

Phase 1 study of BGB-B2033 (GPC3 x 4-1BB bispecific antibody) Monotherapy: First Disclosure of Dose Optimization (DO) and Dose Escalation (DE) Update in Advanced Hepatocellular Carcinoma (HCC)

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Background: BGB-B2033 is a bispecific antibody targeting glypican-3 (GPC-3) on tumor cells and 4-1BB, an inducible co-stimulatory receptor expressed on T-cells. BGB-B2033 is being evaluated in a phase 1 trial as a single agent or as combination therapy in patients (pts) with advanced solid tumors (NCT06427941). The preliminary safety and antitumor activity for the DE cohort have been previously presented. The first results from DO and DE updates with 3 additional months (mo) of follow-up in pts with HCC are reported here.

Methods: Pts with HCC and ≥ 1 prior line of therapy (LoT) were randomized to receive 450 or 900 mg BGB-B2033 for DO; pts with HCC treated at doses from the DE and DO cohorts (300-1000 mg) were included in pooled analyses. Primary endpoints were safety and determining the recommended Phase 2 dose (RP2D); a secondary endpoint was ORR by investigator per RECIST v1.1.

Results: As of April 26, 2026, 110 (60 DE; 50 DO) pts with HCC were enrolled. Overall, 72% of pts had ≥ 2 LoTs and 66% had prior anti-PD-(L)1 and TKI exposure. Adverse events (AE) occurred in 82 (75%) pts; TRAEs occurred in 57 (52%) pts. Six (5%) pts experienced Grade 3 TRAEs; no grade 4 or 5 TRAEs were reported. Median study follow-up was 6.4 mo (range: 0.3–13.3) for pts receiving 300, 600, and 1000 mg, and 4.1 mo (range: 0.4–5.9) for pts receiving 450 and 900 mg. Robust antitumor activity was demonstrated across doses in DE and DO cohorts (**Table**); among pts enrolled to DE at doses ≥ 300 mg, 6-mo DOR was 72.7% (37.1%–90.3%).

Conclusions: BGB-B2033 is well tolerated in pts with HCC, with limited and manageable AEs. RP2D was determined to be 450 mg. With longer follow up, including DO cohorts, ORR of this first-in-class molecule remains highly encouraging and exhibits early evidence of durability in heavily treated HCC. Overall, these findings support continued development of BGB-B2033.

	Dose escalation			Dose optimization	
	300 mg N=14	600 mg N=14	1000 mg N=10	450 mg N=23	900 mg N=25
Confirmed ORR, n (%)	4 (28.6)	5 (35.7)	2 (20.0)	5 (21.7)	4 (16.0)
CR	1 (7.1)	0	0	0	0
PR	3 (21.4)	5 (35.7)	2 (20.0)	5 (21.7)	4 (16.0)
SD	6 (42.9)	4 (28.6)	6 (60.0)	9 (39.1)	13 (52.0)
PD	4 (28.6)	5 (35.7)	1 (10.0)	8 (34.8)	8 (32.0)
NE	0	0	1 (10.0)	1 (4.3)	0
Unconfirmed ORR, n (%)	4 (28.6)	5 (35.7)	3 (30.0)	8 (34.8)	6 (24.0)

CR	1 (7.1)	0	0	1 (4.3)	1 (4.0)
PR	3 (21.4)	5 (35.7)	3 (30.0)	7 (30.4)	5 (20.0)
SD	6 (42.9)	4 (28.6)	5 (50.0)	6 (26.1)	11 (44.0)
PD	4 (28.6)	5 (35.7)	1 (10.0)	8 (34.8)	8 (32.0)
NE	0	0	1 (10.0)	1 (4.3)	0
NE, non-evaluable					