A new biomarker of recent interest in the cancer field is folate receptor alpha (FRA), a membrane-bound protein with high affinity for binding and transporting folate into cells. Overexpression of FRA can confer a growth advantage to tumors by increasing folate uptake and affect cell proliferation via alternative cell signaling pathways (1). FRA levels have been found to be elevated in tumors of epithelial origin compared to normal tissue, including TNBC (2). Due to an absence of potential targeted therapy for this breast cancer subtype, the finding that a significant number of TNBCs express abundantly FRA suggests an important population of patients may benefit from FRA-targeting therapy. Eighty-five percent of preclinical agents entrusting oncology clinical trials fail to demonstrate sufficient safety or efficacy to gain regulatory approval (3). This failure rate shows a weak understanding of the complexity of human cancer, the continued limitations of the predictive value of existing preclinical safety or efficacy to gain regulatory approval (3). This failure rate shows a weak understanding of the complexity of human cancer, the continued limitations of the predictive value of existing preclinical safety or efficacy to gain regulatory approval (3). This failure rate shows a weak understanding of the complexity of human cancer, the continued limitations of the predictive value of existing preclinical safety or efficacy to gain regulatory approval (3).

The national IMODI (Innovative MODels Initiative) consortium collection preclinical setting. It is now evidenced that patient derived xenograft (PDX) recapitulate human expression abundantly FRA suggests an important population of patients may benefit from FRA-targeting therapy. The HER2 receptor are refractory to available targeted therapies for breast cancer, treatment in FRA-expressing tumours.

FRA expression could be used as MORAb-202 activity biomarker, Antitumour activity of MORAb-202 is dependent on FRA expression, At equivalent dose MORAb-202 showed a higher antitumour activity when compared to free eribulin. In highly expressive FRA tumour, to observe similar antitumour activity the dose of eribulin without vectorization would require to be enhanced by 32-fold compared to targeted eribulin. At this dose of eribulin, a body weight loss is observed and a tumor relapse occurred in all treated animals whereas no relapse was observed for mice treated with MORAb-202.

Triple-Negative Breast Cancer that does not express estrogen, progesterone or the HER2 receptor.

In INTRODUCTION
A new biomarker of recent interest in the cancer field is folate receptor alpha (FRA), a membrane-bound protein with high affinity for binding and transporting folate into cells. Overexpression of FRA can confer a growth advantage to tumors by increasing folate uptake and affect cell proliferation via alternative cell signaling pathways (1). FRA levels have been found to be elevated in tumors of epithelial origin compared to normal tissue, including TNBC (2). Due to an absence of potential targeted therapy for this breast cancer subtype, the finding that a significant number of TNBCs express abundantly FRA suggests an important population of patients may benefit from FRA-targeting therapy.

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In RESULTS

In vivo anti-proliferation activity (PDX: OD-BRE-589 FRA negative tumor)

Vehicle IV Q1Dx1

MORAb-202 5 mg/kg IV Q1Dx1 (0.1 mg/kg eq. Eribulin, B)

Eribulin 0.1 mg/kg IV Q1Dx1

MORAb-202-eribulin 5 mg/kg IV Q1Dx1 (0.1 mg/kg eq. Eribulin)

Vehicle IV Q1Dx1

MORAb-202 5 mg/kg Q1Dx1 (0.1 mg/kg eq. Eribulin)

MORAb-202 1 mg/kg IV Q1Dx1 (0.02 mg/kg eq. Eribulin)

Vehicle IV Q1Dx1

Eribulin 0.1 mg/kg IV Q1Dx1

In vivo anti-proliferation activity (PDX: OD-BRE-589 FRA positive tumor)

Vehicle IV Q1Dx1

MORAb-202 5 mg/kg IV Q1Dx1 (0.1 mg/kg eq. Eribulin)

Eribulin 0.1 mg/kg IV Q1Dx1

MORAb-202 5 mg/kg IV Q1Dx1 (0.1 mg/kg eq. Eribulin)

MORAb-202-eribulin 5 mg/kg IV Q1Dx1 (0.1 mg/kg eq. Eribulin)

Vehicle IV Q1Dx1

In vivo anti-proliferation activity (PDX: 03-BRE-5F9 FRA positive tumor)

Vehicle IV Q1Dx1

MORAb-202 5 mg/kg IV Q1Dx1 (0.1 mg/kg eq. Eribulin)

Eribulin 0.1 mg/kg IV Q1Dx1

MORAb-202 5 mg/kg IV Q1Dx1 (0.1 mg/kg eq. Eribulin)

Vehicle IV Q1Dx1

In vivo anti-proliferation activity (PDX: 03-BRE-631 FRA positive tumor)

Vehicle IV Q1Dx1

MORAb-202 5 mg/kg IV Q1Dx1 (0.1 mg/kg eq. Eribulin)

Eribulin 0.1 mg/kg IV Q1Dx1

MORAb-202 5 mg/kg IV Q1Dx1 (0.1 mg/kg eq. Eribulin)

Vehicle IV Q1Dx1

Conclusions and perspectives

FRA expression could be used for MORAb-202 activity biomarker, Antitumour activity of MORAb-202 is dependent on FRA expression, At equivalent dose MORAb-202 showed a higher antitumour activity when compared to free eribulin. In highly expressive FRA tumour, to observe similar antitumour activity the dose of eribulin without vectorization would require to be enhanced by 32-fold compared to targeted eribulin. At this dose of eribulin, a body weight loss is observed and a tumor relapse occurred in all treated animals whereas no relapse was observed for mice treated with MORAb-202.

Triple-Negative Breast Cancer that does not express estrogen, progesterone or the HER2 receptor are refractory to available targeted therapies for breast cancer treatment, such as HER2-directed therapy (Trastuzumab, T-DXR and endocrine therapies (Tamoxifen or letrozole) should be sensitive to MORAb-202 treatment in FRA-expressing tumours.

References