Phase Ib study of BI 836880 (VEGF/Ang2 nanobody®) in combination with ezabenlimab (BI 754091; anti-PD-1 antibody) in patients with solid tumours

#532P

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Introduction

- VEGF/VEGFR2 and Ang/Tie2 signalling have key roles in tumour angiogenesis[1,2]
- Combining anti-VEGF/Ang2 with anti-PD-1 agents promotes an immunopermissive state, supportive of tumour cell destruction mediated by T cells[1–4]
- BI 836880, a humanised bispecific nanobody® that targets VEGF and Ang2, and ezabenlimab (BI 754091), an anti-PD-1 monoclonal antibody, have both shown safety and preliminary antitumour activity as monotherapies[5,6]
- This ongoing Phase Ib study aims to assess BI 836880 and ezabenlimab in patients with advanced or metastatic solid tumours. In Part 1, the RP2D was defined as BI 836880 720 mg + ezabenlimab 240 mg intravenously q3w in patients with PD-L1 positive metastatic NSCLC[7]

Ang, angiopoietin; NSCLC, non-small cell lung cancer; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; q3w, every 3 weeks; RP2D, recommended Phase II dose; VEGF, vascular endothelial growth factor; VEGFR2, VEGF receptor 2

Objective

- In Part 2, the primary objective is to assess the antitumour activity of BI 836880 in combination with ezabenlimab in patients with advanced or metastatic solid tumours
- Secondary and further objectives are to evaluate the safety, pharmacokinetics, and pharmacodynamics

Methods

Part 2: Cohort expansion: BI 836880 720 mg + ezabenlimab 240 mg intravenously q3w

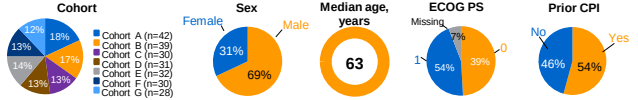
- **Cohort A (n=42*)** mNSCLC after CPI monotherapy
- **Cohort B (n=40)** mNSCLC after CT + CPI therapy
- **Cohort C (n=30*)** mSCLC after CT ± CPI therapy
- **Cohort D (n=31*)** Recurrent GBM (1st and 2nd recurrences)
- **Cohort E (n=32*)** Immunotherapy-resistant mMEL
- **Cohort F (n=30*)** HCC after prior sorafenib or lenvatinib
- **Cohort G (n=30)** Previously untreated unresectable HCC

Primary endpoint: Shrinkage estimator of objective response, defined as best overall response (RECIST v1.1)
Secondary endpoints: Adverse events, disease control, duration of response, progression-free survival, pharmacokinetics, tumour shrinkage

*Recruitment completed. CPI, checkpoint inhibitor; CT, chemotherapy; GBM, glioblastoma; HCC, hepatocellular carcinoma; m, metastatic; MEL, melanoma; RECIST, Response Evaluation Criteria in Solid Tumours; SCLC, small cell lung cancer

Results

- As of 28 June 2021, 232 patients have received treatment in Part 2 and 85 remain on treatment



ECOG PS, Eastern Cooperative Oncology Group performance status

Key findings and conclusions

- A total of 232 patients have been treated in Part 2 of this ongoing Phase Ib study evaluating BI 836880 and ezabenlimab in patients with advanced or metastatic solid tumours
- BI 836880 in combination with ezabenlimab had a manageable safety profile; the most common AEs were asthenia (25%) and hypertension (19%)
- Clinical activity was observed across all cohorts, with particularly promising activity observed in the HCC, SCLC, and GBM cohorts
- A total of 85 patients remain on treatment in Part 2 and continue to be followed up

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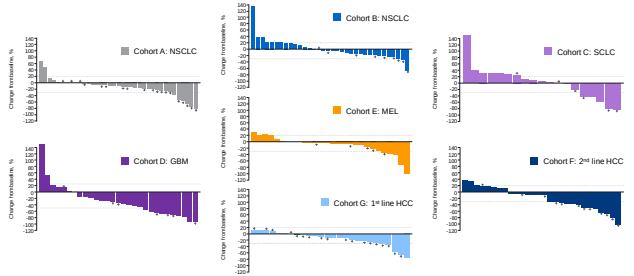
Efficacy

Confirmed best overall response

	Total	A	B	C	D	E	F	G*
Evaluable, n	217	40	36	26	30	32	29	24
Complete response, n (%)	1 (<1)	0	0	0	0	0	1 (3)	0
Partial response, n (%)	35 (16)	6 (15)	1 (3)	5 (19)	6 (20)	3 (9)	11 (38)	3 (13)
Stable disease, n (%)	114 (53)	26 (65)	20 (56)	4 (15)	19 (63)	16 (50)	11 (38)	18 (75)
Progressive disease, n (%)	51 (24)	5 (13)	12 (33)	10 (38)	5 (16)	12 (38)	4 (14)	3 (13)
Discontinued with <2 post-baseline scans, n (%)	16 (7)	3 (8)	3 (8)	7 (27)	0	1 (3)	2 (7)	0

Evaluable patients are those with at least two post-baseline scans or who discontinued treatment. *Cohort G was the last to recruit; patients in this cohort do not have sufficient duration of treatment and continue to be followed for response



Positive values indicate tumour growth, while negative values indicate tumour shrinkage. Only valid post-baseline sums of target lesion diameters are used to generate the figures above. Some patients have sufficient tumour shrinkage to qualify for target partial response or complete response but have overall progressive disease due to non-target progressive disease and/or appearance of new lesions. + indicates ongoing patients

Safety

N=232	All grades n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)
Any AE*	210 (91)	34 (15)	81 (35)	74 (32)	12 (5)	9 (4)
Asthenia	57 (25)	27 (12)	24 (10)	6 (3)	0	0
Hypertension	45 (19)	8 (3)	21 (9)	15 (6)	0	0
Diarrhoea	37 (16)	22 (10)	12 (5)	3 (1)	0	0
Decreased appetite	30 (13)	20 (9)	8 (3)	2 (1)	0	0
Fatigue	27 (12)	17 (7)	7 (3)	3 (1)	0	0
Treatment-related AE	134 (58)	48 (21)	49 (21)	32 (14)	5 (2)	0
Immune-related AE	34 (15)	10 (4)	15 (7)	5 (2)	4 (2)	0
Serious AE	76 (33)	2 (1)	19 (8)	36 (16)	10 (4)	9 (4)

*Maximum Common Terminology Criteria for Adverse Events grade. AE, adverse event

References

1. Fukumura D, et al. Nat Rev Clin Oncol 2018;15:325–40; 2. Hofmann I, et al. Poster presentation at the 8th Euro Global Summit on Cancer Therapy 2015; 3. Gerald D, et al. Cancer Res 2013;73:1649–57; 4. Huang H, et al. Nat Rev Cancer 2010;10:575–85; 5. Le Tourneau C, et al. J Clin Oncol 2018; 36(Suppl15):12024; 6. Johnson ML, et al. J Clin Oncol 2018;36(Suppl5):212; 7. Girard N, et al. J Clin Oncol 2020;38(Suppl15):9566

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