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AACR 2022 Investor Event

April 8, 2022

Forward-Looking Statements and Disclaimer

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Today's Agenda

1. **ZN-c3 (Wee1 inhibitor) Updates**
   - Phase 1 monotherapy update from USC cohort
   - Phase 1b chemotherapy combination data in ovarian cancer
2. **ZN-c5 (oral SERD) Updates**
3. **ZN-d5 (Bcl-2 inhibitor) Updates**
4. **Summary and Catalysts**

Company Overview

Lead Program: Wee1i (ZN-c3) potentially first- and best-in-class

- Monotherapy responses in 4 solid tumor types, with 3 Exceptional Responders & additional responses in USC
- Promising data in ovarian cancer when combined with chemotherapy
- Potential accelerated approval paths for USC* and biomarker-driven trials
- Orphan drug and rare pediatric disease designations granted in osteosarcoma

Oral SERD (ZN-c5): potentially best-in-class profile as monotherapy and in combination, including with ZN-c3

BCL-2 inhibitor (ZN-d5): broad applicability as anti-apoptotic target; potential as monotherapy and in combination, including with ZN-c3

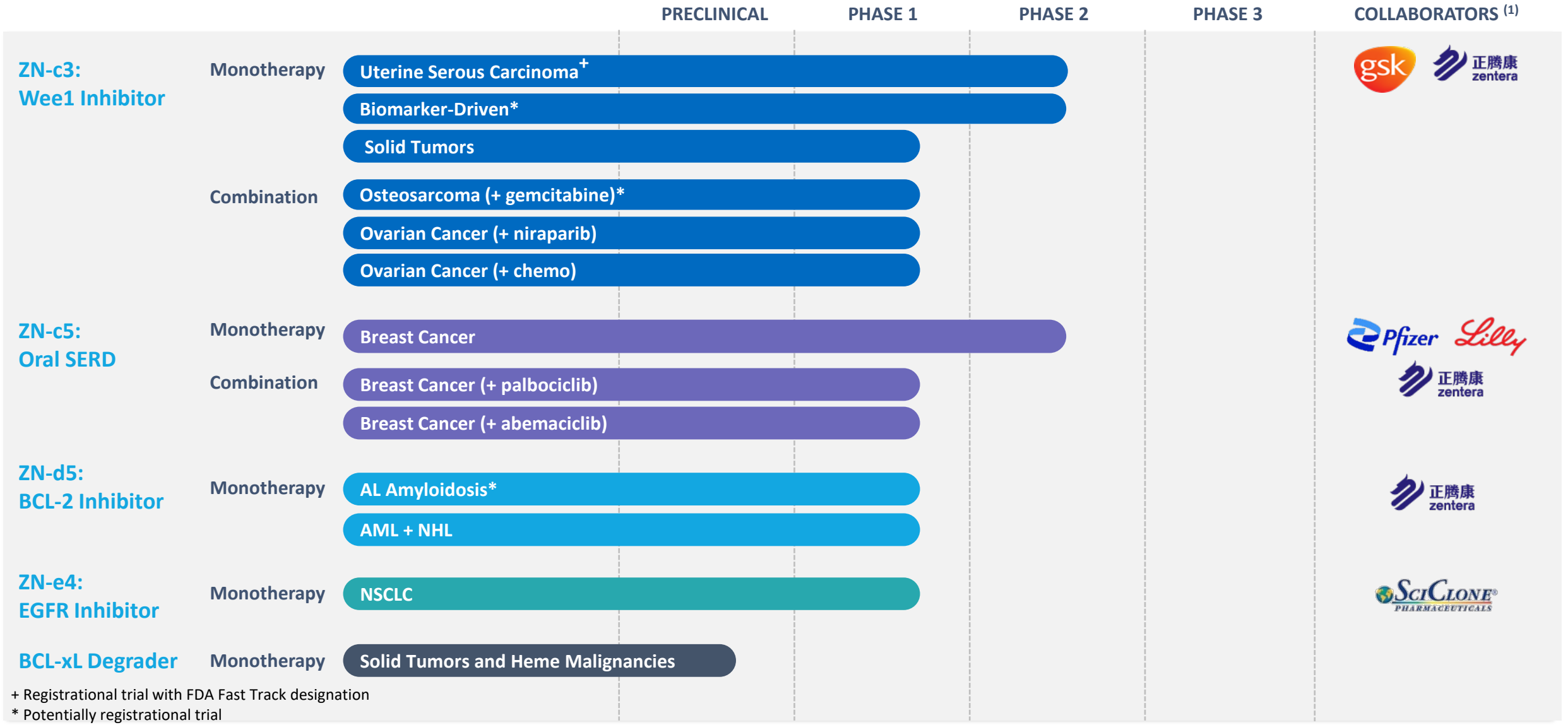
Additional programs targeting fundamental cancer pathways: EGFR inhibitor (ZN-e4) & BCL-xL heterobifunctional degrader

Investigating internal & third-party combinations, including ZN-d5 + ZN-c3 for liquid tumors and ZN-c5 + ZN-c3 for CDK4/6i-resistant tumors

Integrated Discovery Engine: 4 FDA-cleared INDs within the first 5 years

* Fast Track designation granted.

Broad Oncology Pipeline Designed to Improve Patient Outcomes



+ Registrational trial with FDA Fast Track designation
* Potentially registrational trial

(1) Zentalis is currently evaluating ZN-c5 in combination with palbociclib (Ibrance®), as part of a clinical research collaboration with Pfizer, evaluating ZN-c5 in combination with abemaciclib (Verzenio®), as part of a clinical research collaboration with Lilly. Zentalis intends to evaluate ZN-c3 in combination with niraparib (ZEJULA®), as part of a clinical research collaboration with GlaxoSmithKline. Zentalis maintains full ownership of ZN-c5 and ZN-c3 in each such collaboration. SciClone has development and commercial rights to ZN-e4 in Greater China (including Macau and Hong Kong), South Korea, Taiwan and Vietnam. Zentera, our joint venture, has development and commercial rights to ZN-c5, ZN-c3 and ZN-d5 in select Asian countries (including China). Zentera received CTA acceptances in China for ZN-c3, ZN-c3 in combination, ZN-c5 and ZN-d5 and four clinical trials are ongoing.

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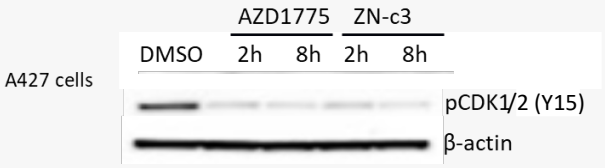
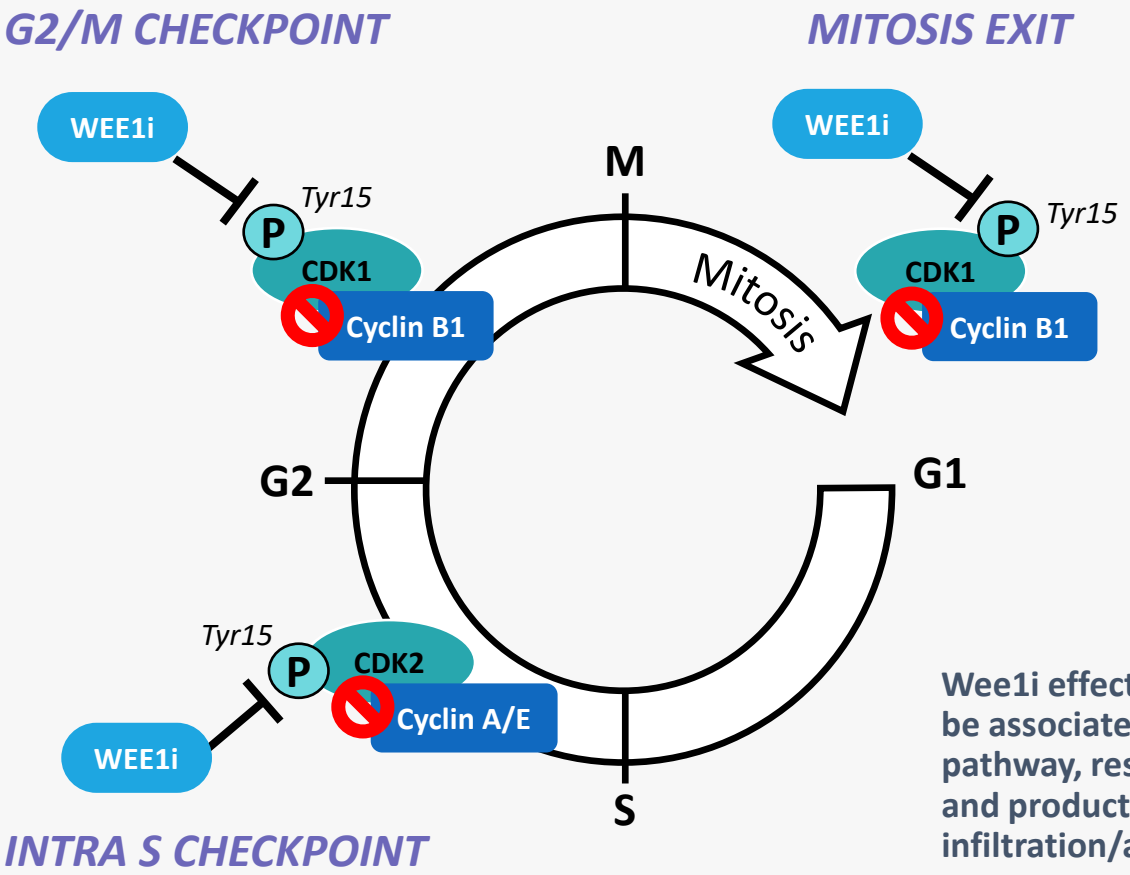
ZN-c3: Wee1 Inhibitor Background

Wee1 Inhibition: Clinically Proven DDR Target for Cancer



ZN-c3 inhibits CDK1/2 phosphorylation

Wee1 inhibition causes cancer cells to proceed to mitosis without repairing DNA damage, resulting in premature mitotic entry and apoptosis



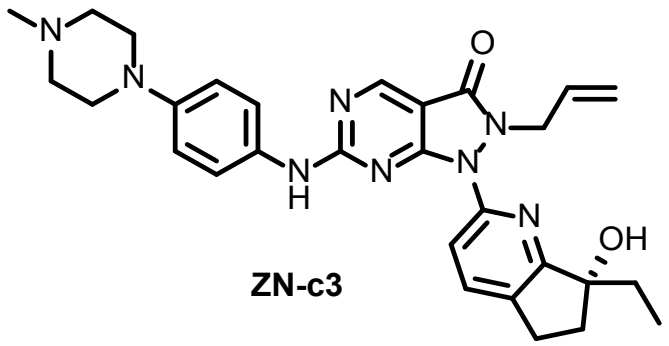
Inhibition of Wee1 may cause tumor cell death by:

- Aberrant origin firing causing exhaustion of the replication protein A1 (RPA1)[(1)]
- Degradation of ribonucleotide reductase subunit leading to exhaustion of dNTP pools[(2)]

Wee1i effects on cell cycle and DNA damage may be associated with activation of cGAS/STING pathway, resulting in Type I interferon response and production of cytokines driving immune cell infiltration/activation into tumor[(3-5)]

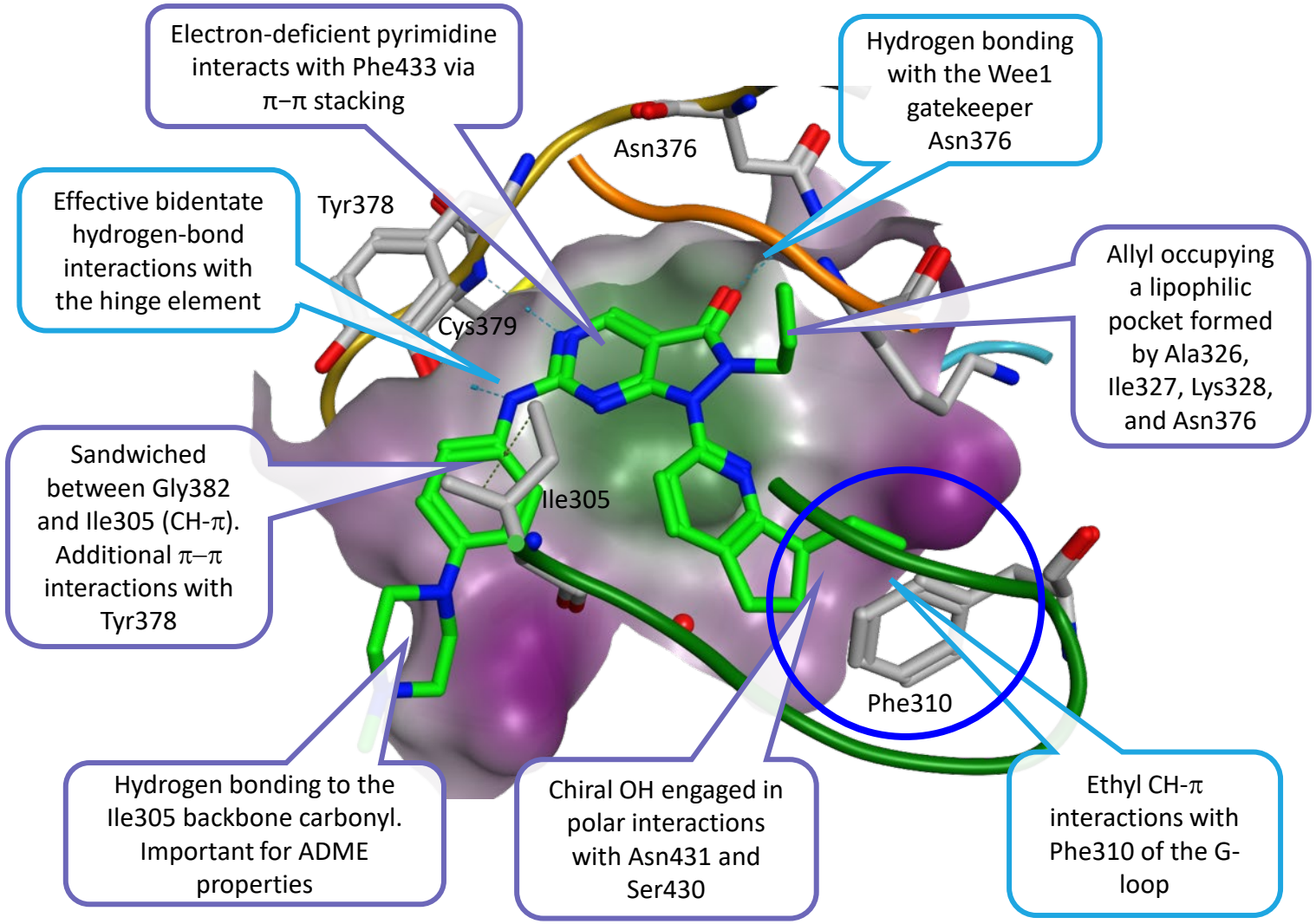
(1) Di Rora AGL et al. J Hematol Oncol. 2020 Sep 21;13(1):126
(2) Pfister SX et al. Cancer Cell. 2015 Nov 9; 28(5): 557–568
(3) Keenan et al. Clin Canc Res. (2021)
(4) Hai J et al. Clin Cancer Res. 2020 Jul 1;26(13):3431-3442
(5) Guo e et al. J. Exp. Med. 2021 Vol. 219 No. 1

Structure-Based Drug Design (SBDD) Led to the Discovery of a Highly Potent and Selective Wee1 Inhibitor ZN-c3 with Improved ADME Properties(1)



ZN-c3

ZN-c3 potency and ADME	
Wee1 IC_{50}	3.8 nM
H23 IC_{50}	103 nM
A427 IC_{50}	75 nM
Log *D*	2.4
*h*PPB	66%
*h*Hep	<18 mL/min/kg
solubility	> 2000 µM
CYP3A4	7 µM
hERG	> 30 µM



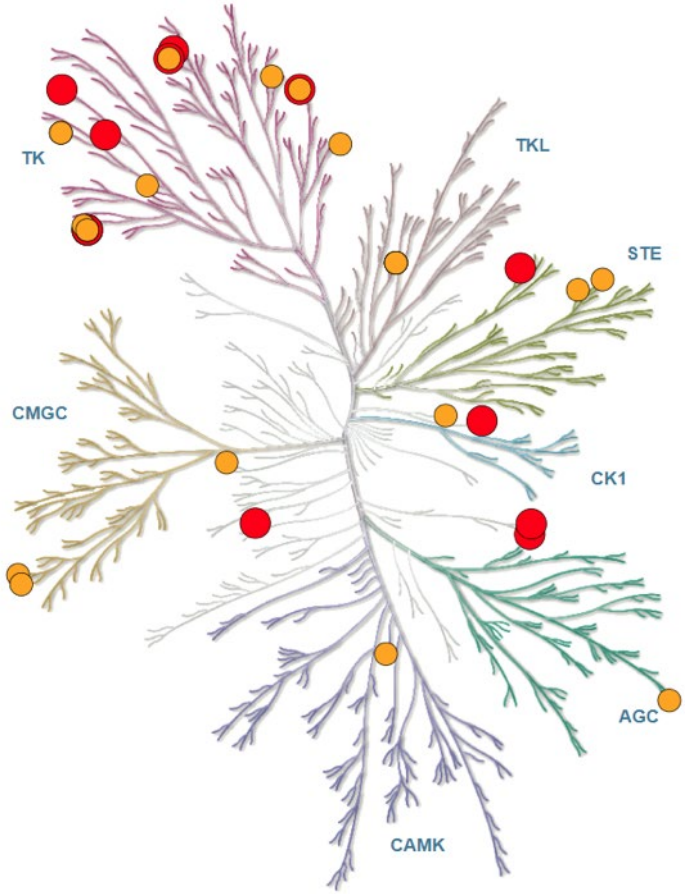
(1) Huang, PQ; *et al.* J. Med. Chem. **2021**, *64*, 13004-13024

ZN-c3: Differentiated Selectivity Profile(1)

Adavosertib

% Inhibition (@ 1µM)

- 90+ 13 kinases
- 75-89 24 kinases



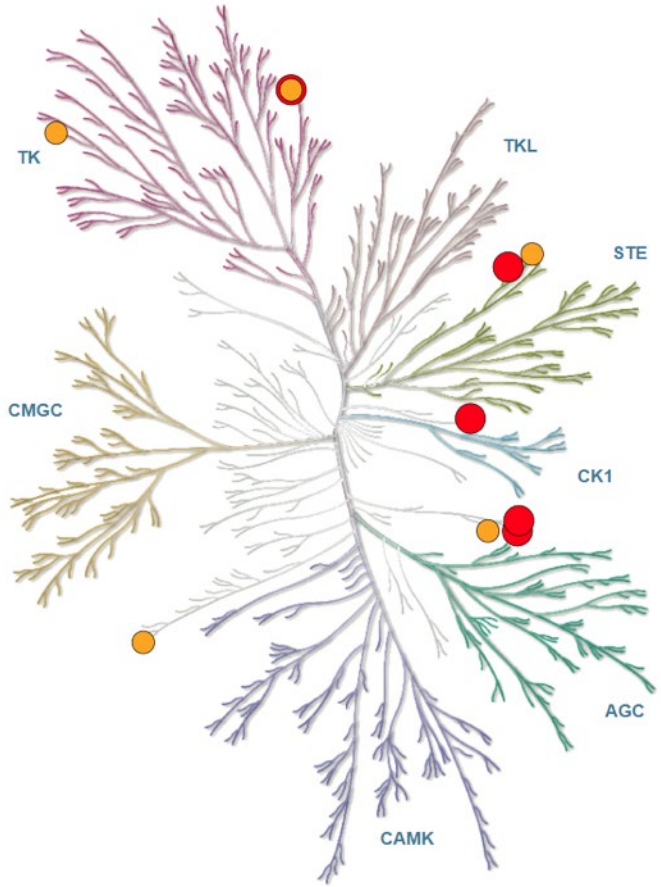
ASSAY	adavosertib	ZN-c3
WEE1	106	102
PLK2	101	96
MAP3K19 (YSK4)	92	95
EGFR (ErbB1) d747-749	90	93
PLK3	91	92
EGFR (ErbB1) d746-750	78	79
PLK1	70	79
NEK1	73	76
MAP3K3 (MEKK3)	66	76
LCK	87	75
DDR2 T654M	83	72
STK33	83	72
SYK	66	69
GAK	93	68
YES1	92	68
HIPK2	62	67
CDK4/cyclin D1	60	67
PKMYT1	86	65
RET S891A	43	64
NEK4	25	64
FLT3 D835Y	83	62
HIPK4	44	62
FES (FPS)	47	61
ABL1 G250E	85	59
EGFR (ErbB1) L858R	53	59
JAK3	81	58
MAP3K2 (MEKK2)	32	56
MUSK	101	55
FGR	91	55
EGFR (ErbB1) L861Q	53	54
DDR2 N456S	96	53
CDK4/cyclin D3	68	52
BMX	63	52
EIF2AK2 (PKR)	51	51
FYN	64	50
EGFR (ErbB1)	54	50
PEAK1	81	48
SNF1LK2	71	48
MAP4K5 (KHS1)	78	47
FRK (PTK5)	75	44
JAK2	63	44
JAK2 JH1 JH2 V617F	48	43
ABL1 Q252H	94	42
ABL1 M351T	90	42
SRC N1	88	42
ABL1 Y253F	85	41
ERBB4 (HER4)	26	41
ABL1 H396P	92	40
EPHB1	44	40
ABL2 (Arg)	82	39
NIM1K	43	39
CDK6/cyclin D1	65	38
JAK2 JH1 JH2	58	37
TYRO3 (RSE)	46	37
ABL1	84	36
SRC	74	36

>470 kinases

ZN-c3

% Inhibition (@ 1µM)

- 90+ 5 kinases
- 75-89 5 kinases



(1) Illustrations reproduced courtesy of Cell Signaling Technology, Inc. (www.cellsignal.com)

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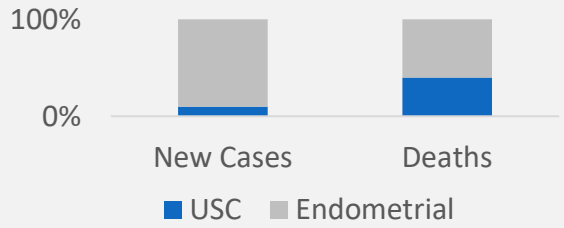
ZN-c3: Phase 1 USC Monotherapy Update

The Unmet Need in Uterine Serous Carcinoma is Significant

UNMET NEED

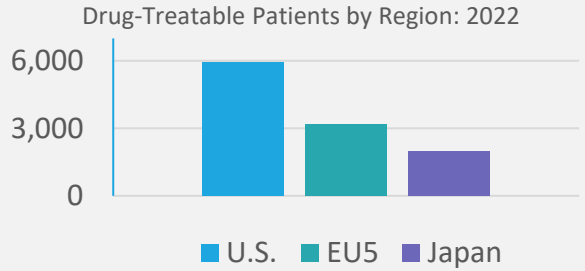
- USC results in **~40% of endometrial cancer deaths** despite comprising only 10% of cases



  - **Prior to pembro+len approval, ORR of 9.5% with PLD was chemo SOC for third-line USC**(1)
  - The 5-year survival rate for late-stage USC is 33% (2)
- >90% of USC patients have TP53 mutations(3)

PATIENT POPULATION

- In 2022, the total number of drug treatable **third line** advanced or recurrent endometrial cancer patients is approximately **10,000 in the United States, EU5 and Japan**(4)



- **Improvement in efficacy while limiting toxicities** would make a meaningful difference for patients

COMPETITIVE LANDSCAPE

- Current standard of care for third line, USC is single-agent chemotherapy, with some limited use of bevacizumab and pembrolizumab monotherapies(5)
- There is a **high need** for a therapeutic option in later line patients **after prior platinum containing chemotherapy and pembrolizumab + lenvatinib treatment**(1)
  - Another Wee1 inhibitor (adavosertib) is also in late-stage clinical evaluation
- ZN-c3 is potentially a best in-class treatment option for USC

ZN-c3's efficacy and tolerability profile are well positioned for the USC population

(1) Muggia, J Clin Oncol, 2002 (2) Hamilton CA et al. Br J Cancer. 2006 Mar 13;94(5):642-6. (3) Liu JF et al. J Clin Oncol. 2021 Mar 11:JCO2003167. (4) Decision Resources Group; data on file. (5) CancerMPact, Future Trends and Insights Endometrial cancer June 2021; data on file.

Safety and clinical activity of single-agent ZN-c3, an oral Wee1 inhibitor, in a Phase 1 trial in subjects with recurrent or advanced uterine serous carcinoma (USC)

F. Meric-Bernstam[1], P. Chalasani[2], H. Mamdani[3], C. Zheng[4], M. Viana[4], R. Lambersky[4], P. Pultar[4], A. Tolcher[5]

[1]MD Anderson Cancer Center, Houston, TX, USA; [2]University of Arizona Cancer Center, Tucson, AZ, USA; [3]Karmanos Cancer Center, Detroit, MI, USA; [4]Zentalis Pharmaceuticals, New York, NY, USA; [5]Texas Oncology Babcock, San Antonio, TX, USA

Updated monotherapy data from USC cohort dose ≥300mg QD will be presented as part of a mini-symposium on Monday, April 11th at 2:50pm CT

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ZN-c3: Chemo Combination in Ovarian Cancer

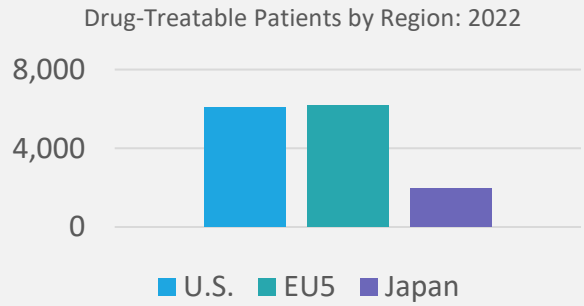
Platinum-Resistant/Refractory Ovarian Cancer Remains an Unmet Need

UNMET NEED

- Platinum-resistant and -refractory ovarian cancer represents a **high unmet need**
- It is associated with a poor prognosis and limited treatment options
  - **ORR of 11.8% with SOC[(1)] for platinum resistant patients**
- **Improvement in efficacy with acceptable safety profile** would make a meaningful difference for patients

PATIENT POPULATION

- In 2022, the total number of drug-treatable second line platinum-resistant ovarian cancer patients is estimated to be **>14,000 in the United States, EU5 and Japan[(2)]**



COMPETITIVE LANDSCAPE

- Current standard of care for second line platinum-resistant ovarian patients is single-agent chemotherapy ± bevacizumab[(3)]
- Ongoing pivotal trials focus on novel MOAs, including ADCs, and combinations with either PARPi or chemotherapy.[(3)] Of note, ADCs only work in a sub-population of patients
- ZN-c3 is potentially a first-in-class treatment option that works synergistically with other anticancer therapies

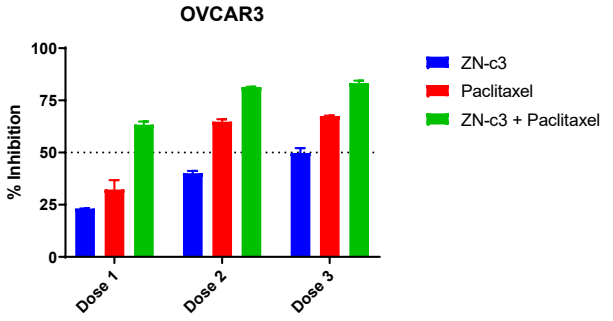
ZN-c3's efficacy and tolerability profile are well-positioned for the platinum-resistant/refractory ovarian population

(1) Pujade-Lauraine et al. J Clin Oncol 2014; 32:1302-1308; AURELIA study (2) Decision Resources Group; data on file. (3) CancerMPact Treatment Architecture Ovarian cancer July 2021; data on file.

ZN-c3 Combined with Chemotherapy is Highly Active *in vitro* Against OVCAR3 Ovarian Cancer Cells

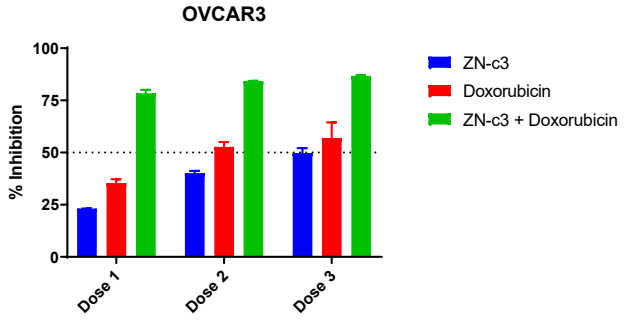
- Inhibition of Wee1, combined with DNA-damaging agents (**doxorubicin** and **carboplatin**) or inducers of replication stress (**paclitaxel** and **gemcitabine**), causes mitotic entry without completion of DNA repair, leading to mitotic catastrophe(1-3)
  - **Paclitaxel:** shown to induce degradation of the Wee1 protein by causing mitotic arrest
  - **Gemcitabine:** inhibits the enzyme RRM2* essential for synthesis of deoxyribonucleotides and causes replication stress
- In addition, Wee1 inhibition elicits an immune response which may synergize with the immune activation mediated by chemotherapy (Immunogenic Cell Death)

ZN-c3 + Paclitaxel



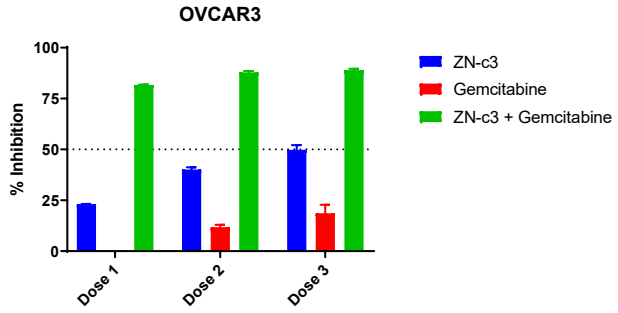
	Dose 1	Dose 2	Dose 3
ZN-c3	200 nM	300 nM	500 nM
Paclitaxel	5 nM	10 nM	20 nM

ZN-c3 + Doxorubicin



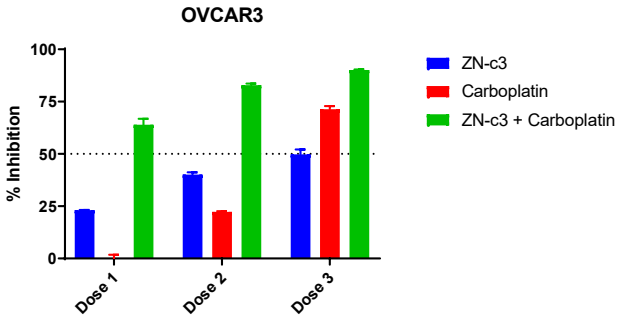
	Dose 1	Dose 2	Dose 3
ZN-c3	200 nM	300 nM	500 nM
Doxorubicin	500 nM	750 nM	1 uM

ZN-c3 + Gemcitabine



	Dose 1	Dose 2	Dose 3
ZN-c3	200 nM	300 nM	500 nM
Gemcitabine	10 nM	20 nM	50 nM

ZN-c3 + Carboplatin

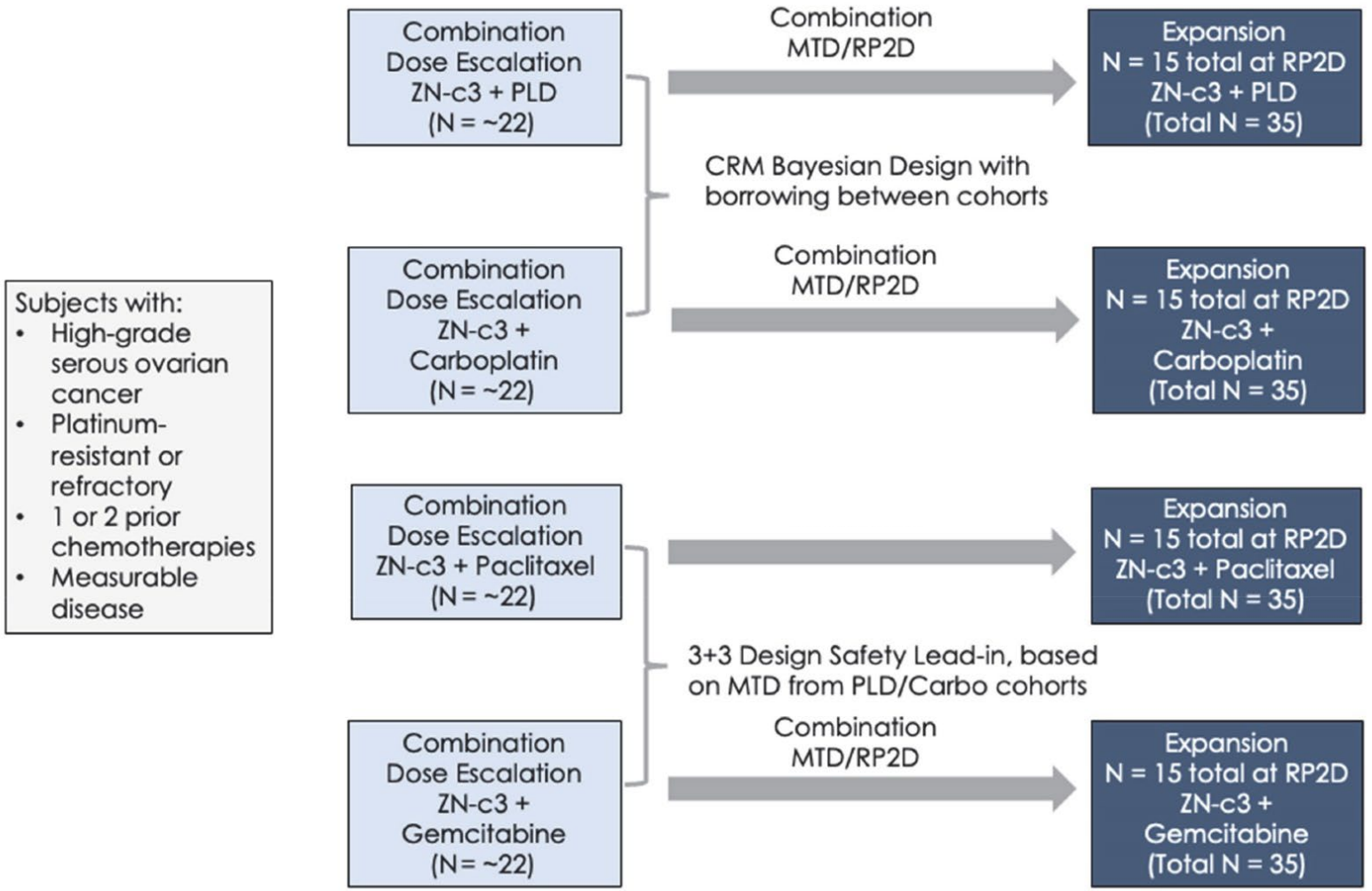


	Dose 1	Dose 2	Dose 3
ZN-c3	200 nM	300 nM	500 nM
Carboplatin	20 uM	30 uM	50 uM

(1) L Ghelli et al. J Hematol Oncol. 2020; 13:126
(2) NYL Ngoi et al. Trends Cancer. 2021; 7:930-957
(3) M Aarts et al. Cancer Discov. 2012;2:524-39

* Ribonucleoside-diphosphate reductase subunit M2

ZN-c3-002: Study Design



MTD= maximum tolerated dose; N= number of subjects; RP2D= recommended Phase 2 dose; CRM= continual reassessment method; PLD= liposomal doxorubicin

ZN-c3-002: Baseline Characteristics

Baseline Characteristics (All Cohorts)

Characteristic	ZN-c3 + PLD (n = 30)	ZN-c3 + Carboplatin (n = 17)	ZN-c3 + Paclitaxel (n = 9)	Total[1,2] (N = 56)
Median age, years (range)	55 (34–75)	61 (49–74)	67 (51–74)	58.5 (34–75)
Race, n (%)				
White	29 (97)	17 (100)	8 (89)	54 (96)
Asian	1 (3)	0 (0)	1 (11)	2 (4)
ECOG status, n (%)				
0	20 (67)	8 (47)	8 (89)	36 (64)
1	10 (33)	9 (53)	1 (11)	20 (36)
Prior lines of therapy, n (%)				
1	19 (63)	9 (53)	5 (56)	33 (59)
2	11 (37)	8 (47)	4 (44)	23 (41)
Prior bevacizumab, n (%)	13 (43)	9 (53)	4 (44)	26 (46)
Prior PARP inhibitor, n (%)	3 (10)	4 (24)	1 (11)	8 (14)
Prior therapy status, n (%)				
Resistant	24 (80)	15 (88)	9 (100)	48 (86)
Platinum refractory	6 (20)	2 (12)	0 (0)	8 (14)

100% of patients became resistant/refractory to platinum within the first 2 lines of therapy indicating an aggressive phenotype

(1) No subjects have been enrolled in the gemcitabine arm as of January 28, 2022.
(2) Full patient genetic background analysis ongoing.

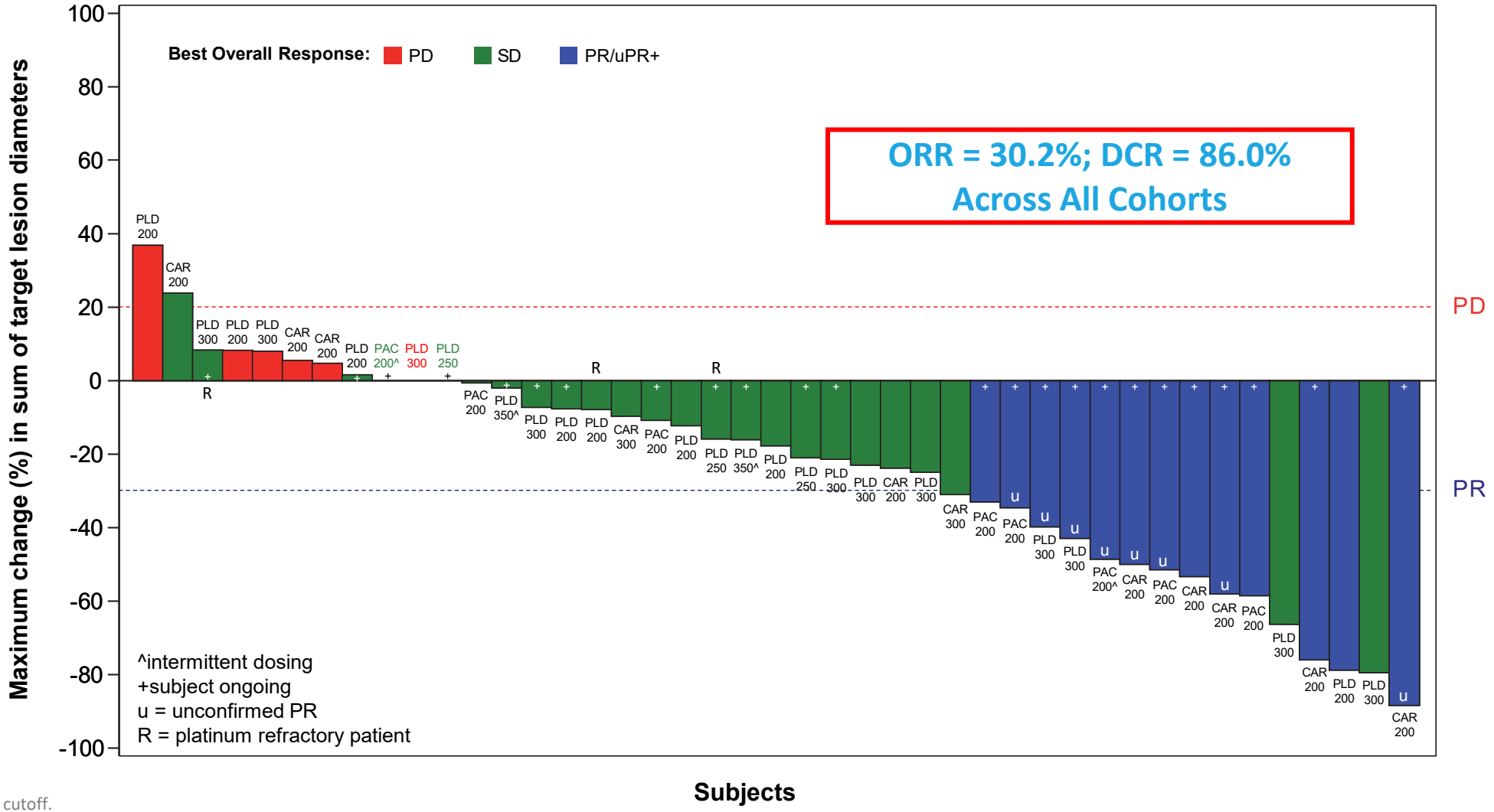
Expectations for Efficacy in Recurrent Ovarian Cancer Patients

Study Name / Author	Drug	Platinum Refractory	Prior Bevacizumab Treatment	ORR	Overall Survival for Wee1 Inhibitor
AURELIA (Phase 3, Randomized Trial) [1]	Chemotherapy (PLD, paclitaxel, topotecan) in control arm	Not included	None	11.8%	N/A
Moore KM, CCR (Phase 2, Open Label) [2]	Adavosertib + chemotherapy	Not included	34% overall	11-33% range (High dose C2 arm not tolerated)	N/A
Lheureux S, Lancet (Phase 2, DB, PC, Randomized Trial) [3]	Adavosertib + gemcitabine	Included Plat Refractory (10%)	Unknown	23% (6% chemo alone)	**mOS = 11.4 mos; HR = 0.56 vs gemcitabine alone (p=0.017)**
ZN-c3-002	ZN-c3 + chemotherapy	Included Plat Refractory (7%)[4]	46% overall		

A response rate >20% may lead to significant PFS and OS advantages in larger trials

(1) Pujade-Lauraine E et al. [AURELIA study] *J Clin Oncol* 2014; 32:1302-1308.
(2) Moore KM et al. *Clin Cancer Res* 2022;28:36–44
(3) Lheureux S et al. *Lancet* 2021; 397: 281–92
(4) Platinum refractory population of 7% in evaluable population

ZN-c3-002: Maximum Reduction in Sum of Target Lesion Diameters All Patients (n=43*)(1)



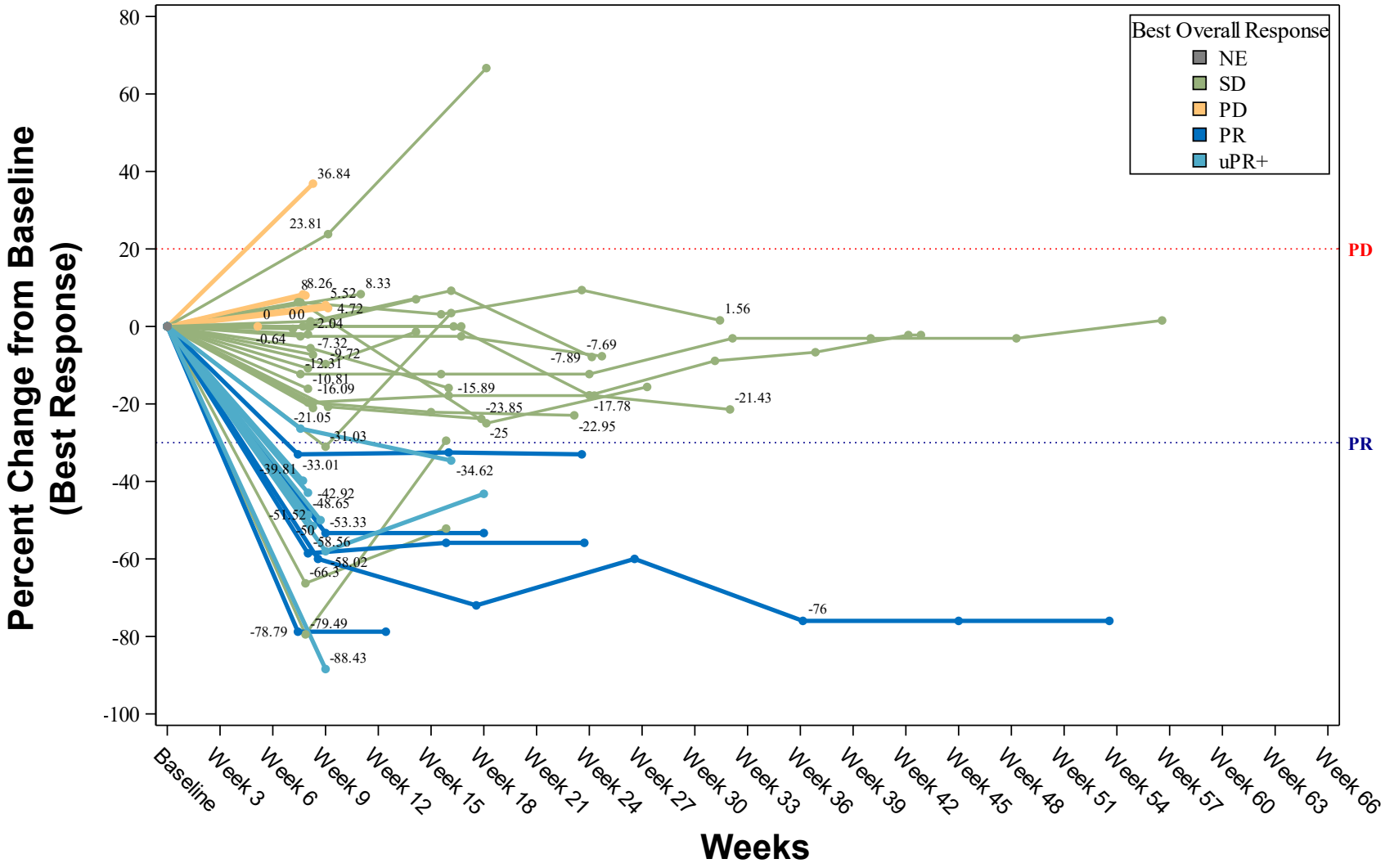
(1) January 28, 2022 data cutoff.

Note: Excluding platinum refractory patients ORR = 32.5% and DCR = 85%.

* Evaluable patients; Measurable disease per Response Evaluation Criteria in Solid Tumors (RECIST), version 1.1; Patients with measurable disease and at least one post-baseline scan

ZN-c3-002: Robust Disease Control Rate Observed Across All Cohorts

Responders experienced a meaningful duration of response



Data cutoff January 28, 2022.

ZN-c3-002: Responder #1 Background

Ovarian Cancer – Platinum-resistant

- 52-year-old female, Stage III Ovarian Cancer, metastases to the liver, abdomen, mesentery (lymph node). ECOG PS 0
- Two prior lines of therapy in the advanced/ metastatic setting
- ZN-c3 starting dose: 200 mg QD + Paclitaxel 80 mg/m^2
- The subject remained on the study for 214 days (Cycle 7) until clinical disease progression
- Patient experienced decreased CA-125 tumor marker from 1122 ng/mL at baseline to 254 ng/mL at Cycle 4

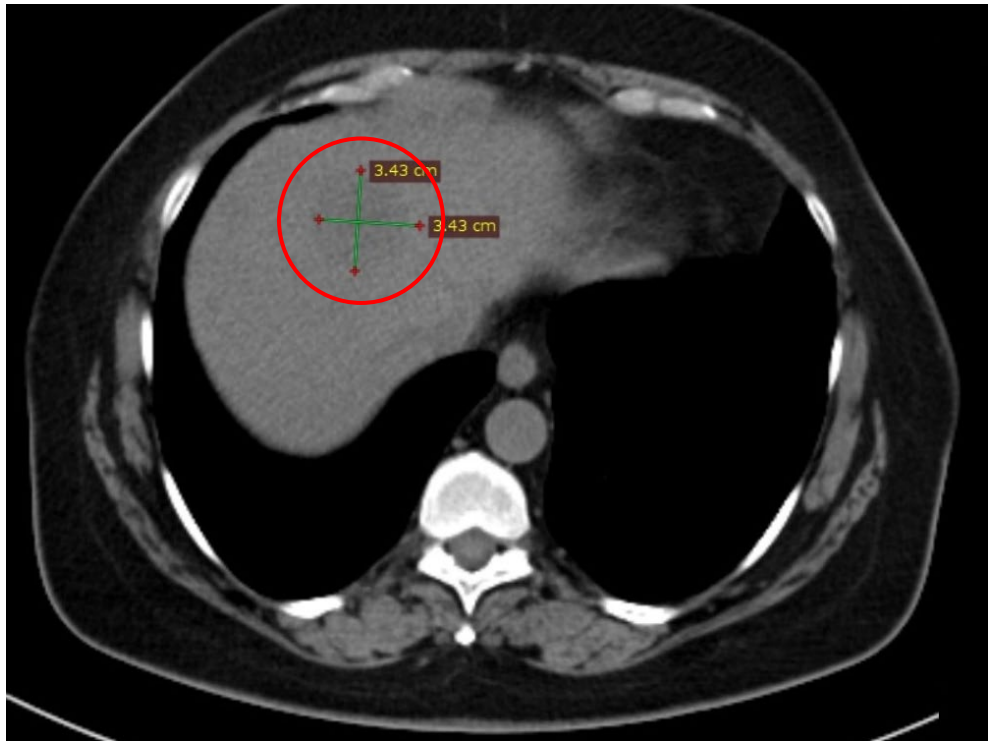
Confirmed PR with 56% reduction overall

Previous Therapy Experience

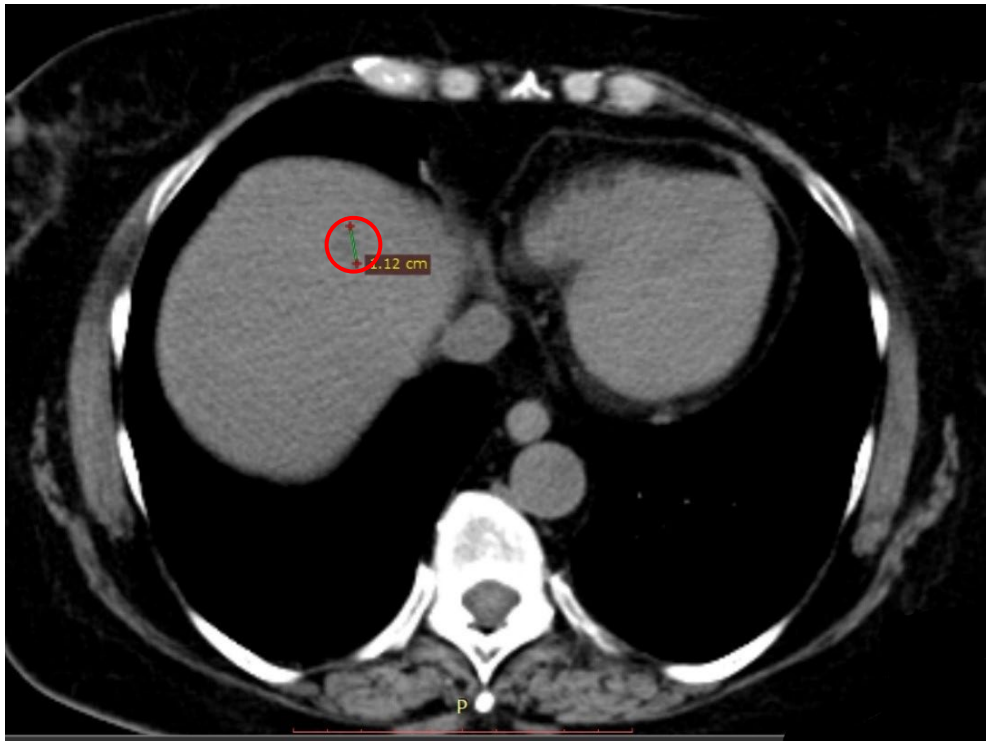
Intent of Treatment	Regimen	Start	Stop	Best Response
Advanced/ Metastatic	Carboplatin / Paclitaxel	Jul-17	Sep-17	SD
Advanced/ Metastatic	Carboplatin / Doxorubicin	Dec-20	Apr-21	PD

ZN-c3-002: Responder #1 Baseline and Follow-up (Liver Lesion)

Baseline (July 2021)



4th Assessment (Jan 2022)



ZN-c3-002: Responder #2 Background

Ovarian Cancer – Platinum-resistant

- 72-year-old female, Stage IV Ovarian Cancer, metastases to the greater omentum, spleen capsule, pararectal, Liver capsule, peritoneum. ECOG PS 0
- Two prior lines of therapy in the advanced/ metastatic setting
- ZN-c3 starting dose: 300 mg QD + PLD 40 mg/m^2
- The subject remains on the study, currently Cycle 5
- Patient experienced decreased CA-125 tumor marker from 381 ng/mL at baseline to <50 ng/mL at Cycle 5

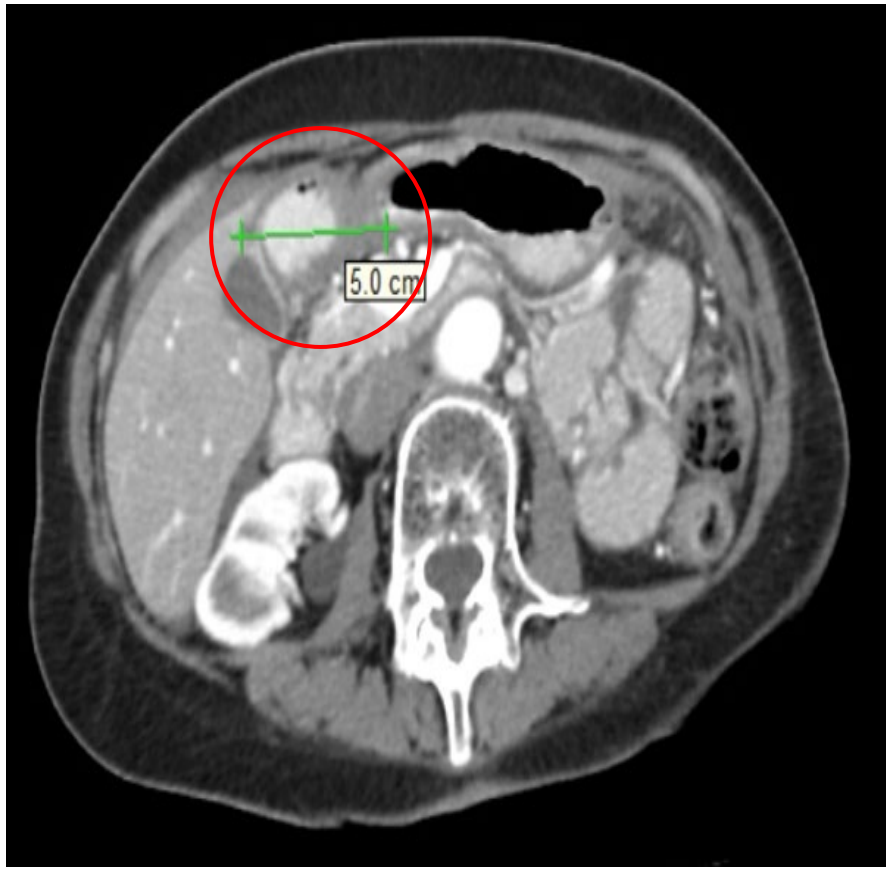
Confirmed PR with 46% reduction overall

Previous Therapy Experience

Intent of Treatment	Regimen	Start	Stop	Best Response
Advanced/ Metastatic	Carboplatin / Paclitaxel	Oct-19	Mar-20	SD
Advanced/ Metastatic	Carboplatin / Paclitaxel	Dec-20	May-21	PD

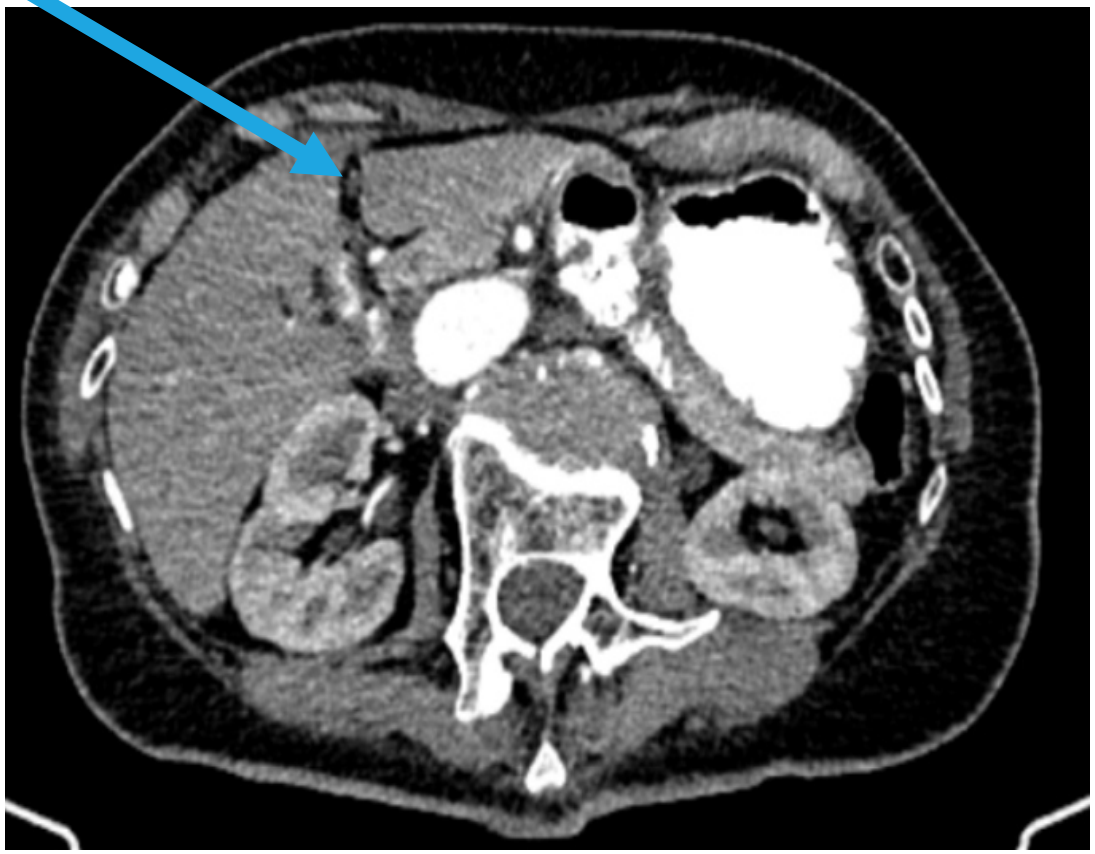
ZN-c3-002: Responder #2 Baseline and Follow-up (Liver Lesion)

Baseline (October 2021)



Complete disappearance

2nd Assessment (December 2021)



ZN-c3-002: Summary of Clinical Activity

Summary of Clinical Activity (All Cohorts)

Group	N	Evaluable* (n)	PR/uPR+ (n)	SD/SD+ (n)	PD (n)	DCR (%)	ORR (%)
Total	56	43	13	24	6	86.0	30.2
ZN-c3 + PLD	30	24	3	17	4	83.3	12.5
ZN-c3 + Carboplatin	17	11	5	4	2	81.8	45.5
ZN-c3 + Paclitaxel	9	8	5	3	–	100	62.5

Measurable disease per Response Evaluation Criteria in Solid Tumors (RECIST), version 1.1

* Patients with measurable disease and at least one post-baseline scan

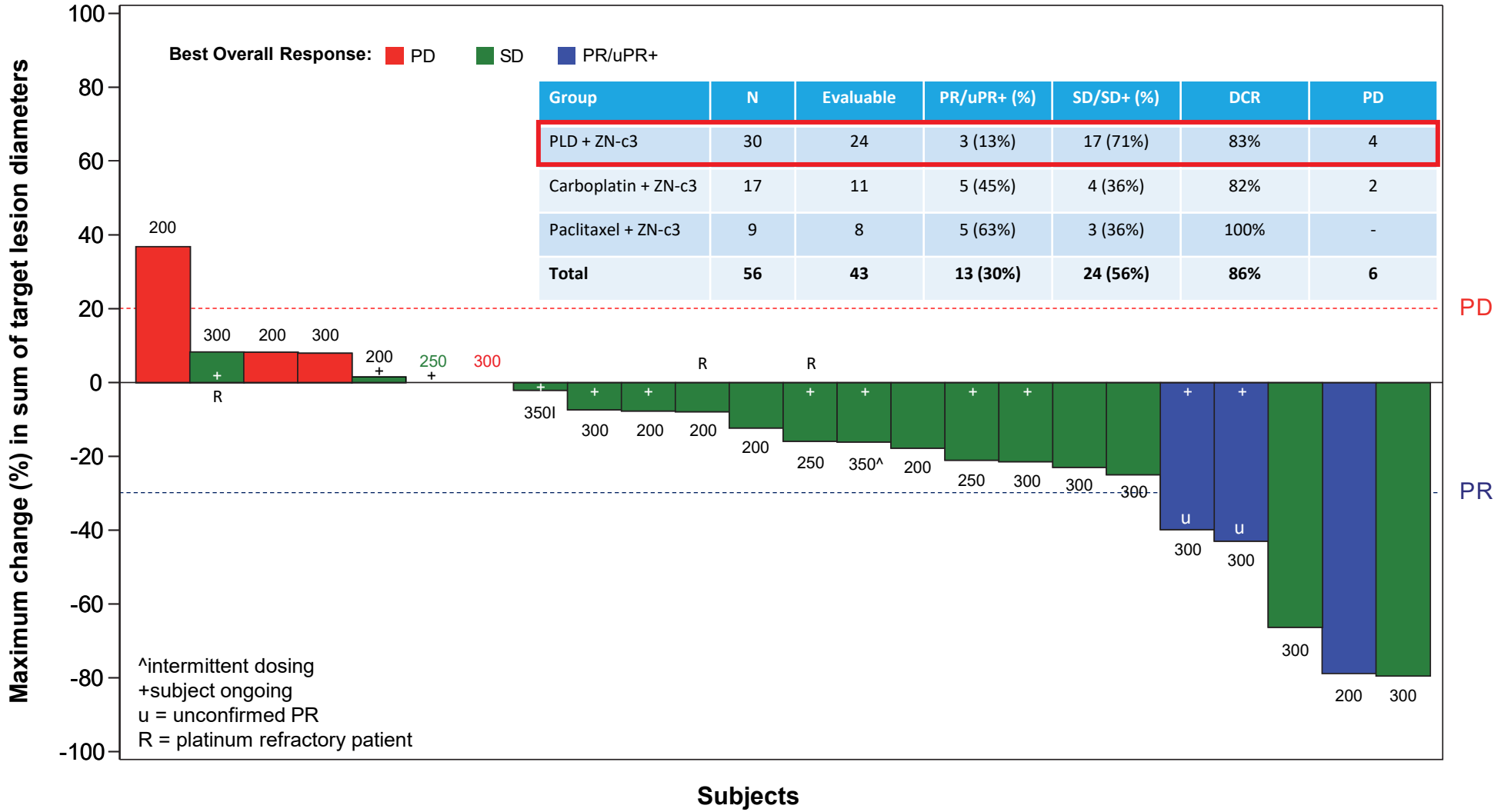
Of evaluable subjects, ORR is percentage with PR/uPR; and DCR is percentage with ORR + SD/SD+

+ Indicates treatment is ongoing for this subject

PR = partial response; uPR = unconfirmed partial response; ORR = objective response rate; DCR = disease control rate; SD = stable disease; PD = progressive disease

Data cutoff January 28, 2022

ZN-c3-002: Maximum Reduction in Sum of Target Lesion Diameters PLD Patients(1)

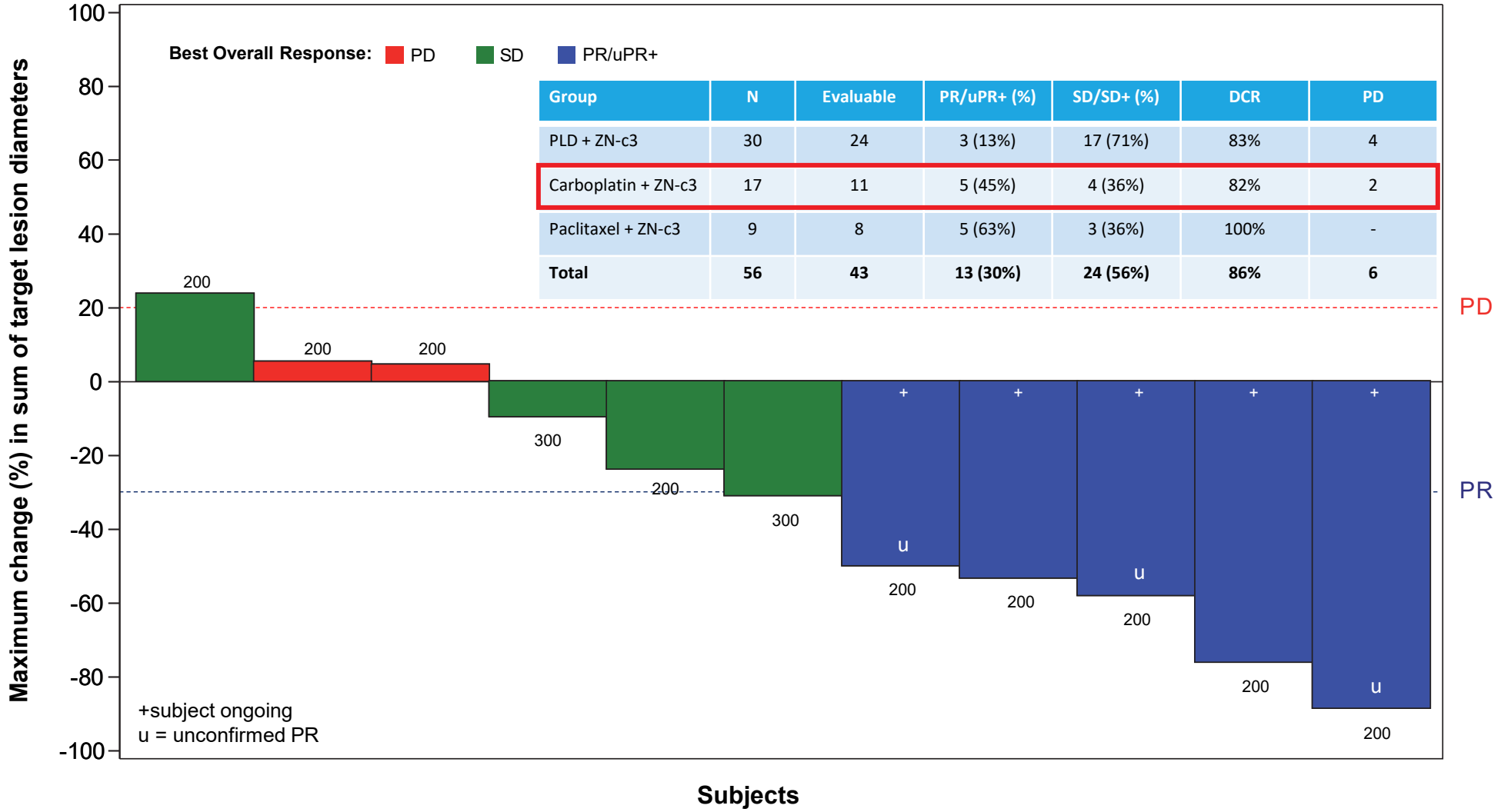


Group	N	Evaluable	PR/uPR+ (%)	SD/SD+ (%)	DCR	PD
PLD + ZN-c3	30	24	3 (13%)	17 (71%)	83%	4
Carboplatin + ZN-c3	17	11	5 (45%)	4 (36%)	82%	2
Paclitaxel + ZN-c3	9	8	5 (63%)	3 (36%)	100%	-
Total	**56**	**43**	**13 (30%)**	**24 (56%)**	**86%**	**6**

(1) January 28, 2022 data cutoff.
Note: Excluding platinum refractory patients ORR = 14.3% and DCR = 81%.

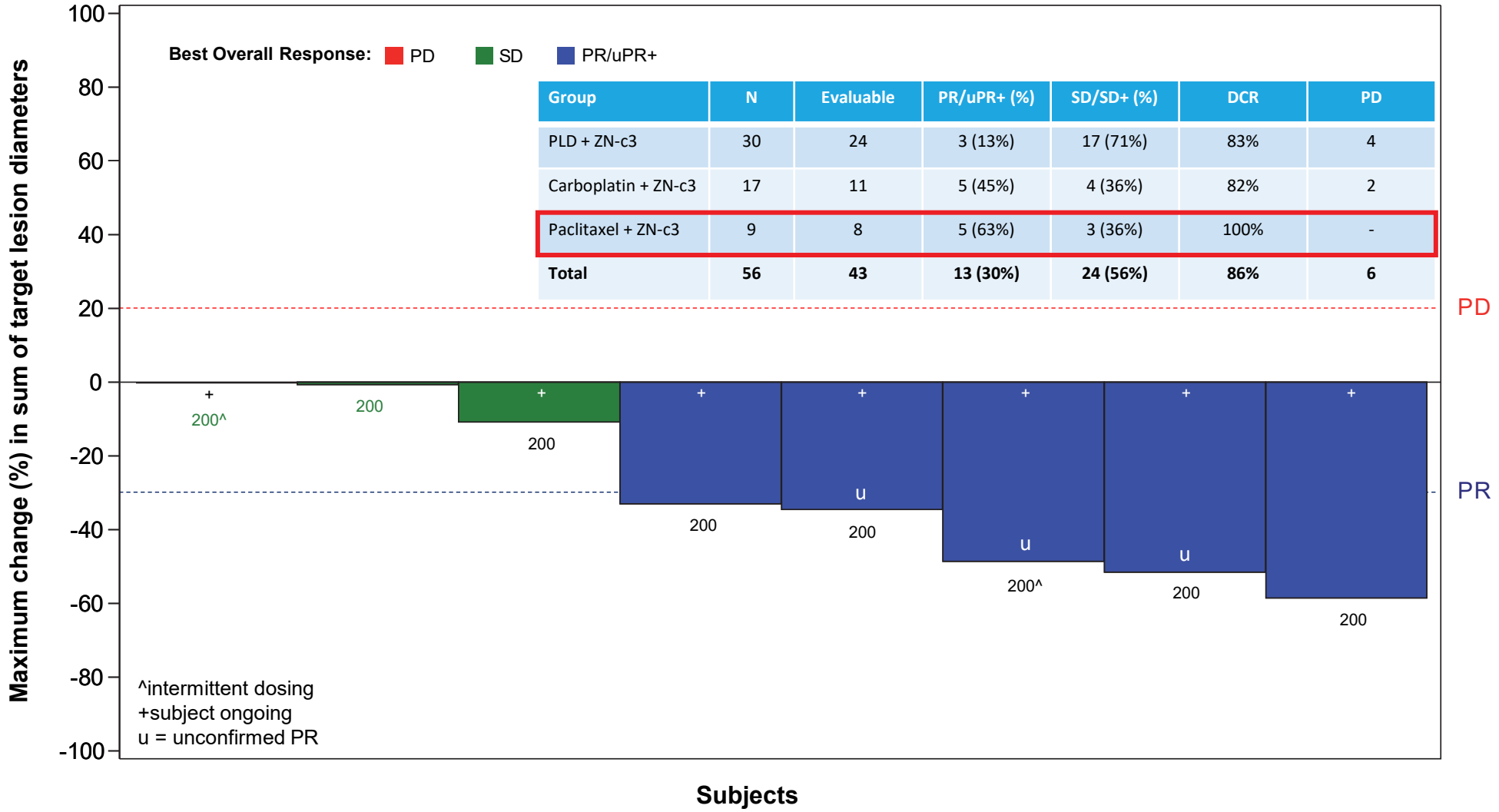
ZN-c3-002: Maximum Reduction in Sum of Target Lesion Diameters Carboplatin Patients(1)

Group	N	Evaluable	PR/uPR+ (%)	SD/SD+ (%)	DCR	PD
PLD + ZN-c3	30	24	3 (13%)	17 (71%)	83%	4
Carboplatin + ZN-c3	17	11	5 (45%)	4 (36%)	82%	2
Paclitaxel + ZN-c3	9	8	5 (63%)	3 (36%)	100%	-
Total	**56**	**43**	**13 (30%)**	**24 (56%)**	**86%**	**6**



(1) January 28, 2022 data cutoff.

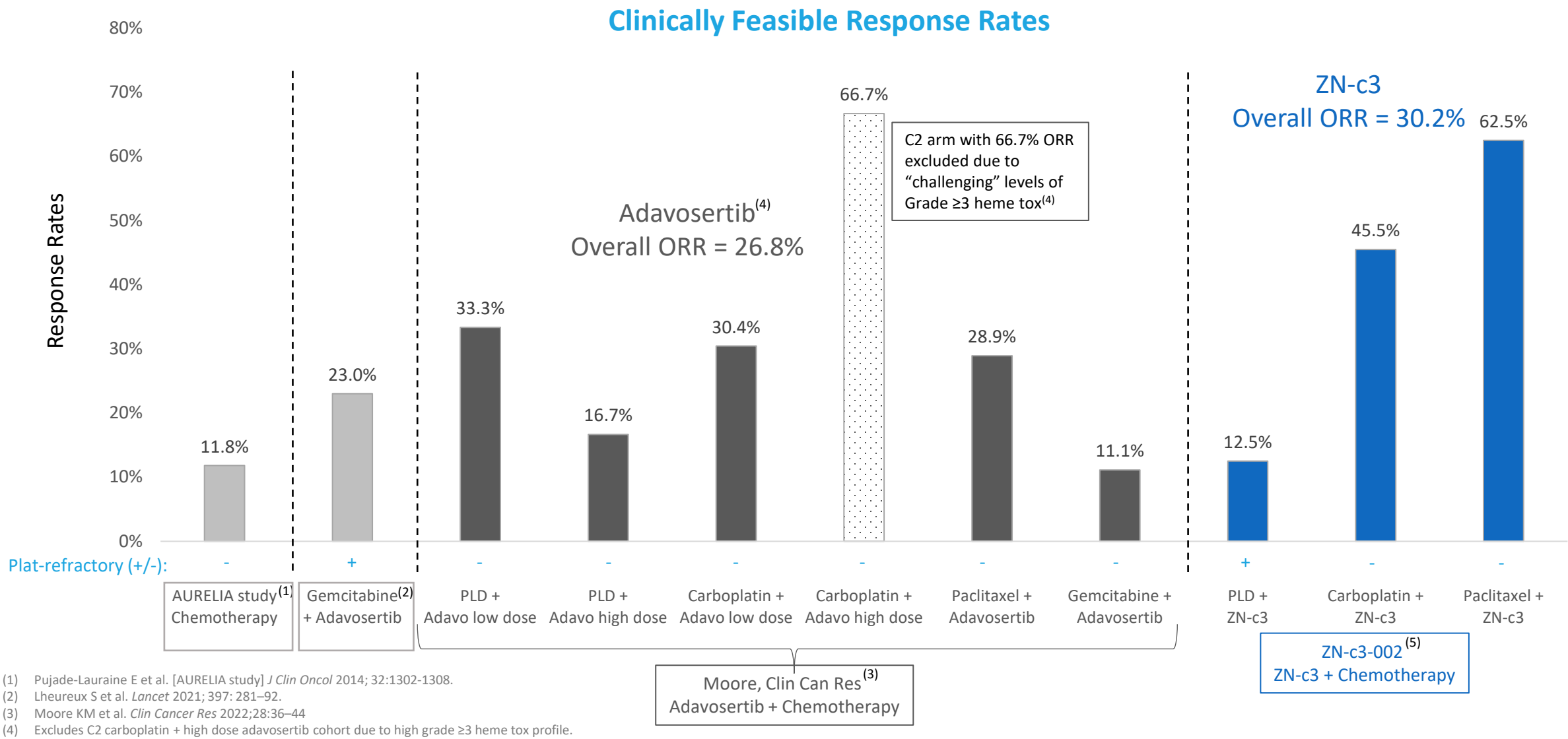
ZN-c3-002: Maximum Reduction in Sum of Target Lesion Diameters Paclitaxel Patients(1)



Group	N	Evaluable	PR/uPR+ (%)	SD/SD+ (%)	DCR	PD
PLD + ZN-c3	30	24	3 (13%)	17 (71%)	83%	4
Carboplatin + ZN-c3	17	11	5 (45%)	4 (36%)	82%	2
Paclitaxel + ZN-c3	9	8	5 (63%)	3 (36%)	100%	-
Total	**56**	**43**	**13 (30%)**	**24 (56%)**	**86%**	**6**

(1) January 28, 2022 data cutoff.

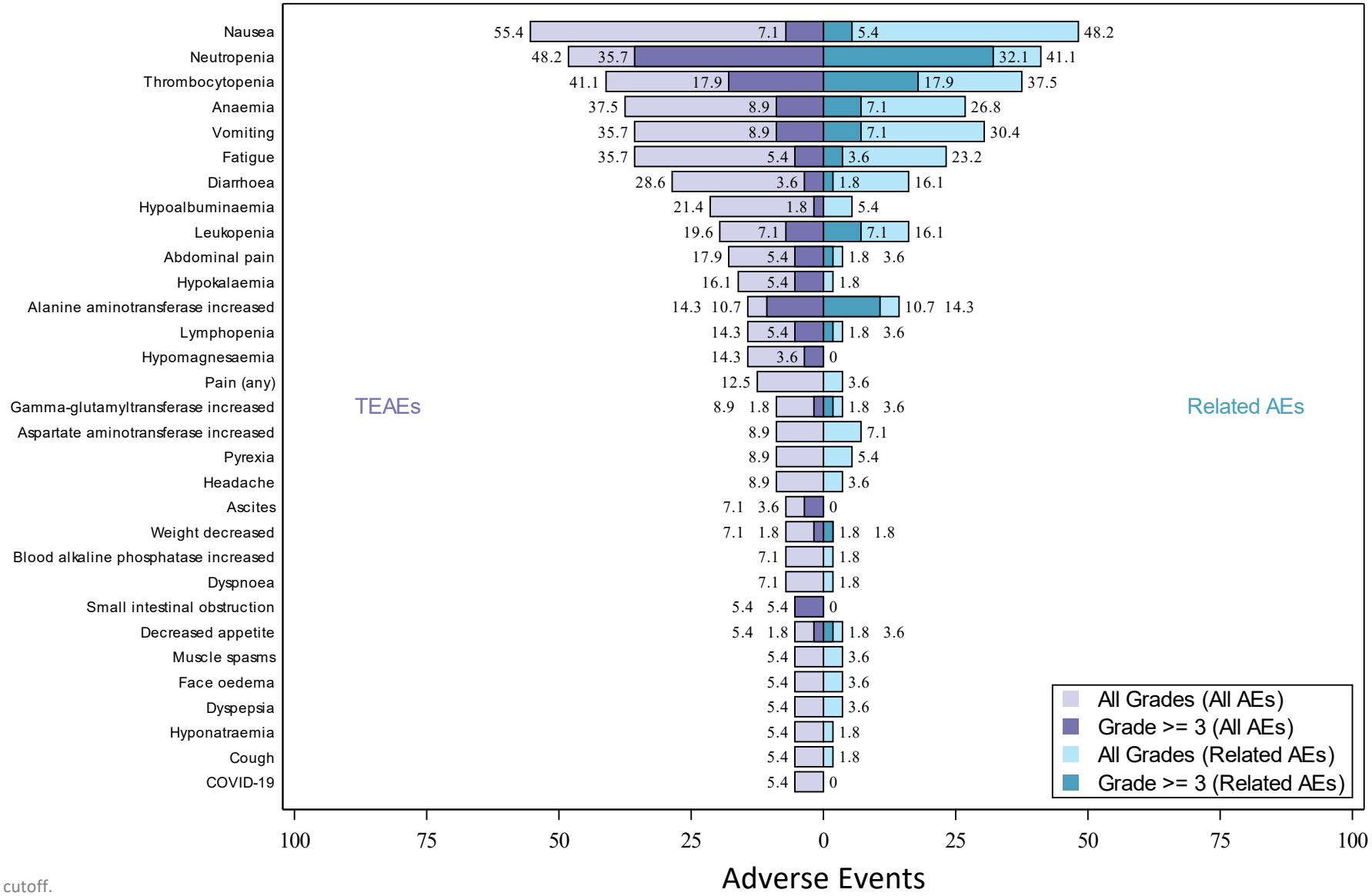
Clinically Feasible Response Rates for ZN-c3 and Competitors in Ovarian Cancer*



(1) Pujade-Lauraine E et al. [AURELIA study] *J Clin Oncol* 2014; 32:1302-1308.
(2) Lheureux S et al. *Lancet* 2021; 397: 281–92.
(3) Moore KM et al. *Clin Cancer Res* 2022;28:36–44
(4) Excludes C2 carboplatin + high dose adavosertib cohort due to high grade ≥3 heme tox profile.
(5) ZN-c3 January 28, 2022 data cutoff.

* Non-head-to-head comparison. Results of a head-to-head comparison may differ significantly from those set forth herein. In addition, because our Phase 1 clinical trial for ZN-c3 and the clinical trials of those other compounds above were separate trials, differences between the results of the trials may not be statistically or clinically meaningful.

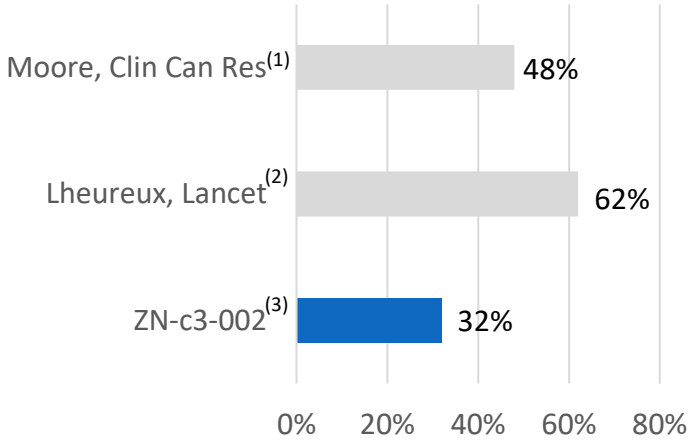
ZN-c3-002: TEAEs ≥5% for All Patients (N=56)[1]



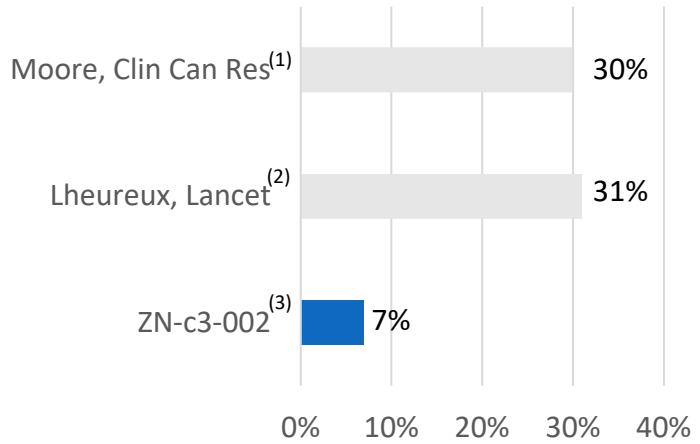
(1) January 28, 2022 data cutoff.

ZN-c3 Exhibits Lower Hematologic Toxicity vs Adavosertib When Combined with Chemotherapy – Grade ≥ 3 TRAEs*

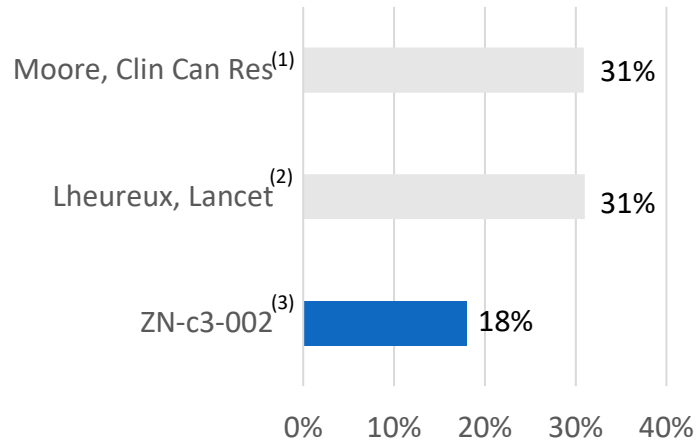
Neutropenia



Anemia



Thrombocytopenia



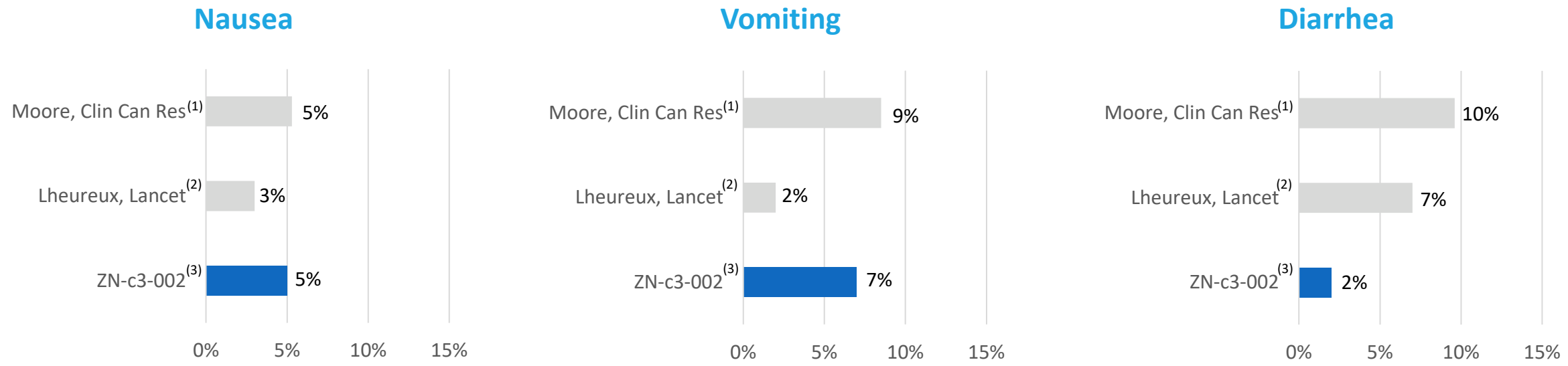
- Target ZN-c3 dosing was QD continuously throughout the treatment cycle across all chemotherapy cohorts
- Adavosertib's dosing schedule was intermittent to manage expected tolerability concerns, creating hurdles for commercial adoption

ZN-c3 demonstrated a potentially best-in-class hematologic tolerability profile versus adavosertib even with a higher total drug load

(1) Moore KM et al. *Clin Cancer Res* 2022;28:36–44
(2) Lheureux S et al. *Lancet* 2021; 397: 281–92 (as reported)
(3) ZN-c3-002 data cutoff January 28, 2022.

* Non-head-to-head comparison. Results of a head-to-head comparison may differ significantly from those set forth herein. In addition, because our Phase 1 clinical trial for ZN-c3 and the Adavosertib clinical trials were separate trials, differences between the results of the trials may not be statistically or clinically meaningful.

ZN-c3 GI Tolerability Profile is Better than Adavosertib When Combined with Chemotherapy – Grade ≥ 3 TRAEs*



- Target ZN-c3 dosing was QD continuously throughout the treatment cycle across all chemotherapy cohorts
- Adavosertib's dosing schedule was intermittent to manage expected tolerability concerns, creating hurdles for commercial adoption

ZN-c3's GI tolerability profile is potentially better than adavosertib even with a higher total drug load

(1) Moore KM et al. *Clin Cancer Res* 2022;28:36–44
(2) Lheureux S et al. *Lancet* 2021; 397: 281–92 (as reported)
(3) ZN-c3-002 data cutoff January 28, 2022.
* Non-head-to-head comparison. Results of a head-to-head comparison may differ significantly from those set forth herein. In addition, because our Phase 1 clinical trial for ZN-c3 and the Adavosertib clinical trials were separate trials, differences between the results of the trials may not be statistically or clinically meaningful.

ZN-c3 Oral Dosing Regimen is Convenient and Currently in Dose Escalation

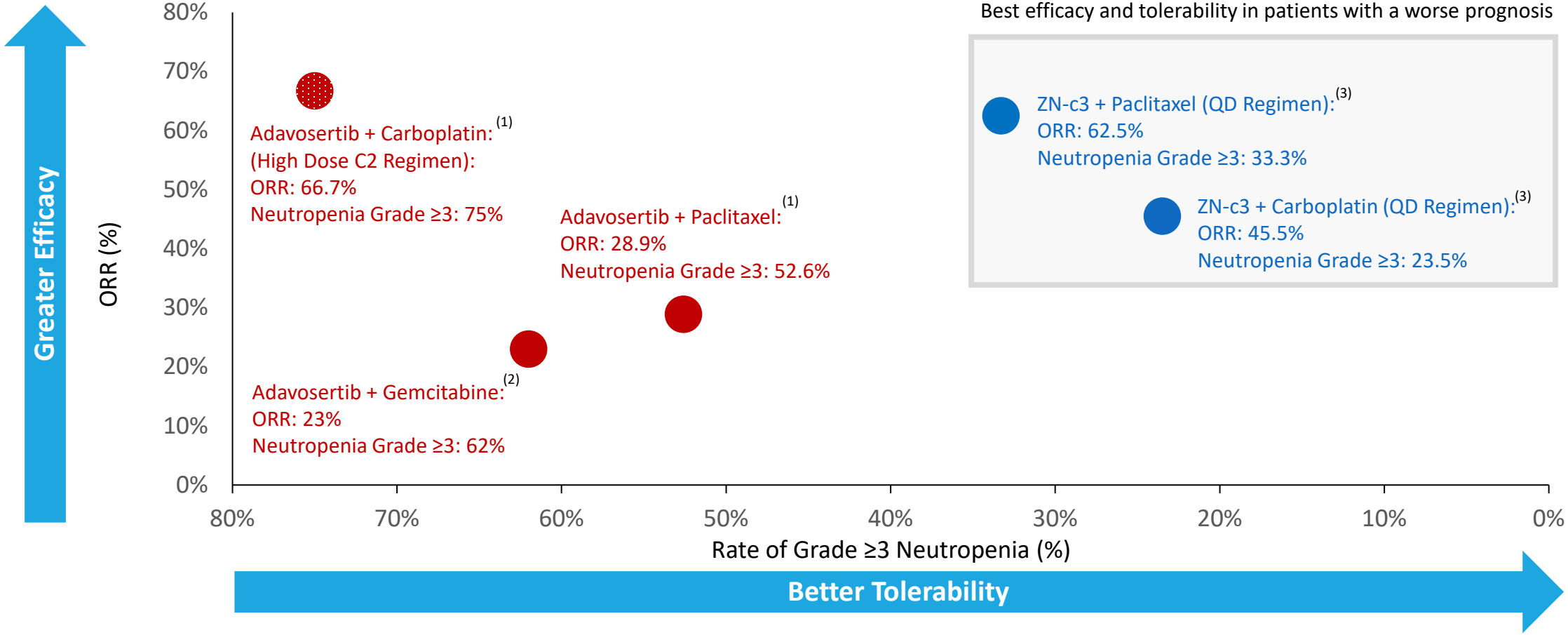
	Paclitaxel	Carboplatin	PLD
	Wee1i Dose *(per cycle-28D)*	Wee1i Dose *(per cycle-21D)*	Wee1i Dose *(per cycle-28D)*
ZN-c3-002[1] (Dose escalation)	200 mg QD	200 mg QD	300 mg QD
Adavosertib (High Dose)[2]	225 mg BID Days 1-3, 8-10, 15-17	225 mg BID Days 1-3, 8-10, 15-17	225 mg BID Days 1-3
Adavosertib (Low Dose)[2]	N/A	225 mg BID Days 1-3	175 mg BID Days 1-3

- Oral continuous dosing regimen for ZN-c3 is enabled by its potentially best-in-class tolerability profile
- Continuous ZN-c3 dosing in combination with chemotherapy is better tolerated than intermittent dosing with an adavosertib/chemotherapy combination
- ZN-c3-002 is an ongoing trial and continues to enroll patients in dose escalation

(1) ZN-c3 January 28, 2022 data cutoff.
(2) Moore KM et al. *Clin Cancer Res* 2022;28:36–44
Note: Non-head-to-head comparison. Results of a head-to-head comparison may differ significantly from those set forth herein. In addition, because our Phase 1 clinical trial for ZN-c3 and the Adavosertib clinical trials were separate trials, differences between the results of the trials may not be statistically or clinically meaningful.

ZN-c3 Demonstrates Superior Efficacy with Greater Safety/ Tolerability in Patients with a Worse Prognosis*

Efficacy Versus Tolerability



Utilizing a continuous dosing regimen, ZN-c3 is able to achieve very high ORRs with markedly better safety / tolerability profile versus Adavosertib

(1) Moore KM et al. *Clin Cancer Res* 2022;28:36–44
(2) Lheureux S et al. *Lancet* 2021; 397: 281–92
(3) ZN-c3 January 28, 2022 data cutoff.

* Non-head-to-head comparison. Results of a head-to-head comparison may differ significantly from those set forth herein. In addition, because our Phase 1 clinical trial for ZN-c3 and the Adavosertib clinical trials were separate trials, differences between the results of the trials may not be statistically or clinically meaningful.

ZN-c3-002: Summary of Chemotherapy Combination in Ovarian Cancer

CLINICAL ACTIVITY

- **Strong clinical activity** in combination with chemotherapy agents for platinum-resistant ovarian cancer patients (ORR = 30%)
  - Paclitaxel combo: ORR = 63%
  - Carboplatin combo: ORR = 46%
- ZN-c3-002 enrolled a **more advanced patient population** (higher prior bevacizumab treatment and allowed platinum-refractory patients) than related adavosertib trial [1,3]

SAFETY PROFILE

- ZN-c3 is **well-tolerated** in combination with chemotherapy at oral doses ≥ 200 mg QD in subjects with platinum-resistant or -refractory ovarian cancer
- **Superior tolerability** profile for ZN-c3 enabled continuous initial dosing and **higher dose intensity** than adavosertib[1,2]
- Overall **lower rates** of hematological adverse events compared to adavosertib combinations[1-3]
- Dosing regimen for ZN-c3 is **more patient friendly**, which should boost compliance

REGULATORY PATH

- **Promising interim results** support development of a Phase 3 study for potential approval of ZN-c3 in ovarian cancer
- Randomized **Phase 3 study in planning** to support full approval
  - 2nd line platinum-resistant ovarian cancer – in combination with chemotherapy (*tbd*)
- Future development plan details forthcoming

ZN-c3 is well-tolerated with chemotherapy and supports potential use in additional indications

(1) Moore KM et al. *Clin Cancer Res* 2022;28:36–44
(2) Lheureux S et al. *Lancet* 2021; 397: 281–92
(3) Non-head-to-head comparison. Results of a head-to-head comparison may differ significantly from those set forth herein. In addition, because our Phase 1 clinical trial for ZN-c3 and the Adavosertib clinical trials were separate trials, differences between the results of the trials may not be statistically or clinically meaningful.

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ZN-c5: Oral SERD Data Update

ZN-c5 Combination with CDK 4/6i – Efficacy Data

Palbociclib Combination

Phase 1 Dose (mg/day)	N	ORR	CBR	mPFS (months)
25 mg QD + Palbo	10	1/7* (14%)	2/7*(29%)	**
50 mg QD + Palbo	18	2/13 (15%)	6/18 (33%)	3.6
>50 mg + palbo (includes 25 BID)	22	0/14	8/22 (36%)	3.7
Overall	**50**	**3/34 (9%)**	**16/47 (34%)**	**3.7 [95% CI: 2.2-5.7]**

Data as of Jan 31, 2022
*# of subjects with 24 weeks + 10 days opportunity for f/u
** median not estimable due to very few PD events
ClinicalTrials.gov Identifier: NCT03560531

Abemaciclib Combination

Dose (mg/day)	N	ORR	CBR*	mPFS (months)
50 mg ZN-c5 QD + 150 mg abema BID	4	-	0/4	2.0
25 mg ZN-c5 QD + 150 mg abema BID	5	-	1/1	Not estimable
25 mg ZN-c5 QD + 150 mg abema BID (fed conditions)	1	-	-	No on-treatment scans yet
Overall	**10**	**-**	**1/5 (20%)**	**4.0**

Data as of Jan 11, 2022
*Subjects with opportunity for follow-up > 24 weeks
ClinicalTrials.gov Identifier: NCT04514159

- At the selected doses the combination of ZN-c5 and Palbociclib had a clinical benefit rate of 34% in ER+/HER2- breast cancer patients
- DDI was seen at 50 mg of ZN-c5 with a 35% decrease in palbociclib exposure relative to historical patient data

- In a small Phase 1 cohort of ER+/HER2- breast cancer patients receiving ZN-c5 and abemaciclib, a 20% CBR rate was observed, based on interim immature data
- DDI was seen at the 50 mg dose of ZN-c5 with a 67% decrease in abemaciclib exposure at steady state

ZN-c5 Combination with CDK 4/6i – Tolerability Profile (TEAE ≥20%)

Palbociclib Combination (N=50)

Treatment Emergent Adverse Events	All Grades (%)	Grade ≥ 3 (%)
Any adverse event	98.0	66.0
Neutrophil count decreased	72.0	40.0
While blood cell count decreased	72.0	24.0
Anemia	52.0	0.0
Fatigue	36.0	0.0
Lymphocyte count decrease	32.0	10.0
Nausea	32.0	0.0
Hyperglycemia	32.0	0.0
Arthralgia	30.0	4.0
Platelet count decreased	28.0	0.0
Hypertriglyceridema	22.0	0.0

Data as of Jan 31, 2022
ClinicalTrials.gov Identifier: NCT03560531

Abemaciclib Combination (N=10)

Treatment Emergent Adverse Events	All Grades (%)	Grade ≥ 3 (%)
Any adverse event	90.0	50.0
Neutropenia	60.0	20.0
Diarrhea	60.0	0.0
Nausea	40.0	0.0
Fatigue	30.0	10.0
Anemia	20.0	0.0
Hypertension	20.0	20.0

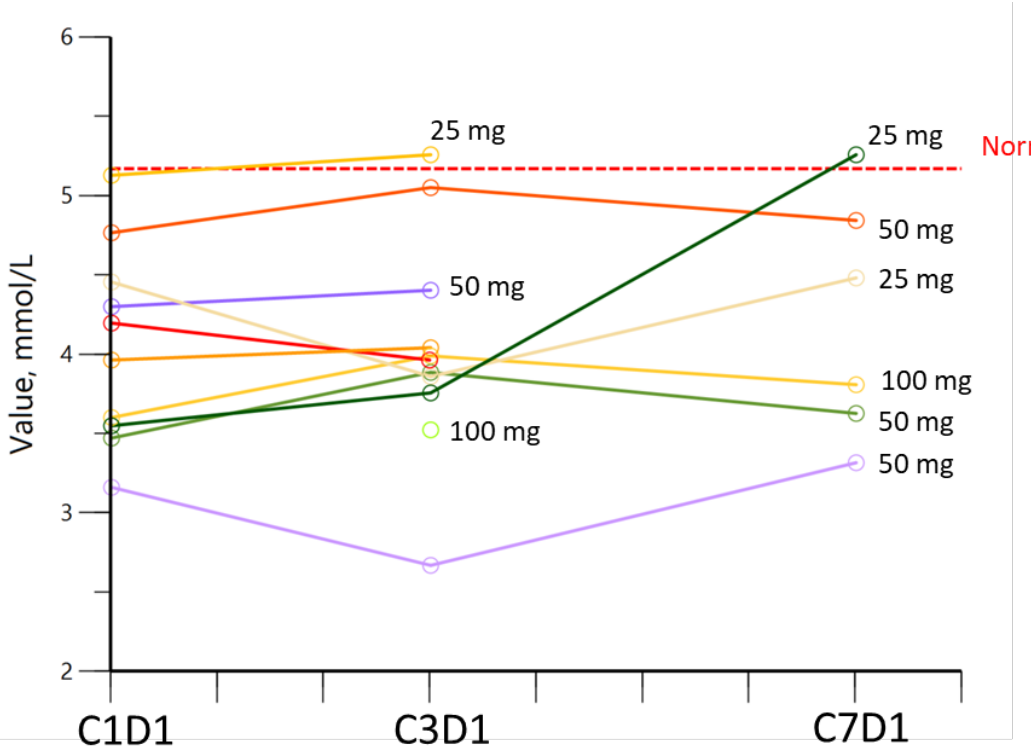
Data as of Jan 11, 2022
ClinicalTrials.gov Identifier: NCT04514159

ZN-c5 is well-tolerated across all dose cohorts and in combination with selected CDK 4/6 inhibitors

ZN-c5 is not Expected to have DDI with Commonly Used Medicines at Relevant Doses

- We have not identified potential for any relevant interaction of ZN-c5 with drugs from 50 most prescribed drugs list
- Well established drugs such as apalutamide and enzalutamide are known CYP3A inducers
- Atovarstatin is a CYP3A substrate and is one of the most prescribed drugs in the United States

Example: For subjects taking atovarstatin, Cholesterol remains well-controlled regardless of ZN-c5 dose

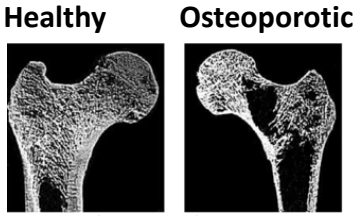


Based on modeling no significant DDI expected in the ZN-c5 + ZN-c3 combination studies

(1) Ibrance™ Clin Pharmacology Review 2014 Aug 13. Weighted average from Pfizer studies-1001c and 1003d (AUC 1801 hr*ng/mL)

ZN-c5 Safety Profile and Bone Protective Activity Versus Other Oral SERDs Supports Use in Adjuvant Settings

- Loss of estrogen associated with osteoporosis in post-menopausal women(1)

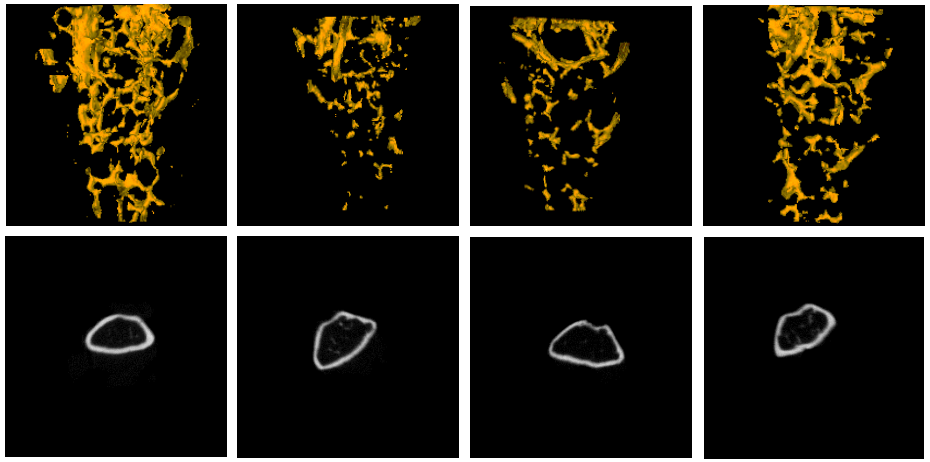


ResearchGate / Thesis / Ehsan Basafa (2013)

- Advanced breast cancer patients suffer from osteolytic bone metastasis(1)
- Treatment with fulvestrant is associated with osteolysis(1)
- ZN-c5 opportunity:
  - **ZN-c5 combines anti-tumor effect with bone-protective effect**

Micro-CT of Trabecular Bone

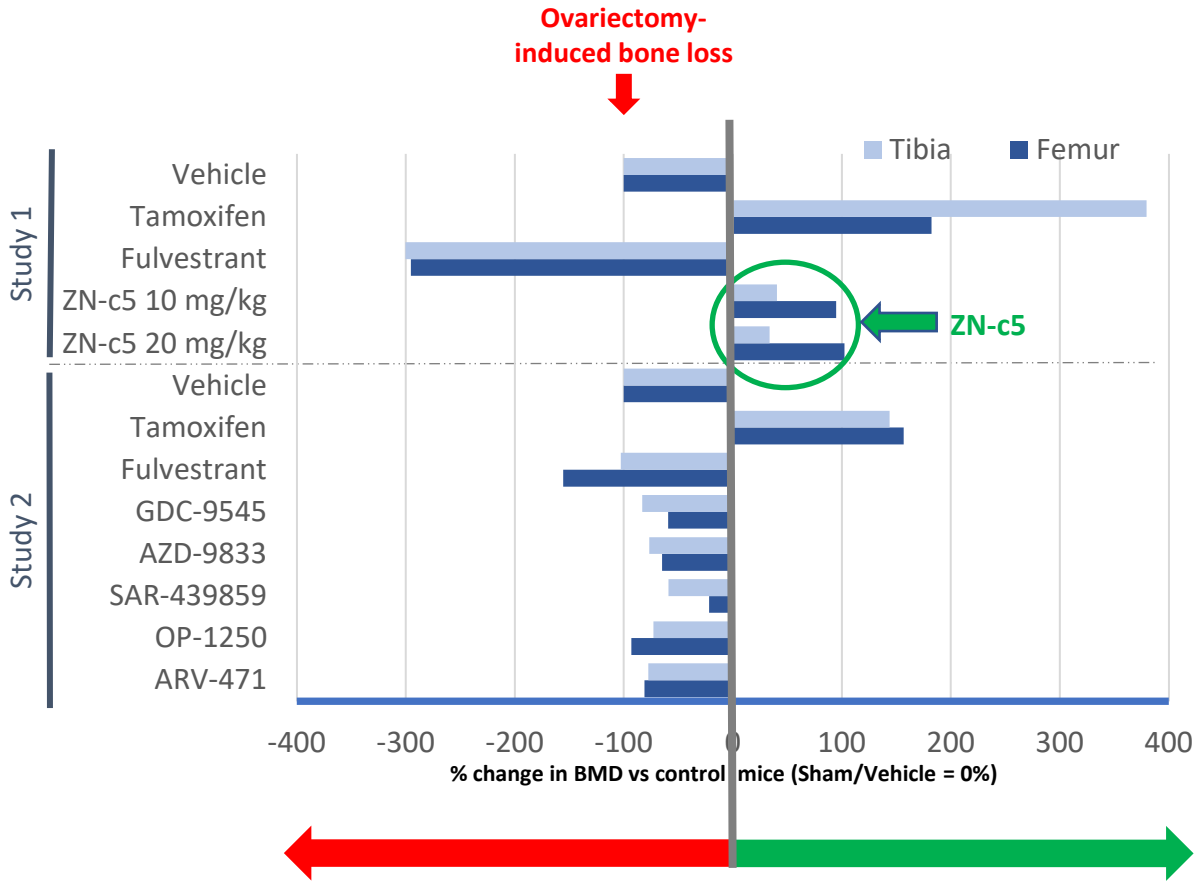
12 weeks; Femur



Sham Vehicle	OVX Vehicle	OVX Fulvestrant	OVX ZN-c5 10mpk

Note: Fulvestrant was dosed sc QW, ZN-c5 was dosed po QD

Bone Mineral Density in Ovariectomized Mice (Interim Look, 9 weeks)



Starting 2-3 weeks after ovariectomy, mice were treated with compounds for 12 weeks. Study 2, investigating oral SERDs, is still ongoing. The 2 independent studies are compared after 9 weeks of treatment and have been normalized to maximum bone mass density loss by ovariectomy (-100%) in each study. SERDs and tamoxifen were dosed daily PO at 10 mg/kg (+ 20 mg/kg for ZN-c5, twice daily for SAR-439859), fulvestrant was dosed once weekly SC at 25 mg/kg

(1) Bado, I. et. al., Oncogene 2017; 36, 4527-4537

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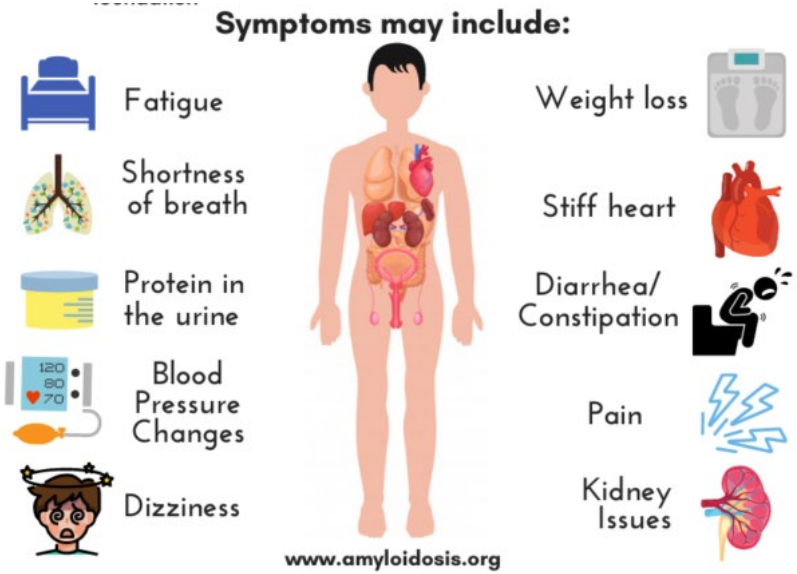
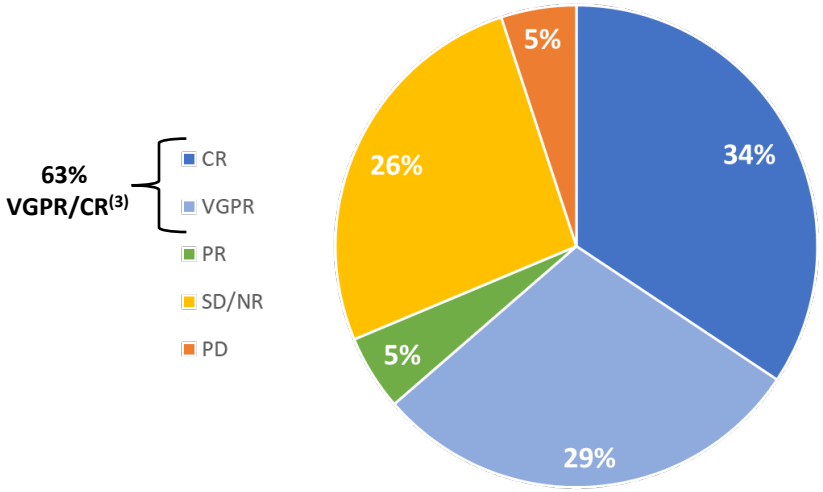
ZN-d5: BCL2 Inhibitor

ZN-d5 in AL (Primary) Amyloidosis





- AL Amyloidosis: Deposition of immunoglobulin light chains
  - Clonal plasma cell population secretes misfolding light chain
  - Progressive systemic amyloid accumulation causes widespread organ damage
  - **High morbidity and mortality**
- Orphan disease
  - Estimated worldwide prevalence is 75,000(1)
  - About 4k new cases/year in the US(2)
- Not a cancer, but treated like one
  - Agents active in multiple myeloma used in first-line and relapsed/refractory settings
  - Daratumumab only approved therapy, for first-line use with CyBorD
- **Relapsed/refractory setting is a high unmet medical need**

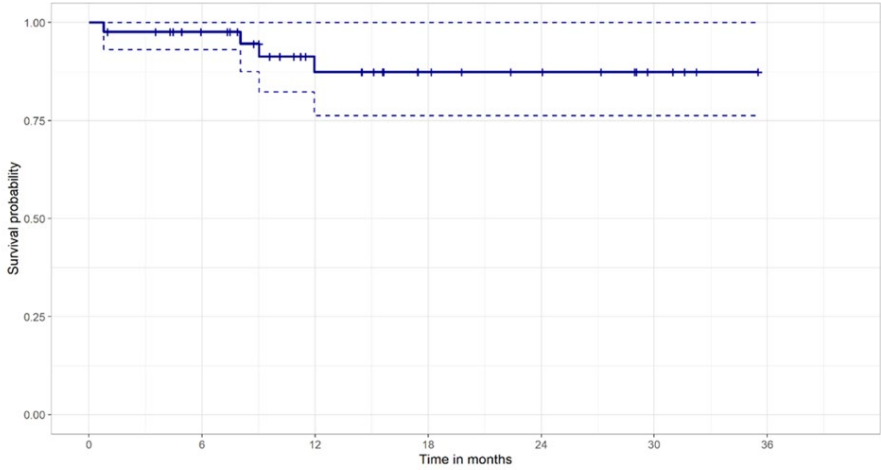
AL Amyloidosis study is currently enrolling patients

(1) Zhang et al. Clin Lymphoma Myeloma Leuk. 2019;19(suppl 10):e339
(2) Kyle et al, Mayo Clin Proc. 2019;94:465-471
(3) Premkumar et al, Blood Cancer J 2021;11:10; hematologic response rate in 38 evaluable patients.

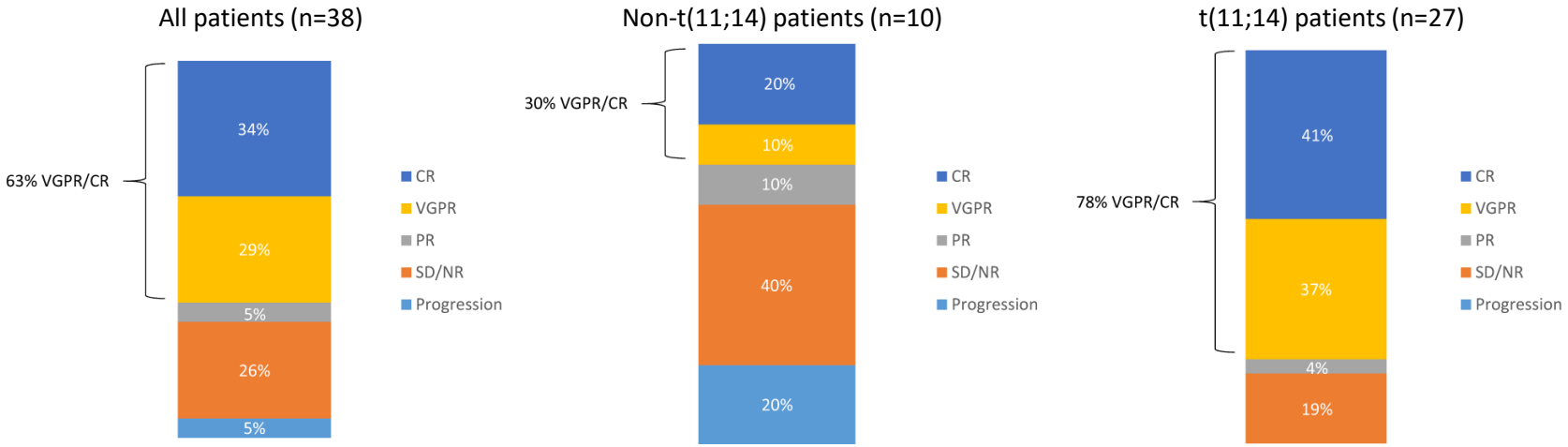
BCL-2 Inhibition has Shown Robust Clinical Activity in AL Amyloidosis (1)

- Patients with the t(11;14) translocation have a worse prognosis than the general AL amyloidosis community
- BCL-2 inhibition showed an improved response rate in the t(11;14) cohort with a trend towards better survival

OS for All Patients



Best Response in Evaluable Patients



(1) Premkumar et al, Blood Cancer J 2021;11:10; hematologic response rate in 38 evaluable patients.

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ZN-d5 + ZN-c3: Activity in Hematologic Malignancies and Solid tumors

AACR American Association for Cancer Research ANNUAL MEETING 2022 New Orleans

JOIN US APRIL 8-13!

BH3 mimetics synergize with the Wee1 inhibitor ZN-c3 by activating caspases which induce DNA damage and degrade key proteins

Hooman Izadi, Noah Ibrahim, Tiffany Hoang, Jianhui Ma, Petrus R. De Jong, Joseph Pinchman, Kevin D. Bunker, Ahmed A. Samatar, Fernando Doñate

AACR American Association for Cancer Research ANNUAL MEETING 2022 New Orleans

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Combination of the BCL-2 inhibitor ZN-d5 with the Wee1 inhibitor ZN-c3 shows additive or synergistic anti-tumor activity in acute myeloid leukemia (AML)

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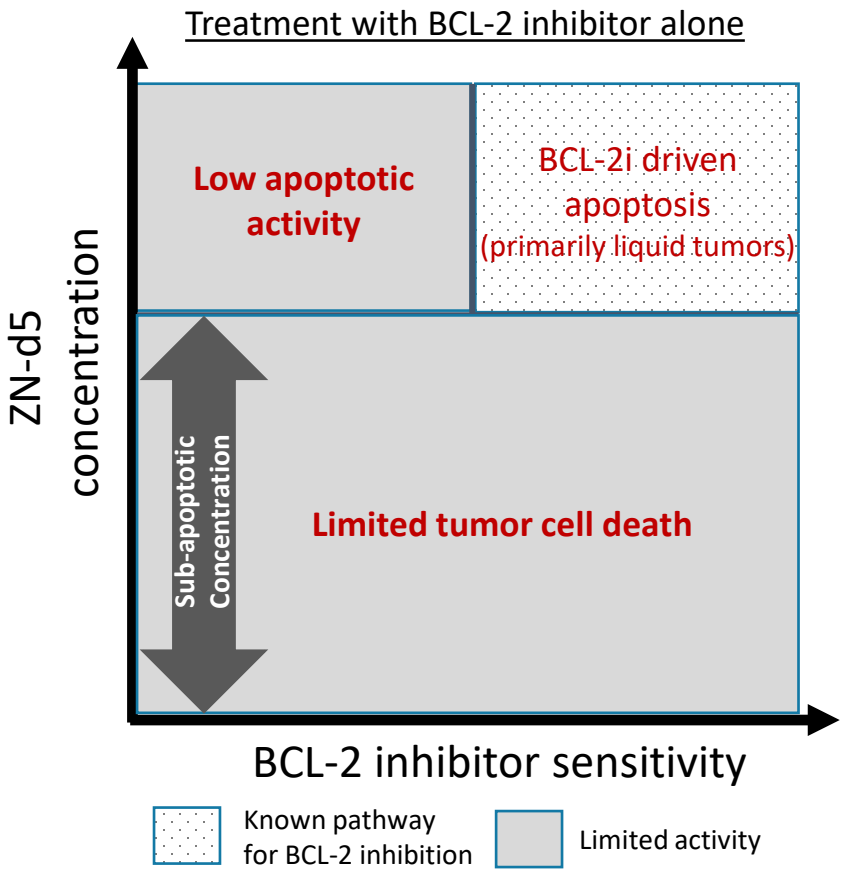
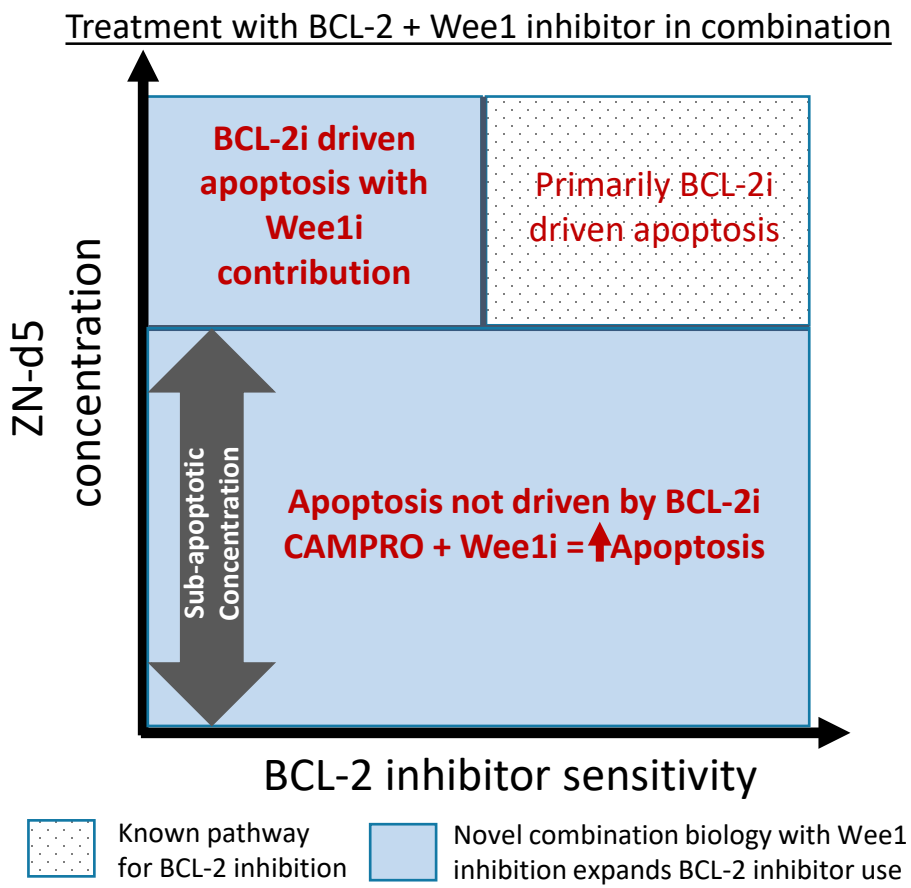
Novel Biology Supports Synergy of BCL-2 and Wee1 Inhibition – *CAMPRO (CAspase Mediated PROteolysis)*

BCL-2 inhibition (BCL-2i) induces CAMPRO of multiple proteins, including DNA damage repair (DDR) proteins

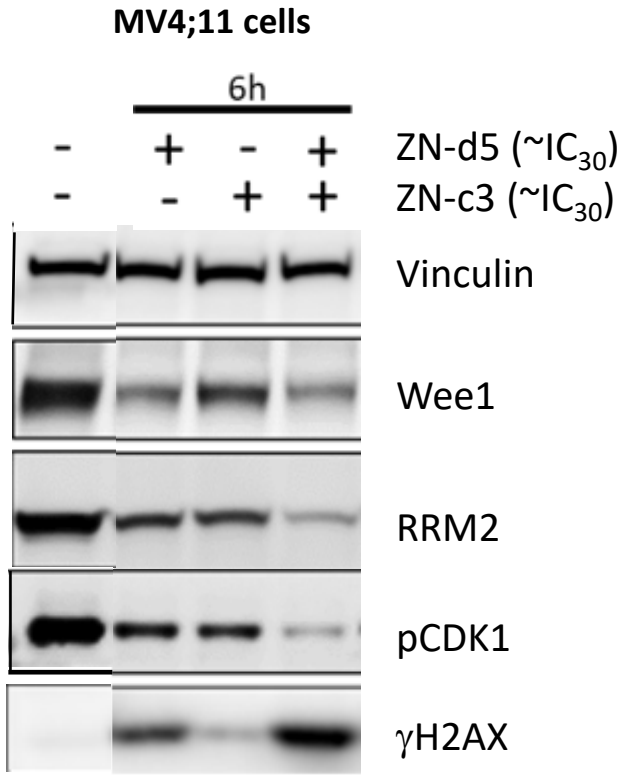




This novel synergistic finding supports the use of ZN-d5 + ZN-c3 in both sensitive and less sensitive tumor cells, opening a large market opportunity across both solid and liquid tumors

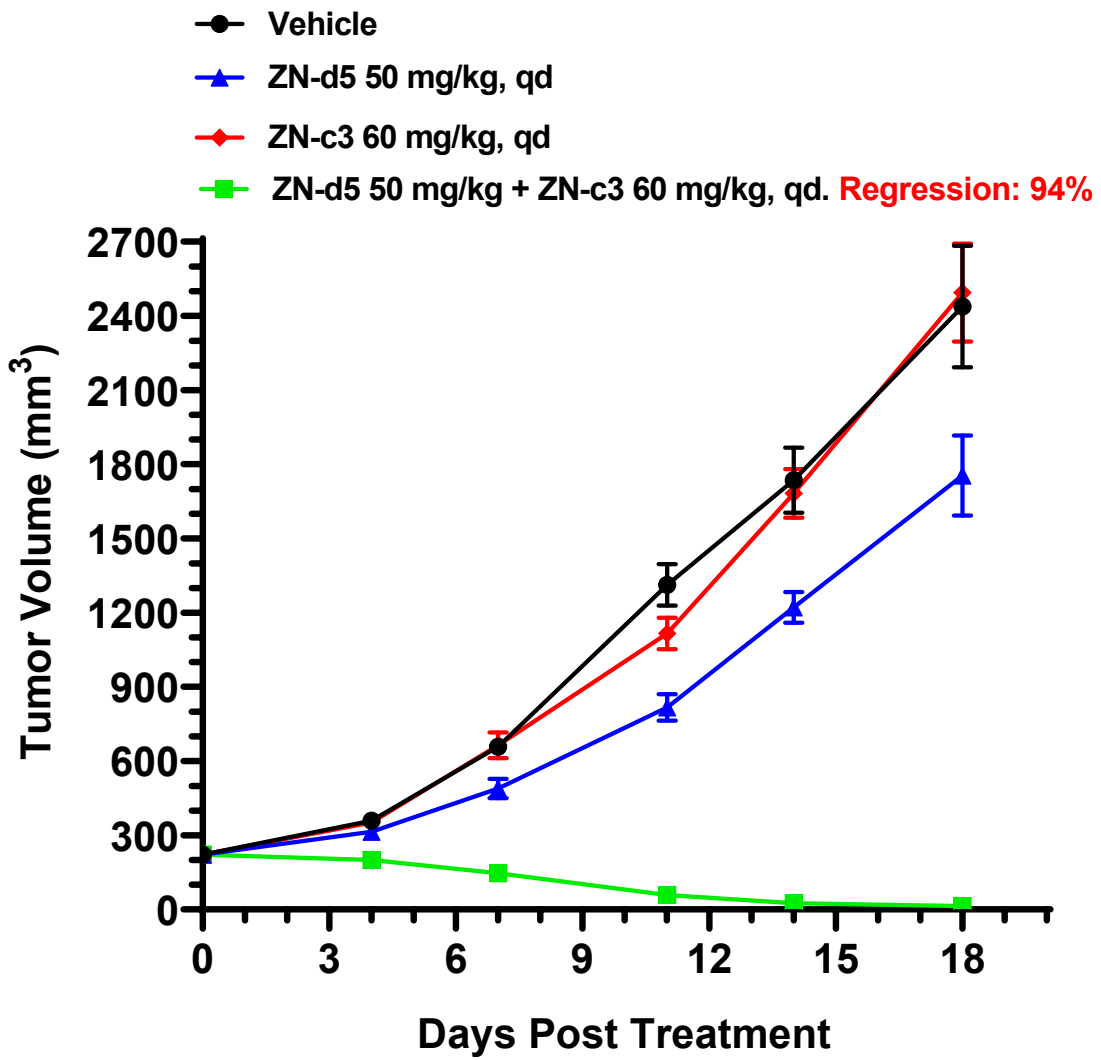
ZN-d5 + ZN-c3 Combination Treatment Also Results in Decreased Levels of DDR Proteins

- **ZN-d5 at subtherapeutic doses activates caspases leading to:**
  - DNA damage (increased in γH2AX)
  - Degradation or decrease of DDR related proteins (Wee1 and RRM2)
  - **These effects are increased when combined with ZN-c3**
- **This, in turn, results in inhibition of multiple relevant pathways (e.g. pCDK1) and synergistic anti-tumor activity when combined with ZN-c3**



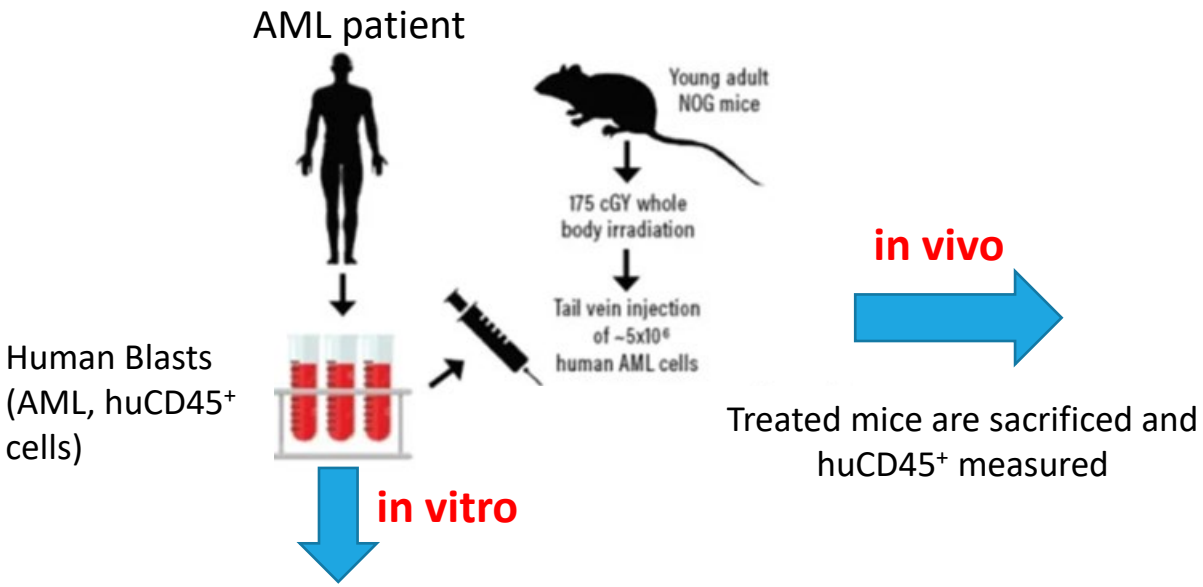
The Combination of BCL-2 and Wee1 Inhibitor Results in Synergism in Several Tumor Models Including AML

HL-60 AML model



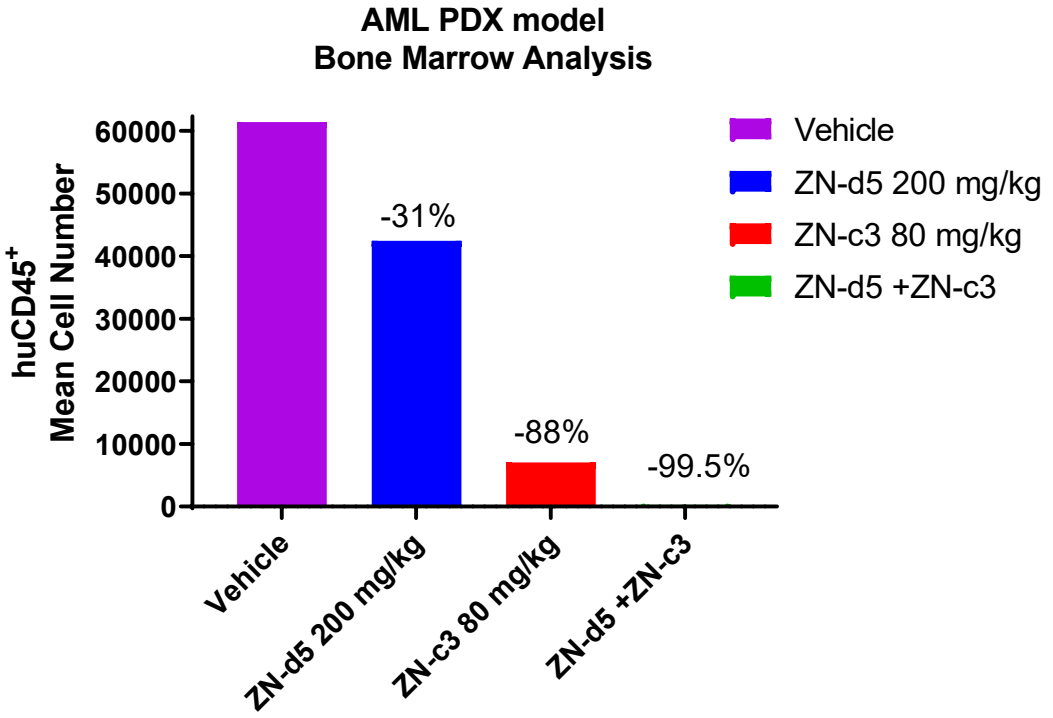
- The combination of ZN-d5 and ZN-c3 represents a novel therapeutic approach
- Significant enhancement of activity than single agent in several indications, including AML
- Combination regimen was well-tolerated in mice
- **Zentalis is the only company known to have both inhibitors in clinical development**

ZN-d5 Combined with ZN-c3 is Active in Patient-Derived AML Samples



Clinical				In vitro (ZN-d5+ZN-c3)	
Patient	Blasts % (before treatment)	Post- Collection Treatment	Blasts % (After Treatment)	ZN-d5/ZN-c3 Treatment (nM)	Blasts % (After Treatment)
3930	93.4	Vidaza/Venetoclax	Residual AML (33% blast) (~2 months post-treatment)	120/500	4.6
3977	62.1	Vidaza/Venetoclax	Residual AML (68% blast) (~2 months post-treatment)	65/100	0
3978	41.1	Gilteritinib/Venetoclax	Residual AML (32% blast) (~1 month post-treatment)	65/500	3.6

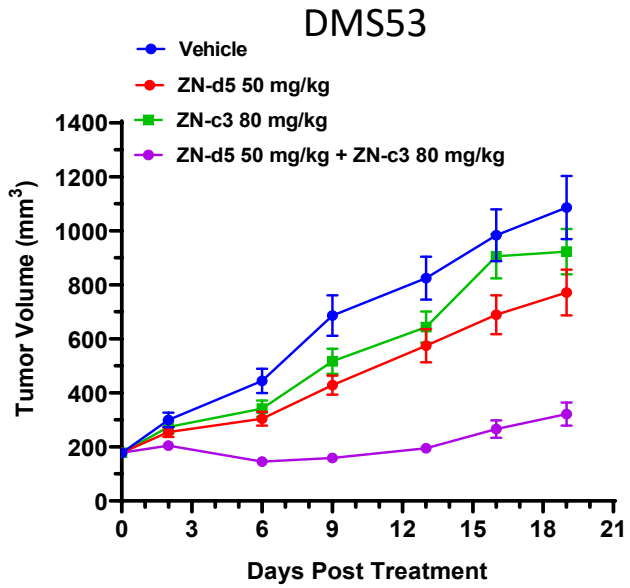
- The combination of ZN-d5+ ZN-c3 is active *in vitro* in **3/3 samples from patients who progressed on venetoclax**
- The combination of ZN-d5 + ZN-c3 is active *in vitro* in 29 patient's derived AML samples independently of TP53 mutation

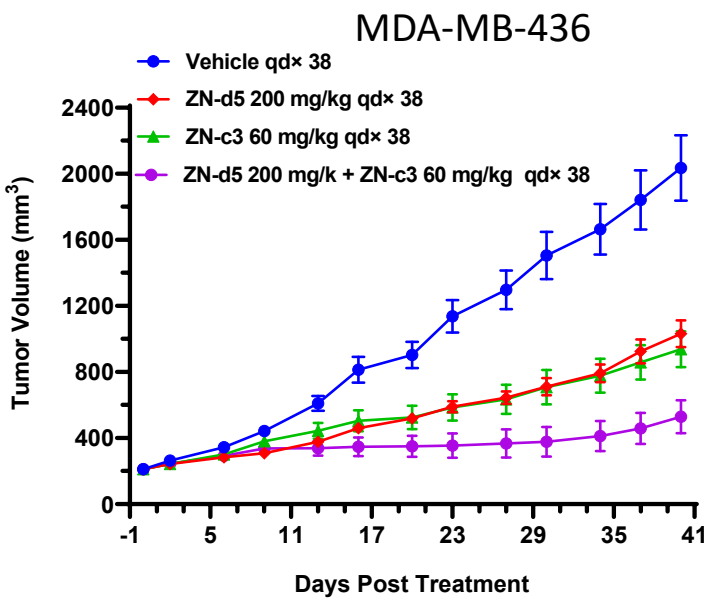


n= 6 or 10, qd x 17 treatment

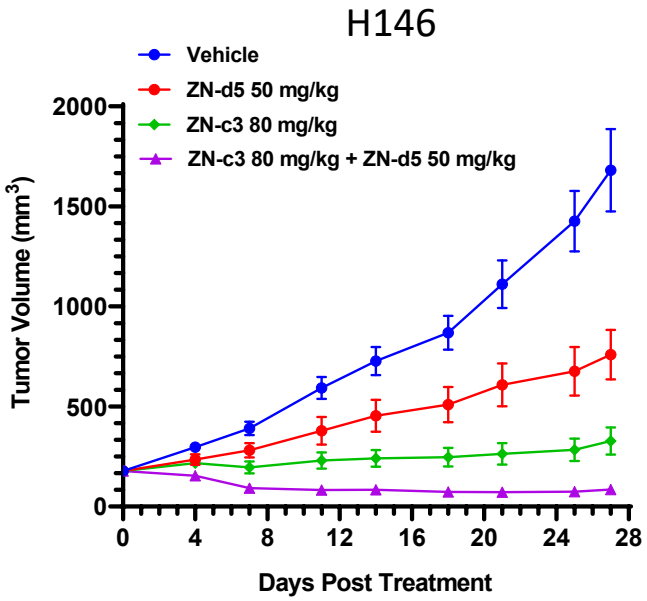
ZN-d5 + ZN-c3 shows promising activity in samples from AML patients progressing on venetoclax

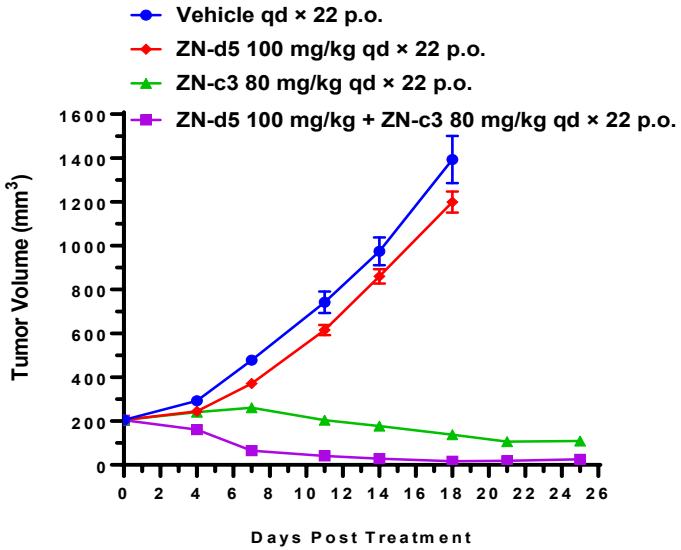
Antitumor Activity in Solid Tumor Models with the ZN-d5 + ZN-c3 Combination Represents Market Expansion Opportunities





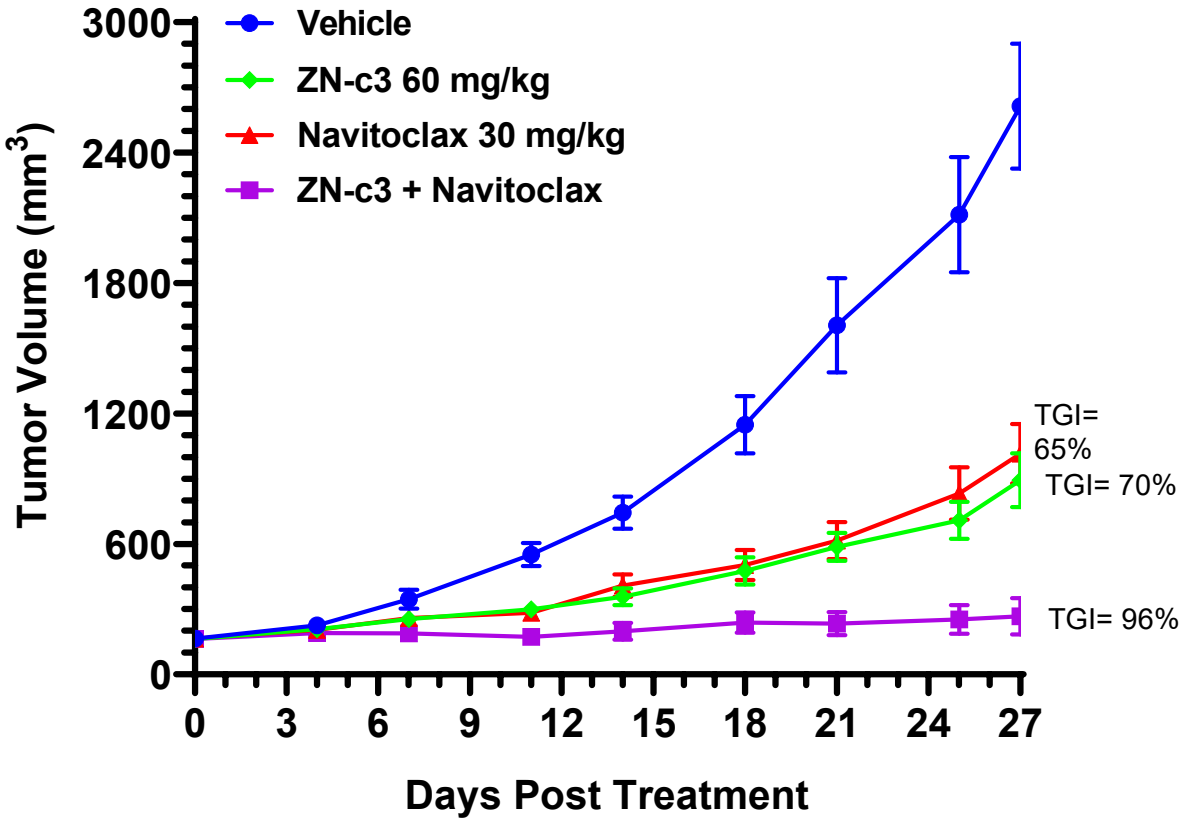
Cell Line	Indication
DMS53	SCLC
MDA-MB-436	TNBC





Cell Line	Indication
H146	NSCLC
H660	Neuroendocrine Prostate

ZN-c3 Combined with a Low Dose of Navitoclax (BCL-xL Inhibitor) Results in Enhanced Anti-tumor Activity in the ALL model MOLT-4



The MOA of the combination of ZN-d5 and ZN-c3 represents a novel therapeutic approach which also applies to combinations of ZN-c3 with other inhibitors of anti-apoptotic proteins

- Navitoclax enhances the anti-tumor activity of ZN-c3 at one-third of the active dose used as a single agent in xenografts (30 versus 100 mg/kg)
- Opportunity to overcome the toxicity observed with navitoclax

TGI: Tumor Growth Inhibition
ALL: Acute Lymphoblastic Leukemia
MOLT-4 model is BCL-xL dependent, but is not on BCL-2

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Summary

Summary

ZN-c3 Wee1 Inhibitor: A Potential Cornerstone Treatment

- ZN-c3 showed **strong clinical activity** and **good tolerability** in USC and in combination with chemotherapy in ovarian cancer
- Observed overall potential superior profile compared to adavosertib[(1-3)] in both monotherapy and in combination
- ZN-c3 is currently in a potentially registrational trial in USC; planning is underway for a Phase 3 trial in combination with chemotherapy in ovarian cancer
- In addition, ZN-c3 has **shown broad preclinical activity across multiple models** in both monotherapy and in combination:
  - Osteosarcoma, colorectal, prostate, *neuroendocrine prostate*, breast cancer (ER+, HER2+, and TNBC), AML, NHL, *ALL*, *SCLC*, NSCLC
- ZN-c3's potentially best-in-class/first-in-class profile and underlying biology may establish it as a potential cornerstone treatment, creating a significant market opportunity across a broad range of solid and liquid tumors

ZN-c5 Oral SERD

- ZN-c5 continues to show clinical activity and potentially best-in-class tolerability data, suggesting potential superiority amongst the oral SERDs
  - Decision made to not to pursue CDK 4/6i combination
- ZN-c5 showed bone protective activity in a preclinical model - unlike other investigational SERDs - positioning ZN-c5 well for an adjuvant setting
- Initiating combination of ZN-c5 + ZN-c3 in $ER^+/HER2^-$ CDK 4/6i-resistant patients in 2022

ZN-d5 Bcl-2 Inhibitor

- Preclinical combination data of ZN-d5 + ZN-c3 utilizing novel biology showed synergistic and additive activity across multiple indications in both solid and liquid tumors, often at subtherapeutic doses
- First patient enrolled in a potentially registrational study evaluating ZN-d5 monotherapy in AL amyloidosis

(1) Liu JF et al. J Clin Oncol. 2021 Mar 11:JCO2003167
(2) Moore KM et al. Clin Cancer Res 2021.
(3) Lheureux et al. Lancet 2021.
Italics indicate new data presented today

Key Milestones

ZN-c3: Wee1 Inhibitor

1H 2022	✓	Initial readout on Phase 1 USC expansion cohort
1H 2022	✓	Initial readout on Phase 1b ovarian chemotherapy combo
2H 2022		Initial enrollment/safety update on Phase 2 USC trial[+]
2H 2022		Initial readout on Phase 1/2 chemotherapy combo in osteosarcoma*

ZN-c5: Oral SERD

1H 2022	✓	Phase 1b combination study topline results with Pfizer's palbociclib
1H 2022	✓	Phase 1b combination study topline results with Lilly's abemaciclib
2H 2022		Initiate Phase 1b combination study of ZN-c5 + ZN-c3 in CDK4/6i resistant breast cancer

ZN-d5: BCL-2 Inhibitor

1Q 2022	✓	Initiate Phase 1/2 monotherapy study in amyloidosis*
1H 2022		Initiate Phase 1/2 combination study of ZN-d5 + ZN-c3 in AML
2H 2022		Updated results from Phase 1 dose escalation study in AML and NHL

ZN-e4: EGFR Inhibitor

2H 2022	Report results on Phase 1 NSCLC trial

Integrated Discovery Engine

2022	Initiate IND enabling studies for an internal program

Zentera

2022	Maximize value from investment in and partnership with Zentera

[+] Registrational trial with FDA Fast Track designation
* Potentially registrational trial

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