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

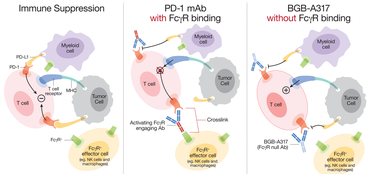
T. Meniawy[1], G. Richardson[2], A. Townsend[3], J. Desai[4], H. Gan[5], M. Friedlander[6], L. Horvath[7], M.B. Jameson[8], S. Sandhu[4], Z. Wu[9], Z. Qin[10], J. Kang[10], B. Markman[11]

[1]Linear Clinical Research Limited, Nedlands, WA, Australia; [2]Cabrini Hospital Malvern, Malvern, VIC, Australia; [3]Queen Elizabeth Hospital, Woodville, SA, Australia; [4]Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; [5]Olivia Newton-John Cancer Research Institute, Heidelberg, VIC, Australia; [6]Prince of Wales Hospital, Randwick, NSW, Australia; [7]Chris O'Brien Lifehouse, Camperdown, NSW, Australia; [8]Waikato Hospital, Hamilton, New Zealand; [9]BeiGene USA, Inc, Fort Lee, NJ, United States; [10]BeiGene (Beijing) Co., Ltd., Beijing, China; [11]Monash Cancer Center, Monash Health, Melbourne, VIC, Australia

INTRODUCTION

- Ovarian cancer (OC) is the seventh most commonly diagnosed cancer among women in the world[1] and has the highest fatality rate among the gynecologic cancers; the majority of patients present at an advanced stage, with widely metastatic disease within the peritoneal cavity[2]
- Monoclonal antibodies against the immune checkpoint inhibitory receptor, programmed cell death-1 (PD-1), have demonstrated antitumor activity across multiple malignancies[3], including OC[4]
- 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 FcγR 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[3]
- Here we present the preliminary results, as of 8 June 2017, of patients with recurrent/refractory ovarian cancer enrolled in this Phase 1A/1B study. The trial is ongoing to collect more mature safety and antitumor activity data

Figure 1: Lack of FcγR Binding Prevents Macrophage-Mediated T Cell Clearance



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

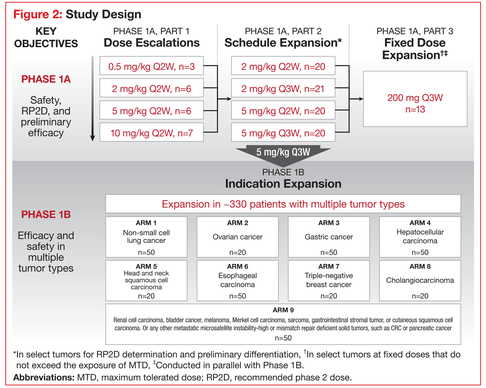
METHODS

- 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
- Tumor assessments, including CA125, occurred approximately every 9 weeks and response was collected according to both RECIST 1.1 and Gynecological Cancer Intergroup (GCIC) criteria

Key Eligibility Criteria of the OC Subset

- Adult patients (aged ≥18 years) with histologically or cytologically confirmed advanced/metastatic OC, 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 OC treated at different dose levels (0.5, 2, 5, 10 mg/kg intravenously [IV] every 2 weeks [Q2W] in dose escalation, or at 2 or 5 mg/kg IV Q2W or Q3W, or 200 mg IV Q3W in dose expansion, or 5 mg/kg IV Q3W in indication expansion)
- As of 8 June 2017, 51 patients with advanced OC (median age 62.0 [range: 19–80]) had enrolled in this study (**Table 1**)
  - A total of 6 patients remained on treatment

Table 1: Patient Demographics and Disease Characteristics of OC Patients

		OC Population (N=51)
Median age, years (range)		62 (19–80)
Race	Caucasian	45
	Asian	3
	Other	3
Median prior anti-cancer therapy regimens (range)		3 (0–12)
Prior anti-cancer therapy regimens, n	0	1*
	1	5
	2	13
	≥3	32
Response to platinum therapy†	Sensitive	12
	Resistant/refractory	37
BRCA status	BRCA WT	2
	BRCA1/2 mutation	5
	Unknown	44

*Patient has received adjuvant treatment; †Subjects are platinum-sensitive if disease progression occurred >6 months after last platinum chemotherapy; platinum-resistant if disease progression occurred <6 months after their last platinum chemotherapy but after post-treatment evaluation; platinum-refractory if disease progressed while receiving platinum chemotherapy, up to the date of post-treatment evaluation.

Preliminary Antitumor Activity

- As of 8 June 2017, 50 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)
  - Two patients achieved a confirmed PR and 20 patients achieved best overall response as stable disease (SD)
  - Disease control rate (DCR=PR+SD) was 44% (n=22/50)
  - Median treatment duration in patients with OC was 71 days (range: 29–540)
- Antitumor activity of BGB-A317 is presented in **Figures 3–6**

Figure 3: Duration of Treatment and Response in Patients with OC

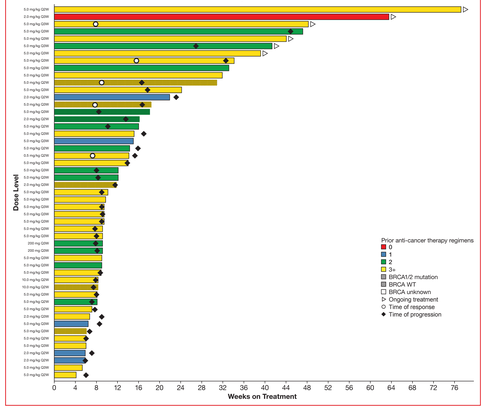


Figure 4: Percent Change in CA125 from Baseline

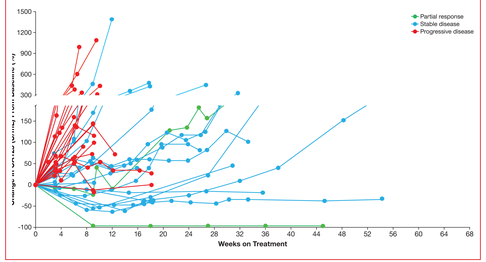
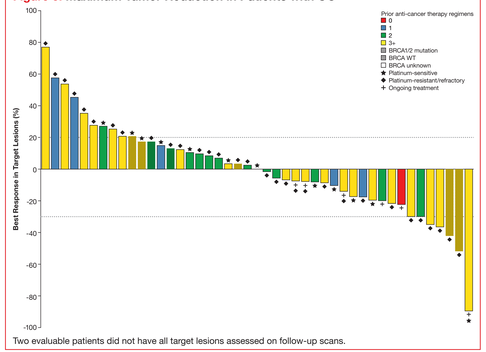
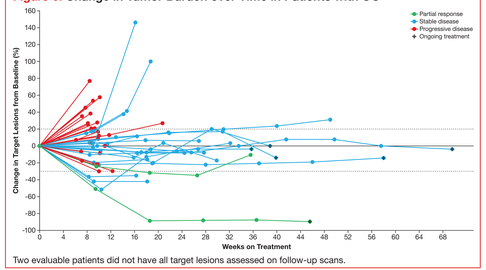


Figure 5: Maximum Tumor Reduction in Patients with OC



Two evaluable patients did not have all target lesions assessed on follow-up scans.

Figure 6: Change in Tumor Burden over Time in Patients with OC



Two evaluable patients did not have all target lesions assessed on follow-up scans.

Safety and Tolerability

- Treatment-related adverse events (TRAEs) occurred in 28 of the 51 patients with OC (**Table 2**)
  - The most common events were fatigue (n=9) and pruritus, rash, and diarrhea (n=5 each)
  - The majority of these TRAEs were grade ≤2 in severity
    - A total of 3 patients with OC reported a TRAE of Grade ≥3 (pyrexia, stomatitis, and diarrhea, n=1 each)
- Serious adverse events considered related to treatment occurred in 3 patients with OC (colitis, mucosal inflammation, and pyrexia, n=1 each)
- No patient experienced an adverse event that led to death

CONCLUSIONS

- Treatment with BGB-A317 was generally well tolerated in pretreated patients with advanced OC
  - As of 8 June, 2017, 12% of patients (n=6/51) remained on treatment; median treatment duration is 71 days (range: 29–540 days)
- Adverse events reported in this cohort were consistent with the overall safety profile observed in the study and were generally of low severity, manageable, and reversible
- Of the 50 evaluable patients, tumor reduction meeting the definition of confirmed partial response were observed in 2 patients; 20 patients achieved a confirmed best overall response of stable disease
- Combination therapy of BGB-A317 with BGB-290, a potent and selective poly (ADP-ribose) polymerase 1/2 inhibitor, is currently under investigation in patients with advanced solid tumors likely to harbor DNA damage repair deficiencies, such as advanced OC[6]

Table 2: TRAEs Occurring in ≥2 Patients with OC

	OC Population (N=51)	
	All Grades	Grade ≥3
Any TRAE	**28**	**3***
Fatigue	9	0
Pruritus	5	0
Rash	5	0
Diarrhea	5	1
Lethargy	3	0
Nausea	3	0
Abdominal pain	2	0
Dry eye	2	0
Dry skin	2	0
Onychoclasis	2	0
Maculo-papular rash	2	0

*Pyrexia and stomatitis were TRAEs of grade ≥3 severity (n=1 each).
Abbreviations: TRAE, treatment-related adverse events.

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