#12060: An Anti-EpCAM x Anti-CD3 Bispecific Antibody, M701, for the Treatment of Malignant Ascites Due to Epithelial Cancer: Interim Results of a Prospective Randomized Controlled Phase II Trial

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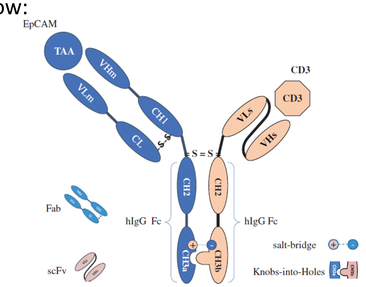
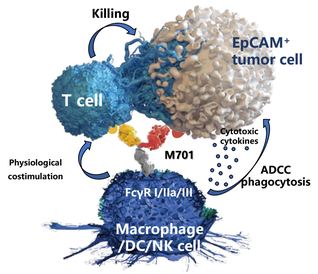
Background:

Malignant ascites (MA) : A significant complication in advanced cancer patients, associated with poor prognosis, reduced quality of life and severe symptoms.
M701: An anti-EpCAM x CD 3 bispecific antibody, sharing same targets as Catumaxomab (EMA approved in 2009). The structure and MOA were illustrated below:





Study design:

MA patients with advanced epithelial solid tumors with at least 2 prior treatments (N=84)

Key eligibility criteria
- >2L gastrointestinal tumors, platinum resistant ovarian cancer
- ECOG PS: 0-2
- Moderate-large volume ascites

Stratification factors
- Cancer Types
- Whether change the regime of systemic treatment.

R 1:1

Arm E: IP infusion of M701 (N=43)

Transfer after re-puncture

Arm C: Paracentesis (N=41)

Both Arms received systemic tumor treatment as per the investigators' instructions

Primary endpoints:
- Puncture-free survival (PuFS)

Secondary endpoints:
- PFS, OS
- Safety
- popPK, immunogenicity

The experimental arm (Arm E) of the study receives intraperitoneal (IP) infusion of M701 at doses of 50, 400, 400, and 400μg of M701 on days 1, 4, 11, and 18 respectively, with additional infusions available every 2 weeks without requiring further punctures. The control arm (Arm C) receives paracentesis as needed from day 1 to day 18 without M701 administration.
The primary endpoint of the study is puncture-free survival (PuFS), defined as the time from Day 18 to the next puncture or death, whichever occurs first.

Results:

As of Dec 15, 2023, 84 patients were enrolled, with 43 in Arm E and 41 in Arm C. 1 patient in Arm C dropped out before any treatment, and 7 patients transferred from Arm C to Arm E after the re-puncture. The FAS comprised 43 patients in Arm E and 40 in Arm C, while the Safety Set included 50 patients in Arm E and 40 in Arm C.

M701 (Anti-EpCAM x Anti-CD3) IP infusions significantly prolonged the puncture interval of patients with malignant ascites (54 VS 24 days)!

- M701 IP infusion is **SAFE** in MA patients combined with systemic treatment.
- M701 IP infusion showed the trend to prolong the OS in MA patients.
- Survival benefits achieved in the **Gastric** cancer population (128 VS 64 days, p=0.0438).

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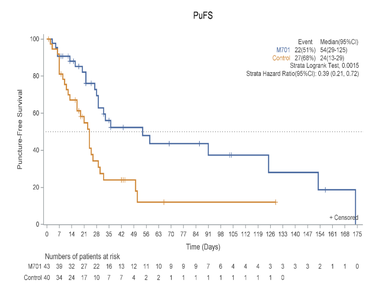
1) Baseline: The characteristics were listed below:

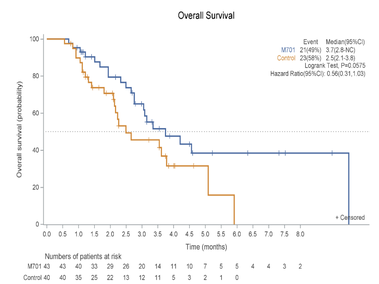
Characteristics	Arm E (N=43)	Arm C (N=41)
Age (yrs), Median	54	54
Gender, Male	33%	34%
ECOG (0-1)	89%	88%
Cancer Type		
Gastric	49%	49%
Ovarian	30%	32%
Colorectal	19%	17%
Previous paracentesis	63%	54%
Previous IP chemotherapy	58%	56%

2) Safety: M701 IP infusion was well tolerated and did not pose a higher risk compared to control arm. Low CRS incidence and grade were observed.

Safety	Arm E (N=50)	Arm C (N=40)
TEAE	98%	98%
Grade 3 TEAE	52.0%	57.5%
SAE	38.0%	50.0%
CRS (grade 1-2)	4%	0%

3) Efficacy: M701 IP infusion extended the PuFS with significance (54 days VS 24days, HR = 0.39, **p=0.001**), and indicated a trend toward prolonged overall survival (OS) (113 days VS 76 days, HR= 0.56, p= 0.0575) . Specifically, in gastric cancer patients, the median OS were 128 days VS 64 days, HR = 0.45, **p = 0.0438**.





The PuFS rate and OS rate were listed below:

PuFS rate	Arm E (N=43)	Arm C (N=40)	OS rate	Arm E (N=43)	Arm C (N=40)
Half a month % (95%CI)	88.0 (73.5, 94.8)	67.1 (49.4, 79.8)	2-month % (95%CI)	72.7 (56.8, 83.6)	70.7 (53.2, 82.7)
1-month % (95%CI)	62.8 (44.2, 76.7)	27.4 (13.3, 43.6)	3-month % (95%CI)	59.5 (42.9, 72.7)	45.6 (27.5, 62.0)
2-month % (95%CI)	43.6 (25.2, 60.6)	12.0 (2.5, 29.4)	6-month % (95%CI)	35.2 (19.2, 51.7)	15.8 (1.60, 44.1)

Future Directions:

A pivotal trial of M701 as a novel treatment for MA has been launched based on the data of phase II trial. Meanwhile, combination therapy of M701 with ICIs or ADC, as well as adjuvant therapy with M701 in gastrointestinal and ovarian cancer will be explored.