Phase 1/2 study of novel HER-targeting, TLR7/8 immune-stimulating antibody conjugate (ISAC) BDC-1001 with or without immune checkpoint inhibitor in patients with advanced HER2-expressing solid tumors

Marish N. Sharma, 1 Ecartera Ileana Dumbrava, 1 Richard D. Carvajal, 1,7,8 Daniel Cataneo, 1,7,8,9 Leshia A. Emens, 1 Glen J. Hanna, 1 Dejan Juric, 1 Yoon-Koo Kang, 1 Jeeyun Lee, 1 Keun-Wook Lee, 1 Bob T. Lii, 1 Kathleen Moore, 1 Mark D. Pegg, 1,8,9 Paul R. Pohlmann, 1,2,3,4,5,6,7,9 Dave Rasco, 1,2,3,4,5,6,7,9 Alexander Spira, 1,2,3,4,5,6,7,9 Antonette R. Tan, 1,2,3,4,5,6,7,9 Ding Wang, 1,2,3,4,5,6,7,9 Shelley E. Ackerman, 1,2,3,4,5,6,7,9,10 Heidi LeBlanc, 1,2,3,4,5,6,7,9,10 David Domanic, 1,2,3,4,5,6,7,9,10 Marcis Konwaten, 1,2,3,4,5,6,7,9,10 Michael N. Alonso, 1,2,3,4,5,6,7,9,10 Edith A. Perez, 1,2,3,4,5,6,7,9,10

1 Boltbody, Redwood City, CA; 2 The University of Texas MD Anderson Cancer Center, Houston, TX; 3 Columbia University Cancer Center, New York, NY; 4 Stepenson Cancer Center, Pittsburgh, PA; 5 Dana-Farber Cancer Institute, Boston, MA; 6 Massachusetts General Hospital, Boston, MA; 7 Memorial Sloan Kettering Cancer Center, New York, NY; 8 Stephenson Cancer Center, Oklahoma City, OK; 9 Stanford University, Stanford, CA; 10 Combiphar Comprehensive Cancer Center, Georgetown University, Washington, DC; 11 Memorial Sloan Kettering Cancer Center, New York, NY; 12 Stephenson Cancer Center, Pittsburgh, PA; 6 Dana-Farber Cancer Institute, Boston, MA; 7 Massachusetts General Hospital, Boston, MA. Presented at SITC 2020.

ABSTRACT 401

BACKGROUND

• In a phase of advances made in the management of patients with human epidermal growth factor receptor 2 (HER2)-expressing or -driven solid tumors, there remains a significant unmet need for novel approaches to improve patient outcomes.

• Intratumoral delivery of antitumor antibodies and immunomodulatory adjuvants such as Toll-like receptor (TLR) agonists has been shown to drive potent antitumor responses via activating myeloid cells, presentation of tumor antigens to T cells that mediate antitumor immunity.

• BDC-1001 is delivered systemically and has demonstrated superior preclinical biology. This novel ISAC consists of an investigational HER2-targeting antibody (BDC-1001) covalently linked to a TLR7/8 agonist agent. The implicated endogenous TLR7/8 pathway is shown to activate innate immune responses in a TLR- and FcR-dependent manner.

• Importantly, BDC-1001 did not induce systemic activation of the immune system, thrombocytopenia, or thrombosis in preclinical human primary studies.

• A 2-cohort, 1.5Bolt body trial in HER2-expressing PD-1+ patients in HER2-expressing advanced solid tumors.

• Overall response rate using RECIST v1.1 and iRECIST, disease control rate of confirmed complete response, partial response, lasting 4 or more weeks following the initiation of BDC-1001, duration of response, progression-free survival, and overall survival.

• Antitumor activity in lesions with different levels of HER2 and PD-L1 expression.

• Study design: a multi-centric, open-label, phase 1/2 study to evaluate BDC-1001 alone and in combination with pembrolizumab for patients with HER2-expressing advanced solid tumors.

• Primary objectives:
  1. Overall response rate using RECIST v1.1 and iRECIST, disease control rate of confirmed complete response, partial response, lasting 4 or more weeks following the initiation of BDC-1001, duration of response, progression-free survival, and overall survival.
  2. Antitumor activity in lesions with different levels of HER2 and PD-L1 expression.

• Secondary objectives:
  1. Evaluate pharmacokinetic and pharmacodynamic (PK/PD) biomarkers associated with activity.
  2. Evaluate exploratory pharmacodynamic biomarkers and potential biomarkers associated with biological activity.

• Safety, PK, Efficacy, PD Biomarkers

• Study Design

  1. Phase 1/2 data anticipated to provide clinical proof of concept.

  2. Phase 1 dose escalation: 6 patients per cohort, 3 patients per cohort in combination with pembrolizumab.

  3. Phase 2 dose expansion: 16 patients per cohort, 14 patients per cohort in combination with pembrolizumab.

• Following the phase 1 dose escalation of BDC-1001, cohorts of 16 patients in HER2+ breast cancer, patients with advanced HER2+ solid tumors (BC, other solid tumors IHC3+ or gene amplification).

• For HER2 low breast cancer HER2 IHC2+

• Hypersensitivity to pembrolizumab or particular excipients that are used for formulation.

• History of treatment with a TLR7//8, or TLR8 agonist.

• Use of another investigational agent or anticancer therapy within 4 weeks prior to dose 1 or within 5 estimated elimination half-lives, whichever is shorter.

• History of severe hypersensitivity to any ingredient of the study drug(s), including trentalucind.

• Anti-PD1 Combination Therapy Exclusions

• Prior use of immune-modulating agents.

• Patient has a history of autoimmune disease with the exception of autoimmune endocrinopathies that are stable on hormone replacement therapy.

• Resistant to prednisone or other immunosuppressors.

• Exclusion Criteria

• Anti-PD1 Combination Therapy Exclusions

• Prior use of immune-modulating agents.

• Patient has a history of autoimmune disease with the exception of autoimmune endocrinopathies that are stable on hormone replacement therapy.

• Resistant to prednisone or other immunosuppressors.

• Baseline (archival or freshly collected) tumor sample, and blood mandated for all patients.

• Baseline tumor sample required if the tumor is no longer available.

• Baseline sample must be obtained within 4 weeks of the first dose of BDC-1001.

• Investigate PD biomarkers to demonstrate that BDC-1001 is biologically active, and support dose selection.

• Evaluate potential predictive biomarkers of response to BDC-1001.

• Use of another investigational agent or anticancer therapy within 4 weeks prior to dose 1 or within 5 estimated elimination half-lives, whichever is shorter.

• History of severe hypersensitivity to any ingredient of the study drug(s), including trentalucind.

• Anti-PD1 Combination Therapy Exclusions

• Prior use of immune-modulating agents.

• Patient has a history of autoimmune disease with the exception of autoimmune endocrinopathies that are stable on hormone replacement therapy.

• Resistant to prednisone or other immunosuppressors.

• Baseline (archival or freshly collected) tumor sample, and blood mandated for all patients.

• Baseline tumor sample required if the tumor is no longer available.

• Baseline sample must be obtained within 4 weeks of the first dose of BDC-1001.

• Investigate PD biomarkers to demonstrate that BDC-1001 is biologically active, and support dose selection.

• Investigate potential predictive biomarkers of response to BDC-1001.

• Use of another investigational agent or anticancer therapy within 4 weeks prior to dose 1 or within 5 estimated elimination half-lives, whichever is shorter.

• History of severe hypersensitivity to any ingredient of the study drug(s), including trentalucind.