MORAb-202, a novel antibody-drug conjugates (ADC) comprised of farletuzumab conjugated with eribulin, exhibits long-lasting targeted antitumor activity and payload-mediated bystander effects on the tumor microenvironment.

Introduction

Farletuzumab, a humanized antibody targeting human fraktor receptor alpha (HFRα), has been investigated in patients with metastatic breast cancer (MBc) who have previously received at least 2 chemotherapy regimens for the treatment of metastatic disease. Prior therapy should include an anthracycline and a taxane in the adjuvant or metastatic setting. Subpopulation analysis of a phase 3 trial revealed that patients with TNBC, a subtype of BC that demonstrates very poor survival, had a longer OS compared to patients with HER2+ BC (i.e. for overall survival [OS] = $P_{0.05}$). In addition, 100 patients with HER2+ BC were observed in the abirateron arms and compared to the comparator arm for new metastases (i.e. HR).

To date, it has been demonstrated that eribulin blocks microtubule growth by binding to microtubule [H] ends (i.e. modified from ref 12). Eribulin also blocks microtubule growth by binding to microtubule [H] ends (i.e. modified from ref 12). Eribulin also blocks microtubule growth by binding to microtubule [H] ends (i.e. modified from ref 12). Eribulin also blocks microtubule growth by binding to microtubule [H] ends (i.e. modified from ref 12). Eribulin also blocks microtubule growth by binding to microtubule [H] ends (i.e. modified from ref 12). Eribulin also blocks microtubule growth by binding to microtubule [H] ends (i.e. modified from ref 12). Eribulin also blocks microtubule growth by binding to microtubule [H] ends (i.e. modified from ref 12). Eribulin also blocks microtubule growth by binding to microtubule [H] ends (i.e. modified from ref 12). Eribulin also blocks microtubule growth by binding to microtubule [H] ends (i.e. modified from ref 12). Eribulin also blocks microtubule growth by binding to microtubule [H] ends (i.e. modified from ref 12). Eribulin also blocks microtubule growth by binding to microtubule [H] ends (i.e. modified from ref 12). Eribulin also blocks microtubule growth by binding to microtubule [H] ends (i.e. modified from ref 12). Eribulin also blocks microtubule growth by binding to microtubule [H] ends (i.e. modified from ref 12).

Figure 1: Structure of MORAb-202

Figure 2: In vitro cytotoxicity of MORAb-202

Figure 3: Competitive inhibition of the cytotoxic activity of MORAb-202 by farletuzumab

Figure 4: Bystander effect of MORAb-202 against PFA-negative cancer cells

Figure 5: In vivo efficacy of MORAb-202

Figure 6: In vivo efficacy of MORAb-202 in a triple negative breast cancer PDX model

Summary

1. Eribulin conjugation to farletuzumab using a cathepsin-cleavable linker (i.e. MORAb-202) demonstrated FKA-specific in vitro cytotoxicity.

2. MORAb-202 demonstrated bystander killing against FKA-negative cells in the presence of FKA-positive cells, while little off-target killing was observed against the non-targeted FKA-negative cells.

3. In vivo anti-tumor efficacy of MORAb-202 was observed in human cancer cell line xenograft models and TNBC PDX models including a FKA-lower tumor model.

4. MORAb-202 demonstrated no visible adverse events in the murine efficacy models.

5. MORAb-202 exhibited demonstrable effects on the tumor microenvironment.

These data strongly support that MORAb-202 is a promising ADC drug candidate.

References

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