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BL-B01D1, an EGFR x HER3 Bispecific Antibody-drug Conjugate (ADC), in Patients with Locally Advanced or Metastatic Urothelial Carcinoma (UC)

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DECLARATION OF INTERESTS

Dr. Ye reports institutional support for the following:

Biokin Pharmaceutical: Steering committee member & trial chair

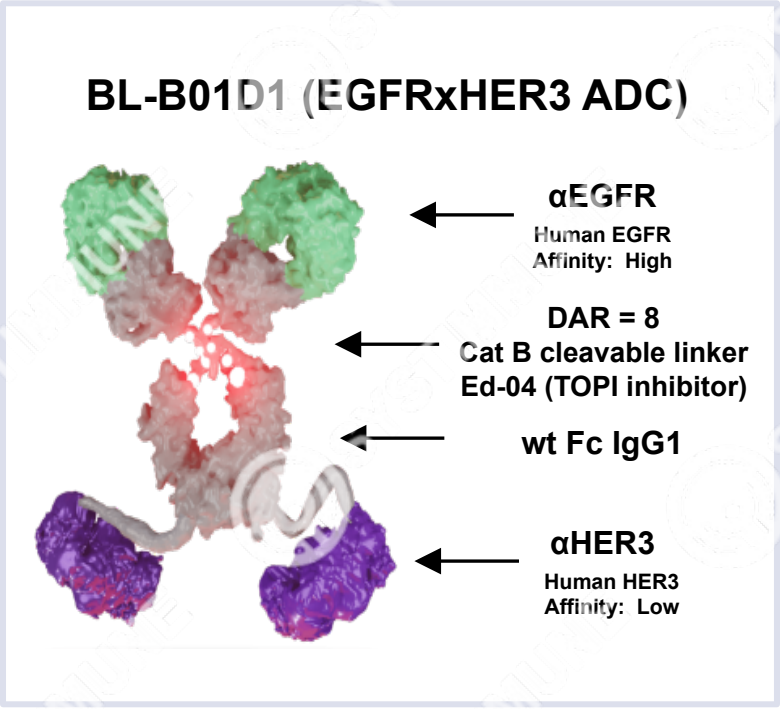
Dr. Ye reports personal compensation for the following:

AstraZeneca: Advisory board

Lilly: Advisory board

Bayer: Advisory board

Background

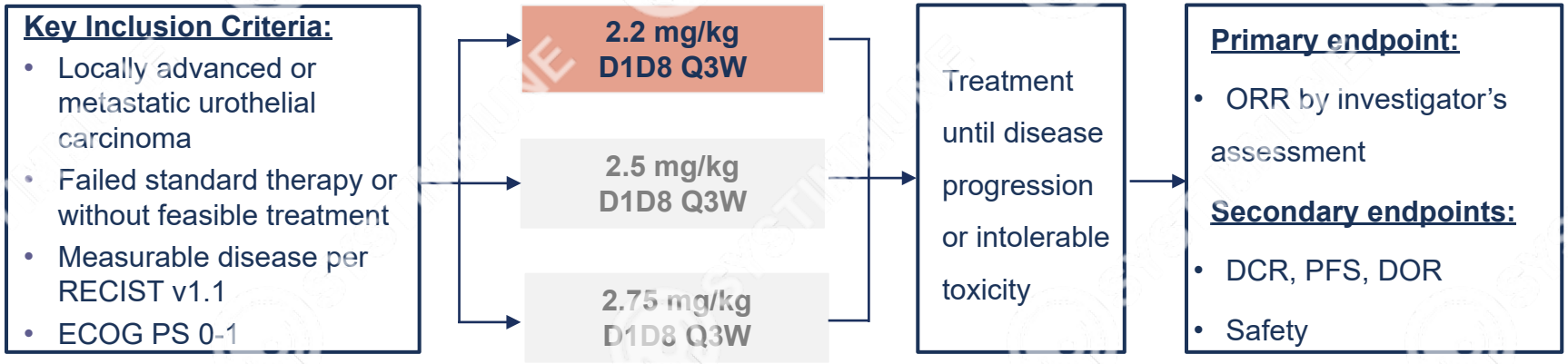


wt: wild type; Cat B: cathepsin B; TOPI: Topoisomerase I
*: Chow NH, Chan SH, Tzai TS, Ho CL, Liu HS. *Clin Cancer Res.* 2001 Jul;7(7):1957-62.

- EGFR and HER3 are highly expressed in urothelial carcinoma*. Targeting EGFR and HER3 could provide a promising therapeutic option for urothelial carcinoma.
- BL-B01D1 is a potential first-in-class (FIC) ADC consisting of an EGFRxHER3 bispecific antibody bound to a novel topoisomerase I inhibitor payload via a cleavable linker.
- Results for safety, tolerability and preliminary efficacy in previously treated patients with locally advanced or metastatic urothelial carcinoma (UC) in phase II study (BL-B01D1-201) are presented.

Study Design of BL-B01D1 in UC

Non-randomized, phase II study (BL-B01D1-201, NCT05785039)



ECOG PS: Eastern Cooperative Oncology Group performance status;
DCR: disease control rate;
DOR: duration of response;
ORR: objective response rate;
PFS: progression-free survival;
RECIST: Response Evaluation Criteria in Solid Tumors;
Standard therapy including platinum-based chemotherapy (PBC) or PD-1 + ADC.

Baseline Characteristics

	Total (N = 41)	2.2 mg/kg D1D8Q3W (N = 34)	2.5 mg/kg D1D8Q3W (N = 4)	2.75 mg/kg D1D8Q3W (N = 3)
Sex (Male), n(%)	32 (78.0)	26 (76.5)	4 (100)	2 (66.7)
Age, median (range)	62.0 (42.0, 74.0)	61.5 (42.0, 74.0)	56.5 (51.0, 68.0)	70.0 (68.0, 72.0)
BMI, mean (SD)	23.3 (3.2)	23.3 (3.1)	22.6 (3.9)	23.6 (4.8)
ECOG-PS Score, n(%)				
0	17 (41.5)	15 (44.1)	1 (25.0)	1 (33.3)
1	24 (58.5)	19 (55.9)	3 (75.0)	2 (66.7)
Primary tumor sites, n(%)				
Bladder	22 (53.7)	17 (50.0)	3 (75.0)	2 (66.7)
Upper urinary tract	19 (46.3)	17 (50.0)	1 (25.0)	1 (33.3)
Histologic type, n(%)				
Urothelial only	34 (82.9)	27 (79.4)	4 (100)	3 (100)
Urothelial carcinoma with squamous differentiation	5 (12.2)	5 (14.7)	0	0
Urothelial with other components*	2 (4.9)	2 (5.9)	0	0
Prior line of chemotherapy, n(%)				
1	18 (43.9)	16 (47.1)	0	2 (66.7)
PBC	15 (36.6)	13 (38.2)	0	2 (66.7)
ADC	2 (4.9)	2 (5.9)	0	0
PD(L)-1+ chemo	1 (2.4)	1 (2.9)	0	0
2+	23 (56.1)	18 (52.9)	4 (100)	1 (33.3)
Prior anti-PD(L)-1, n(%)	38 (92.7)	31 (91.2)	4 (100)	3 (100)

*: One urothelial carcinoma with sarcomatoid variant and one urothelial carcinoma with glandular differentiation.

BMI: body mass index; ADC: antibody-drug conjugates.

Data cutoff: June 30, 2024

Preliminary Efficacy in UC

	2.2 mg/kg D1D8Q3W	
	Total (N = 27)[1]	1 Prior line of chemo (PBC or ADC) (N=12)[2]
Prior line of therapy, median (range)	2 (1-7)	1 (1-2)
Best Overall Response (BOR), n		
PR	11	9
Confirmed PR	9	9
SD	15	3
PD	0	0
NE	1	0
ORR, % (95%CI)	40.7 (22.4, 61.2)	75.0 (42.8, 94.5)
cORR, % (95%CI)	33.3 (16.5, 54.0)	75.0 (42.8, 94.5)
DCR, % (95%CI)	96.3 (81.0, 99.9)	100 (73.5, 100.0)
Median DOR (months) (95% CI)	NR (NR, NR)	NR (NR, NR)
6-month DOR rate, %, (95% CI)	100 (100.0, 100.0)	100 (100.0, 100.0)
Median PFS (months) (95% CI)	NR (4.2, NR)	NR (NR, NR)
6-month PFS rate, %, (95% CI)	62.4 (32.2, 82.2)	100 (100.0, 100.0)

[1] Among of the 27 patients, 24 patients had received anti-PD-(L)1, 24 patients had received PBC, and 14 patients had received 1-2 prior lines of ADCs.

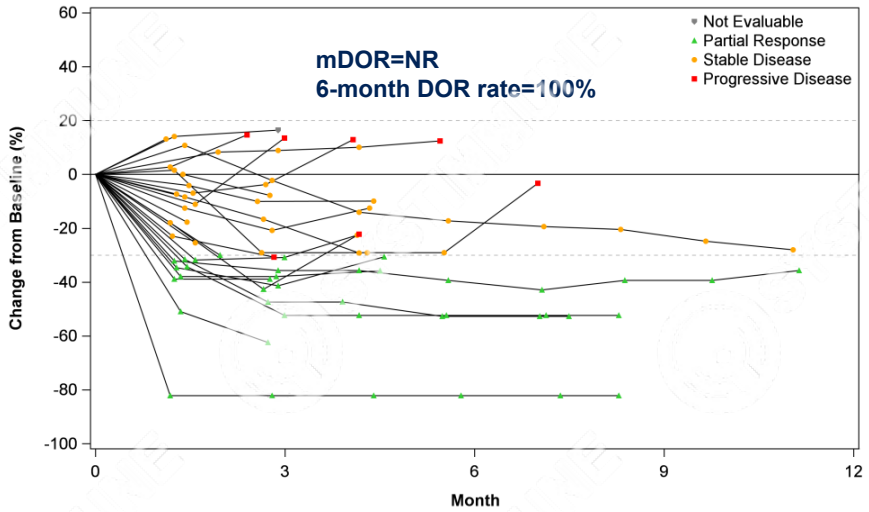
[2] Among of the 12 patients, 11 patients had received anti-PD-(L)1, 9 patients had received PBC, 2 patients had received ADCs, and 1 patient had received anti-PD-(L)1 + gemcitabine.

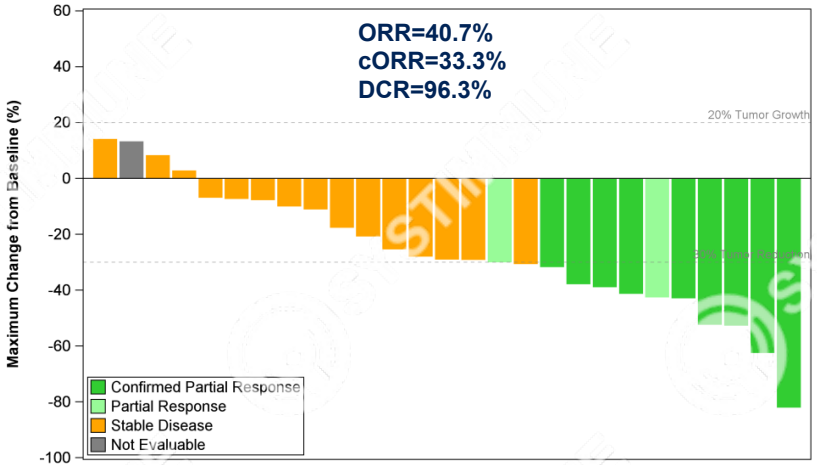
ORR was calculated based on response evaluable population defined as at least 1 post-baseline scan; CI: confidence interval; cORR: confirmed objective response rate; NE: not evaluable; NR: not reached; PD: progressive disease; PR: partial response; SD: stable disease.

Data cutoff: June 30, 2024

Depth and Duration of Response

Patients at 2.2 mg/kg D1D8 Q3W (N=27)

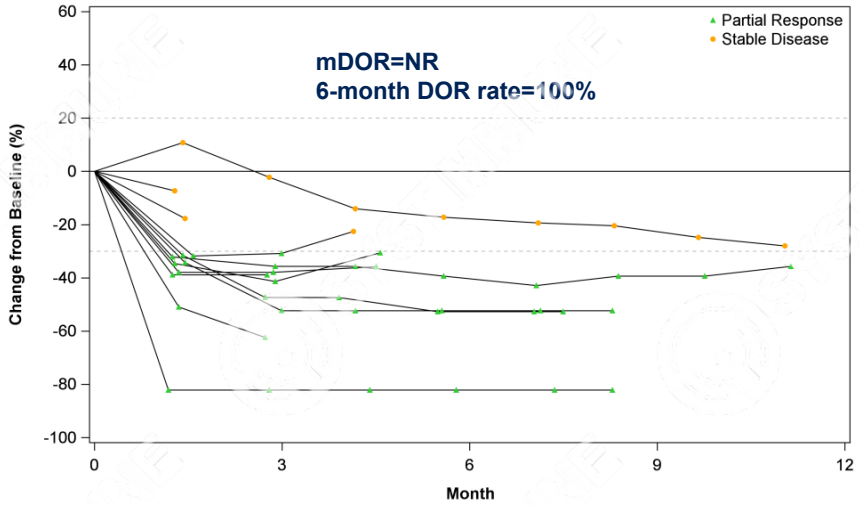


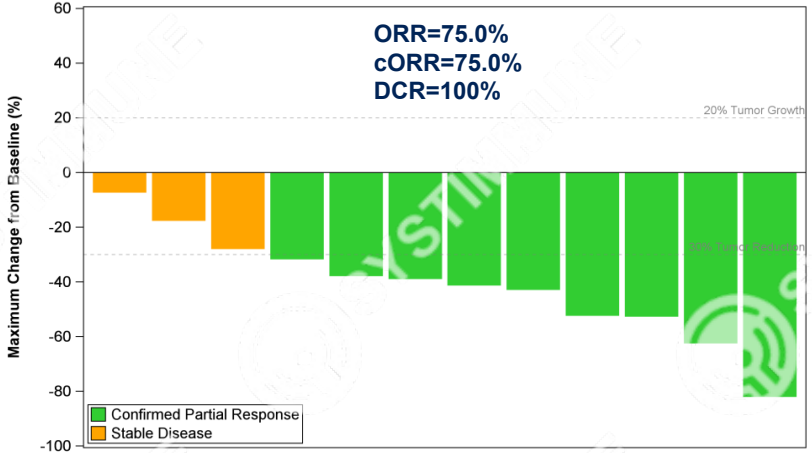


Data cutoff: June 30, 2024

Depth and Duration of Response

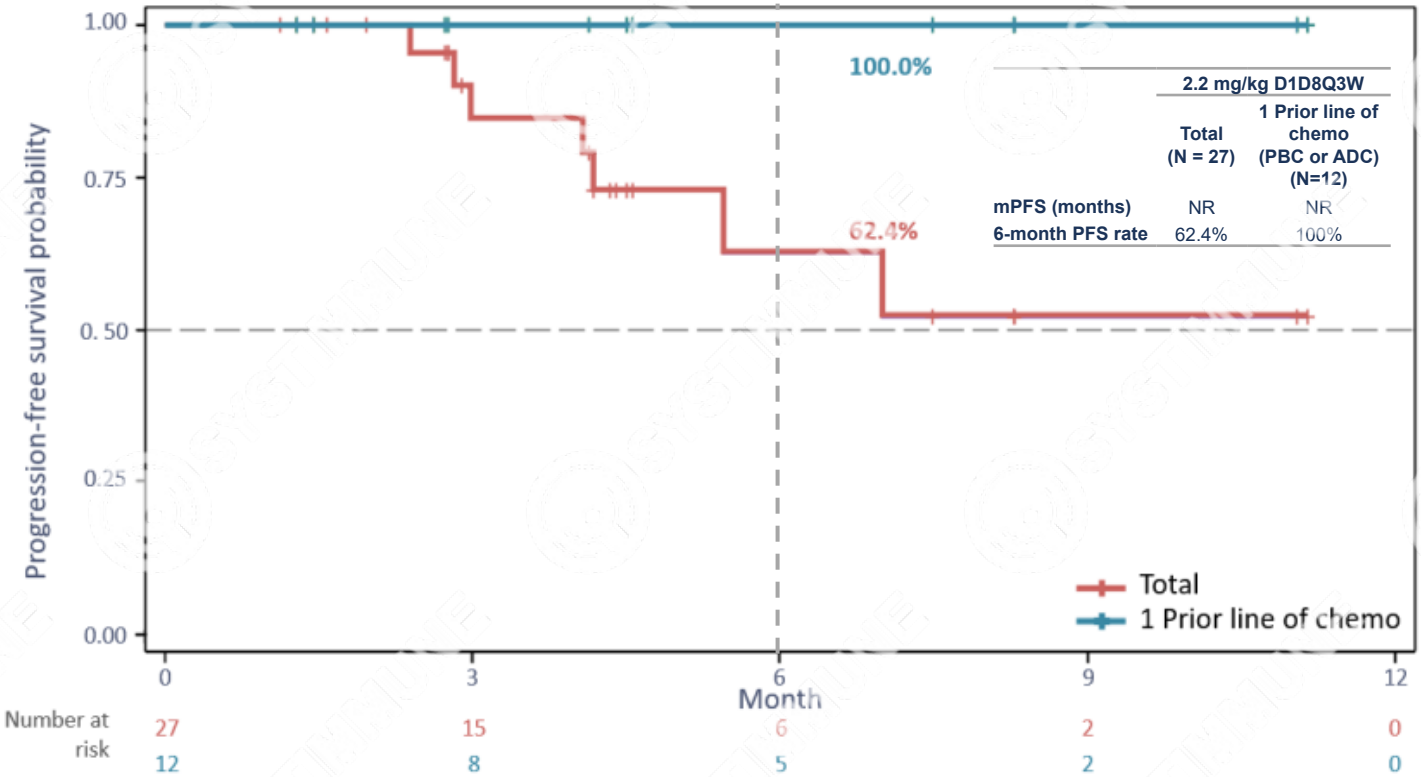
Patients with 1 Prior line of chemo at 2.2 mg/kg D1D8 Q3W (N=12)





Data cutoff: June 30, 2024

PFS at 2.2 mg/kg D1D8 Q3W



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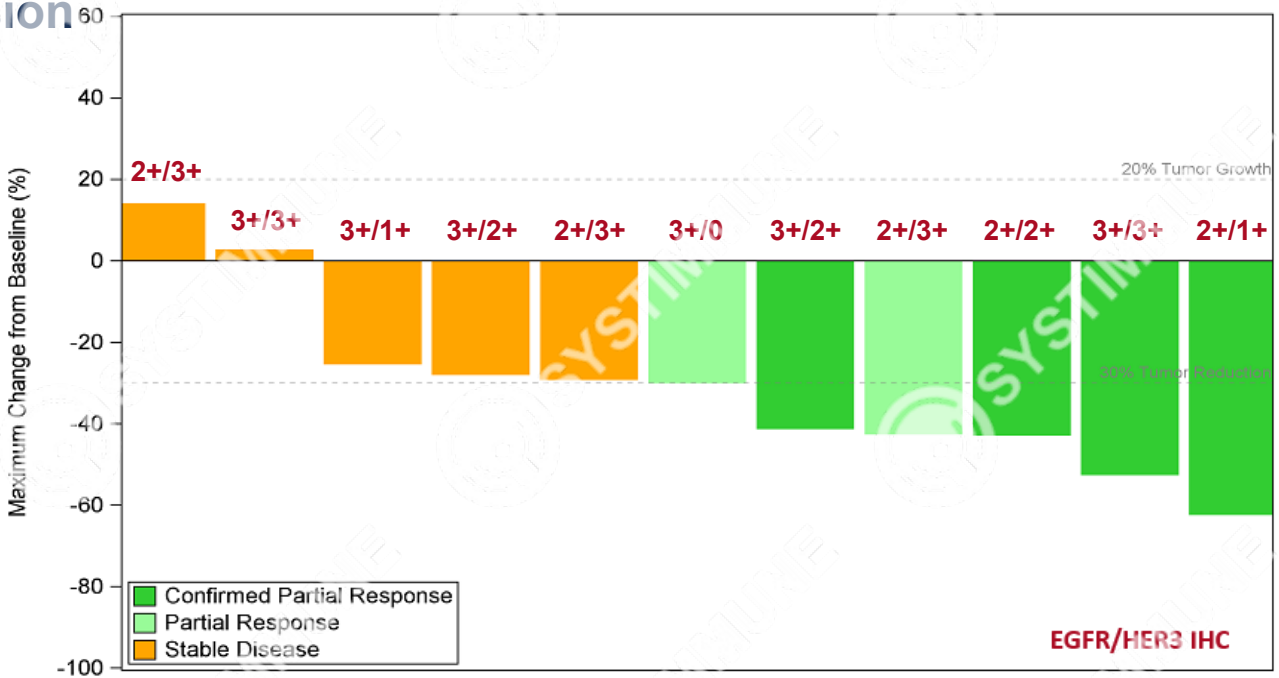
Data cutoff: June 30, 2024

Biomarker analysis at 2.2 mg/kg D1D8 Q3W

Clinical activity seen across various levels of EGFR and HER3 expression



Biomarker analysis was performed only for patients with tissue samples.

Data cutoff: June 30, 2024

Overall Safety Summary

TRAEs, n(%)	2.2 mg/kg D1D8Q3W (N = 34)
Median Follow-up (months)	4.6
Treatment Related AE (TRAE)	34 (100)
TRAE leading to death	0
TRAE leading to discontinuation	2 (5.9)
TRAE leading to dose reduction	5 (14.7)
Grade ≥3 TRAE	18 (52.9)
Treatment Related-SAE	12 (35.3)

AE: adverse event; SAE: serious adverse event; TRAE: treatment related adverse event.

Data cutoff: June 30, 2024

TRAEs Occurring ≥15% in UC Patients

	2.2 mg/kg D1D8Q3W (N = 34)		
Preferred Term (PT), n(%)	All Grade	Grade 3	Grade 4
Hematological AE			
Anemia	28 (82.4)	9 (26.5)	0
Leukopenia	24 (70.6)	6 (17.6)	4 (11.8)
Thrombocytopenia	21 (61.8)	4 (11.8)	5 (14.7)
Neutropenia	19 (55.9)	7 (20.6)	4 (11.8)
Lymphocyte count decreased	7 (20.6)	2 (5.9)	0
Non-Hematological AE*			
Decreased appetite	16 (47.1)	1 (2.9)	0
Nausea	15 (44.1)	1 (2.9)	0
Hypoalbuminemia	9 (26.5)	0	0
Vomiting	9 (26.5)	0	0
Alopecia	8 (23.5)	0	0
Asthenia	6 (17.6)	0	0
Constipation	6 (17.6)	0	0
Diarrhea	6 (17.6)	0	0
Stomatitis	6 (17.6)	0	0

* Rash was 11.8% (4/34). All cases were G1.

- No treatment related deaths.
- The most common TRAEs were hematological toxicities.
- The non-hematological toxicities were mostly Grade 1 or 2.
- No interstitial lung disease (ILD) was observed. No new safety signals were observed.

Data cutoff: June 30, 2024

Conclusions

- BL-B01D1 showed encouraging preliminary efficacy and favorable safety profile at 2.2 mg/kg D1D8 Q3W in previously treated urothelial carcinoma, especially at second line.
- Biomarker analysis demonstrated that clinical activity was seen across various levels of EGFR and HER3 expression.
- The most common TRAEs were hematological toxicities, which were manageable.
- The incidence and severity of toxicities related to EGFR and HER3 targeting were relatively low, and no new safety signals were observed.
- Given the promising results, plans are underway for registrational studies

Data cutoff: June 30, 2024

Acknowledgments

- Thanks to all the patients and their families for their participation.
- Thanks to the investigators, study nurses, and other staffs for their contributions to this study.