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

#2579

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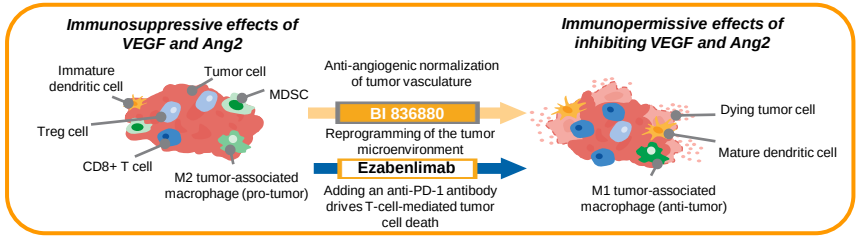
Introduction

Please scan the QR code for additional introduction information

- Combining anti-VEGF/Ang2 with anti-PD-1 agents promotes an immunopermissive state, supportive of tumor cell destruction mediated by T cells[1–4]
- BI 836880, a humanized bispecific nanobody® that targets VEGF and Ang2, and ezabenlimab (BI 754091), an anti-PD-1 monoclonal antibody, have both shown safety and preliminary anti-tumor activity as monotherapies[5,6]



Ang2, angiopoietin 2; CD8+, cluster of differentiation 8+; MDSC, myeloid-derived suppressor cell; PD-1, programmed cell death protein 1; Treg, regulatory T cell; VEGF, vascular endothelial growth factor

Objective

- This ongoing Phase Ib study aims to assess the safety and anti-tumor activity of BI 836880 and ezabenlimab in patients with advanced or metastatic solid tumors

Methods

Please scan the QR code for additional methods

Part 1: Dose escalation
14 patients with PD-L1 positive mNSCLC (non-squamous)
In Part 1, the RP2D was defined as BI 836880 720 mg + ezabenlimab 240 mg intravenously every 3 weeks[7]

Primary endpoint:
MTD or RP2D based on dose limiting toxicities
Secondary endpoints:
Adverse events, pharmacokinetics
Further endpoints include:
Best overall response

Part 2: Cohort expansion
All patients to receive the RP2D: BI 836880 720 mg + ezabenlimab 240 mg intravenously every 3 weeks

- **Cohort A (n=40)** 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 metastatic melanoma
- **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 version 1.1)
Secondary endpoints: Adverse events, disease control, duration of response, progression-free survival, pharmacokinetics, tumor shrinkage

*Recruitment completed. CPI, checkpoint inhibitor; CT, chemotherapy; GBM, glioblastoma; HCC, hepatocellular carcinoma; m, metastatic; MTD, maximum tolerated dose; PD-L1, programmed death ligand-1; RECIST, Response Evaluation Criteria in Solid Tumours; RP2D, recommended Phase II dose

Key findings and conclusions

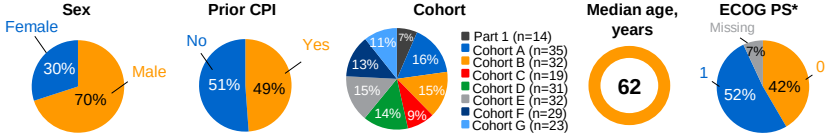
- This ongoing Phase Ib study is evaluating the safety and anti-tumor activity of BI 836880 and ezabenlimab in patients with advanced or metastatic solid tumors
- As of March 2021, 215 patients have been treated
- Overall, 183 (85%) patients have experienced an adverse event, most commonly asthenia (22%) and hypertension (19%)

- Of the 179 patients evaluable for response at data cut-off, 1 patient with HCC had a confirmed complete response, 22 patients had partial response, and 110 patients had stable disease
- At data cut-off, 106 patients remain on treatment
- BI 836880 plus ezabenlimab had a manageable safety profile. Preliminary antitumor activity was observed in a range of tumor types

Data were originally presented: JSMO 2021. *Corresponding author email address: nicolas.girard2@curie.fr

Results

- As of March 1, 2021, 215 patients have been treated



ECOG PS, Eastern Cooperative Oncology Group performance status. *Total percentage exceeds 100% due to rounding

Safety

Patients with:	All grades n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)
Any adverse event*	183 (85)	37 (17)	74 (34)	59 (27)	5 (2)	8 (4)
Asthenia	48 (22)	27 (13)	15 (7)	6 (3)	0	0
Hypertension	41 (19)	7 (3)	18 (8)	16 (7)	0	0
Diarrhea	30 (14)	20 (9)	9 (4)	0	0	0
Nausea	27 (13)	16 (7)	10 (5)	1(<1)	0	0
Decreased appetite	25 (12)	15 (7)	9 (4)	1 (<1)	0	0
Fatigue	22 (10)	14 (7)	6 (3)	2 (1)	0	0
Treatment-related adverse event	118 (55)	42 (20)	43 (20)	28 (13)	4 (2)	1 (<1)
Immune-related adverse event	35 (16)	9 (4)	18 (8)	4 (2)	4 (2)	0
Serious adverse event	65 (30)	2 (1)	19 (9)	30 (14)	5 (2)	8 (4)

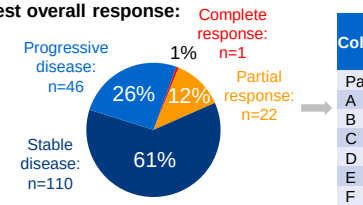
- Grade 4 adverse events included hyperkalemia plus cardiac arrest, laryngospasm, gastrointestinal perforation (all non-drug-related) and drug-related anaphylactic reaction, cholestatic hepatitis, acute pancreatitis, and increased transaminases
- Grade 5 adverse events included COVID-19 pneumonia, epilepsy, intracranial hemorrhage, cardio-respiratory arrest, hemoptysis, hepatic failure, general physical health deterioration, Glasgow coma scale abnormal plus shortness of breath (all non-drug-related) and drug-related tracheal hemorrhage

*Maximum Common Terminology Criteria for Adverse Events grade

Efficacy

- At data cut-off, 179 patients were evaluable for response and 106 patients were still on treatment

Best overall response:



Cohort	Evaluable, n	Complete response, n	Partial response, n	Stable disease, n	Progressive disease, n
Part 1	14	0	2	9	3
A	24	0	4	17	3
B	30	0	0	19	11
C	17	0	5	4	8
D	28	0	4	19	5
E	31	0	3	18	10
F	25	1	3	18	3
G	10	0	1	6	3

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