PS4-06-17: First Clinical Data of DB-1310 (a HER3-targeted Antibody-Drug Conjugate), in Patients with Pretreated Hormone Receptor-positive/HER2-negative Breast Cancer: Efficacy and Safety Data from a Phase 1/2a Trial

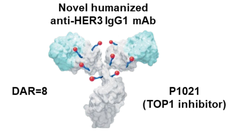
[1]Y. Yin, [2]A. Spira, [3]H. Lan, [4]M. Zhao, [5]Y. Mao, [6]W. Yao, [7]Y. Sun, [8]J. Wu, [9]X. Sun, [9]S. Liu, [9]H. Mu, [9]K. Wang, [10]Y. Qiu, [11]E.Hamilton

[1]Department of Oncology, The First Affiliated Hospital of Nanjing Medical University, Nanjing, CHINA. [2]Clinical Research, Next Oncology, Fairfax, VA. [3]Department of Medical Oncology, Sichuan Provincial People's Hospital, Sichuan Academy of Medical Sciences, School of Medicine UESTC, Chengdu, CHINA. [4]Department of Medical Oncology, The First Affiliated Hospital of China Medical University, Shenyang, CHINA. [5]Department of Oncology, The Affiliated Hospital of Jiangnan University, Jiangsu, CHINA. [6]Department of Thoracic Medical Oncology, Sichuan Cancer Hospital, Chengdu, CHINA. [7]Phase I Clinical Research Center, The Affiliated Cancer Hospital of Shandong First Medical University, Jinan, CHINA. [8]Department of Radiotherapy, The First Affiliated Hospital of Hainan Medical University, Haikou, CHINA. [9]Clinical Development, Dualitybiologics, Shanghai, CHINA. [10]R&D, Dualitybiologics, Shanghai, CHINA. [11]Breast Cancer Research Program, Sarah Cannon Research Institute, Nashville, TN

Introduction

DB-1310 is an investigational ADC composed of a humanized anti-HER3 IgG1 mAb conjugated to a proprietary DNA inhibitor (P1021) via a cleavable tetra-peptide linker, with a DAR of approximately 8.0.

- **DB-1310 is engineered to target HER3-expressing tumors via multiple mechanisms: direct cytotoxicity upon internalization, bystander killing of adjacent cells, blockade of HER3 ligand binding, and ADCC.**



- 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

Building upon the established safety and efficacy of DB-1310 in solid tumors, notably EGFR-mutated non-small cell lung cancer (Lisberg et al., ASCO2025, abstract 3000), herein we first disclose the clinical data of DB-1310 as a monotherapy in HR+/HER2- BC patients progressing after prior ET, CDK4/6 inhibitors and chemotherapy. These findings suggest a favorable safety profile and preliminary efficacy in this difficult-to-treat population.

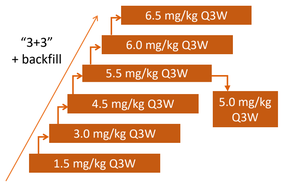
Method

Study Design: Multicenter, open-label, first-in-human Phase 1/2a Study of DB-1310 in advanced/metastatic solid tumors unselected for HER3 expression

Key Eligibility Criteria:

- ≥ 18 years
- Advanced or metastatic solid tumor progressing on/after standard systemic therapy
- ≥ 1 measurable lesion (per RECIST v1.1)
- ECOG PS 0–1
- Adequate organ function
- Treated, asymptomatic brain metastases allowed
- No prior HER3 targeted therapy
- No prior TOP1 ADC therapy

Phase 1 Stage: DB-1310 Dose escalation



Backfill Rule: Once the SMC confirms the safety of a dose level following "3+3" escalation rule, additional patients with HR+/HER2- BC will be backfilled to this dose level, with a total of up to 20 patients.

Endpoints:

- **Primary endpoints** include safety and MTD/RP2D.
- **Secondary endpoints** include ORR, DoR, DCR, TTR, PFS, OS, PK and ADA.

ADA= anti-drug antibody; ADC= antibody-drug conjugate; ADCC= antibody-dependent cellular cytotoxicity; BC= breast cancer; DAR= drug-to-antibody ratio; DCR= disease control rate; DoR= duration of response; ECOG PS= Eastern Cooperative Oncology Group Performance Status; EGFR= epidermal growth factor receptor; ET= endocrine therapy; HER2= human epidermal growth factor receptor 2; HER3= human epidermal growth factor receptor 3; HR= hormone receptor; RECIST= Response Evaluation Criteria in Solid Tumors; IgG1= immunoglobulin G1; mAb= monoclonal antibody; MTD= maximum tolerated dose; ORR= objective response rate; OS= overall survival; PFS= progression-free survival; PK= pharmacokinetics; Q3W= once every 3 weeks; RP2D= recommended phase 2 dose; SMC= safety monitoring committee; TKI= tyrosine kinase inhibitor; TOP1= topoisomerase 1; TTR= time to response.

Results

Baseline Character

As of the DCO date (September 19, 2025), 246 patients in Phase 1 had received DB-1310 across 7 dose levels (1.5-6.5 mg/kg) Baseline characteristics were as follows: median age, 61.0 [range: 29-81] years ; Male, 51.2%; ECOG PS 1, 83.3%; White, 22.8%; Asian, 72.8%. The median follow-up duration was 6.24 (range: 0.1-22.9) months.

Among the total enrolled population, 24 were HR+/HER2- BC patients (3.0 mg/kg, n=1; 4.5 mg/kg, n=1; 5 mg/kg, n=10; 5.5 mg/kg, n=12) (Table 1).

- **A total of 18 patients (75.0%) remained on DB-1310 treatment.**

Table 1 Baseline and Characteristics

	5-5.5 mg/kg (N=22)	Total (N=24)
Age, median (range)	56.5 (34, 71)	57.0 (34, 71)
Female, n (%)	21 (95.5)	23 (95.8)
Race, n (%)		
White	2 (9.1)	4 (16.7)
Chinese	19 (86.4)	19 (79.2)
Black or African American	1 (4.5)	1 (4.2)
ECOG PS, n (%)		
0	3 (13.6)	4 (16.7)
1	19 (86.4)	20 (83.3)
Number of Prior Systemic Regimens, median (range)	4.0 (2, 11)	4.0 (2, 11)
Prior ET+CDK 4/6 inhibitor	22 (100.0)	24 (100.0)
Prior Chemotherapy at metastasis stage	20 (90.9)	22 (91.7)
Site of metastasis, n (%)		
Liver	15 (68.2)	17 (70.8)
Lungs	12 (54.5)	12 (50.0)
Bones	13 (59.1)	15 (62.5)
HER2 IHC subgroup, n (%)		
IHC 0	11(50)	12 (50)
IHC 1+	8 (36.4)	9 (37.5)
IHC 2+/ISH-	2(9.1)	2(8.3)

CDK= cyclin-dependent kinase; DCO= data cut-off; N= total number; n= subset of the total number; ET= endocrine therapy ; L= line; IHC= Immunohistochemistry; ISH= In Situ Hybridization.

Efficacy Results

Among HR+/HER2- BC patients, 20 were efficacy evaluable, with a median follow-up duration of 6.32 (range: 1.5-22.9) months.

- **The unconfirmed ORR was 50.0% (10/20) and the confirmed DCR was 90.0% (18/20) per RECIST v1.1 (Table 2).**

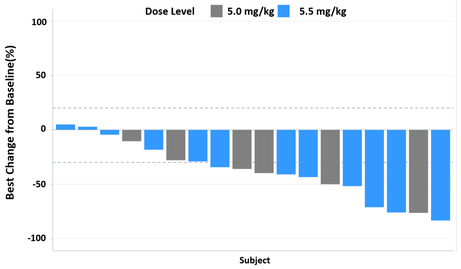


Figure 1 Waterfall Plot of Best Percentage Change from Baseline on Sum of Target Lesion Diameters (Investigator Assessed) with DB-1310 monotherapy at 5.0-5.5 mg/kg in HR+/HER2- BC Patients with Postbaseline Scans (N=18)

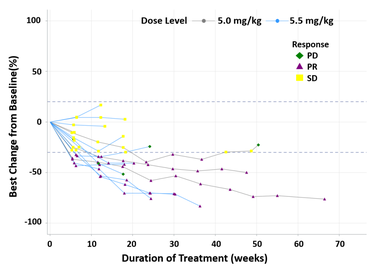


Figure 2 Spider Plot of Percentage Change from Baseline on Sum of Target Lesion Diameters (Investigator assessed) with DB-1310 monotherapy at 5.0-5.5 mg/kg in HR+/HER2- BC patients with Postbaseline Scans (N=18)

Table 2 Efficacy for HR+/HER2- BC patients

	5 mg/kg (N=6)	5.5 mg/kg (N=12)	5-5.5 mg/kg (N=18)	Total (N=20)
Unconfirmed ORR, n(%)	4 (66.7)	6 (50.0)	10 (55.6)	10 (50.0)
95%CI	22.28, 95.67	21.09, 78.91	30.76, 78.47	27.20, 72.80
Confirmed ORR, n(%)	3 (50.0)	6 (50.0)	9 (50.0)	9 (45.0)
95%CI	11.81, 88.19	21.09, 78.91	26.02, 73.98	23.06, 68.47
Pending confirmation, n (%)	1 (16.7)	0 (0)	1 (5.6)	1 (5.0)
Confirmed DCR, n(%)	6 (100.0)	11 (91.7)	17 (94.4)	18 (90.0)
95%CI	54.07, 100.00	61.52, 99.79	72.71, 99.86	68.30, 98.77
Confirmed DoR, months, median	NR	NR	NR	NR
95%CI	6.28 ,NE	3.02 ,NE	3.02 ,NE	3.02 ,NE
PFS, months, median	NR	NR	11.60	11.60
95% CI	11.60 ,NE	4.44 ,NE	4.44 ,NE	4.44 ,NE
6-month PFS, rate(%)	100.0	57.3	71.4	69.4
95% CI	100.0 ,100.0	14.6 ,85.1	33.0 ,90.3	35.9 ,87.8

BC= breast cancer; CI= Confidence Interval; DCR= disease control rate; DoR= duration of response; HER2= human epidermal growth factor receptor 2; HR= hormone receptor; N= total number; n= subset of the total number; NE= not estimable; NR= not reached; ORR= objective response rate; PFS= progression-free survival.

Safety Results

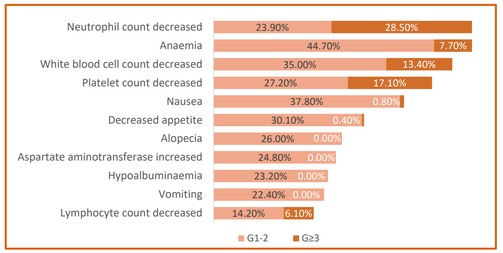


Figure 3 TRAE in ≥ 20% of total participants

Overall, DB-1310 was well-tolerated and demonstrated a favorable safety profile.

- **The median duration of treatment was 4.14 (range: 0.7-23.1) months.**
- **The most common TRAEs were mainly hematologic and gastrointestinal events, primarily Grade 1–2 (Figure 3).**
- **ILD/pneumonitis occurred in 10 participants (4.1%) (Grade 1, n=9; Grade 2, n=1).**
- **One treatment-related death was reported (PT: subarachnoid haemorrhage, 5.0 mg/kg).**
- **The safety profile of 24 HR+/HER2- BC patients was consistent with the overall Phase 1 population.**

Table 3 Summary of Overall Safety

	1.5 mg/kg (N=3)	3.0 mg/kg (N=10)	4.5 mg/kg (N=25)	5.0 mg/kg (N=84)	5.5 mg/kg (N=113)	6.0 mg/kg (N=7)	6.5 mg/kg (N=4)	Total (N=246)
Any TRAEs, n (%)	0 (0.0)	8 (80.0)	21 (84.0)	76 (90.5)	111 (98.2)	5 (71.4)	4 (100.0)	225 (91.5)
Grade≥3	0 (0.0)	1 (10.0)	7 (28.0)	31 (36.9)	68 (60.2)	3 (42.9)	3 (75.0)	113 (45.9)
Serious AEs	0 (0.0)	0 (0.0)	2 (8.0)	7 (8.3)	24 (21.2)	0 (0.0)	3 (75.0)	36 (14.6)
lead to drug discontinuation	0 (0.0)	0 (0.0)	1 (4.0)	4 (4.8)	6 (5.3)	0 (0.0)	0 (0.0)	11 (4.5)
lead to dose reduction	0 (0.0)	0 (0.0)	2 (8.0)	11 (13.1)	27 (23.9)	2 (28.6)	1 (25.0)	43 (17.5)
lead to dose interruption	0 (0.0)	1 (10.0)	2 (8.0)	6 (7.1)	27 (23.9)	1 (14.3)	1 (25.0)	38 (15.4)

AE= adverse event; G= grade; ILD= interstitial lung disease; PT= preferred term; TRAE= treatment-related adverse events

Conclusions

- **DB-1310 was well-tolerated with manageable toxicity. The rate of TRAEs leading to discontinuation was 4.8% at 5.0 mg/kg and 5.3% at 5.5 mg/kg.**
- **Encouraging preliminary antitumor activity of DB-1310 was observed in HR+/HER2- BC patients with resistant to ET, CDK4/6 inhibitor and chemotherapy. At DB-1310 doses of 5.0-5.5 mg/kg, confirmed ORR was 50.0% and confirmed DCR was 94.4%, with 18 patients (75.0%) still on treatment.**
- **The enrollment of HR+/HER2- BC patients in the DB-1310 monotherapy cohorts is ongoing.**

Acknowledgment

We thank the patients who participated in this study, as well as their families and caregivers.

Contact

Duality Biologics
Email: xiaodong.sun@dualitybiologics.com
Website: https://www.dualitybiologics.com
Phone: 021-2601 8730

References

1. Li X, Liang L, Zhu Z, Hua H, Qiu Y. DB-1310, a HER3-targeting antibody-drug conjugate, has synergistic anti-tumor activity with trastuzumab in HER2- and HER3-expressing breast cancer. Cancer Biol Med. 2025 Mar 19;22(3):231–6. doi: 10.20892/j.issn.2095-3941.2024.0586.
2. Li X, Yao J, Qu C, Luo L, Li B, Zhang Y, Zhu Z, Qiu Y, Hua H. DB-1310, an ADC comprised of a novel anti-HER3 antibody conjugated to a DNA topoisomerase I inhibitor, is highly effective for the treatment of HER3-positive solid tumors. J Transl Med. 2024 Apr 17;22(1):362. doi: 10.1186/s12967-024-05133-7.

This presentation is the intellectual property of the author/presenter. Contact them at xiaodong.sun@dualitybiologics.com for permission to reprint and/or distribute.

© Poster Template by Genigraphics® 1.800.790.4001 www.genigraphics.com