

Phase 1b/2 Trial of BGB-A445 (OX40 Agonist) With or Without Tislelizumab in Urothelial Carcinoma, Renal Cell Carcinoma, and Melanoma

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Background: OX40 is a costimulatory receptor expressed by T cells. BGB-A445 is a monoclonal antibody OX40 agonist. Here we report the results of the phase 1b/2 trial evaluating BGB-A445 alone and with tislelizumab (TIS) in advanced urothelial carcinoma (UC), renal cell carcinoma (RCC), and melanoma (NCT05661955).

Methods: Enrolled patients (pts) received BGB-A445 alone or with TIS every 3 weeks. PD-L1 and OX40 were assessed by immunohistochemistry (IHC). Pharmacodynamics biomarkers in cohort E were determined by multiplex IHC. Primary endpoint was objective response rate by investigator per RECIST v1.1 (INV per RECIST). Secondary endpoints were disease control and clinical benefit rates by INV per RECIST, and safety.

Results: At trial end (May 27, 2025), with 9.92 months of median follow-up (range, 3.76-15.92), 113 pts were enrolled across cohorts A to H. Efficacy data are summarized in the Table. Among 15 pts with melanoma who switched from BGB-A445 to BGB-A445 + TIS after progressive disease, 4 had an unconfirmed partial response, including 2 with durable responses lasting 15.1 and 20.8 months and maximum tumor shrinkage of 53.5% and 86.5%, respectively. Grade ≥ 3 treatment-related adverse events (TRAEs) occurred in 23 pts

(20%), the most common being anemia (4%). One death (cerebral infraction) related to BGB-A445 occurred. Three TRAEs led to treatment discontinuation. No correlation between PD-L1 and OX40 expression was observed. Multiplex IHC of posttreatment tumor samples from Cohort E demonstrated an upward trend in OX40⁺CD4⁺ effector T cells and a downward trend in Ki67⁺Foxp3⁻ Treg cells compared with baseline.

Conclusions: BGB-A445 demonstrated a tolerable safety profile and preliminary antitumor activity as monotherapy or combined with TIS. PD biomarkers indicated the potential functional activity of BGB-A445, consistent with its mechanism of action.

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Table. Antitumor Activity of BGB-A445 With or Without Tislelizumab								
	2-3 LoT UC		2-3 LoT RCC		2-3 LoT Melanoma		1 LoT UC	Nonmucosal Melanoma
Cohort	A (N=18)	B (N=17)	C (N=19)	D (N=15)	E (N=19)	F (N=6)	G (N=1)	H (N=10)
Treatment	BGB-A455	BGB-A455 + TIS	BGB-A455	BGB-A455 + TIS	BGB-A455	BGB-A455 + TIS	BGB-A455 + TIS	BGB-A455 + TIS
ORR, n (%)	0	5 (29.4)	0	3 (20)	0	1 (16.7)	1 (100)	1 (10)
CR	0	1	0	0	0	0	0	0
PR	0	4	0	3	0	1	1	1
DCR, n (%)	6 (33.3)	12 (70.6)	7 (36.8)	8 (53.3)	5 (26.3)	4 (66.7)	1 (100)	2 (20.0)
CBR, n (%)	0	7 (41.2)	3 (15.8)	4 (26.7)	1 (5.3)	2 (33.3)	1 (100)	1 (10.0)
CR, complete response; CBR, clinical benefit rate; DCR, disease control rate; LoT, prior lines of therapy; ORR, objective response rate; PR, partial response; TIS, tislelizumab.								