1371P An Anti-EpCAM x CD3 Bispecific Antibody, M701, for the Treatment of Malignant Pleural Effusion in NSCLC patients: Intermediate Results of a Prospective Multicenter Phase Ib Trial

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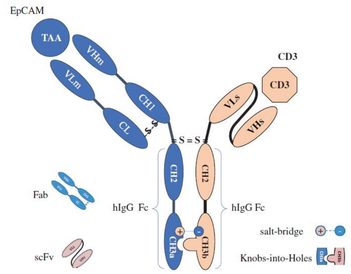
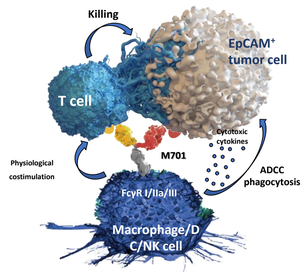
Background:

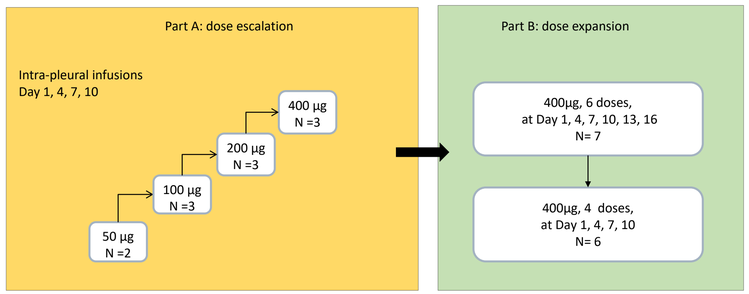
Malignant Pleural Effusion (MPE) : A significant complication in patients with advanced NSCLC and other epithelial cancers, associated with poor prognosis, reduced quality of life and severe symptoms.

M701: An anti-EpCAM x CD 3 bispecific antibody, engaging the T cells to EpCAM positive tumor cells and activating T cells and other immune cells (Macrophage/DC/NK) to kill the tumor cells. The structure of M701 and MOA were illustrated below:





Study design:



NSCLC patients with symptomatic MPE who had failed in at least 1 line of systemic treatment were enrolled. During the dose escalation phase, patients were enrolled across four cohorts. Each cohort received intra-pleural(IP) infusion of M701 at doses of 50, 100, 200, and 400 μg, administered every 3 days on days 1, 4, 7 and 10, respectively. During dose expansion phase, patients received different infusion of M701 with the recommended dose. All patients received systemic treatment during the study.

The primary endpoint of this Phase Ib study is RP2D, including the dosage and frequency of M701 infusion. The efficacy of M701 treating MPE was evaluated via imaging and puncture interval. All kinds of adverse events were collected to evaluate the safety of M701 IP infusion.

M701 (Anti-EpCAM x Anti-CD3) Intra-pleural infusion was SAFE and showed great potential of efficacy!

- M701 Intra-pleural infusion was **SAFE and well tolerated** in NSCLC patients combined with systemic treatment.
- M701 Intra-pleural infusion showed the trend to prevent the accumulation of pleural effusion with **61.5%** successful pleurodesis and **237 days** of puncture-free survival.
- Most EpCAM positive cells in the pleural effusions were eliminated after 3 intra-pleural infusions of M701.

This study was sponsored by Wuhan YZY Biopharma Co. Ltd.(Wuhan, China)

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Results:

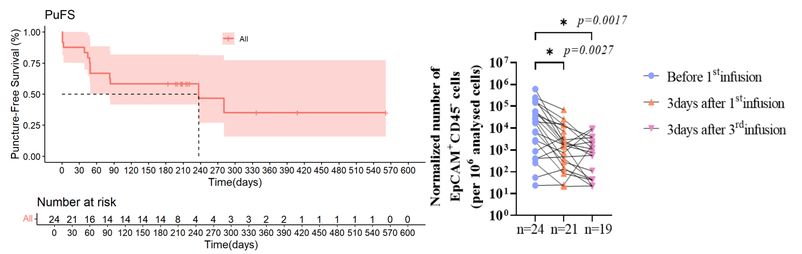
As of April 19, 2024, 24 patients were enrolled. Among them, 11 patients in the dose escalation phase received M701 doses ranging from 50-400μg, while 6 and 7 patients in the dose expansion phase received 4 or 6 doses of M701 every 3 days, respectively.

1) **Baseline:** The characteristics were listed below:

Characteristics	N=24
Age (yrs)，Median	65
Gender，Female	17(70.8%)
ECOG (0-1)	21(87.5%)
Baseline Pleural effusions volume	
<500 mL	6 (25%)
500-1000 mL	10 (41.7%)
> 1000 mL	8 (33.3%)
Previous thoracentesis history	14 (58.3%)
Harboring EGFR mutations	14 (58.3%)
Median prior lines of treatment	3

2) **Safety:** M701 IP infusion was well tolerated and did not report DLT during the dose escalation phase. The SAE incidence was 16.7%, all unrelated to M701. The only 1 case of ≥ Grade 3 TRAE was neutropenia.

3) **Efficacy:** At 4 weeks from the 1st infusion of M701, 61.5% patients in the dose expansion phase achieved MPE objective response (≥ 50% volume decreased) and successful pleurodesis. At 8 weeks, the MPE ORR was 53.8% and the successful pleuraodesis rate was kept at 61.5%. The median Puncture-free survival (PuFS) of 24 patients was 237 days. Flow cytometry analysis revealed that EpCAM+ cells in effusions were significantly eliminated after the initial 3 infusions of M701.



Future Directions:

A phase II trial comparing the efficacy of IP infusion of M701 with IP infusion of cisplatin in NSCLC patients with MPE is currently ongoing. The major endpoint is PuFS which is the preferred indicator of controlling re-accumulation of pleural effusion. Secondary endpoints included MPE ORR, successful pleurodesis rate, safety and PK characters.