Poster No: 389P
European Society for Medical Oncology
08-12 Sept 2017
Madrid, Spain

PRELIMINARY RESULTS FROM PATIENTS WITH ADVANCED HEAD AND NECK SQUAMOUS CARCINOMA IN A DOSE-ESCALATION AND DOSE-EXPANSION STUDY OF BGB-A317, AN ANTI-PD-1 MONOCLONAL ANTIBODY

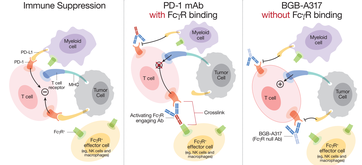
L. Horvath[1], J. Desai[2], S. Sandhu[3], A. O'Donnell[4], A. Hill[5], S. Deva[6], B. Markman[7], M. Jameson[8], Z. Chen[9], X. Tan[10], J. Hou[11], A. Lim[12]

[1]Chris O'Brien Lifehouse, Camperdown, NSW, Australia; [2]Royal Melbourne Hospital, Parkville, VIC, Australia; [3]Peter MacCallum Cancer Centre-East Melbourne, East Melbourne, VIC, Australia; [4]Wellington Hospital, Wellington, New Zealand; [5]Tasman Oncology Research Ltd, Southport, QLD, Australia; [6]Auckland City Hospital, Auckland, New Zealand; [7]Monash Health and Monash University, Clayton, VIC, Australia; [8]Waikato Hospital, Hamilton, New Zealand; [9]BeiGene USA Inc., Fort Lee, NJ, United States; [10]BeiGene (Beijing) Co., Ltd., Beijing, China; [11]BeiGene USA, Inc., Emeryville, CA, United States; [12]Linear Clinical Research Limited, Nedlands, WA, Australia

INTRODUCTION

- Head and neck squamous cell carcinoma (HNSCC) is a leading cause of cancer-related death with 600,000 cases reported worldwide annually[1]
- Monoclonal antibodies against the immune checkpoint inhibitory receptor, programmed cell death-1 (PD-1), have demonstrated antitumor activity across multiple malignancies[2], including HNSCC[3,4]
- 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[5]
- Here, we present the preliminary results, as of 8 June 2017, of patients with HNSCC 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.

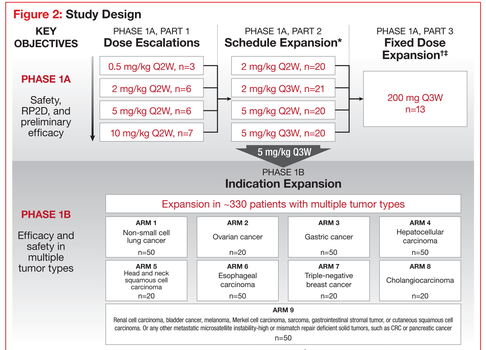
METHODS

- The study design is detailed in **Figure 2**
  - In Phase 1A, 10 mg/kg Q2W was the maximum administered dose; maximum tolerated dose (MTD) was not reached
  - All patients in Phase 1B received BGB-A317 as a 5 mg/kg IV infusion Q3W
  - Radiographic assessment was performed every 9 weeks per RECIST v1.1

Key Eligibility Criteria of the HNSCC Subset

- Adult patients (aged ≥18 years) with histologically or cytologically confirmed advanced HNSCC who have at least one measurable lesion as defined per RECIST Version 1.1, received standard therapy but 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 HNSCC treated with 5 mg/kg Q3W
- As of 8 June 2017, 18 patients with recurrent HNSCC had enrolled in this study (**Table 1**); of these 17 patients had either a prior exposure of cisplatin or carboplatin. The patient who was platinum naive had prior surgery and multiple rounds of radiation
  - A total of 3 patients remained on treatment

Table 1: Patient Demographics and Disease Characteristics of HNSCC Patients

		HNSCC Population (N=18)
Median age, years (range)		63 (25–78)
Sex	Male/female	16/2
Race	Caucasian	12
	Black/African-American	1
	Asian	2
	Other	3
Prior anti-cancer therapy regimens, n	0*	6
	1	7
	2	4
	≥3	1

*Four patients have received adjuvant treatment; 1 patient has received neoadjuvant treatment; 1 patient has received neither adjuvant or neoadjuvant therapy

Preliminary Antitumor Activity

- As of 8 June 2017, 17 HNSCC 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)
  - Three patients achieved a confirmed partial response (PR) and 6 patients achieved a stable disease (SD)
  - Disease control rate (DCR=PR+SD) was 53% (n=9/17)
  - Median treatment duration in HNSCC patients was 104 days (range: 30–339)
- Antitumor activity of BGB-A317 is presented in **Figures 3–6**

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

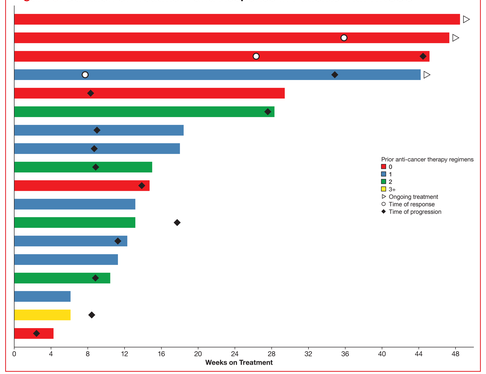
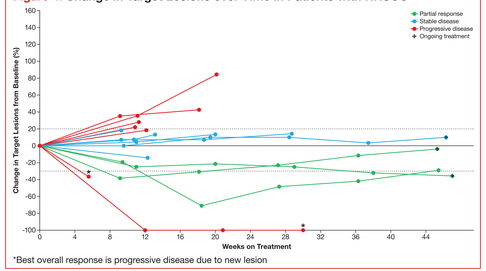
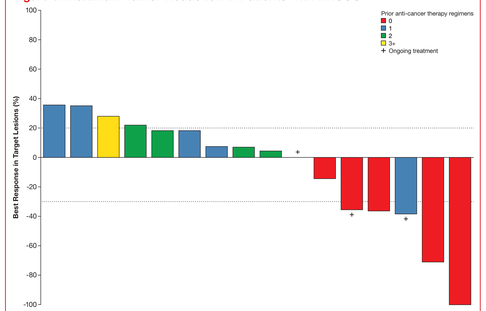


Figure 4: Change in Target Lesions over Time in Patients with HNSCC



*Best overall response is progressive disease due to new lesion

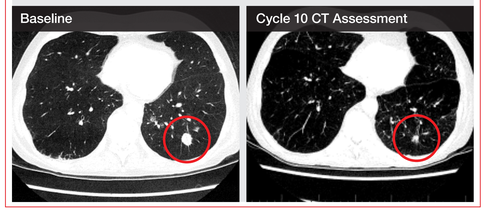
Figure 5: Maximum Tumor Reduction in Patients with HNSCC



Of the 17 evaluable patients, 1 patient had disease progression prior to the first post baseline assessment.

Figure 6: Case Example, Radiographic Images of a Patient with Partial Response

65-year old white male with HNSCC, moderately differentiated squamous cell carcinoma metastatic to lymph nodes and lung



Safety and Tolerability

- Treatment with BGB-A317 was generally well tolerated in pretreated patients with advanced HNSCC
- Treatment-related adverse events (TRAEs) occurred in 7 of the 18 patients with HNSCC (**Table 2**)
  - The only AE considered related to treatment in ≥2 patients with HNSCC was fatigue
- Nausea (n=1) was the only adverse event considered related to treatment that was grade ≥3 in severity
- No patient discontinued treatment due to a TRAE
- Of the 9 deaths reported in the patients with HNSCC, none were considered to be associated with the treatment

CONCLUSIONS

- Treatment with BGB-A317 was generally well tolerated in pretreated patients with advanced HNSCC
  - As of 8 June 2017, 3 patients remained on treatment; median treatment duration was 104 days (range: 30–339 days)
- Adverse events reported in patients with HNSCC were consistent with the overall safety profile observed in the study and were generally of low severity, manageable, and reversible
- Of the 17 evaluable patients, tumor reductions meeting the definition of partial response were observed in 3 patients; 6 patients achieved a confirmed best overall response of stable disease
- The preliminary safety profile and antitumor activity support continued development of BGB-A317 in patients with advanced/metastatic HNSCC

Table 2: TRAEs Occurring in Patients with HNSCC

	HNSCC Population (N=18)	
	All grades	Grade ≥3
Any TRAE	7	1
Fatigue	2	0
Back pain	1	0
Diarrhea	1	0
Enteritis	1	0
Face oedema	1	0
Headache	1	0
Hyperthyroidism	1	0
Hypothyroidism	1	0
Increased ALT	1	0
Increased blood alkaline phosphatase	1	0
Increased GGT	1	0
Myalgia	1	0
Nausea	1	1
Ocular hyperaemia	1	0
Pruritus (generalized)	1	0
Thrombocytopenia	1	0
Tongue oedema	1	0
Vomiting	1	0

Abbreviations: ALT, alanine aminotransferase; GGT, gamma-glutamyl transferase;TRAE, treatment-related adverse event

REFERENCES

1. Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer.* 2015;136(5):E359-86.
2. Topalian SL, Hodi FS, Brahmer JR, et al. Safety, activity, and immune correlates of anti-PD-1 antibody in cancer. *N Engl J Med.* 2012;366(26):2443–2454.
3. Seiwert TY, Burtness B, Mehra R, et al. Safety and clinical activity of pembrolizumab for treatment of recurrent or metastatic squamous cell carcinoma of the head and neck (KEYNOTE-012): an open-label, multicentre, phase 1b trial. *Lancet Oncol.* 2016;17(7):956-965.
4. Ferris RL, Blumenschein G, Fayette J, et al. Nivolumab for recurrent squamous-cell carcinoma of the head and neck. *N Engl J Med.* 2016;375(19):1856–1867.
5. Desai J, Markman B, Sandhu SK, et al. Updated safety, efficacy, and pharmacokinetics (PK) results from the phase I study of BGB-A317, an anti programmed death-1 (PD-1) mAb in patients with advanced solid tumors. *J Immunother Cancer.* 2016;4(Suppl 1):P154.

ACKNOWLEDGMENTS

The authors wish to acknowledge the investigative center study staff and study patients, as well as recognize those from BeiGene who have substantially contributed to the development of this presentation. BeiGene, Ltd., provided financial support for this presentation, including writing and editorial assistance by Aarati Rai, PhD, of SuccinctChoice Medical Communications, Chicago, IL.

Please address any questions or comments regarding this poster to Clinicaltrials@beigene.com.