1880P A Phase II, randomized, controlled, open label study of M701 Intra-pleural infusion in patients with Malignant Pleural Effusion caused by NSCLC: Intermediate Results

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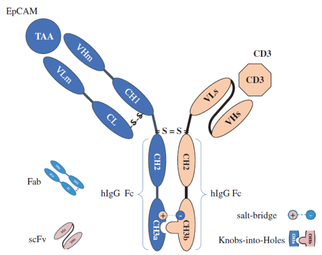
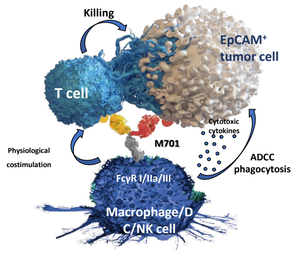
Background:

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. In China, local chemotherapy is a common treatment method that can provide non-durable control of MPE.

M701: An anti-EpCAM x CD3 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 mechanism of action were illustrated below:





Study design:

NSCLC patients with MPE at least 1 prior treatments (N=92)

Key eligibility criteria
- >1L systemic treatment
- ECOG PS: 0-2
- Symptomatic, moderate-large volume MPE(Seated ultrasound showing pleural effusion depth ≥4 cm, estimated volume ≥500 mL.)

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- **Thoracentesis + Intra-pleural infusion of M701 (N=46)[a]**
- **Thoracentesis + Intra-pleural infusion of Cisplatin (N=46)[b]**

Primary endpoints:
- Puncture-free survival (PuFS)

Secondary endpoints:
- MPE ORR
- TTNP
- PRO (Patients reported outcome)
- PD
- immunogenicity

a. receive M701 infusion （25/400μg） at Day 1,4,7,10;
b. receive Cisplatin infusion （40mg）at Day 1, 7.

NSCLC patients with symptomatic MPE who had failed in at least 1 line of systemic treatment were enrolled. Enrolled subjects were assigned into 2 arms randomly. M701 arm received intra-pleural(IP) infusion of M701 at doses of 25-400-400-400μg, administered on days 1, 4, 7 and 10). Control arm received IP infusion of Cisplatin at 2 doses of 40mg, on days 1 and 7. The catheter was removed on Day 10 after sufficient drainage . All patients received systemic treatment during the study.

The primary endpoint is Puncture-free Survival (PuFS), defined as the survival time from Day 10 to the day of intolerance of MPE or death, which is a composed time to event endpoint. Secondary end points included MPE objective response rate (ORR), Time to next puncture (TTNP), symptoms and signs related to MPE, pharmacodynamic and immunogenicity.

M701 (Anti-EpCAM x Anti-CD3) Intra-pleural infusion showed favorable efficacy in MPE!

- In driven gene-negative NSCLC patients or NSCLC patients who had prior intra-pleural chemotherapy, M701 infusion showed significant efficacy of preventing the re-accumulation of pleural effusion (mPuFS **253 days vs. 71 days, p=0.021**).

Results:

As of Mar 07, 2025, 54 subjects were enrolled, 26 in M701 arm and 28 in cisplatin arm.

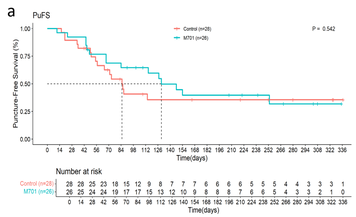
1） Baseline: The characteristics were listed below:

Characteristics	M701 Arm N= 26	Control Arm N=28
Age (yrs)，Median	66.5	61.5
Gender，Female	15(57.7%)	14(50.0%)
ECOG (0-1)	24(92.3%)	27(96.4%)
Baseline Pleural effusions volume		
<500 mL	5(19.2%)	6 (21.4%)
≥500 mL	17 (65.4%)	19 (67.9%)
Previous thoracentesis history	17 (65.4%)	20 (71.4%)
Driven gene mutations-positive	20 (76.9%)	22 (78.6%)
Previous systematic treatment		
TKIs	20 (76.9%)	22 (78.6%)
chemotherapies	16(61.5%)	16(57.1%)

2) **Safety:** Both M701 and Cisplatin intra-pleural infusion were safe and well tolerated in the subjects (≥Gr 3 TEAE 34.6% VS 35.7%). The common TRAEs in the M701 arm were increased lipase (19.2%), while the common TRAEs in the control arm were nausea (17.9%) and vomiting (10.7%).

3) **Efficacy:** The primary endpoint was median PuFS, data showed below. The best MPE ORR were 72.7% and 41.7% in the M701 and Control arms, respectively. The results showed that NSCLC patients who have received chemotherapy, whether they underwent systemic therapy or local therapy, all exhibited a very good response to M701 local treatment.

mPuFS (days)	M701	Control	HR	P value
All patients (n=26 vs 28) (Fig. a)	130	85	0.8	0.542
Driven gene negative NSCLC patients （n= 6 vs 6） (Fig. b)	Not reached	44.5	<0.01	<0.001
NSCLC patients with prior IP chemotherapy （n= 11 vs 10） (Fig. c)	253	72	0.31	0.076
Driven gene positive NSCLC patients without prior IP chemotherapy (n=13 vs 14)	127	114	1.58	0.366



Flow cytometry analysis revealed that EpCAM+ CD45- tumor cells in pleural effusions were significantly decreased after M701 infusions, but not in the control arm with Cisplatin infusions (Fig. d).

Future Directions:

This Phase II trial is ongoing and has demonstrated promising potential in preventing the re-accumulation of pleural effusion, particularly in driver gene-negative NSCLC patients, or driver gene-positive NSCLC patients who had prior intrapleural chemotherapy. A pivotal phase III trial is planned for 2026 to validate its efficacy and safety in a large-scale Chinese population.

Contract Dr. Song for more details of this trial: songzb@zjcc.org.cn (Dr. Zhengbo Song)