ESMO 2024 Presentation Materials

- **Tropion-PanTumor03**
  - Oaknin, A. et al., ESMO 2024 714MO (Oral)
- **ICARUS-Breast01**
  - Pistilli, B. et al., ESMO 2024 340O (Oral)
- **First in human study of DS-9606**
  - Patel, M. R. et al., ESMO 2024 610O (Oral)

This document does not cover all the company related topics presented at ESMO 2024.

Datopotamab deruxtecan (Dato-DXd) in patients with Ovarian or Endometrial Cancer: Results from the Phase 2 TROPION-PanTumor03 Study

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Background

- TROP2 is a transmembrane protein that is highly expressed in a majority of ovarian and endometrial cancers[1]
- Dato-DXd is a TROP2-directed ADC that delivers a potent Topo-I inhibitor payload into tumour cells,[2] and has several unique properties:*
  - Optimised drug to antibody ratio ≈ 4†
  - Plasma-stable, tumour-selective cleavable linker-payload
  - High potency of payload with short systemic half-life†
  - Bystander antitumour effect
- Dato-DXd has demonstrated clinically relevant efficacy and manageable safety in Phase 3 trials in patients with pretreated non-squamous NSCLC and HR+/HER2– breast cancer[3,4]

Dato-DXd: Humanised anti-TROP2 IgG1 monoclonal antibody[5]

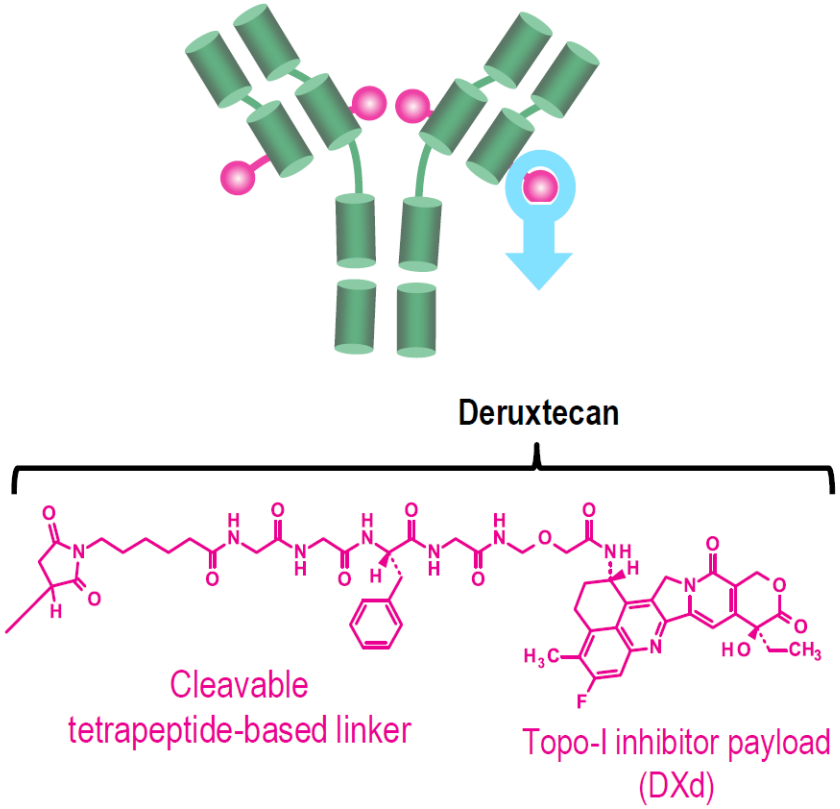


Image is for illustrative purposes only; actual drug positions may vary.

*The clinical relevance of these features is under investigation. †Based on animal data.
ADC, antibody-drug conjugate; Dato-DXd, datopotamab deruxtecan; HR+, hormone receptor positive; HER2–, human epidermal growth factor receptor 2 negative; IgG, immunoglobulin G; NSCLC, non-small cell lung cancer; TROP2, trophoblast cell-surface antigen 2; Topo-I, topoisomerase-I.

1. Shvartsure A, et al. Genes Cancer 2015;6:84–105; 2. Okajima D, et al. Mol Cancer Ther 2021;20:2329–40; 3. Ahn M-J, et al. Ann Oncol 2023;34:S1665–66; 4. Bardia A, et al. Ann Oncol 2023;34(suppl_2):S1264–5; 5. Dent R, et al. Future Oncol 2024;19:2349–59.

TROPION-PanTumor03 Study Design

A Phase 2, open-label, global study (NCT05489211) evaluating Dato-DXd as monotherapy and in combination with various anticancer agents across several tumour types

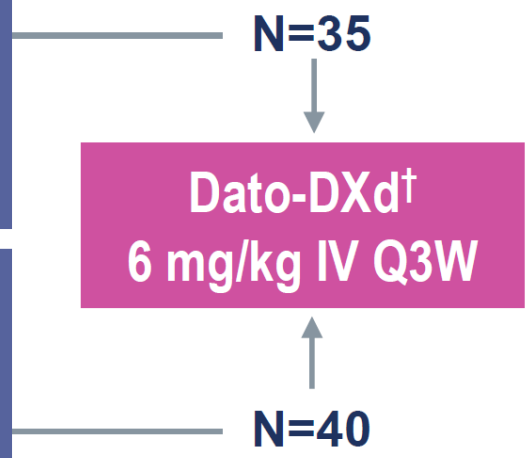
- Here, we present results of Dato-DXd monotherapy in the ovarian and endometrial cancer cohorts

Ovarian cancer (TROP2 expression unselected)

- High-grade serous or endometrioid ovarian, fallopian tube, or primary peritoneal carcinoma
- ECOG PS 0 or 1
- Progressed on ≥1 line of platinum chemotherapy but no more than 2 lines of therapy for advanced or metastatic disease; platinum-sensitive and resistant disease allowed*

Endometrial cancer (TROP2 expression unselected)

- Advanced/metastatic endometrial carcinoma
- All histologies (except sarcoma)
- ECOG PS 0 or 1
- Progressed on ≥1 line of platinum chemotherapy but no more than 2 lines of therapy for advanced or metastatic disease



Endpoints

Primary

- ORR by investigator per RECIST v1.1
- Safety & tolerability

Secondary

- PFS, DoR, DCR by investigator
- PK and immunogenicity

Exploratory

- OS
- Biomarker analyses

*Platinum-sensitive is defined as relapse/progression ≥6 months after completion of platinum-based chemotherapy; platinum-resistant is defined as progression <6 months of platinum-based therapy, including primary-refractory patients who progressed on or within 3 months of platinum-based chemotherapy (modified definition implemented by IMG); †Patients continued to receive treatment until they met one of the discontinuation criteria, including disease progression, unacceptable toxicity, withdrawal of consent, or study termination. Per protocol, a daily oral care protocol for stomatitis prophylaxis was provided to all patients prior to initiation of Dato-DXd; the use of a steroid-containing mouthwash was highly recommended.
DCR, disease control rate; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IMG, International Medical Graduates; IV, intravenous; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetics; Q3W, every 3 weeks; RECIST v1.1, Response evaluable criteria in solid tumours version 1.1.

Baseline Characteristics and Demographics

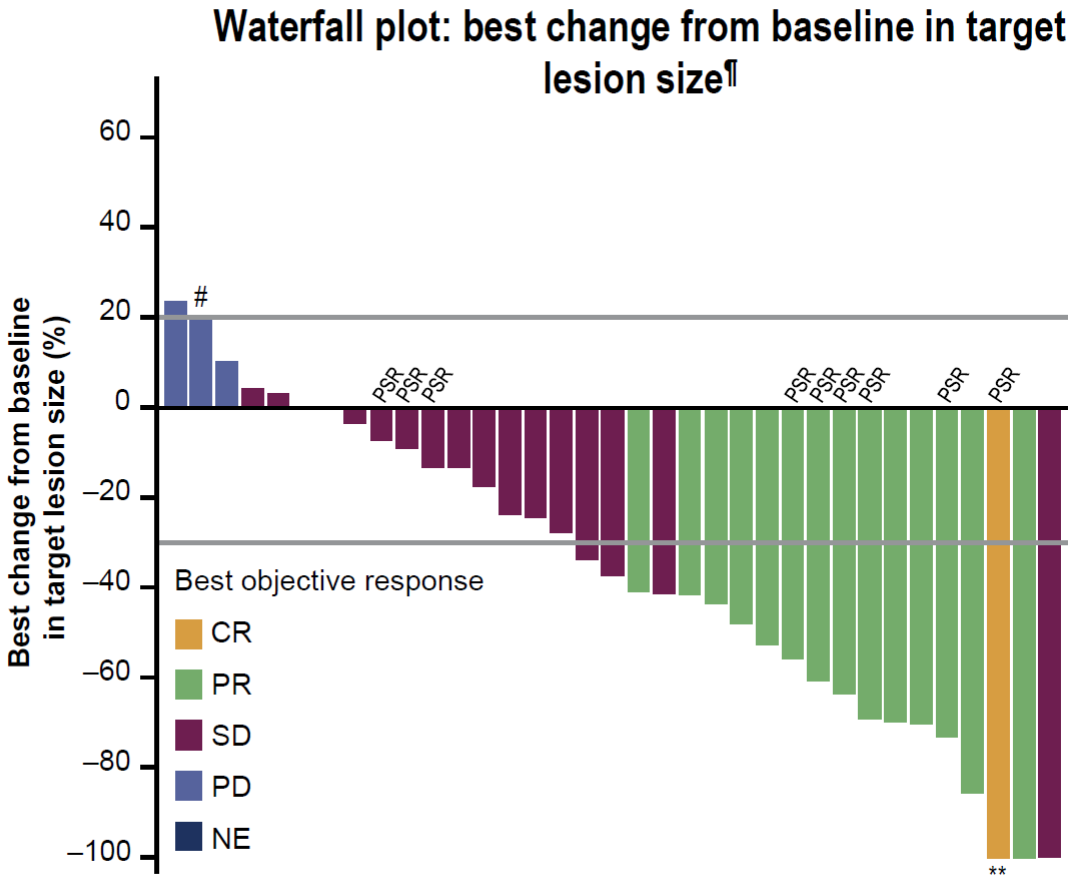
Characteristic		Ovarian (N=35)	Endometrial (N=40)
Age	Median (range), years	61.0 (35–80)	66.5 (48–78)
Race, n (%)	Asian	8 (22.9)	16 (40.0)
	White	23 (65.7)	18 (45.0)
	Other or not reported	4 (11.4)*	6 (15.0)†
ECOG PS, n (%)	0	21 (60.0)	25 (62.5)
	1	14 (40.0)	15 (37.5)
Major histology types, n (%)	High-grade endometrioid	0 (0.0)	11 (27.5)
	High-grade serous	27 (77.1)	10 (25.0)
	Low-grade endometrioid	0 (0.0)	7 (17.5)
	Clear cell	6 (17.1)	3 (7.5)
	Other‡	2 (5.7)	9 (22.5)
Previous lines of therapy, n (%)§	1	11 (31.4)	29 (72.5)
	≥2	24 (68.6)	11 (27.5)
Prior therapy, n (%)‖	Platinum therapy	35 (100)	40 (100)
	Bevacizumab/Lenvatinib	25 (71.4)	8 (20.0)
	PARP inhibitors	18 (51.4)	1 (2.5)
	Immunotherapy	2 (5.7)	9 (22.5)
	Hormone therapy	0 (0.0)	5 (12.5)
Platinum-sensitivity	Platinum-resistant¶	26 (74.3)	–
	Platinum-sensitive	9 (25.7)	–

*Including other (n=1), missing (n=1) and not reported (n=2); †Including American Indian or Alaska Native (n=1), Black or African American (n=1), not reported (n=3) and missing (n=1); ‡Including carcinosarcoma; §A patient who has received multiple lines of therapy is counted under the higher line of therapy only. No more than 2 previous lines of systemic therapy in the advanced or metastatic setting were allowed, neoadjuvant/adjuvant was counted as a line of therapy in the ovarian cohort; ‖A patient can be counted in multiple rows since more than one therapy can be taken. Within each row, a patient is counted only once; ¶Includes patients with platinum-refractory disease, defined as progression within 3 months of platinum therapy. PARP, Poly-ADP ribose polymerase.

Efficacy in Ovarian Cancer

- As of June 14, 2024, median duration of follow-up* was 14.5 months (range 10.4–15.4) in the ovarian cohort

	Ovarian		
	Total (N=35)	Platinum-sensitive (n=9)	Platinum-resistant (n=26)
Confirmed ORR, % (95% CI)	42.9 (26.3–60.6)	66.7 (29.9–92.5)	34.6 (17.2–55.7)
Best overall response, n (%)			
CR	1 (2.9)	1 (11.1)	0 (0.0)
PR	14 (40.0)	5 (55.6)	9 (34.6)
SD†	17 (48.6)	3 (33.3)	14 (53.8)
PD‡	3 (8.6)	0 (0.0)	3 (11.5)
NE§	0 (0.0)	0 (0.0)	0 (0.0)
Median time to response, months (range)	1.4 (1.2–8.2)	–	–
Median DoR, months (95% CI)	5.7 (2.9–NC)	8.5 (2.7–NC)	5.6 (2.9–NC)
DCR at 12 weeks,‖ % (80% CI)	85.7 (75.1–92.9)	100 (77.4–100.0)	80.8 (67.2–90.3)
Median PFS, months (95% CI)	5.6 (4.1–7.0)	–	–



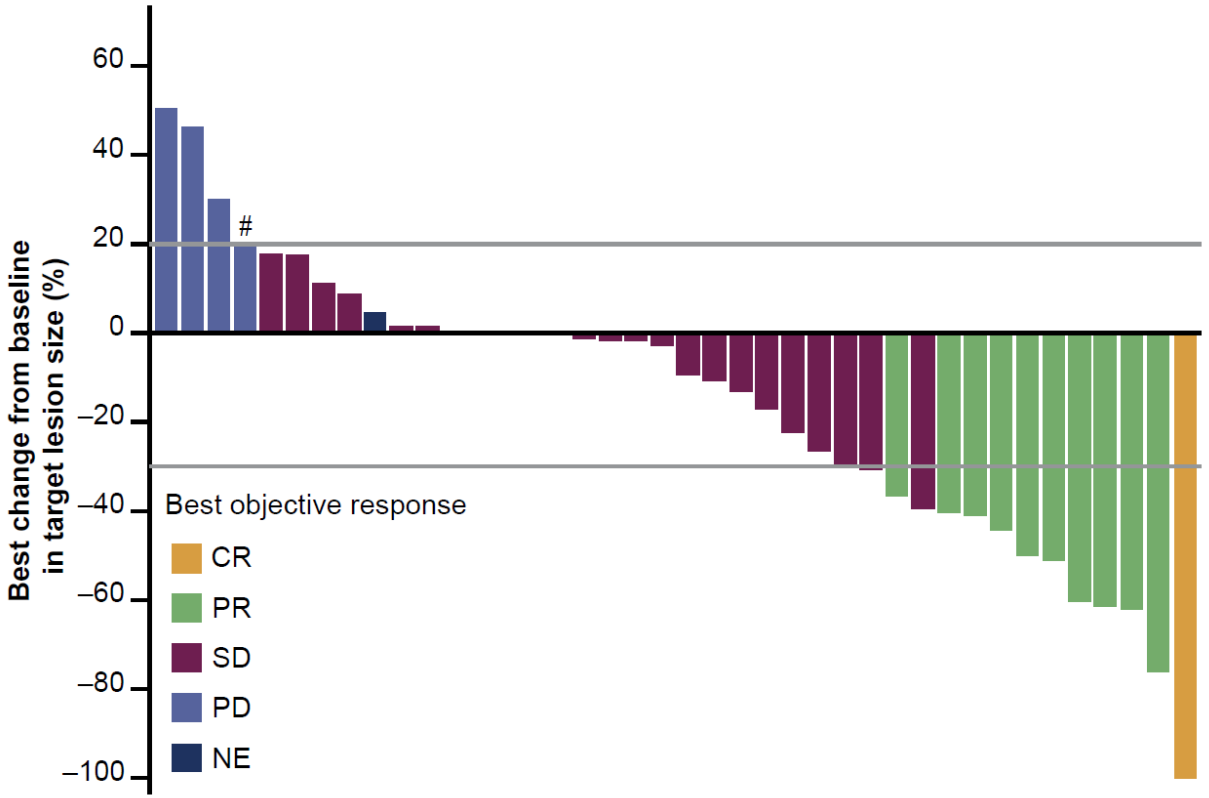
*Duration of follow-up calculated as the median time from randomisation to the date of censoring, in censored patients only; †Unconfirmed CR/PR, or SD ≥35 days; ‡RECIST progression or death ≤13 weeks; §SD <35 days, no valid baseline assessment or evaluable follow-up assessment; ‖Defined as the percentage of patients who achieved CR, PR or SD; ¶Best change in target lesion size is the maximum reduction from baseline or the minimum increase from baseline in the absence of a reduction. Lines at -30% and 20% indicate thresholds for PR and PD, respectively. If best percentage change cannot be calculated due to missing data, +20% will be imputed as the best percentage change in the following situations (otherwise left as missing): patient has no post-baseline assessment, has died, has new lesions or progression of lesions, or has withdrawn due to PD and has no evaluable target lesion data. Patients with imputed values marked with #; **Patient had PR at the first visit (with a change from baseline in the target lesion of 100%) and PD at the subsequent two visits and was therefore an unconfirmed PR and classified as SD. CI, confidence interval; CR, complete response; NC, not calculable; NE, not evaluable; PD, progressive disease; PR, partial response; PSR, platinum-sensitive relapsed; SD, stable disease.

Efficacy in Endometrial Cancer

- As of June 14, 2024, median duration of follow-up* was 13.6 months (range 2.1–19.6) in the endometrial cohort

	Endometrial (N=40)
Confirmed ORR, % (95% CI)	27.5 (14.6–43.9)
Best overall response, n (%)	
CR	1 (2.5)
PR	10 (25.0)
SD†	23 (57.5)
PD‡	5 (12.5)
NE§	1 (2.5)
Median time to response, months (range)	2.8 (1.4–4.2)
Median DoR, months (95% CI)	16.4 (7.1–NC)
DCR at 12 weeks,‖ % (80% CI)	57.5 (46.1–68.3)
Median PFS, months (95% CI)	6.3 (2.8–NC)

Waterfall plot: best change from baseline in target lesion size¶



*Duration of follow-up calculated as the median time from randomisation to the date of censoring, in censored patients only; †Unconfirmed CR/PR, or SD ≥35 days; ‡RECIST progression or death ≤13 weeks; §SD <35 days, no valid baseline assessment or evaluable follow-up assessment; ‖Defined as the percentage of patients who achieved CR, PR or SD; ¶Best change in target lesion size is the maximum reduction from baseline or the minimum increase from baseline in the absence of a reduction. Lines at -30% and 20% indicate thresholds for PR and PD, respectively. If best percentage change cannot be calculated due to missing data, +20% will be imputed as the best percentage change in the following situations (otherwise left as missing): patient has no post-baseline assessment, has died, has new lesions or progression of lesions, or has withdrawn due to PD and has no evaluable target lesion data. Patients with imputed values marked with #.

Exposure and Safety

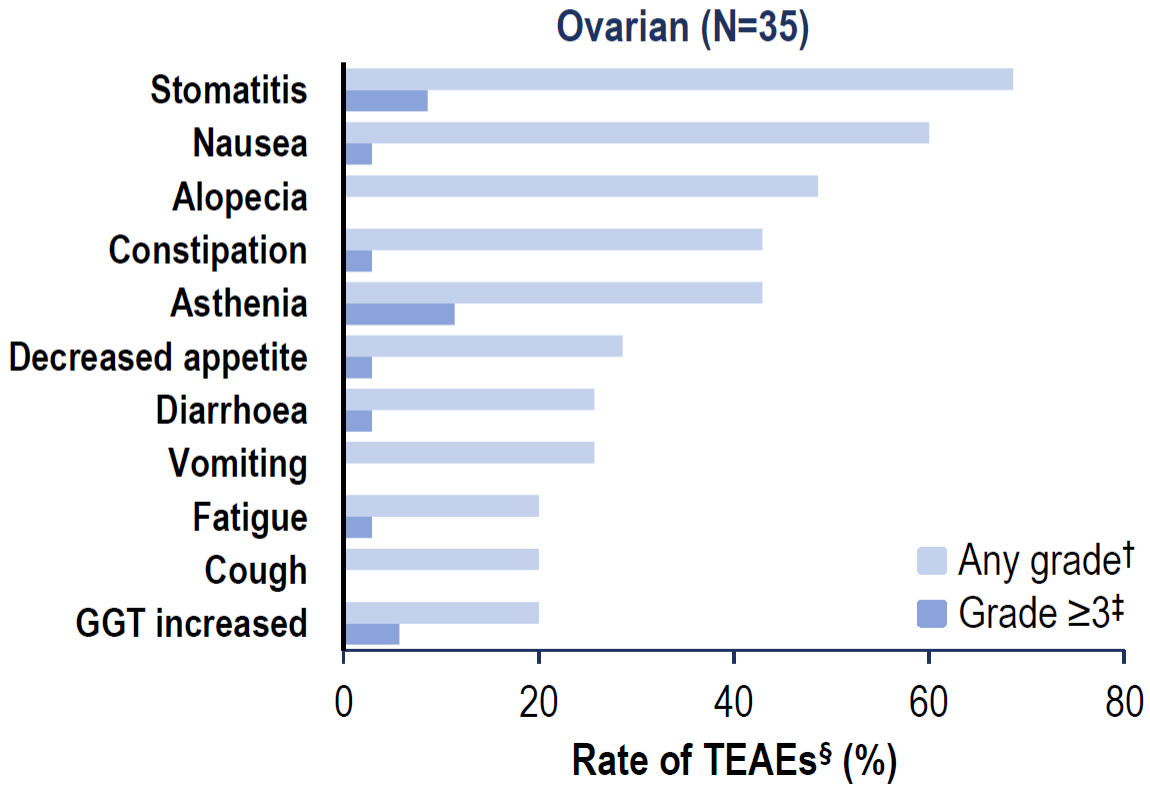
- The median treatment duration* for Dato-DXd was 5.6 months (range 1.4–14.8) in the ovarian cohort and 5.2 months (range 0.7–19.3) in the endometrial cohort

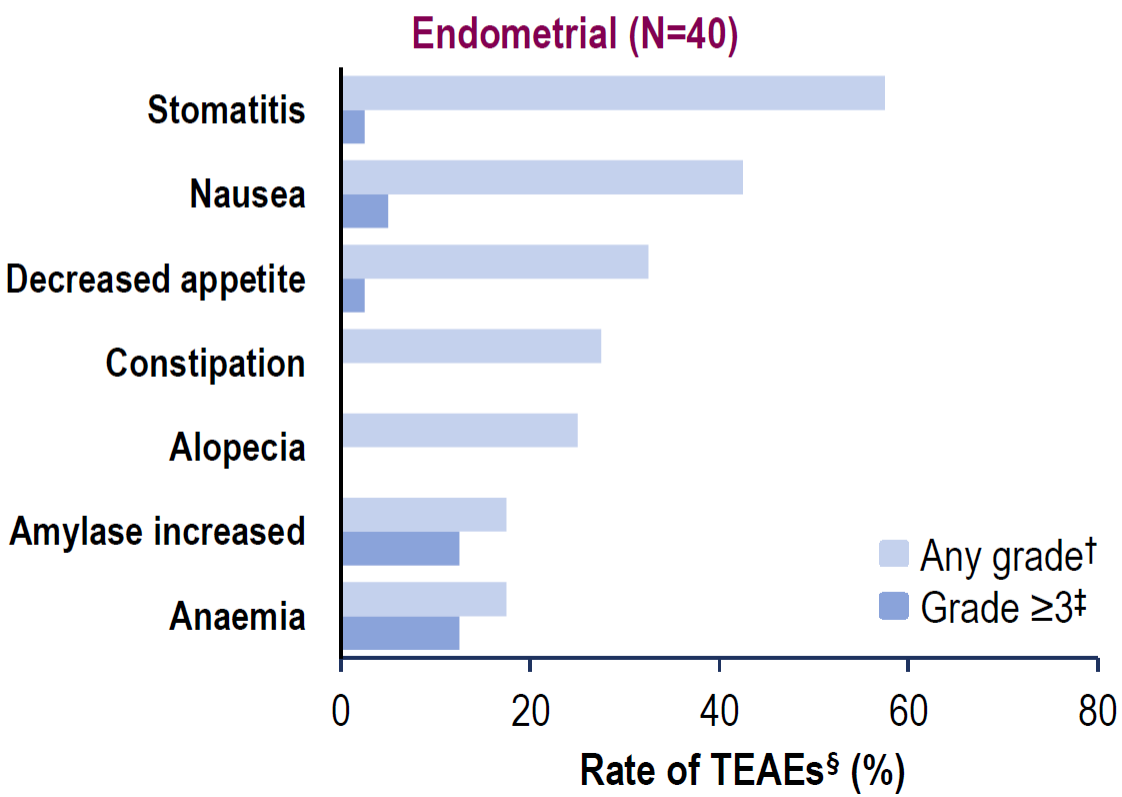
TEAEs, n (%)†	Ovarian (N=35)	Endometrial (N=40)
All grade	35 (100.0)	39 (97.5)
Grade ≥3‡	19 (54.3)	23 (57.5)
Serious	10 (28.6)	11 (27.5)
Leading to		
Dose reduction§	13 (37.1)	10 (25.0)
Dose interruption‖	16 (45.7)	14 (35.0)
Discontinuation¶	2 (5.7)	3 (7.5)
Death	0 (0)	0 (0)

*Actual treatment duration, defined as the total treatment duration (period from the first dose data of study drug to earliest of date of study discontinuation, date of death, data cutoff) minus the total duration of interruptions;
†Patients with multiple events in the same category are counted only once in that category. Patients with events in more than one category are counted once in each of those categories;
‡According to Common Terminology Criteria for Adverse Events (CTCAE) v5.0; §The most common reason for dose reduction in both cohorts was stomatitis (ovarian cohort: n=4; endometrial cohort: n=7); ‖The most common reasons for dose interruptions were punctate keratitis (n=2), vision blurred (n=2), and stomatitis (n=2) in the ovarian cohort and COVID-19 (n=2), keratitis (n=3) and amylase increased (n=2) in the endometrial cohort; ¶Reasons for discontinuation were pneumonitis (n=2) in the ovarian cohort and syncope (n=1), dry eye and ulcerative keratitis (n=1) and ILD (n=1) in the endometrial cohort. ILD, interstitial lung disease; TEAEs, treatment-emergent adverse events.

Most Frequent TEAEs

- The most common TEAEs in both cohorts were stomatitis* and nausea; the majority of cases were grade 1–2
- Adjudicated drug-related ILD* was reported in 1 patient in each cohort; both cases were grade 3
- Ocular surface events* were reported in 40.0% (grade 3: 0%) and 27.5% (grade 3: 5%) of patients in the ovarian and endometrial cohorts, respectively; there were no grade 4 or 5 events





*Adverse events of Special Interest. Ocular surface events and ILD are reported as group terms; †TEAEs that occurred at any grade in ≥20% of patients shown; ‡According to CTCAE v5.0; grade ≥3 AEs that occurred in ≥5 patients included; §Patients with multiple events in the same category are counted only once in that category. Patients with events in more than one category are counted once in each of those categories.
GGT, gamma-glutamyltransferase.

Conclusions

- **Dato-DXd monotherapy** demonstrated **encouraging efficacy** in patients with **advanced/metastatic ovarian and endometrial cancer** who had disease progression on prior platinum chemotherapy
  - In the ovarian cohort, ORR was 42.9% and median DoR was 5.7 (95% CI: 2.9–NC) months
    - In platinum-sensitive patients, ORR was 66.7% and median DoR was 8.5 (95% CI: 2.7–NC) months
    - In platinum-resistant patients, ORR was 34.6% and median DoR was 5.6 (95% CI: 2.9–NC) months
  - In the endometrial cohort, ORR was 27.5% and median DoR was 16.4 (95% CI: 7.1–NC) months

- The **safety profile** of Dato-DXd monotherapy was **manageable** and **consistent** with that of previous studies
  - Few TEAEs led to drug discontinuation and there were no TEAEs that led to death
  - The most common TEAEs were stomatitis and nausea; mostly grade 1/2
  - Rates of adjudicated drug-related ILD were low

Efficacy, safety and biomarker analysis of ICARUS-BREAST01: a phase 2 Study of Patritumab Deruxtecan (HER3-DXd) in patients with HR+/HER2 advanced breast cancer

B. Pistilli[1,15], L. Pierotti[2], M. Lacroix-Triki[3], C. Vicier[4], J.S. Frenel[5], V. D'Hondt[6], F. Dalenc[7], T. Bachelot[8], A. Ducoulombier[9], M.A Benderra[10], D. Loirat[11], D. Mayeur[12], G. Nachabeh[13], A. Sporchia[14], F.Suto[14], S.Michiels[2], N. Corcos[15], F. Mosele[1,16], F. André[1,16,17], G. Montagnac[15]

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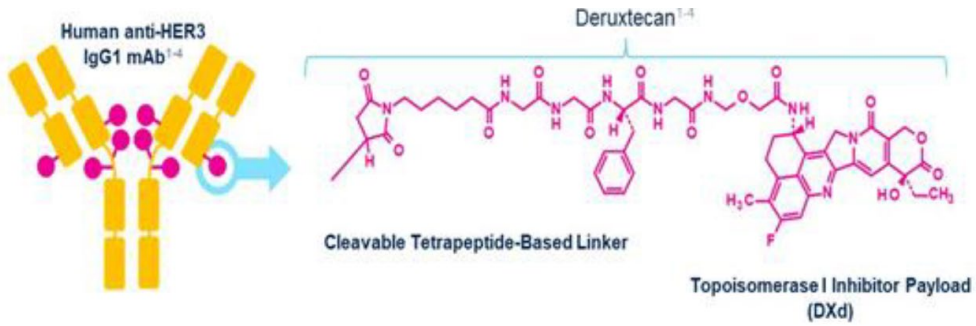
ESMO 2024 340O (Oral)

Background

- Despite the improved clinical outcomes achieved with endocrine therapy + CDK4/6 inh in HR+/HER2- advanced breast cancer, effective therapeutic options are limited after disease progression[1-3]
- **High expression of Human Epidermal Growth Factor Receptor-3 (HER3)** is associated with **poor prognosis** and plays a key role in **resistance to PI3K/AKT/mTOR inh, HER2-targeting therapies and endocrine therapy**[4-12]
- **HER3-DXd** is an antibody-drug conjugate composed of an anti-HER3 monoclonal antibody conjugated to a topoisomerase-I inh by a cleavable peptide linker[13-16]
- Prior phase I and II studies showed **promising activity of HER3-DXd** across breast cancer subtypes and across a range of HER3 membrane expression[17-20]



1. Gennari A, et al. *Ann Oncol* 2021;32:1475-1495; 2. Wolff AC, et al. *J Clin Oncol* 2023;41:3867–72;3. Moy B, et al. *J Clin Oncol* 2023;41:1318–20; 4..Jura N, et al, Proc Natl Acad Sci USA 2009, 106:21608-13; 5.Hynes NE et al, Nat Rev Cancer 2005, 5(5): 341-354; 6.Ocana et al, J Natl Cancer Inst 2013, 105:266–273; 7.Chandarlapaty S et al, Cancer Cell, 2011, 19:58-71; 8. Rodrik-Outmezguine VS et al, Cancer Discov 2011, 1:248-59; 9.Chakrabarty A et al, Proc Natl Acad Sci U S A 2012;109: 2718–23; 10. Huang X et al, Cancer Res 2010, 70:1204-14; 11.Liu B et al, Int J Cancer 2007;120:1874-82.; 12. Morrison MM et al, Oncogene (2016) 35, 1143–1152; 13.Hashimoto Y, et al. Clin Cancer Res. 2019;25(23):7151-7161; 14. Nakada T, et al. Chem Pharm Bull (Tokyo). 2019;67(3):173-185; 15. OgitaniY, et al. Clin Cancer Res. 2016;22(20):5097-5108; 16. KoganemaruS, et al. Mol Cancer Ther. 2019;18(11):2043-2050. 17; Krop I et al, JCO 2023, 18.Hamilton E et al, ASCO 2023.; 19 Oliveira M et al, Ann Oncol 2023; 20. Braso-Maristany et al, Nature Communications 2024

Background

UNLOCK BY GUSTAVE ROUSSY

Ph1/2 translationnal studies

Biopsies timepoints

Mechanisms of action and resistance of innovative drugs
Current portfolio: platform of 10 phase II dedicated trials and 9 phase I trials

ICARUS

Mechanisms of actions and resistance to Dato-DXd and HER3-DXd

Dato-DXd

ICARUS LUNG

ICARUS BREAST

HER3-DXd

ICARUS BREAST01: Study Design

Multi-center, single-arm, phase 2 study (NCT04965766)

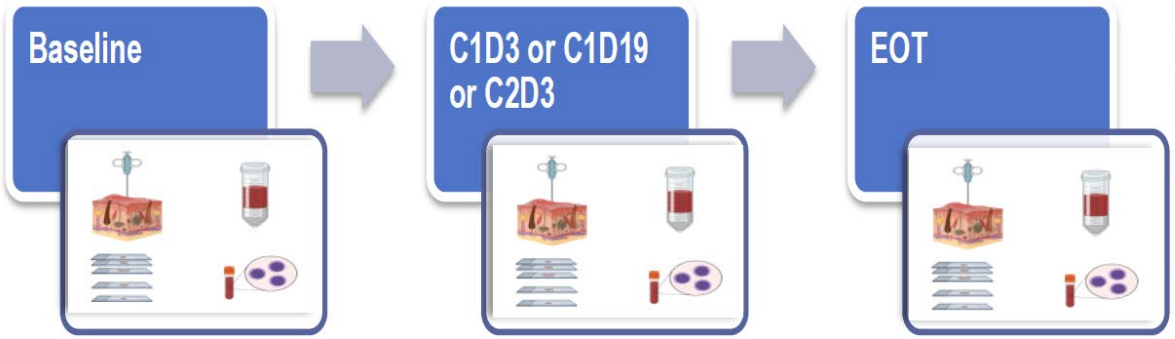
KEY ELIGIBILITY CRITERIA*:
-unresectable locally advanced/metastatic BC
-HR+/HER2-neg[a]
-progression on CDK4/6inh + ET
-progression on 1 prior chemotherapy for ABC
-prior PI3K/AKT/mTORinh allowed
-no prior T-DXd

HER3-DXd 5.6 mg/kg every 3 weeks until PD or unacceptable toxicity

Primary Endpoint:
- Investigator-assessed confirmed ORR

Secondary Endpoints:
- DOR, PFS, CBR, OS
- Safety and tolerability

Mandatory:
-tumor biopsy (1 frozen + 3 FFPE)
-blood (whole blood + serum)



Exploratory Endpoints:
- Predictors of response/resistance
- Dynamics of HER3 expression before and after treatment
- CTCs levels during treatment

***HER3-expression prescreening (75% of membrane positivity at 10x) was removed by amendment on April 21st 2022[b]**

a. Either IHC2+ and in situ hybridization [ISH] negative, or IHC1+ or IHC0+; b. The study was initially designed to include only patients with HER3-membrane expression ≥ 75% with 10x in tumor biopsies at baseline, however this inclusion criterion was deleted by amendment on 21st of April, 2022, after including the first 29 patients, and afterwards recruitment proceeded regardless of HER3 expression. This decision was taken because of the lack of a clear correlation between HER3 expression and response in other datasets. ABC: advanced breast cancer; CBR: clinical benefit rate; CTC: circulating tumor cells; DOR: duration of response; ET: endocrine therapy, T-DXd: Trastuzumab deruxtecan; ORR: objective response rate; OS: overall survival; PFS: progression-free survival;

Statistical considerations and methods

Investigator-initiated, multi-center trial in 11 French sites

Primary endpoint: confirmed ORR according to the investigator

Evaluation RECIST (V1.1) every 6 weeks (±7 days) for the first 12 months and then every 12 weeks (±7 days)

Confirmation of response had to be demonstrated with an assessment 4 weeks or later from the initial response

Sample size: ***99 patients required to provide 85% power to test H0: ORR ≤ 12% at a one-sided 5% significance level, assuming ORR = 23% under the alternative***

Data cut-off: Apr 16th, 2024; median follow-up: 15.3 months [95%CI 13.0;17.2]

Demographics and baseline characteristics

PATIENTS N=99

Age	
Median [range], years	57.0 (48.0;66.0)
Sex, n (%)	
Female	99 (100.0)
HR status, n (%)[a]	
ER+	94 (94.9)
PR+	42 (42.4)
HER2 expression, n (%)[b]	
IHC 0*	39 (39.4)
IHC 1+	22 (22.2)
IHC 2+	7 (7.1)
IHC 3+	1 (1.0)
Unknown	30 (30.3)[c]
HER3 expression[b]	
Membrane H-score, median (IQR)	180 (144;215)
Overall membrane positivity at 10x, n (%):	
<25%	16 (16.2)
25-74%	7 (7.1)
≥75%	49 (49.4)
Unknown	27 (27.3)
Median number of systemic therapies for ABC, n [range]	2 [1;4]
Prior treatment with CDK4/6inh, n (%)	98 (99.0)[d]
Median duration, months [range]	13.7 [6.5;19.7][e]
Prior PI3K/AKT/mTOR inh for ABC, n (%)	35 (35.4)
Prior chemotherapy for ABC, n (%)[f]	99 (100.0)

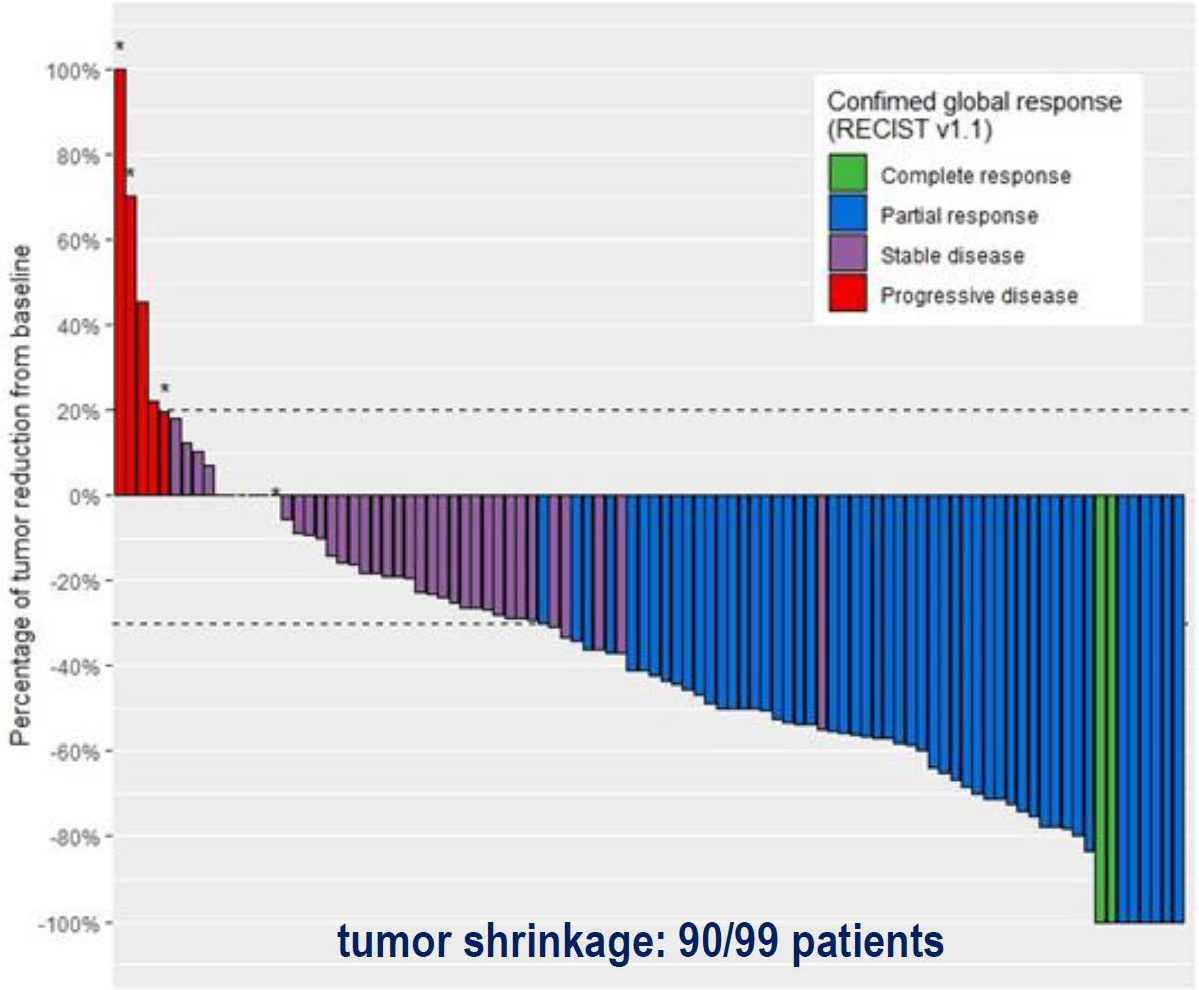
a. As assessed on initial tumor biopsy at diagnosis; b. Centrally assessed on tumor biopsy at study entry; c. Insufficient tumor sample available; d. 96 patients had CDK4/6inh for ABC, 2 patients for early breast cancer; 1 patient was enrolled by mistake as did not receive any prior treatment with CDK4/6inh; e. assessed in 73 patients; f. only 1 line of chemotherapyr allowed; *20 with HER2 membrane staining 1-10 %

Patient Disposition and treatment exposure

PATIENTS N=99	
HER3-DXd treatment status, n (%)	
Ongoing	19 (19.2)
Discontinued	80 (80.8)
Primary reason for discontinuation, n (%)	
Disease progression	64 (64.6)
Adverse events	8 (8.1)[a]
Other	7 (7.1)
Number of HER3-DXd cycles, median [IQR]	11.0 [6.0;18.0]
Median treatment duration, days [IQR]	251.0 [144.5;402.0]
At least one dose modification, n (%)	
No	67 (67.7)
Yes	32 (32.3)

a.n=2 adjudicated HER3-DXd-related grade 1 ILD, n=2 grade 3 nausea/vomiting; n=1 grade 3 fatigue; n=1 grade 3 thrombocytopenia, n=1 grade 3 hepatic fibrosis; n=1 patient died from concurrent medical condition, with last tumor assessment showing PR

Confirmed Objective Response Rate



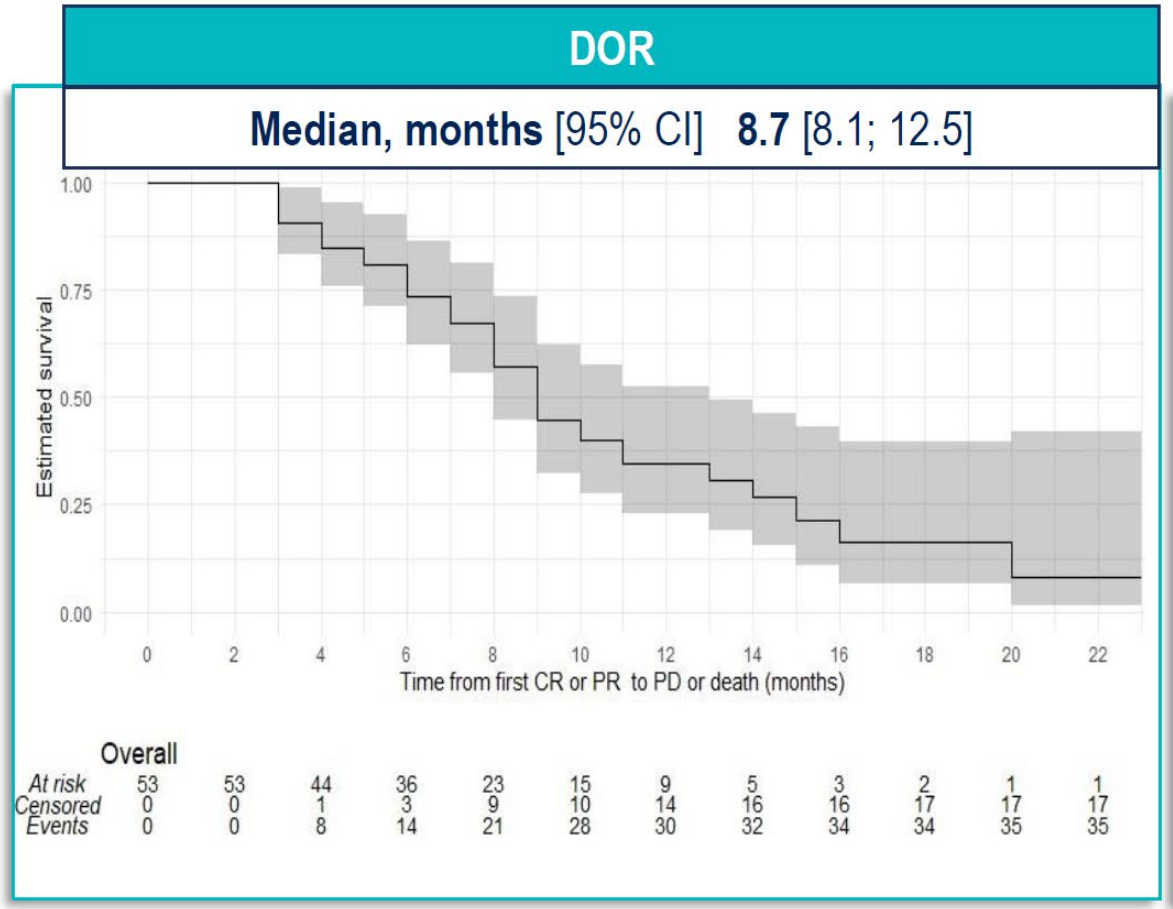
tumor shrinkage: 90/99 patients

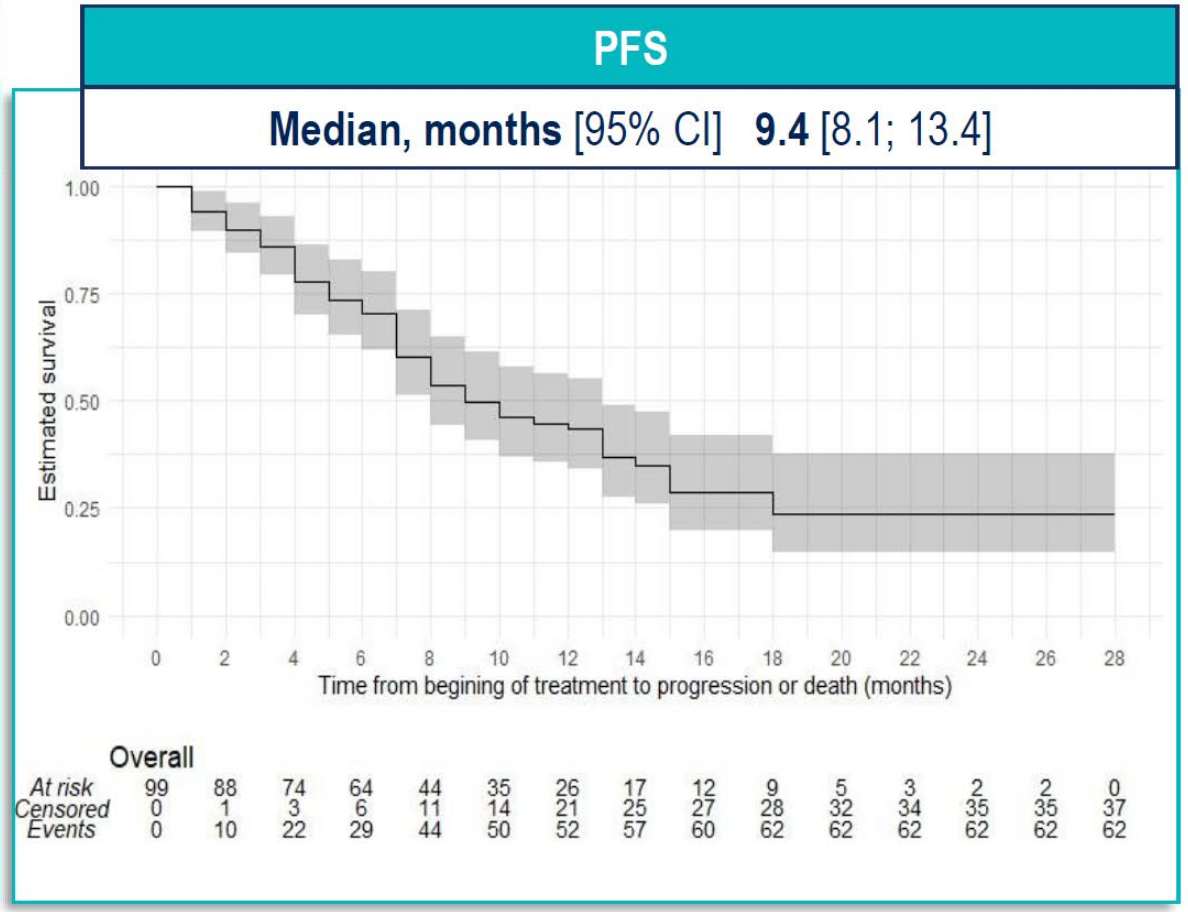
	N=99 n	% [95%CI][a]
Confirmed ORR[b]	**53**	**53.5** [43.2; 63.6]
CR	2	2.0 [0.2;7.1]
PR	51	51.5 [41.3; 61.7]
SD	37	37.4 [27.8; 47.7]
PD	7	7.1 [2.9; 14.0]
NE[c]	2	2.0 [0.2;7.1]
CBR[d]	**62**	**62.6** [52.3;72.1]

No significant association between HER2 expression and ORR (*p-value 0.8*)[e]

a. Clopper-Pearson (Exact) method was used for confidence interval; b. Confirmation of response must be demonstrated with a new tumor assessment 4 weeks or later from the initial response; c. 2 patients were not evaluable for ORR: one patient had only one tumor assessment with PR and then treatment discontinued due to clinical progression, a second patient had not evaluable as global response of target lesions. d. CBR is defined as the presence of at least a confirmed PR or CR, or a stable disease (SD) >6 months; e. logistic regression model was performed to estimate association between HER2 expression and ORR

Duration of Response and Progression-free Survival





Median follow-up: 15.3 months [95%CI 13.0;17.2]

No significant association between HER2 expression and PFS (*p-value 0.6*)[a]

a. Cox regression model was performed to estimate association between HER2 expression and PFS

Overall safety data

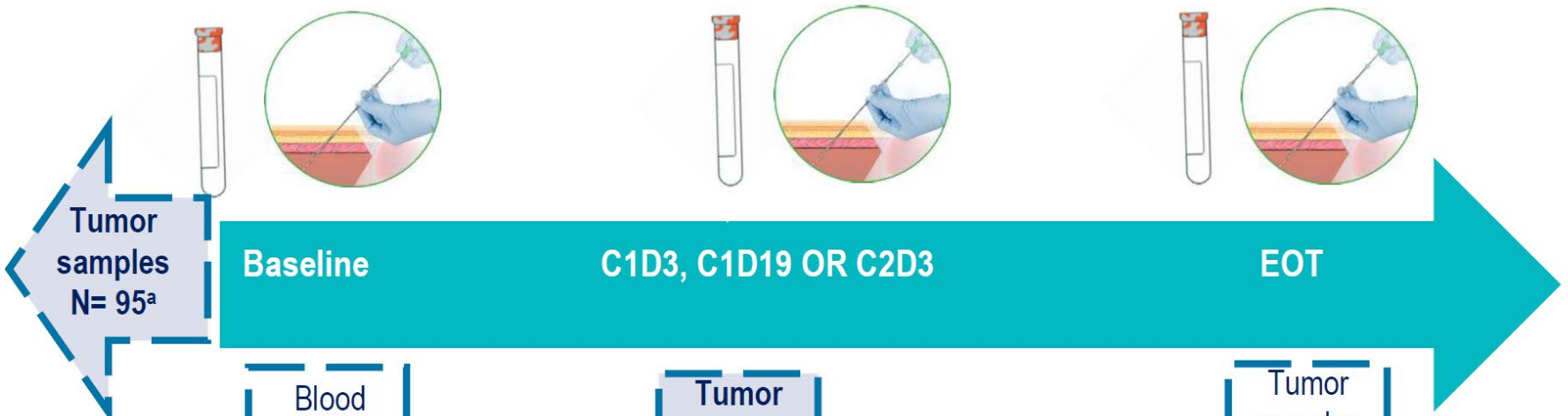
Overall safety profile, n (%)	
• **Patients with any grade TEAEs**	**97 (98.0)**
Grade ≥3 TEAEs	**54 (54.5)**
• **Patients with any grade TRAEs**	**97 (98.0)**
Grade ≥3 TRAEs	**50 (50.1)**
• TEAEs leading to HER3-DXd discontinuation	11 (11.1)
• TEAEs leading to HER3-DXd interruption	26 (26.3)
• TEAEs leading to HER3-DXd dose reduction	20 (20.2)
• TEAEs leading to death	1 (1.0)[a]
• **Adjudicated treatment-related ILD**	**7 (7.1)[b]**
Grade 1	7

TRAEs occurring in ≥ 10% of patients

	Any grade, n (%)	Grade ≥ 3, n (%)
Fatigue	82 (82.8)	10 (10.1)
Nausea	74 (74.7)	14 (14.1)
Diarrhea	52 (52.5)	10 (10.1)
Alopecia	40 (40.4)	0
Constipation	21 (21.2)	0
Vomiting	18 (18.2)	3 (3.0)
Anorexia	16 (16.2)	1 (1.0)
Neutrophil count decrease	14 (14.1)	12 (12.1)
Abdominal pain	11 (11.1)	0
Stomatitis	10 (10.1)	0
Anemia	10 (10.1)	0

TEAEs: Treatment-Emergent Adverse Events; ILD: Interstitial Lung Disease ; a. one patient died due to a massive pleural effusion not related to study treatment; b.Among the 13 cases identified as suspected during the treatment period, 7 case was adjudicated as HER3-DXd-related ILD, 2 of them led to treatment discontinuation

Exploratory biomarker analysis



- *HER3 expression by IHC, n=72[b]*
- *HER3 spatial distribution, ML, n=69[c]*
- *Genomic alterations associated with response/resistance WES, n= 43[d]*
- *Gene expression modulation, bulk RNA-seq, n=22[e]*
- *Characterization of tumor/TME IMC, n=61[f]*

- *CTC (n=36), ctDNA (n=99) (Baseline, C1D3 or C2D3 or C2D19, C2D1, EOT)*

- *HER3-DXd distribution, IMC, n= 57[g]*
- *Gene expression modulation, bulk RNA-seq, n=22[h]*

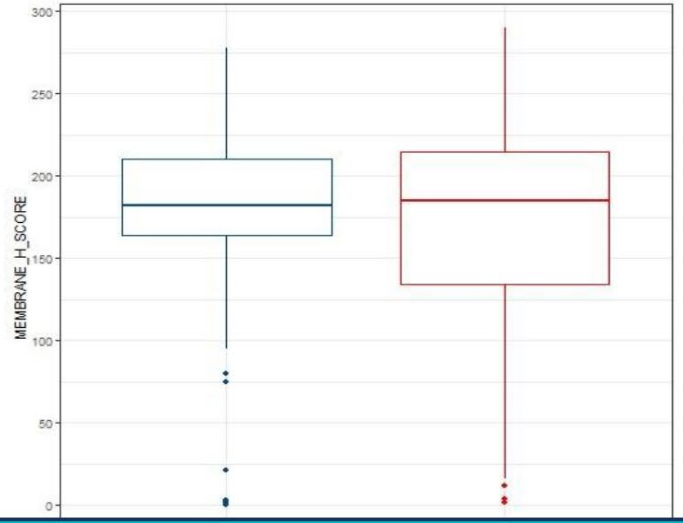
- *Genomic alterations associated with resistance, WES*
- *HER3 expression, IHC*
- *HER3-DXd distribution, remodeling TME, IMC*

a.4 biopsies not performed/collected; b. 23 samples < 10%; c.25 excluded after pathologist's review; d. 15 fresh biopsies not collected/provided by centers, 28 < 200 ng DNA or < 10% tumor cell; 13 failed quality control; e. 15 fresh biopsies not provided by centers, 28 < 200 ng RNA or < 30% tumor cell, 5 failed quality control, 29 did not have the matched on-T sample; f. 15 fresh biopsies were not provided centers, 28 < 200 ng RNA or < 30% tumor cell, 5 failed the quality control, 29 did not have matched on-T sample; g. 12 samples inadequate staining; h. 22 fresh biopsies not provided by centers, 39 < 200 ng RNA or < 30% tumor cell, 1 sample failed the quality control, 15 did not have matched BL sample;
IHC: Immunohistochemistry, RNAseq: RNA Sequencing, IMC: Imaging Mass Cytometry, WES: Whole Exome Sequencing; ML: machine learning; HER3 IHC: clone SP438

HER3 expression and outcome

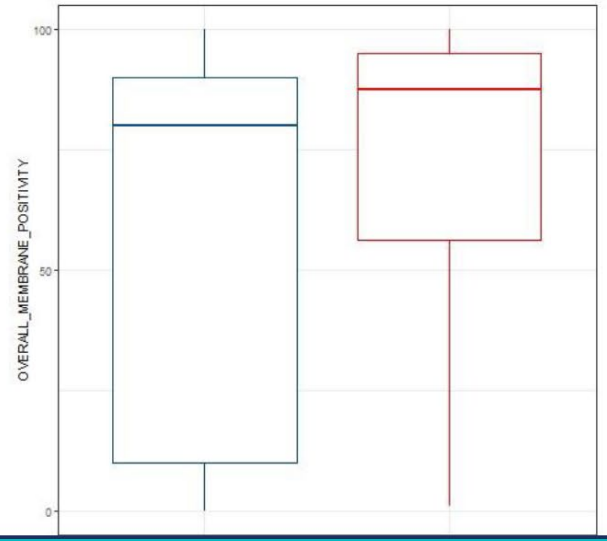
IHC analysis on tumor samples at baseline

HER3 membrane H-score



Non-responders (SD, PD) Median, [IQR]; n=34	Responders (CR,PR) Median, [IQR]. n=38
180.0 [165.0;210.0]	185.0 [134.0; 215.0]

HER3 membrane positivity 10x



Non-responders (SD, PD) Median, [IQR]; n=34	Responders (CR,PR) Median, [IQR]; n=38
80.0 [16.2;90.0]	87.5 [56.2;95.0]

No significant difference in HER3-membrane expression between responders and non-responders

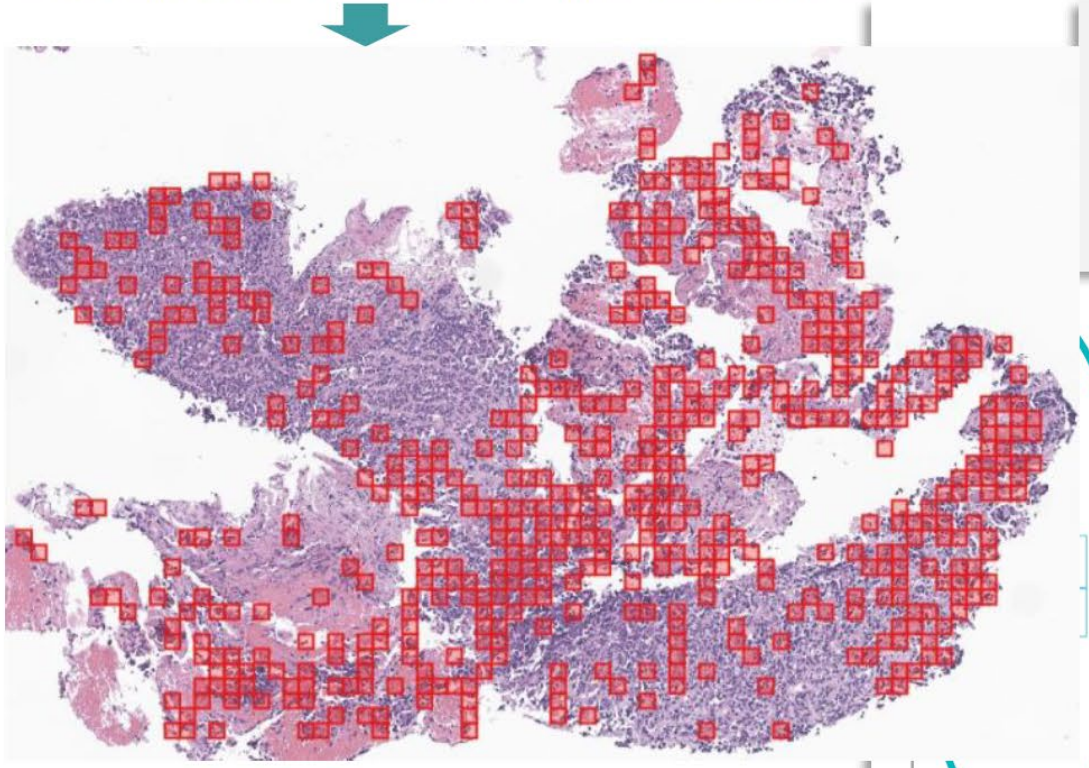
(*p-value 0.8 and 0.4*, respectively with HER3 H-score and 10x membrane positivity) *

72 patients at baseline, of whom 29 enrollment before study amendment ; *Logistic regression models were used to estimate the association of ORR and HER3 expression as continuous or categorical variable; HER3 assessment made by Roche CDx CAP/CLIA Laboratory (Tucson) using clone SP438

HER3 spatial distribution and outcome

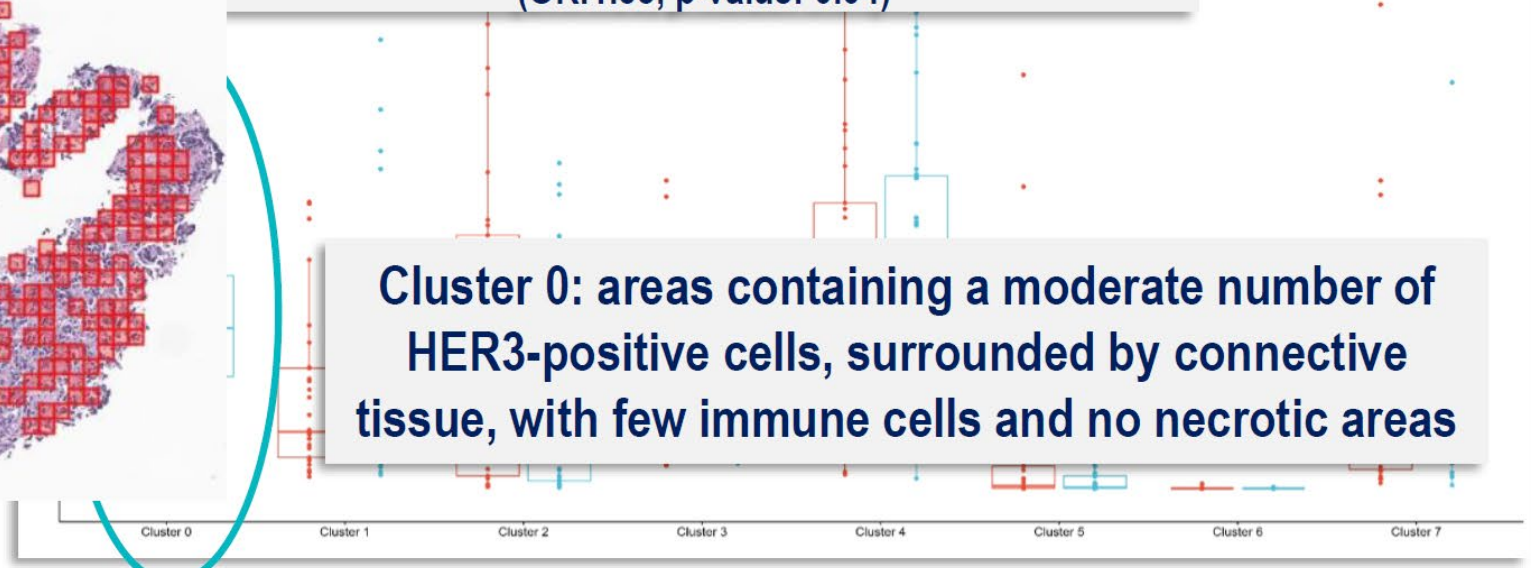
AI-digital pathology analysis on tumor samples at baseline

1. HER3 (DAB) stained slides overlapped with H&E slide



Tumors containing a higher proportion of clusters 0 had a higher likelihood of responding to the treatment

(OR:1.53, p-value: 0.04)*



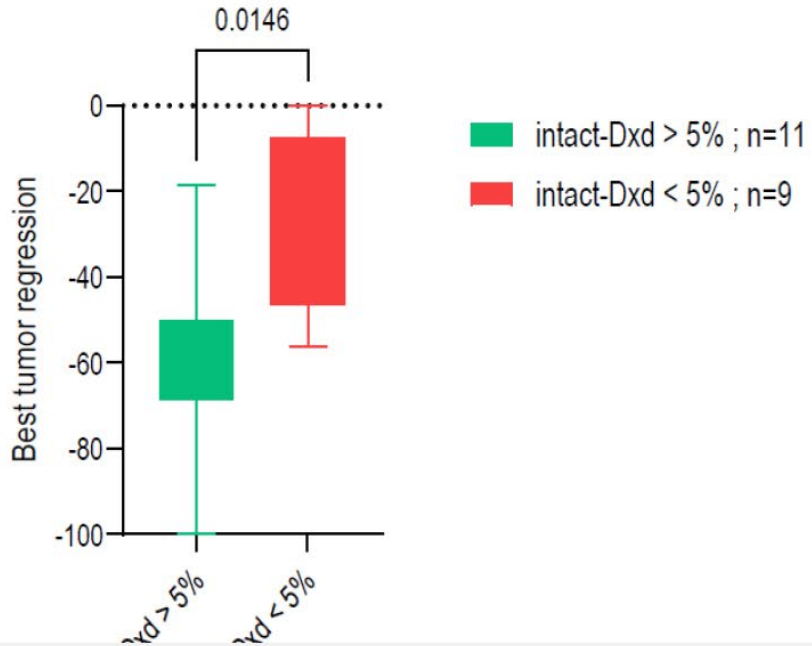
Cluster 0: areas containing a moderate number of HER3-positive cells, surrounded by connective tissue, with few immune cells and no necrotic areas

*63 samples at baseline, upon pathologist's review and exclusion of samples with non-optimal registration quality control ; . For all these analysis, using R version 4.1.2, we applied Dirichlet regression to identify which clusters were significantly associated with the objective response to treatment, and logistic regression to obtain odds ratios. 1. Hörst F, Rempe M, Heine L, et al. CellViT: Vision Transformers for precise cell segmentation and classification. Medical Image Analysis 2024;94:103143

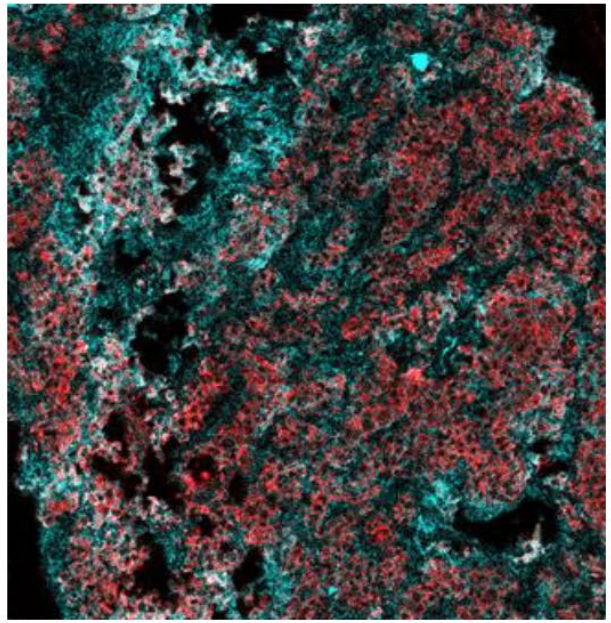
HER3 DXd distribution and treatment response

Imaging Mass Cytometry on tumor samples on-treatment

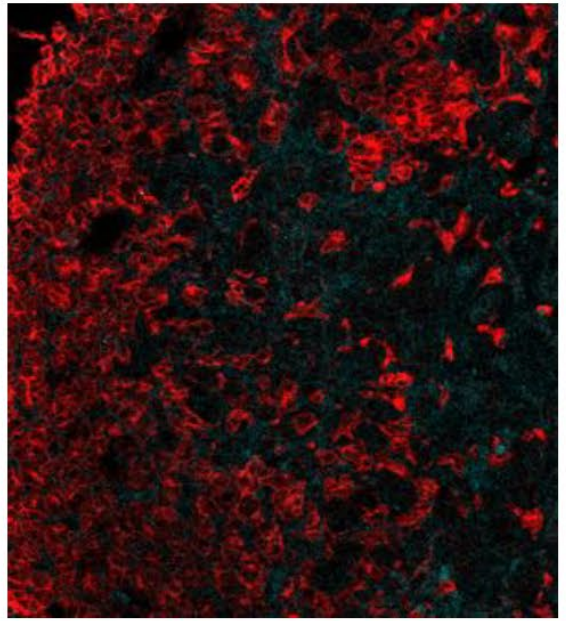
Tumor shrinkage/HER3-DXd-positive cells



HER3-DXd staining > 5% of tumor cells at C1D3; Tumor shrinkage: -52.5%



HER3-DXd staining < 5% of tumor cells at C1D3; Tumor shrinkage: -26.0%

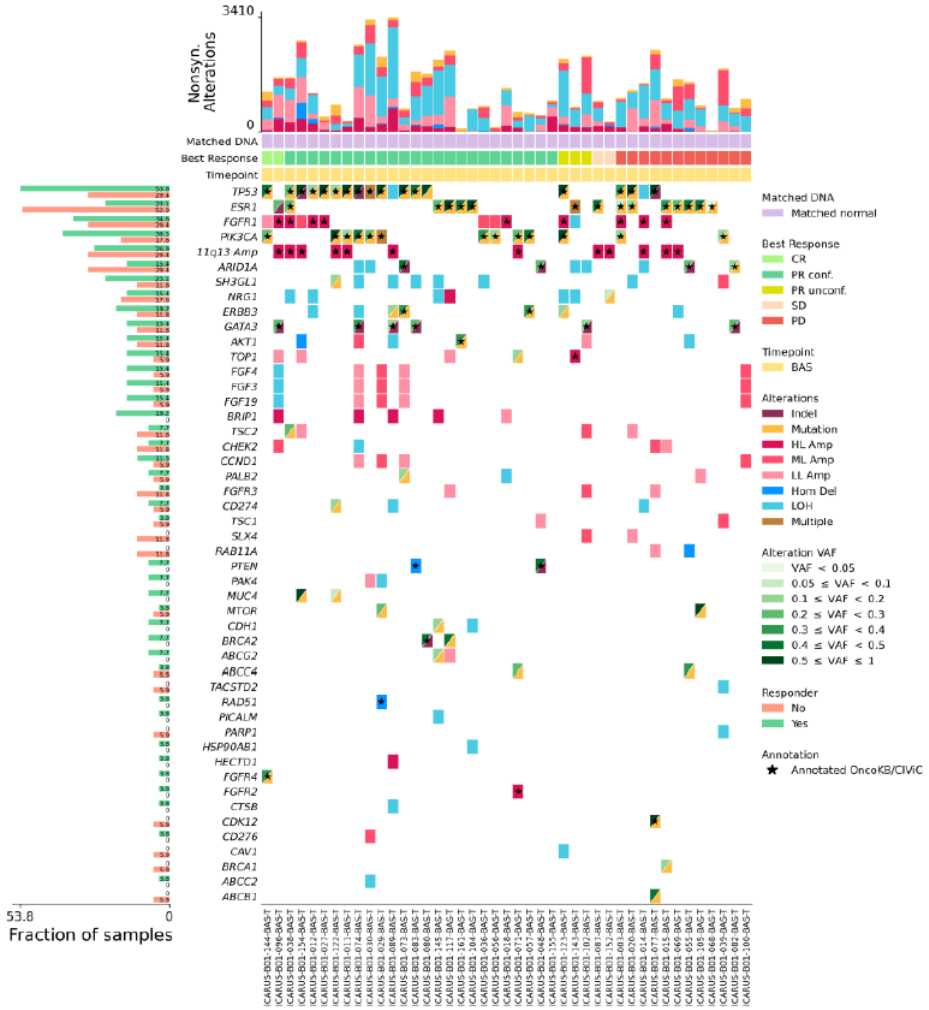


Greater tumor shrinkage in patients with HER3-DXd-positive cells > 5% (n=11) compared to HER3-DXd-positive cells <5% (n=9) at Cycle 1 Day 3 (t-test, *p-value 0.0146*)

Results to be interpreted with cautions due to the small sample size

Genomic alterations and treatment response

WES on 43 tumor samples at baseline: 73 genes of interest (selected before the study initiation)



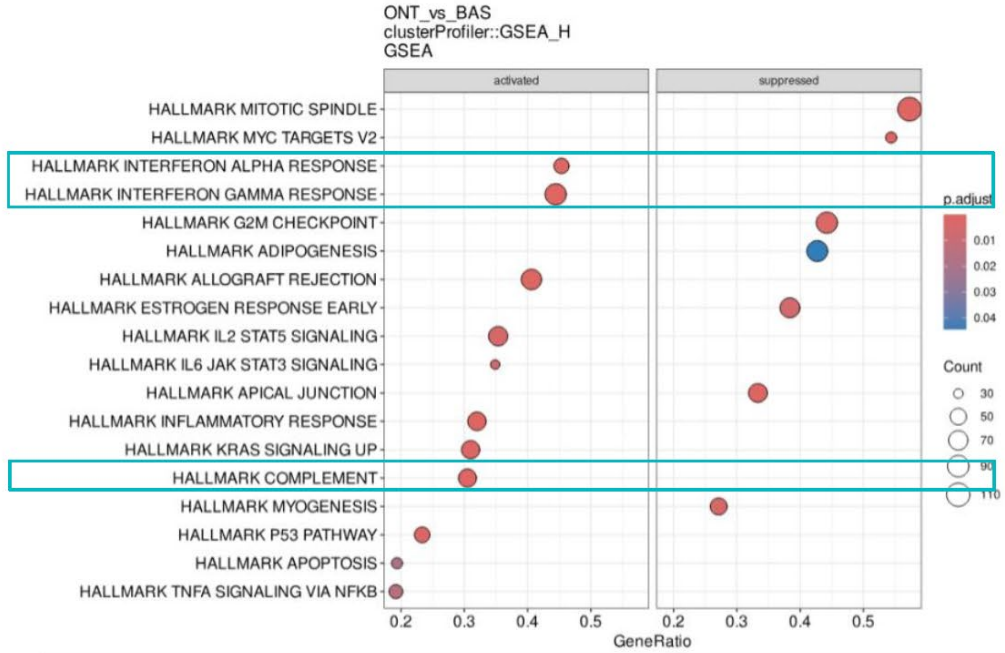
Gene alterations	Responders (CR, PR) n= 26 (%)	Non-responders (PD, SD) n=17 (%)
TP53	14 (53.8)	5 (29.4)
PIK3CA	10 (38.5)	3 (17.6)
ESR1	6 (23.1)	9 (52.9)
ERBB3	3 (11.5)	1 (5.9)

43 frozen tumor biopsies at baseline were analyzed for WES. Forty-three blood samples were used as germline control. Overall, at baseline, 15 fresh biopsies were either not collected or not provided by the participating centers, 28 were excluded due to < 200 ng DNA or < 10% tumor cell and 13 failed the quality control. Point muts. and indels were identified with Mutect2 following best practices while CNAs were called with FACETS.

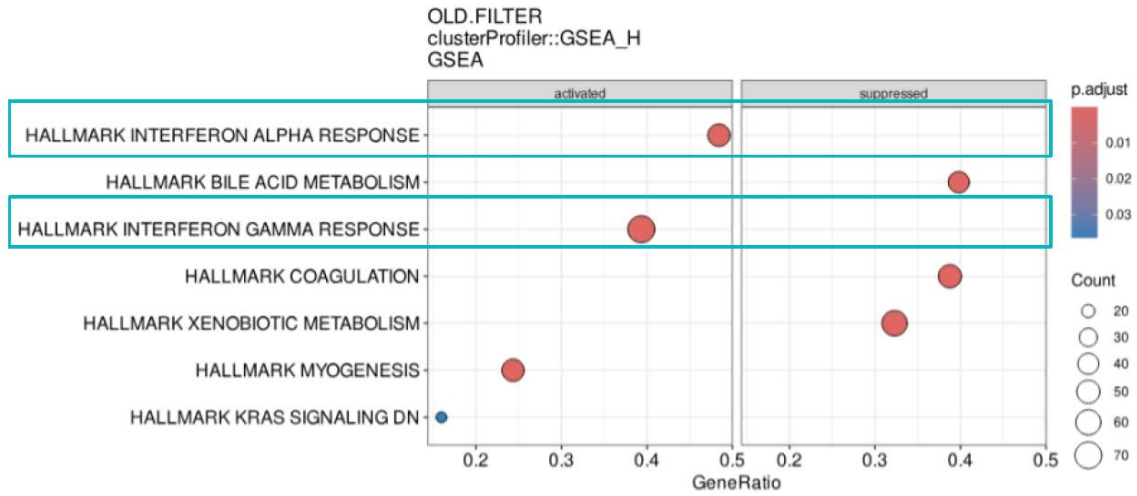
Gene expression modulation by HER3 DXd

- **22 pairs of baseline/on-treatment biopsies from <u>all analyzable samples</u>**
- Gene Set Enrichment Analysis (GSEA) using the Gene Sets “Hallmarks”*

Regardless of treatment response (n=22)



Responders (n=14)

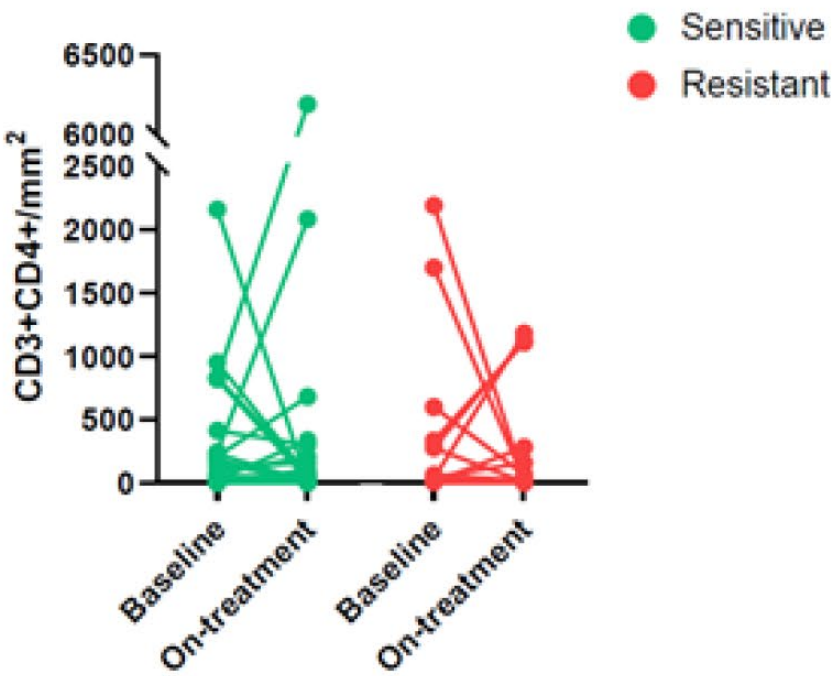


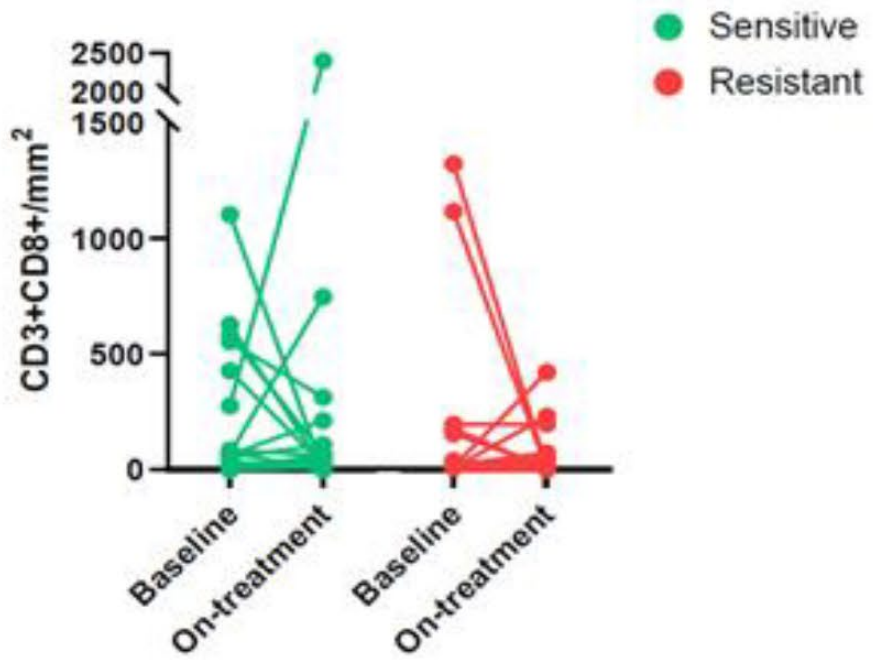
Up-regulation of pathways involved in immune response, interferon alpha and gamma and complement signaling, enriched in the whole cohort and in responders (*adj p-value ≤0.05*)

At baseline, 15 fresh biopsies not provided by centers, 28 were excluded due to < 200 ng RNA or < 30% tumor cell, 5 failed the quality control, 29 did not have the matched on-T sample. On-treatment (n=12 at C1D3, n=4 at C1D19, n=6 at C2D3), 22 fresh biopsies not provided by centers, 39 were excluded due to < 200 ng RNA or < 30% tumor cell, 1 sample failed the quality control, and 15 did not have the matched BL sample; ”P_Value_Adj” by Benjamini-Hochberg method

Immune modulation of TME

Imaging Mass Cytometry on tumor samples at baseline and on-treatment





IMC analysis on paired tumor samples at baseline and on-treatment showed a notable T-cell expansion and activation (increase of CD4+, CD8+, CD8+GzmB+ and CD8+CD107a+) at C1D3 in two patients who responded to the treatment

Conclusion and perspectives

- HER3-DXd showed clinically meaningful activity and manageable safety profile in patients with HR+/HER2- ABC progressing after 2 or more lines of therapy, including CDK4/6inh:
  ORR 53.5% [95%CI, 43.2; 63.6]; mDoR 8.7 [8.1; 12.5]; mPFS 9.4 mos [95%CI 8.1; 13.4]

- Activity of HER3-DXd was observed **across a range of tumor HER3 and HER2 membrane expression by IHC**

- Although with the limitations of the small sample size, exploratory biomarker analysis suggest that:
  -distribution of HER3-DXd in the tumor may play a role in determining a better treatment response
  -up-regulation of genes involved in immune response, particularly interferon alpha and gamma were significantly enriched in the entire cohort and among responders

- **Efficacy and safety profile of HER3-DXd make this ADC an optimal candidate for further larger trials in patients with HR+/HER2- ABC after failure of CDK4/6 inhibitors**

Preliminary results from a Phase 1, first-in-human study of DS-9606, a Claudin 6 (CLDN6)-directed antibody–drug conjugate, in patients with tumor types known to express CLDN6

Manish R. Patel,[1,2] Erika Hamilton,[2] Sarina A. Piha-Paul,[3] Jason Henry,[4] Udai Banerji,[5] Mohammed Najeeb Al Hallak,[6] Hiroyuki Okada,[7] Meng Qian,[7] Xinyuan Zhang,[7] Nabil Said,[7] Valery Chatikhine,[7] Elisa Fontana[8]

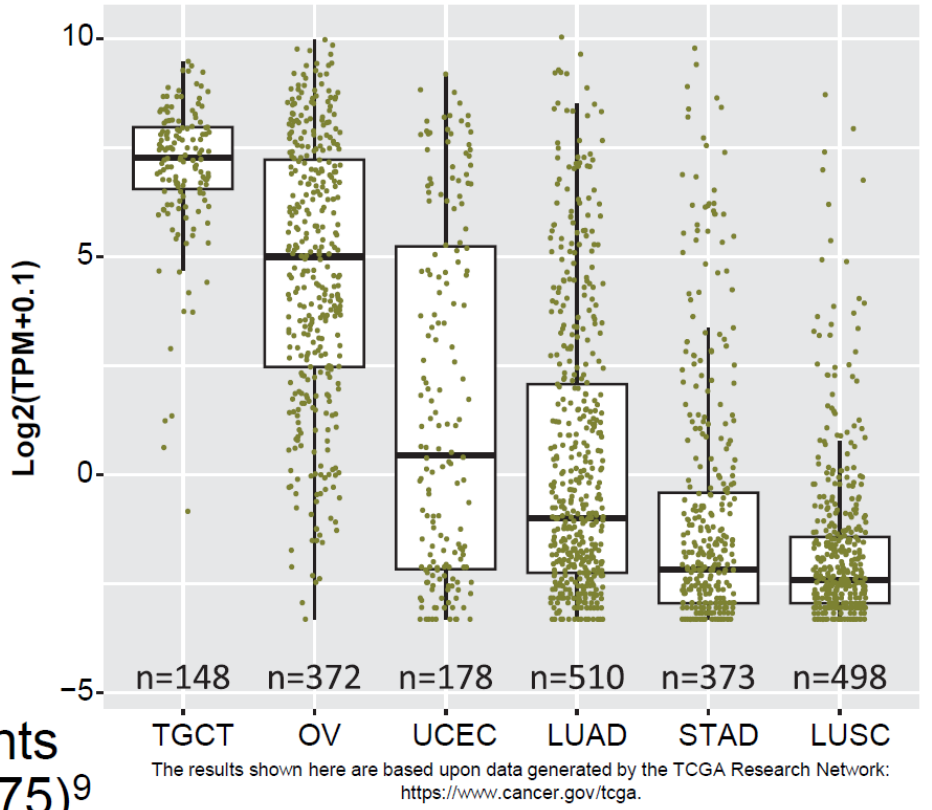
[1]Florida Cancer Specialists, Sarasota, FL, USA; [2]Sarah Cannon Research Institute, Nashville, TN, USA; [3]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [4]Sarah Cannon Research Institute, Denver, CO, USA; [5]Institute of Cancer Research and the Royal Marsden Hospital, London, UK; [6]Karmanos Cancer Institute, Detroit, MI, USA; [7]Daiichi Sankyo Inc., Basking Ridge, NJ, USA; [8]Sarah Cannon Research Institute, London, UK.

ESMO 2024 610O (Oral)

Background

- **DS-9606 is an ADC composed of[1]:**
  - Humanized anti-CLDN6 mAb
  - Cleavable linker
  - Modified PBD payload
- **CLDN6**
  - Important component of cell-to-cell tight junctions[2]
  - Plays a role in the regulation of epithelial and endothelial cell proliferation and differentiation[2]
  - Nearly absent in normal adult tissue but expressed in several tumor types, including ovarian, endometrial, and gastric cancers, GCTs, and NSCLC[3–8]
  - Can be associated with poor prognosis[7]
- First report from an ongoing Phase 1 trial of DS-9606 in patients with locally advanced or metastatic solid tumors (NCT05394675)[9]

CLDN6 expression in select solid tumors



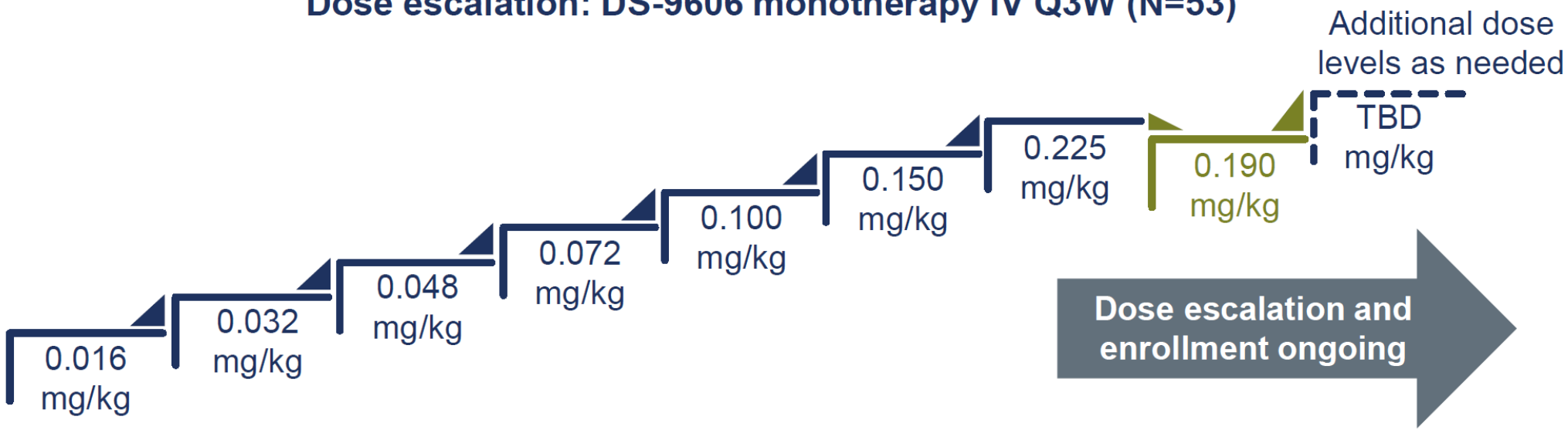
ADC, antibody–drug conjugate; CLDN6, Claudin 6; GCT, germ cell tumor; LUAD, lung adenocarcinoma; LUSC, lung squamous cell carcinoma; mAb, monoclonal antibody; NSCLC, non-small cell lung cancer; OV, ovarian serous cystadenocarcoma; PBD, pyrrolobenzodiazepine; STAD, stomach adenocarcinoma; TCGA, The Cancer Genome Atlas; TGCT, testicular GCT; TPM, transcripts per million; UCEC, uterine corpus endometrial carcinoma.

1. Data on file. Daiichi Sankyo, Inc. DS9606-137 protocol, version 6; 2023. 2. Du H, et al. *Mol Med Rep*. 2021;24:677. 3. Wang L, et al. *Diagn Pathol*. 2013;8:190. 4. Ushiku T, et al. *Histopathology*. 2012;61:1043–1056. 5. Kojima M, et al. *Cancers (Basel)*. 2020;12:2748. 6. Micke P, et al. *Int J Cancer*. 2014;135:2206–2214. 7. Zhang C, et al. *Front Cell Dev Biol*. 2021;9:726656. 8. Yu S, et al. *Cell Death Dis*. 2019;10:949. 9. ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT05394675. Accessed August 15, 2024.

First-in-human Phase 1 study of DS-9606[1,2]

Preliminary safety and efficacy analysis of dose-escalation

Dose escalation: DS-9606 monotherapy IV Q3W (N=53)



Key enrollment criteria:

- Adults with locally advanced or metastatic solid tumors known to express CLDN6 (CLDN6 expression was not required for selection[a])
- PD with SOC treatment for metastatic disease (any number of prior LOTs)
- ECOG PS 0–1
- No prior CLDN6-targeted agents or ADCs that deliver a PBD payload
- Adequate cardiac and pulmonary function, including no history of or current ILD/pneumonitis

Data cutoff: June 14, 2024

[a]Archived tumor tissue, or fresh tumor biopsy if archived tissue was not available, was tested retrospectively; patients with GCTs without archived tumor tissue may be allowed with medical monitor approval.

ADC, antibody–drug conjugate; CLDN6, Claudin 6; ECOG PS, Eastern Cooperative Oncology Group performance status; GCT, germ cell tumor; ILD, interstitial lung disease; IV, intravenous; LOT, line of therapy; PBD, pyrrolobenzodiazepine; PD, progressive disease; Q3W, every 3 weeks; SOC, standard-of-care; TBD, to be determined.

1. ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT05394675. Accessed August 15, 2024. 2. Data on file. Daiichi Sankyo, Inc. DS9606-137 protocol, version 6; 2023.

Baseline characteristics and disposition

Patients were heavily pretreated, and baseline characteristics were balanced across dose groups

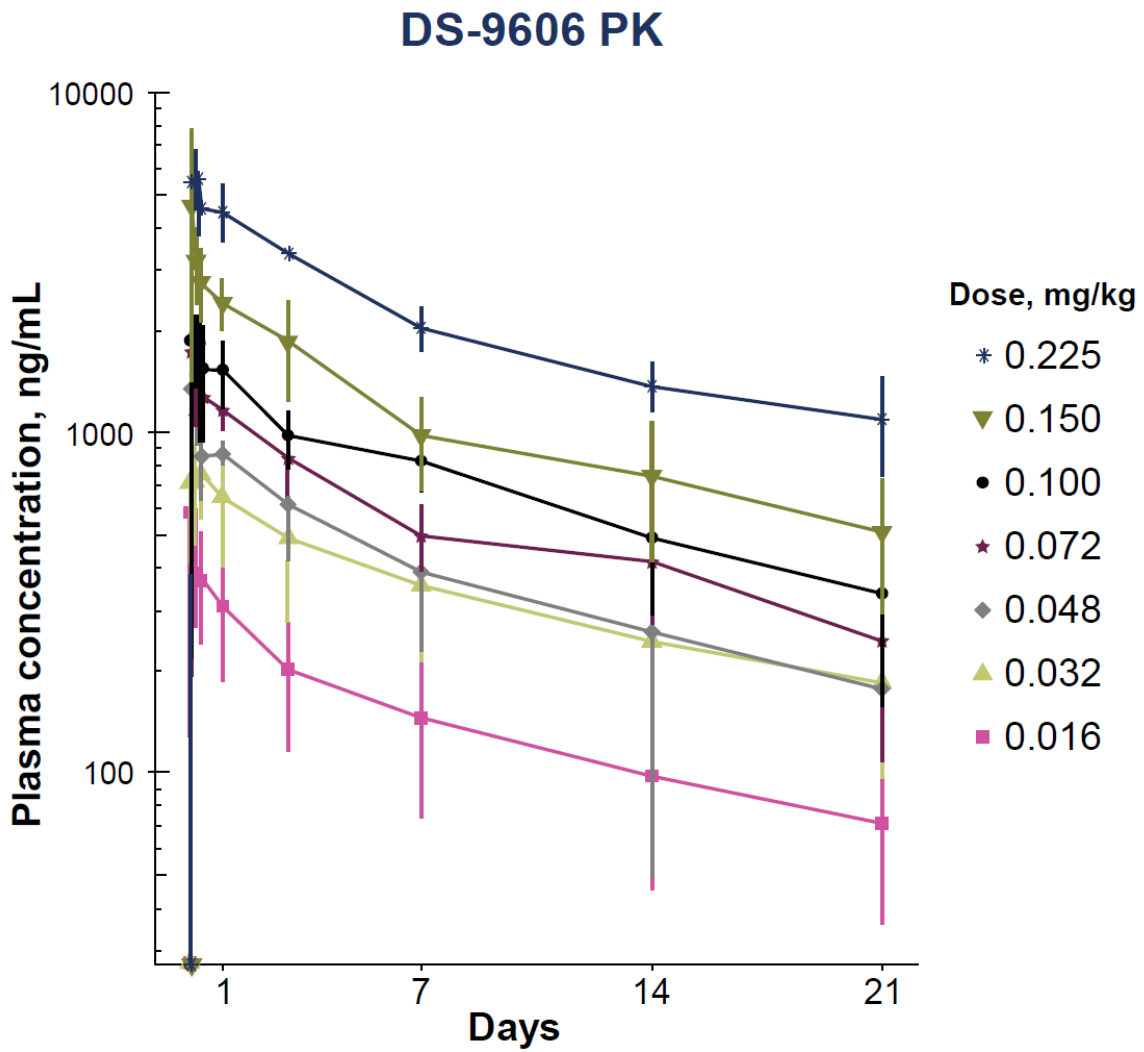
DS-9606 dose, mg/kg	0.016 (n=3)	0.032 (n=7)	0.048 (n=7)	0.072 (n=6)	0.100 (n=7)	0.150 (n=14)	0.190 (n=3)	0.225 (n=6)	Total (N=53)
Age, median (range), years	67 (52–72)	52 (24–72)	63 (51–68)	48 (29–68)	63 (55–75)	58 (31–84)	65 (37–75)	54 (32–66)	58 (24–84)
Sex, n (%)									
Male	1 (33.3)	3 (42.9)	1 (14.3)	3 (50.0)	1 (14.3)	10 (71.4)	2 (66.7)	3 (50.0)	24 (45.3)
Female	2 (66.7)	4 (57.1)	6 (85.7)	3 (50.0)	6 (85.7)	4 (28.6)	1 (33.3)	3 (50.0)	29 (54.7)
ECOG PS, n (%)									
0	1 (33.3)	2 (28.6)	3 (42.9)	0	1 (14.3)	5 (35.7)	0	1 (16.7)	13 (24.5)
1	2 (66.7)	5 (71.4)	4 (57.1)	6 (100.0)	6 (85.7)	9 (64.3)	3 (100.0)	5 (83.3)	40 (75.5)
Primary diagnosis, n (%)									
Ovarian cancer[a]	1 (33.3)	2 (28.6)	5 (71.4)	2 (33.3)	5 (71.4)	2 (14.3)	0	2 (33.3)	19 (35.8)
GCT[b]	0	2 (28.6)	0	3 (50.0)	0	4 (28.6)	1 (33.3)	1 (16.7)	11 (20.8)
G/GEJ/E-AC[c]	0	0	0	0	1 (14.3)	3 (21.4)	0	3 (50.0)	7 (13.2)
NSCLC	0	0	0	0	0	5 (35.7)	2 (66.7)	0	7 (13.2)
Pancreatic cancer	1 (33.3)	2 (28.6)	2 (28.6)	0	0	0	0	0	5 (9.4)
Breast cancer	0	1 (14.3)	0	0	1 (14.3)	0	0	0	2 (3.8)
Endometrial cancer	1 (33.3)	0	0	1 (16.7)	0	0	0	0	2 (3.8)
No. prior LOT, median (range)	3.0 (3–3)	3.0 (2–8)	4.0 (1–8)	3.5 (1–8)	6.0 (3–9)	4.0 (1–9)[d]	3.0 (2–5)	5.5 (2–8)	4.0 (1–9)
Ongoing in study, n (%)	0	1 (14.3)	1 (14.3)	1 (16.7)	0	10 (71.4)	3 (100.0)	5 (83.3)	21 (39.6)

Data cutoff: June 14, 2024

[a]Includes ovarian cancer (n=18) and fallopian tube cancer (n=1). [b]Includes anterior mediastinal tumor (n=1), mediastinal GCT (n=1), embryonal cell carcinoma of the right testis (n=1), and testicular cancer (n=8). [c]Includes gastric cancer (n=1), stomach cancer (n=1), gastrointestinal carcinoid tumor (n=1), gastroesophageal junction cancer (n=2), and esophageal cancer (n=2). [d]Information on prior systemic anticancer therapy missing for one patient.

ECOG PS, Eastern Cooperative Oncology Group performance status; G/GEJ/E-AC, gastric/gastroesophageal junction/esophageal adenocarcinoma; GCT, germ cell tumor; LOT, line of therapy; NSCLC, non-small cell lung cancer.

Pharmacokinetics



- Intact ADC (DS-9606) exposures increased in an approximately dose-proportional manner across 0.016–0.225 mg/kg doses[a]
- Unconjugated payload undetectable[b]
- Intact DS-9606 elimination half-life approximately 12–16 days, supporting Q3W dosing

Data cutoff: June 14, 2024

[a]No PK data were available for the 0.190 mg/kg dose. [b]Below the lower limit of quantification of PK assay (10 pg/mL); only 1 PK sample in the study had detectable payload exposures.

ADC, antibody–drug conjugate; PK, pharmacokinetics; Q3W, every 3 weeks.

Safety: Overview of TEAEs and related TEAEs

- 45 patients (84.9%) had TEAEs; 28 patients (52.8%) had related TEAEs
- No treatment withdrawals due to related TEAEs; related TESAEs occurred at the highest dose level
- No DLTs to date; MTD and RDE not yet determined

DS-9606 dose, mg/kg	0.016 (n=3)	0.032 (n=7)	0.048 (n=7)	0.072 (n=6)	0.100 (n=7)	0.150 (n=14)	0.190 (n=3)	0.225 (n=6)	Total (N=53)
TEAEs, n with event (%)									
Any grade	3 (100.0)	6 (85.7)	7 (100)[a]	6 (100)	5 (71.4)	13 (92.9)	1 (33.3)	4 (66.7)	45 (84.9)
Related	0	5 (71.4)	5 (71.4)[a]	4 (66.7)	2 (28.6)	8 (57.1)	0	4 (66.7)	28 (52.8)
Grade ≥3	1 (33.3)	2 (28.6)	3 (42.9)	2 (33.3)	2 (28.6)	4 (28.6)	0	2 (33.3)	16 (30.2)
Related	0	1 (14.3)	1 (14.3)	0	0	0	0	1 (16.7)	3 (5.7)
Serious[b]	1 (33.3)	1 (14.3)	3 (42.9)	2 (33.3)	2 (28.6)	4 (28.6)	0	3 (50.0)	16 (30.2)
Related	0	0	0	0	0	0	0	2 (33.3)	2 (3.8)
Associated with:									
Treatment interruption	0	2 (28.6)[c]	2 (28.6)	2 (33.3)	0	2 (14.3)	0	1 (16.7)	9 (17.0)
Related	0	0	0	0	0	0	0	1 (16.7)	1 (1.9)
Dose reduction	0	0	1 (14.3)[a]	0	0	1 (7.1)	0	1 (16.7)	3 (5.7)
Related	0	0	1 (14.3)[a]	0	0	1 (7.1)	0	1 (16.7)	3 (5.7)
Treatment withdrawal	0	0	0	0	0	1 (7.1)	0	0	1 (1.9)
Related	0	0	0	0	0	0	0	0	0
Death	0	0	0	0	0	0	0	0	0

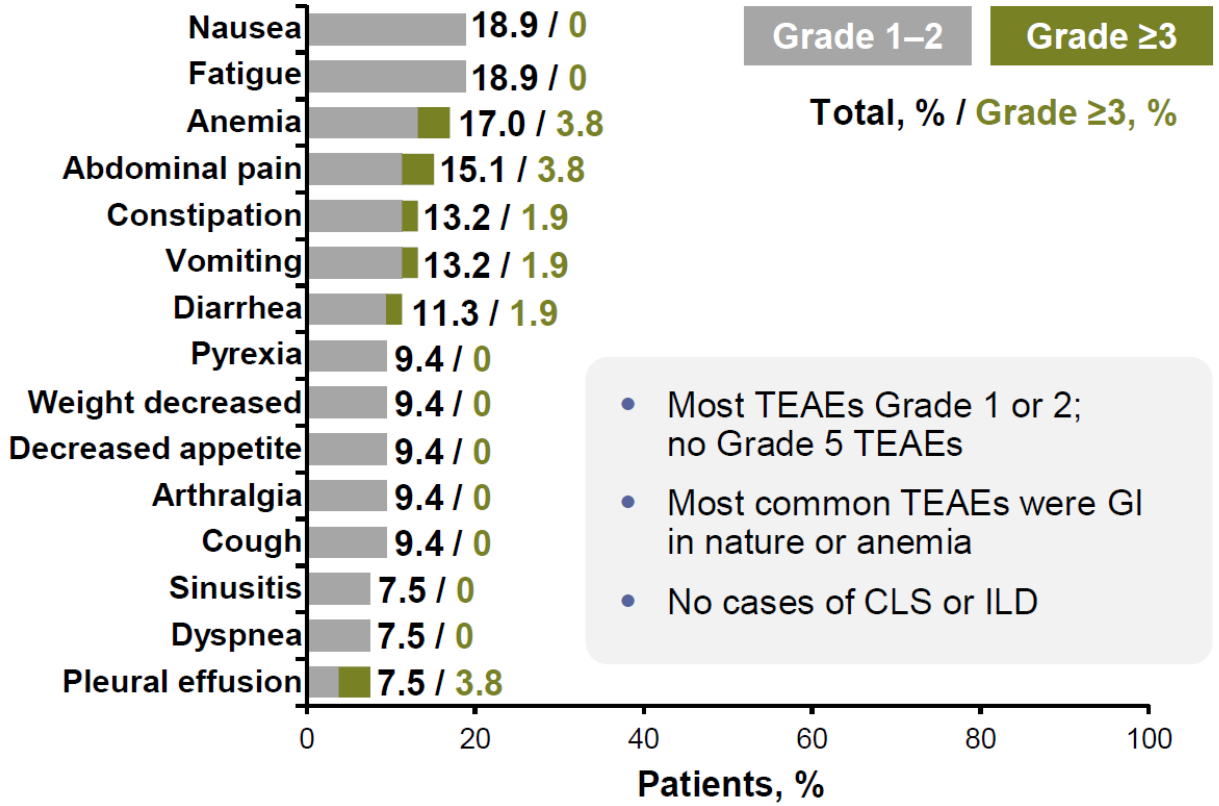
Data cutoff: June 14, 2024

[a]One intra-patient dose escalation (IPDE), with the patient receiving DS-9606 0.048 mg/kg from Cycle 1–10, 0.100 mg/kg from Cycle 11–14, and then 0.048 mg/kg from Cycle 15 through end of treatment. Dose reduction occurred at 0.100 mg/kg. Per the protocol, IPDE was allowed if the investigator determined IPDE was favorable from a benefit–risk standpoint; the patient had completed at least 6 cycles of treatment at the current dose level; no Grade ≥3 related TEAEs or any AE leading to dose reduction were observed at the current dose level; the totality of the patient's available data had been reviewed by the medical monitor; and the sponsor had granted approval. [b]Per the protocol, AEs were considered serious if they resulted in any of death, a life-threatening AE, inpatient hospitalization of ≥24 hours or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, a congenital anomaly/birth defect, or an important medical event. [c]Includes 1 IPDE, with the patient receiving DS-9606 0.032 mg/kg from Cycle 1–23, 0.048 mg/kg from Cycle 24–25, and 0.032 mg/kg from Cycle 26 through end of treatment. AE, adverse event; DLT, dose-limiting toxicity; IPDE, intra-patient dose escalation; MTD, maximum tolerated dose; RDE, recommended dose for expansion; TEAE, treatment-emergent adverse event; TESAE, treatment-emergent serious adverse event.

Safety: Most common TEAEs and related TEAEs[a]

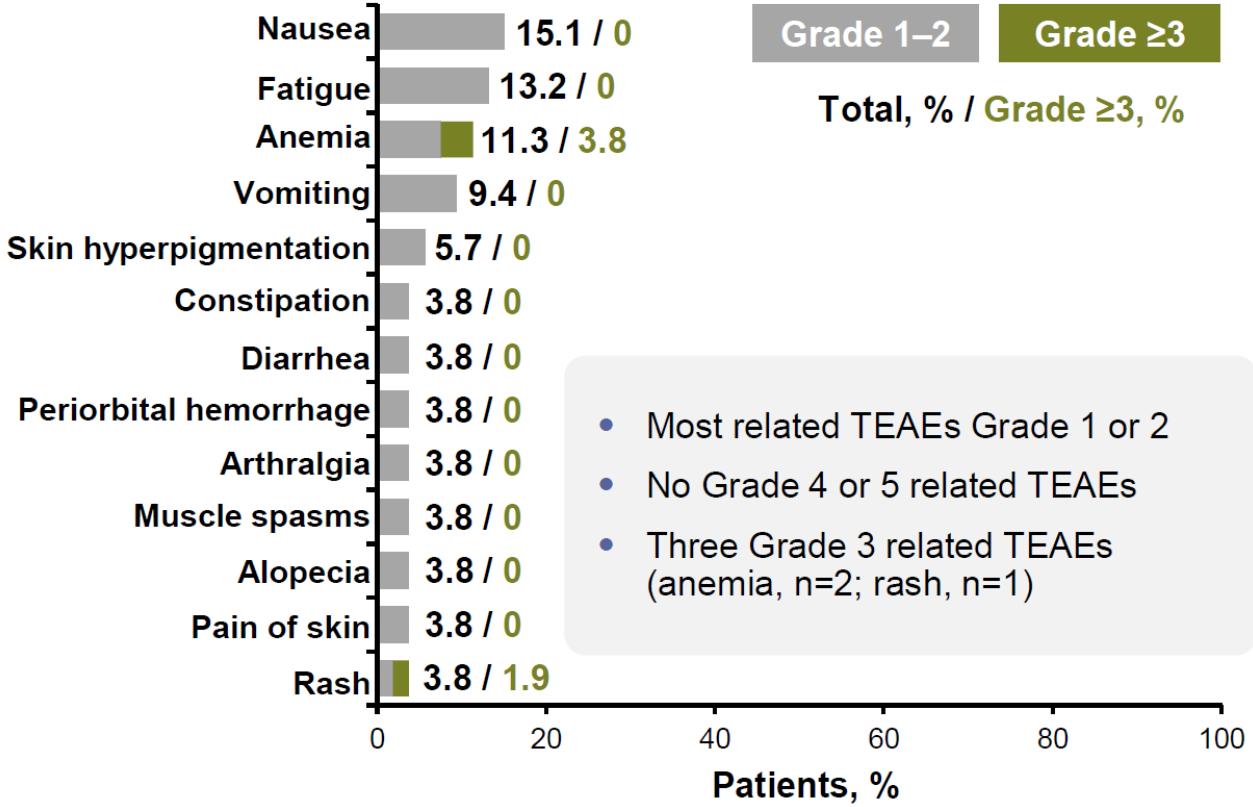
DS-9606 safety was manageable and tolerable

Any-grade TEAEs (≥7.5% of patients)[b]



- Most TEAEs Grade 1 or 2; no Grade 5 TEAEs
- Most common TEAEs were GI in nature or anemia
- No cases of CLS or ILD

Any-grade related TEAEs (≥3.8% of patients)



- Most related TEAEs Grade 1 or 2
- No Grade 4 or 5 related TEAEs
- Three Grade 3 related TEAEs (anemia, n=2; rash, n=1)

- When grouped, events of cutaneous toxicity (AESI) were the most common TEAEs and related TEAEs

Data cutoff: June 14, 2024

[a]Overall population (N=53). TEAEs occurring at any grade in ≥7.5% of patients and Grade ≥3 TEAEs occurring for those preferred terms. Related TEAEs occurring at any grade in ≥3.8% of patients and Grade ≥3 related TEAEs occurring for those preferred terms. [b]Five TEAEs in 4 patients were not coded at the data cutoff (all Grade 1 or 2).

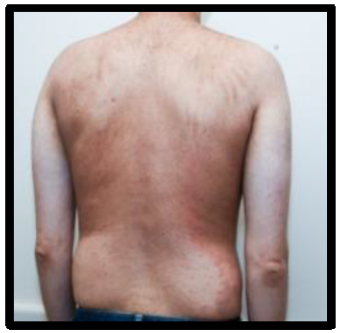
AESI, adverse event of special interest; CLS, capillary leak syndrome; GI, gastrointestinal; ILD, interstitial lung disease; TEAE, treatment-emergent adverse event.

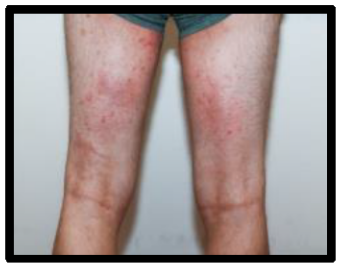
Safety: Cutaneous toxicity (AESI)

- All cutaneous toxicity TEAEs were Grade 1, except for:
  - One patient[a] with Grade 2 skin hyperpigmentation (0.100 mg/kg, resulted in dose reduction)
  - One patient with Grade 3 rash (0.225 mg/kg, improved to Grade 1 with dose modification)

DS-9606 dose, mg/kg	0.016 (n=3)	0.032 (n=7)	0.048 (n=7)	0.072 (n=6)	0.100 (n=7)	0.150 (n=14)	0.190 (n=3)	0.225 (n=6)	Total (N=53)
Treatment-emergent cutaneous toxicity, n with event (%)									
Any	**0**	**0**	**1 (14.3)[a]**	**0**	**1 (14.3)**	**5 (35.7)**	**0**	**2 (33.3)**	**9 (17.0)**
Skin hyperpigmentation	0	0	1 (14.3)[a]	0	0	2 (14.3)	0	0	3 (5.7)
Pain of skin	0	0	1 (14.3)[a]	0	0	1 (7.1)	0	0	2 (3.8)
Periorbital hemorrhage	0	0	0	0	1 (14.3)	1 (7.1)	0	0	2 (3.8)
Rash	0	0	0	0	1 (14.3)	0	0	1 (16.7)	2 (3.8)
Maculo-papular rash	0	0	0	0	0	1 (7.1)	0	0	1 (1.9)
Papular rash	0	0	0	0	0	1 (7.1)	0	0	1 (1.9)
Seborrheic dermatitis	0	0	0	0	0	1 (7.1)	0	0	1 (1.9)
Skin discoloration	0	0	0	0	0	0	0	1 (16.7)	1 (1.9)

Example of skin rash



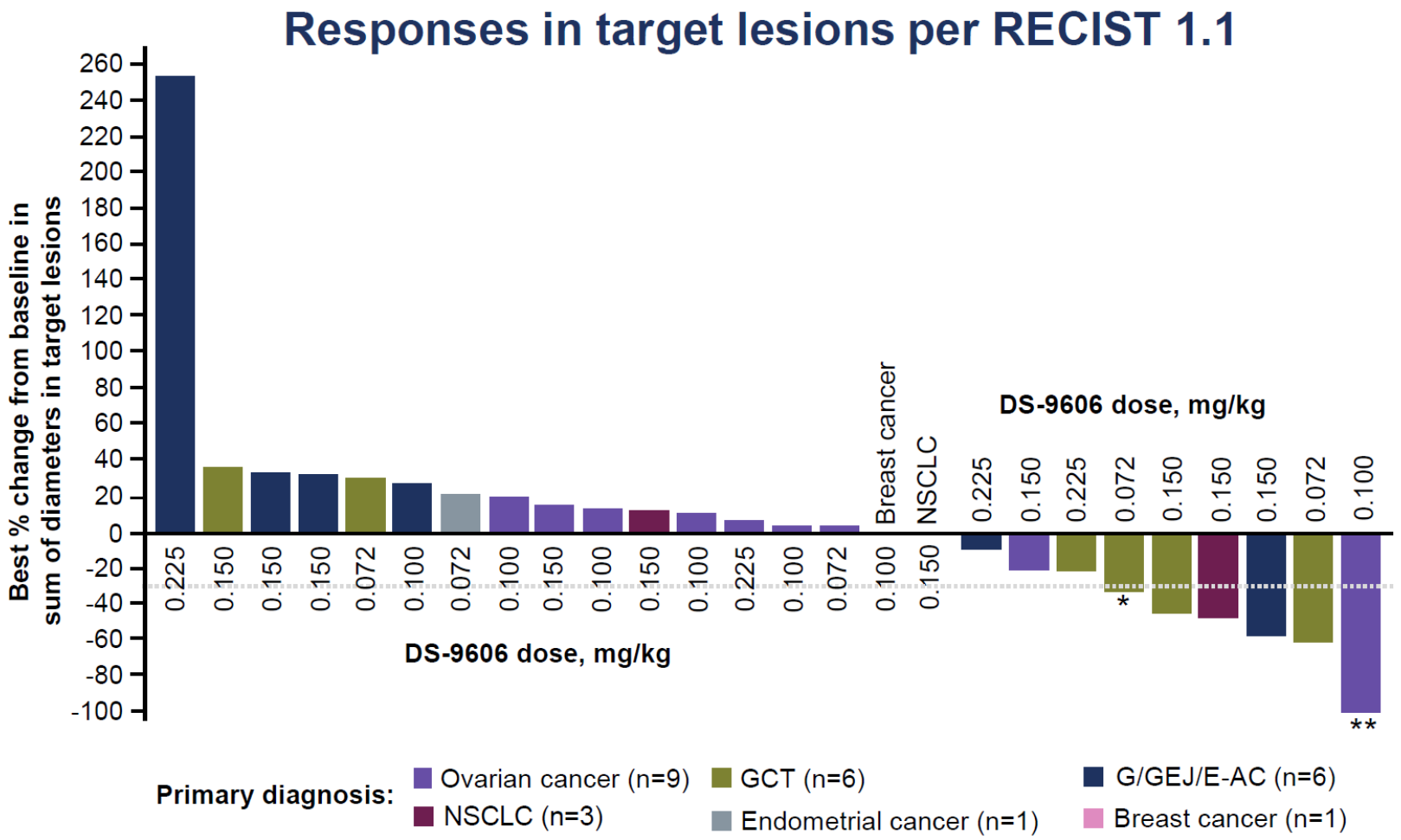


Data cutoff: June 14, 2024

[a]Includes 1 IPDE, with the patient receiving DS-9606 0.048 mg/kg from Cycle 1–10, 0.100 mg/kg from Cycle 11–14, and 0.048 mg/kg from Cycle 15 through end of treatment. Dose reduction occurred at 0.100 mg/kg.

AESI, adverse event of special interest; IPDE, intra-patient dose escalation; TEAE, treatment-emergent adverse event.

Preliminary efficacy[a]: All tumor types



- Confirmed objective responses seen across tumor types (RECIST 1.1)
  - GCT, n=2
  - G/GEJ/E-AC, n=1
  - NSCLC, n=1
  - Response highest with 0.150 mg/kg (3/12[b] patients)

Data cutoff: June 14, 2024

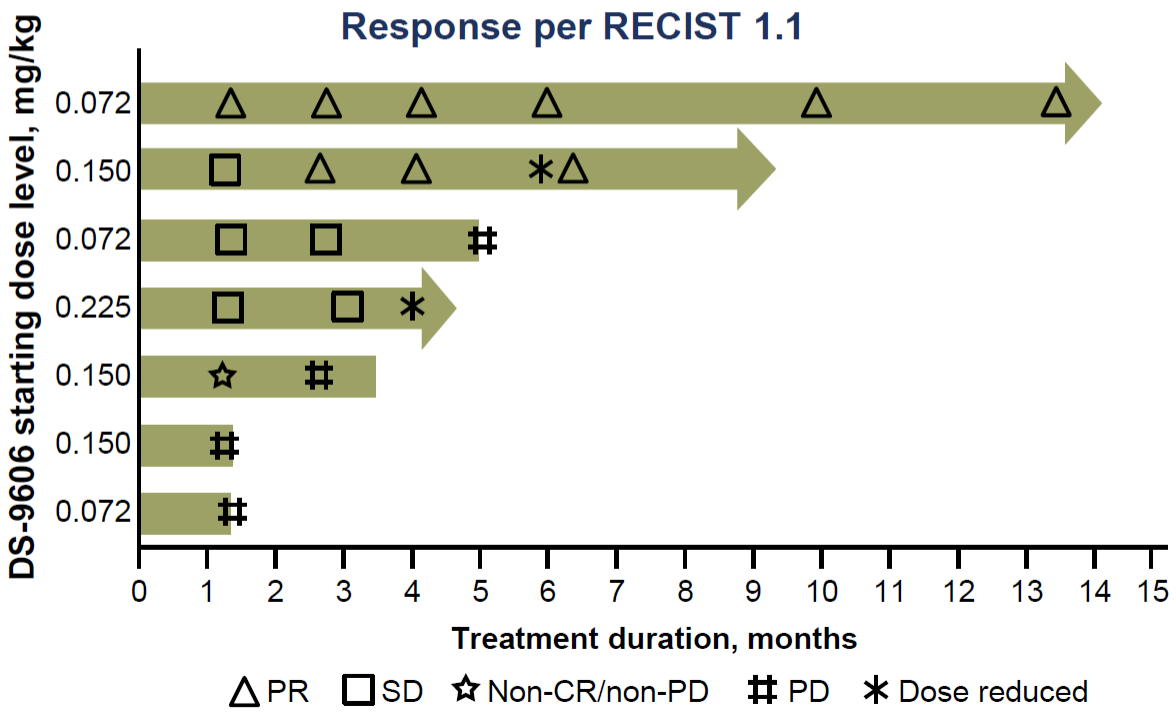
[a]DS-9606 doses ≥0.072 mg/kg, except 0.190 mg/kg due to immature data. [b]Includes only 12 of 14 patients; patients were included if they had ≥2 post-baseline scans and/or had discontinued treatment for any reason.
*Patient did not have confirmed PR due to new lesion observed at disease assessment. **Patient did not have a confirmed PR due to progression at subsequent assessment.

GCT, germ cell tumor; G/GEJ/E-AC, gastric/gastroesophageal junction/esophageal adenocarcinoma; NSCLC, non-small cell lung cancer; PR, partial response; RECIST 1.1, Response Evaluation Criteria in Solid Tumours, version 1.1.

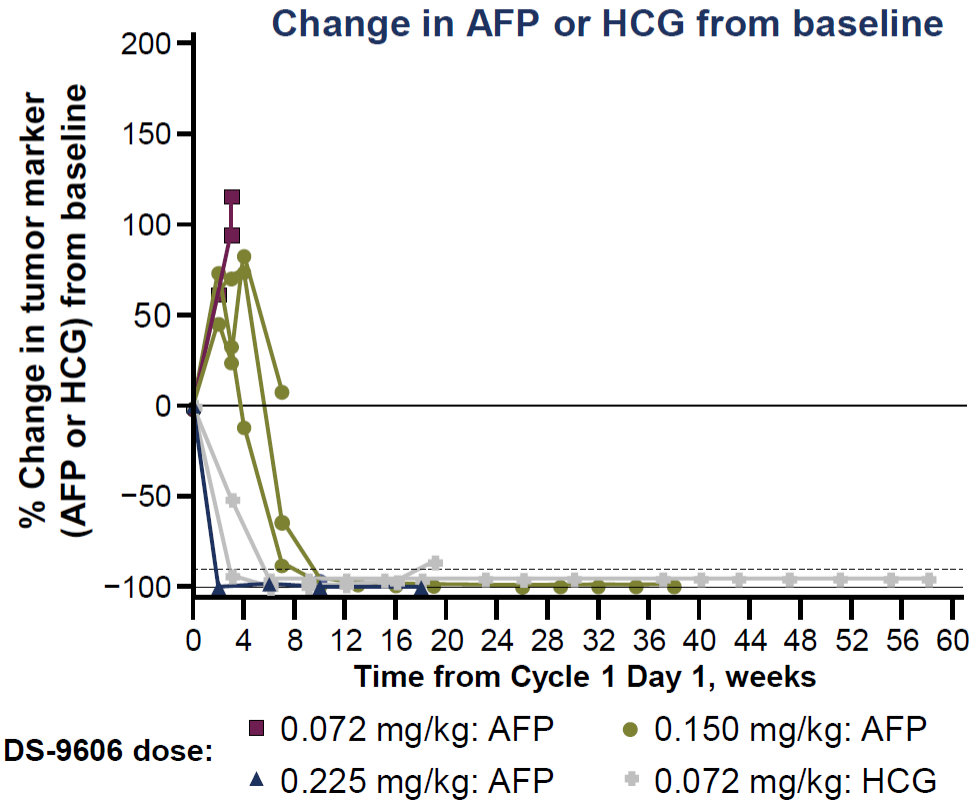
Preliminary efficacy[a]: GCT responses

Responses in patients with GCTs who were heavily pretreated/refractory to prior treatment

- 2/7 patients had PR as best response (RECIST 1.1) and remained on treatment >6 months



- 5/7 patients had ≥90% reduction in tumor markers



Data cutoff: June 14, 2024

[a]DS-9606 doses ≥0.072 mg/kg, excluding 0.190 mg/kg due to lack of efficacy data availability.

AFP, alpha-fetoprotein; CR, complete response, GCT, germ cell tumor; HCG, human chorionic gonadotropin; PD, progressive disease; PR, partial response; SD, stable disease.

Conclusions

- In this heavily pretreated population, interim data with DS-9606 show:
  - **Manageable and tolerable safety profile**
    - No DLTs or discontinuations due to related TEAEs. Most TEAEs and related TEAEs were Grade 1 or 2
    - No cases of CLS or ILD, and mostly low-grade cutaneous toxicity
  - **Promising preliminary efficacy,** with responses across tumor types
    - Encouraging efficacy in GCTs based on several tumor markers
- Enrollment and dose escalation are ongoing with MTD and RDE not yet determined

Data cutoff: June 14, 2024

CLS, capillary leak syndrome; DLT, dose-limiting toxicity; GCT, germ cell tumor; ILD, interstitial lung disease; MTD, maximum tolerated dose; RDE, recommended dose for expansion; TEAE, treatment-emergent adverse event.