First-in-human study of DM005, an anti-EGFR/c-MET bispecific antibody-drug conjugate, in patients with advanced solid tumors

#545808
ASCO 2026

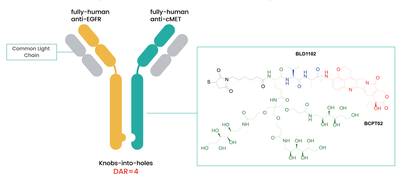
Authors: Jin-Ji Yang, Meili Sun, Yuping Sun, Yong Fang, Jim Coward, Alexander Spira, Reva Schneider, Andrew Parsonson, Meiyu Fang, Zhixiang Zhuang, Adrian Pokorny, Yi-Long Wu

Organizations: Guangdong Provincial People's Hospital, Guangdong, China; Jinan Central Hospital, Shandong, China; Shandong Cancer Hospital, Shandong, China; Sir Run Run Shaw Hospital, Zhejiang University School Of Medicine, Zhejiang, China; ICON Cancer Centre, QLD, Australia; NEXT Oncology Virginia, Virginia, USA; Sarah Cannon Research Institute at Mary Crowley, Texas, USA; Macquarie University Hospital, Sydney, Australia; Zhejiang Cancer Hospital, Zhejiang, China; The Second Hospital Affiliated to Suzhou University, Jiangsu, China; Chris O'Brien Lifehouse, NSW, Australia; Guangdong Provincial People's Hospital, Guangdong, China.

Corresponding Author: Yi-Long Wu, E-mail: syylwu@live.cn.

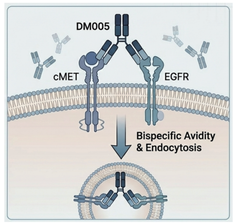
Background

Figure 1: DM005 Molecular Design



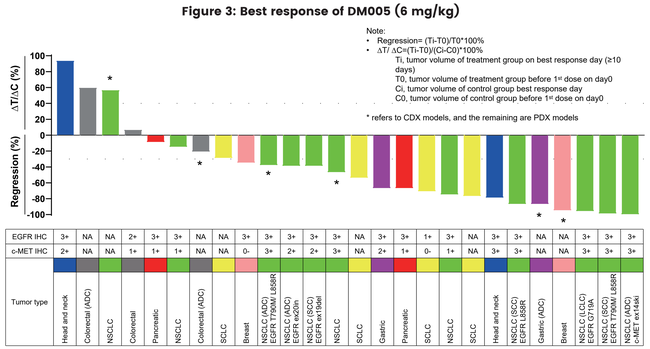
	Sample	ka (1/Ms)	kd (1/s)	KD (M)
DM005	hEGFR-His	1.92E+05	1.65E-02	8.59E-08
	hMET-His	5.95E+04	2.24E-03	3.76E-08

Figure 2: Proposed Mechanism of DM005



- **Mechanism of Action**: DM005 is a novel, first-in-class bispecific antibody-drug conjugate (BsADC) targeting EGFR and c-MET, engineered to overcome resistance mechanisms associated with standard-of-care targeted therapies.(**Figure 2**).
- **Payload & Design**: It utilizes a fully humanized bispecific antibody conjugated to a highly potent DNA topoisomerase I inhibitor (BCPT02) via a proprietary cleavable linker, with an optimized drug-to-antibody ratio (DAR) of 4. (**Figure 1**).
- **Dual-Targeting Rationale**: EGFR and c-MET are frequently co-expressed across various solid tumors (e.g., NSCLC, HNSCC, CRC) and drive tumor progression and treatment resistance. Dual targeting enhances tumor-specific internalization and selectively delivers the cytotoxic payload, overcoming resistance associated with single-pathway inhibition. Preclinical studies demonstrated robust and durable antitumor activity across multiple PDX/CDX models, supporting further clinical development of DM005(**Figure 3**).

Figure 3: Best response of DM005 (6 mg/kg)



Results

Figure 5: Antitumor activity of DM005 in solid tumors

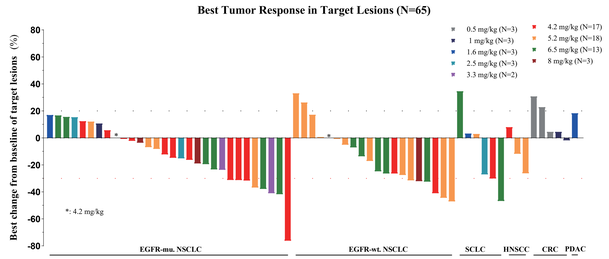
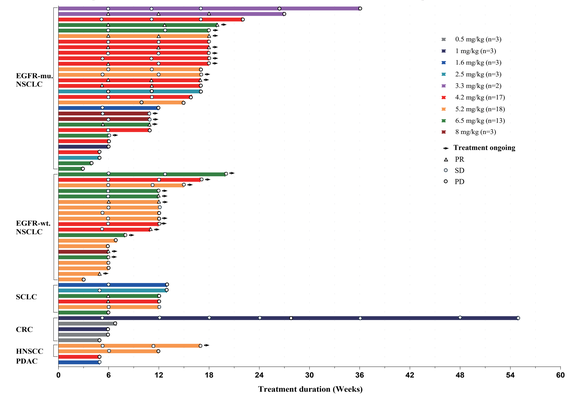


Figure 6: Swimmer plot of treatment time and antitumor activity of DM005 in solid tumors



Preliminary Efficacy

- **Encouraging Antitumor Activity**: Among 65 heavily pretreated patients evaluable for tumor assessment at the data cutoff, DM005 demonstrated robust preliminary clinical benefit across multiple dose cohorts.
- **Broad Efficacy**: Deep and durable tumor regression was observed in NSCLC patients with EGFR-mutant and wild-type, small cell lung cancer (SCLC), and HNSCC.

Table 1: Baseline Characteristics (N=70)

Median age, years (range)	**60 (40-76)**
Sex, n (%)	
Female	**35 (50%)**
Male	**35 (50%)**
Race	
Asian	**58 (82.9%)**
White	**12 (17.1%)**
Baseline ECOG PS, n (%)	
0	**8 (11.4%)**
1	**62 (88.6%)**

Table 2: TEAEs and TRAEs occurring in ≥20% of patients

System Organ Class Preferred Term	TEAE, Overall (N=74), N (%)		TRAE, Overall (N=74), N (%)	
	Any Grade	≥ G 3	Any Grade	≥ G 3
Related to EGFR inhibition				
Constipation	27(36.5)	0	15(20.3)	0
Related to MET inhibition				
Hypoalbuminaemia	24(32.4)	0	15(20.3)	0
Elevation of AST	16(21.6)	0	14(18.9)	0
Related to MET/EGFR inhibition				
Nausea	39(52.7)	2(2.7)	36(48.6)	2(2.7)
Others				
Decreased appetite	31(41.9)	1(1.4)	29(39.2)	1(1.4)
Hypoalbuminaemia	24(32.4)	0	15(20.3)	0
Hypocalcaemia	17(23.0)	0	8(10.8)	0
Hyponatraemia	17(23.0)	1(1.4)	8(10.8)	0
Leukopenia	27(36.5)	7(9.5)	27(36.5)	7(9.5)
Lymphopenia	24(32.4)	9(12.2)	20(27.0)	7(9.5)
Neutropenia	20(27.0)	11(14.9)	20(27.0)	11(14.9)
Aspartate aminotransferase increased	16(21.6)	0	14(18.9)	0
Anaemia	36(48.6)	3(4.1)	34(45.9)	3(4.1)
Fatigue	25(33.8)	1(1.4)	23(31.1)	1(1.4)
Body weight loss	16(21.6)	0	12(16.2)	0

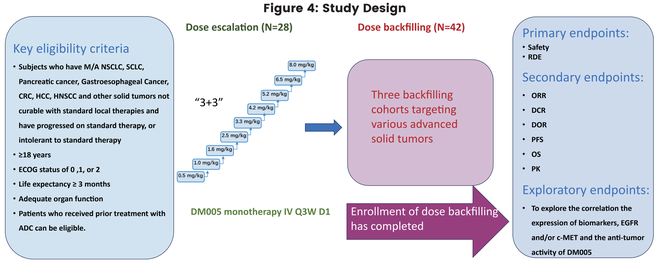
Note: N: number of subject; number of subjects 74 also includes 4 expansion cohort subjects.

Safety Profile

- **Favorable Tolerability**: DM005 was generally well-tolerated at dose levels up to 8.0 mg/kg. The MTD has not been reached, and no DLTs or treatment-related deaths were reported.
- **No ILD and IRR**: Importantly, there were no reports of treatment-related interstitial lung disease (ILD), pneumonitis, or infusion-related reactions (IRRs).
- **Predictable Adverse Events**: The most common treatment-related adverse events (TRAEs) were primarily gastrointestinal and hematologic, including nausea (48.6%) and anemia (45.9%), which were mostly Grade 1 or 2.
- **High-Grade Events**: The most frequent Grade ≥3 TRAEs were neutropenia (14.9%), lymphopenia (9.5%), and leukopenia (9.5%).

Methods

Figure 4: Study Design



- **Study Design**: This is an ongoing, first-in-human, multicenter, open-label Phase 1/2a study (NCT06515990) evaluating DM005 in patients with advanced solid tumors.
- **Dose Escalation (Part 1)**: Utilizes a standard 3+3 design to determine the maximum tolerated dose (MTD) and recommended dose for expansion (RDE).
- **Administration**: DM005 is administered via a single intravenous (IV) infusion every 3 weeks (Q3W), with a 21-day dose-limiting toxicity (DLT) observation period.
- **Assessments**: Tumor response is evaluated by investigator assessment per RECIST v1.1 criteria.

DM005 exhibited a favorable pharmacokinetic profile

The systemic exposure of DM005 increased approximately proportional to dose with the mean $T_{1/2}$ of 52~140 h. The PK parameters of total antibody were similar to those of DM005, suggesting that DM005 was stable in the circulation. The BCPT02 exposure in the blood was much lower than that of DM005.

Conclusions

- DM005 exhibits a highly favorable safety and tolerability profile in patients with heavily pretreated advanced solid tumors, with no DLTs, MTD not reached (up to 8.0 mg/kg), and notably, zero incidence of treatment-related ILD or pneumonitis.
- Through dual EGFR/c-MET targeting and a potent topoisomerase I inhibitor payload, DM005 demonstrates highly encouraging preliminary efficacy, particularly in NSCLC, SCLC, and HNSCC.
- Dose optimization and expansion cohorts are actively enrolling patients across multiple tumor types to further validate these promising early clinical findings.

Acknowledgements

The authors would like to thank all the participants and their families.

All authors have no conflicts of interest to disclose.