AFM24 and atezolizumab combination in patients with advanced epidermal growth factor receptor-expressing (EGFR+) solid tumors: Initial results from the Phase 1 dose-escalation study

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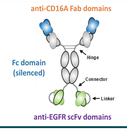
BACKGROUND

- Tumor immune escape through suppression of immune effector cell activity is a major hurdle for the eradication of solid tumors by a patient's own innate and adaptive immune responses[1,2]
- Antibody-based immunotherapies that reinvigorate and enhance the activity of endogenous immune responses are becoming increasingly relevant across a range of onco-therapy areas[3–5]
- AFM24, a bispecific innate cell engager (ICE®), binds to EGFR on solid tumor cells, and CD16A on natural killer (NK) cells or macrophages, resulting in redirection and activation of these cells, enhancing anti-tumor antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis, respectively[5]
- Preclinical studies have shown that AFM24 induces NK cell-mediated cytotoxicity of EGFR$^+$ solid tumor cell lines[6], and a well-managed safety profile has been observed in an ongoing monotherapy trial[7]
- Atezolizumab, a PD-L1 inhibitor that relieves tumor immunosuppression of cytotoxic T cells, is approved for the treatment of several types of solid malignancies[8,9]
- Combining AFM24 with atezolizumab may utilize the cross-talk between the innate and adaptive immune responses to synergistically enhance anti-tumor activity and clinical outcomes in patients with EGFR$^+$ solid tumors

AFM24 STRUCTURE

AFM24 is a tetravalent EGFR/CD16A-specific IgG1-scFv fusion antibody (scFv-IgAb) with a silenced IgG1 Fc domain derived from the ROCK® platform

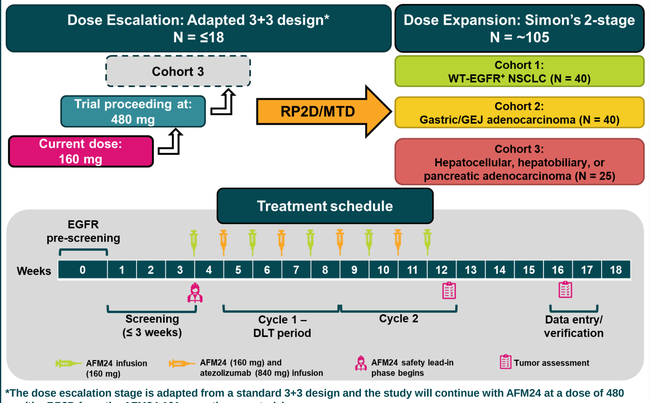


AFM24-102 PHASE 1 PRIMARY OBJECTIVE

An open-label, non-randomized, multicenter, dose escalation study (NCT05109442) is establishing the recommended phase 2 dose(s) (RP2D) or maximum tolerated dose (MTD) and investigating the safety and tolerability of the combination of AFM24 and atezolizumab

STUDY DESIGN

Key inclusion criteria: Patients must be aged 18 or over; have confirmed EGFR expression in ≥1% tumor cells; have a diagnosis of any of the solid tumors eligible for the dose expansion phase; have progressed on all relevant standard-of-care therapies; have an Eastern Cooperative Oncology Group (ECOG) score of 0–1; have evaluable or measurable disease per Response Evaluation Criteria in Solid Tumors (RECIST v1.1)



***The dose escalation stage is adapted from a standard 3+3 design and the study will continue with AFM24 at a dose of 480 mg (the RP2D from the AFM24-101 monotherapy study).**

DLT, dose-limiting toxicity; EGFR, epidermal growth factor receptor; GEJ, gastro-esophageal junction; MTD, maximum tolerated dose; NSCLC, non-small cell lung cancer; RP2D, recommended Phase 2 dose; WT, wild-type.

RESULTS

- As of 07 June 2022, a total of four patients were enrolled in the study; baseline characteristics are shown in Table 1

Table 1: Summary of demographics and patient characteristics

	n (%), n=4
Age: Mean (range)	60 (50–73)
Sex: Female	4 (100)
ECOG PS 0 1	 3 (75) 1 (25)
Ethnicity: Caucasian	4 (100)
Number of prior lines: Median (range)	3.5 (3–4)
Tumor type Gastric cancer Pancreatic adenocarcinoma	 1 (25) 3 (75)

ECOG, Eastern Cooperative Oncology Group; PS, performance score.

Safety of AFM24 + atezolizumab

- Three out of four patients completed the safety lead-in phase with AFM24 at 160 mg
  - One patient withdrew from the study after a Grade 2 infusion-related reaction (IRR) in the safety lead-in phase; this patient was not included in the DLT evaluation
- Two serious adverse events (SAEs) were reported, both during the safety lead-in phase
  - One Grade 1 medication error which did not have a deleterious effect on the patient; one Grade 2 IRR requiring prolonged hospital admission for administrative reasons
- IRRs were reported in two patients in the safety population (Table 2)
  - All observed IRRs occurred exclusively during the first AFM24 infusion, were manageable, and controlled with anti-histamines
- There were no on-study deaths
- No grade 3–4 skin toxicities were reported (Table 3) and no dose-limiting toxicities (DLTs) occurred
- Transient and reversible Grade 3 TEAEs were reported in two patients

Table 2: Summary of TEAEs by incidence

Adverse event, n (patients)	All (n=4)	AFM24-related (n=4)	Atezolizumab-related (n=4)
Infusion-related reactions	3 (2)	3 (2)	0
TEAE ≥Grade 3	3 (2)	3 (2)	1 (1)
Serious TEAE	2 (2)	2 (2)	0
Fatal TEAE	0	0	0
TEAE leading to study drug discontinuation	1 (1)	1 (1)	0

TEAE, treatment-emergent adverse event.

Table 3: Summary of TEAEs by grade

Adverse event, n (patients)	Grade 1/2	Grade 3*	Overall
Any study drug-related TEAE	33 (4)	3 (2)	36 (4)
Lymphocytopenia	13 (4)	3 (2)	16 (4)
Anemia	4 (2)	0	4 (2)
Neutropenia	4 (2)	0	4 (2)
Infusion-related reactions	3 (2)	0	3 (2)
Thrombocytopenia	2 (1)	0	2 (1)
Cough	1 (1)	0	1 (1)
Dyspnea	1 (1)	0	1 (1)
Vomiting	1 (1)	0	1 (1)
Fever	1 (1)	0	1 (1)
Asthenia	1 (1)	0	1 (1)
Ascites	1 (1)	0	1 (1)
Medication error	1 (1)	0	1 (1)

*No Grade 4/5 TEAEs were reported. TEAE, treatment-emergent adverse event.

Among the three patients evaluated in Cohort 1, one patient has shown a partial response, and another has exhibited stable disease

A patient with gastric cancer achieved a partial response after two cycles of AFM24 in combination with atezolizumab

- **50-year-old female**
- **Gastric adenocarcinoma**
  - Diffuse type, signet ring histology
  - Microsatellite stable (MSS), HER2-negative, PD-L1 not evaluated
  - *TP53* (V172F) mutation
  - Stage IV (cutaneous, subcutaneous, bone and peritoneal metastases)
  - EGFR+ H-score:190
- **Diagnosed October 2020**

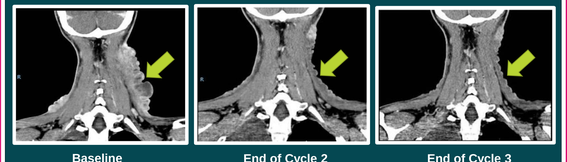
Treatment history

Nov 2020 – Mar 2021	Apr 2021 – Jul 2021	Aug 2021 – Dec 2021	Aug 2021 – Dec 2021
Oxaliplatin + Capecitabine + Pembrolizumab	Paclitaxel	Irinotecan	FOXP3 inhibitor
Partial response; Progressed	Progressive disease	Progressive disease	Progressive disease

The patient's skin metastases did not respond to any prior treatment lines

An ongoing partial response was observed following two cycles of AFM24 in combination with atezolizumab

Computerized tomography (CT) scans



Informed consent was obtained from the patient for the publication of these images.

A patient with pancreatic adenocarcinoma exhibited stable disease after two cycles of the combination therapy

- **65-year-old female**
- **Pancreatic adenocarcinoma**
  - Microsatellite stable (MSS)
  - Loco-regional recurrence
  - Pelvic mass and ascites
  - EGFR+ (H-score: 130)
- **Diagnosed June 2020**

Treatment history

Jul 2020 – Aug 2020	Sep 2020 – Sep 2021	Sep 2021 – Dec 2021
Gemcitabine + Nab-paclitaxel	FOLFOX	FOLFIRI
Progressive disease	Partial response; progressed	Progressive disease

As of the data cut-off, this patient is exhibiting stable disease

Informed consent was obtained from the patient for the publication of these images.

FOLFOX, leucovorin-fluorouracil-oxaliplatin; FOLFIRI, leucovorin-fluorouracil-irinotecan.

A further patient was awaiting their first tumor assessment at the time of data cut-off

- **73-year-old female**
- **Pancreatic adenocarcinoma**
  - Microsatellite stable (MSS)
  - Loco-regional recurrence
  - Lung and peritoneal metastases
  - EGFR+ (H-score: 160)
- **Diagnosed with localized disease in January 2019; diagnosed with local relapse and lung metastases in June 2019**

Treatment history*

Jul 2019 – Apr 2020	Jul 2020 – Dec 2020 – Feb 2021	Feb 2021 – Mar 2021	Jun 2021 – Feb 2022
Gemcitabine + Nab-paclitaxel	FOLFOX – capecitabine	FOLFIRI	Gemcitabine
Stable disease; progressed	Stable disease; progressed	Progressive disease	Stable disease; progressed

*Treatment at initial diagnosis: surgery. The patient but did not receive adjuvant chemotherapy due to fatty liver disease. She received capecitabine as a maintenance therapy from Dec 2020 to Feb 2021.

FOLFOX, leucovorin-fluorouracil-oxaliplatin; FOLFIRI, leucovorin-fluorouracil-irinotecan.

CONCLUSIONS

- **AFM24 at 160 mg in combination with atezolizumab demonstrated a well-managed safety profile; no DLTs were reported**
- **Clinical activity was observed in two patients as of June 7, 2022**
- **The study is ongoing and dose escalation is proceeding at a dose of 480 mg AFM24**

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