

## AFM24 AND ATEZOLIZUMAB COMBINATION IN PATIENTS WITH ADVANCED EPIDERMAL GROWTH FACTOR RECEPTOR-EXPRESSING (EGFR<sup>+</sup>) SOLID TUMORS: INITIAL RESULTS FROM THE PHASE 1 DOSE-ESCALATION STUDY

<sup>1</sup>Omar Saavedra Santa Gadea\*, <sup>2</sup>Daniela Morales-Espinosa, <sup>3</sup>Juanita Lopez, <sup>4</sup>Eric Christenson, <sup>5</sup>Anthony El-Khoueiry, <sup>6</sup>Andrés Cervantes, <sup>2</sup>Christa Raab, <sup>2</sup>Ulrike Gärtner, <sup>2</sup>Kerstin Pietzko, <sup>2</sup>Laura Kohlhas, <sup>2</sup>Daniel Schütz, <sup>2</sup>Gabriele Hintzen, <sup>2</sup>Paulien Ravenstijn, <sup>2</sup>Michael Emig, <sup>7</sup>Pilar Nava-Parada. <sup>1</sup>Vall D'Hebron University Hospital, Barcelona, Spain; <sup>2</sup>Affimed GmbH, Heidelberg, Germany; <sup>3</sup>Royal Marsden Hospital, London, UK; <sup>4</sup>John Hopkins University Hospital, Baltimore, MD, USA; <sup>5</sup>University of Southern California, Los Angeles, CA, USA; <sup>6</sup>Hospital Clínico, University of Valencia, Valencia, Spain; <sup>7</sup>Affimed Inc., New York, NY, USA

**Background** AFM24 is an innate cell engager binding EGFR on tumor cells, and CD16A on natural killer cells and macrophages; AFM24 activates and redirects these cells to EGFR<sup>+</sup> tumors to enhance antibody-dependent cellular cytotoxicity and antibody-dependent phagocytosis, respectively. Atezolizumab, a PD-L1 inhibitor, has been approved in patients with solid tumors. Combining AFM24 with atezolizumab may synergistically enhance the innate and adaptive immune responses, respectively, to target EGFR<sup>+</sup> tumors.

**Methods** AFM24-102 (NCT05109442) is a Phase 1/2a open-label, non-randomized, multicenter, dose escalation, and expansion study evaluating AFM24 in combination with atezolizumab in patients with selected EGFR<sup>+</sup> advanced solid malignancies whose disease has progressed after treatment with previous anticancer therapies. Phase 1 will follow a 3+3 design to establish the maximum tolerated dose or recommended phase 2 dose of AFM24; patients will receive AFM24 IV QW at an escalating dose per cohort and 840 mg atezolizumab IV once fortnightly in a 4-week cycle until disease progression, intolerable toxicity, termination by the investigator, or patient withdrawal. Secondary endpoints include pharmacokinetic, pharmacodynamic, and immunogenicity analysis. A starting dose of 160 mg QW of AFM24 was selected based on data from an ongoing Phase 1/2a first-in-human trial of AFM24 monotherapy.

**Results** Four patients have been enrolled in the first dose cohort, with three completing the safety lead-in phase and receiving 160 mg AFM24 and atezolizumab. Patients are female with gastric (n=1) or pancreatic (n=3) adenocarcinomas (median [range] age was 60 years [50–73], number of prior therapies was 3.5 [3–4], with 90% EGFR expression [70–100%] by immunohistochemistry). All patients have European Cooperative Oncology Group scores of 0–1. Adverse events (AEs) (n≥2) included lymphopenia, anemia, neutropenia, and infusion-related reactions. No dose-limiting toxicities (DLTs) occurred. Serious AEs likely related to AFM24 treatment were one Grade 2 IRR and one Grade 1 medication error. In the patient with gastric cancer and skin metastases, who had rapidly progressed following four prior lines of therapy, including a PD-L1 inhibitor, an ongoing partial response has been confirmed after two cycles of AFM24 treatment. A still ongoing stable disease of 4+ months and symptomatic improvement has been observed in a patient with pancreatic adenocarcinoma that had rapid disease progression after three lines of previous therapy.

**Conclusions** AFM24 at 160 mg in combination with atezolizumab was adequately tolerated. No DLTs were reported. Clinical activity was observed in two patients. Dose escalation is proceeding at 480 mg and enrollment has begun.

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**Trial Registration** NCT05109442

**Ethics Approval** The study is being conducted in accordance with ICH GCP, the Declaration of Helsinki, the European Union Clinical Trials Directive 2001/20/EC, the GCP Directive 2005/28/EC, the requirements of local IRB/EC, and the US Code of Federal Regulations, Title 21 CFR Part 50. The principles of informed consent in the Declaration of Helsinki and GCP guidelines are being implemented before any protocol-specific procedures or interventions are carried out.

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