MADRID 2026 ESMO congress

Phase 1 Study of BGB-B2033 (GPC3 x 4-1BB Bispecific Antibody) Monotherapy: First Disclosure of Dose Optimization and Dose Escalation Update in Advanced Hepatocellular Carcinoma

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24 October 2026

ESMO

Declarations of Interest

Honoraria: Eisai, Roche, ONO, MSD, Bristol Myers Squibb, BeOne Medicines, Sanofi, Servier, AstraZeneca, Boryung

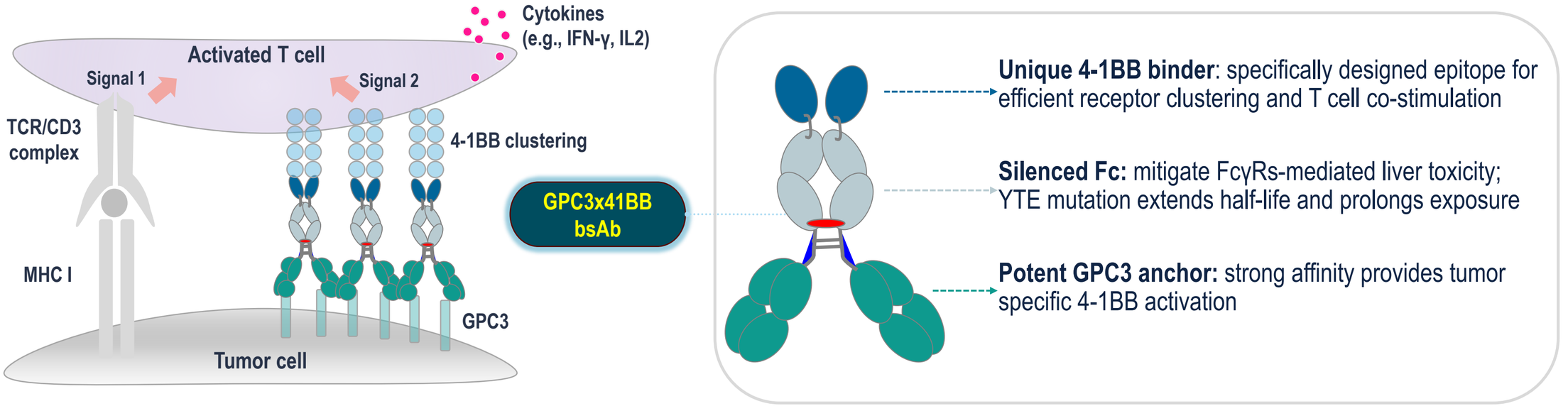
Consulting or Advisory Role: Eisai, Roche, ONO, MSD, Bristol Myers Squibb, BeOne Medicines, Servier, AstraZeneca, Boryung; IMBDx; Aptamer Science

Research Funding: Roche, BeOne Medicines; IMBDx; Dong-A ST; Boryung

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Background

- **BGB-B2033** is a novel, rationally designed IgG-based GPC3 x 4-1BB bispecific antibody that binds a unique epitope of 4-1BB
  - **GPC3:** tumor-associated antigen highly expressed in multiple tumors, including in ~90% of HCC with any staining[1]
  - Activates **4-1BB** on CD8+ T-cells only in the presence of GPC3-expressing tumor cells, enabling targeted tumor activity
  - Has an engineered Fc region designed to extend PK exposure while maintaining localized immune activation[2]
  - Demonstrated ~linear PK and prominent PD effect of soluble 4-1BB increase at dose levels ≥300 mg[3]



1. Ishiguro et al, *Sci. Transl. Med*. 2017;9, eaal4291. 2. Li et al. Poster #6009 AACR 2025. 3. Chon et al. *J Clin Oncol* 2026;44:3016.

bsAb; bispecific antibody; GPC3, glypican-3; HCC, hepatocellular carcinoma; PD, pharmacodynamics; PK, pharmacokinetics; YTE, M252Y/S254T/T256E.

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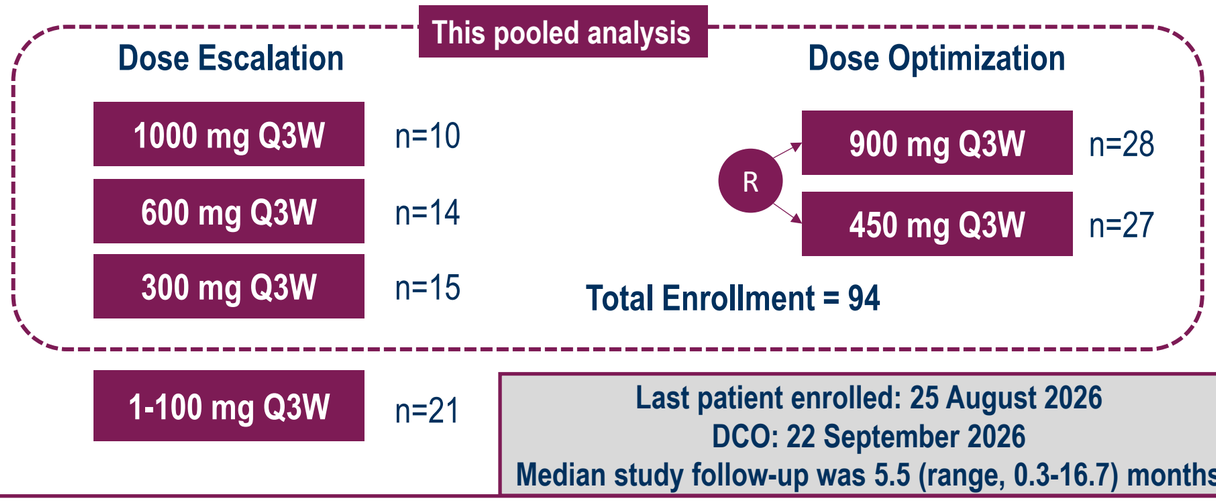
Study Design (NCT06427941)

Phase 1/2 study of BGB-B2033 alone or in combination with tislelizumab with or without bevacizumab in patients with advanced solid tumors

Key Eligibility Criteria

- Patients with aHCC who received at least 1 line of systemic therapy
  - Child Pugh A
  - BCLC C or BCLC B that is not amenable to or progressed after locoregional therapy and not amenable to curative treatment
- ECOG PS 0-1
- At least 1 measurable lesion by RECIST 1.1
- Archival tissue or fresh biopsy for GPC3 testing

Monotherapy Dose Escalation and Dose Optimization BGB-B2033 Q3W in Patients with aHCC



IV infusion Q3W

Infusion duration
Cycle 1/2: 60 ± 5 min
Cycle ≥3: 30 ± 5 min

Endpoints

Primary
- Safety
- Recommended dose for expansion
- MTD

Secondary
- Objective response rate by investigator per RECISTv1.1
- Pharmacokinetics/ pharmacodynamics
- Immunogenicity

aHCC, advanced hepatocellular carcinoma; BCLC, Barcelona Clinic Liver Cancer; DCO, data cut-off; ECOG PS, Eastern Cooperative Oncology Group Performance Status; GPC3, Glypican-3; MTD, maximum tolerate dose; Q3W, every 3 weeks; R, randomized; RECIST, Response Evaluation Criteria in Solid Tumors.

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Baseline Demographics and Disease Characteristics

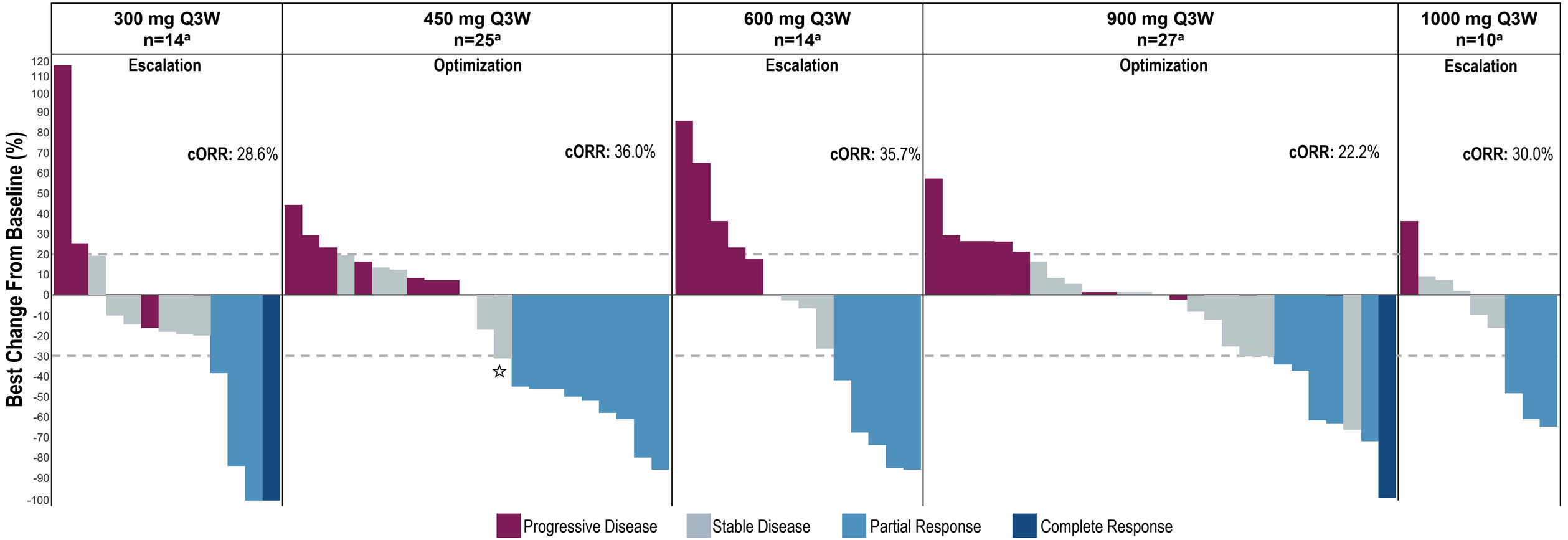
Parameters		Total (N=94)
Age, median (range), years		56.5 (24-85)
Male, n (%)		79 (84.0)
Country, n (%)	China	44 (46.8)
	Korea	38 (40.4)
	New Zealand	7 (7.4)
	USA	5 (5.3)
ECOG PS, n (%)	0	51 (54.3)
	1	43 (45.7)
Etiology of hepatitis, n (%)	HBV	82 (87.2)
	HCV	4 (4.3)
	Uninfected	8 (8.5)
Number of prior lines, median (range)		2 (1-8)
Number of prior lines, n (%)	1	30 (31.9)
	2	41 (43.6)
	≥3	23 (24.5)
Prior systemic therapy, n (%)	PD-(L)1	88 (93.6)
	TKI	64 (68.1)
	PD-(L)1 and TKI	58 (61.7)

Data cut-off: 22 September 2026

ECOG PS, Eastern Cooperative Oncology Group Performance Score; HBV, Hepatitis B; HCV, Hepatitis C; PD-(L)1, programmed cell death protein (ligand) 1; TKI, tyrosine kinase inhibitor.

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Consistent Antitumor Activity with BGB-B2033 was Observed Across Dose Escalation and Optimization Cohorts



- 450 mg RP2D was selected based on linear PK, exposure-efficacy, PD plateau, and a flat exposure-safety relationship

Data cut-off: 22 September 2026

[a]Investigator assessed and efficacy-evaluable patients

cORR, confirmed objective response rate; PD, pharmacodynamic; PK, pharmacokinetic; RP2D, recommended phase 2 dose.

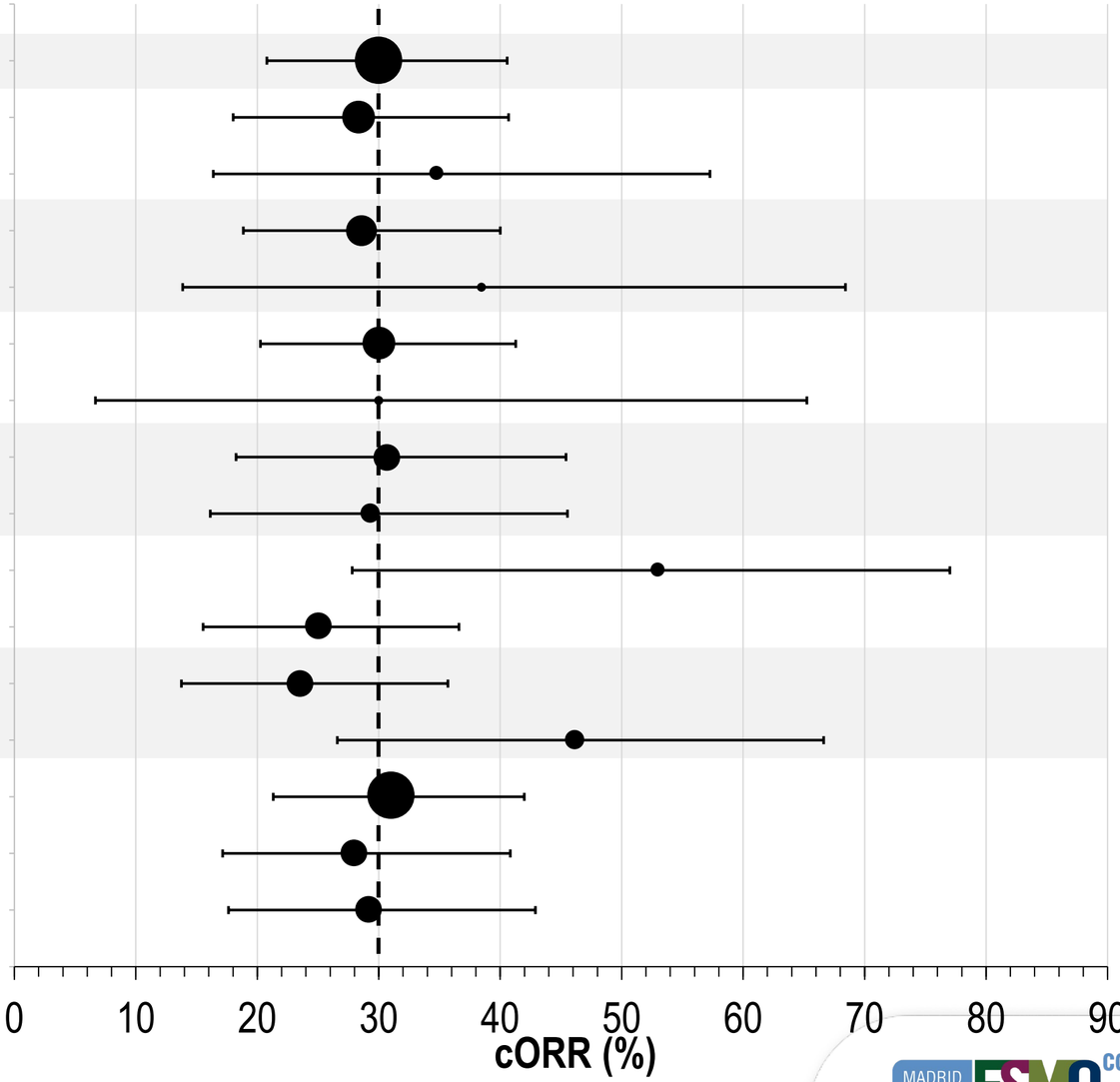
☆The patient has an unconfirmed partial response, remains on treatment and is awaiting confirmation

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Responses With BGB-B2033 Were Observed Across All Clinically Relevant Subgroups

		N[a]	Responders	cORR
Overall		**90**	**27**	**30.0**
Age	<65	67	19	28.4
	≥65	23	8	34.8
Sex	Male	77	22	28.6
	Female	13	5	38.5
Region	Asia	80	24	30.0
	ROW	10	3	30.0
ECOG PS	0	49	15	30.6
	1	41	12	29.3
BCLC Stage[b]	B	17	9	52.9
	C	72	18	25.0
Extra-hepatic Metastasis at Study Entry	Yes	64	15	23.4
	No	26	12	46.2
Prior Systemic Therapy	PD-(L)1	84	26	31.0
	TKI	61	17	27.9
	PD-(L)1 and TKI	55	16	29.1



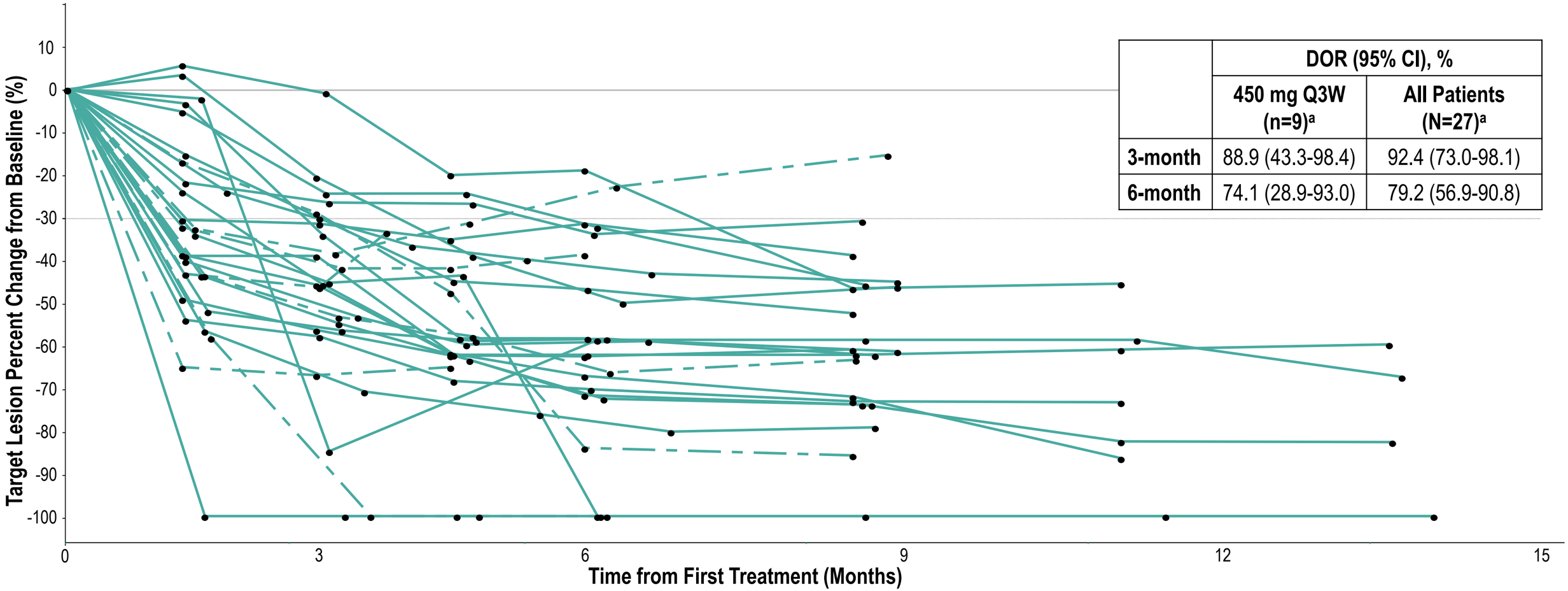
Data cut-off: 22 September 2026

[a]Investigator-assessed and efficacy-evaluable patients. [b]Data missing for one patient

BCLC, Barcelona Clinic Liver Cancer; cORR, confirmed objective response rate; ECOG PS, Eastern Cooperative Oncology Group Performance Score; PD-(L)1, programmed cell death protein (ligand) 1; TKI, tyrosine kinase inhibitor.

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Among Patients With a Confirmed Response[a] to BGB-B2033, Tumor Reductions Were Sustained Over Time Across Cohorts



	DOR (95% CI), %	
	450 mg Q3W (n=9)[a]	All Patients (N=27)[a]
3-month	88.9 (43.3-98.4)	92.4 (73.0-98.1)
6-month	74.1 (28.9-93.0)	79.2 (56.9-90.8)

Data cut-off: 22 September 2026

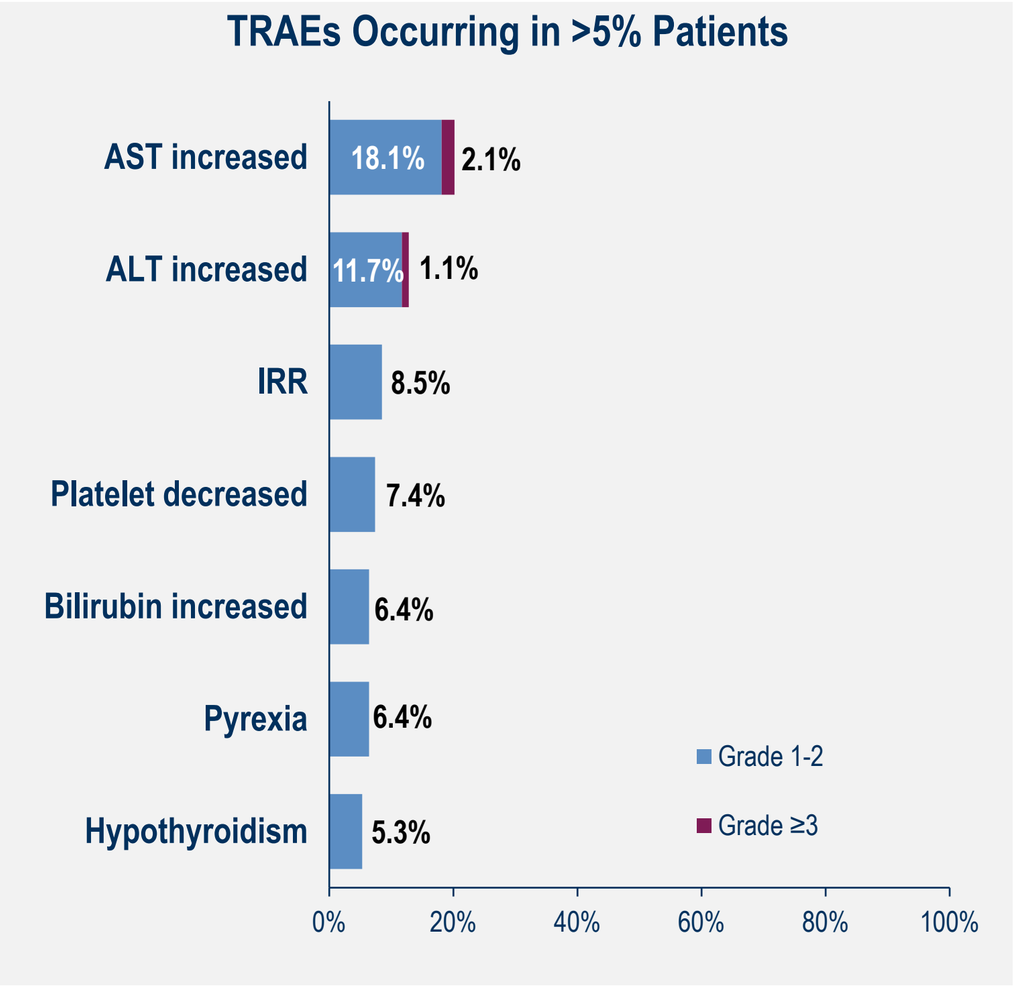
[a]Investigator-assessed confirmed responders.

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BGB-B2033 Was Well Tolerated, With Limited Grade ≥3 TRAEs

Parameter, n (%)	Dose escalation			Dose optimization		
	300 mg n=15	600 mg n=14	1000 mg n=10	450 mg n=27	900 mg n=28	Total (N=94)
Any TEAEs	11 (73.3)	9 (64.3)	10 (100)	26 (96.3)	22 (78.6)	78 (83.0)
Leading to Discontinuation	0	0	2 (20.0)	1 (3.7)	0	3 (3.2)
Grade ≥3 TEAEs	5 (33.3)	1 (7.1)	6 (60.0)	5 (18.5)	4 (14.3)	21 (22.3)
Any Serious TEAEs	0	2 (14.3)	4 (40.0)	5 (18.5)	4 (14.3)	15 (16.0)
Any TRAEs	9 (60.0)	7 (50.0)	5 (50.0)	18 (66.7)	15 (53.6)	54 (57.4)
Leading to Discontinuation	0	0	1 (10.0)[a]	1 (3.7)[b]	0	2 (2.1)
Grade ≥3 TRAEs	2 (13.3)	0	1 (10.0)	1 (3.7)	1 (3.6)	5 (5.3)
IMAEs	2 (13.3)[c]	1 (7.1)[d]	0	5 (18.5)[e]	4 (14.3)[f]	12 (12.8)



Data cut-off: 22 September 2026

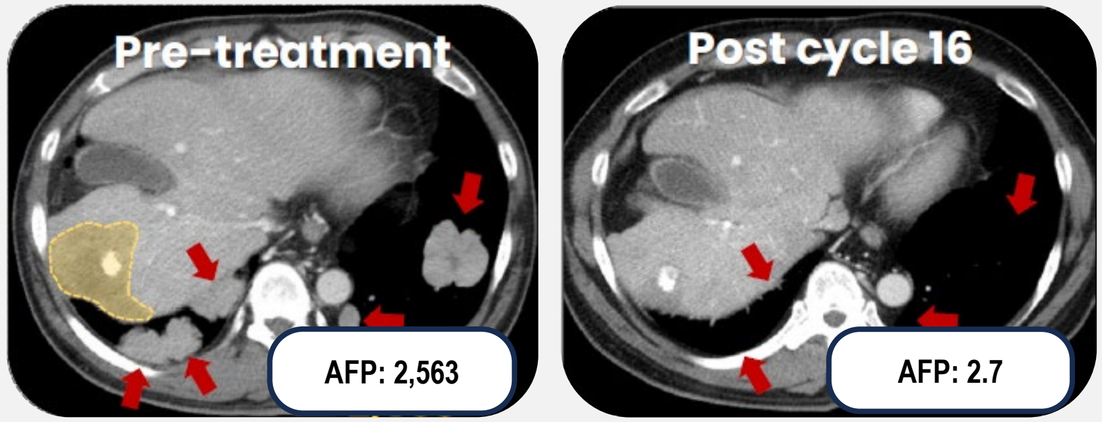
[a]Drug eruption (grade 3). [b]IRR (grade 2). [c]Hypothyroidism (n=2). [d]Rash (n=1). [e]Hypothyroidism (n=2), maculo-papular rash (n=1), rash (n=2). [f]Hypothyroidism (n=1), immune-mediated hepatitis (n=1), pancreatitis (n=1; grade 3), rash (n=1).

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; IMAE, immune-mediated adverse events; IRR, infusion-related reaction; TEAE, treatment emergent adverse event; TRAE, treatment-emergent treatment-related adverse event.

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Individual patient cases

Patient 1



PATIENT PROFILE

53-year-old male
HCC with liver and lung metastasis

HBV+ [Prior TACE]

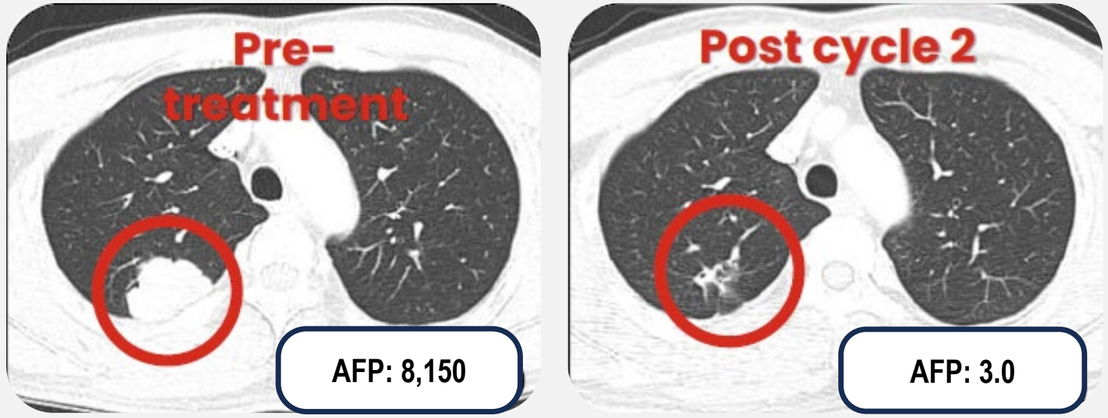
PRIOR SYSTEMIC THERAPY

1L Atezolizumab + bevacizumab

2L GARP + PD-1 (clinical trial)

3L Lenvatinib

Patient 2



PATIENT PROFILE

52-year-old male
HCC with lung metastasis

HBV+ [Prior left liver resection]

PRIOR SYSTEMIC THERAPY

1L Atezolizumab + bevacizumab

2L Atezolizumab + Lenvatinib (clinical trial)

3L Sorafenib

- BGB-B2033 introduced responses that are not commonly observed in this treatment setting, further supporting the activity signal seen in the broader dataset

AE, adverse event; AFP, alpha-fetoprotein; ALT, alanine aminotransferase; AST, aspartate aminotransferase; HBV, Hepatitis; HCC, hepatocellular carcinoma; IMAE, immune-mediated adverse events; IRR, infusion-related reaction; PD-1, programmed cell death protein 1; TACE, trans arterial chemoembolization; TEAE, treatment emergent adverse event; TRAE, treatment-emergent treatment-related adverse event.

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Conclusion

1. With longer follow up, BGB-B2033, a first-in-class GPC3 x 4-1BB bispecific antibody, continues to demonstrate compelling antitumor activity in patients with heavily pretreated aHCC
2. At the RP2D (450 mg Q3W), cORR was 36% and the 6-month DOR was 74%
3. The favorable tolerability profile is notable as patients with heavily pretreated aHCC often have underlying liver disease that limits therapeutic options
4. Given the compelling antitumor activity and favorable safety profile, global registrational studies are planned to be initiated by the end of the year

aHCC, advanced hepatocellular carcinoma; cORR, confirmed objective response rate; DOR, duration of response; GPC3, glypican-3; ORR, objective response rate; RP2D, recommended phase 2 dose; Q3W, every 3 weeks.

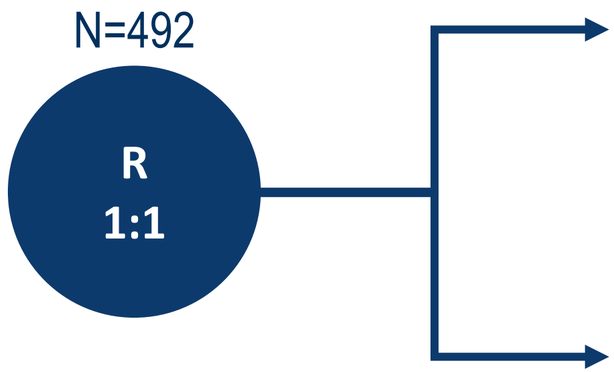
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GroundBBreaker 301 Study (NCT07836530)

Phase 3 study of BGB-B2033 vs investigator's choice of sorafenib or lenvatinib in patients with HCC who progressed on prior systemic treatment

Key Eligibility Criteria

- Adults (≥18 years) with histologically confirmed HCC not amenable to curative surgical or locoregional therapies
- GPC3 expression level for stratification
- Previously treated with up to 2 systemic regimens, including PD-(L)1 inhibitors
- Measurable disease per RECIST v1.1
- ECOG PS 0 or 1
- Adequate organ function



BGB-B2033

- 450mg Q3W intravenous administration
- Until disease progression, unacceptable toxicity, or other discontinuation criteria

Investigator's choice

- Sorafenib BID or lenvatinib QD
- Until disease progression, unacceptable toxicity, or other discontinuation criteria

Primary endpoint
OS

Secondary endpoints

ORR, PFS, and DOR per BICR and investigator assessment

Safety

PROs

BICR, blinded independent central review; BID, twice daily; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; GPC3, glypican-3; HCC, hepatocellular carcinoma; ORR, objective response rate; OS, overall survival; PD-(L)1, programmed cell death protein (ligand) 1; PFS, progression-free survival; PRO, patient-reported outcome; Q3W, every 3 weeks; QD, daily; RECIST, Response Evaluation Criteria in Solid Tumors.

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Thank you!

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