BACKGROUND

EGFR is overexpressed in many solid cancers and can be an indicator of poor prognosis.1,2 Clinically used EGFR signaling inhibitors have various limitations including:

1. Resistance related to the inhibition of EGFR signaling in healthy tissues.3,4
2. Intrinsically and acquired resistance.5-7 AFM24 engages CD16A on NK cells and macrophages with a higher affinity than therapeutic monoclonal antibodies; once engaged, AFM24 can trigger responses against EGFR-expressing cancer cells including:

- NK cell-mediated antibody-dependent cellular cytotoxicity (ADCC)
- Macrophage-mediated antibody-dependent cellular phagocytosis (ADCP)

This mechanism of action may be instrumental to the efficacy of AFM24, especially in macrophage-rich tumors.

OBJECTIVE

To assess the ability of AFM24 to induce antibody-dependent cellular phagocytosis in solid tumor cell lines expressing wildtype EGFR or EGFR signaling pathway mutations.

RESULTS

AFM24 is more efficacious than cetuximab in inducing ADCP of EGFR+ (wildtype and KRAS mutant) tumor cells.

CONCLUSIONS

- AFM24 enhances macrophage-mediated ADCP of various EGFR expressing tumor cell lines, irrespective of the EGFR signaling pathway; this has been confirmed using two independent methods over 24 h kinetics.
- AFM24 can induce ADCP mediated by various macrophage subtypes.
- This mechanism of action may be instrumental to the efficacy of AFM24, especially in macrophage-rich tumors.
- AFM24 is superior to cetuximab in induction of ADCP.

REFERENCES


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AFM24 is superior to cetuximab at inducing phagocytosis of EGFR+ (wildtype and KRAS mutant) cells in live cell imaging analysis over 24 hours.

Monocyte-differentiated macrophages (M0) from healthy donor PBMCs were co-cultured for 4 hours with CMFDA-labelled wildtype EGFR-expressing or KRAS mutant tumor cells in the presence of 10 µg/mL AFM24 or cetuximab. ADCP was assessed by flow cytometry (FACS). Shown are representative plots from 1 donor; n= 2-3.

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M0 macrophages were co-cultured with pHRodoTM-labelled tumor cells in the presence of 10 µg/mL AFM24 or cetuximab and phagocytosis was assessed by live cell-imaging analysis (IncuCyte®) over 24 hours. Data shown represent 1 donor; n= 2-3.