Long-Term Exposure (LTE) to Tislelizumab, an Investigational Anti-PD-1 Antibody, in a First-in-Human Phase 1 Study

Jayesh Desai[1,2], Benjamin Markman[3], Michael Friedlander[4], Hui Gan[5], Lisa Horvath[6], Amanda Townsend[7], Michael Millward[8], Michael Jameson[9], Chia-Jui Yen[10], Ming-Mo Hou[11], Jeannie Hou[12], John Wu[12], Liang Liang[13], Sanjeev Deva[14]

[1]Peter MacCallum Cancer Centre, Melbourne, Australia; [2]Royal Melbourne Hospital, Parkville, Australia; [3]Monash Health and Monash University, Melbourne, Australia; [4]Prince of Wales Hospital, Randwick, New South Wales, Australia; [5]Austin Hospital, Heidelberg, Victoria, Australia; [6]Chris O'Brien Lifehouse, Camperdown, Australia; [7]The Queen Elizabeth Hospital, Woodville South, South Australia, Australia; [8]Linear Clinical Research, Nedlands, Australia; [9]Regional Cancer Centre, Waikato Hospital, and the University of Auckland Waikato Clinical Campus, Hamilton, New Zealand; [10]National Cheng Kung University Hospital, Tainan, Taiwan; [11]ChangGung Memorial Hospital, Linkou, Taiwan; [12]BeiGene USA, Inc., San Mateo, California, United States; [13]BeiGene (Beijing) Co., Ltd., Beijing, China [14]Auckland City Hospital, Auckland, New Zealand

Background Tislelizumab (BGB-A317), an investigational monoclonal antibody with high affinity and specificity for PD-1, was engineered to minimize binding to FcγR on macrophages in order to abrogate antibody-dependent phagocytosis, a potential mechanism of resistance to anti-PD-1 therapy. Previous reports from early phase studies suggest tislelizumab was generally well tolerated and had antitumor activity in patients (pts) with advanced solid tumors. Clinical effects of tislelizumab LTE (>12 mo) in pts enrolled in the first-in-human study (NCT02407990) are presented here.

Methods Patients with advanced solid tumors received IV tislelizumab 0.5, 2, 5, or 10 mg/kg Q2W, 2 or 5 mg/kg administered Q2W or Q3W, or 200 mg IV Q3W. Antitumor activity was assessed by RECIST v1.1 criteria; PD-L1 expression was retrospectively assessed with the VENTANA PD-L1 (SP263) assay.

Results As of 31 Aug 2018, 63 of the 451 pts received tislelizumab for >12 mo. In these 63 pts, median age was 64 yr and 70% had received ≥1 prior systemic therapy. Tislelizumab LTE was most common in NSCLC (n=9), HCC (n=7), and bladder and ovarian (n=5 each) cancers. Four of the 5 pts who achieved CR during this study had LTE to tislelizumab (**Table**); all 4 pts were PD-L1+ (≥1% expression on tumor cells). Across the LTE cohort, ORR was 66.7%; PR and SD were observed in both PD-L1+ and PD-L1– tumors. The median time to CR/PR (3.7 mo) and duration of CR/PR (21.1 mo) were longer in pts with LTE than pts who responded but did not remain on treatment for >12 mo (2.1 and 6.3 mo, respectively). Rash was the only treatment-related AE (TRAE) reported in ≥15% of pts. Most TRAEs were of mild or moderate severity; arthritis, diarrhea, fatigue, granuloma, hyperglycemia, and lichenoid keratosis (n=1 each) were the only grade ≥3 TRAEs reported with tislelizumab LTE.

Conclusion Tislelizumab remained well tolerated for >12 mo and elicited durable responses in pts with a variety of tumor types regardless of PD-L1 status.

Best Overall Response in Patients With Long-Term Exposure (>12 month) to Tislelizumab by PD-L1 Status				
	PD-L1+ (n=35)	PD-L1– (n=22)	Missing (n=6)	Total (N=63)
CR	4	0	0	4 (6.3%)
PR	21	13	4	38 (60.3%)
SD	9	9	2	20 (31.7%)
PD	1	0	0	1 (1.6%)
Abbreviations: CR, complete response; PD, progressive disease; PR, partial response; SD stable disease.				