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# PRELIMINARY RESULTS FROM PATIENTS WITH ADVANCED GASTRIC CANCER AND ESOPHAGEAL CARCINOMA IN A DOSE-ESCALATION/EXPANSION STUDY OF BGB-A317, AN ANTI-PD-1 MONOCLONAL ANTIBODY


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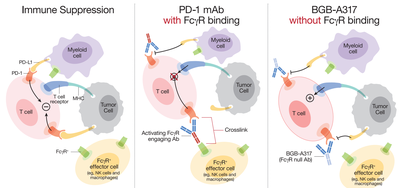
## INTRODUCTION

- Gastric cancer (GC) and esophageal cancer (EC) are commonly diagnosed cancers that pose a major clinical challenge due to limited treatment options[1,2]
- Monoclonal antibodies against the immune checkpoint inhibitory receptor, programmed cell death-1 (PD-1), have demonstrated antitumor activity across multiple malignancies[3]
- BGB-A317 is a humanized IgG4 monoclonal antibody (mAb) with high affinity and binding specificity against PD-1
- BGB-A317 was specifically engineered to minimize binding to $Fc\gamma R$ on macrophages, thereby abrogating antibody-dependent phagocytosis, a potential mechanism of T-cell clearance (**Figure 1**)
- Previous reports from an ongoing Phase 1A/1B study (NCT02407990) of BGB-A317 in patients with advanced solid tumors suggested that BGB-A317 is tolerable. In addition, its toxicity profile demonstrates that adverse events (AEs) are generally of low severity, manageable, and reversible[4]
- Here we present the preliminary results, as of 8 June 2017, of patients with advanced GC and EC enrolled in this Phase 1A/1B study. The trial is ongoing to collect more mature safety and antitumor activity data

**Figure 1: Lack of $Fc\gamma R$ Binding Prevents Macrophage-Mediated T Cell Clearance**




Adapted from Dahan et al, *Cancer Cell*. 2015;28:285–295.

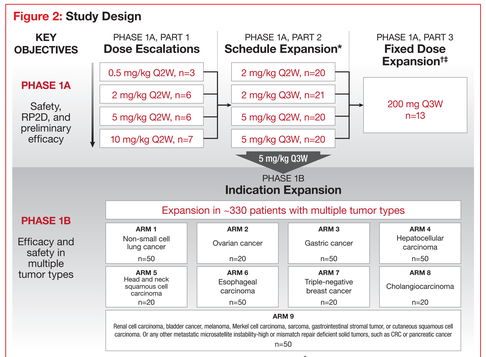
## METHODS

- The study design is detailed in **Figure 2**
  - In Phase 1A, 10 mg/kg Q2W was the maximum administered dose; maximum tolerated dose was not reached
  - All patients in Phase 1B received BGB-A317 as a 5 mg/kg IV infusion Q3W
  - Radiographic assessment was performed approximately every 9 weeks

### Key Eligibility Criteria of the GC and EC Subsets

- Adult patients (aged ≥18 years) with histologically or cytologically confirmed advanced/metastatic GC or EC, who have at least one measurable lesion, have not received prior anti-PD-1 or PD-L1 treatment, and an Eastern Cooperative Oncology Group (ECOG) performance status of ≤1 were enrolled
- Patients were excluded if they had a history of severe hypersensitivity reactions to other mAbs or if they had a prior malignancy active within the previous 2 years

**Figure 2: Study Design**




*In select tumors for RP2D determination and preliminary differentiation, †In select tumors at fixed doses that do not exceed the exposure of MTD, ‡Conducted in parallel with Phase 1B.
**Abbreviations:** MTD, maximum tolerated dose; RP2D, recommended phase 2 dose.

## RESULTS

### Patient Disposition

- Results presented here include patients with advanced/metastatic GC or EC treated with 2 mg/kg or 5 mg/kg every two weeks (Q2W) or Q3W
  - A total of 7 patients from the phase 1A schedule dose-expansion arm were included
  - All but one patient who received BGB-A317 5 mg/kg Q3W were from the phase 1B indication-expansion arm
- As of 8 June 2017, 83 patients with GC (n=46; median age 60.5 years [range: 22–81]) or EC (n=37; median age of 62 years [range: 32–80]) have been enrolled in this study (**Table 1**)
  - A total of 27 patients (n=18, GC; n=9, EC) remained on treatment

**Table 1: Patient Demographics and Treatment Profile of GC and EC Populations**

| | | Patients with GC or EC | |
|---|---|---|---|
| | | GC (n=46) | EC (n=37) |
| Median age, years (range) | | 60.5 (22–81) | 62.0 (32–80) |
| Sex | Male/female | 25/21 | 28/9 |
| Race | Caucasian | 21 | 26 |
| | Black/African-American | 1 | 1 |
| | Asian | 21 | 7 |
| | American Indian/Alaska Native | 0 | 1 |
| | Native Hawaiian/Other Pacific Islander | 1 | 0 |
| | Other | 2 | 2 |
| Median prior anti-cancer therapy regimens for advanced disease (range) | | 2 (0–9) | 2 (0–7) |
| Prior anti-cancer therapy regimens for advanced disease, n | 0* | 9 | 6 |
| | 1 | 13 | 11 |
| | 2 | 11 | 10 |
| | ≥3 | 13 | 10 |
| Histological subtypes for EC | Adeno | | 23 |
| | Squamous | | 13 |
| | Adenosquamous | | 1 |
| Prior radiotherapy for EC | Yes | | 28 |
| | No | | 9 |
| Prior gastrectomy for GC | Yes | 17 | |
| | No | 29 | |

*All but one patient with GC received chemotherapy in the adjuvant or neoadjuvant setting

### Preliminary Antitumor Activity

- As of 8 June 2017, 65 GC (n=34) and EC (n=31) patients were evaluable (defined as having a measurable baseline tumor assessment and at least one evaluable post-baseline tumor response assessment or had progressed or died prior to the initial tumor assessment)
  - Six patients achieved a confirmed PR (n=4, GC; n=2, EC) and 12 patients (n=3, GC; n=9, EC) achieved a best overall response (BOR) of stable disease (SD)
    - Three of the 9 patients with EC who achieved SD also have achieved an unconfirmed PR, one of whom remains on study awaiting confirmation
  - Across the 2 populations, disease control rate (DCR=PR+SD) was 28% (n=18/65); DCR for patients with GC=21% and DCR for patients with EC=36%
  - Median treatment duration in patients with GC was 44.5 days (range: 4–457); median treatment duration in EC patients was 50 days (range: 1–246)
- Antitumor activity of BGB-A317 is presented in **Figures 3–5**

**Figure 3: Maximum Tumor Reduction in Patients with GC (A) or EC (B)**

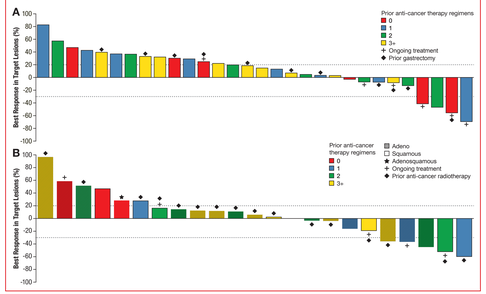



**Figure 4: Change in Tumor Burden over Time in Patients with GC (A) or EC (B)**

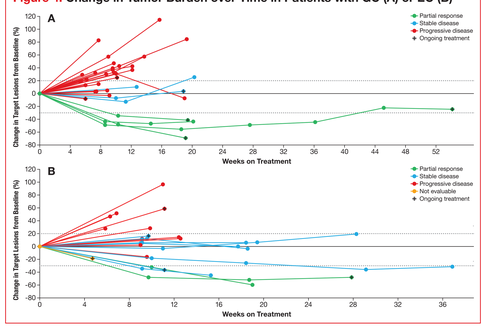
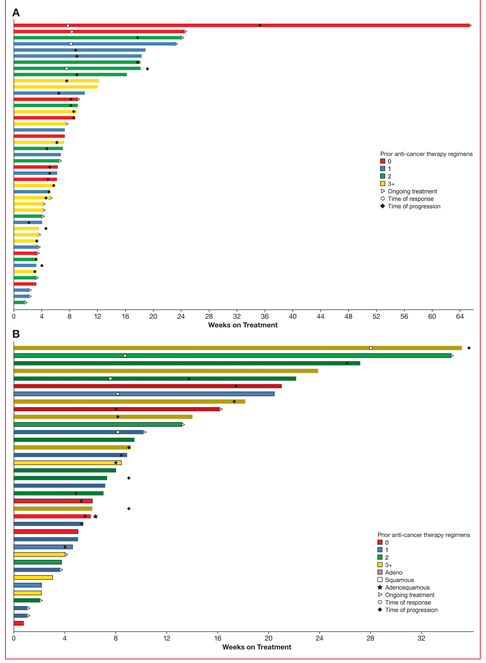



**Figure 5: Duration of Treatment and Response in Patients with GC (A) or EC (B)**




### Safety and Tolerability

- Treatment-related adverse events (TRAEs) occurred in 30 patients with GC or EC (**Table 2**)
  - Across the cohorts, fatigue, decreased appetite, abdominal pain, and nausea were the most commonly reported TRAEs
  - The majority of these TRAEs were grade ≤2 in severity
    - Only one patient in each cohort reported a TRAE of grade ≥3 (proteinuria [GC]; dermatitis [EC])
- Serious adverse events considered related to treatment occurred in 2 patients with GC (diarrhea, n=1; pyrexia, n=1)
- A total of 8 patients from these cohorts (n=2 GC; n=6 EC) had a TEAE with a fatal outcome, none were assessed as related to treatment

## CONCLUSIONS

- Treatment with BGB-A317 was generally well tolerated in pretreated patients with advanced GC and EC
  - As of 8 June 2017, 65 of 83 patients with GC or EC were evaluable for response, and 27 remained on treatment
    - Median treatment duration in patients with GC was 44.5 days (range: 4–457); median treatment duration in EC patients was 50 days (range: 1–246)
- Adverse events reported in these cohorts were consistent with the overall safety profile observed in the study and were generally of low severity, manageable, and reversible
- Of the 65 evaluable patients, tumor reductions meeting the definition of confirmed partial response were observed in 6 patients with GC or EC; 12 patients achieved a confirmed best overall response of stable disease including 3 with unconfirmed partial response
- The preliminary safety profile and antitumor activity support continued development of BGB-A317 in patients with advanced/metastatic GC or EC

**Table 2: TRAEs Occurring in ≥2 Patients with GC or EC Across Cohorts**

| | All grades | | Grade ≥3 | |
|---|---|---|---|---|
| | GC (n=46) | EC (n=37) | GC (n=46) | EC (n=37) |
| **Any TRAE** | **15** | **15** | **1** | **1** |
| Fatigue | 3 | 6 | 0 | 0 |
| Nausea | 3 | 3 | 0 | 0 |
| Decreased appetite | 4 | 2 | 0 | 0 |
| Abdominal pain | 4 | 0 | 0 | 0 |
| Pruritus | 2 | 1 | 0 | 0 |
| Diarrhea | 1 | 1 | 0 | 0 |
| Arthralgia | 1 | 1 | 0 | 0 |
| Dermatitis | 1 | 1 | 0 | 1 |
| Proteinuria | 1 | 1 | 1 | 0 |
| Infusion-related reaction | 0 | 2 | 0 | 0 |
| Myalgia | 0 | 2 | 0 | 0 |

**Abbreviations:** TRAE, treatment-related adverse event.

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