A Phase 3 Open-Label, Randomized, Multicenter Study of Imprime PGG in Combination with Cetuximab in Patients with KRAS Wild Type Colorectal Cancer

Jeffrey Meyerhardt¹, Vivek Sharma², Michele M. Grady³, Jamie Lowe⁴, Michele A. Gargano⁵, Richard D. Huhn⁶, Ada Braun⁷
¹Center for Gastrointestinal Cancer, Dana Farber Cancer Institute, Boston, US; ²Medical Oncology/Hematology, University of Louisville Research Foundation, Louisville, US; ³Biothera, Inc., Eagan, MN, United States of America; ⁴Presenting Author

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Background

- Colorectal cancer (CRC) is one of the most common malignancies worldwide and the second leading cause of cancer-related deaths in Europe.⁸
- For patients with KRAS wild type (WT), epidermal growth factor receptor (EGFR) expressing, metastatic colorectal cancer (mCRC) who failed oxaliplatin- and irinotecan-based therapy or who are intolerant of irinotecan, EGFR-targeted antibodies with or without irinotecan are a standard care option.⁹
- Single-agent cetuximab, in this setting, is associated with a 12.8% objective response rate (ORR) and median progression-free survival (PFS) of 3.7 months.¹⁰

Rationale

- EGFR is highly expressed in over 75% of mCRC and has been associated with tumor formation and progression.¹¹
- Binding of cetuximab to EGFR can induce complement deposition (opsonization) in vivo. Although complement-dependent cytotoxicity (CDC) is a potent mechanism of cell killing, CDC has not been identified as a significant mechanism of action for cetuximab.¹²
- Imprime PGG is a novel innate immune modulator (complex carbohydrate biologic), which harnesses innate immune cells to enhance killing of antibody-targeted tumor cells. Imprime PGG binds complement receptor 3 (CR3) on innate immune cells (including neutrophils, monocytes and macrophages) and primes these cells to exert anti-tumor activity against tumor cells that have been opsonized by complement (CR3b) following targeting by anti-tumor antibodies.¹³,¹⁴

Hypothesis

- Imprime PGG in combination with cetuximab will improve overall survival (OS) compared to cetuximab alone in patients with advanced, refractory KRAS wild type mCRC.

Study Design

- Study BT-CL-PGG-CRC1031 (PRIMUS) is an international, phase 3, open-label, randomized, active-controlled study
- Approximately 795 patients will be randomized in a 2:1 ratio to
  - Imprime PGG plus Cetuximab, or
  - Cetuximab alone

Study Treatment:

- Imprime PGG 4 mg/kg IV is administered weekly preceding the administration of cetuximab
- Cetuximab is administered weekly at an initial dose of 400 mg/m² and subsequent doses of 250 mg/m²
- Patients will receive treatment until documented disease progression (PD) per RECIST 1.1 or intolerable toxicity
- Following treatment discontinuation, patients will be monitored for survival until death or loss to follow-up

Key Study Endpoints

- Overall Survival (OS)
- Progression-Free Survival (PFS)
- Objective Response Rate (ORR)
- Median Progression-Free Survival (PFS)
- Quality of Life (QOL)
- Incidence of treatment-emergent adverse events
- Analysis of safety parameters will be performed on the intent to treat population

General Statistical Methods

- This study has 80% power to detect an increase in median OS from approximately 32 weeks in the control group to approximately 40 weeks in the Imprime PGG group (a hazard ratio of approximately 0.8) at a two-sided 5% significance level.

Study Oversight

- An independent Data Safety Monitoring Board is conducting regular safety reviews for this study.

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Disclosures

- This trial is sponsored by Biothera. Author disclosures: Meyerhardt J, Sharma V: No disclosures
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Corresponding Author

Michele A. Gargano, MSc (mgargano@biothera.com)

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