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Corporate Presentation

April 2024

Nasdaq: ZNTL

Forward Looking Statements and Disclaimer

Zentalis Pharmaceuticals, Inc. (“we,” “us,” “our,” “Zentalis” or the “Company”) cautions that this presentation (including oral commentary that accompanies this presentation) contains forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995. All statements contained in this presentation that do not relate to matters of historical fact should be considered forward-looking statements, including without limitation statements regarding the potential for azenosertib (ZN-c3) to be first-in-class and best-in-class; the potential for azenosertib to be a blockbuster opportunity; the potential applicability of azenosertib to a broad array of tumor types, including in combination with molecularly targeted agents; the potential timing of filing our first New Drug Application for azenosertib; potential for azenosertib to have real impact for patients; our positioning to execute; our projected cash runway; our development approach for our product candidates; planned clinical trials for our product candidates, including our strategy with respect to azenosertib in platinum sensitive ovarian cancer; the potential that we are generating registrational data; the potential of azenosertib to address large unmet need across a broad array of tumor types; the potential for studies to be registrational; the potential and suitability of azenosertib to address tumors with high genomic instability; the opportunity for azenosertib in first-line maintenance in homologous repair proficient platinum sensitive ovarian cancer; the opportunity for a monotherapy approval of azenosertib in platinum resistant ovarian cancer; our strategy for azenosertib development and the potential benefits thereof, including in platinum sensitive ovarian cancer; the potential for our development approach in platinum sensitive ovarian cancer to be practice changing; pursuit of a fast-to-market strategy for azenosertib; the potential for azenosertib to provide prolonged benefit for the greatest number of ovarian cancer patients in the first-line maintenance setting; the potential for CCNE1 amplification and Cyclin E1 IHC as potential patient enrichment strategies; the opportunity to address unmet need in relapsed or refractory acute myeloid leukemia by combining azenosertib and ZN-d5; the potential for building the azenosertib franchise, including the potential that the franchise opportunity for azenosertib more than doubles as it expands beyond gynecologic malignancies; the potential unmet need in a particular indication and/or patient population; potential for generating datasets with value-creating potential; potential for combinations including our product candidates and the potential benefits thereof; our potential positioning for success with the azenosertib franchise; the potential benefits of the designs of our product candidates; the target profiles and potential benefits of our product candidates and their mechanisms of action, including as a monotherapy and/or in combination; the market opportunities for and market potential of our product candidates, including the number of potential patients per year; the timing and content of our anticipated milestones, including the timing of initiation of clinical trials and disclosure of clinical data, as well as statements that include the words such as “anticipate,” “building,” "continue," "could," “estimate,” “expect,” “milestone,” “opportunity,” “plan,” “positioned,” “potential,” “predictive,” “strategy,” "support," “will” and similar statements of a future or forward-looking nature. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, the following: our limited operating history, which may make it difficult to evaluate our current business and predict our future success and viability; we have and expect to continue to incur significant losses; our need for additional funding, which may not be available; our plans, including the costs thereof, of development of any diagnostic tools; the outcome of preclinical testing and early trials may not be predictive of the success of later clinical trials; failure to identify additional product candidates and develop or commercialize marketable products; potential unforeseen events during clinical trials could cause delays or other adverse consequences; risks relating to the regulatory approval process or ongoing regulatory obligations; failure to obtain U.S. or international marketing approval; our product candidates may cause serious adverse side effects; inability to maintain our collaborations, or the failure of these collaborations; our reliance on third parties; effects of significant competition; the possibility of system failures or security breaches; risks relating to intellectual property; our ability to attract, retain and motivate qualified personnel, and risks relating to management transitions; and significant costs as a result of operating as a public company. Other risks and uncertainties include those identified under the caption “Risk Factors” in our most recently filed periodic reports on Forms 10-K and 10-Q and subsequent filings with the U.S. Securities and Exchange Commission in the future could cause actual results to differ materially from those indicated by the forward-looking statements made in this presentation. Any such forward-looking statements represent management’s estimates as of the date of this presentation. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. While we may elect to update these forward-looking statements at some point in the future, we assume no obligation to update or revise any forward-looking statements except to the extent required by applicable law. Although we believe the expectations reflected in such forward-looking statements are reasonable, we can give no assurance that such expectations will prove to be correct. 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This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and other data about our industry. These data involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such data and estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk. Neither we nor our affiliates, advisors or representatives makes any representation as to the accuracy or completeness of that data or undertake to update such data after the date of this presentation.

Zentalis’ product candidates are investigational drugs and have not yet been approved by the U.S. Food and Drug Administration or any other regulatory authority.

Advancing Azenosertib

First-in-class WEE1 Inhibitor with Broad Franchise Potential

Highly Specific Agent Targeting WEE1

- Clinical-stage asset generating potentially registrational data
- Intermittent dosing allows for maximized efficacious exposures
- Differentiated from and years ahead of other agents against this target in development

Real Impact for Patients

- Monotherapy efficacy; 37% ORR and 6.5 month mPFS in heavily pretreated ovarian and USC*
- Excellent safety and tolerability profile compared to other commercially successful anti-cancer agents
- Established dosing and efficacy in combination with multiple chemotherapeutic agents

Blockbuster Opportunity

- At least 2 gynecologic malignancies (PROC/USC)
- Expanding to a broad array of tumor types in combination with molecularly targeted agents
- More than 10 ongoing and planned trials
- Potential first NDA in 2026

Positioned to Execute

- Deep oncology expertise
- Industry-leading scientific and clinical advisors
- Partnerships with Pfizer and GSK
- Cash runway into 2026

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Abbreviations: PROC, platinum resistant ovarian cancer; USC, uterine serous carcinoma; ORR, objective response rate; NDA, New Drug Application; mPFS, median progression free survival
Statements comparing azenosertib to other agents, not head-to-head comparisons

*Data cut-off: October 25, 2023

Building Azenosertib Franchise in Gynecologic Cancers and Beyond

		INDICATION	TRIAL NAME + DEVELOPMENT APPROACH	Phase 1	Phase 1b	Phase 2	Phase 3	EXPECTED MILESTONES
Azenosertib WEE1 Inhibitor	GYNECOLOGIC MALIGNANCIES	Platinum Sensitive Ovarian Cancer	Planned trial in 1L maintenance setting					Add'l details **2H 2024,** Expect initiation **2025**
		Platinum Resistant Ovarian Cancer	**DENALI (ZN-c3-005)** Monotherapy					Topline data anticipated **1H 2025**
		PARPi Resistant Ovarian Cancer	**MAMMOTH (ZN-c3-006)** Azenosertib monotherapy, or with niraparib				GSK	Topline data anticipated **2H 2024**
		Uterine Serous Carcinoma	**TETON (ZN-c3-004)** Monotherapy, FDA Fast Track Designation					Topline data anticipated **2H 2025**
		Platinum Resistant Ovarian Cancer	**ZN-c3-002** Azenosertib + multiple chemo backbones					Data presented ASCO 2023
		Solid Tumors	**ZN-c3-001** Monotherapy					Final results anticipated **2H 2024**
	OTHER TUMOR TYPES	Osteosarcoma	**ZN-c3-003** Azenosertib + gemcitabine					Final results anticipated **1H 2024**
		BRAF Mutant Colorectal Cancer	**ZN-c3-016** Azenosertib + encorafenib and cetuximab		Pfizer			Initial data anticipated **2H 2024**
		Pancreatic Cancer	Azenosertib + gemcitabine					*Investigator initiated study*
		Breast Cancer	**ZAP-IT** Azenosertib + carboplatin + pembrolizumab					*Investigator initiated study*
ZN-d5 BCL-2 Inhibitor		Acute Myeloid Leukemia	**ZN-d5-004C** ZN-d5 + azenosertib					Initial data anticipated **2H 2024**

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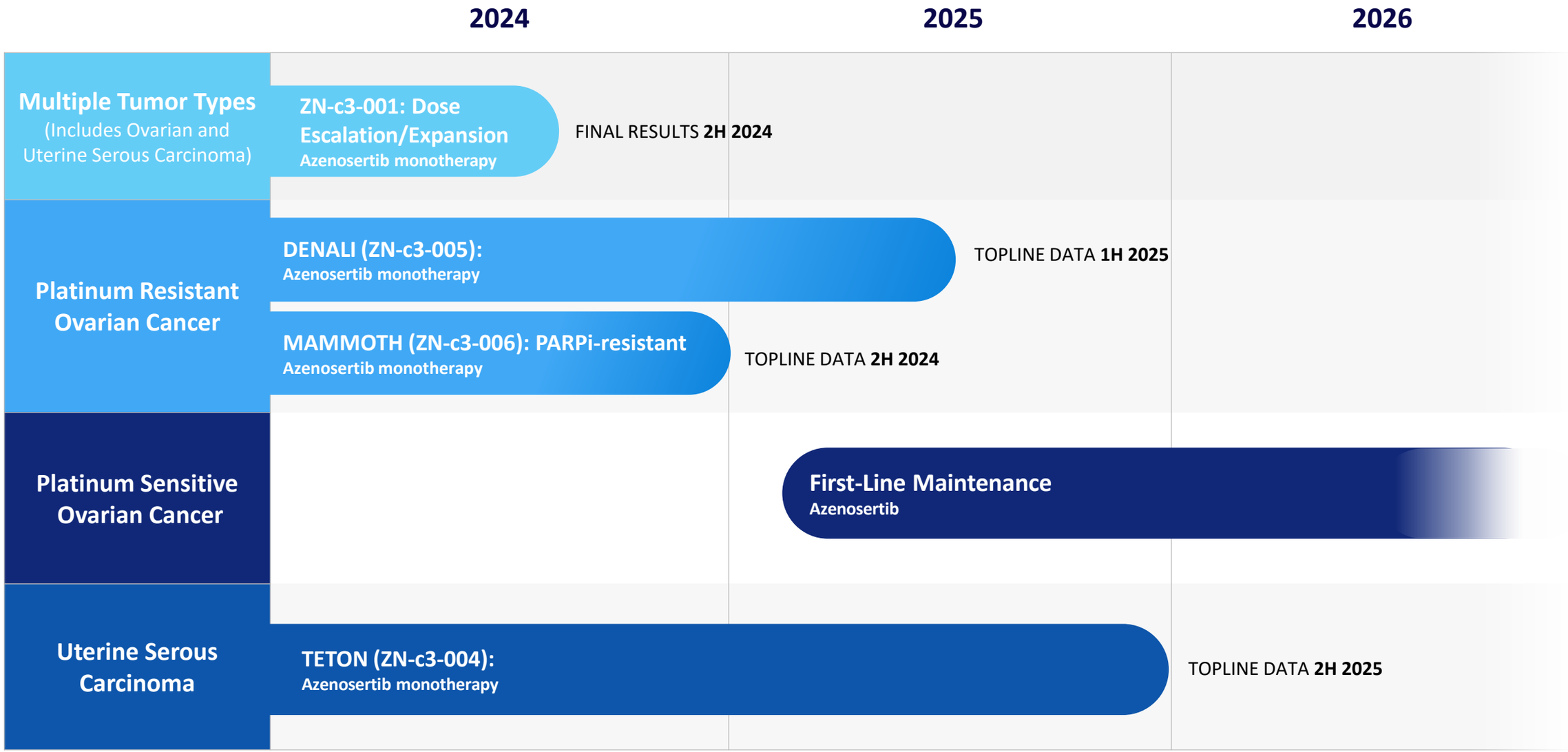
Clinical Programs Position Zentalis for Multiple Datasets with Value-creating Potential

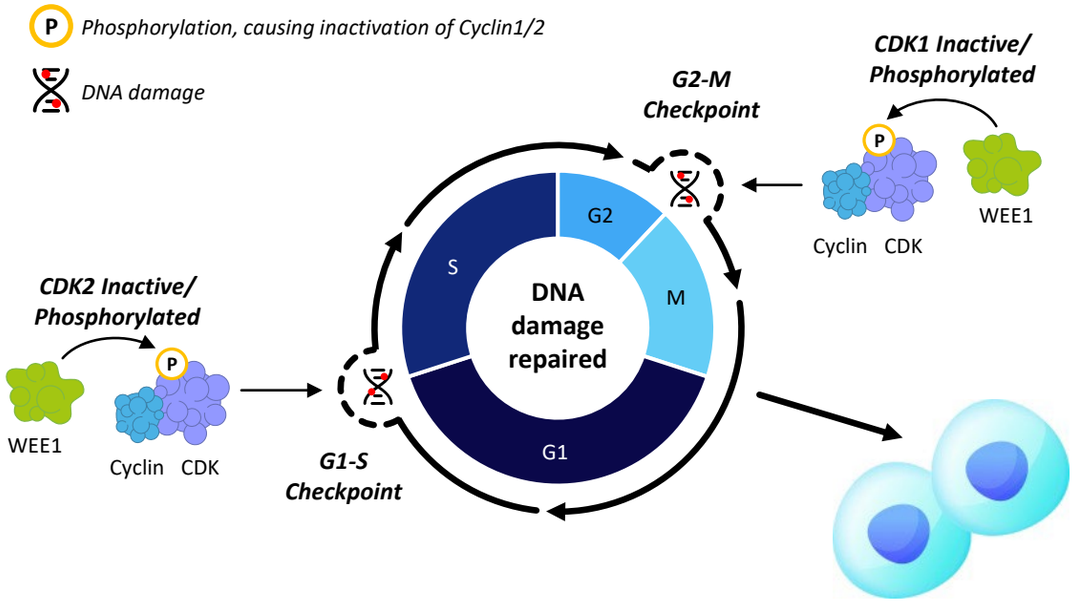


Abbreviations: 1H, first half; 2H, second half

Azenosertib Mechanism of Action – Inhibitor of WEE1, Master Cell Cycle Regulator

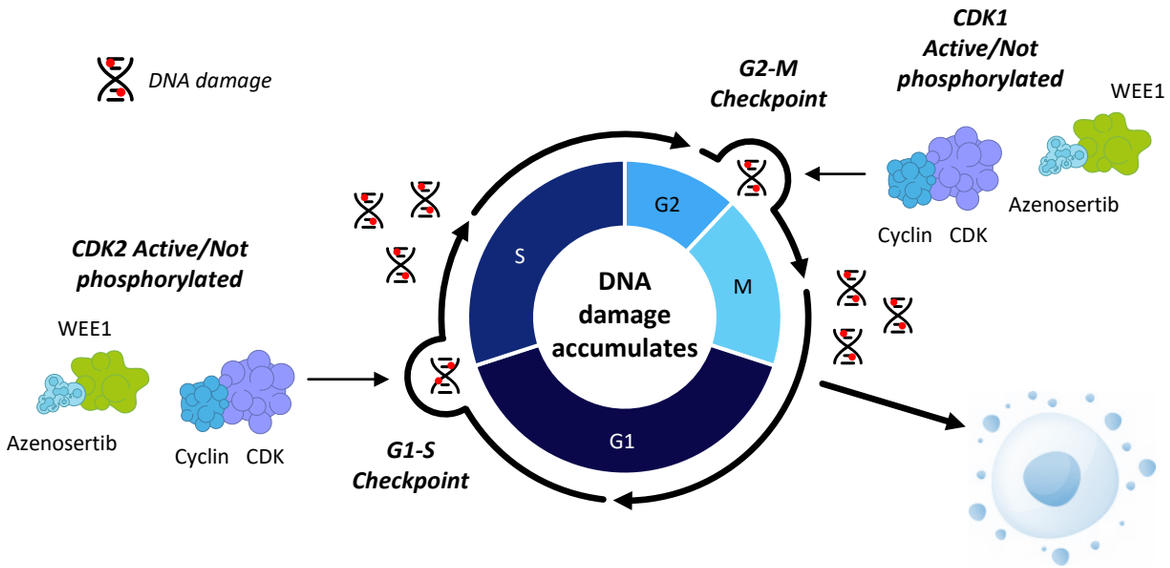
Normal Cell Cycle Regulation

- CDKs and their cyclin binding partners promote progression through the cell cycle
- Following DNA damage, WEE1 kinase phosphorylates and inactivates Cyclin/CDK complexes at both G1-S and G2-M checkpoints to halt the cell cycle and allow for repair
- Upon DNA repair, cells progress through the cell cycle and proliferate

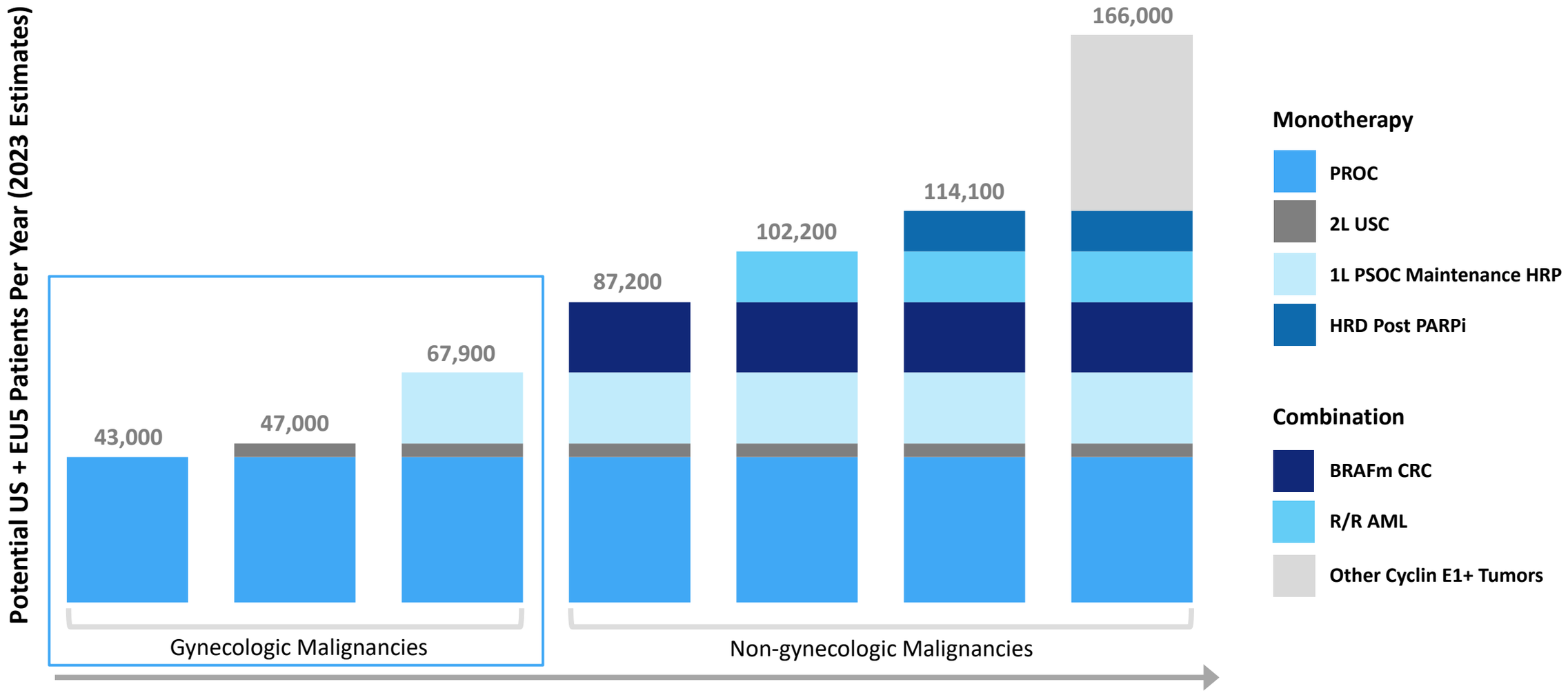


Cancer Cell and Azenosertib

- In cancer cells, oncogene induced replication stress (e.g. Cyclin E1 activation or a driver mutation) leads to high levels of DNA damage and genomic instability
- Cancers with high levels of replication stress are sensitized to WEE1 inhibition via azenosertib
- Inhibition of WEE1 activates CDKs and increases DNA damage to intolerable levels, resulting in mitotic catastrophe and cell death



Azenosertib Treatable Patient Population More Than Doubles as Franchise Expands to Non-Gynecologic Malignancies



'Drug treatable' estimates from DRG Clarivate. For 'Other Cyclin E1+ tumors' used incidence reported by SEER and ECIS.
HRD Post PARPi tumor types: Prostate, Pancreas and Breast; Other Cyclin E1+ Tumor Types include bladder, stomach, esophageal, lung, and breast cancer
Abbreviations: PROC, platinum resistant ovarian cancer; 2L, second line; USC, uterine serous carcinoma; PSOC, platinum sensitive ovarian cancer; HRD, homologous recombination repair deficient; PARPi, poly-ADP ribose polymerase inhibitor; BRAFm CRC, BRAF V600E mutant colorectal cancer; R/R AML, relapsed or refractory acute myeloid leukemia

Azenosertib Monotherapy Results

Monotherapy Anti-tumor Activity in Gynecologic Malignancies with Favorable Safety and Tolerability Profile

Longer Follow Up Improves Duration of Benefit

Strong Safety and Tolerability of Azenosertib Monotherapy

CORPORATE CALL
June 6, 2023

- **37% Objective Response Rate** using intermittent dosing in ovarian and USC patients
- Established monotherapy **RP2D** of 400 mg 5:2
- **Doubled steady state drug exposure** compared to continuous dosing

UPDATED DATA
Nov 6, 2023

- **Median follow up has increased by nearly 5 months and mPFS has increased to 6.5 months**
- **Maintained excellent safety and tolerability with intermittent dosing**

Abbreviations: USC, uterine serous carcinoma; RP2D: recommended Phase 2 dose; 5:2 refers to administration schedule of five days on therapy and two days off; mPFS, median progression free survival

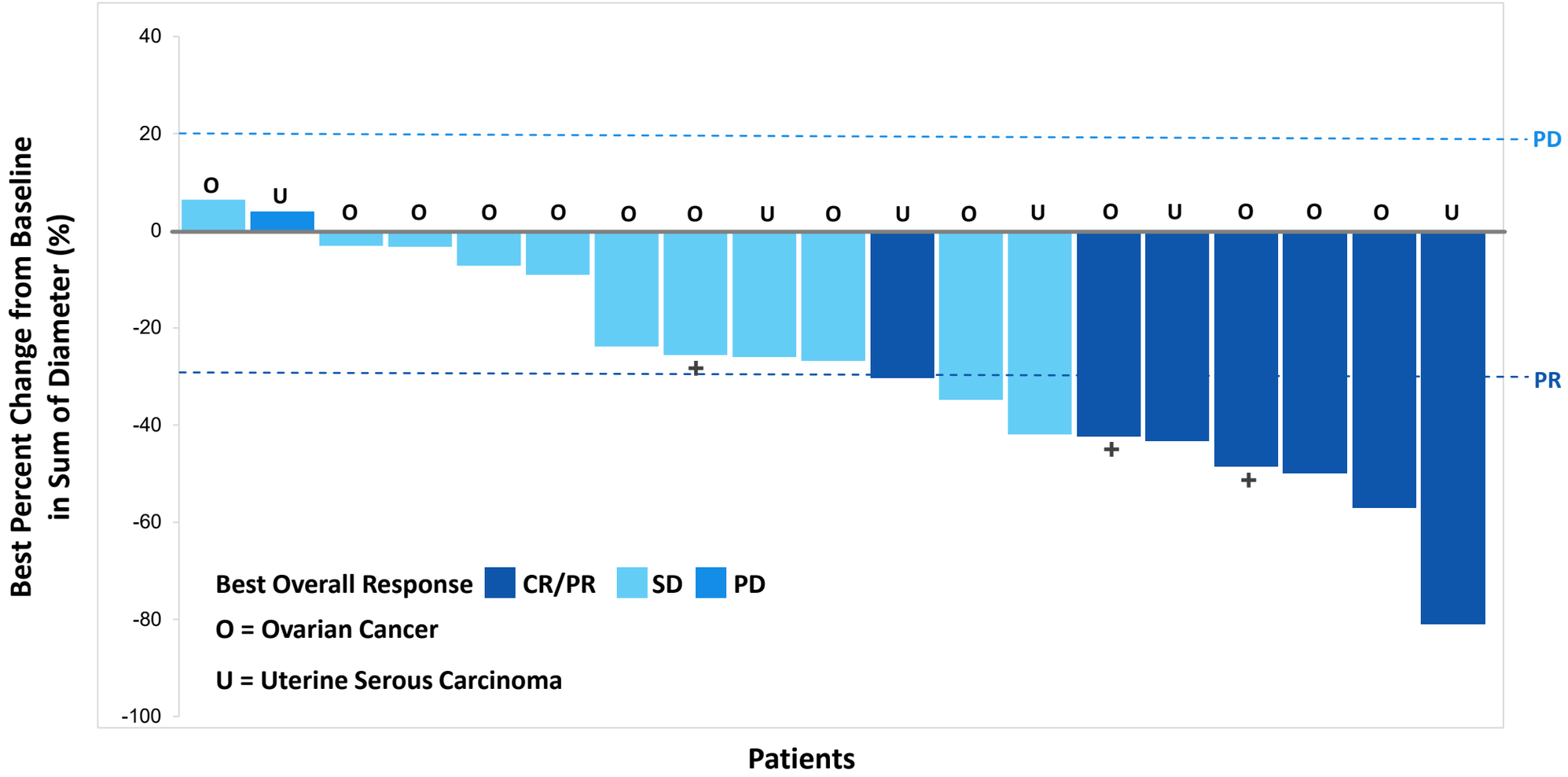
Intermittent Monotherapy Patient Population Was Heavily Pretreated and Treatment Refractory

	USC	HGSOC
	N=6	N=13
Prior Lines of Treatment		
Median (Range)	3.5 (1-6)	6 (2-11)
Platinum Resistant* (N, %)	5 (83.3)	5 (38.5)
Platinum Refractory** (N, %)	NA	8 (61.5)
Prior Therapies (N, %)		
Prior PARP Inhibitor	1 (16.7)	10 (76.9)
Prior Experimental Agents	0 (0.0)	5 (38.5)
Prior VEGF Inhibitor	5 (83.3)	11 (84.6)
Prior Anti-PD-1/PD-L1	6 (100)	1 (7.7)

USC and HGSOC subjects who received at least one dose of azenosertib with intermittent dosing schedule, have baseline measurable disease by RECIST 1.1, and at least one post-baseline scan.
*Platinum Resistant: For USC patients, received prior platinum therapy. For HGSOC patients, progression within 90-180 days of prior dose of a platinum-based regimen in any line of therapy.
**Platinum Refractory: Progression within 90 days of prior dose of a platinum-based regimen in any line. Progression date based on progression date if available or start date of next therapy.
Abbreviations: USC, uterine serous carcinoma; HGSOC, high grade serous ovarian cancer; PARP, poly-ADP ribose polymerase; VEGF, vascular endothelial growth factor; PD-1/PD-L1, programmed cell death protein 1/programmed death ligand 1.

Monotherapy Azenosertib Results in a 37% Confirmed Response Rate

In Both Platinum Resistant Ovarian Cancer and Uterine Serous Carcinoma

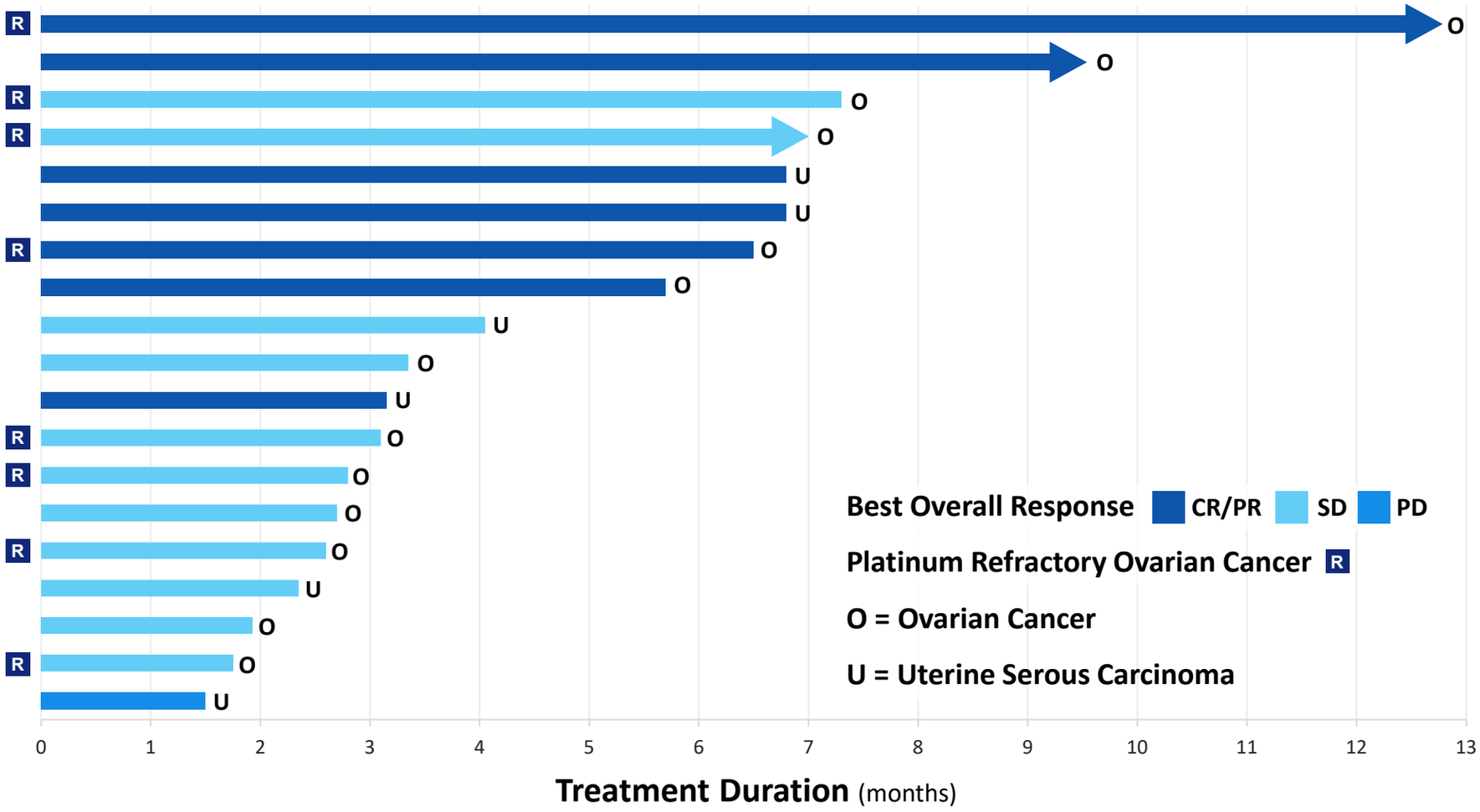


ORR = 36.8%

Subjects who received at least one dose of azenosertib with intermittent dosing schedule, have baseline measurable disease by RECIST 1.1, and at least one post-baseline scan.
Abbreviations: +, patients remain on therapy at the time of data cut-off; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; ORR, objective response rate

Data cut-off: October 25, 2023

Monotherapy Azenosertib Has Meaningful and Durable Benefit to Platinum Resistant Ovarian Cancer/USC Patients



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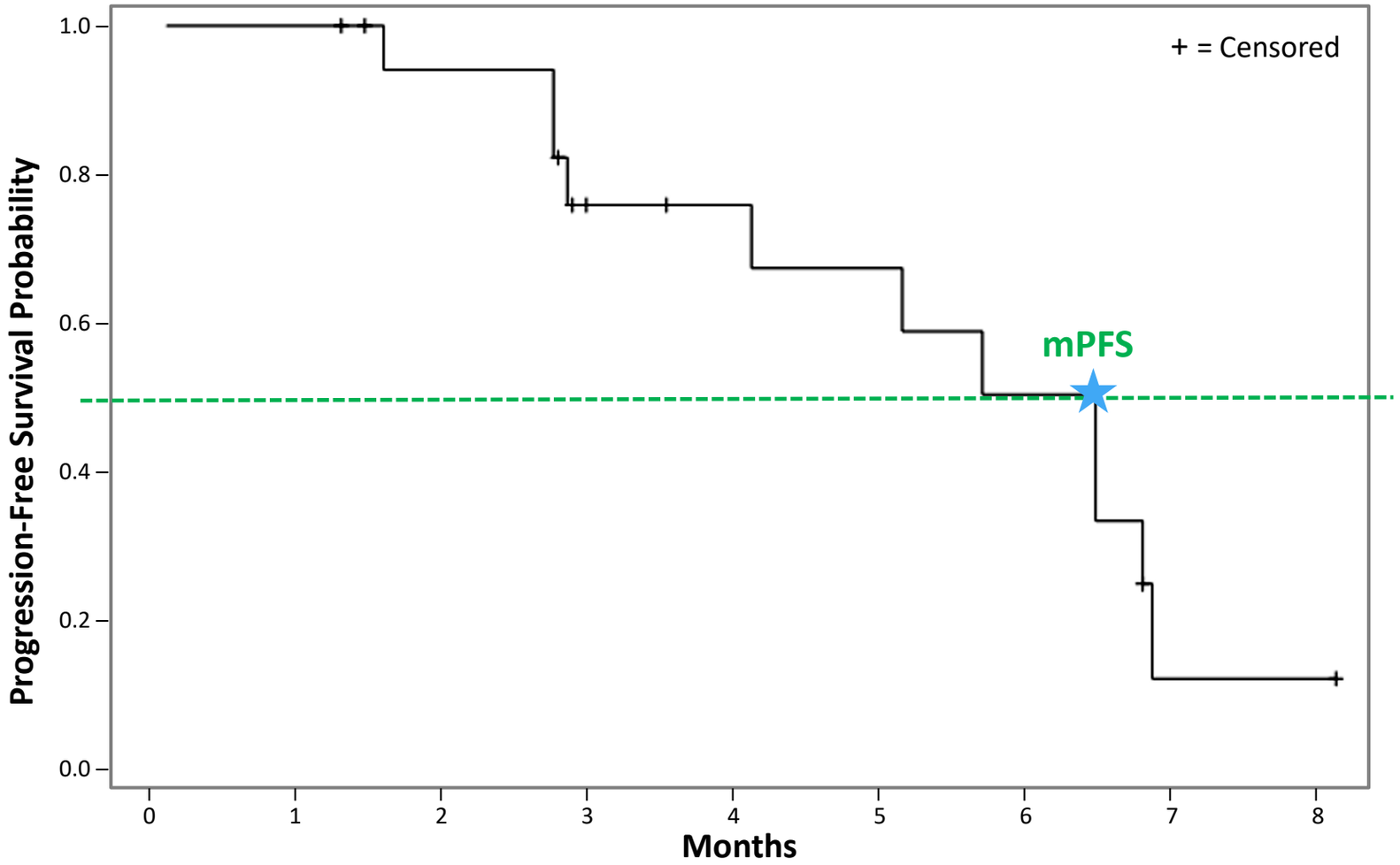
* Subjects who received at least one dose of azenosertib with intermittent dosing schedule, have baseline measurable disease by RECIST 1.1, and at least one post-baseline scan.
Abbreviations: PROC, platinum resistant ovarian cancer; USC, uterine serous carcinoma; CR, complete response; PR, partial response;
SD, stable disease; PD, progressive disease; Platinum Refractory: Progression within 90 days of last dose of a platinum-based regimen in any line.

Monotherapy Azenosertib Has Meaningful and Durable Benefit to Platinum Resistant Ovarian Cancer/USC Patients



At Risk	19	19	16	10	9	8	6	1	1

mPFS (95% CI):
6.5 months (2.79, 6.87)

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* Subjects who received at least one dose of azenosertib with intermittent dosing schedule, have baseline measurable disease by RECIST 1.1, and at least one post-baseline scan.
Abbreviations: USC, uterine serous carcinoma; mPFS, median progression-free survival

Azenosertib Monotherapy Continues to Demonstrate Excellent Safety Profile with Additional Patients Across Tumor Types*

Treatment Related AEs, n (%)

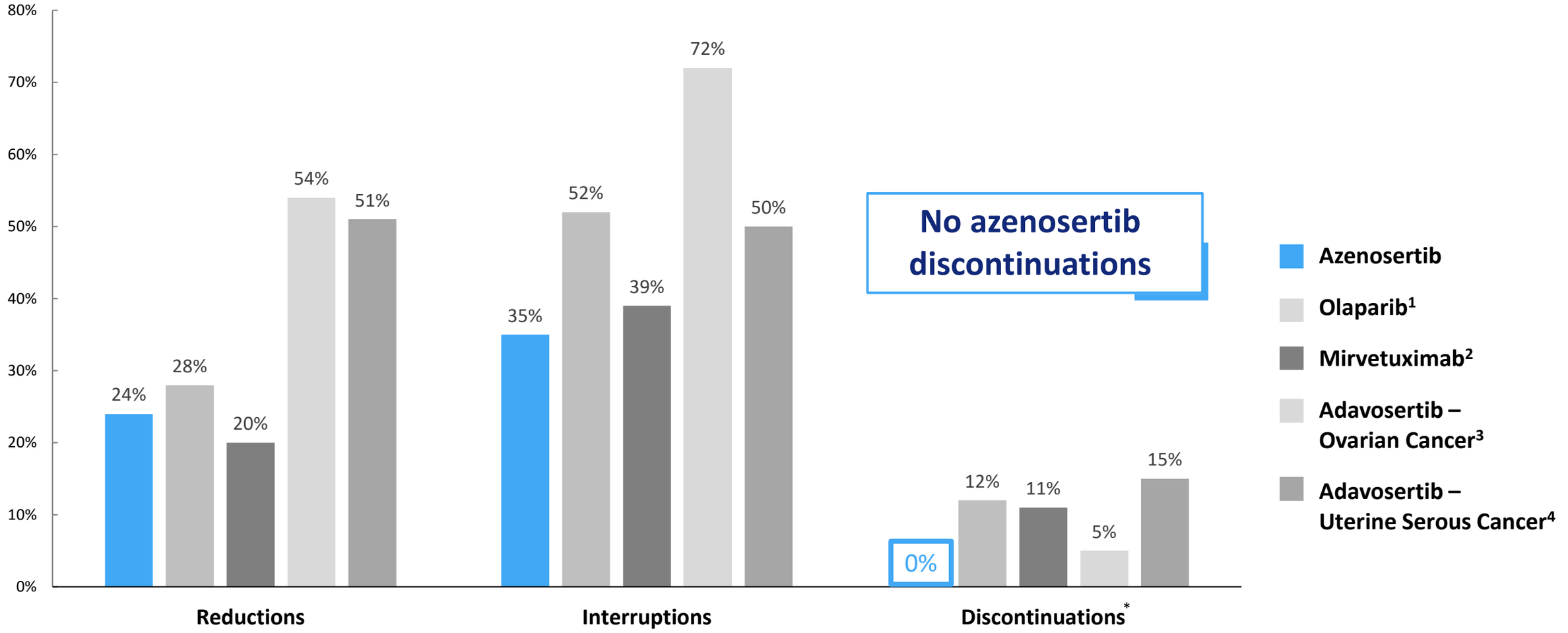
	ALL GRADES	GRADE 3/4
Gastrointestinal		
Nausea	20 (43.5)	2 (4.3)
Diarrhea	22 (47.8)	4 (8.7)
Vomiting	8 (17.4)	1 (2.2)
Decreased appetite	4 (8.7)	1 (2.2)
Dehydration	5 (10.9)	0

	ALL GRADES	GRADE 3/4
Fatigue		
	18 (39.1)	5 (10.9)
Hematologic		
Anemia	11 (23.9)	5 (10.9)
Thrombocytopenia	9 (19.6)	4 (8.7)
Neutropenia	9 (19.6)	7 (15.2)

No cases of febrile neutropenia or sepsis

*Safety Evaluable Population (All tumor types; n=46) as of Sept 27, 2023 versus n=27 reported on June 6, 2023 corporate call: Received at least one dose of drug; Intermittent 350 5:2 and 400 5:2; Treatment Related AEs > 10% for entire trial and treatment related AEs of interest. Abbreviations: AE, adverse event; 5:2, 5-days of treatment followed by 2-days off treatment

Azenosertib is Well Tolerated with Similar or Better Tolerability Compared to Other Gynecologic Malignancy Therapies



Safety Evaluable Population (All tumor types; n=46): Received at least one dose of drug; Intermittent 350 5:2 and 400 5:2; Not head-to-head comparisons; *Discontinuations due to treatment related adverse events

1 Poveda A, et al. Lancet Oncol 2021;22:620-631; 2 Moore K, et al. J Clin Oncol 2023;41:abstr LBA5507; 3 Westin S, et al. J Clin Oncol 2021 39:15_suppl, 5505;
4 Liu JF, et al. Society of Gynecologic Oncology Annual Meeting on Women's Cancer; March 25-28; Tampa, Florida. Abstract 219

Monotherapy Conclusions

Data Supports Ongoing Azenosertib Monotherapy Potentially Registrational Studies in Ovarian Cancer and Uterine Serous Carcinoma

MONOTHERAPY EFFICACY

37% confirmed ORR

mPFS of 6.5 MONTHS

EXCELLENT TOLERABILITY & SAFETY

Consistent or better than other available agents

DEFINITIVE DATA

Supports differentiation from other clinical WEE1 inhibitors

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Abbreviations: ORR, objective response rate; mPFS, median progression free survival; Comparisons to other agents are not head-to-head.

Phase 2 Trials of Azenosertib

Potential Paths to Registration in Platinum Resistant Ovarian Cancer and Uterine Serous Carcinoma

Platinum Resistant Ovarian Cancer: High Unmet Need Provides Opportunity for Monotherapy Approval

Untreated Stage III/IV Ovarian Cancer

First Line Therapy

Carboplatin + Paclitaxel

BRCAm/HRD

HRP

First Line Maintenance

PARP Inhibitor or Bevacizumab + Olaparib

Bevacizumab

PFI>6m

PFI≤6m

Second Line Therapy

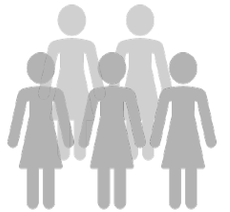
Combination Chemotherapy
Platinum Doublet

PFI≤6m

Unmet Need

Platinum Resistant

Single Agent Chemotherapy or Mirvetuximab (~35% pts)[2]



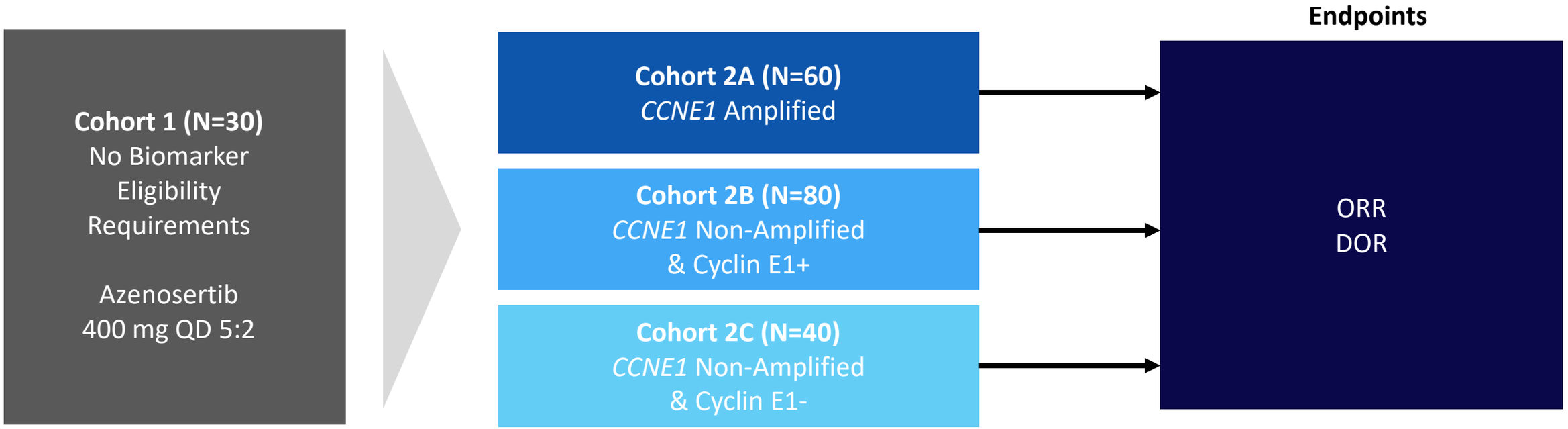
42,981 Treatable Patients[1] US/EU5

1 Figures represent Company estimates of U.S. and EU5 patients with conditions covered by the Company's targeted indications; Source: IQVIA, DRG Clarivate;
2 Matulonis U. JCO 2023 41:13:2436-2445; Abbreviations: BRCAm, BRCA mutant; HRD, homologous-recombination repair deficient; HRP, homologous-recombination repair proficient; PFI, platinum-free interval

DENALI (ZN-c3-005): Prospective Evaluation of *CCNE1* Amplification and Cyclin E1+ in Platinum Resistant High-Grade Serous Ovarian Cancer

CURRENTLY ACCRUING

Key Eligibility: 1-5 prior lines of therapy in Cohort 1 (1-4 prior lines in Cohort 2); Mandatory Sufficient Tissue; Cannot be Platinum Refractory (DFI < 3month from last platinum based therapy)



Topline data 1H 2025

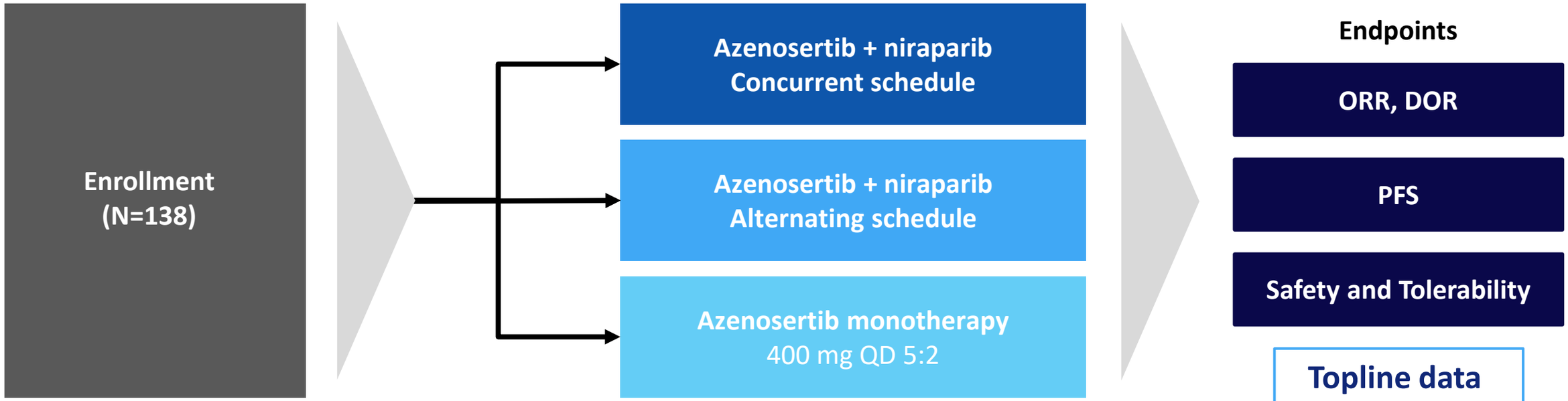
Note: Cyclin E1+ refers to protein overexpression determined by immunohistochemistry
Abbreviations: QD, once daily; 5:2, 5-days of treatment followed by 2-days off treatment; ORR, objective response rate; DOR, Duration of Response; 1H, first half

NCT05128825

MAMMOTH (ZN-c3-006): Phase 1/2 Study of Azenosertib in Combination with Niraparib or Alternating with Niraparib or as a Monotherapy in Patients with PARP-Resistant High-Grade Epithelial Ovarian Cancer

CURRENTLY ACCRUING

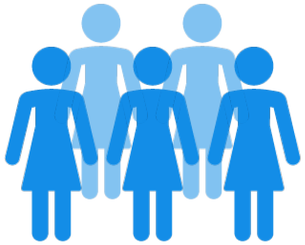
Key Eligibility: 1-5 prior lines of therapy; platinum-resistant, progressed while receiving an approved PARP inhibitor; Mandatory Sufficient Tissue; Cannot be Platinum Refractory (DFI < 3 months from last platinum based therapy)



NCT05198804

Abbreviations: PARP, poly-ADP ribose polymerase; QD, once daily; 5:2, 5-days of treatment followed by 2-days off treatment; ORR, objective response rate DOR, duration of response; PFS, progression-free survival; 2H, second half

New Treatment Options Needed in 2L+ Uterine Serous Carcinoma

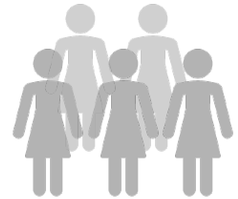


Stage IV
or Recurrent USC

1L Carboplatin + Paclitaxel + Pembrolizumab/Dostarlimab

Unmet Need

2L+ Single-Agent Chemotherapy



4,103
Treatable Patients[1] US/EU5

1 Figures represent Company estimates of U.S. patients with conditions covered by the Company's targeted indications and are dependent upon regulatory approvals; Source: IQVIA, DRG Clarivate, Kantar Health;
Abbreviations: 2L+, second line maintenance plus; USC, uterine serous carcinoma; 1L, first line

TETON (ZN-c3-004): Azenosertib Monotherapy in Women with ≥2L Advanced Uterine Serous Carcinoma

CURRENTLY ACCRUING - FDA Fast Track Designation

Key Eligibility: ≥1 prior platinum-based chemotherapy regimen; prior anti-PD(L)1

Patients (N=130)
Azenosertib
400 mg QD 5:2

Endpoints

- **ORR**
- **DOR**
- **Safety and Tolerability**

Topline data 2H 2025

Abbreviations: 2L, two lines; QD, once daily; 5:2, 5-days of treatment followed by 2-days off treatment; ORR, objective response rate; DOR, duration of response; 2H, second half;
The FDA granted Fast Track designation in November 2021 to azenosertib in patients with advanced or metastatic USC who have received at least one prior platinum-based chemotherapy regimen for management of advanced or metastatic disease.

NCT04814108

Azenosertib in Platinum Sensitive Ovarian Cancer

1L Maintenance Opportunity to Provide Prolonged Benefit for a Larger Number of Patients

Opportunity for Azenosertib in First Line Maintenance in Homologous Repair Proficient (HRP) Platinum Sensitive Ovarian Cancer

Untreated Stage III/IV Ovarian Cancer

First Line Therapy

Carboplatin + Paclitaxel

BRCAm/HRD

HRP

First Line Maintenance

PARP Inhibitor or Bevacizumab + Olaparib

Bevacizumab

PFI>6m

Second Line Therapy

Combination Chemotherapy

Platinum Doublet

PFI≤6m

PFI≤6m

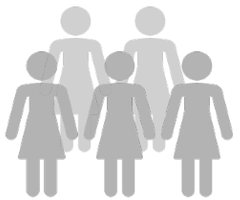
Platinum Resistant

Single Agent Chemotherapy or Mirvetuximab (~35% pts)[3]

Unmet Need

~40% patients are HRP/not eligible for maintenance PARP[1]

Platinum Sensitive



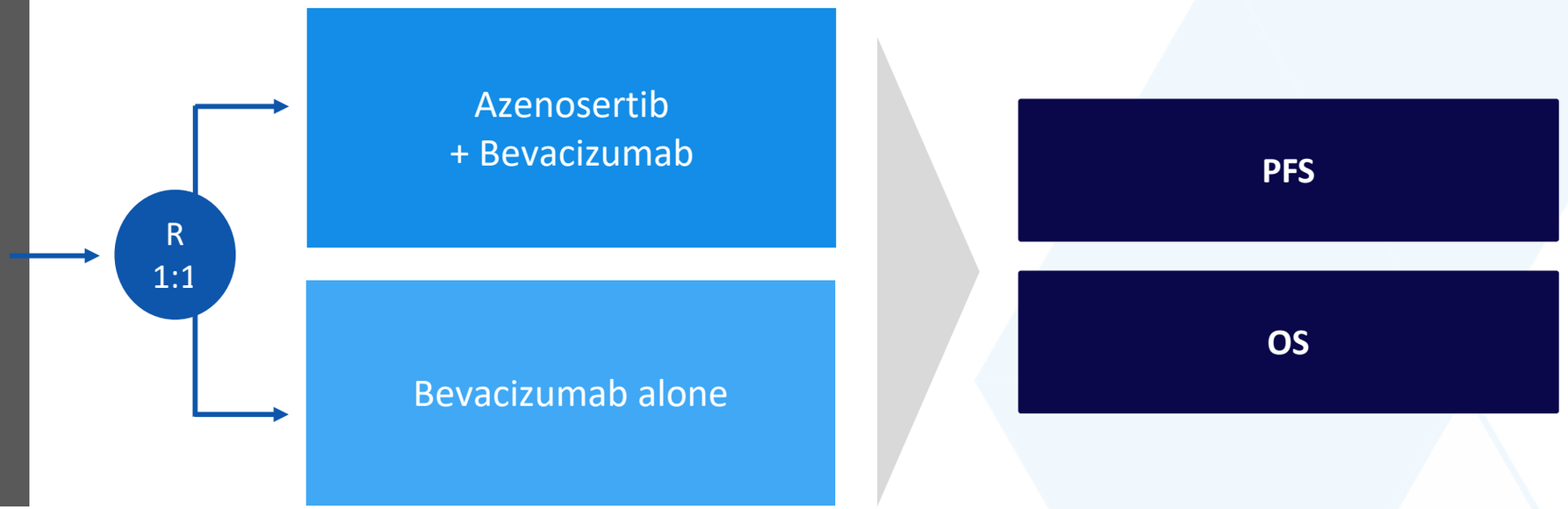
20,905

Treatable Patients[2] US/EU5

1 Ray-Coquard I. N Engl J Med 2019; December 2019 381:2416-2428; 2 Figures represent Company estimates of U.S. and EU5 patients with conditions covered by the Company's targeted indications; Source: IQVIA, DRG Clarivate;
3 Matulonis U. JCO 2023 41:13:2436-2445; Abbreviations: BRCAm, BRCA mutant; HRD, homologous-recombination repair deficient; HRP, homologous-recombination repair proficient; PFI, platinum-free interval

Azenosertib in 1L Maintenance Setting for Platinum Sensitive Ovarian Cancer

- Advanced Ovarian Cancer following 6 cycles of first line therapy with Carboplatin and Paclitaxel
- Homologous Recombination Proficient (HRP)



Abbreviations: 1L, one line; PFS, progression free survival; OS, overall survival; 2H, second half

Potential for Azenosertib to Impact the Greatest Number of Ovarian Cancer Patients in the 1L Maintenance Setting

2x as **many patients**

receive 1L maintenance treatment compared to 2L treatment[1]

Evolving labels and prescribing practice for PARPi **presents an opportunity**

for a new 1L maintenance oral therapy for patients with HRP/unknown tumors

40% of **1L maintenance patients**

are HRP[2] and not eligible to receive a PARPi

Azenosertib uniquely positioned for success in maintenance setting

Oral non-chemotherapy agent
Clear global regulatory pathways

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1 Figures represent Company estimates of U.S. and EU5 patients with conditions covered by the Company's targeted indications; Source: IQVIA, DRG Clarivate Kantar and DRG;
2 Ray-Coquard I., N Engl J Med 2019; December 2019 381:2416-2428; Abbreviations: 1L, first line treatment; 2L, second line treatment; HRP, homologous-recombination repair proficient; PARPi, poly-ADP ribose polymerase inhibitor

Azenosertib as 1L Maintenance Therapy in Platinum Sensitive Ovarian Cancer Patients

Additional trial details in 2H 2024

"Zentalis' frontline maintenance study of WEE1 inhibition could be practice changing for our patients with poor prognosis ovarian cancer"

Professor Alexandra Leary, MD, PhD
Deputy Chair of Medical Oncology,
Institut de Cancérologie Gustave Roussy, France
GINECO and ENGOT Investigator

"Advancing azenosertib into the first-line HRP maintenance setting has the potential to reach the largest number of patients with ovarian cancer"

Professor Premal Thaker, MD, MS
Distinguished Chair of Obstetrics and Gynecology
Washington University School of Medicine in St. Louis
GOG Investigator

Azenosertib Combination with Chemotherapy

Clinical Data Shows Strong Efficacy and Favorable Safety Profile in Platinum Resistant Ovarian Cancer

ZN-c3-002: Phase 1b Combination Study in Platinum Resistant Ovarian Cancer

Key Eligibility: Platinum-resistant/refractory; Up to 3 prior lines of chemotherapy

Dose Finding guided by a CRM

Cohort assignment by availability and investigator preference

Azenosertib + Paclitaxel

Paclitaxel: 80 mg/m^2 on D1, D8, D15 (28-day cycles)

Azenosertib + Carboplatin

Carboplatin: AUC 5 mg/mL*min on D1 (21-day cycles)

Azenosertib + Gemcitabine

Gemcitabine: D1, D8 (21-day cycles)

Azenosertib + PLD

PLD: 40 mg/m^2 D1 (28-day cycles)

Objectives

Primary: Safety and Tolerability MTD and/or RP2D

Key Secondary: Clinical Activity (Endpoints: ORR, DOR, PFS, CA 125)

NCT04516447

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Liu JF, et al. Journal of Clinical Oncology 41, no. 16_suppl (June 01, 2023) 5513-5513; Abbreviations: CRM, continuous reassessment model; QD, once daily; D, day; AUC, area under the curve; PLD, pegylated liposomal doxorubicin; MTD, maximum tolerated dose; RP2D, recommended Phase 2 dose; ORR, objective response rate; DOR, duration of response; PFS, progression-free survival

Encouraging Efficacy and Durability with Azenosertib* in Combination with Chemotherapy in Platinum Resistant Ovarian Cancer

Endpoint	Azenosertib + Paclitaxel (N=26)	Azenosertib + Carboplatin (N=36)	Azenosertib + Gemcitabine (N=18)	Azenosertib + PLD (N=35)	Total (N=115)
Response-Evaluable* (N)	22	28	13	31	94
ORR (confirmed), N (%)	11 (50.0)	10 (35.7)	5 (38.5)	6 (19.4)	32 (34.0)
Median DOR (95% CI) in months	5.6 (3.8-NE)	11.4 (8.3-NE)	6.2 (NE)	7.3 (1.5-NE)	8.3 (5.6-12.4)
Clinical Benefit Rate (CR + PR + SD for ≥ 16 weeks), N (%)	18 (81.8)	16 (57.1)	6 (46.2)	24 (77.4)	64 (68.1)
Median PFS (95% CI) in months	7.4 (5.5-NE)	10.4 (3.3-14.5)	8.3 (3.3-NE)	6.3 (3.7-11.0)	9.0 (5.8-13.7)

*Response-evaluable subjects are treated subjects with baseline measurable disease per RECIST version 1.1 and at least one post-baseline assessment. All objective responses were confirmed per RECIST v 1.1. Data include patients on all schedules of azenosertib plus chemotherapy. Liu JF, et al. Journal of Clinical Oncology 41, no. 16_suppl (June 01, 2023) 5513-5513; Abbreviations: PLD, pegylated liposomal doxorubicin; ORR, objective response rate; DOR, duration of response; CI, confidence interval; NE, not estimable; CR, complete response; PR, partial response; SD, stable disease; PFS, progression-free survival; RECIST, response evaluation criteria in solid tumors

Azenosertib* in Combination with Chemotherapy Demonstrates Favorable Safety Profile

Treatment-Related Adverse Event ≥20% N (%)		Azenosertib + Paclitaxel (N=19)		Azenosertib + Carboplatin (N=14)		Azenosertib + Carboplatin (N=8)		Azenosertib + Gemcitabine (N=10)		Azenosertib + PLD (N=8)		Total (N=59)	
		All Doses*		All Doses		Doses ≤ MTD		All Doses**		All Doses*			
Grade		All Gr	Gr ≥3	All Gr	Gr ≥3	All Gr	Gr ≥3	All Gr	Gr ≥3	All Gr	Gr ≥3	All Gr	Gr ≥3
Hematologic	Neutropenia	11 (57.9)	5 (26.3)	7 (50.0)	1 (7.1)	4 (50.0)	0	7 (70.0)	4 (40.0)	3 (37.5)	3 (37.5)	28 (54.9)	13 (25.5)
	Thrombo-cytopenia	4 (21.1)	0	9 (64.3)	5 (35.7)	4 (50.0)	2 (25.0)	8 (80.0)	6 (60.0)*	3 (37.5)	3 (37.5)	24 (47.1)	14 (27.5)
	Anemia	8 (42.1)	1 (5.3)	10 (71.4)	4 (28.6)	4 (50.0)	1 (12.5)	5 (50.0)	2 (20.0)	2 (25.0)	1 (12.5)	25 (49.0)	8 (15.7)
Gastro-intestinal	Nausea	7 (36.8)	1 (5.3)	6 (42.9)	0	3 (37.5)	0	5 (50.0)	0	4 (50.0)	1 (12.5)	22 (43.1)	2 (3.9)
	Vomiting	2 (10.5)	1 (5.3)	2 (14.3)	0	2 (25.0)	0	1 (10.0)	0	4 (50.0)	1 (12.5)	9 (17.6)	2 (3.9)
	Diarrhea	6 (31.6)	1 (5.3)	5 (35.7)	0	3 (37.5)	0	6 (60.0)	0	2 (25.0)	0	19 (37.3)	1 (2.0)
Other	Fatigue	8 (42.1)	2 (10.5)	5 (35.7)	1 (7.1)	4 (50.0)	0	6 (60.0)	2 (20.0)	2 (25.0)	0	21 (41.2)	5 (9.8)

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*All doses were at or below MTD and were intermittent; **A MTD for gemcitabine + azenosertib has not been determined, further dose cohorts are ongoing.
Liu JF, et al. Journal of Clinical Oncology 41, no. 16_suppl (June 01, 2023) 5513-5513; Abbreviations: MTD, maximum tolerated dose; PLD, pegylated liposomal doxorubicin

Addition of Azenosertib to Single Agent Chemotherapy Increases Response Rates and Durability of Response in Ovarian Cancer Compared to Chemotherapy Alone

50%

50% Objective Response Rate with 7.4-month Progression Free Survival in paclitaxel combination

Superior durability in carboplatin combination with **10.4-month Progression Free Survival** and 36% Objective Response Rate

Overall tolerability of paclitaxel and carboplatin combinations **compares favorably to SOC** chemotherapy doublets paclitaxel-carboplatin or PLD-carboplatin

Cyclin E1+ status associated with **superior Objective Response Rate and longer Progression Free Survival** across response-evaluable patient population

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Liu JF, et al. Journal of Clinical Oncology 41, no. 16_suppl (June 01, 2023) 5513-5513; Abbreviations: SOC, standard of care; PLD, pegylated liposomal doxorubicin

Targeting Tumors with High Genomic Instability Using Azenosertib

Multiple Mechanisms Leading to Genomic Instability Enhance Sensitivity to Azenosertib

High Genomic Instability[1] Can be Caused By:

Cyclin E1+ Activation

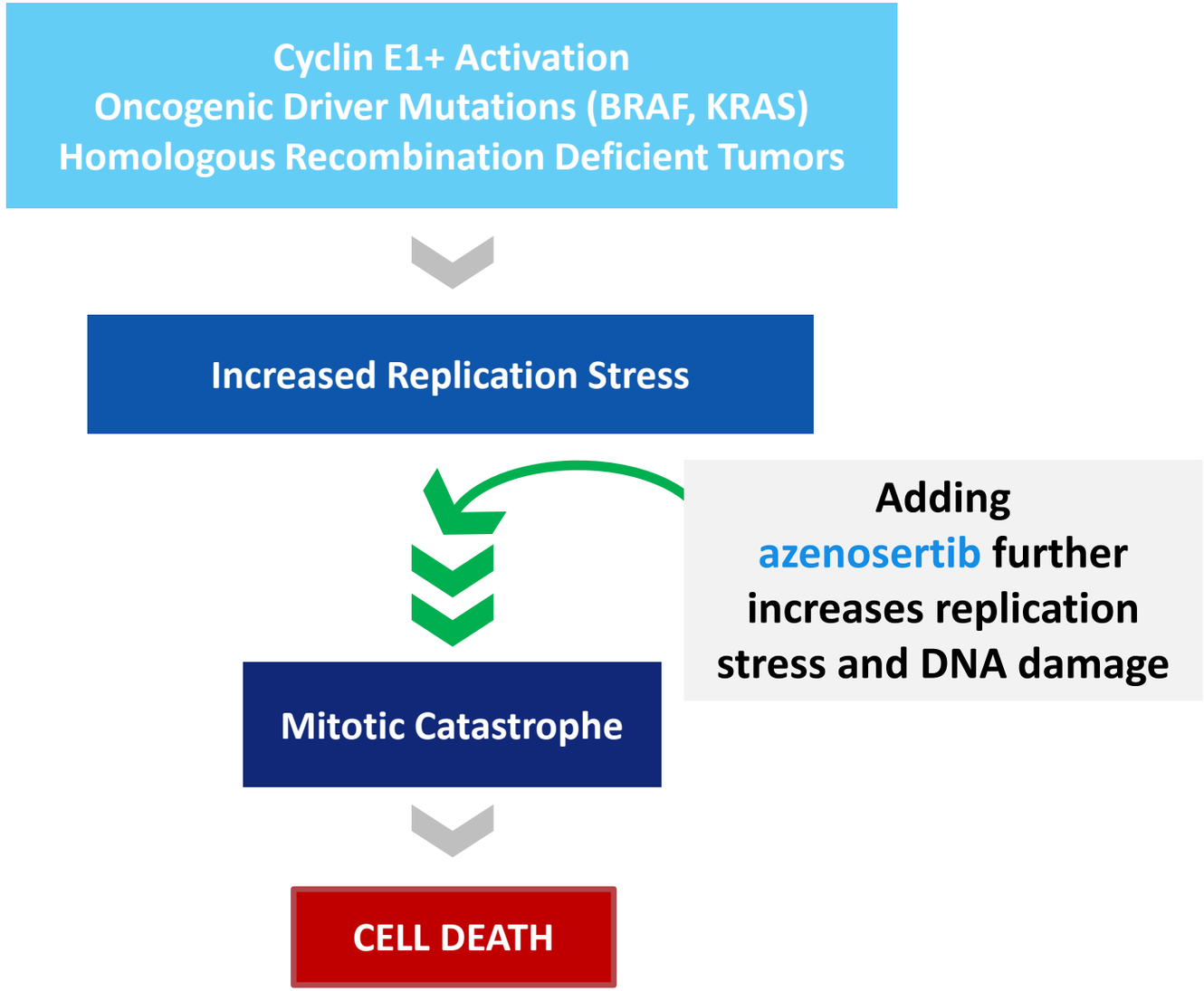
- Activation of Cyclin E1/CDK2 increases cell proliferation, resulting in higher replication stress and contributing to genomic instability

Tumors with Oncogenic Driver Mutations[2]

- Driver mutations, such as BRAF or KRAS, accelerate G1/S cell cycle transition, inducing DNA replication stress, leading to DNA damage and genomic instability

Homologous Recombination Deficient Tumors[3]

- Genomic instability results from inability to repair double stranded DNA breaks



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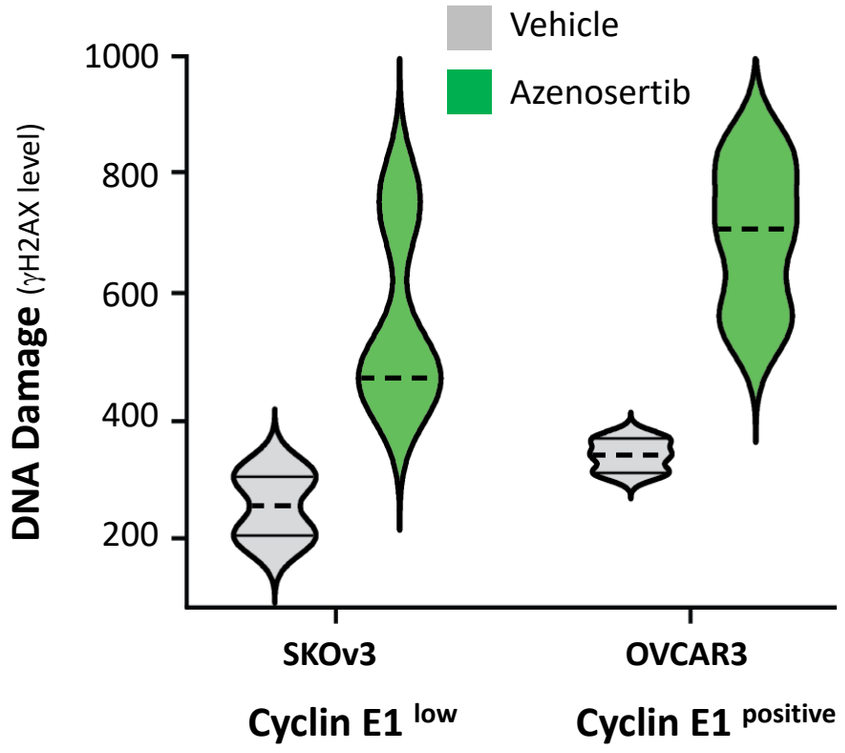
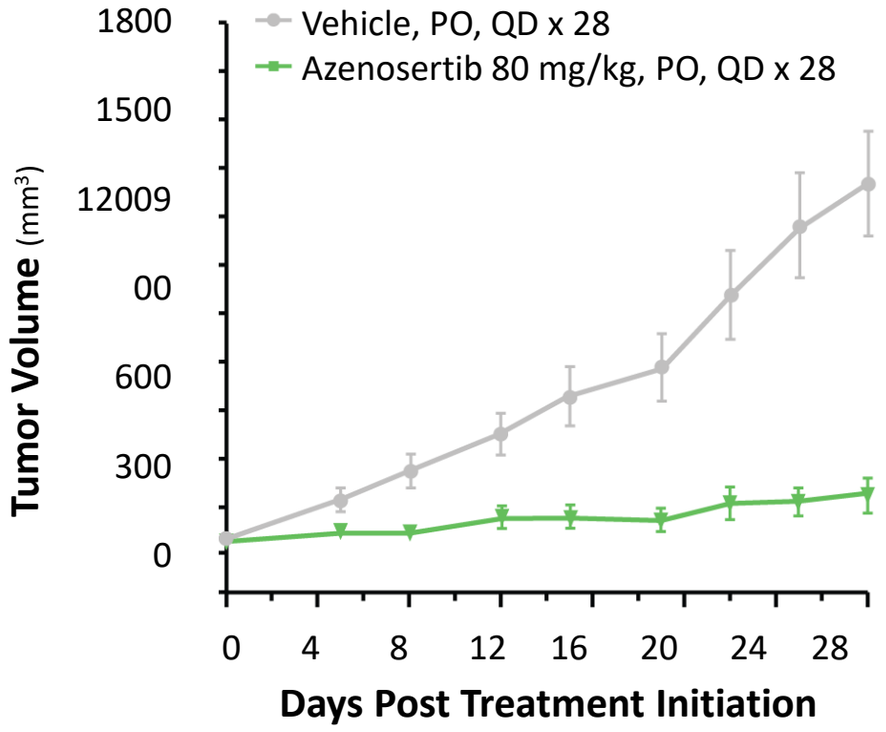
1 Fagundes R, et al. Front Cell Dev Biol. 2021; 2 Stewart MD, Oncologist. 2022; 3 Zhang, J, et al. Genes 2016; Abbreviations: BRAF, V-Raf Murine Sarcoma Viral Oncogene Homolog B; KRAS, Kirsten rat sarcoma viral oncogene homolog

Azenosertib Results in Higher Levels of DNA Damage and Tumor Growth Inhibition in Cyclin E1 Positive Tumors



- OVCAR3 tumors (Cyclin E1 ^{positive}) have higher baseline levels of DNA damage than SKOV3 tumors (Cyclin E1 ^{low})
- **Azenosertib treatment further increases DNA damage**



- Azenosertib treatment results in 88% Tumor Growth Inhibition (TGI) in xenografted Cyclin E1 ^{positive} OVCAR3 tumors

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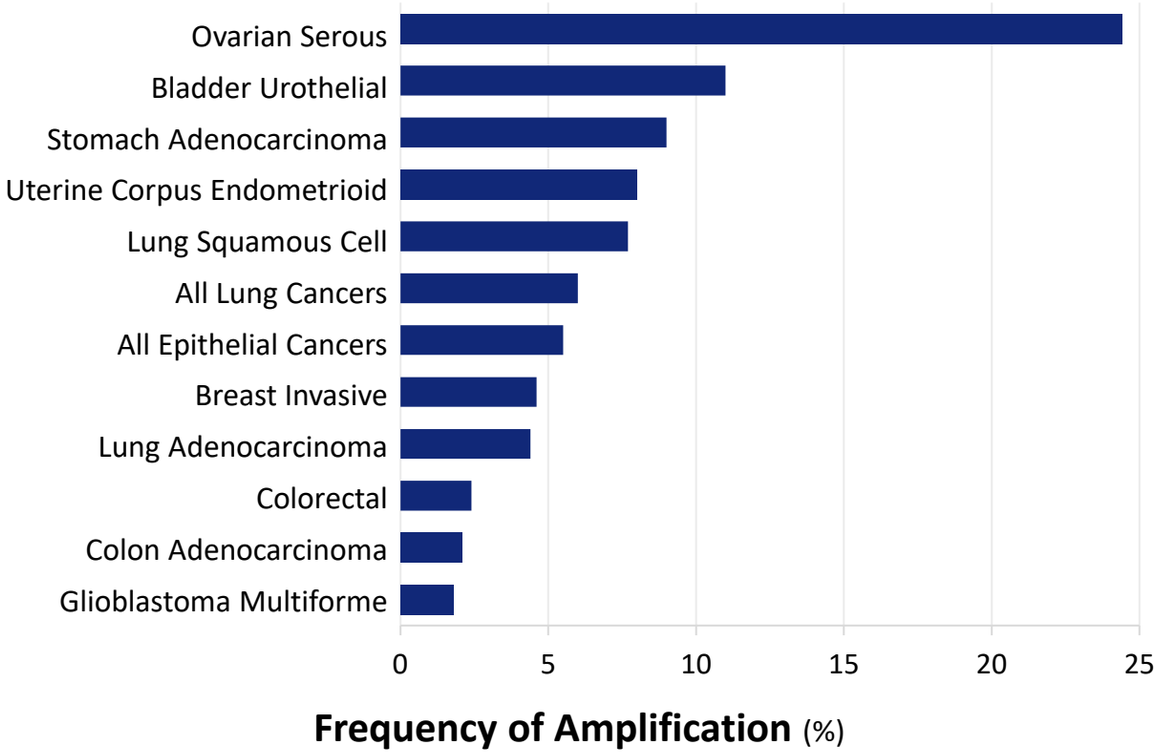
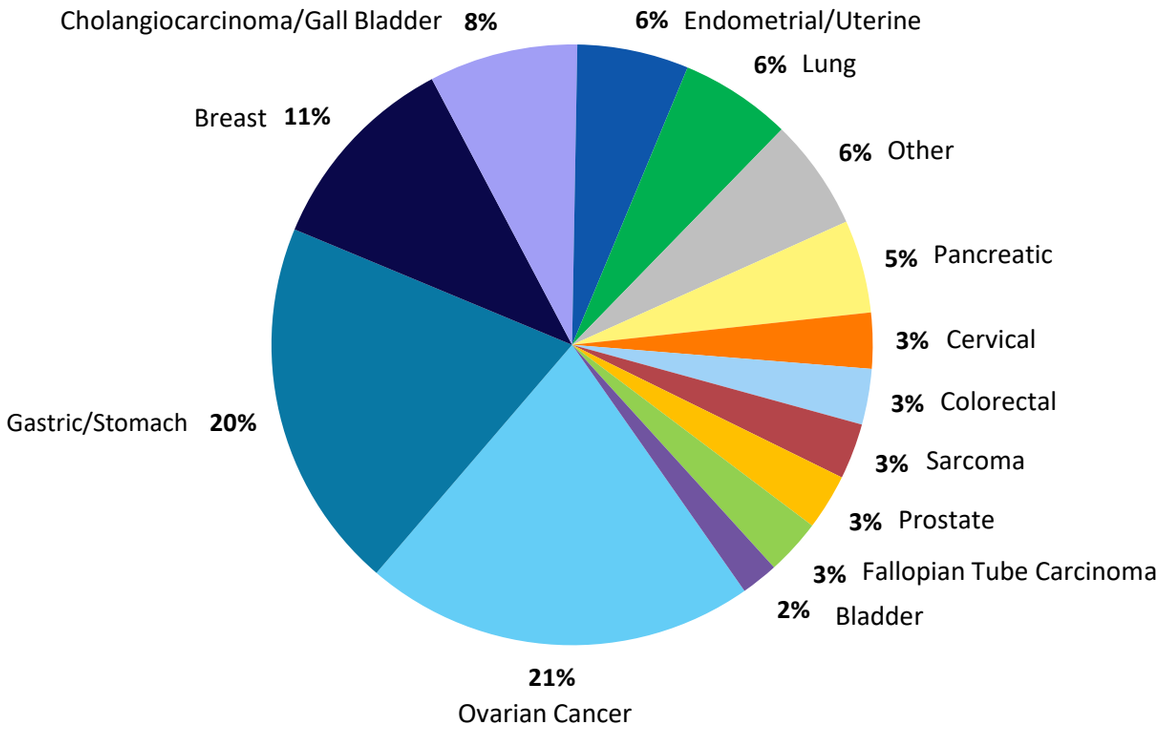
Ma, et al. Cancer Res (2023) 83 (7_Supplement): 2153; Abbreviations: PO, orally; QD, daily

Cyclin E1 Amplification Particularly Prevalent in Gynecologic Malignancies But Occurs in Many Other Tumor Types

TCGA Pan Cancer Analysis (6547 samples)[1]



Frequency of *CCNE1* Amplification Across Tumor Types[2]



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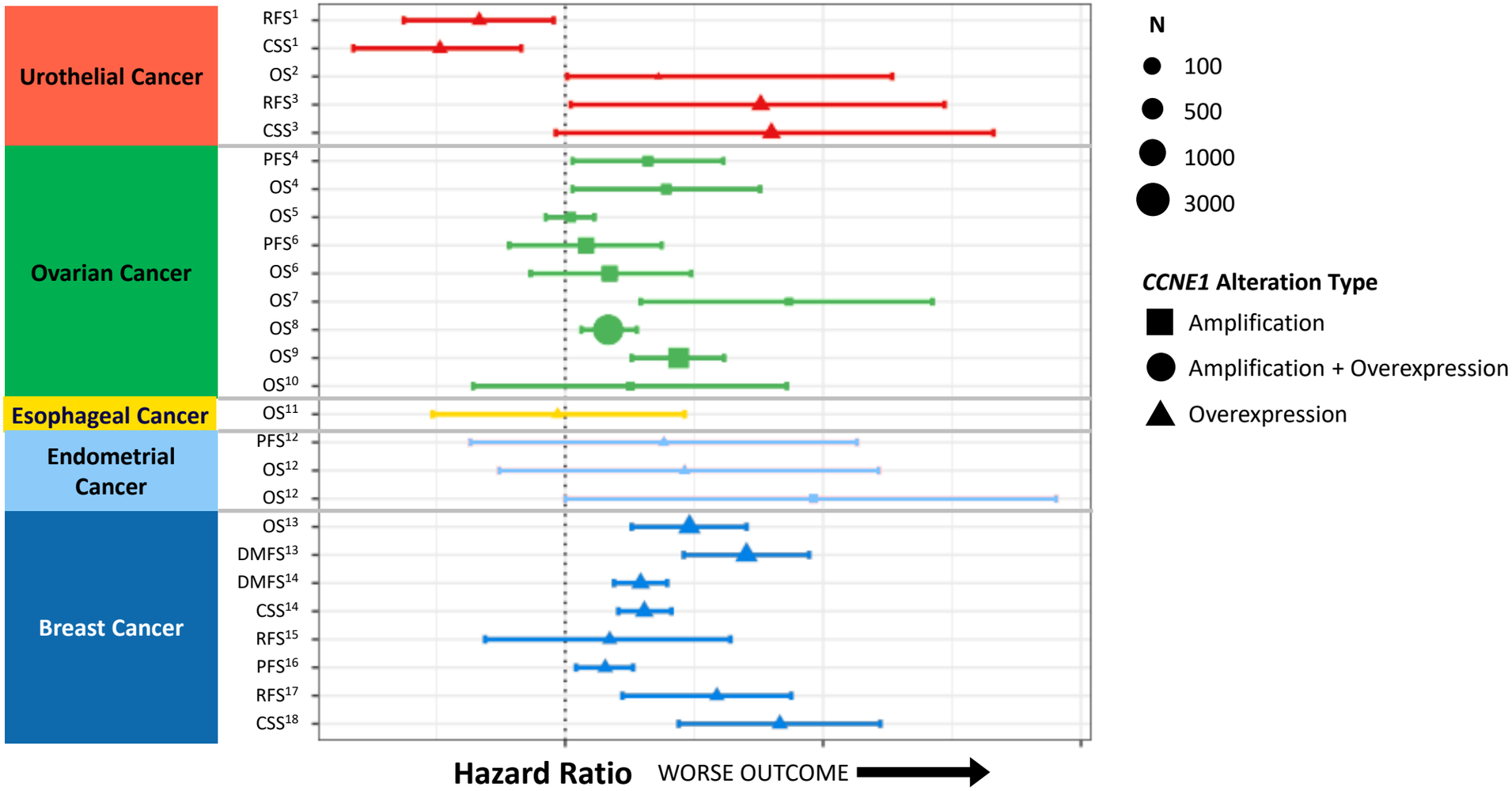
1 Etemadmoghadam D., et al. Proc Natl Acad Sci USA 2013; 2 Yao, S., et al. Sci Rep 12, 8701 2022. 3. TCGA GENIE: 2161/119807 (1.8%). 4. Foundation Insights database: 18802/541919 (3.5%)

CCNE1 Amplified and/or Cyclin E1+ Cancers Have a Worse Outcome Across Multiple Tumor Types

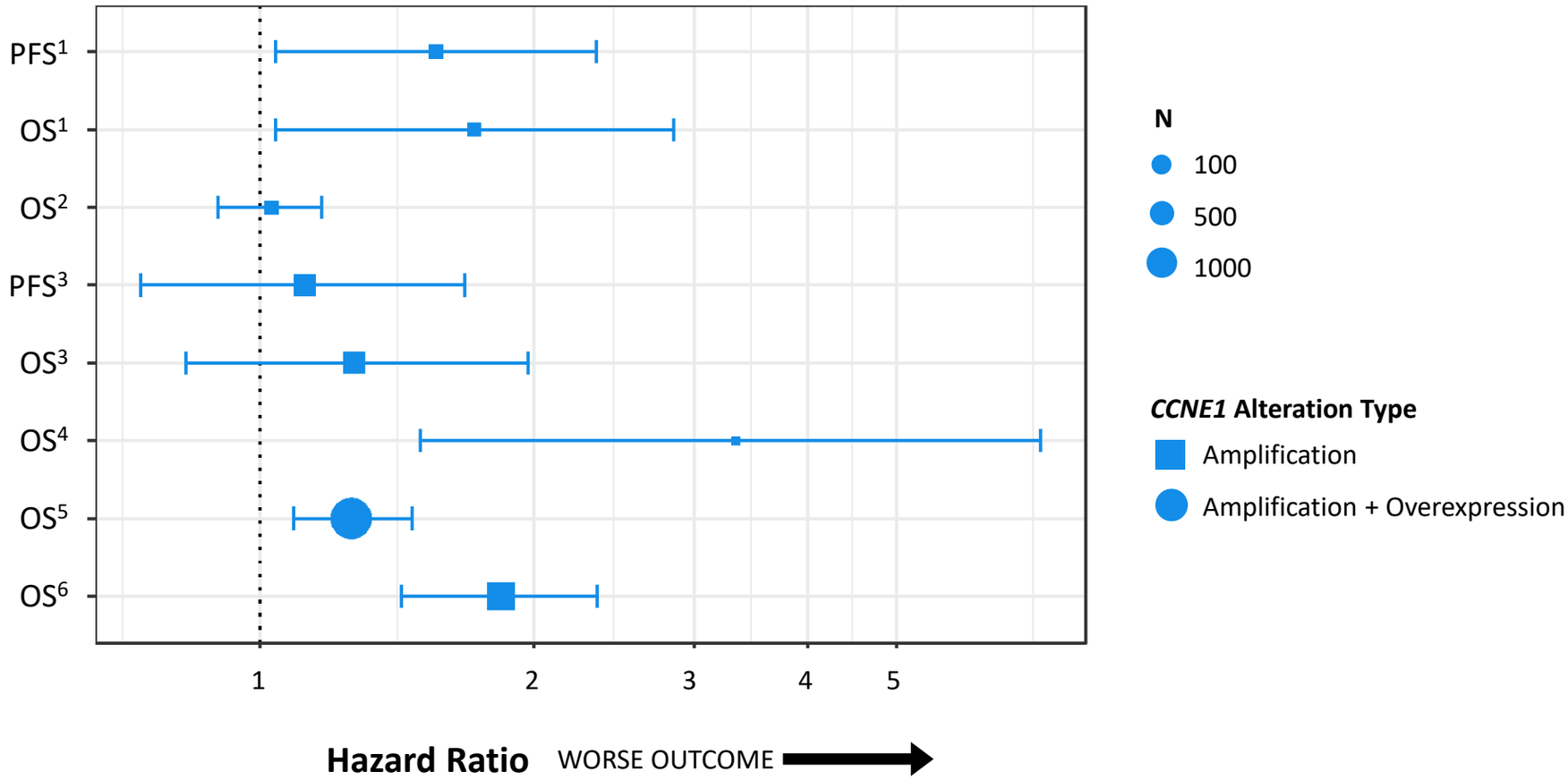


1 Shariat SF, et al. Human Path. 2006; 2 Matsushita R, et al. British J Cancer 2015; 3 Lotan Y, et al. Euro Assoc Urology 2013; 4 Stronach E, et al. Mol Cancer Res 2018; 5 Pils D, et al. Euro J Cancer 2014;
6 Petersen S, et al. Gynecol Oncol 2020; 7 Nakayama N, et al. Cancer 2010; 8 Kang E, et al. Cancer 2023; 9 Chan A, et al. J Path: Clin Res 2020; 10 Ayhan A, et al. Mod Path 2017; 11 Zhou Z, et al. BMC Gastroenterology 2014;
12 Nakayama K J Oncol. 2016; 13 Sieuwerts AM, et al. Clin Cancer Res 2006; 14 Lundgren C, et al. Acta Oncologica 2015; 15 Luhtala S, et al. Tumor Biol 2016; 16 Jansen MP, et al. Breast Cancer Res Treat 2012;
17 Desmedt C, et al. Int J Cancer 2006; 18. Chappuis PO, et al. Annals of Oncology 2005
Abbreviations: RFS, recurrence free survival, CSS; cancer specific survival, OS; overall survival; PFS, progression free survival; DMFS; distant metastasis free survival

Ovarian Cancer Patients with *CCNE1* Amplified and/or Cyclin E1+ Cancers Have a Worse Outcome Following Platinum-Based Chemotherapy Treatment Independent of Platinum-Sensitivity Status

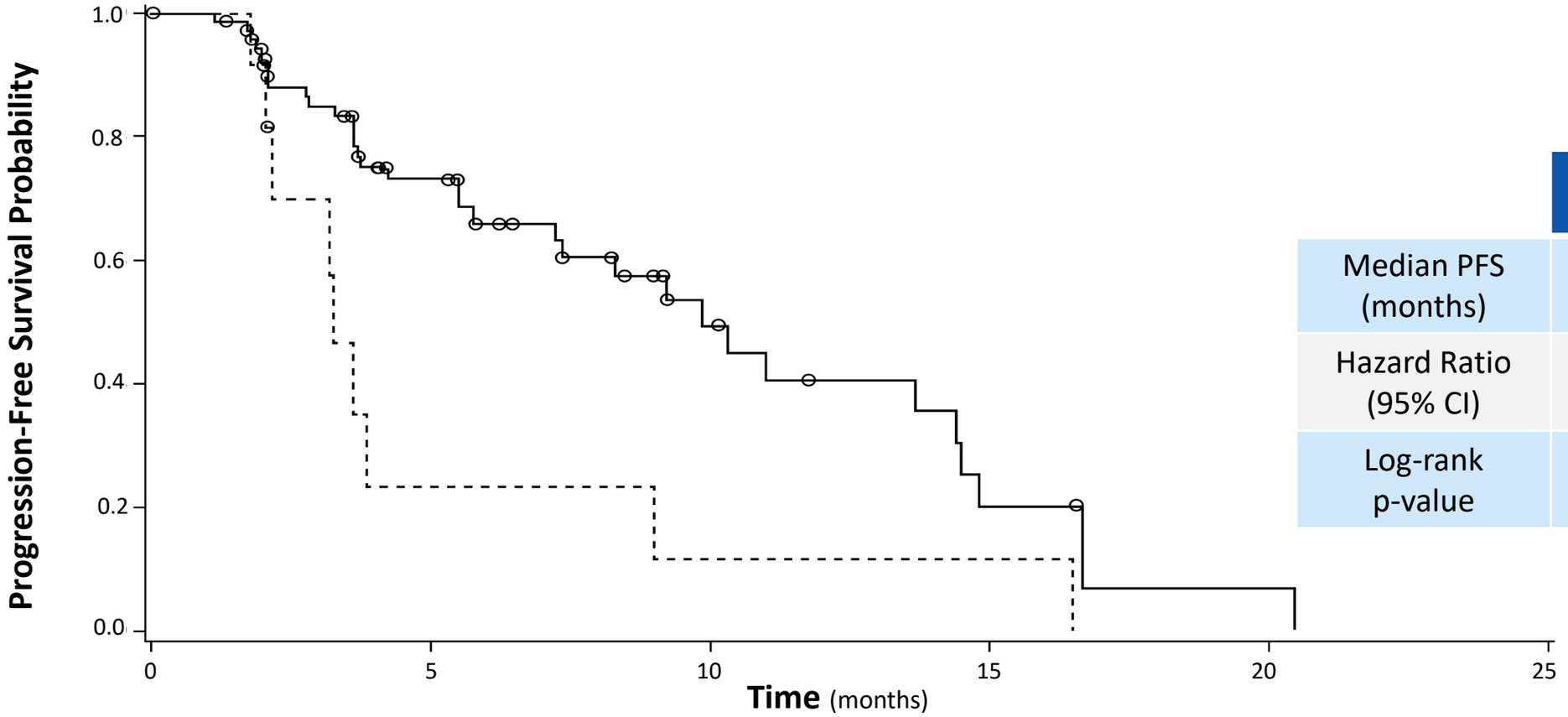
6 Studies; n=5,404

- 4 studies where timing of tissue collection was available- all were platinum sensitive tissue collected after ≤ 1 course of chemotherapy; 3,533/5,404 (65%)
- Other 2 studies did not disclose timing of tissue collection



1 Stronach, et al. Mol Cancer Res 2018;16:1103-11; 2 Pils, et al. Eur J Cancer 2014;50:99-110; 3 Peterson, et al. Gynecol Oncol 2020;157:405-10; 3 Nakayama, et al. Cancer 2010;116:2621-34; 5 Kang, et al. Cancer 2023;129:697-713; 6 Chan, et al. J Pathol Clin Res 2020;6:252-62; *Timing of tissue collection was not disclosed. Abbreviations: PFS: progression free survival, OS; overall survival

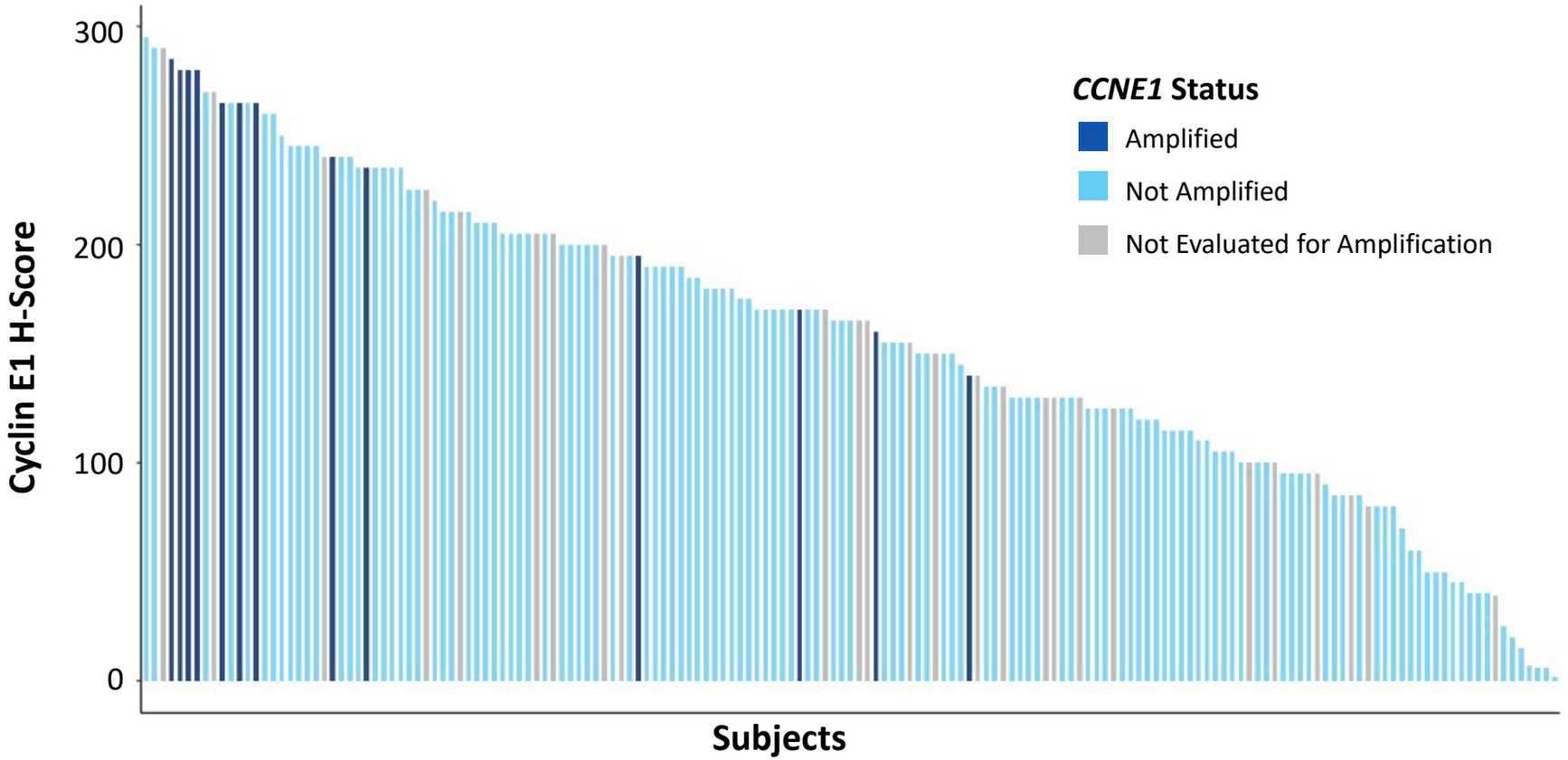
Progression Free Survival Triples in Patients with Cyclin E1+ Tumors Compared to Cyclin E1- Tumors in Azenosertib Chemotherapy Combinations (ZN-c3-002)



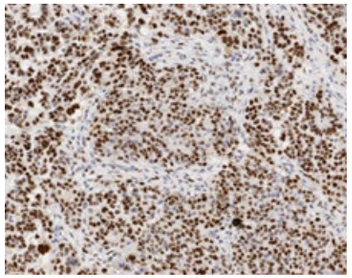
	H-Score ≤ 50 (N=12)	H-Score > 50 (N=78)
Median PFS (months)	3.25	9.86
Hazard Ratio (95% CI)	0.37 (0.18 – 0.79)	
Log-rank p-value	0.0078	

H-scores calculated by multiplying the percentage of cells (0 to 100%) with intensity of Cyclin E1 expression (0 to 3); Liu JF., et al. Journal of Clinical Oncology 41, no. 16_suppl (June 01, 2023) 5513-5513;
Abbreviations: CI, confidence interval; PFS, progression free survival

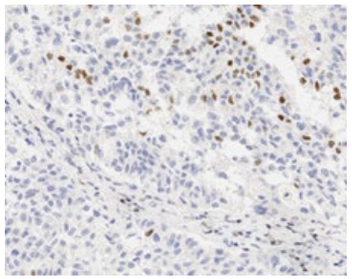
Analysis of Zentalis Clinical Trial Samples Confirms Cyclin E1 Protein Expression is High in the Majority of Ovarian Cancers



Cyclin E1^{+} by IHC



Cyclin E1^{-} by IHC

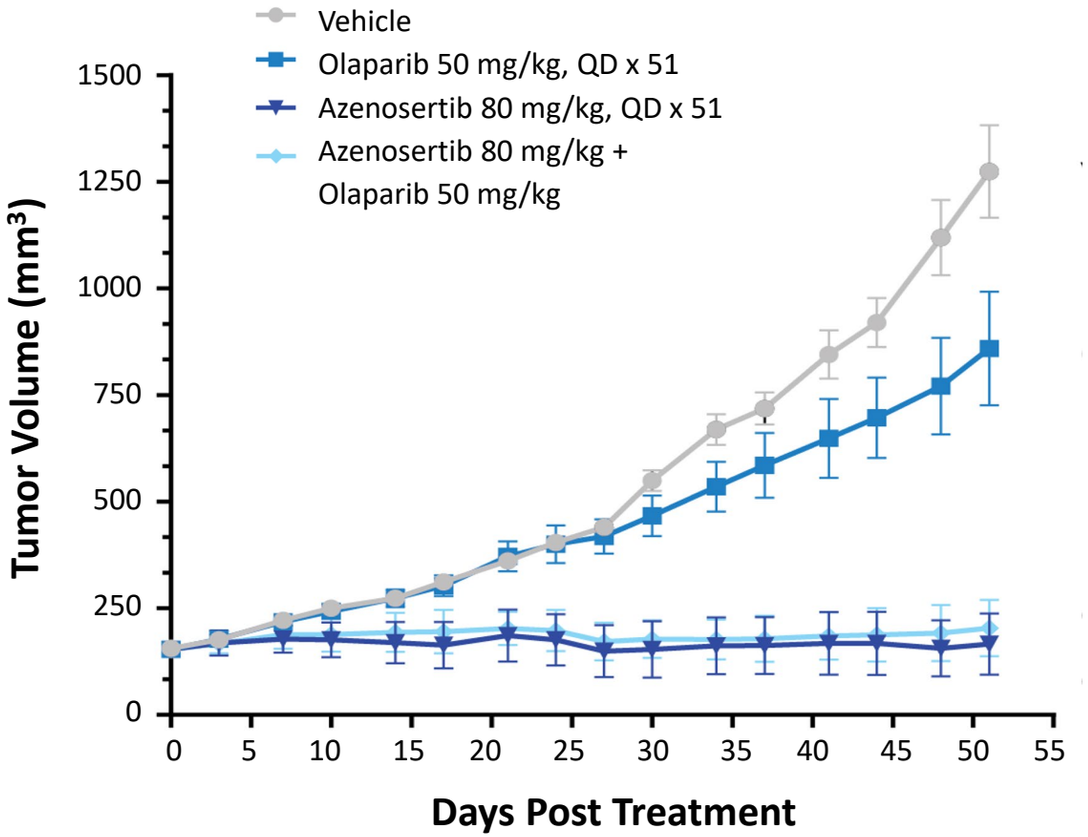


- HGSOC samples from an ongoing azenosertib clinical trial (ZN-c3-002, N=111) as well as 56 procured samples
- Cyclin E1 H-scores* were determined using a validated IHC assay and *CCNE1* amplification status was determined by tissue-based NGS
- Cyclin E1 IHC positivity is prevalent and occurs in tumors both with and without *CCNE1* amplification

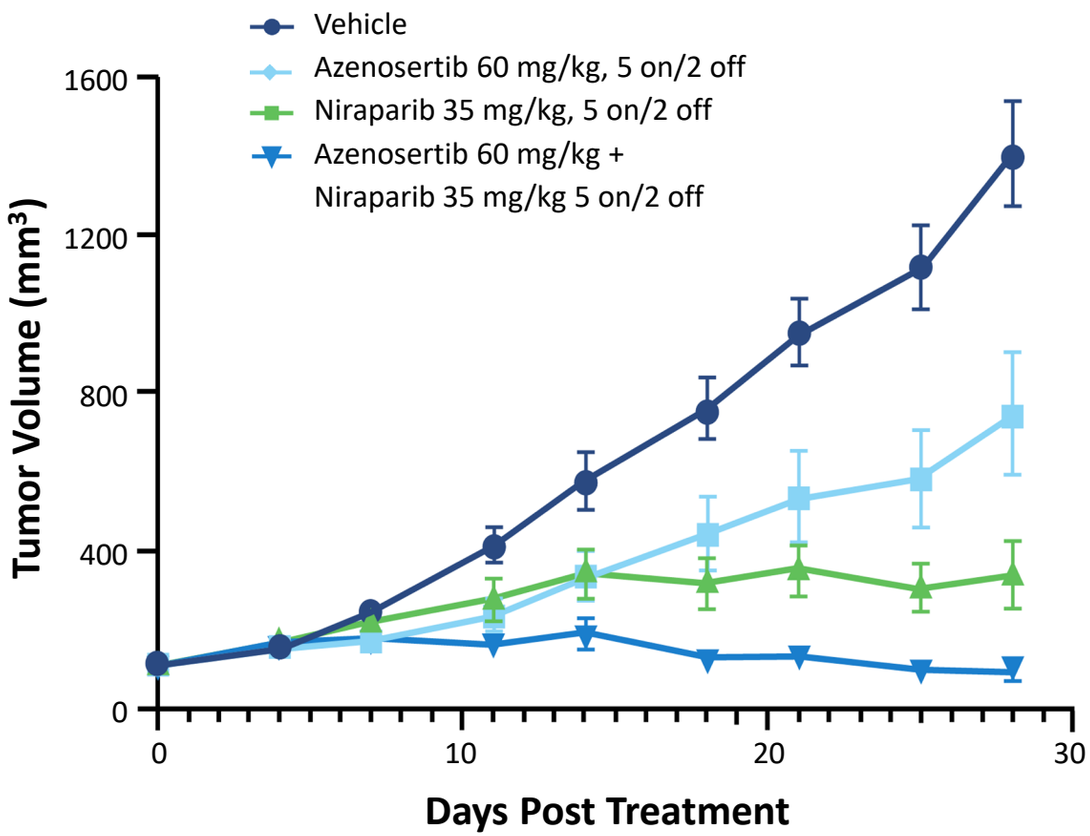
*H-scores calculated by multiplying the percentage of cells (0 to 100%) with intensity of Cyclin E1 expression (0 to 3).
Harismendy, et al. Presented at the AACR Special Conference in Cancer Research: Ovarian Cancer. October 5 - 7, 2023 - Boston, MA; Abbreviations: HGSOC, high-grade serous ovarian cancer; IHC, immunohistochemistry; NGS, next generation sequencing

Monotherapy Azenosertib +/- PARP Inhibitor Combinations are Active in HRD Tumors, Including Models with Acquired PARP Resistance

CDX Model PARPi Resistant Model (MDA-MB-436; *BRCA1*mt)



PDX TNBC Model (HBCx-10; *BRCA2*mt)



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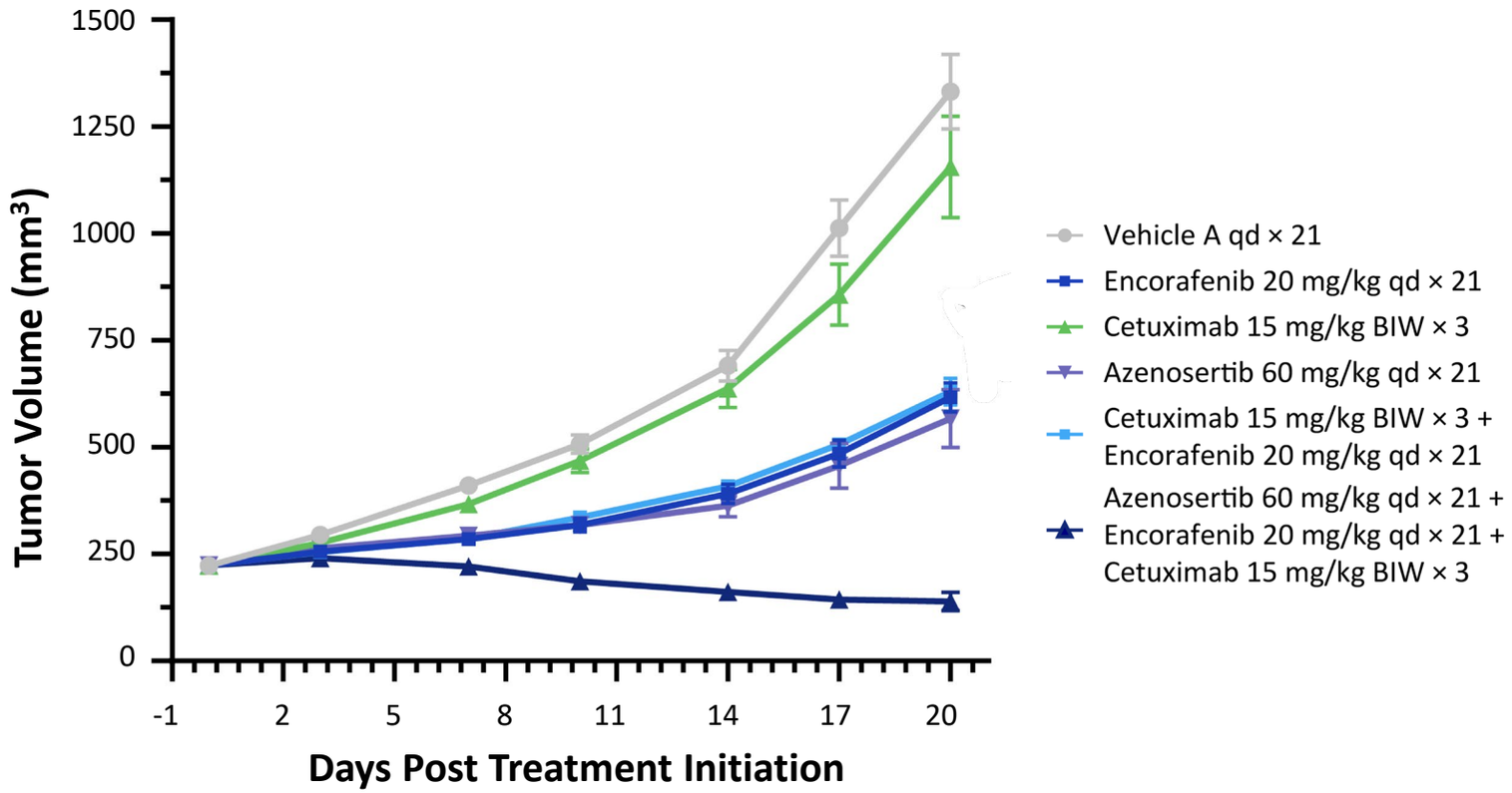
Zentalis data on file; Abbreviations: PARP, poly-ADP ribose polymperase; HRD, homologous recombination repair deficient; PARPi, PARP inhibitor; CDX, cell line derived xenograft; PDX, patient derived xenograft; TNBC, triple-negative breast cancer

Preclinical Data Supports the Combination of Azenosertib with Encorafenib and Cetuximab (BEACON Regimen)

LS411N (BRAF mutant CRC model)



- Oncogene-induced replication stress in mutationally driven cancers leads to DNA damage and genomic instability[1]
- Azenosertib further increases replication stress and DNA damage, providing mechanistic basis for synergy with EGFR/BRAF inhibition
- Addition of azenosertib to the BEACON regimen is well tolerated and provides superior efficacy in an *in vivo* model of BRAF mutant CRC

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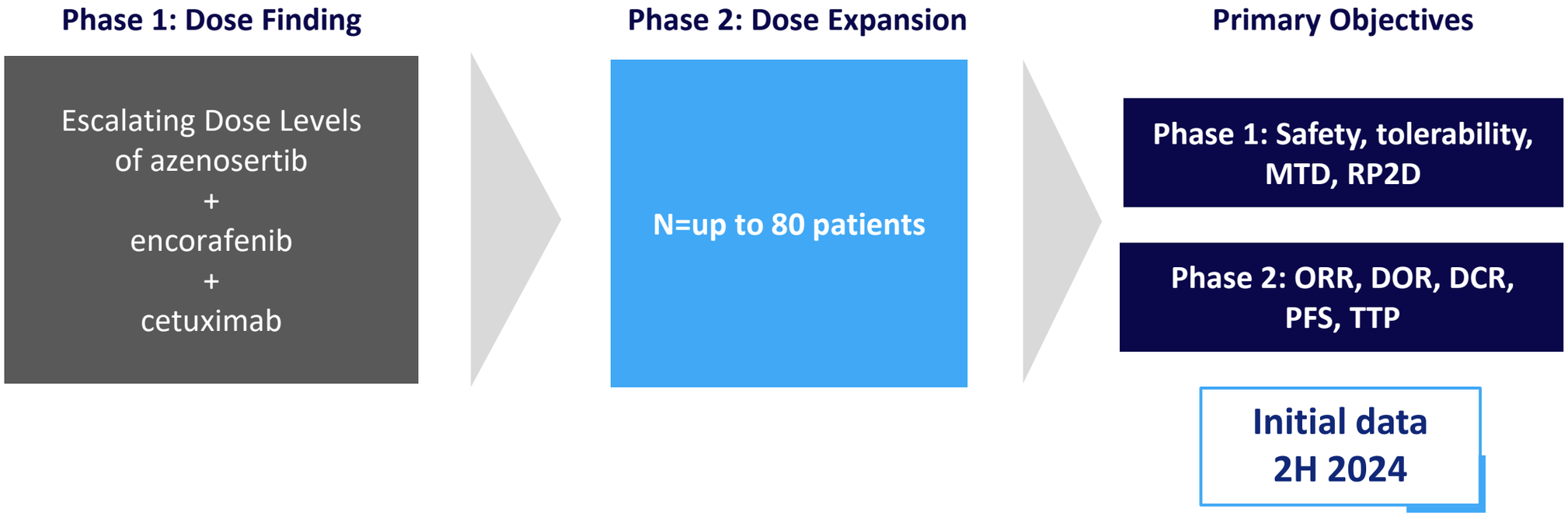
Zentalis Data on File; 1. Kotsantis P, et al. Cancer Discov. 2018. Abbreviations: BRAF, V-Raf Murine Sarcoma Viral Oncogene Homolog B; CRC, colorectal cancer; EGFR, epidermal growth factor receptor

ZN-c3-016: Phase 1/2 Trial in BRAF mCRC in Collaboration with Pfizer

Key Eligibility: BRAF V600E mutated mCRC; Disease progression after 1 or 2 previous regimens for metastatic disease; Prior therapy may include BRAF and/or EGFR directed therapy (e.g., may have progressed after BEACON regimen)

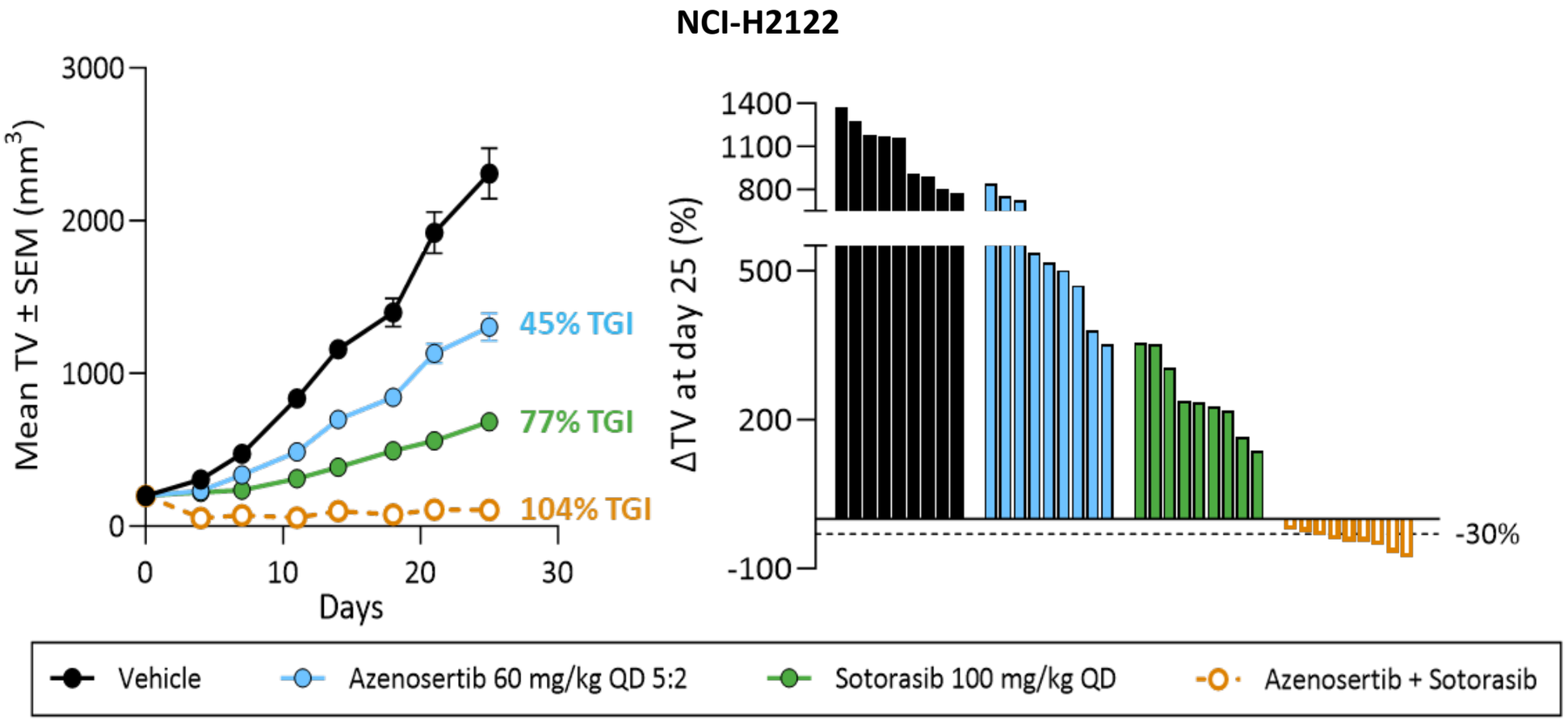


Encorafenib in combination with cetuximab (BEACON) is the standard of care for 2L treatment of BRAF V600E mCRC

NCT05743036

Abbreviations: BRAF, V-Raf Murine Sarcoma Viral Oncogene Homolog B; mCRC, metastatic colorectal cancer; EGFR, epidermal growth factor receptor; MTD, maximum tolerated dose; RP2D, recommended phase 2 dose; ORR, objective response rate; DOR, duration of response; DCR, disease control rate; PFS, progression free survival; TTP, time to progression; 2H, second half; 2L, second line

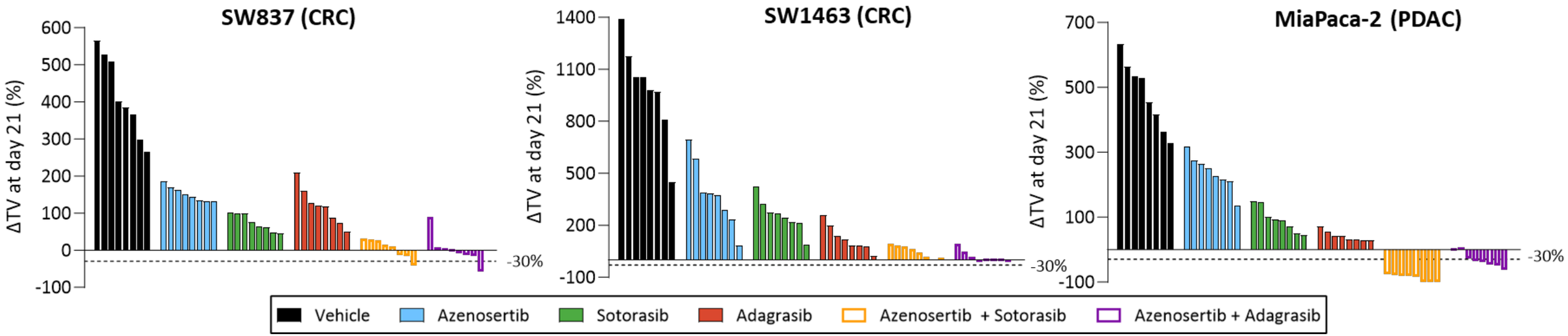
The Combination of Azenosertib with the KRAS^{G12C} Inhibitor Sotorasib Demonstrates Tumor Regressions in a NSCLC Model



Source: Zentalis AACR poster 2024, Jameson, et al

Abbreviations: TV, tumor volume; SEM, standard error of the mean; TGI, tumor growth inhibition; ΔTV, change in tumor volume; NSCLC, non small cell lung cancer

Combination of Azenosertib with KRAS^{G12C} Inhibitors Improves Efficacy and Drives Tumor Regression in Colorectal (CRC) and Pancreatic (PDAC) Models



Source: Zentalis AACR poster 2024, Jameson, et al

Abbreviations: ΔTV, change in tumor volume

Strong Rationale Supports Ongoing Clinical Development of Azenosertib in Cancers with High Genomic Instability

1 Cyclin E1 status is predictive of azenosertib sensitivity in preclinical models

- DENALI (ZN-c3-005) is prospectively evaluating *CCNE1* amplification and Cyclin E1 IHC as potential patient enrichment strategies

2 Azenosertib has monotherapy activity in multiple HRD models

- MAMMOTH (ZN-c3-006) is evaluating monotherapy and combination with niraparib in PARP resistant, platinum resistant ovarian cancer

3 Azenosertib enhances the efficacy of BRAF + EGFR inhibition in preclinical models of colorectal cancer

- ZN-c3-016 is evaluating azenosertib in combination with encorafenib and cetuximab in BRAFV600E metastatic colorectal cancer

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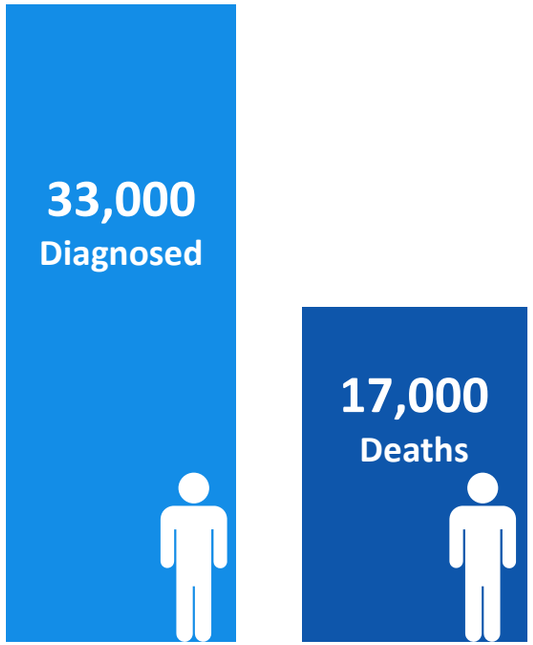
Abbreviations: IHC, immunohistochemistry; PARP, poly-ADP ribose polymerase; BRAF, V-Raf Murine Sarcoma Viral Oncogene Homolog B; EGFR, epidermal growth factor receptor; HRD, homologous recombination repair deficient

BCL-2 Inhibitor (ZN-d5) in Combination with Azenosertib

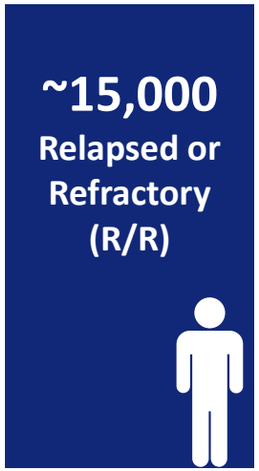
Represents Opportunity to Address Acute Myeloid Leukemia Patients with Known Poor Prognosis and High Unmet Need

Relapsed/Refractory Acute Myeloid Leukemia Remains a Devastating Disease and Represents a Major Unmet Medical Need

2023 US/EU5 Estimated New Cases and Patient Deaths[1]



2023 US/EU5 Drug Treatable[2]

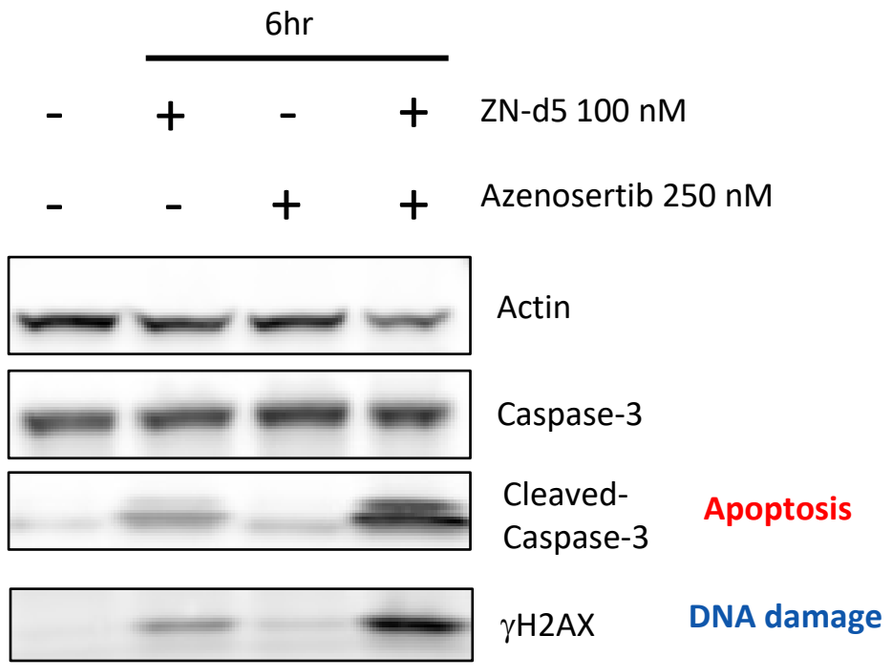


- Most common form of acute leukemia in adults; estimated 5-yr survival ~10% for patients ≥ 60 years old[3]
- 57% of patients either relapse after CR, are primary refractory, or die within 12 months[3]
- R/R patients have particularly dismal prognosis with median OS 3-6 months[3]
- BCL-2 inhibitors (e.g., venetoclax) are foundational treatments for AML[4]

1. American Cancer Society. Cancer Facts & Figures 2023, SEER and ECIS. 2 Figures represent company best estimates based on US patients with conditions covered by the companies target indication. Sources DRG Clarivate, Kantar Health 3 Shimony, S, et al. Am J Hematol. 2023; 98(3): 502-526; 4 Maiti A, et al. The Cancer Journal 28(1) 2022
Abbreviations: CR, complete response; R/R, relapsed/refractory; OS, overall survival; AML, acute myeloid leukemia

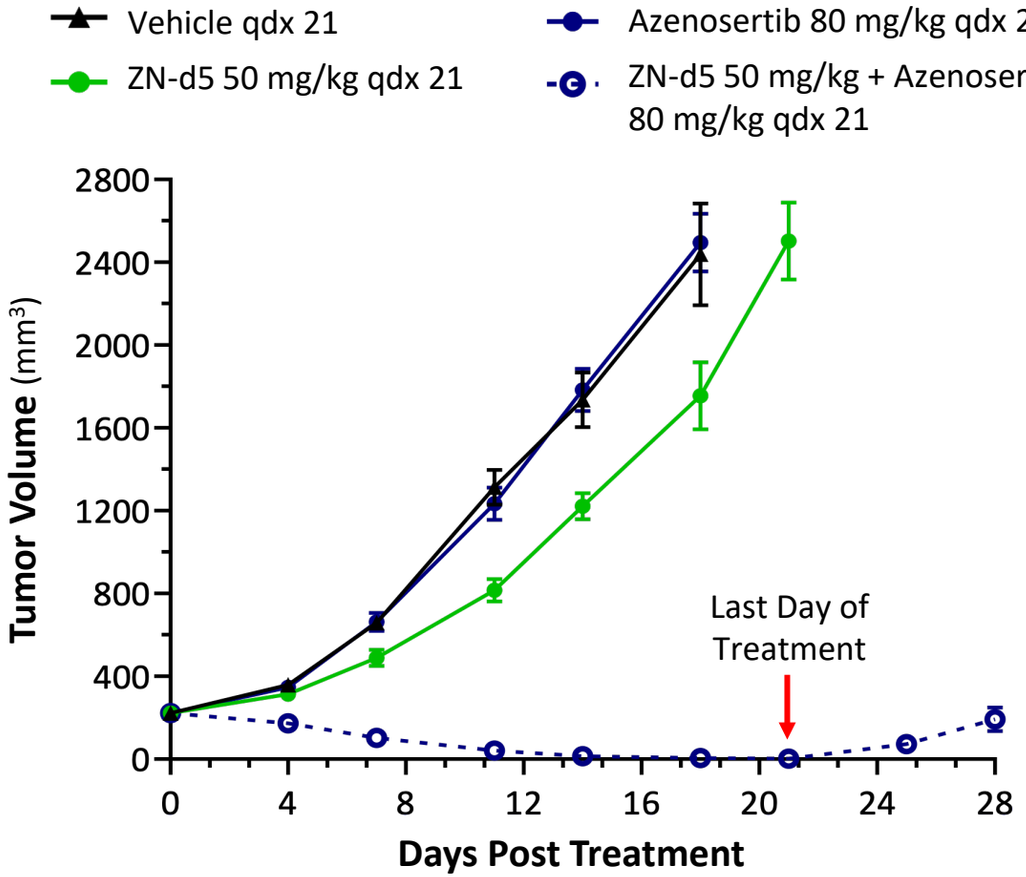
Combination of ZN-d5 and Azenosertib Results in Enhanced Apoptosis, DNA Damage and Synergistic Anti-Tumor Activity in an AML Model

HL-60 (in vitro)



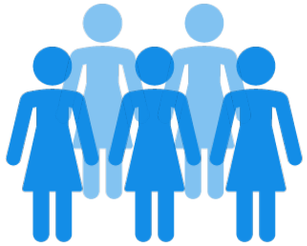
Synergistic effects seen at sub-efficacious doses of both agents

HL-60 (in vitro)



Izadi H, et al. AACR 2022 Cancer Res (2022) 82 (12_supplement):2591; Data / Report On File, Zentalis Pharmaceuticals

Despite Recent Progress and Evolving Treatment Paradigm in AML, Many Patients Still Lack Treatment Options After Relapse



AML Incidence (2021)
US + EU5 = ~33,212

Newly Diagnosed: Front Line → **Maintenance** → **Relapsed/Refractory**

Unmet Need

1st Relapse Chemo/SCT Ineligible: Without Actionable Mutation

~10,500
treatment eligible

2nd Relapse: After Mutation Directed Therapy

~4,500
treatment eligible

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Adapted from Heuser, Y. et. Al. Annals of Oncology 31 (6) 697-712 2020; Abbreviations: AML, acute myeloid leukemia; SCT, stem cell transplant

ZN-d5-004C: Enrolling Phase 1/2 Study of ZN-d5 and Azenosertib in R/R AML

Key Eligibility: R/R AML; Must have received at least 1 prior line of therapy for AML

Part A

Azenosertib Monotherapy and ZN-d5 + Azenosertib Dose Escalation Combination

- Azenosertib Monotherapy Dose Escalation
- ZN-d5 + Azenosertib Dose Escalation

Part B

Dose Expansion

ZN-d5 + Azenosertib at Combination RP2D(s)

Endpoints

- Safety, tolerability, PK, RP2D(s)
- ORR (CR + CRi + MLFS + PR); CRh; DoR

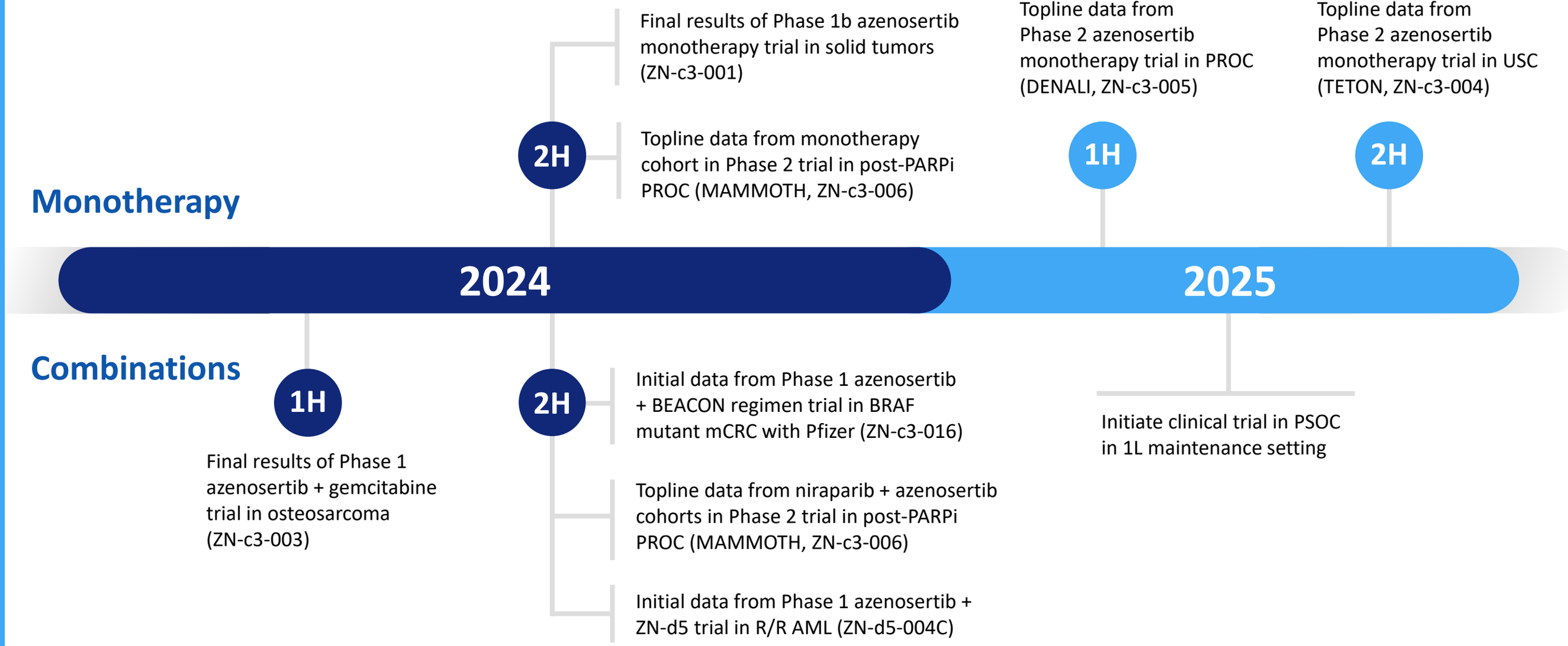
Initial data 2H 2024

NCT05682170

Abbreviations: R/R, relapsed/refractory; AML, acute myeloid leukemia; RP2D, recommended Phase 2 dose; PK, pharmacokinetics; ORR, objective response rate; CR, complete response; CRi: complete response with incomplete count recovery; MLFS: morphologic leukemia free state; PR, partial response; CRh: complete response with partial hematologic recovery; DoR; duration of response; 2H, second half

Executing on the Franchise Potential of Azenosertib

Upcoming Clinical Milestones



Abbreviations: 1H, first half; 2H second half; BRAF, V-Raf murine sarcoma viral oncogene homolog B; mCRC, metastatic colorectal cancer; PARPi, poly-ADP ribose polymerase inhibitor; R/R AML, relapsed or refractory acute myeloid leukemia; PROC, platinum resistant ovarian cancer; USC, uterine serous carcinoma; PSOC, platinum sensitive ovarian cancer; 1L, first line

Zentalis is Positioned for Success with Azenosertib Franchise

Potentially First- and Best-in-Class WEE1 Inhibitor

- Monotherapy efficacy; 37% ORR and 6.5 months mPFS in heavily pretreated ovarian and USC*
- Efficacy and safety clearly differentiate azenosertib from other WEE1 inhibitors
- Years ahead of other WEE1 inhibitors in development

Clinical Strategy Supports Blockbuster Opportunity

- Pursuing fast-to-market strategy with azenosertib monotherapy in platinum resistant ovarian cancer (PROC), ~43,000 treatable patients[1]
- Planned trial as 1L maintenance in ovarian cancer offers potential to benefit greatest number of patients, ~21,000 treatable patients[1]
- Expanding to a broad array of tumor types in combination with targeted agents

Multiple Near-Term Value Inflection Points

- Readouts from 3 Phase 2 trials in 2024 and 2025 in addition to other data updates
- Potential first NDA in 2026
- Supported by strong cash balance and runway into 2026

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1 Figures represent Company estimates of U.S. and EU5 patients with conditions covered by the Company's targeted indications; Source: IQVIA, DRG Clarivate
Abbreviations: mPFS: median progression free survival; ORR, objective response rate; USC, uterine serous carcinoma; 1L, first line NDA, New Drug Application; Statements comparing azenosertib to other agents, not head-to-head comparisons

*Data cut-off: October 25, 2023

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