2025 ASCO ANNUAL MEETING

DB-1310, a HER3-targeted ADC, in patients with advanced solid tumors: Preliminary results from the Phase 1/2a trial

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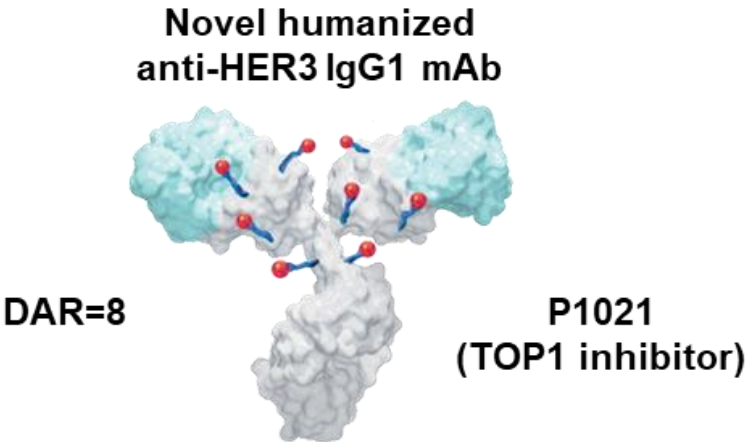
Key Takeaway Points/Conclusions

DB-1310, a novel HER3 ADC, is well-tolerated and demonstrates encouraging efficacy in advanced solid tumors (NCT05785741)

- **DB-1310 showed encouraging antitumor activity, particularly in patients with EGFR-mutant NSCLC**
  - All Solid Tumors (n=123): uORR 31%, DCR 84%, mPFS 5.5mo, mOS 14.5mo
  - EGFR-mutant NSCLC (n=46): uORR 44%, DCR 91%, mPFS 7.0mo, mOS 18.9mo
    - uORR 37.5% at 5 mg/kg (n=16), 66.7% at 5.5 mg/kg (n=12)
- **DB-1310 was well-tolerated with a manageable safety profile**
  - Predominantly Grade 1-2 Heme/GI treatment-related toxicities
  - Low (3.5%) treatment-related discontinuation rate
- **DB-1310 global development ongoing in NSCLC and beyond**



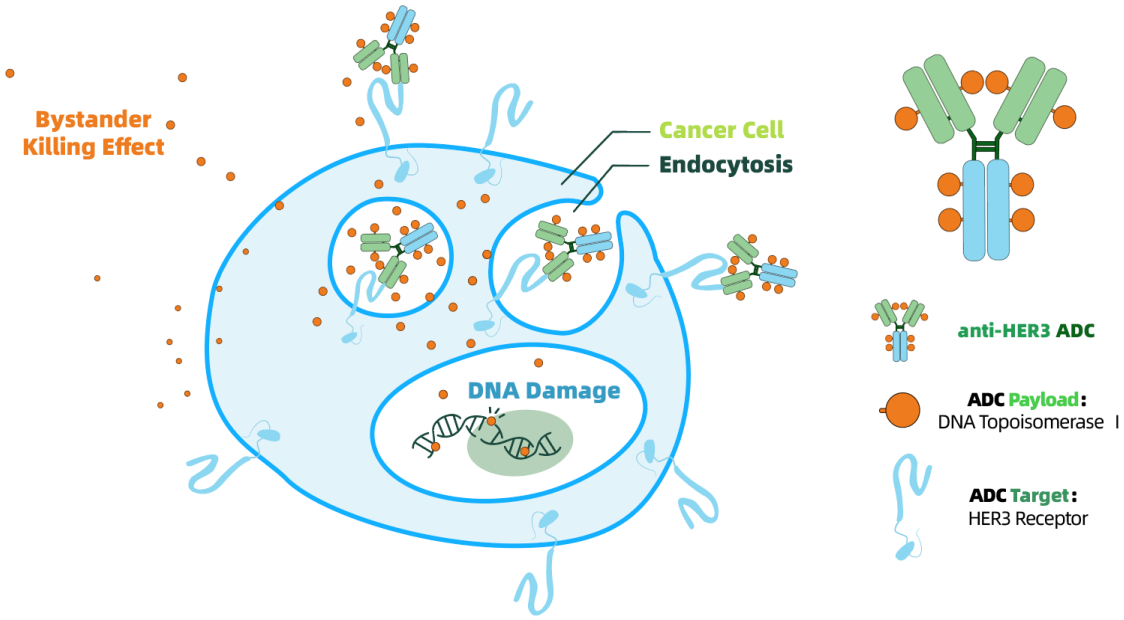
- **Binds a novel epitope on Domain I of HER3→ Blocking HER2/HER3 & NRG/HER3 interaction**
- **High internalization capability**
- **Synergy when combined with HER2 therapy and EGFR TKIs**

Background: DB-1310, a novel HER3 ADC

HER3 is overexpressed in many solid tumors and correlates with poor prognosis: [1]

- Advanced disease
- Inferior survival
- Resistance to standard therapies

HER3 represents a validated pan-tumor target, with HER3-directed therapies demonstrating clinical activity in a variety of solid tumors. [2-4]



DB-1310 is an investigational, next-generation HER3-targeting ADC with a proprietary topoisomerase-I-inhibitor payload (P1021). [5-6]

Preclinical studies showed potent antitumor activity and a favorable PK profile, as well as synergy when combined with EGFR TKIs and HER2 targeted therapies.[5-6]

ADC, antibody–drug conjugate; HER3, human epidermal growth factor receptor 3; EGFR, epidermal growth factor receptor.

1. Heidi M. Haikala, et al. Clin Cancer Res. 2021; 27(13): 3528-3539; 2. Ian E. Krop et al. JCO 41, 5550-5560(2023); 3. Helena A. Yu et al. JCO 41, 5363-5375(2023); 4. Ying C, et al. ASCO2024, Poster179; 5. Xi L, et al. AACR 2023, Poster 2967; 6. Aaron Lisberg, et al. AACR2024, Poster CT168.

DB-1310-O-1001 Study design (NCT05785741)

Phase 1/2, multicenter, first-in-human study of DB-1310 in patients with advanced/metastatic solid tumors unselected for HER3 expression

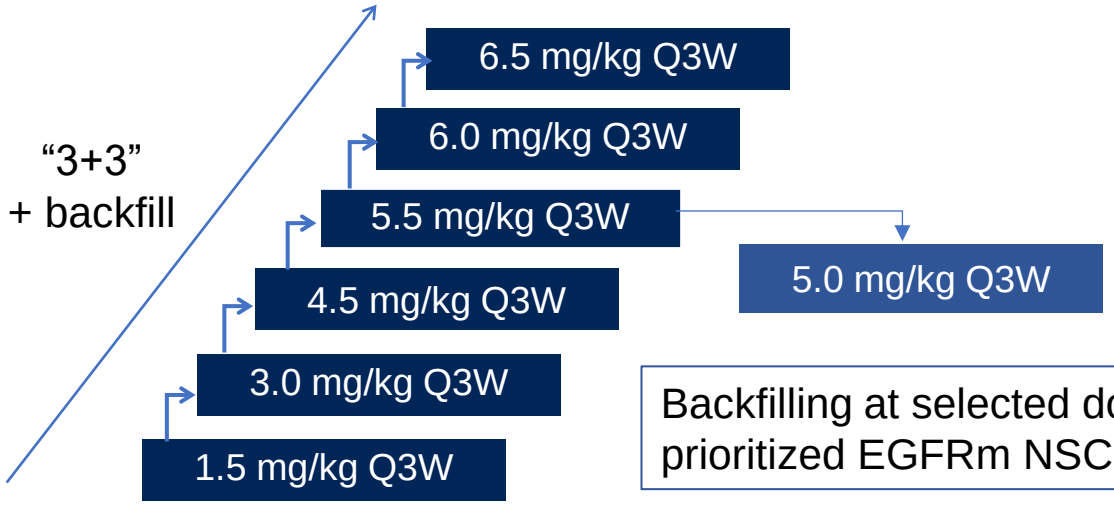
Key Inclusion Criteria:

- ≥18 years of age
- Advanced or metastatic solid tumor that progressed on/after standard systemic treatments
- ≥1 measurable lesion per RECIST v1.1
- ECOG PS 0–1
- Adequate organ function
- Treated and asymptomatic brain metastases are allowed

Key Exclusion Criteria:

- Prior treatment with HER3 targeted therapy
- Prior treatment with TOP1 ADC

Phase 1: Dose escalation



Backfilling at selected doses prioritized EGFRm NSCLC

- **Primary endpoint:** DLT/MTD, safety.
- **Secondary endpoints:** ORR, DCR, DOR, PFS, OS, PK, and ADA

Herein, we present the first clinical data for DB-1310 monotherapy

ADA, anti-drug antibody; ADC, antibody–drug conjugate; DLT, dose-limiting toxicity; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; HER3, human epidermal growth factor receptor 3; IV, intravenous; MTD, maximum tolerable dose; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetics; Q3W, once every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; TOP1, topoisomerase 1.

Overall baseline characteristics

172 patients treated [China (n=103), USA (n=69)], 81 (47.1%) remain on treatment.

62.8% (108/172) of patients had NSCLC, 5.8% (10/172) had HR+/HER2- BC, and 5.8% (10/172) had CRPC.

14.0% (24/172) had brain metastases.

		Overall (N=172)*	1.5 mg/kg (n=3)	3 mg/kg (n=10)	4.5 mg/kg (n=25)	5 mg/kg (n=53)	5.5 mg/kg (n=74)	6 mg/kg (n=4)	6.5 mg/kg (n=3)
Age, years	Median (range)	61.0 (29, 81)	68.0 (59, 70)	59.0 (40, 79)	58.0 (32, 79)	64.0 (42, 81)	58.0 (29, 77)	56.5 (43, 69)	60.0 (55, 75)
Sex, n(%)	Male	87 (50.6%)	1 (33.3%)	1 (10.0%)	12 (48.0%)	29 (54.7%)	41 (55.4%)	2 (50.0%)	1 (33.3%)
	Female	85 (49.4%)	2 (66.7%)	9 (90.0%)	13 (52.0%)	24 (45.3%)	33 (44.6%)	2 (50.0%)	2 (66.7%)
Race,* n(%)	Asian	112 (65.1%)	0 (0.0%)	5 (50.0%)	11 (44.0%)	25 (47.2%)	65 (87.8%)	3 (75.0%)	3 (100.0%)
	White	50 (29.1%)	2 (66.7%)	4 (40.0%)	13 (52.0%)	23 (43.4%)	7 (9.5%)	1 (25.0%)	0 (0.0%)
	Black	7 (4.1%)	1 (33.3%)	0 (0.0%)	0 (0.0%)	4 (7.5%)	2 (2.7%)	0 (0.0%)	0 (0.0%)
ECOG PS, n(%)	0	30 (17.4%)	0 (0.0%)	2 (20.0%)	11 (44.0%)	7 (13.2%)	8 (10.8%)	2 (50.0%)	0 (0.0%)
	1	142 (82.6%)	3 (100.0%)	8 (80.0%)	14 (56.0%)	46 (86.8%)	66 (89.2%)	2 (50.0%)	3 (100.0%)
Prior lines, n	Median (range)	3.0 (1, 11)	5.0 (3, 5)	2.5 (2, 7)	2.0 (1, 9)	3.0 (1, 11)	3.0 (1, 9)	2.0 (1, 3)	1.5 (1, 2)

CRPC, castration-resistant prostate cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; HR+/HER2- BC, hormone receptor positive/human epidermal growth factor receptor 2 negative breast cancer; NSCLC, non-small cell lung cancer; USA, United States of America.

*all patients who had received at least one dose of DB-1310.

Overall safety profile of DB-1310

Manageable safety profile (MTD has not been established yet).
No TRAEs leading to death were reported.

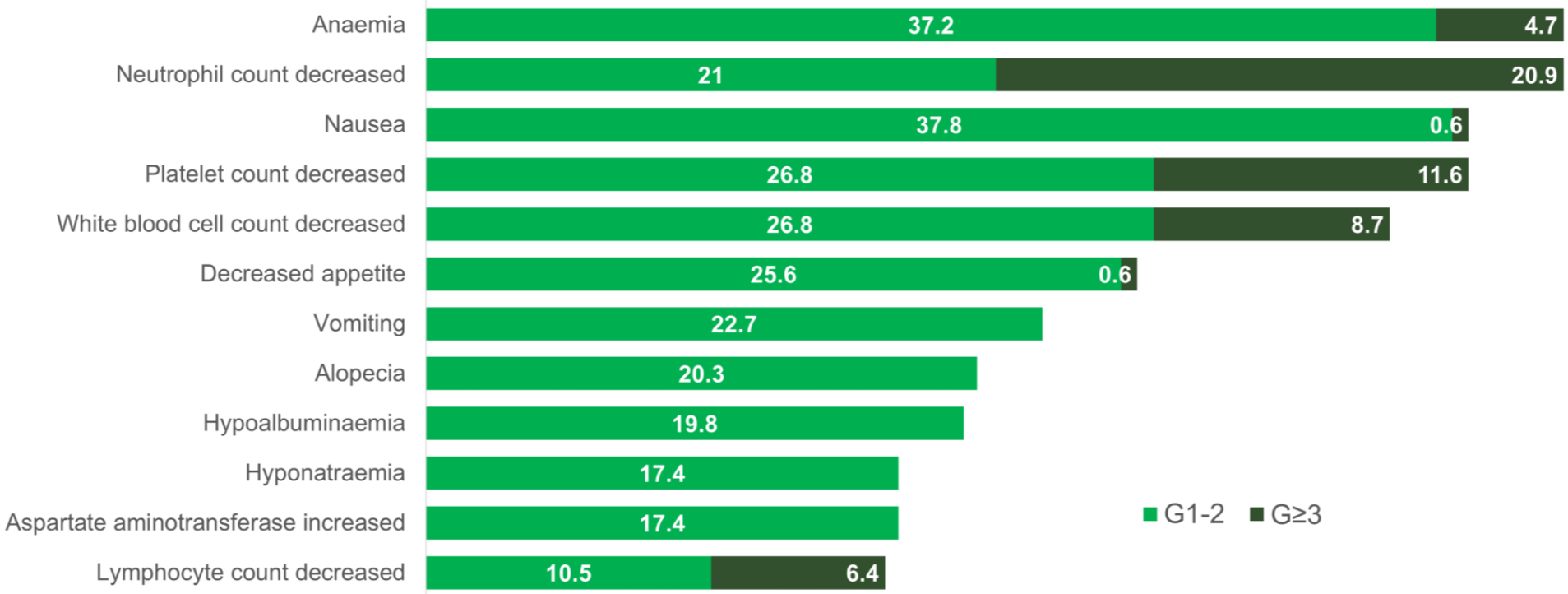
n(%)	Overall (N=172)*	1.5 mg/kg (n=3)	3 mg/kg (n=10)	4.5 mg/kg (n=25)	5 mg/kg (n=53)	5.5 mg/kg (n=74)	6 mg/kg (n=4)	6.5 mg/kg (n=3)
Any TEAE	165 (95.9%)	2 (66.7%)	9 (90.0%)	25 (100.0%)	51 (96.2%)	71 (95.9%)	4 (100.0%)	3 (100.0%)
Grade ≥3 TEAE	86 (50.0%)	0 (0.0%)	2 (20.0%)	15 (60.0%)	32 (60.4%)	33 (44.6%)	2 (50.0%)	2 (66.7%)
Any TRAE	152 (88.4%)	0 (0.0%)	8 (80.0%)	21 (84.0%)	48 (90.6%)	68 (91.9%)	4 (100.0%)	3 (100.0%)
Grade ≥3 TRAE	62 (36.0%)	0 (0.0%)	1 (10.0%)	7 (28.0%)	19 (35.8%)	31 (41.9%)	2 (50.0%)	2 (66.7%)
TRAE leading to:								
Interruption	26 (15.1%)	0 (0.0%)	1 (10.0%)	2 (8.0%)	6 (11.3%)	14 (18.9%)	2 (50.0%)	1 (33.3%)
Dose reduction	21 (12.2%)	0 (0.0%)	0 (0.0%)	2 (8.0%)	8 (15.1%)	11 (14.9%)	0 (0.0%)	0 (0.0%)
Discontinuation	6 (3.5%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	3 (5.7%)	2 (2.7%)	0 (0.0%)	0 (0.0%)

DLT, dose-limiting toxicity; MTD, maximum tolerable dose; TRAE, treatment-related adverse event.
*all patients who had received at least one dose of DB-1310.

Overall safety profile of DB-1310

Hematologic and gastrointestinal events, primarily Grade 1–2, were the most common TRAEs.

TRAEs≥15% of patients across all dose levels (N=172)



Unadjudicated ILD/pneumonitis reported in 9 patients (5.2%), all Grade 1-2 (Grade 1: 4.5 mg/kg n=2, 5 mg/kg n=3, 5.5 mg/kg n=3; Grade 2: 5 mg/kg n=1). ILD adjudication is ongoing.

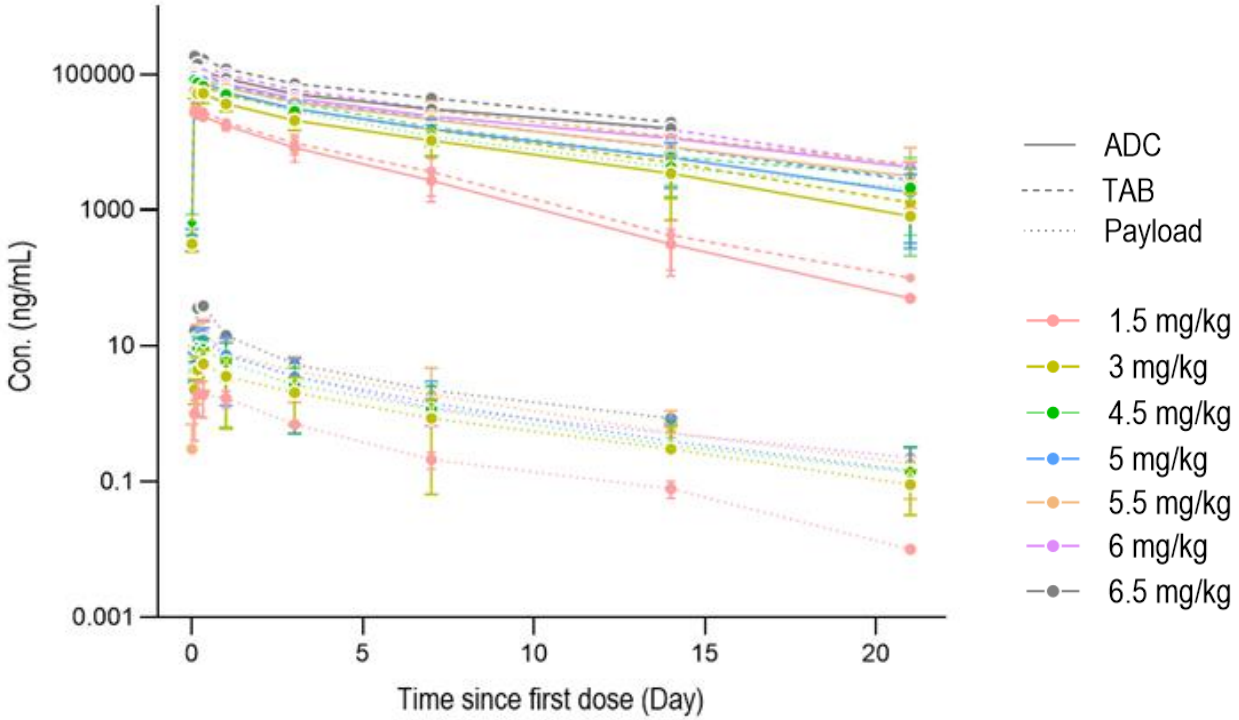
G, grade; ILD, interstitial lung disease; TRAE, treatment-related adverse event.

PK profile of DB-1310

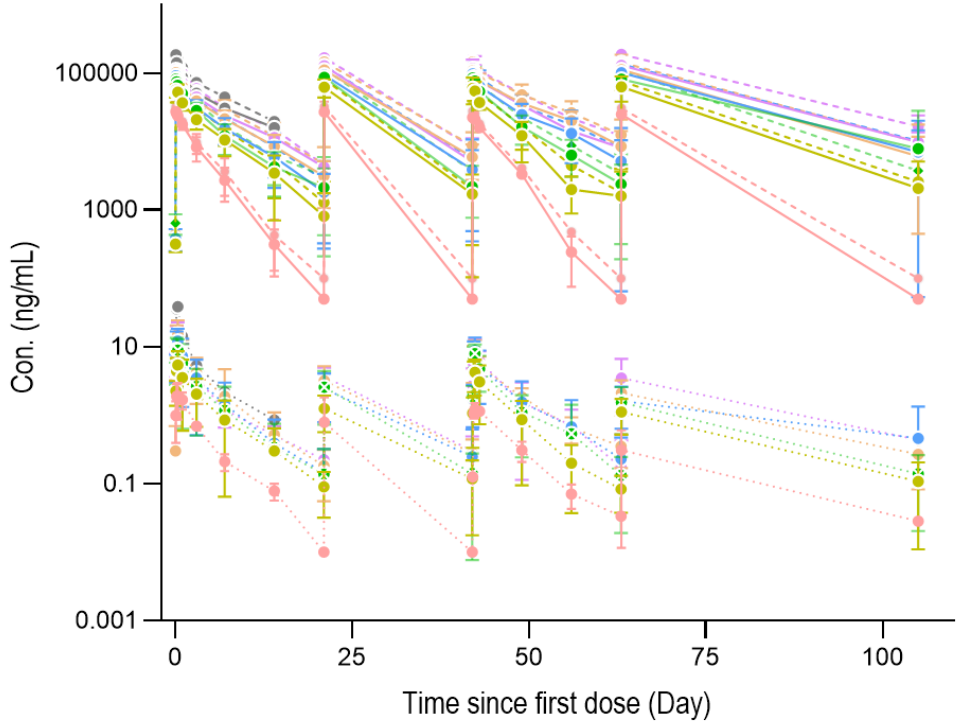
Half-life ~3-5 days for the ADC and ~3-6 days for the payload (3.0-6.5 mg/kg dose range).

DB-1310 ADC exposures in circulation are about 50-fold higher than those of the payload on a molar basis, reflecting the stability of the linker.

PK Profile (Mean ± SD) of DB-1310 (Cycle 1)



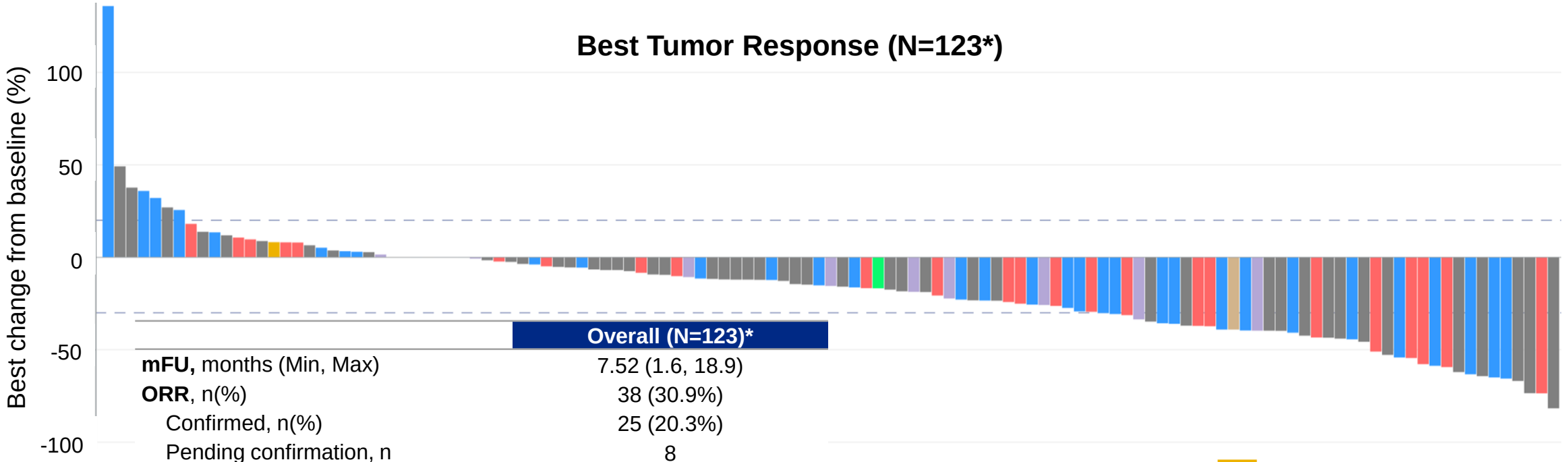
PK Profile (Mean ± SD) of DB-1310 (Cycle 1-4)



ADC, antibody-drug conjugate; SD, standard deviation; PK, pharmacokinetics; TAB, total antibody.

Overall efficacy of DB-1310 in advanced solid tumors

Promising antitumor activity across heavily pretreated patients



	Overall (N=123)*
mFU, months (Min, Max)	7.52 (1.6, 18.9)
ORR, n(%)	38 (30.9%)
Confirmed, n(%)	25 (20.3%)
Pending confirmation, n	8
DoR, months (95% CI)	6.28 (4.14, NE)
DCR, n(%)	103 (83.7%)
mPFS, months (95% CI)	5.49 (4.30 ,6.93)
mOS, months (95% CI)	14.42 (10.68, NE)

CI, confidence interval; DCR, disease control rate; DOR, duration of response; mFU, median follow-up duration; mPFS, median progression-free survival; NE, not evaluable; NR, not reached; ORR, objective response rate.

* All patients who had received at least one dose of DB-1310 and had at least one post-baseline efficacy assessment.

Focus on EGFR Mutant NSCLC: Baseline characteristics

Advanced Disease (62 Pts, 29 [46.8%] on treatment): 27% with brain mets / 18% with liver mets at baseline

Heavily pretreated [Median prior lines 3 (1-11)]: 86% 3rd generation TKI, 92% PBC, 39% ICI.

		Overall (N=62)*	5 mg/kg (n=16)	5.5 mg/kg (n=27)
Age, years	Median (range)	56.5 (36, 79)	60.0 (43, 72)	54.0 (36, 73)
Sex, n(%)	Male	32 (51.6%)	10 (62.5%)	12 (44.4%)
	Female	30 (48.4%)	6 (37.5%)	15 (55.6%)
Race, n(%)	Asian	49 (79.0%)	12 (75.0%)	25 (92.6%)
	White	10 (16.1%)	3 (18.8%)	1 (3.7%)
	Black	1 (1.6%)	0 (0.0%)	1 (3.7%)
ECOG PS, n(%)	0	7 (11.3%)	3 (18.8%)	0 (0.0%)
	1	55 (88.7%)	13 (81.3%)	27 (100.0%)

		Overall (N=62)*	5 mg/kg (n=16)	5.5 mg/kg (n=27)
Metastases at baseline, n(%)	Brain	17 (27.4%)	6 (37.5%)	5 (18.5%)
	Liver	11 (17.7%)	3 (18.8%)	4 (14.8%)
EGFR Mutations, n(%)	19Del	35 (56.5%)	4 (25.0%)	17 (63.0%)
	L858R	23 (37.1%)	11 (68.8%)	8 (29.6%)
Prior lines	Median (range)	3.0 (1, 11)	3.0 (1, 11)	3.0 (1, 9)
Prior 3rd G TKI	Yes, n(%)	53 (85.5%)	15 (93.8%)	21 (77.8%)
Prior PBC		57 (91.9%)	13 (81.3%)	25 (92.6%)
Prior ICI		24 (38.7%)	6 (37.5%)	8 (29.6%)

ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; G, generation; ICI, immune checkpoint inhibitor; NSCLC, non-small cell lung cancer; PBC, platinum-based chemotherapy; pt, patient; TKI, tyrosine kinase inhibitor; USA, United States of America.

*All patients who had received at least one dose of DB-1310 (dose range: 3.0 mg/kg - 6.0 mg/kg).

Focus on EGFR Mutant NSCLC: DB-1310 Safety

The safety profile is manageable and consistent with the overall population.

n(%)	Overall (N=62)*	3 mg/kg (n=7)	4.5 mg/kg (n=9)	5 mg/kg (n=16)	5.5 mg/kg (n=27)	6 mg/kg (n=2)	6.5 mg/kg (n=1)
Any TEAE	59 (95.2%)	6 (85.7%)	9 (100.0%)	15 (93.8%)	26 (96.3%)	2 (100.0%)	1 (100.0%)
Grade ≥3 TEAE	29 (46.8%)	2 (28.6%)	6 (66.7%)	9 (56.3%)	10 (37.0%)	1 (50.0%)	1 (100.0%)
Any TRAE	57 (91.9%)	5 (71.4%)	9 (100.0%)	15 (93.8%)	25 (92.6%)	2 (100.0%)	1 (100.0%)
Grade ≥3 TRAE	22 (35.5%)	1 (14.3%)	4 (44.4%)	6 (37.5%)	9 (33.3%)	1 (50.0%)	1 (100.0%)
TRAE leading to:							
Interruption	13 (21.0%)	1 (14.3%)	2 (22.2%)	1 (6.3%)	8 (29.6%)	1 (50.0%)	0 (0.0%)
Dose reduction	6 (9.7%)	0 (0.0%)	1 (11.1%)	2 (12.5%)	3 (11.1%)	0 (0.0%)	0 (0.0%)
Discontinuation	2 (3.2%)	0 (0.0%)	0 (0.0%)	1 (6.3%)	1 (3.7%)	0 (0.0%)	0 (0.0%)

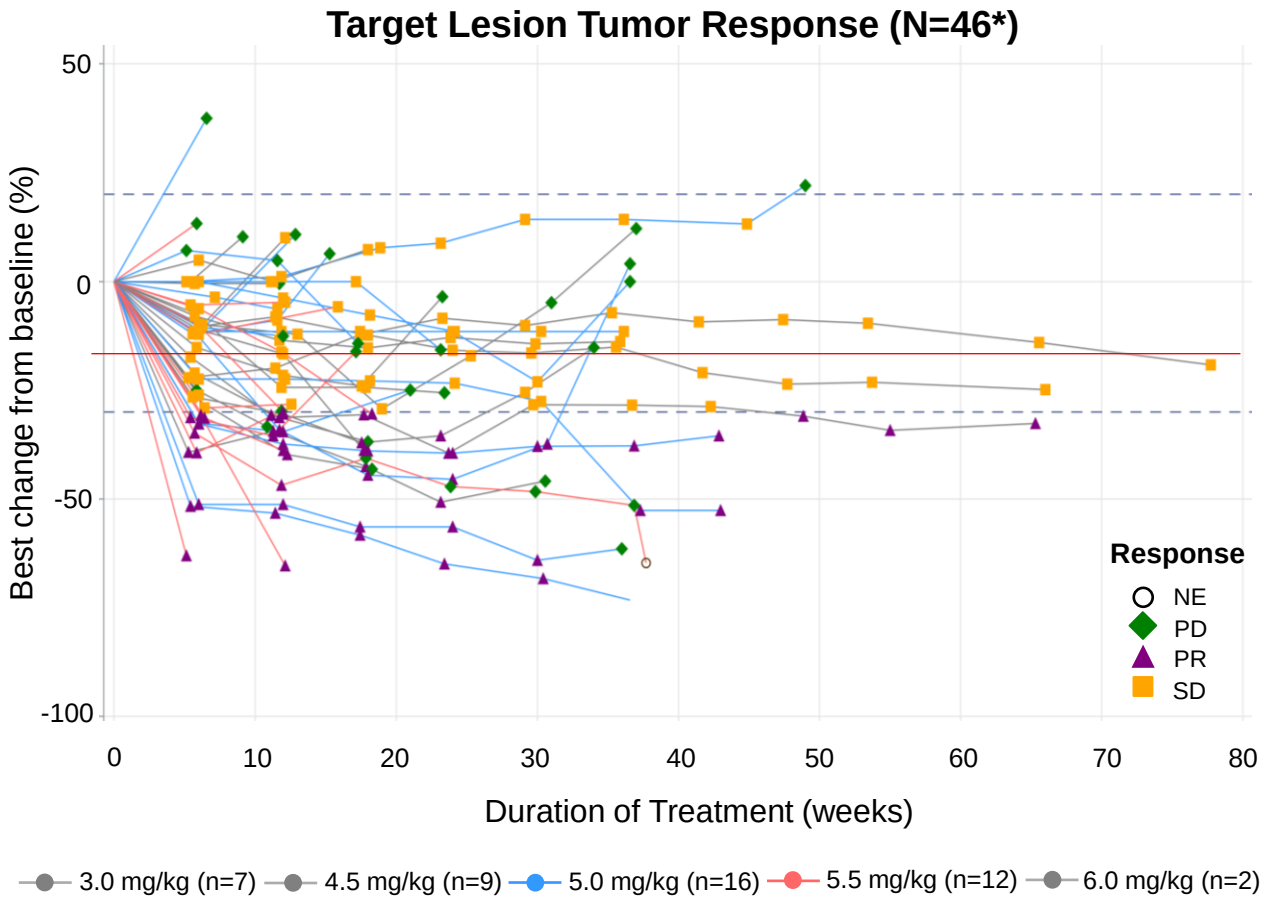
TRAE, treatment-related adverse event.
*all patients who had received at least one dose of DB-1310.

Focus on EGFRm NSCLC: DB-1310 Efficacy

Encouraging antitumor activity in EGFRm NSCLC

	Overall (N=46)*	5 mg/kg (n=16)	5.5 mg/kg (n=12)
mFU, mo (Min, Max)	7.52 (1.7, 18.9)	9.97 (1.7, 12.5)	4.24 (3.4, 9.4)
ORR, n(%)	20 (43.5%)	6 (37.5%)	8 (66.7%)
Confirmed, n(%)	13 (28.3%)	6 (37.5%)	4 (33.3%)
Pending confirmation, n	3†	0	2†
DoR, mo (95%CI)	5.80 (2.73, NE)	6.93 (3.48, NE)	2.78 (2.73, NE)
DCR, n(%)	42 (91.3%)	14 (87.5%)	11 (91.7%)
mPFS, mo (95%CI)	7.03 (4.14, 8.41)	8.28 (2.96, NE)	4.11 (2.73, NE)
mOS, mo (95%CI)	18.89 (11.63, NE)	NR (7.10, NE)	NR (NE, NE)

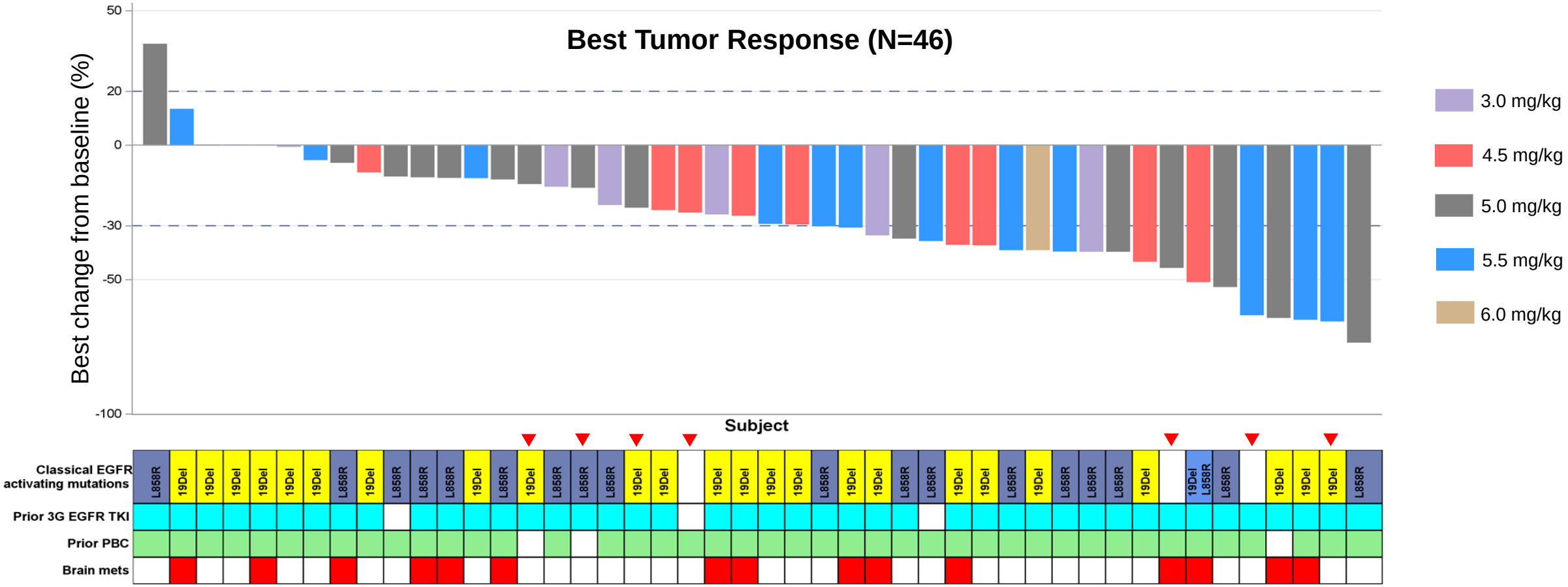
†Response confirmations were pending for three patients, which were confirmed post DCO.



DCR, disease control rate; DOR, duration of response; mFU, median follow-up duration; mPFS, median progression-free survival; NE, not evaluable; NR, not reached; NSCLC, non-small cell lung cancer; ORR, objective response rate.
*All patients who had received at least one dose of DB-1310 (dose range: 3.0 mg/kg – 6.0 mg/kg) and had at least one post-baseline efficacy assessment.

Focus on EGFRm NSCLC: DB-1310 Efficacy

Encouraging antitumor activity in EGFRm NSCLC



DCR, disease control rate; DOR, duration of response; mPFS, median progression-free survival; NSCLC, non-small cell lung cancer; ORR, objective response rate.

*All patients who had received at least one dose of DB-1310 and had at least one post-baseline efficacy assessment. ▼indicates the presence of other EGFR mutations, such as T790M, 20Ins, L718V, G719X, C797S, or L792F.

Conclusions

DB-1310: A novel HER3 ADC demonstrating encouraging efficacy and a manageable safety profile

- **DB-1310 was well tolerated:** Nausea and hematological events were the most common TRAEs
  - Hematologic TRAEs primarily Grade 1/2 and low treatment-related discontinuation rate
- **DB-1310 showed encouraging anti-tumor activity** across advanced solid tumors, particularly in EGFR-mutant NSCLC
  - **All Solid Tumors (n=123):** uORR 31%, DCR 84%, mPFS 5.5mo, mOS 14.5mo
  - **EGFR-mutant NSCLC (n=46):** uORR 44%, DCR 91%, mPFS 7.0mo, mOS 18.9mo
    - uORR 37.5% at 5 mg/kg (n=16), 66.7% at 5.5 mg/kg (n=12)
- **Study is ongoing** and will evaluate additional solid tumor indications, as well as combination approaches in EGFR-mutant NSCLC (+ EGFR TKI) and HER2+ Breast Cancer (+ HER2 therapy)

DB-1310 had a manageable safety profile and promising antitumor activity, particularly in patients with advanced/metastatic EGFR-mutant NSCLC

Acknowledgments

Thank You

The authors would like to thank participants, their families, study staff, research coordinators, and the investigators.

Funding

This Study was sponsored by DualityBiologics.

Medical writing assistance was provided by Lily Zhang and Qing Yang of Duality Biologics, Shanghai, China. Editorial support was provided in accordance with Good Publication Practice guidelines.