A Phase 1/2a Open Label, Multi-Center Study to Assess the Safety, Tolerability, Pharmacokinetics, and Efficacy of AFM24 in Patients with Advanced Solid Cancers: Study Design and Rationale

TPS2672

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BACKGROUND

EGFR IS A KEY THERAPEUTIC TARGET

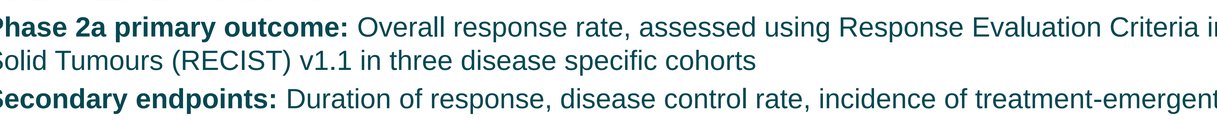
- Epidermal growth factor receptor (EGFR) is frequently overexpressed on the cell surface in solid tumors making it an ideal therapeutic target[1]
- Overexpression is typically a strong prognostic indicator[1], but not all patients respond to EGFR inhibitors[2], and in patients who are responsive, acquired resistance invariably occurs[3]; therefore, novel therapies acting independently of EGFR signaling are required

AFM24

- Derived from the Redirected Optimized Cell Killing (ROCK®) antibody platform, AFM24 is a first-in-class, bispecific, tetravalent, Innate Cell Engager (ICE®) that targets EGFR
- AFM24 has four binding sites: two for CD16A, the Fcγ receptor expressed by natural killer (NK) cells and macrophages, and two for EGFR
- AFM24 engages CD16A on NK cells and macrophages with a higher affinity than monoclonal antibodies and triggers antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP), respectively, directed at EGFR-expressing ($EGFR^+$) cancer cells[4]
- Preclinical data have shown that AFM24 can induce NK cell-mediated killing of $EGFR^+$ solid tumor cell lines, independent of EGFR mutational status and that AFM24 monotherapy has a well-managed safety profile in cynomolgus monkeys[5]
- An ongoing Phase 1/2a open-label, non-randomized, first-in-human, multi-center study (NCT04259450) was initiated in April 2020; an estimated 156 patients will be enrolled

PHASE 1 SUMMARY: DOSE ESCALATION

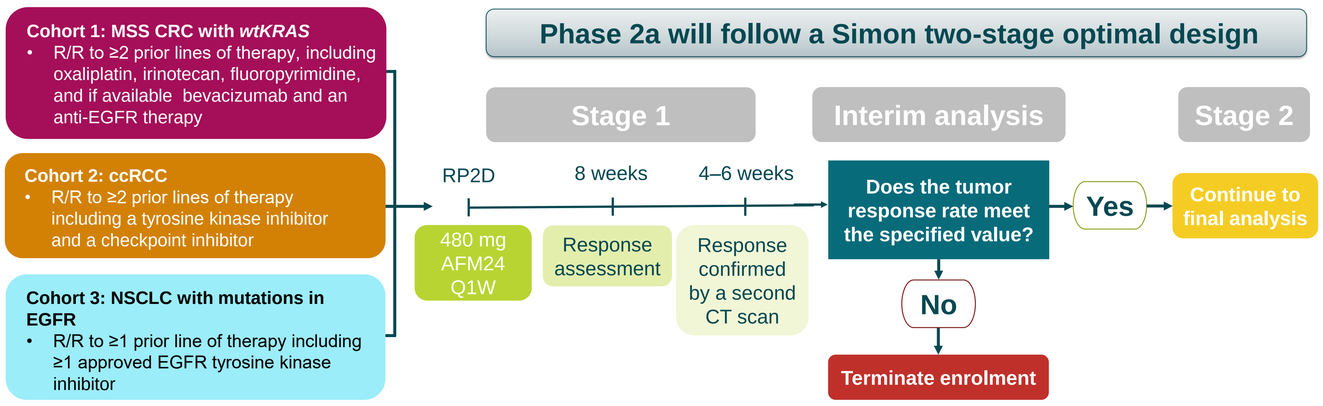
- Phase 1 was designed to establish the maximum tolerated dose (MTD) and/or the recommended Phase 2 dose (RP2D) of AFM24
- The primary outcome was to assess the incidence of dose-limiting toxicities, assessed by National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) v5.0
- AFM24 was administered intravenously once weekly at 14-720 mg in 28-day cycles and tumor assessment was performed every 8 weeks until disease progression, intolerable toxicity, patient withdrawal, or termination at the investigator's discretion
- As of April 2022, 34 patients were enrolled and treated
- AFM24 had a well-managed safety profile and a RP2D was established as 480 mg[6]
  - Dose escalation at 720 mg is ongoing



STUDY DESIGN

PHASE 2A: DOSE EXPANSION

- The dose-expansion phase will use the RP2D determined in Phase 1 and is designed to collect preliminary evidence of efficacy and to further confirm the safety of AFM24
- The first patient was enrolled in the Phase 2a study in January 2022



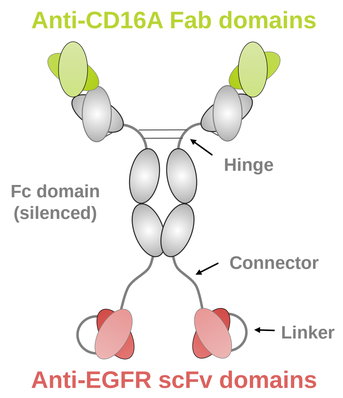
ccRCC, clear cell renal cell carcinoma; CRC, colorectal cancer; CT, computed tomography; EGFR, epidermal growth factor receptor; MSS, microsatellite stable; NSCLC, non-small cell lung cancer; RP2D, recommended Phase 2 dose; TKI, tyrosine kinase inhibitor; wt, wild-type.

STUDY ENDPOINTS

- **Phase 2a primary outcome:** Overall response rate, assessed using Response Evaluation Criteria in Solid Tumours (RECIST) v1.1 in three disease specific cohorts
- **Secondary endpoints:** Duration of response, disease control rate, incidence of treatment-emergent and serious adverse events and assessment of PK/PD and immunogenicity of AFM24

AFM24 STRUCTURE

AFM24 is a tetravalent EGFR/CD16A-specific IgG1-scFv fusion antibody (scFv-IgAb) with a silenced IgG1 Fc region.



OBJECTIVE

To assess the safety, tolerability, pharmacokinetics and efficacy of AFM24 monotherapy in locally advanced or metastatic, treatment-refractory, $EGFR^+$ solid tumors

STUDY ELIGIBILITY CRITERIA

Inclusion criteria	
General	Aged ≥18 years
	Adequate organ function
Phase 1	Histologically or cytologically confirmed, advanced or metastatic, solid malignancies known to express EGFR
	Previously treated with ≥1 line of anticancer therapy plus documented disease progression during or after most recent line of therapy, plus either there is no further standard of care (SOC) therapy for the patient or the remaining SOC therapies are deemed inappropriate by the investigator
	≥1 tumor site that is accessible for biopsy
Phase 2a	Measurable disease per RECIST 1.1
	Confirmed advanced or metastatic select solid malignancies (as shown in the study design), with EGFR positivity in >1% of tumor cells as determined by immunohistochemistry
Exclusion criteria	
General	Treatment with systemic anticancer therapy (excluding hormonal therapy or radiotherapy) within 4 weeks (6 weeks if therapy was mitomycin C and/or nitrosoureas), or within 5 half-lives of the agent if half-life is known and it is shorter, before first dose of study drug
	Radiation therapy within 2 weeks before 1st dose of study drug or unresolved toxicity from previous radiotherapy
	History of any other invasive malignancy, unless previously treated with curative intent and the subject has been disease free for ≥3 years. Examples of acceptable previous malignancies include completely removed in situ cervical intra-epithelial neoplasia, non-melanoma skin cancer, ductal carcinoma in situ, and early-stage prostate cancer that has been adequately treated
	Currently participating in a study and receiving study therapy, or participated in a study of an investigational agent and received study therapy or used an investigational device within 4 weeks of the first dose of study treatment

KEY POINTS

- A Phase 1/2a study is assessing the safety, tolerability and efficacy of the EGFR-targeting ICE® molecule, AFM24, as a monotherapy in patients with $EGFR^+$ solid tumors
- Phase 1 indicated that AFM24 monotherapy has a well-managed safety profile and has established the RP2D as 480 mg
- Phase 2a will collect preliminary efficacy data and further confirm the safety of AFM24 monotherapy in three cohorts of tumor types, namely CRC, ccRCC and NSCLC

REFERENCES

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