

ORAL PRESENTATION

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Interim results of an ongoing Phase I, dose escalation study of MGA271 (Fc-optimized humanized anti-B7-H3 monoclonal antibody) in patients with refractory B7-H3-expressing neoplasms or neoplasms whose vasculature expresses B7-H3

John Powderly¹, Gregory Cote², Keith Flaherty², Russell Z Szmulewitz³, Antoni Ribas⁴, Jeffrey Weber⁵, Deryk Loo⁶, Jan Baughman⁶, Francine Chen⁶, Paul Moore⁷, Ezio Bonvini⁷, James Vasselli^{7*}, Jon Wigginton⁷, Roger Cohen⁸, Howard Burris⁹, Bartosz Chmielowski¹⁰

From 30th Annual Meeting and Associated Programs of the Society for Immunotherapy of Cancer (SITC 2015)
National Harbor, MD, USA. 4-8 November 2015

Background

MGA271 is a humanized IgG1 monoclonal antibody-targeting B7-H3 (CD276), a member of the B7 family. MGA271 has been Fc-engineered to enhance binding to activating FcγR (CD16A), decrease binding to inhibitory FcγR (CD32B), and potentiate ADCC. B7-H3 has limited expression in normal tissues but highly expressed in a broad range of tumors, making it an attractive target for cancer immunotherapy. We initiated a Phase I investigation of the safety, tolerability, pharmacokinetics, pharmacodynamics and antitumor activity of MGA271.

Methods

This Phase I study included dose escalation (complete) and an ongoing two-component cohort expansion (NCT01391143). Dose escalation utilized single-patient, intra-patient escalation, followed by a conventional 3+3 design, using MGA271 doses of 0.01-15mg/kg. MGA271 was administered weekly on a 4-week on, 4-week off schedule during cycle 1, and 3 out of every 4 weeks in subsequent cycles. Initial expansion cohorts enrolled patients (N=15/cohort) with melanoma, prostate carcinoma and other B7-H3+ tumors. Major modifications

were subsequently made to enhance the functionality of the study prior to enrolling additional expansion cohorts. MGA271 administration was changed to uninterrupted weekly dosing, corticosteroid infusion reaction prophylaxis was reduced and immune-related response criteria and management principles were implemented. The additional expansion cohorts (N=16/cohort) were initiated in patients with melanoma (post checkpoint inhibitor), squamous cell head and neck carcinoma, renal cell carcinoma, triple-negative breast carcinoma, and high-B7-H3 expressing tumors including bladder and lung carcinoma. Pharmacodynamic testing included serum cytokines and modulation of the lymphocyte phenotype and T cell repertoire in peripheral blood.

Results

MGA271 was well tolerated, with no dose-limiting toxicity and no maximum tolerated dose defined up to 15 mg/kg. Patients were frequently heavily pre-treated, with a median of 3 (0-7) prior therapies. Any grade treatment-related AEs occurred in 71% of patients, including fatigue (30%), infusion-related reaction (26%), nausea (19%), chills (17%) and vomiting (13%). Grade 3/4 drug related AEs were noted in 6% of patients. No drug-related AEs led to study drug discontinuation. MGA271 showed linear PK. As of 30 July

⁷MacroGenics, Rockville, MD, USA

Full list of author information is available at the end of the article

2015, 20 of 46 patients treated under the new study design continue on study drug. Patients experienced disease stabilization (>12 weeks) and tumor shrinkage (2-69%) across several tumor types. The study continues to enroll patients and generate more mature data.

Conclusions

MGA271 has a favorable safety profile and initial evidence of anti-tumor activity across several tumor types. These data support continued evaluation of MGA271 monotherapy and in combination with other immune modulators, including checkpoint inhibitors.

Trial Registration

ClinicalTrials.gov Identifier NCT01391143.

Authors' details

¹Carolina BioOncology Institute, Huntersville, NC, USA. ²Department of Oncology, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA. ³University of Chicago, Chicago, IL, USA. ⁴University of California at Los Angeles Medical Center, Los Angeles, CA, USA. ⁵H. Lee Moffitt Cancer Center, Tampa, FL, USA. ⁶MacroGenics, San Francisco, CA, USA. ⁷MacroGenics, Rockville, MD, USA. ⁸University of Pennsylvania, Philadelphia, PA, USA. ⁹Sarah Cannon Research Institute, Nashville, TN, USA. ¹⁰Division of Hematology - Medical Oncology, UCLA Jonsson Comprehensive Cancer Center, Los Angeles, CA, USA.

Published: 4 November 2015

doi:10.1186/2051-1426-3-S2-O8

Cite this article as: Powderly *et al.*: Interim results of an ongoing Phase I, dose escalation study of MGA271 (Fc-optimized humanized anti-B7-H3 monoclonal antibody) in patients with refractory B7-H3-expressing neoplasms or neoplasms whose vasculature expresses B7-H3. *Journal for ImmunoTherapy of Cancer* 2015 **3**(Suppl 2):O8.

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