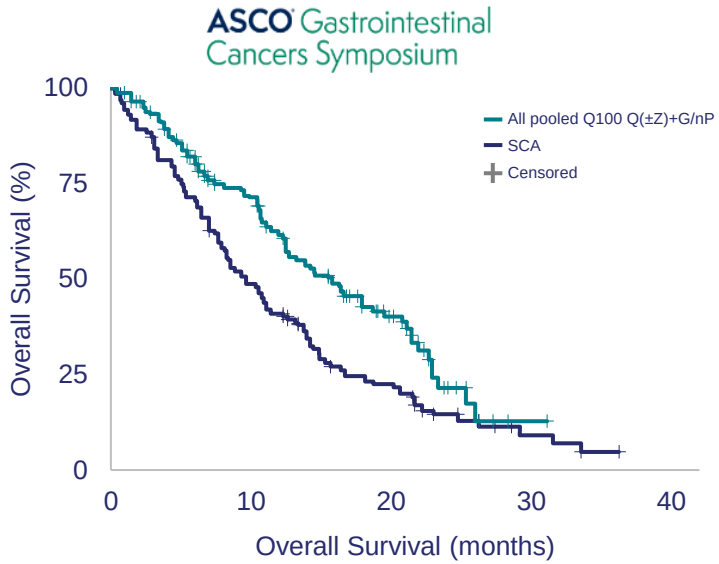
ARC-9




## 1L Metastatic PDAC

**quemli** ± zim + G/nP (n=122)

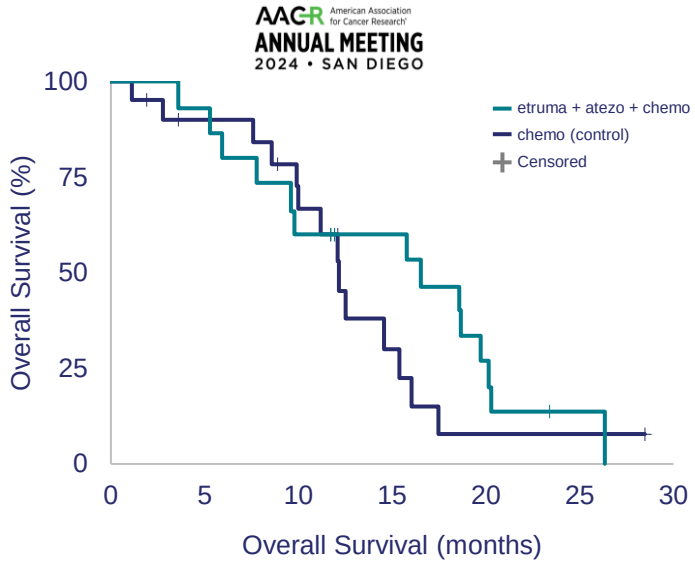
ARC-8




## 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)**

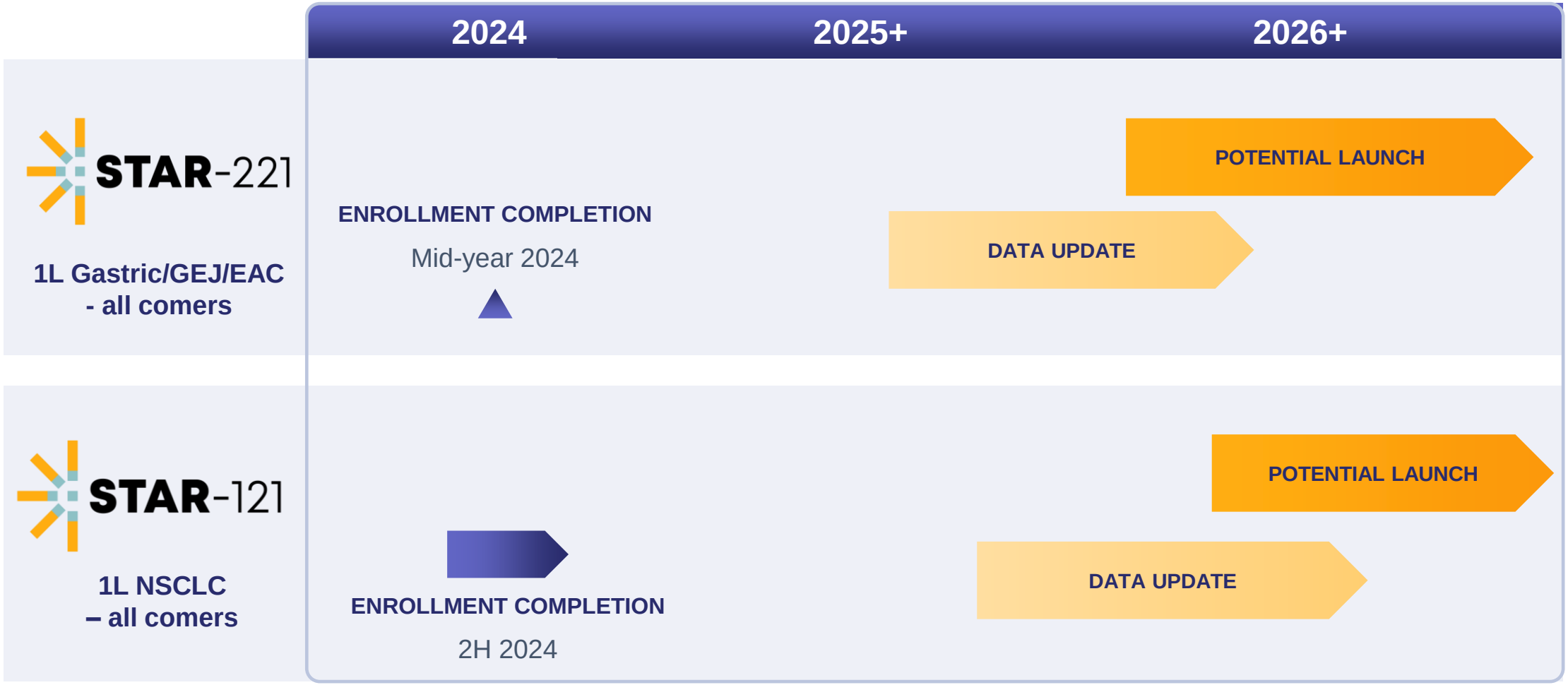
1L: first line; 3L: third line; atezo: atezolizumab; bev: bevacizumab; chemo: chemotherapy; E/etruma: etrumadenant; EZFB, etrumadenant + zimberelimab + mFOLFOX6 + bevacizumab; FOLFOX: oxaliplatin 85 mg/m2 IV; G/nP: gemcitabine/nab-paclitaxel; HR: hazard ratio; mOS: median overall survival; PDAC: pancreatic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



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# Approaching Pivotal Data & Launch Windows for Dom + Zim




1L: first line; 2H: second half; dom: domvanalimab; EAC: esophageal adenocarcinoma; GEJ: gastroesophageal junction; NSCLC: non-small cell lung cancer; zim: zimberelimab



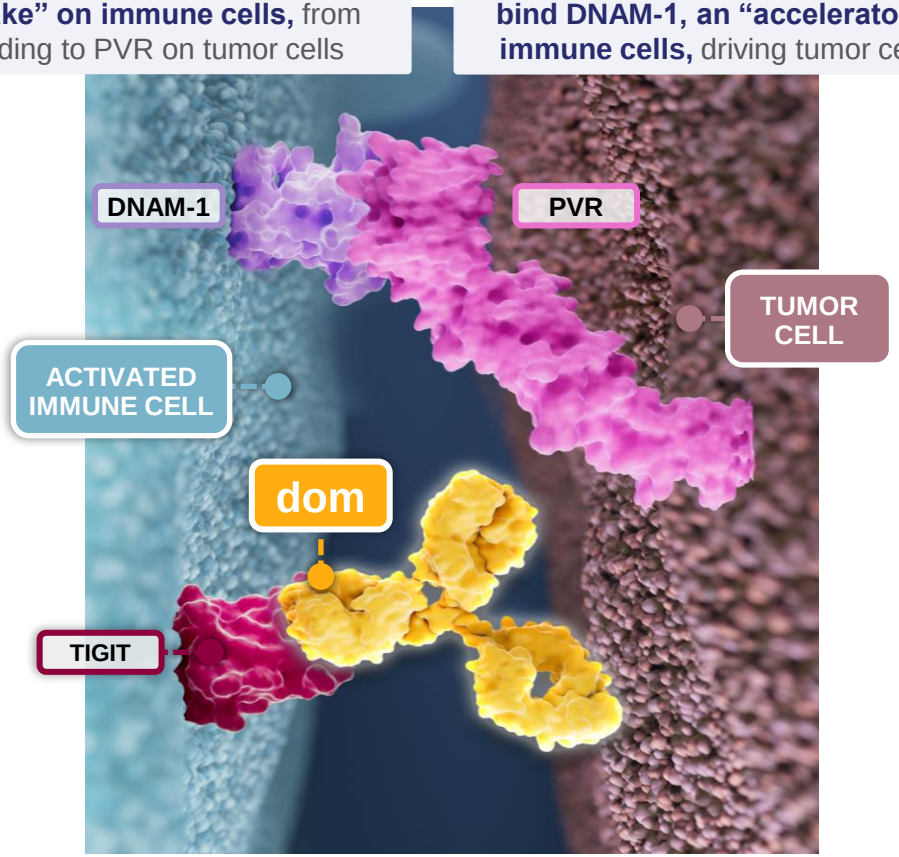
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# Dom is the Most Clinically Advanced Fc-Silent Anti-TIGIT Antibody in Development

## 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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# Domvanalimab + Zimbereliamb in Upper Gastrointestinal Cancers

ASCO 2024: Updated EDGE-Gastric Data

*Dr. Dimitry S.A. Nuyten*

*CMO, Arcus Biosciences*



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# Nivo + Chemo is Standard of Care in 1L HER2- Gastric / GEJ Based on CM-649; mPFS Consistently ~7-8 Months

## Efficacy Benchmarks in Phase 3 Studies Have Fallen in a Narrow Range

| RANDOMIZED TRIAL | TUMOR TYPE | REGIMEN | N | ORR | mDOR | mPFS | mOS |
|---|---|---|---|---|---|---|---|
| **CheckMate-649[1]** | 1L HER2- Gastric, GEJ, EAC | Nivo + Chemo (XELOX or FOLFOX) | 789 (ITT)<br>473 (CPS ≥ 5)<br>316 (CPS < 5) | 58% (ITT, n=603)<br>60% (CPS ≥ 5, n=378)<br>55% (CPS < 5) | 8.5m (ITT, n=350)<br>9.5m (CPS ≥ 5, n=226) | **7.7m (ITT)**<br>**7.7m (CPS ≥ 5)**<br>**7.5m (CPS < 5)** | 13.8m (ITT)<br>14.4m (CPS ≥ 5)<br>12.4m (CPS < 5) |
| **KEYNOTE-859[2]** | 1L HER2- Gastric, GEJ | Pembro + Chemo (FP or CAPOX) | 790 (ITT) | 51% (ITT)<br>61% (CPS ≥ 10) | 8.0m (ITT, n=405)<br>10.9m (CPS ≥ 10, n=169) | **6.9m (ITT)**<br>**8.1m (CPS ≥ 10)** | 12.9m (ITT)<br>13.0m (CPS ≥ 1)<br>15.7m (CPS ≥ 10) |
| **RATIONALE-305[3]** | 1L HER2- Gastric, GEJ | Tislelizumab + Chemo (XELOX or FP) | 501 (ITT)<br>274 (TAP ≥ 5) | 47% (ITT)<br>50% (TAP ≥ 5) | 8.6m (ITT, n=237)<br>9.0m (TAP ≥ 5, n=138) | **6.9m (ITT)**<br>**7.2m (TAP ≥ 5)** | 15.0m (ITT)<br>16.4m (TAP ≥ 5) |

1. Phase 3: Janjigian Lancet 2021 (12.1m minimum follow up)
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)

1L: first line; chemo: chemotherapy; CPS: combined positive score; EAC: esophageal adenocarcinoma; GEJ: gastroesophageal junction; IO: immuno-oncology; ITT: intent-to-treat; mDOR: median duration of response; mOS: median overall surivival; mPFS: median progression-free survival; nivo: nivolumab; ORR: overall response rate; pembro: pembrolizumab; TAP: tumor area positivity


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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 Mar 2024 data cutoff, the median follow-up was 13.9 months

Yelena Janjigian, MD, Memorial Sloan Kettering Cancer Center, New York, NY

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

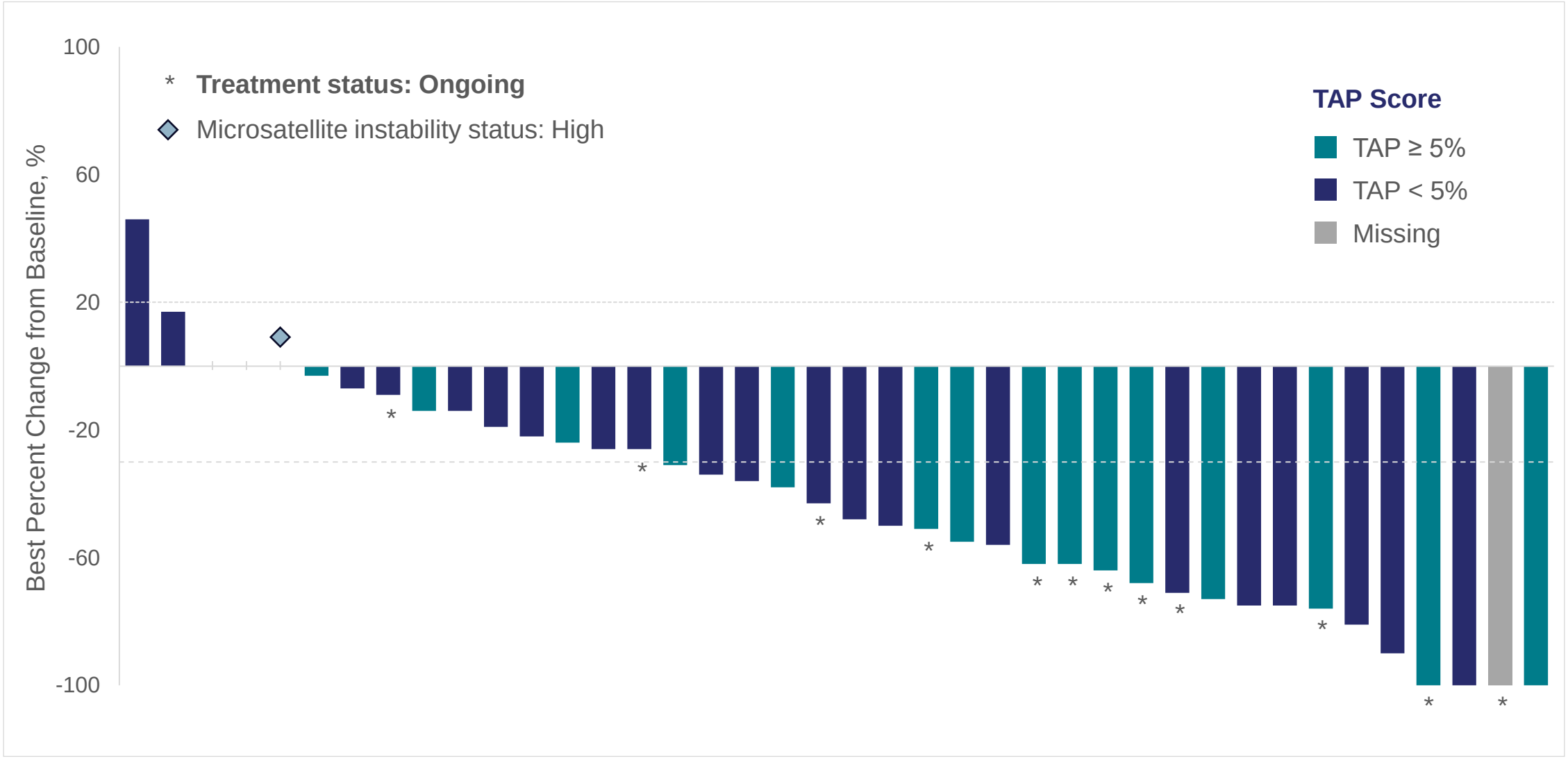
| | Arm A1 N=41, n (%) |
|---|---|
| **Mean age, years (range)** | 61 (30 to 82) |
| **Female** | 17 (41) |
| **Country** | |
| United States/France | 22 (54) |
| Korea | 19 (46) |
| **Baseline ECOG performance status 1** | 25 (61) |
| **Histologically confirmed diagnosis** | |
| Esophageal | 10 (24) |
| 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) |

Yelena Janjigian, MD, Memorial Sloan Kettering Cancer Center, New York, NY
* 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



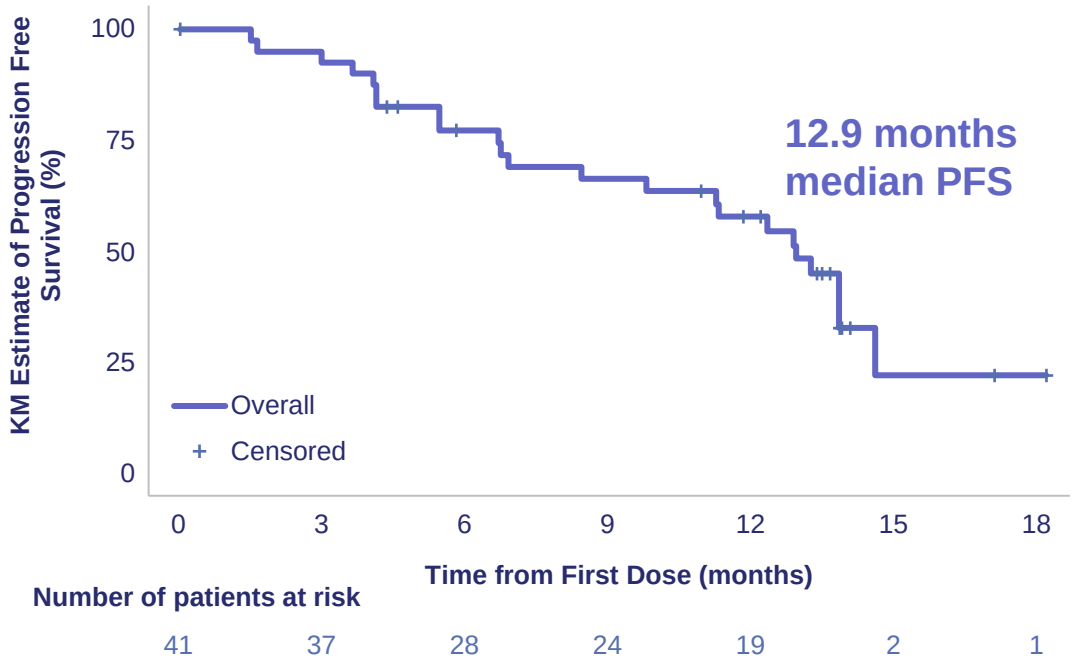

One patient had no tissue available for TAP central lab testing (grey bar). From local lab results, the patient was PD-L1 low via 22-C3 assay.
Yelena Janjigian, MD, Memorial Sloan Kettering Cancer Center, New York, NY
TAP: tumor area positivity


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# Unprecedented Median PFS of 12.9 months in the Overall Population

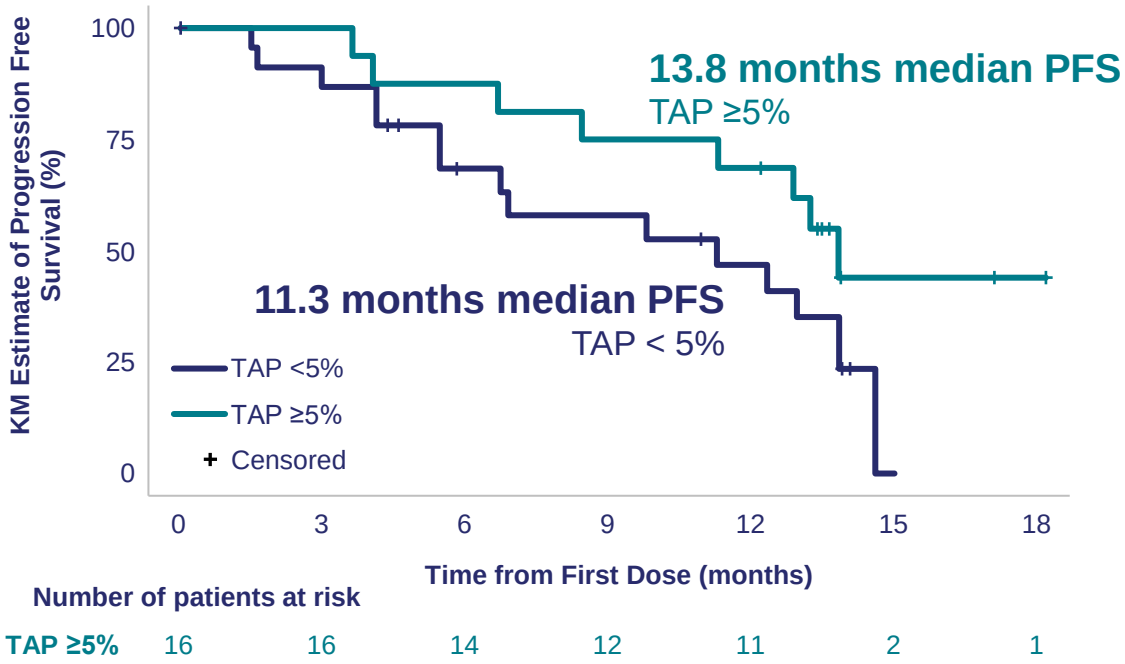
## Efficacy-Evaluable (N=41)

| | 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) |






Yelena Janjigian, MD, Memorial Sloan Kettering Cancer Center, New York, NY
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]<br>8.3m[5] | 8.1m | 7.2m |
| mDOR | ITT | **12.4m** | 8.5m | 8.0m | 8.6m |
| | PD-L1 High | **NE** | 9.5m[4]<br>9.6m[5] | 10.9m | 9.0m |
| ORR | ITT | **59%** | 58%[6] | 51% | 47% |
| | PD-L1 High | **69%** | 60% | 61% | 50% |

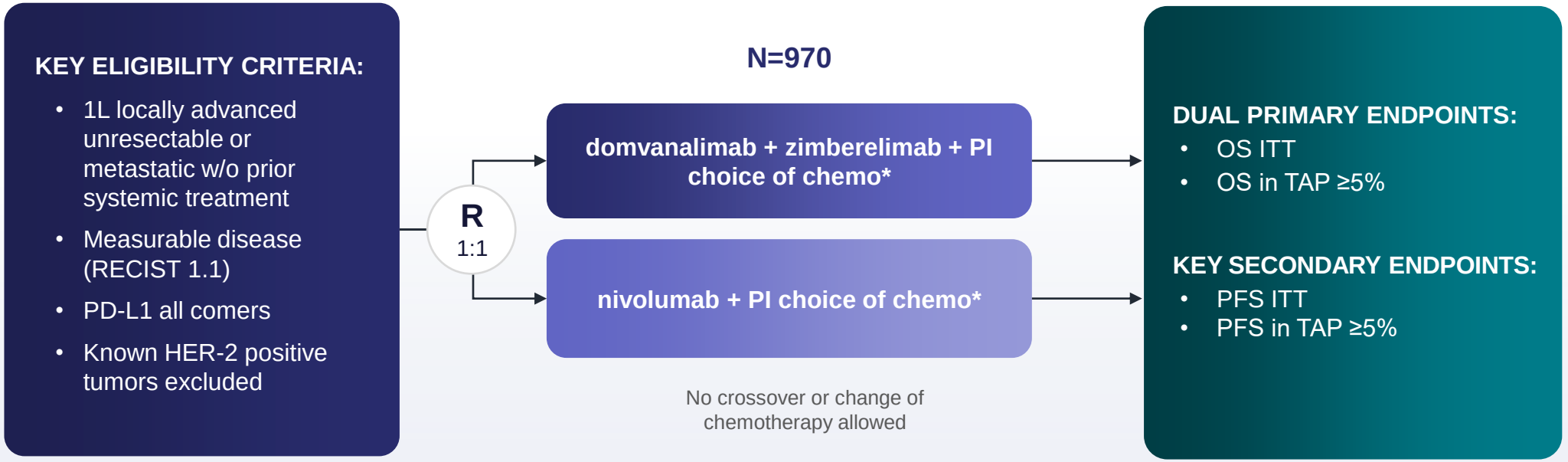
1. Phase 3: Janjigian, 2024. Shitara Nature 2022, Janjigian Lancet 2021, Moehler ASCO 2021 #4003 (36.2m, 24.0m, 12.1m, and 12.1m minimum follow up, respectively)
2. Phase 3: Rha, ESMO Virtual Plenary Feb 2023 and ASCO 2023 #4014 (31.0m median follow up)
3. Phase 3: Moehler, ASCO GI 2023 #286 (15.9m median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




*PI choice of chemo: FOLFOX or CAPOX.
NCT #: NCT05568095
Janjigian et al. ASCO Plenary Series, Nov. 7, 2023; data cut off of Sept. 4, 2023
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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# Domvanalimab + Zimberelimab in Upper Gastrointestinal Cancers: Competitive Landscape

Line-of-Sight to Upcoming Launches

*Eric Matthews*

*CCO, Arcus Biosciences*



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# First-to-Market Opportunity for Dom + Zim in 1L Gastric Cancer

## VALUE PROPOSITION:

- ✓ **First-to-Market opportunity, building on established standard of care**
- ✓ **Two shots on goal (All Comer, TAP ≥ 5)** with STAR-221 vs nivo + chemo SOC
- ✓ **Competitive landscape is quite open**
  - Uptake of anti-claudin 18.2 antibodies expected to be limited by testing, high rate of Gr3+ tox
- ✓ **Dom not expected to add significant AEs** on top of anti-PD-1 + chemo

| TAP <1 | TAP 1-5 | TAP ≥5 |
|---|---|---|
| ~25%[2] patients (26k) | ~30%[2] patients (32k) | ~45%[2] patients (48k) |
| **~$0.5B+** | **~$0.5B+** | **~$2B+** |

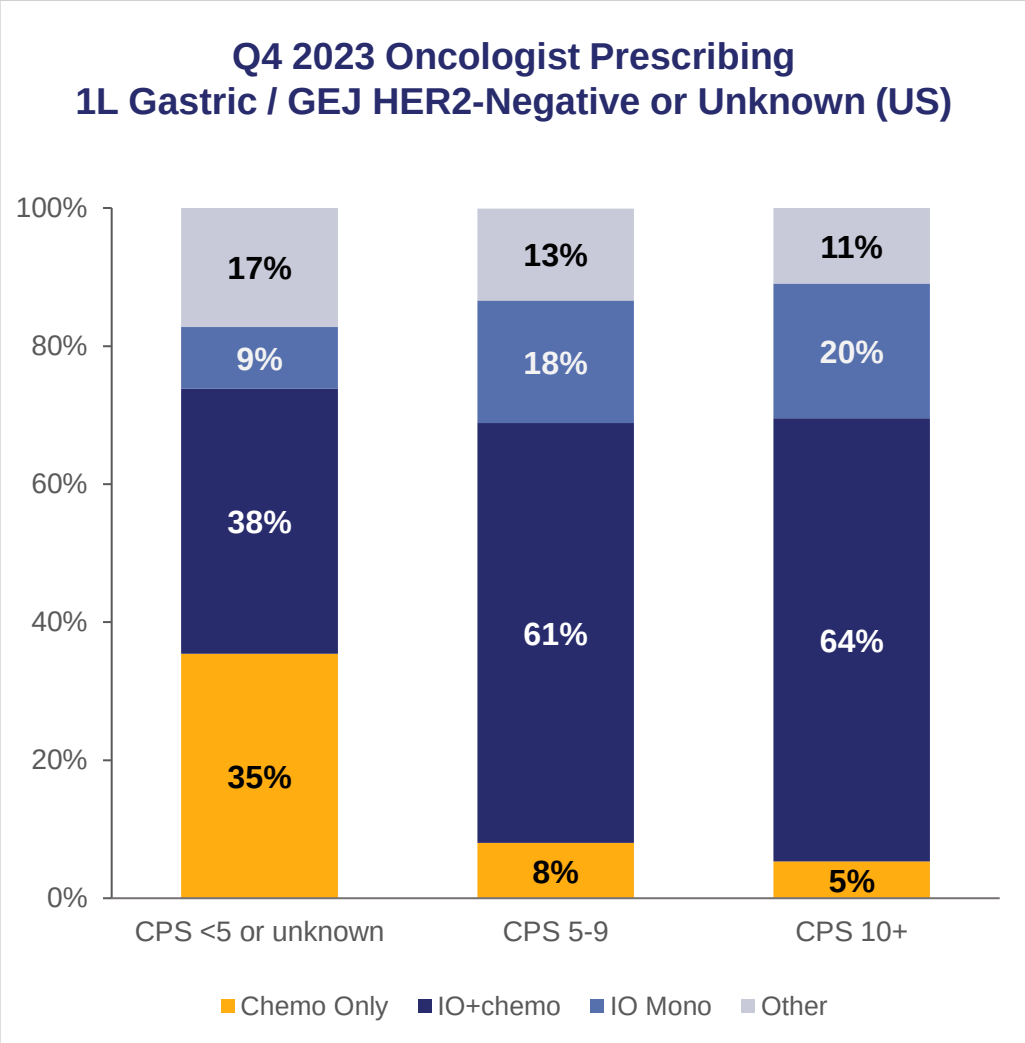
## COMMERCIAL OPPORTUNITY:

- ✓ **106k[1] G7 addressable market** for dom + zim to replace nivo, on top of standard-of-care
- ✓ **~$3B market potential, clear line-of-sight to launch window 2026+**
- ✓ **Rapid uptake of nivo + chemo** validates the potential for an IO doublet, and STAR-221 compares directly to nivo + chemo
- ✓ **Broad utility across market segments** enabled by dual primary endpoints
- ✓ **PD-L1 testing well-established** (>70% sites routinely test in the US)

1) 2023 Drug Treatable Patients, DRG
2) STAR-221 TAP analysis
1L: first line; chemo: chemotherapy; D/dom: domvanalimab; IO: immuno-oncology; nivo: nivolumab; SOC: standard of care; TAP: tumor area positivity; zim: zimberelimab


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# IO Was Rapidly Adopted as 1L SOC in Both Gastric and Esophageal Adenocarcinoma




G7 ADDRESSABLE POPULATION OF >100K PATIENTS
**PROVIDES A LARGE, GLOBAL OPPORTUNITY**

| | Gastric/GEJ (HER2-) | EAC |
|---|---|---|
| | 16k | 8k |
| | 30k | 9k |
| | 42k | 1k |

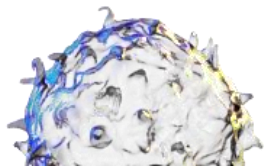
2023 Drug Treatable Patients, DRG

% Patients, Weighted by Patient Load | Arcus Primary Research, Q4 2023 | N = 84
Question: Please assume that you are currently managing 100 HER2-Negative or Unknown/Untested first-line metastatic patients CPS <5 or CPS is unknown, 100 patients CPS 5-9, and 100 patients CPS 10+. Please indicate the number of patients who would receive the following regimens in the first-line metastatic setting. Other includes Lonsurf (+/- chemo) & Cyramza (+/- chemo).
1L: first line; CPS: combined positive score; chemo: chemotherapy; EAC: esophageal adenocarcinoma; G7: Group of Seven; GEJ: gastroesophageal junction; IO: immuno-oncology; SOC: standard of care


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# Casdatifan in Renal Cell Carcinoma







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# Casdatifan in Renal Cell Carcinoma

Current Treatment Landscape

*Dr. Dimitry S.A. Nuyten*

*CMO, Arcus Biosciences*



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# 1L and 2L+ RCC Treatment Landscape

| 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**
- **HIF-2α mono**
  Post-progression on TKI
- **IO re-treatment**

**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; IO: immuno-oncology; mono: monotherapy; NCCN: National Comprehensive Cancer Network; RCC: renal cell carcinoma; TKI: tyrosine kinase inhibitor


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# LITESPARK-005 Data Established Belz as a New SOC in ccRCC

## Key Secondary Endpoint: ORR by BICR per RECIST 1.1

| | 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% |

Insufficient data for response assessment per RECIST 1.1 bNo post-baseline assessment available. *denotes statistical significance.
CR, complete response; PR, partial response. Data cutoff date for IA1: November 1, 2022. Data cutoff date for IA2: June 13, 2023.

**Enrolled only patients that had received 1–3 prior lines of therapy**

Formal data cut-off date of December 15, 2023. Unless otherwise noted, efficacy observations are made as of February 21, 2024.
Scans frequency for ARC-20 is every 6 weeks
*confirmed and unconfirmed ORR
1 Albiges L. et al. Abstract LBA88, ESMO 2023
BICR: blinded independent central review; ccRCC: clear cell renal cell carcinoma; CI: confidence interval; ORR: overall response rate; RECIST: Response Evaluation Criteria in Solid Tumors ;SOC: standard of care

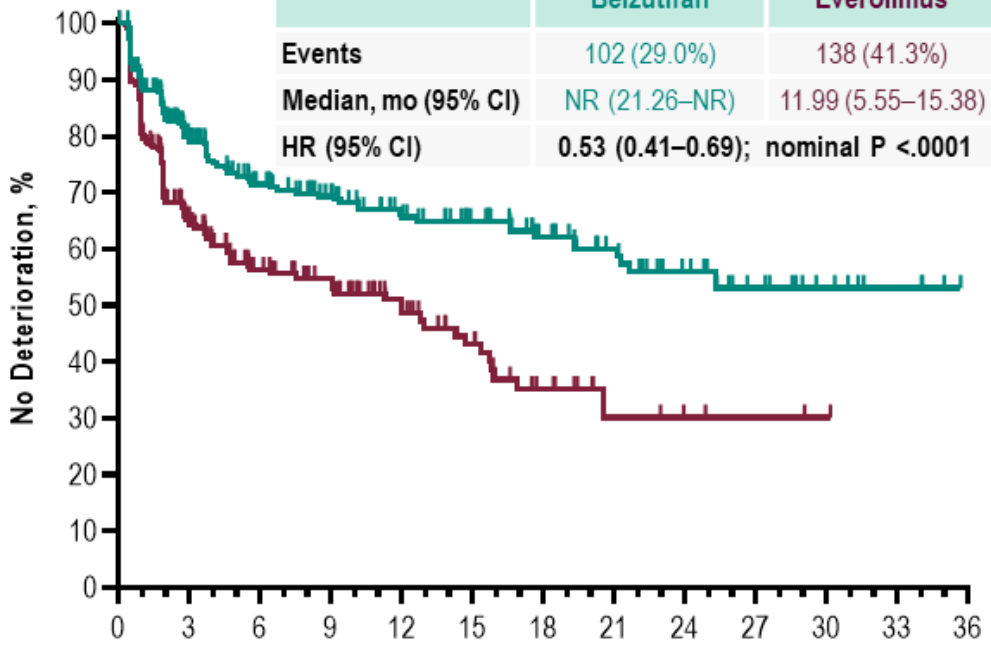

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# PROs Showed a Significant Benefit for Belzutifan over Everolimus

## Patient-Reported Outcomes: Time to Confirmed Deterioration

**FKSI-DRS: TTD**

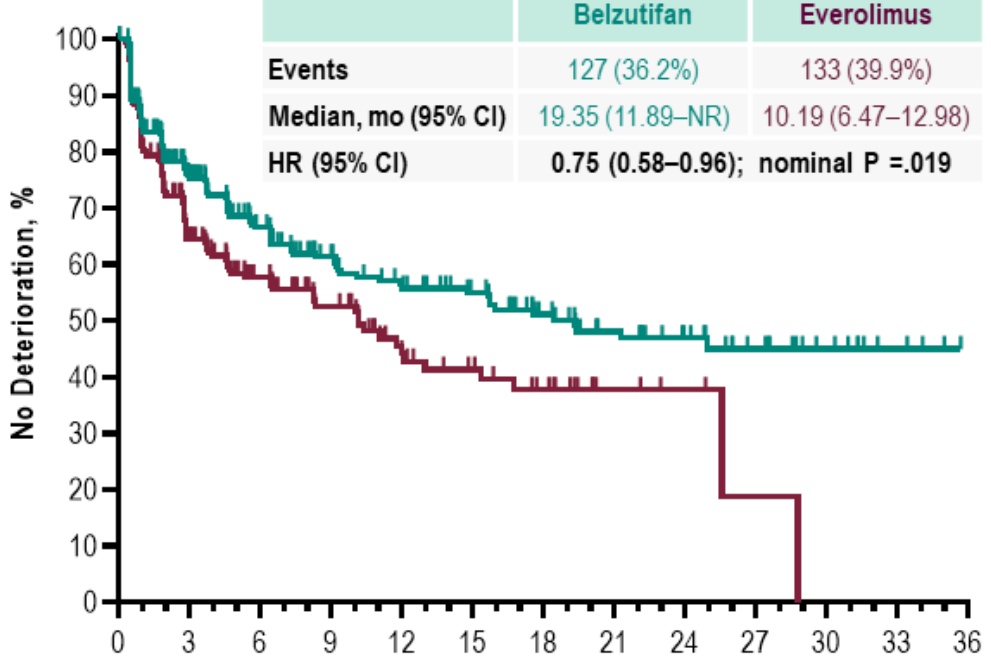
| | Belzutifan | Everolimus |
|---|---|---|
| Events | 102 (29.0%) | 138 (41.3%) |
| Median, mo (95% CI) | NR (21.26–NR) | 11.99 (5.55–15.38) |
| HR (95% CI) | 0.53 (0.41–0.69); nominal P <.0001 | |




| No. at Risk | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Belzutifan | 352 | 192 | 143 | 123 | 100 | 84 | 62 | 46 | 25 | 14 | 8 | 4 | 0 |
| Everolimus | 334 | 137 | 83 | 62 | 41 | 30 | 15 | 6 | 3 | 2 | 1 | 0 | 0 |

**QLQ-C30 GHS/QoL: TTD**

| | Belzutifan | Everolimus |
|---|---|---|
| Events | 127 (36.2%) | 133 (39.9%) |
| Median, mo (95% CI) | 19.35 (11.89–NR) | 10.19 (6.47–12.98) |
| HR (95% CI) | 0.75 (0.58–0.96); nominal P =.019 | |




| No. at Risk | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Belzutifan | 351 | 184 | 131 | 105 | 86 | 75 | 55 | 41 | 28 | 17 | 10 | 4 | 0 |
| Everolimus | 333 | 130 | 80 | 53 | 32 | 25 | 17 | 5 | 3 | 1 | 0 | 0 | 0 |

Time to confirmed deterioration (TTD) was defined as time from baseline to first onset of ≥3 points for FKSI-DRS or ≥10 points for EORTC QLQ-C30 with confirmation by the subsequent vist.
NR, not reached. Data cutoff date for IA2: June 13, 2023.



CI: confidence interval; HR: hazard ratio; PRO: patient reported outcomes

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# LITESPARK-013 Data Presented at ASCO Highlighted Lower ORRs in Patients with More Prior Lines of Therapy

**Background:** In the randomized phase 2 LITESPARK-013 study (NCT04489771), the first-in-class HIF-2α inhibitor belzutifan showed comparable antitumor activity in patients with pretreated advanced ccRCC at 200 mg and 120 mg doses (objective response rate [ORR]: 23.1% vs 23.7%; 1-sided *P*= 0.5312). We present results of a post hoc analysis of the pooled population (200 mg and 120 mg arms) across patient subgroups based on prior therapy and IMDC risk group.

**Results:** A total of 154 patients were enrolled (200 mg, n = 78; 120 mg, n = 76). In the pooled population, the median age was 64.0 years, 127 patients (82.5%) had intermediate/poor risk per IMDC criteria, 110 patients (71.4%) received 1-3 prior tyrosine kinase inhibitor (TKI) regimens, and 81 patients (52.6%) received 2 or 3 prior lines of therapy. As of the data cutoff date, 39 patients (25.3%) in the pooled population remained on treatment. Median follow-up was 20.1 months (range, 14.8-28.4). In the pooled population, ORR was 23.4% (95% CI, 16.9-30.9; 4 complete responses [CRs], 32 partial responses [PRs]) and median duration of response (DOR) was 16.1 months (range, 2.1+ to 23.5+). Additional efficacy analyses for subgroups are presented in the table.

| | ORR, % (95% CI) | DOR, Months (range) |
|---|---|---|
| 1 prior line of therapy<br>n = 73 | 28.8% (18.8-40.6); 3 CRs, 18 PRs | 16.1 (2.6+ to 18.4+) |
| 2 or 3 prior lines of therapy<br>n = 81 | 18.5% (10.8-28.7);<br>1 CR, 14 PRs | 10.2 (2.1+ to 23.5+). |
| Prior anti–PD-(L)1 regimens only<br>n = 44 | 34.1% (20.5-49.9);<br>3 CRs, 12 PRs | Not reached (3.7 to 23.5+) |
| Both prior anti–PD-(L)1 and TKI regimens<br>n = 110 | 19.1% (12.2-27.7);<br>1 CR, 20 PRs | 16.1 (2.1+ to 18.4+). |
| Received TKI regimens containing cabozantinib or lenvatinib<br>n = 40 | 20.0% (9.1-35.6);<br>0 CRs, 8 PRs | 8.4 (2.1+ to 16.1+) |
| Received other TKI regimens<br>n = 70 | 18.6% (10.3-29.7); 1 CR, 12 PRs | 16.1 (2.6+ to 18.4+). |
| Favorable IMDC risk<br>n = 27 | 29.6% (13.8-50.2);<br>0 CRs, 8 PRs | Not reached (2.9 to 15.2+) |
| Intermediate/poor IMDC risk<br>n = 127 | 22.0% (15.2-30.3);<br>4 CR, 24 PRs | 16.1 (2.1+ to 23.5+) |


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# Trial Inclusion Criteria From Other 2L+ RCC Studies

| STUDY DESCRIPTION | PHASE | INCLUSION CRITERIA | # OF LINES OF THERAPY | PRIOR TKI | PRIOR CPI |
|---|---|---|---|---|---|
| **LITESPARK-001**[1] | Ph 1 | • Locally advanced/metastatic ccRCC who previously received ≥1 therapy | • **Median 3 prior lines** | • **91% had prior VEGF TKI** | • 80% had prior CPI |
| **LITESPARK-005**[2] | Ph 3 | • Unresectable, locally advanced or metastatic ccRCC<br>• Disease progression after 1-3 prior systemic regimens, including ≥1 anti-PD-(L)1 and ≥1 VEGFR-TKI<br>• KPS score ≥ 70% | • **1-3 prior lines for inclusion**<br>• **Mostly 2-3 prior lines** | • **100% had prior TKI** | • 100% had prior CPI |
| **LITESPARK-013**[3] | Ph 2 | • Histologically confirmed advanced/metastatic RCC with clear cell component<br>• Measurable disease per RECIST v1.1<br>• Received ≤3 prior systemic therapies for advanced/metastatic disease<br>• Received only 1 prior anti-PD-1/L1 therapy | • **Mostly 1-2 prior lines** | • **71.4% had prior TKI** | • 100% had prior CPI |
| **ARC-20**[4] | Ph 1 | • Histologically confirmed ccRCC<br>• Must have received prior treatment in the metastatic setting (either individually or in combination) with anti-PD-1 and a TKI | • **30% of patients had >3 prior lines** | • **100% had prior TKI** | • 100% had prior CPI |
| **TIVO-3**[5] | Ph 3 | • Histologically or cytologically confirmed metastatic renal cell carcinoma with a clear cell component<br>• Previous unsuccessful treatment with two or three systemic regimens (one of which included a VEGFR-TKI other than tivozanib or sorafenib) | • **Mostly 2 prior lines** | • **100% had prior TKI** | • 27% had prior CPI |

1. belzutifan in previously treated ccRCC (Dose Expansion Cohort) (NCT02974738); refs: Jonasch et al 2024; Choueiri et al 2021; ASCO GU 2021 273
2. belzutifan vs. everolimus in previously treated ccRCC (NCT04195750); ref: ESMO 2023 LBA88
3. belzutifan 120mg vs. 200mg in previously treated ccRCC (NCT04489771); ref: ESMO 2023 1881O
4. casdatafan in previously treated ccRCC (NCT05536141); ref: ct.gov
5. tivozanib vs. sorafenib in previously treated ccRCC (NCT02627963); ref:Rini et al 2020

2L: second line; ccRCC: clear-cell renal cell carcinoma; CPI: checkpoint inhibitor; KPS: Karnofsky Performance Status; Ph: Phase; RECSIT: Response Evaluation Criteria in Solid Tumors; VEGFR-TKI: Vascular endothelial growth factor receptor-tyrosine kinase inhibitor


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# Casdatifan in Renal Cell Carcinoma

Upcoming Milestones and Commercial Opportunity

*Jennifer Jarrett, COO, Arcus Biosciences*

*Eric Matthews, CCO, Arcus Biosciences*



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# ARC-20 Study Design and Inclusion Criteria

## PH 1 DOSE ESCALATION

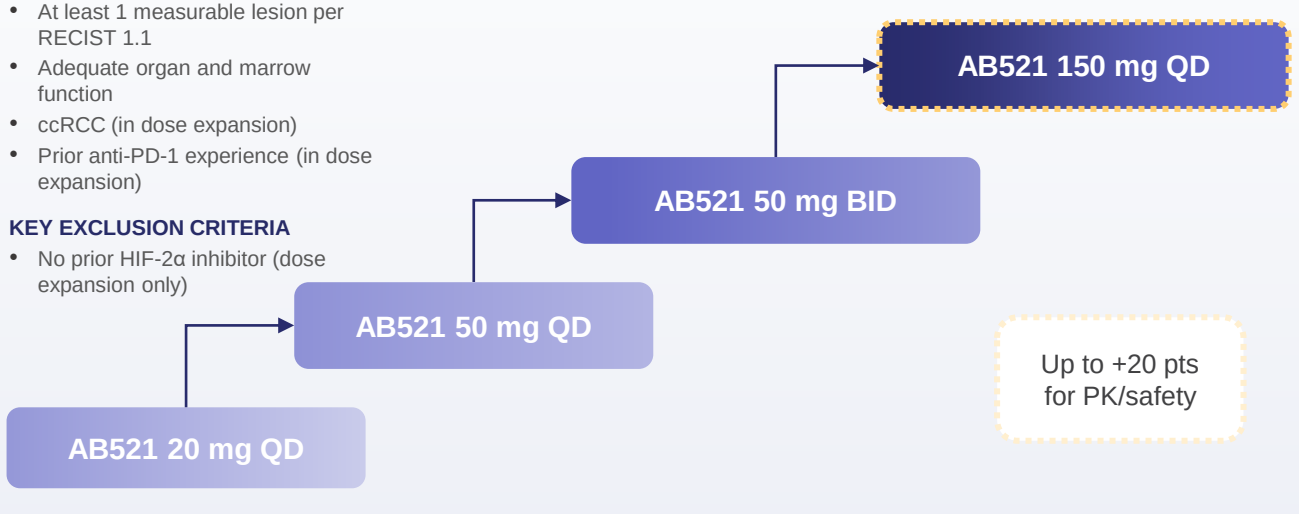
3+3 design with 21-day DLT window **Solid-tumor patients w/o SOC**

**KEY INCLUSION CRITERIA**

- At least 1 measurable lesion per RECIST 1.1
- Adequate organ and marrow function
- ccRCC (in dose expansion)
- Prior anti-PD-1 experience (in dose expansion)

**KEY EXCLUSION CRITERIA**

- No prior HIF-2α inhibitor (dose expansion only)




## EXPANSION COHORTS (2L+ ccRCC)

**50 mg (n=30)**
**COMPLETED ENROLLMENT**

**100 mg (n=30)**
**COMPLETED ENROLLMENT**

**150 mg (n=30)**
**ENROLLING**

**cas + cabo (n=30)**
**PLANNED**

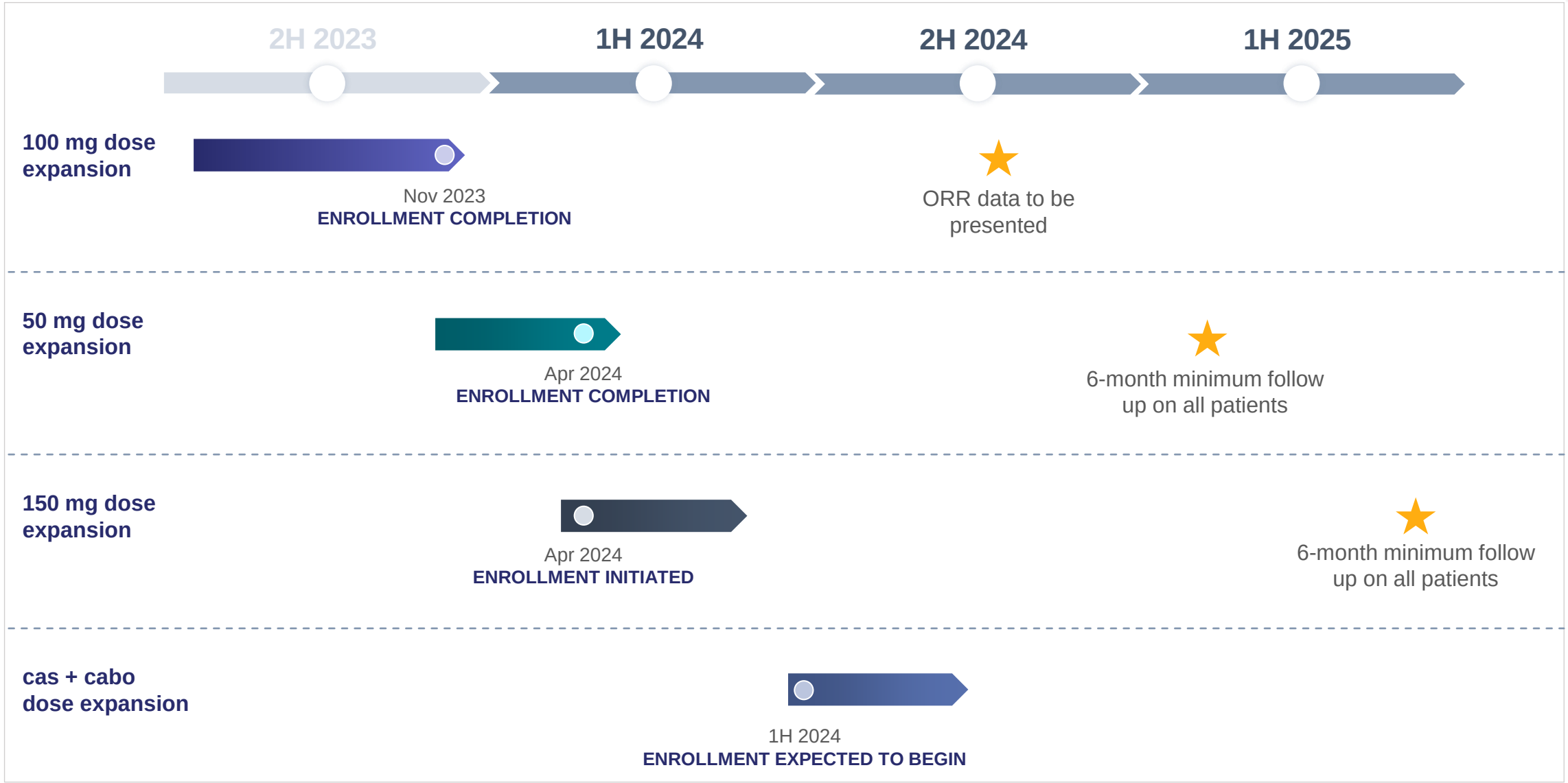
## CURRENT STATUS:

- Dose escalation enrolled 12 patients at the 20 mg QD, 50 mg QD and 50 mg BID doses, 4 of whom had ccRCC (across all three doses) as of Dec. 15, 2023
- **Data from the dose expansion cohort evaluating the 100 mg daily dose (n=30) to be shared 2H:24**

2L: second-line; 2H: second half; BID: twice daily; cabo: cabozantinib; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; DLT: dose limiting toxcicities; PD: pharmacodynamics; Ph: phase; PK: pharmacokinetics; QD: once daily; RECIST: Response Evaluation Criteria in Solid Tumors; SOC: standard of care


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# Multiple Casdatifan Datasets are Expected Over the Next 12 Months






1H: first half; 2H: second half; cabo: cabozantinib; cas: casdatifan; ORR: objective response rate

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# Value Proposition for Casdatifan (AB521), a Potential Best-in-Class HIF-2α Inhibitor

## EFFICACY

### Opportunity to reach greater intra-tumoral HIF-2α inhibition compared to 120 mg dose of belzutifan

**Potential to result in:**

- Lower rate of primary progressive disease
- Higher ORR
- More durable responses
- With a similar safety profile

## NOVEL COMBINATIONS IN 1L AND POST-IO SETTINGS

### Opportunity to create potentially best-in-class & first-in-class combinations

**Post-IO setting (including post-adjuvant):**

- Initiating a cas + cabo cohort in ARC-20
- Clinical collab with Exelixis to combine with zanza, their next-gen TKI

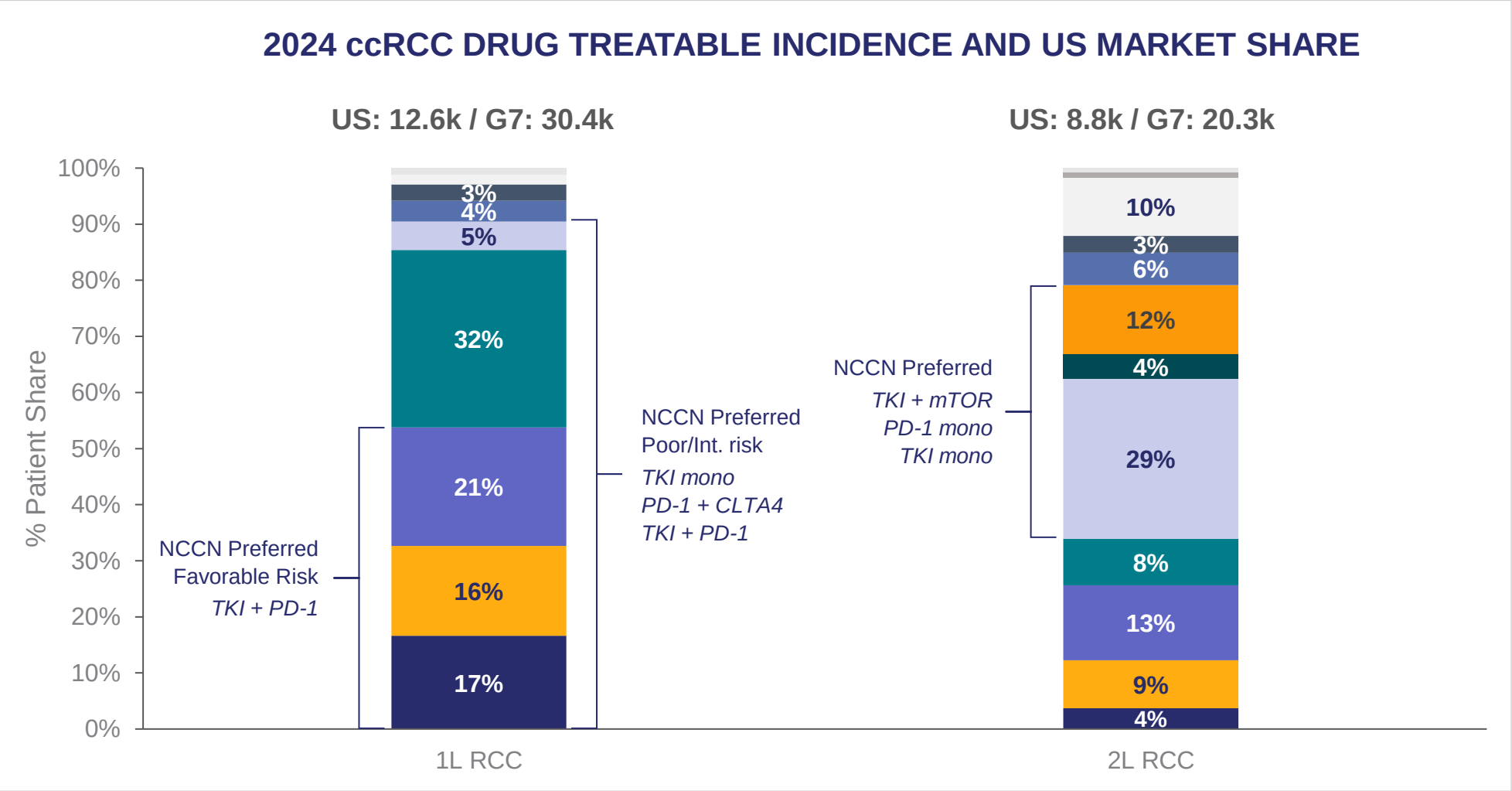
**More to come…**

1L: first line; cabo: cabozantinib; cas: casdatifan; IO: immuno-oncology; ORR: objective response rate; PD: pharmacodynamics; PK: pharmacokinetics; TKI: tyrosine kinase inhibitor; volru: volrustomig; zanza: zanzalintinib



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# RCC Treatment Landscape Favors Tailored Combination Therapies with Multiple TKIs




Sources - Epi: DRG, GlobalData | Share: Arcus primary research, US May 2024 (n=49)
Q1A: Please think of the metastatic clear cell renal cell carcinoma (ccRCC) patients that you have initiated on 1L treatment in the last 6 months. What percent (%) of patients were initiated on each of the following regimens:
Q2: Now please think of the metastatic clear cell renal cell carcinoma (ccRCC) patients that you have initiated on 2L treatment in the last 6 months. What percent (%) of patients were initiated on each of the following regimens:
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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# RCC Patients Have Typically Cycled Through Multiple TKIs Due to Lack of Other Treatment Options

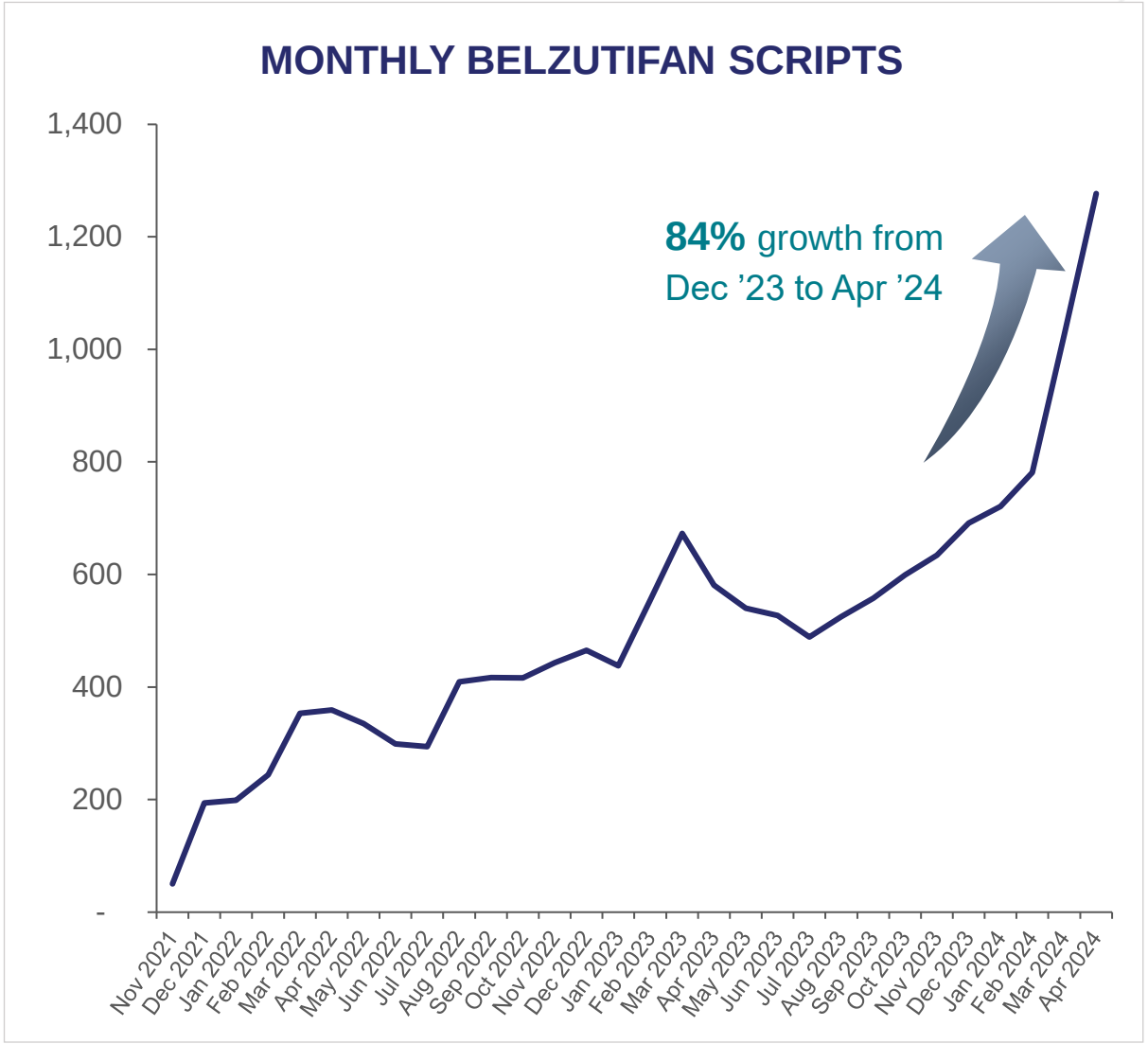
| TKI | GLOBAL 2023 SALES ($M)[1] | REGIMEN | PATIENT POPULATION | APPROVAL |
|---|---|---|---|---|
| **Cabozantinib** | **$2,254** | monotherapy | 1L intermediate-/poor-risk | U.S. (Dec. 2017)<br>E.U. (May 2018)<br>Jp (Mar. 2020) |
| | | nivolumab + cabozantinib | 1L | U.S. (Jan. 2021)<br>E.U. (Mar. 2021)<br>Jp (Aug. 2021) |
| **Lenvatinib** | **$2,199** | pembrolizumab + lenvatinib | 1L | U.S. (Aug. 2021)<br>E.U. (Nov. 2021)<br>Jp (Feb. 2022) |
| **Axitinib** | **$1,036** | pembrolizumab + axitinib | 1L | U.S. (Apr. 2019)<br>E.U. (Sep. 2019) |
| | | avelumab + axitinib | 1L | U.S. (May 2019)<br>E.U. (Oct. 2019)<br>Jp (Mar. 2020) |
| **Sunitinib** | **$180** | monotherapy | 1L | U.S. (Feb. 2007)<br>E.U. (Jan. 2007) |
| **Pazopanib** | **$390** | monotherapy | 1L/2L | U.S. (Oct. 2009)<br>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


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# Doubling of Belzutifan Scripts Since ccRCC Data Release in August 2023

- December 2023: Belzutifan received FDA approval for monotherapy in late-line ccRCC
- **Current Annual Run Rate of: ~$490M**
  - Increase in scripts driven by late-line monotherapy label only
- **Earlier stage settings, with HIF-2α-based combinations, will unlock even greater opportunity**




Source: IQVIA
ccRCC: clear cell renal cell carcinoma



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# Etrumadenant in Colorectal Cancer


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# Treatment Landscape

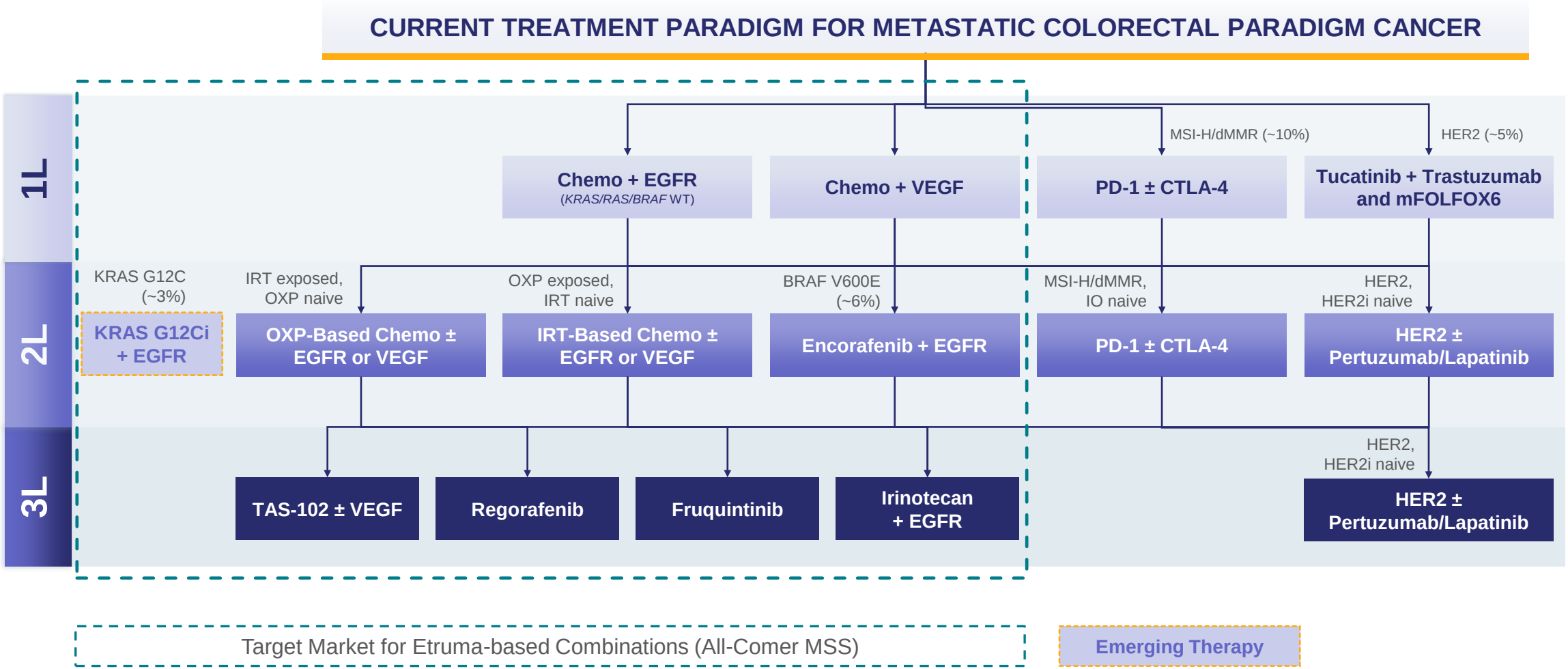
*Dr. Zev Wainberg*

*UCLA*



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# The Current mCRC Treatment Paradigm




*Adapted from NCCN guidelines.
1L: first line; 2L: second line; 3L: third line; 3L+: third line and beyond; chemo: chemotherapy; CTLA-4: cytotoxic T-lymphocyte associated protein 4; dMMR: mismatch repair deficient; EGFR: estimated glomerular filtration rate; HER2+/-, human epidermal growth factor receptor 2 positive/negative; HER2i: HER2 inhibitor; mCRC: metastatic colorectal cancer; MSI-H: microsatellite instability-high; MSS: microsatellite stable; NCCN: National Comprehensive Cancer Network; PD-1: programmed cell death protein-1; VEGF: vascular endothelial growth factor; WT: wild type


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# Phase 3 Benchmarks in 3L+ mCRC Shows mOS Up to 10.8 Months

| STUDY | REGIMEN | N | ORR | mPFS | mOS |
|---|---|---|---|---|---|
| **CORRECT[1] Phase 3** | Regorafenib vs. placebo[1] | 505 (rego)<br>255 (placebo) | 1.0% (5 PR, rego)<br>0.4% (1 PR, placebo) | 1.9m (rego)<br>1.7m (placebo) | **6.4m** (rego)<br>**5.0m** (placebo) |
| **RECOURSE[2] (NCT01607957)** *Phase 3* | TAS-102 (Lonsurf) vs. placebo[2] | 534 (TAS-102)<br>266 (placebo) | 1.6% (n=8 PR/502**, TAS-102)<br>0.4% (n=1 CR/n=258**, placebo) | 2.0m (TAS-102)<br>1.7m (placebo) | **7.2m** (TAS-102)<br>**5.2m** (placebo) |
| **SUNLIGHT[3] Phase 3** | TAS-102 (Lonsurf) + bev vs TAS-102[3] | 246 (TAS-102 + bev)<br>246 (TAS-102) | 6.1% (15 PR, TAS-102 + bev)<br>1.2% (1 CR + 2 PR, TAS-102) | 5.6m (TAS-102 + bev)<br>2.4m (TAS-102) | **10.8m** (TAS-102 + bev)<br>**7.5m** (TAS-102) |

1. Patients who progressed on or within 3m of last administration or were intolerant to standard therapies, including FP, oxa, iri, bev, and cetux/panitumumab (if RASwt); Source: Ph3 Grothey et al, Lancet 2012 and Stivarga Package Insert
2. Patients with two prior lines of chemotherapy which included FP, oxa, iri, bev, cetux/panit (if KRASwt) and progression within 3 months, or intolerance. Adjuvant chemo could be included if the tumor recurred within 6 months; Source: Ph3 Mayer et al, Lancet 2015
3. Patients with no more than two prior treatment regimens (which must have included a FP, Iri, OxPt, VEGF, and/or an EGFR for patients with RASwt and could have included adjuvant chemo if disease had recurred during treatment or within 6 months of the last administration of neo(adjuvant) therapy), and who had progressive disease or were intolerant Source: Ph3 Prager et al, Lancet 2023

Note:* safety population; **efficacy population

3L+: third line and beyond; bev: bevacizumab; CRC: complete response; mCRC: metastatic colorectal cancer; mPFS: median progression-free survival; mOS: median overall survival; ORR: objective response rate; rego: regoragenib; PR: partial response


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# Oxaliplatin Re-Treatment Data in 3L+ mCRC Show mOS of 7-13 Months, with the Vast Majority of Studies Showing ~10 Months

**19** STUDIES ASSESSED

**14** STUDIES INCLUDED
(4 prospective, 10 retrospective)

**665** TOTAL N-SIZE
(across studies)

**1997-2018**
TIME FRAME (across studies)

| mPFS (average, median) | mOS (average, median) |
|---|---|
| **3.8m, 3.7m** | **9.9m, 10.1m** |

### Prospective Study Inclusion/Exclusion Criteria (n=4)

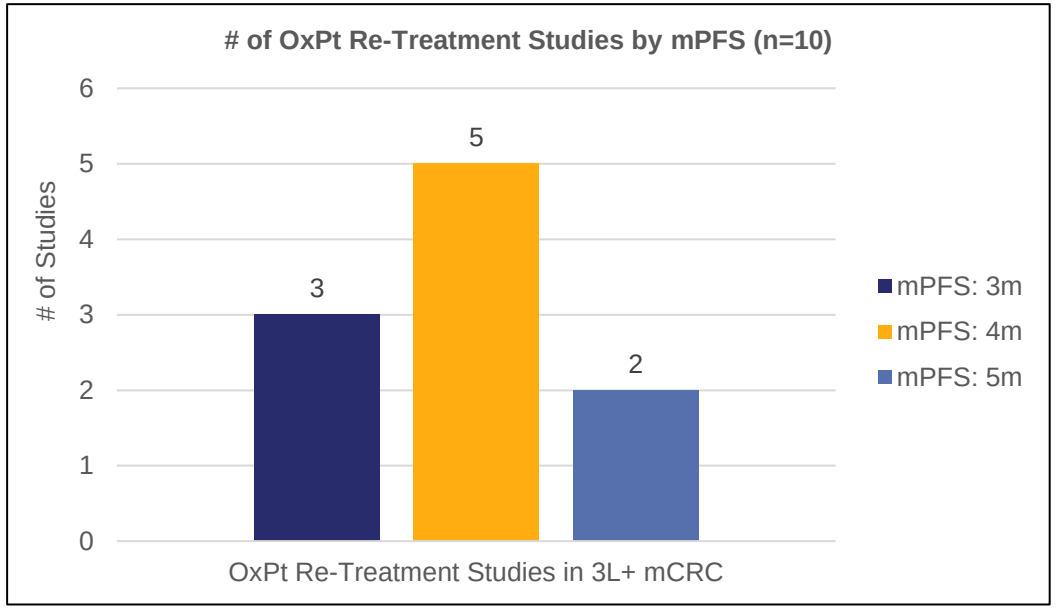
- 3/4 required response of SD or better on prior oxaliplatin
- 2/4 required 6+ month oxaliplatin free interval
- 3/4 excluded patients with severe peripheral neuropathy or peripheral sensory neuropathy

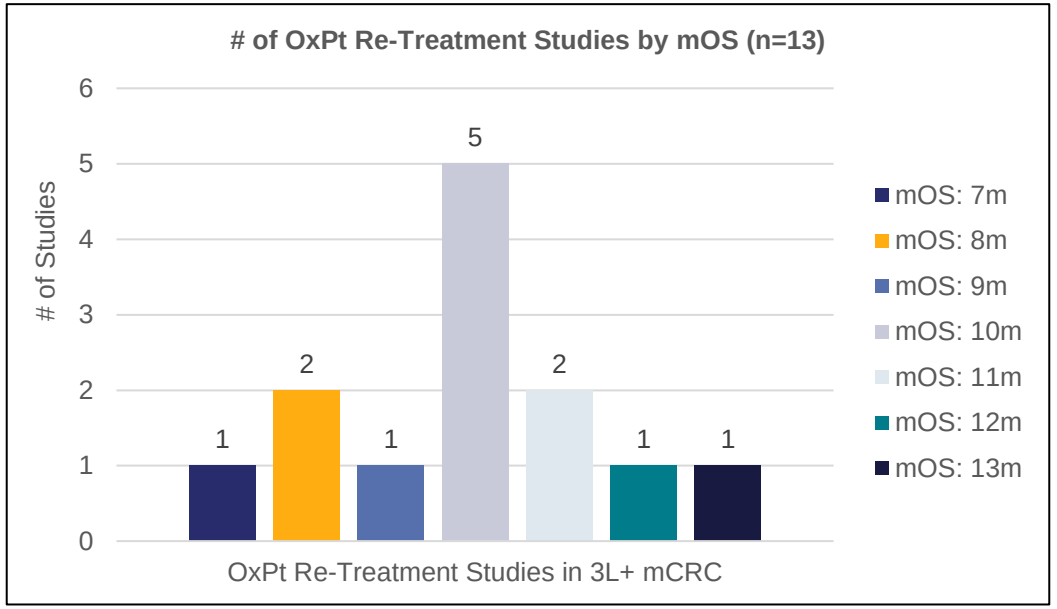
3L+, third line and beyond; m, months; mCRC, metastatic colorectal cancer; m, months; mPFS, median progression-free survival; mOS, median overall survival; SD, stable disease

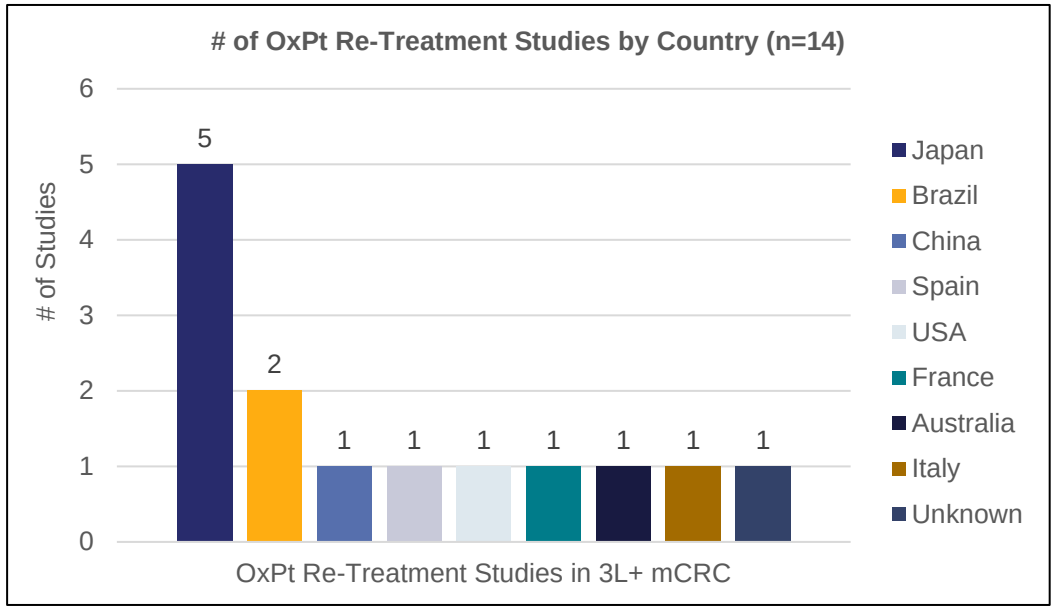


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# Summary of OxPt (+bev) Re-Treatment Data in 3L+ mCRC




- # of Studies Assessed: 19
- **# of Studies Included: 14 (4 prospective, 10 retrospective)**

- Prospective Study Inclusion/Exclusion Criteria (n=4):
  - 4/4 required Prior OxPt
  - 3/4 required response of SD or better on prior OxPt
  - 2/4 required 6+ month OxPt free interval
  - 3/4 excluded patients with severe peripheral neuropathy or peripheral sensory neuropathy

- **mPFS (average, median, and mode): 3.8m, 3.7m, ~4m**
- **mOS (average, median, and mode): 9.9m, 10.1m, ~10m**

- Total n-size (across studies): 665 (from 1997-2018)

3L+: third line and beyond; bev: bevacizumab; mCRC: metastatic colorectal cancer; mOS: median overall survival; mPFS: median progression-free survival; OxPt: oxaliplatin; SD: stable disease; See appendix for references



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# ARC-9 Cohort B Results

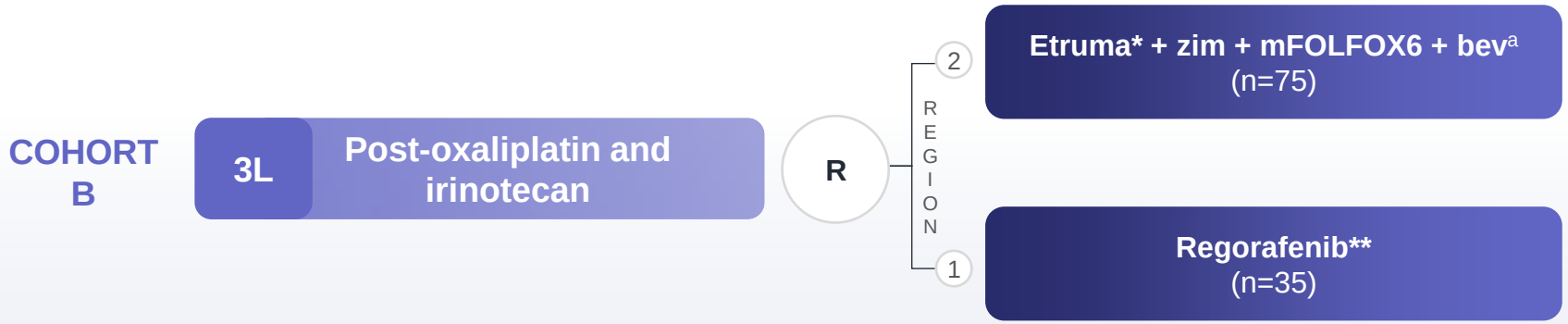
*Dr. Zev Wainberg*

*UCLA*



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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

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

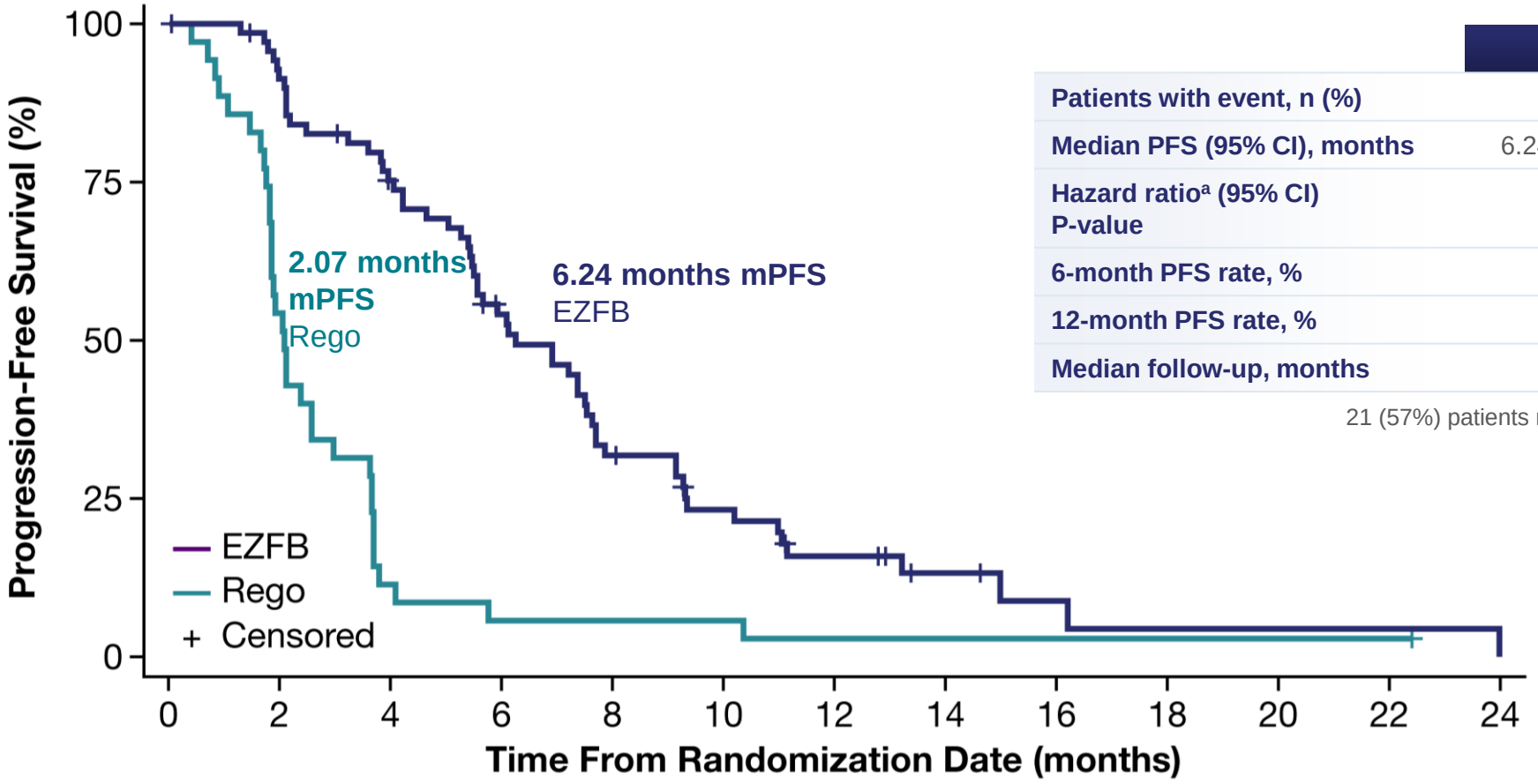
- Patients previously performed in-line with expectations for FOLFOX + bev in  prior lines
- Prior performance in FOLFOX was well-balanced between arms

| | 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) |

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

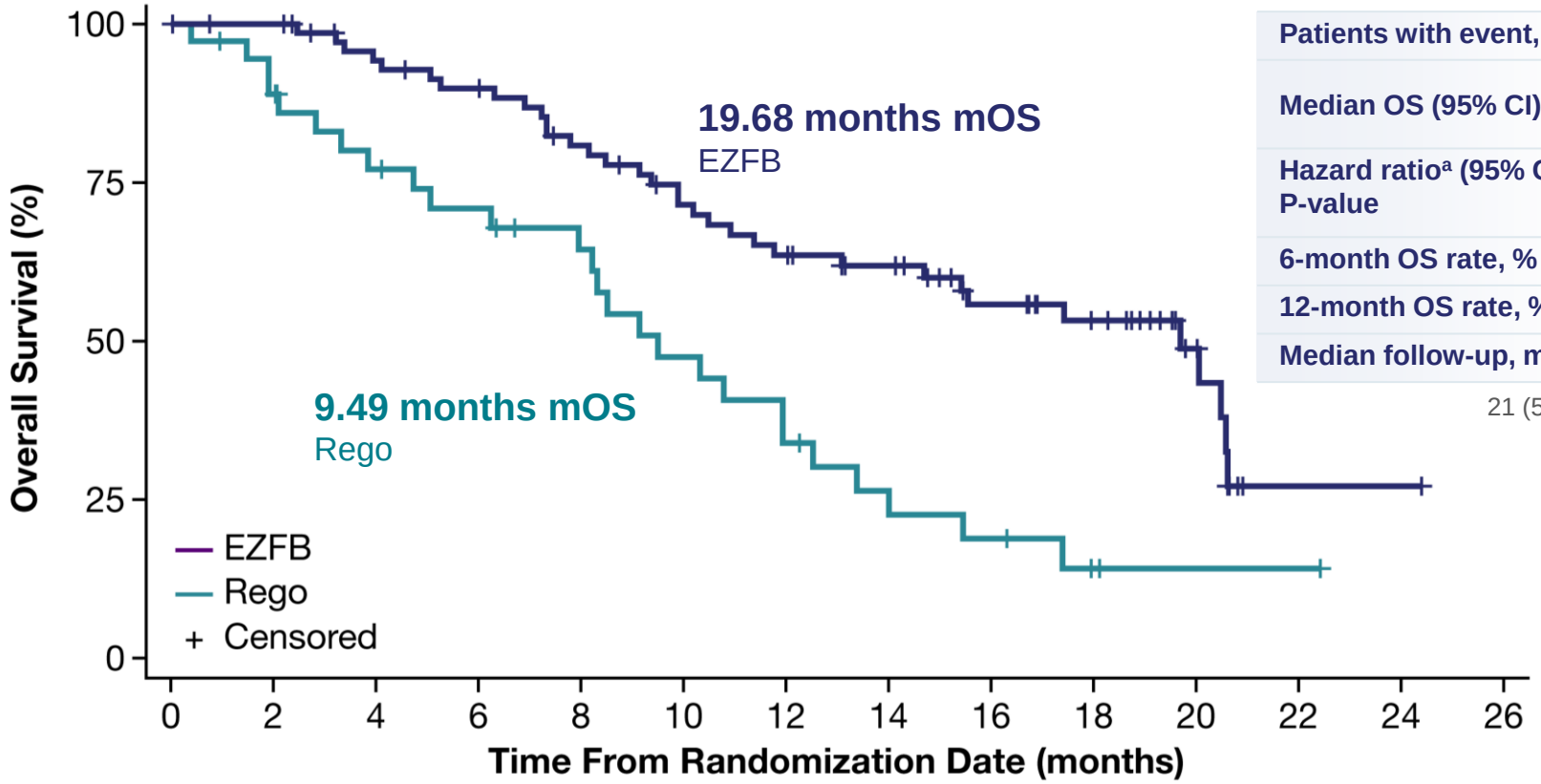
**Number of patients at risk**

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **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 |

Date cutoff date: 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




| | 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

**Number of patients at risk**

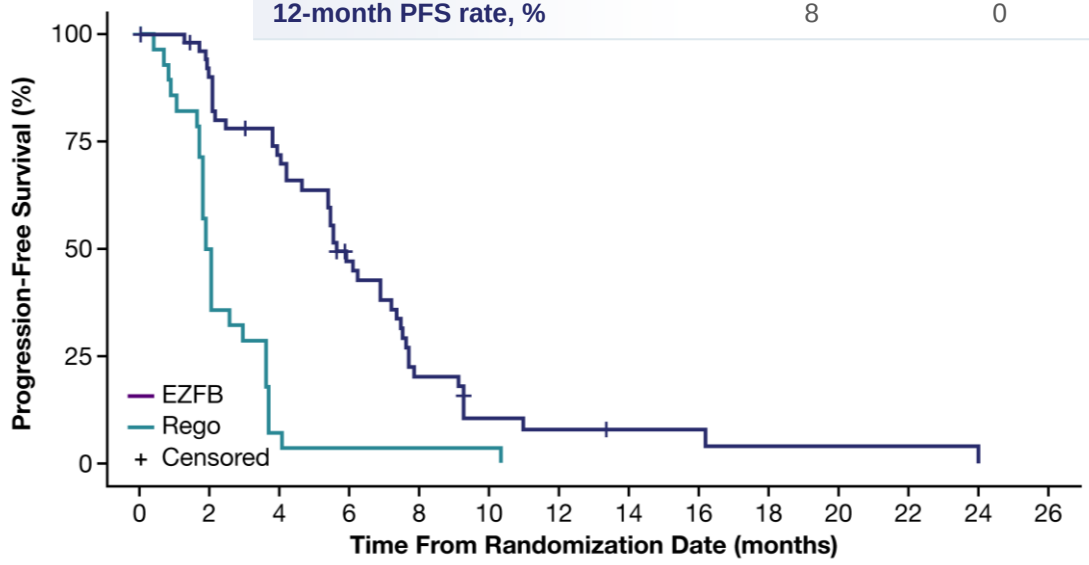
| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **EZFB** | 75 | 73 | 65 | 61 | 53 | 45 | 40 | 35 | 26 | 20 | 10 | 1 | 1 |
| **Rego** | 37 | 32 | 26 | 23 | 19 | 14 | 10 | 6 | 5 | 2 | 1 | 1 | 0 |

Date cutoff date: 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

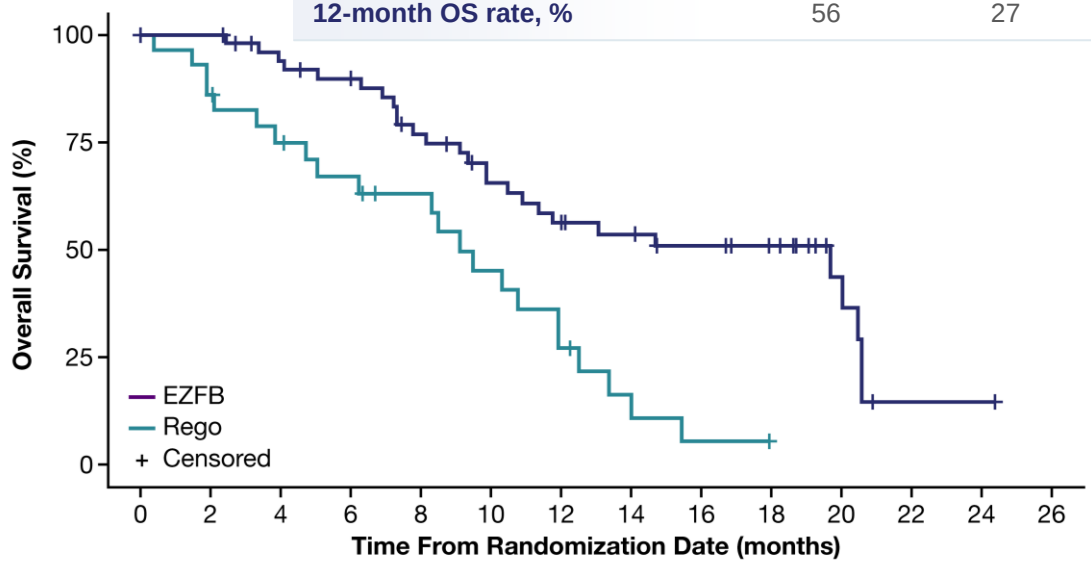
| | EZFB | Rego |
|---|---|---|
| Patients with events , n (%) | 45 (85) | 28 (97) |
| Median PFS, months | 5.65 | 1.97 |
| Hazard ratio (95% CI) | 0.19 (0.10, 0.35) | |
| 6-month PFS rate, % | 47 | 4 |
| 12-month PFS rate, % | 8 | 0 |




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

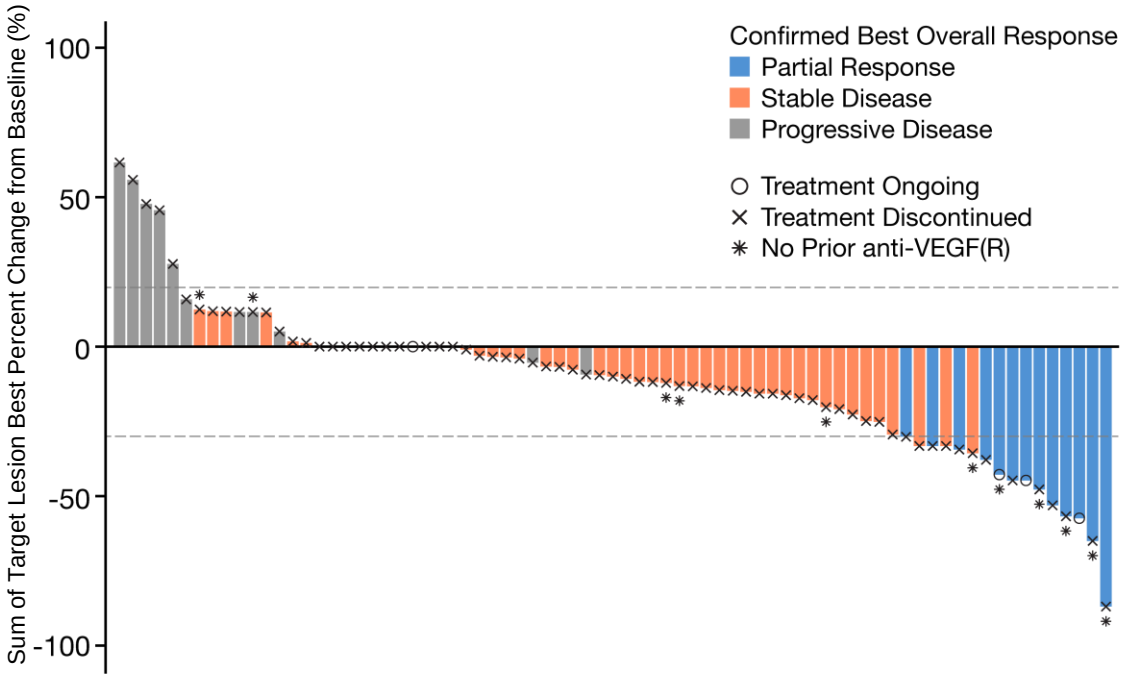
| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| EZFB | 53 | 52 | 46 | 43 | 35 | 28 | 24 | 21 | 18 | 13 | 6 | 1 | 1 | 0 |
| Rego | 29 | 25 | 20 | 17 | 14 | 10 | 6 | 2 | 1 | 0 | | | | |

Date cutoff date: 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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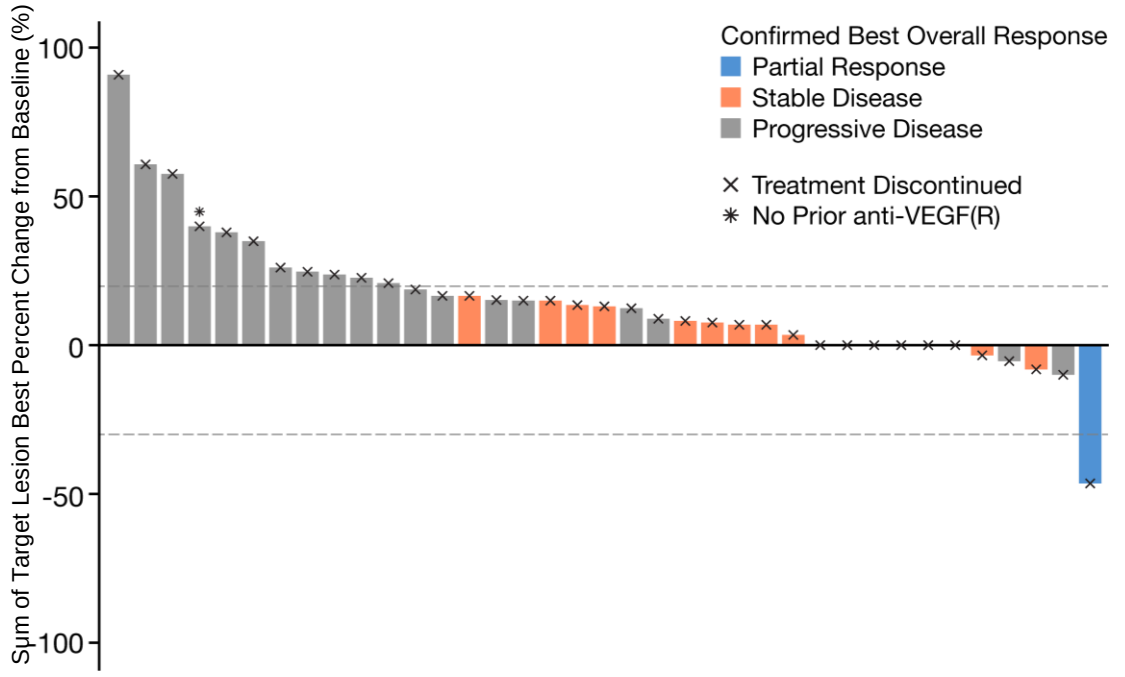
# Two-Thirds (66%) of Patients on EZFB Experienced Tumor Reduction

## 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

Date cutoff date: 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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# Case Study 1: 68 Year-old Male

## PATIENT DETAILS: 68 Year-old Asian Male

**DIAGNOSIS (MAR 2020):** Stage IVB rectal Cancer

## PRIOR REGIMENS:

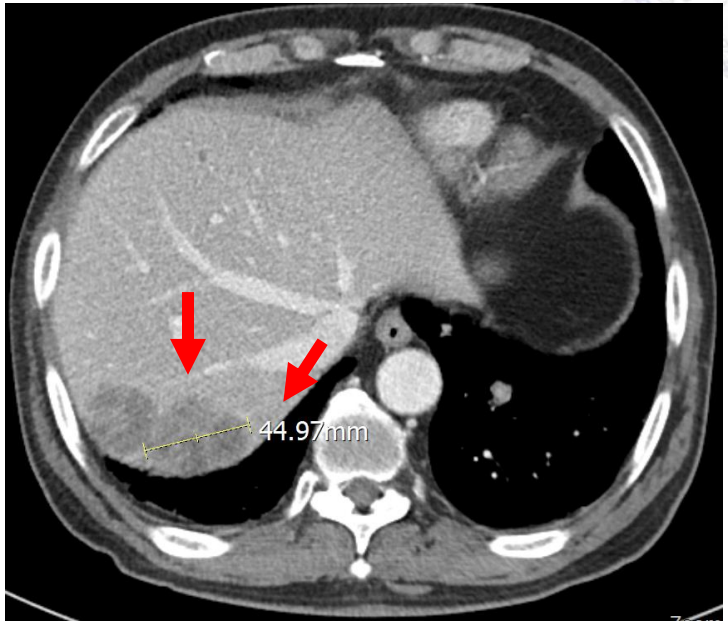
**Regimen #1: mFOLFOX6 + BEV**
- Duration of oxaliplatin: 260 days
- Duration of regimen: 260 days
- BOR: Partial response
- Time to progression: 260 days

**Regimen #2: FOLFIRI + aflibercept**
- Duration of regimen: 252 days
- BOR: Stable disease
- Time to progression: 259 days

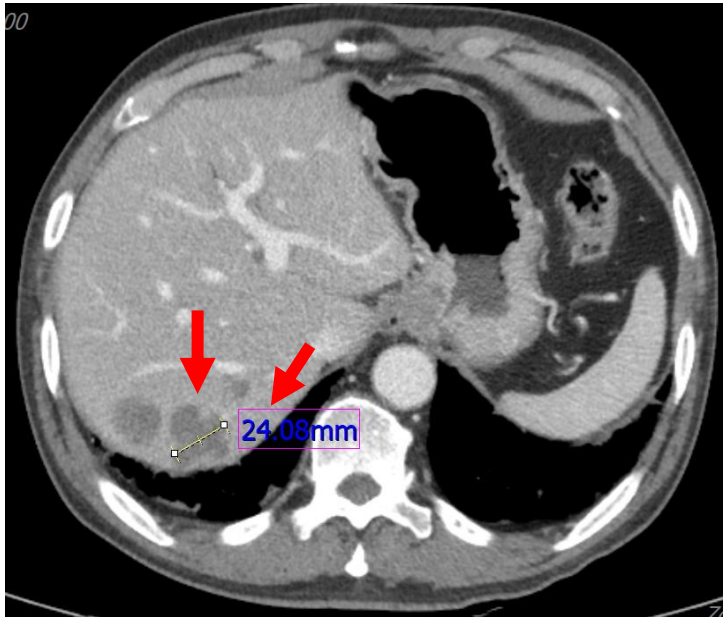
## ARC-9 STUDY DETAILS:

- Baseline disease burden:
  - 4 Target lesions (2x liver and 2x lung) SoD = 135 mm
  - 3 Non-target lesions (rectum, lymph node, lung)
- Duration of oxaliplatin: 91 days
- Duration of regimen: 273 days
- Best overall response: Partial Response
- Time to response: 112 days
- Progression free survival: 284 days (9.3 months)
- Overall survival: 372 days (12.2 months); ongoing at DCO

**BASELINE LIVER TARGET LESIONS**




**ON TREATMENT – WEEK 16**




BOR: best overall response; BEV: bevacizumab; EZFB, etrumadenant + zimberelimab + mFOLFOX6 + bevacizumab; FOLFIRI: 5-fluorouracil + leucovorin + irinotecan; mFOLFOX6, 5-fluorouracil + leucovorin + oxaliplatin



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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].

Date cutoff date: 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**

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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# Value Proposition & Competitive Landscape

Eric Matthews

*CCO, Arcus Biosciences*



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# Value Proposition for Etruma in 3L mCRC

## VALUE PROPOSITION:

- **Median survival with approved therapies is consistently ~8-10 months**
- **Unprecedented ~20 month mOS for etruma-based regimen** (HR=0.37 vs. regorafenib) in 3L mCRC
- **Manageable safety profile** (combination regimen in-line with known profile for FOLFOX/bev)

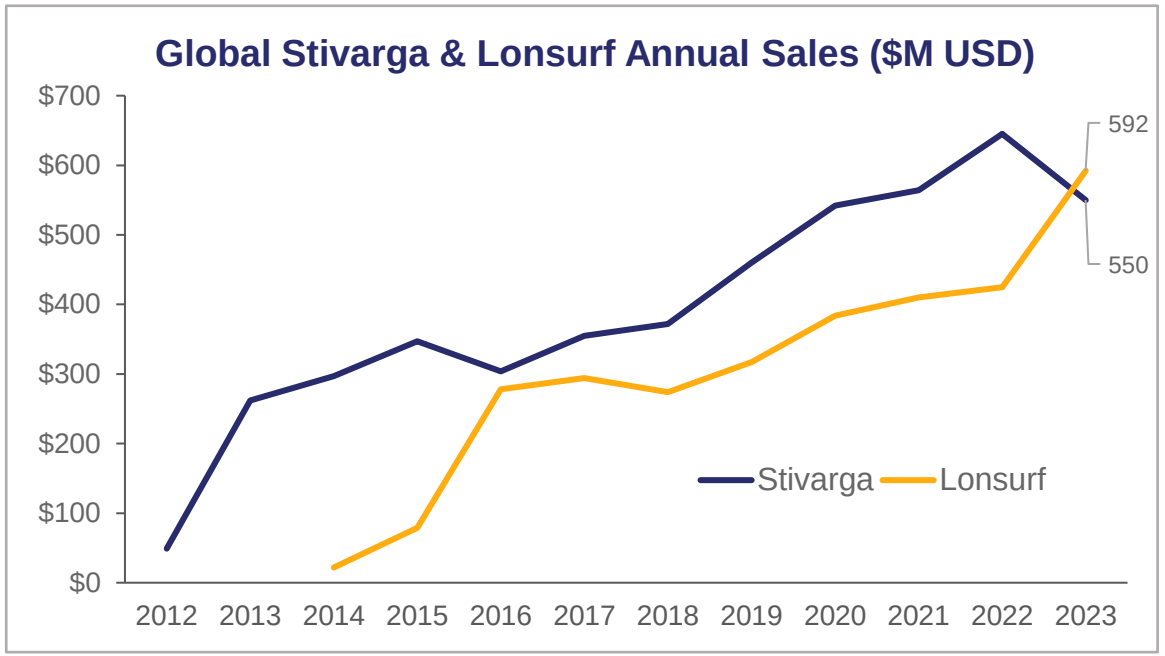
## COMMERCIAL OPPORTUNITY:

- **Treated prevalence of >80,000 3L mCRC patients in G7 markets**
- Lonsurf/bev and rego account for the majority of 3L treatment, with few new options expected[1]
- **3L FOLFOX reintroduction is not SOC, yet there was very rapid enrollment into ARC-9 as a result of the high unmet need**
- Open field for Phase 3 development, especially for an all-comer regimen

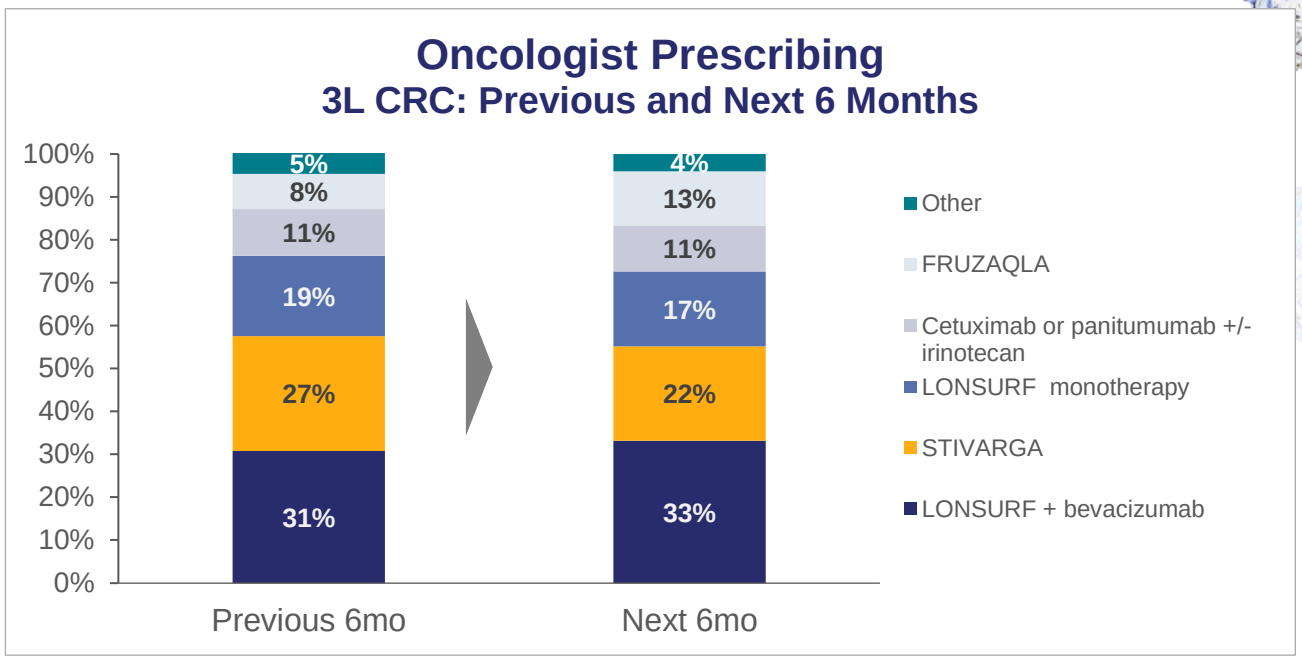
1. Based on Arcus-sponsored primary research.
1L, first-line; 2L, second-line; 3L, third-line; bev, bevacizumab; FOLFOX, 5-fluorouracil + leucovorin + oxaliplatin; G7, Group of Seven; HR: hazard ratio; mCRC, metastatic colorectal cancer; rego, regorafenib; SOC, standard of care


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# Stivarga & Lonsurf Sales Exceed $1.1B/yr Collectively, Despite Limited Time on Treatment, Illustrating the Large Opportunity in Late-line CRC




Globaldata, Annual Reports.




% Patients - Arcus Primary Research, Q1 2024 | N = 50
Please think of the non-biomarker / non-mutant mCRC patients that you initiated on 3L treatment in the last 6 months. What percent (%) of patients did you initiate on each of the following regimens?
Please think of the non-biomarker / non-mutant mCRC patients that you will initiate on 3L treatment in the next 6 months. What percent (%) of patients do you expect to initiate on each of the following regimens?

**Despite limited efficacy and narrow labels, Stivarga & Lonsurf currently generate revenues exceeding $1.1B globally**

**G7 addressable population of >80k patients in 3L with further large opportunities in earlier lines**

| | 1L CRC | 2L CRC | 3L CRC |
|---|---|---|---|
| | 49k | 38k | 25k |
| | 77k | 56k | 36k |
| | 50k | 35k | 21k |

2023 Drug Treatable Patients, DRG



1L: first line; 2L, second line; 3L, third line; G7, Group of Seven; mCRC, metastatic colorectal cancer

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# Concluding Remarks / Q&A



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# Multiple Late-Stage Programs Addressing Unmet Need Across Several Multi-Billion Dollar Markets

| | | Market Potential |
|---|---|---|
| **Dom (+ Zim)**<br>(anti-TIGIT + anti-PD-1)<br><br>**THREE*** PHASE 3 STUDIES UNDERWAY | • Potential to be first-in-class in upper GI cancer and best-in-class in NSCLC<br>• 12.9-13.8 months PFS in EDGE-Gastric is meaningfully higher than benchmark studies | **Upper GI $3B**<br><br>**NSCLC $10B+** |
| **Casdatifan**<br>(HIF-2α)<br><br>AT LEAST **ONE** PHASE 3 STUDY IN PLANNING | • Mechanism validated through the approval of belzutifan<br>• Data from 30-patient 100 mg expansion cohort planned for 2H:24; Multiple datasets from additional expansion cohorts expected to follow<br>• Cas has potential for a best-in-class efficacy profile – and a differentiated development / combination strategy | **RCC $2B** |
| **Quemli / Etruma**<br>(CD73 inhibitor / A2R antagonist)<br><br>**ONE** PHASE 3 STUDY IN PLANNING (PDAC) | • Three recent datasets support the potential of adenosine blockade to prolong survival when combined with chemotherapy<br>• ~20 months overall survival in ARC-9 data is meaningful above benchmark studies in a 3L all comer CRC population | **PDAC $4B**<br><br>**mCRC $2B** |

*includes STAR-121, STAR-221 and PACIFIC-8

2H: second half; 3L: third line; cas: casdatifan; CRC: colorectal cancer; dom: domvanalimab; GI: gastrointestinal; NSCLC: non-small cell lung cancer; PDAC: pancreatic ductal adenocarcinoma; PFS: progression-free survival; zim: zimberelimab



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# Appendix



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# Expansive Development Plan with at least 5 Phase 3 Studies Either Ongoing or Planned

| Program | Disease | Study | Line & Regimen | Ph 1/1b | Ph 2 | Ph 3 | Upcoming Milestones |
|---|---|---|---|---|---|---|---|
| **Dom (Fc-silent anti-TIGIT antibody)** | NSCLC | STAR-121 | **1L, PD-L1 all-comers, metastatic** **dom** + **zim** + chemo vs pembro + chemo | | | | • 2024: Enrollment completion |
| | | STAR-131 | **Perioperative lung cancer** | IN PLANNING | | | |
| | | PACIFIC-8 | **Stage 3:** durva ± **dom** | | | | |
| | | EDGE-Lung | **1L / 2L, all-comers: dom** ± **zim** ± **quemli** ± chemo | | | | |
| | | VELOCITY-Lung | **1L / 2L NSCLC: dom** ± **zim** ± **etruma** ± SG | | | | • 2024: Update expected |
| | Upper GI | STAR-221 | **1L Upper GI Malignancies** **dom + zim +** chemo vs. nivo + chemo | | | | • 2024: Enrollment completion |
| | | EDGE-Gastric | **1L / 2L Upper GI Malignancies** **dom** ± **zim** ± **quemli** ± FOLFOX | | | | ✓ 1H24: ASCO presentation |
| **Cas (HIF-2α inhibitor)** | ccRCC | PEAK-1 | **Post-IO ccRCC** | IN PLANNING | | | • 1H25: Ph 3 initiation |
| | | STELLAR-009 | **2L ccRCC: cas** + zanza | | | | |
| | | ARC-20 | **all-comer cancer; 2L+ ccRCC** **cas** monotherapy | | | | ✓ Early 2024: Dose escalation data<br>• 2H24: Dose expansion data (30 pts, 7m+ follow-up) |
| ADENOSINE **Quemli (CD73 inhib.)** | PDAC | PRISM-1 | **1L quemli +** G/nP vs. GnP | IN PLANNING | | | • Early 2025: Ph 3 initiation |
| | | ARC-8 | **1L: quemli** + **zim** + G/nP vs **quemli** + G/nP | | | | ✓ Jan 2024: Mature OS |
| ADENOSINE **Etruma (A2R antag.)** | CRC | ARC-9 | **2L: etruma** + **zim** + FOLFOX* vs FOLFOX*<br>**3L: etruma** + **zim** + FOLFOX* vs rego | | | | ✓ 1H24: MORPHEUS-PDAC (etruma); mature PFS/OS<br>✓ 1H24: ASCO presentation; mature PFS/OS data in 3L |
| **AB801 (Axl inhibitor)** | NSCLC | ARC-27 | **2L+: AB801** ± chemo | | | | |

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

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



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# Supplemental EDGE-Gastric Data


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# Study Population and Patient Disposition

- As of the 12 Mar 2024 data cutoff, all 41 patients received study treatment* and were included in the analysis of efficacy and safety
- Median treatment duration was 11.4 months
- 28 patients (68%) have discontinued all study treatments
  - Primary reason
  - Disease progression (n=20, 49%)
  - Withdrawal by patient (n=3, 7%)
  - Start of new anticancer therapy (n=2, 5%)
  - Adverse event (n=2, 5%)
  - Death (n=1, 2%)
- 13 patients (32%) discontinued from the study†

Yelena Janjigian, MD, Memorial Sloan Kettering Cancer Center, New York, NY

Efficacy-evaluable: all treated patients with at least 2 post-baseline disease assessments or who discontinued treatment prior to achieving 2 disease assessments

* One patient did not receive leucovorin due to institutional standard practice

† Reasons for discontinuation from study were death (n=8) and withdrawal from study by patient (n=5). Reasons for withdrawal from study were patient withdrawal of consent (n=3), patient relocation (n=1), and patient refusal of further study procedure (n=1)

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# Objective Response Rate per RECIST v1.1

| | Overall N=41* | TAP ≥ 5% n=16 | TAP < 5% n=24 |
|---|---|---|---|
| **Confirmed ORR, % [95% CI]** | 59 [42, 74] | 69 [41, 89] | 50 [29, 71] |
| Complete response, n (%) | 3 (7) | 1 (6) | 1 (4) |
| Partial response, n (%) | 21 (51) | 10 (63) | 11 (46) |
| Stable disease, n (%) | 14 (34) | 5 (31) | 9 (38) |
| Progressive disease, n (%) | 2 (5) | 0 | 2 (8) |
| No post-baseline scan, n (%) | 1 (2) | 0 | 1 (4) |
| **Median Duration of Response, months (95% CI)** | 12.4 (9.9, NE) | NE (11.5, NE) | 10.2 (4.0, 12.4) |

- As of the 12 March 2024 data cutoff, 13 patients (32%) continued on study treatment

Yelena Janjigian, MD, Memorial Sloan Kettering Cancer Center, New York, NY

Investigator-assessed ORR is reported.

* One patient had no tissue available for TAP central lab testing. From local lab results, the patient was PD-L1 low via 22-C3 assay.

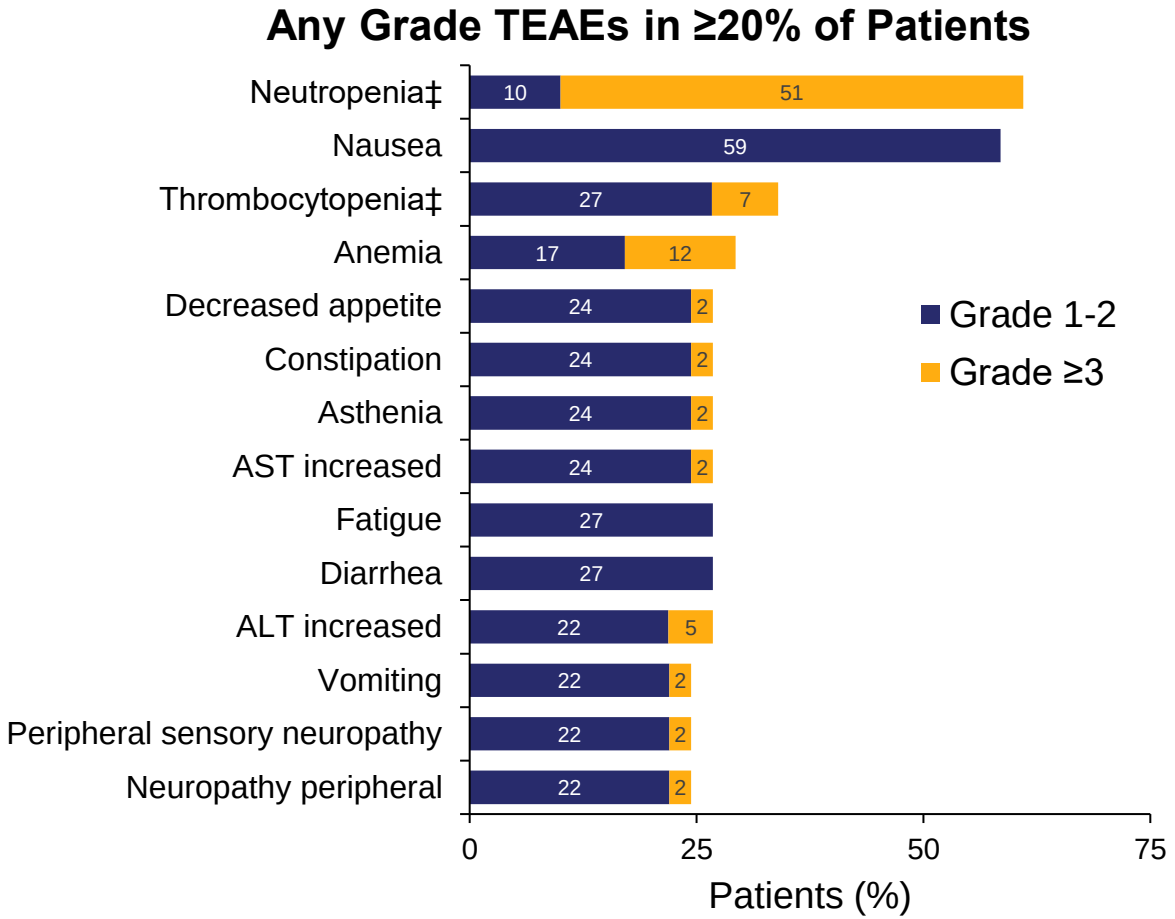
CI: confidence interval; ORR: objective response rate; RECIST: Response Evaluation Criteria in Solid Tumors; TAP: tumor area positivity

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# Overall Safety Summary

| | Arm A1 N=41, n (%) |
|---|---|
| **Any TEAE** | 41 (100) |
| TEAEs related to any study drug* | 40 (98) |
| **Grade ≥3 TEAEs** | 30 (73) |
| Grade ≥3 TEAEs related to dom/zim | 6 (15) |
| Grade ≥3 TEAEs related to FOLFOX | 24 (59) |
| **Serious TEAEs** | 15 (37) |
| Serious TEAEs related to dom/zim | 0 |
| Serious TEAEs related to FOLFOX | 2 (5) |
| **TEAEs leading to discontinuation of any study drug** | 27 (66) |
| TEAEs leading to discontinuation of dom/zim | 4 (10) |
| TEAEs leading to discontinuation of FOLFOX | 26 (63) |
| TEAEs leading to discontinuation all study drugs | 1 (2) |
| **TEAEs leading to dose modification/interruption from any study drug** | 35 (85) |
| **TEAEs resulting in death†** | 1 (2) |

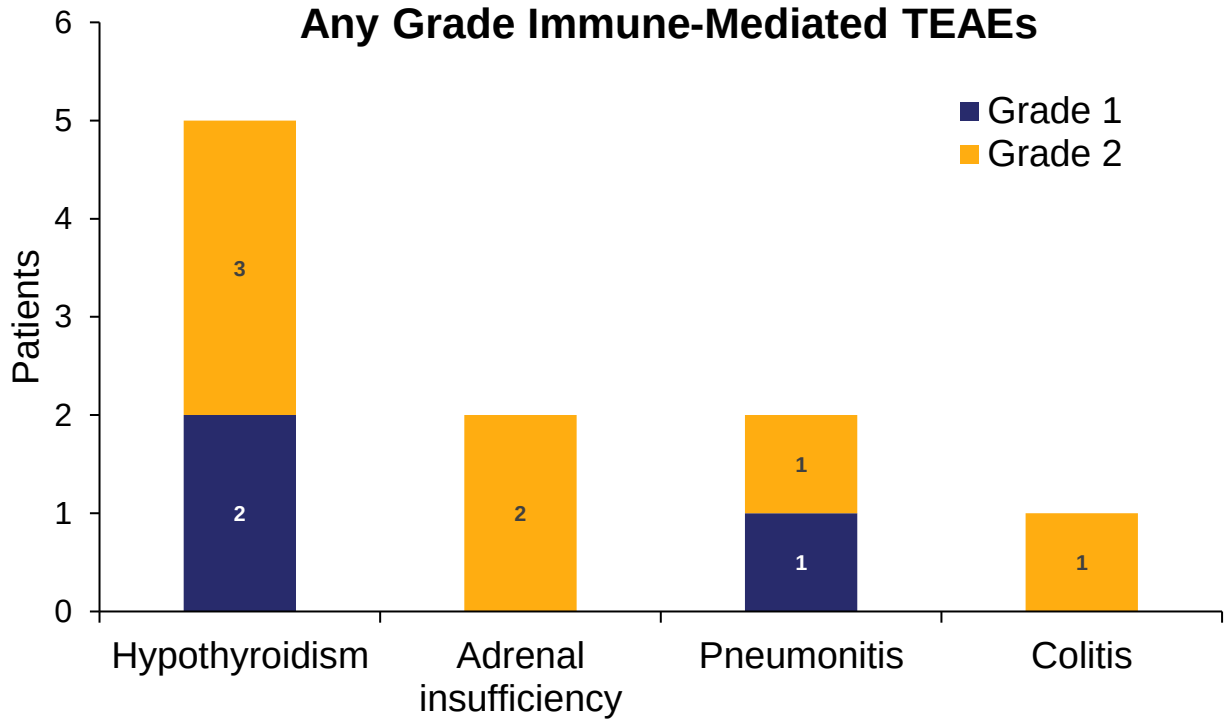



* TEAEs related to zim (n=32), dom (n=32), and FOLFOX (n=39). † Event term is "Death" and assessed as not related to any study medications; query pending.
‡ 'Neutropenia' and 'Neutrophil count decreased' were coded to separate Preferred Terms and combined post-hoc. 'Thrombocytopenia' and 'Platelet count decreased' were coded to separate Preferred Terms and combined post-hoc.
ALT: alanine aminotransferase; AST: aspartate aminotransferase; dom: domvanalimab; TEAE: treatment-emergent adverse event; zim: zimberelimab.


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# Infusion-Related Reactions and Immune-Mediated AEs

| Safety evaluable population | Arm A1 N=41, n (%) |
|---|---|
| **All infusion-related reactions*** | 8 (20) |
| **Infusion-related reactions related to components of FOLFOX** | 7 (17) |
| **All immune-mediated AEs** | 10 (24) |
| Hypothyroidism | 5 (12) |
| Adrenal insufficiency | 2 (5) |
| Pneumonitis | 2 (5) |
| Colitis | 1 (2) |
| **Grade ≥3 immune-mediated AEs** | 0 |
| **Serious immune-mediated AEs** | 0 |




* Infusion-related reactions as assigned by investigator. Two patients reported infusion-related reactions related to domvanalimab/zimberelimab (pruritus n=1, pyrexia n=1).
AEs: adverse events; TEAE: treatment-emergent AE; zim: zimberelimab.


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

**Dom + zim + chemo shows promising ORR, median DOR and median PFS in 1L Gastric/GEJ/EAC, which meaningfully exceeds historical benchmarks**

**Overall:** **Median PFS, 12.9 months; ORR, 59%; median DOR, 12.4 months (9.9, NE)**

**PD-L1-high:** **Median PFS, 13.8 months; ORR, 69%; median DOR, NE (11.5, NE)**

PD-L1-low: Median PFS, 11.3 months; ORR, 50%; median DOR, 10.2 months (4.0, 12.4)

- **OS data remain immature, with 13.9 months of median follow-up**
- AE profile continues to be similar to prior experience with anti-PD-1 plus FOLFOX, with no new safety concerns – these data provide support for the potential advantages of dom's Fc-silent construct
  - Only 10% of patients discontinued due to TEAEs related to dom + zim
  - Only 2% of patients discontinued all study drugs due to TEAEs
  - No serious TEAEs were deemed to be related to dom + zim
  - No grade 3+ immune mediated TEAEs

Yelena Janjigian, MD, Memorial Sloan Kettering Cancer Center, New York, NY
1L: first line; AE: adverse event; chemo: chemotherapy; dom: domvanalimab; DOR, duration of response; EAC: esophageal adenocarcinoma; GEJ: gastroesophageal junction; NE: not estimable; ORR: objective response rate; OS: overall survival; SOC: standard of care;
TEAE: treatment emergent adverse event zim: zimberelimab


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# Supplemental ARC-9 Data


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# Baseline Demographics & Disease Characteristics

| | EZFB (N=75) | REGO (N=37) | TOTAL (N=112) |
|---|---|---|---|
| **Median age, y** | 58.0 | 60.0 | 59.0 |
| **Female, n (%)** | 22 (29) | 15 (41) | 37 (33) |
| **ECOG PS, 0/1, %** | 40 / 60 | 49 / 51 | 43 / 57 |
| **Overall TNM Stage at Initial Diagnosis, n (%)** | | | |
| Stage IV | 56 (75) | 29 (78) | 85 (76) |
| **Primary Diagnosis, n (%)** | | | |
| Colon | 56 (75) | 27 (73) | 83 (74) |
| Rectal | 19 (25) | 10 (27) | 29 (26) |
| **Primary Tumor Location, n (%)** | | | |
| Left | 53 (71) | 23 (62)[a] | 76 (68)[a] |
| **Metastatic Site, n (%)** | | | |
| Liver | 53 (71) | 29 (78) | 82 (73) |
| Peritoneal | 18 (24) | 9 (24) | 27 (24) |
| Lung only | 4 (5) | 2 (5) | 6 (5) |
| **Microsatellite,[b] n (%)** | | | |
| Stable (MSS or MSI-L) | 61 (81) | 30 (81) | 91 (81) |
| Unstable (MSI-H) | 1 (1) | 0 | 1 (1) |
| **KRAS,[c] n (%)** | | | |
| Mutant | 38 (51) | 20 (54) | 58 (52) |
| Wild-Type | 27 (36) | 11 (30) | 38 (34) |
| Missing | 10 (13) | 6 (16) | 16 (14) |

Date cutoff date: November 13, 2023.
Efficacy-evaluable population.
ECOG PS: Eastern Cooperative Oncology Group performance status; EZFB: etrumadenant + zimberelimab + mFOLFOX6 + bevacizumab; rego: regorafenib.
a Unknown n=2; b Microsatellite status based on PCR. c KRAS based on NGS; Indeterminate, n=1 EZFB.


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# Prior Treatment History

| | EZFB (N=75) | REGO (N=37) | TOTAL (N=112) |
|---|---|---|---|
| **Prior Irinotecan, n (%)** | 73 (97) | 37 (100) | 110 (98)[d] |
| **Prior Oxaliplatin,[a] n (%)** | 74 (99) | 36 (97) | 110 (98)[e] |
| Metastatic<br>1L<br>2L+ | 63 (84)<br>53 (71)<br>15 (20) | 31 (84)<br>27 (73)<br>7 (19) | 94 (84)<br>80 (71)<br>22 (20) |
| Adjuvant/Neo Adjuvant | 10 (13) | 5 (14) | 15 (13) |
| Locally Advanced | 4 (5) | 2 (5) | 6 (5) |
| **Prior Anti-VEGF(R),[b] n (%)** | 64 (85) | 36 (97) | 100 (89) |
| **Prior Anti-EGFR, n (%)** | 27 (36) | 11 (30) | 38 (34) |
| **Prior anticancer surgery,[c] n (%)** | 52 (69) | 21 (57) | 73 (65) |
| **Time from first oxaliplatin dose date to progression/discontinuation date of the last prior oxali-containing regimen, n (%)** | 74 (99) | 36 (97) | 110 (98) |
| Median, months | 9.0 | 9.8 | 9.2 |

Date cutoff date: November 13, 2023.
a A patient could be counted more than once if they had prior oxaliplatin in multiple settings. b Includes bevacizumab, ramucirumab, and aflibercept regardless of treatment setting. c Includes curative and non-curative surgery. If a patient had both prior anticancer surgery and prior non-surgical anticancer procedure done, that patient is counted in each respective category. d EDC was subsequently updated after the Data Cut-Off of 13 Nov 2023 showing these 2 patients had received prior irinotecan per the eligibility criteria. e EDC was subsequently updated after the Data Cut-Off of 13 Nov 2023 showing these 2 patients had received prior oxaliplatin per the eligibility criteria .
1L: first line; 2L+: second line and beyond; EZFB: etrumadenant + zimberelimab + mFOLFOX6 + bevacizumab; oxali: oxaliplatin; rego: regorafenib


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# Treatment-Emergent and Immune-Mediated AEs

## Most Common Grade ≥3 TEAEs Occurring in ≥5%

| n (%) | EZFB (N=74) | Rego (N=35) |
|---|---|---|
| Grade ≥3 TEAEs | 61 (82) | 17 (49) |
| Neutropenia[a] | 35 (47) | 0 |
| Nausea | 8 (11) | 0 |
| Bilirubin increased | 7 (9) | 2 (6) |
| Diarrhea | 6 (8) | 0 |
| Hypersensitivity[a] | 6 (8) | 0 |
| WBC count decreased | 6 (8) | 0 |
| Anemia | 5 (7) | 1 (3) |
| Neuropathy[a] | 5 (7) | 0 |
| Vomiting | 5 (7) | 0 |
| Abdominal pain | 4 (5) | 1 (3) |
| Thrombocytopenia[a] | 4 (5) | 1 (3) |

## Immune-Mediated AEs[b]

| n (%) | EZFB (N=74) | Rego (N=35) |
|---|---|---|
| Any grade immune-mediated AE (per sponsor)[b] | 12 (16) | 2 (6) |
| Grade ≥3 event[c] | 4 (5) | 0 |
| Hypothyroidism, any grade | 4 (5) | 2 (6) |
| Adrenal insufficiency, any grade | 2 (3) | 0 |
| Pneumonitis, any grade<br>Grade ≥3 | 2 (3)<br>0 | 0<br>0 |
| Grade ≥3 skin reaction<br>Pruritus<br>Maculopapular rash | 2 (3)<br>1 (1)<br>1 (1) | 0 |
| Hemophagocytic lymphohistiocytosis, any grade | 0 | 1 (3) |
| Hyperthyroidism, any grade | 1 (1) | 0 |

Date cutoff date: November 13, 2023.

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. AE reported terms were coded using the MedDRA version 24.0. Preferred terms are listed unless otherwise noted.

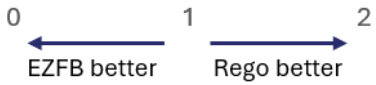
a Indicates grouped term. b Immune-mediated reactions programmatically identified via sponsor-defined preferred terms. c There were no grade 4 or 5 immune-mediated AEs .

AE: adverse event; EZFB: etrumadenant + zimberelimab + mFOLFOX6 + bevacizumab; rego: regorafenib; TEAE: treatment-emergent AE; WBC: white blood cell; zim: zimberelimab

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# PFS Was Consistently Longer in EZFB Arm vs Rego Arm in All Subgroups Analyzed

| | | EZFB #event/N (%); median PFS | Rego #event/N (%); median PFS | HR (95%CI) |
|---|---|---|---|---|
| | Overall | 58/75 (77%); 6.2 | 34/37 (92%); 2.1 | 0.27 (0.17, 0.43) |
| Region | EU + South Korea | 41/49 (84%); 6.9 | 22/23 (96%); 2 | 0.25 (0.14, 0.45) |
| | US | 17/26 (65%); 6.1 | 12/14 (86%); 2.5 | 0.31 (0.14, 0.67) |
| Baseline ECOG PS | D | 20/30 (67%); 7.6 | 16/18 (89%); 2.1 | 0.28 (0.14, 0.56) |
| | 1 | 38/45 (84%); 5.5 | 18/19 (95%); 2 | 0.18 (0.09, 0.38) |
| Baseline liver metastasis | Yes | 45/53 (85%); 5.7 | 28/29 (97%); 2 | 0.19 (0.1, 0.35) |
| | No | 13/22 (59%); 10.2 | 6/8 (75%); 2.6 | 0.4 (0.14, 1.16) |
| Primary diagnosis | Colon | 45/56 (80%); 5.9 | 25/27 (93%); 2 | 0.26 (0.15, 0.44) |
| | Rectal | 13/19 (68%); 7.9 | 9/10 (90%); 3.6 | 0.03 (0, 0.3) |
| Primary tumor location | Left | 40/53 (75%); 7.4 | 21/23 (91%); 2.2 | 0.29 (0.16, 0.51) |
| | Right | 18/22 (82%); 5 | 11/12 (92%); 2.1 | 0.3 (0.12, 0.74) |
| Prior oxaliplatin under metastatic setting | Yes | 49/63 (78%); 6.9 | 30/31 (97%); 2.1 | 0.16 (0.09, 0.28) |
| | No | 9/12 (75%); 5.5 | 4/6 (67%); 3.7 | 0.69 (0.2, 2.37) |
| Time from first prior oxaliplatin dose under metastatic setting to progression or end of regimen in 1L | ≥9 months | 20/25 (80%); 7.5 | 17/17 (100%); 2.1 | 0.18 (0.08, 0.42) |
| | <9 months | 24/28 (86%); 5.6 | 9/10 (90%); 2 | 0.12 (0.04, 0.36) |
| Prior bevacizumab under metastatic setting | Yes | 43/56 (77%); 6.1 | 30/33 (91%); 2.1 | 0.32 (0.19, 0.52) |
| | No | 15/19 (79%); 7.7 | 4/4 (100%); 2.1 | 0.03 (0, 0.27) |




Date cutoff date: November 13, 2023.

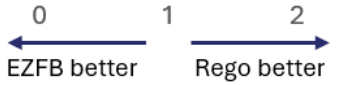
ECOG PS: Eastern Cooperative Oncology Group performance status; EZFB: etrumadenant + zimberelimab + mFOLFOX6 + bevacizumab; PFS: progression-free survival; rego: regorafenib; ROW: rest of the world.



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# OS Was Consistently Longer in EZFB Arm vs Rego Arm in All Subgroups Analyzed

| | | EZFB #event/N (%); median OS | Rego #event/N (%); median OS | HR (95%CI) |
|---|---|---|---|---|
| | Overall | 34/75 (45%); 19.7 | 26/37 (70%); 9.5 | 0.37 (0.22, 0.63) |
| Region | EU + South Korea | 22/49 (45%); 20 | 17/23 (74%); 10.8 | 0.44 (0.23, 0.84) |
| | US | 12/26 (46%); 19.7 | 9/14 (64%); 8.2 | 0.25 (0.1, 0.65) |
| Baseline ECOG PS | 0 | 11/30 (37%); 20.5 | 11/18 (61%); 12.5 | 0.26 (0.1, 0.65) |
| | 1 | 23/45 (51%); 10.9 | 15/19 (79%); 6.2 | 0.34 (0.17, 0.68) |
| Baseline liver metastasis | Yes | 27/53 (51%); 19.7 | 22/29 (76%); 9.1 | 0.36 (0.2, 0.66) |
| | No | 7/22 (32%); NA | 4/8 (50%); 17.4 | 0.66 (0.19, 2.35) |
| Primary diagnosis | Colon | 27/56 (48%); 19.7 | 20/27 (74%); 8.2 | 0.34 (0.18, 0.64) |
| | Rectal | 7/19 (37%); 20 | 6/10 (60%); 11.9 | 0.26 (0.07, 0.98) |
| Primary tumor location | Left | 23/53 (43%); 20 | 17/23 (74%); 9.5 | 0.33 (0.17, 0.63) |
| | Right | 11/22 (50%); 11.8 | 8/12 (67%); 12.5 | 0.49 (0.18, 1.34) |
| Prior oxaliplatin under metastatic setting | Yes | 28/63 (44%); 19.7 | 23/31 (74%); 10.3 | 0.33 (0.19, 0.6) |
| | No | 6/12 (50%); 11.8 | 3/6 (50%); 8.5 | 0.33 (0.07, 1.53) |
| Time from first prior oxaliplatin dose under metastatic setting to progression or end of regimen in 1L | ≥9 months | 13/25 (52%); 19.7 | 14/17 (82%); 9.5 | 0.23 (0.1, 0.57) |
| | <9 months | 12/28 (43%); 20.6 | 7/10 (70%); 8.3 | 0.42 (0.16, 1.13) |
| Prior bevacizumab under metastatic setting | Yes | 25/56 (45%); 19.7 | 22/33 (67%); 10.3 | 0.41 (0.22, 0.75) |
| | No | 9/19 (47%); 20 | 4/4 (100%); 8.4 | 0.16 (0.04, 0.61) |




Date cutoff date: November 13, 2023.

ECOG PS: Eastern Cooperative Oncology Group performance status; EZFB: etrumadenant + zimberelimab + mFOLFOX6 + bevacizumab; OS: overall survival; rego: regorafenib; ROW: rest of the world.



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# Other



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# OxPt (+bev) Re-Treatment in 3L+ mCRC References


1. RE-OPEN (Prospective study at a single center in Japan) *Phase 2: Suenaga et al, DDDT 2015*
2. ORION (prospective study in Japan) *Phase 2: Matsuda et al, IJCO 2015*
3. ORION-2 (prospective study in Japan) *Phase 2: Tanioka et al, IJCO 2019*
4. Prospective study of 22 patients *Ledin et al, Annals of Oncology 2018*
5. Retrospective analysis using the South Australian Metastatic CRC database *Townsend et al, Am JCO 2013.*
6. REOX (Retrospective analysis at AC Camargo Cancer Center, Sao Paulo Brazil) *Costa et al, CCR 2017*
7. Retrospective analysis at Hospital Sírio-Libanês in São Paulo and Brasília, Brazil *Fernandes et al, JGIC 2018*
8. Retrospective analysis of data from 7 hospitals in Japan *Sasaki et al, JCO 2014*
9. Retrospective analysis at Sun Yat-sen University Cancer Center in Guangzhou, China *Yang et al, OT&T 2018*
10. Retrospective analysis at Fondazione Policlinico Universitario in Rome, Italy *Calegari et al, ASCO GI 2019 669*
11. Retrospective analysis at 7 centers in Japan *Nishiura et al, Annals of Oncology 2014*
12. Retrospective analysis of a single center in France *Maindrault-Gœbel et al, Annals of Oncology 2004*
13. Retrospective analysis at Vall d'Hebron University Hospital (in Barcelona, Spain) *Salva et al, ESMO GI 2022*
14. Retrospective analysis at Banner MD Anderson Cancer Center (in Gilbert, AZ) *Chambers et al, JGO 2018*




3L: third line; Bev: bevacizumab; OxPt: oxaliplatin; mCRC: metastatic colorectal cancer

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