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BGB-A333, an Anti-PD-L1 Monoclonal Antibody, in Combination With Tislelizumab in Patients With Urothelial Carcinoma

Juan Martin-Liberal, MD PhD

Consultant Medical Oncologist
Melanoma, Sarcoma and GU Tumors Unit
Early Drug Development Unit

Catalan Institute of Oncology (ICO), Hospitalet, Barcelona, Spain

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Juan Martin-Liberal,[1] Peter Fong,[2] Victor Moreno,[3] Sophia Frentzas,[4,5] Jayesh Desai,[6,7] Tarek Meniawy,[8] Ben Markman,[5,9] Mark Voskoboynik,[5,9,10] Nageshwar Budha,[11] John Wu,[11] Wei Shen,[12] Margaret Singh,[11] Emiliano Calvo[13]

[1]Catalan Institute of Oncology (ICO), Hospitalet, Barcelona, Spain; [2]The University of Auckland and Auckland City Hospital, Auckland, New Zealand; [3]START Madrid-FJD, Hospital Fundación Jiménez Díaz, Madrid, Spain; [4]Monash Health, Victoria, Australia; [5]Monash University, Victoria, Australia; [6]Peter MacCallum Cancer Centre, Victoria, Australia; [7]Royal Melbourne Hospital, Victoria, Australia; [8]Linear Clinical Research, Nedlands, Australia; [9]Alfred Hospital, Melbourne, Australia; [10]Nucleus Network, Melbourne, Australia; [11]BeiGene USA, Inc., San Mateo, CA, United States; [12]BeiGene (Beijing) Co., Ltd., Beijing, China; [13]START Madrid- CIOCC, Centro Integral Oncológico Clara Campal, Madrid, Spain

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Disclosure Information

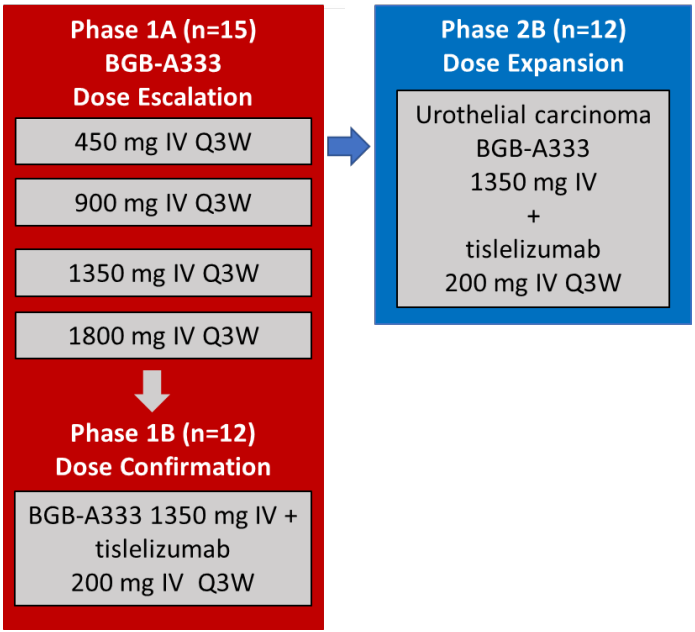
Dr. Martin-Liberal reports:

Advisory fees from Bristol-Myers Squibb, MSD, Novartis, Pierre Fabre, Roche, and Sanofi.

Lecture fees from Astellas, Bristol-Myers Squibb, MSD, Novartis, Pierre Fabre, Pfizer, and Roche.

Travel grants from Bristol-Myers Squibb, Ipsen, MSD, Novartis, Pierre Fabre, Pfizer, and Roche.

BGB-A333 + Tislelizumab Phase 1/2 Study (BGB-900-101)



- Simultaneous PD-L1 and PD-1 blockade has been hypothesized to provide synergistic antitumor effects, as inhibitors may have distinct mechanisms of action[1]
- Patients in phase 2B with locally advanced or metastatic UC (la/mUC) who had progressed after at least one platinum-containing previous regimen received BGB-A333 (anti-PD-L1) 1350 mg IV Q3W + tislelizumab (anti-PD-1) 200 mg IV Q3W
- As of 26 July 2020,12 patients (median age, 69.5 years; 92% male) were enrolled in phase 2B
  - Median duration of treatment was 6.2 months
  - Ten patients (83%) had one prior systemic therapy
  - Median study follow-up was 10 months

[1]Naing A, et al. *J Immunother Cancer*. 2019;7(1):225.

Data cutoff: 26 July 2020

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Safety Profile of BGB-A333 Plus Tislelizumab[a]

TRAEs Occurring in Two or More Patients

	Phase 1A[b] (n=15)		Phase 1B (n=12)		Phase 2B: la/mUC (n=12)		Total (N=39)	
	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3
Any TRAE, n	**8**	**2**	**7**	**3**	**5**	**2**	**20**	**7**
Fatigue	3	0	2	1	0	0	5	1
Rash maculopapular	1	0	2	1	1	0	4	1
Myalgia	2	0	1	0	1	0	4	0
Nausea	2	0	2	0	0	0	4	0
Pruritis	1	0	1	0	1	0	3	0
Asthenia	0	0	0	0	2	0	2	0
Back Pain	2	0	0	0	0	0	2	0
Diarrhea	0	0	1	0	1	0	2	0

Abbreviation: TRAE, treatment-related adverse event.

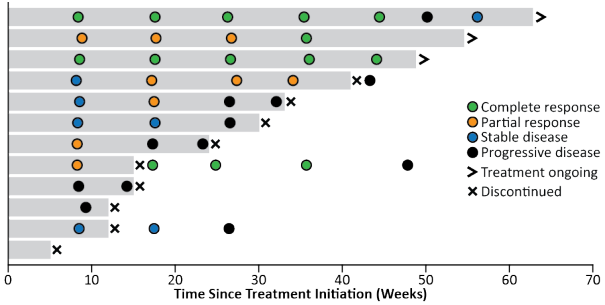
- Across the study, fatigue was the most commonly reported treatment-related adverse event
  - Adverse event profile was consistent with profiles observed during dose-escalation and dose-confirmation across multiple tumor types
- No patients in phase 2B had a fatal treatment-related adverse event
- Two patients in phase 2B experienced four immune-related adverse events (grade 3 endocrine disorders, grade 3 hypophysitis, grade 2 musculoskeletal and connective tissue disorder, grade 2 myositis)

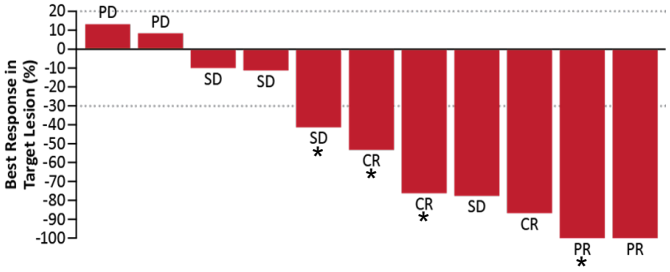
[a]Adverse events were monitored throughout the study per the National Cancer Institute-Common Terminology Criteria for Adverse Events v4.03.
[b]Patients in phase 1A received single-agent BGB-A333.

Data cutoff:
26 July 2020

Combination Treatment Was Associated With Durable Clinical Response[a]

Median duration of response was 9.1 months (95% CI: 6.0-9.6)





Confirmed Responses	PD-L1 High[b] (n=6)	PD-L1 Low[b] (n=6)	Total (N=12)
CR	2	1	3
PR	2	0	2
SD	2	2	4
PD	0	2	2
NE	0	1	1
ORR, % (95% CI)	**67 (22.3, 95.7)**	**17 (0.42, 64.1)**	**42 (15.2, 72.3)**
DCR, % (95% CI)	**100 (54.1, 100.0)**	**50 (11.8, 88.2)**	**75 (42.8, 94.5)**

*Indicates patients with lymph node only disease.
[a]Radiographical assessments were performed every 9 weeks in the first year and every 12 weeks thereafter; reported responses were investigator-assessed per RECIST v1.1.
[b]PD-L1 high was defined as ≥25% of tumor or immune cells with PD-L1 staining using the VENTANA SP263 assay.
Abbreviations: AE, adverse event; CI, confidence interval; CR, complete response; DCR, disease control rate; NE, not evaluable; ORR, objective response rate; PD, progressive disease; PD-L1, programmed death-ligand 1; PR, partial response; SD, stable disease.

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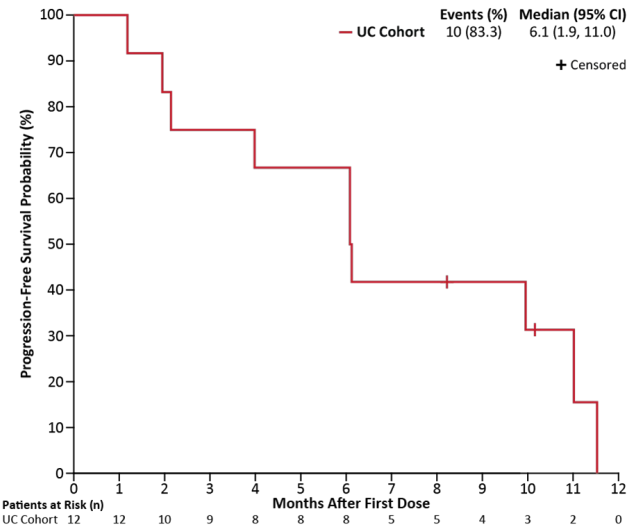
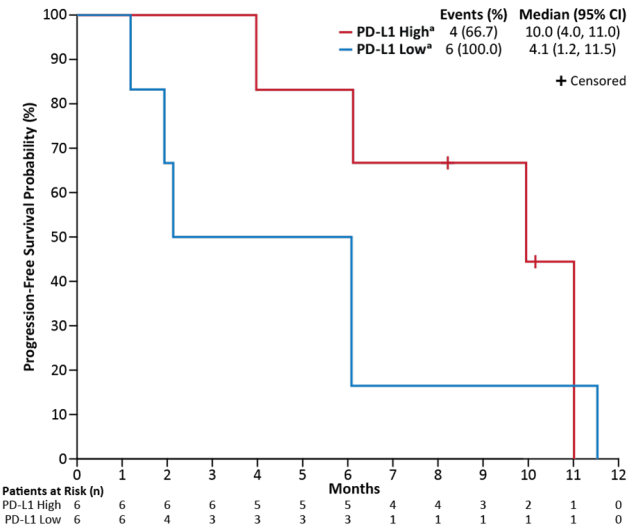
Progression-Free Survival With Combination Treatment

PFS, Overall



PFS, by PD-L1 Expression Status



[a]PD-L1 high was defined as ≥25% of tumor or immune cells with PD-L1 staining using the VENTANA SP263 assay.

Abbreviations: CI, confidence interval; PD-L1, programmed death-ligand 1; PFS, progression-free survival; UC, urothelial carcinoma.

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Conclusions

- BGB-A333 in combination with tislelizumab was generally well tolerated in patients with la/mUC (N=12)
  - Reported treatment-related adverse events were generally of mild or moderate severity
- Preliminary antitumor activity was observed in patients with la/mUC receiving BGB-A333 in combination with tislelizumab
  - Confirmed objective response rate was 42% (5/12 patients), with three patients achieving complete responses and two patients achieving partial response
  - Responses were durable (median duration of response, 9.1 months)
  - Both ORR and PFS were consistent with better efficacy in the PD-L1 high population compared with the PD-L1 low population
- These data have provided insights into combining tislelizumab, a clinical stage anti-PD-1 antibody, with anti-PD-L1 antibodies