Ezabenlimab (BI 754091), an anti-PD-1 antibody, in combination with BI 836880, a VEGF/Ang2-blocking nanobody®: safety and efficacy in patients with previously treated advanced solid tumors

#2582

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Introduction

- The combination of anti-PD-1 antibodies with other immunomodulatory or targeted therapies has the potential for synergistic effects[1]
- VEGF and Ang2 play key roles in tumor angiogenesis and have an immunosuppressive effect in the tumor microenvironment. Combining anti-VEGF/Ang2 with an anti-PD-1 therapy promotes an immunopermissive state supportive of T-cell-mediated tumor cell death.[1,2] An ongoing Phase Ib trial investigating this therapeutic approach has observed manageable safety and preliminary anti-tumor activity[3,4]
- In the current open-label, multicentre, Phase II platform trial (NCT03697304), ezabenlimab, an anti-PD-1 antibody, is being assessed in combination with other agents.[5] Here, we report preliminary data from Module C, which is assessing ezabenlimab in combination with BI 836880, a humanized bispecific nanobody® that targets VEGF and Ang2

Ang2, angiopoietin-2; PD-1, programmed cell death protein 1; VEGF, vascular endothelial growth factor

Objectives

- To investigate the safety and efficacy of ezabenlimab in combination with BI 836880, in patients with previously treated advanced solid tumors

Methods

- 150 patients are being enrolled into five cohorts (approximately 30 per cohort), and will receive intravenous infusions of ezabenlimab (240 mg) and BI 836880 (720 mg) every three weeks

Cohort 1:	Locally advanced/metastatic gastric or gastroesophageal adenocarcinoma with ≥1 prior treatment (anti-PD-[L]1 naïve)
Cohort 2:	Any advanced/metastatic solid tumor (excluding non-squamous NSCLC or melanoma) with prior anti-PD-(L)1 treatment* for ≥2 months, which progressed after achieving at least SD for ≥4 months
Cohort 3:	Advanced/metastatic solid tumors† with no benefit from prior anti-PD-(L)1 treatment* (SD or PD in <4 months)
Cohort 4:	Locally advanced/metastatic microsatellite stable colorectal cancer with ≥1 prior treatment (anti-PD-[L]1 naïve)
Cohort 5:	Advanced metastatic microsatellite stable and mismatch repair-proficient endometrial carcinoma, which progressed after 1 line of chemotherapy (anti-PD-[L]1 naïve)

- All patients are aged ≥18 years, with an Eastern Cooperative Oncology Group performance status of 0–1, and ≥1 measurable lesion according to RECIST version 1.1

Primary endpoint
Objective response per RECIST version 1.1, as assessed by the Investigator
Secondary endpoints
Duration of response
Disease control
Progression-free survival

Further endpoints
Anti-tumor activity by iRECIST
Safety and tolerability of ezabenlimab and BI 836880
Safety and biomarker measurements
Pharmacokinetics and pharmacodynamics
Overall survival

*A maximum of 1 line of prior anti-PD-(L)1-based therapy permitted. †Eligible tumor types: previously treated colorectal cancer; Merkel cell carcinoma; squamous cell skin carcinoma; other squamous cancers (head and neck, cervical, anal, penile, esophageal and vulvar); other gastrointestinal cancers (biliary tract, gastric, esophageal, gastrointestinal stromal tumor); other thoracic cancers (small cell lung cancer, mesothelioma); urothelial cancers; renal cell carcinoma; neuroendocrine tumors; soft-tissue sarcomas; thyroid cancer; gynecological tumors (ovary, endometrial, cervical); other tumor types for which no therapy of proven efficacy exists, or which are not amenable to standard therapies and where anti-PD-(L)1 therapy may be considered in exceptional cases.
iRECIST, immune Response Evaluation Criteria In Solid Tumors; PD, progressive disease; PD-(L)1, programmed death ligand 1; SD, stable disease

Key findings and conclusions

- NCT03697304 is a Phase II platform trial evaluating ezabenlimab (anti-PD-1 antibody) in combination with other agents
- Here, we report data from Module C, evaluating ezabenlimab plus BI 836880 (humanized bispecific antibody that targets VEGF and Ang2)

- As of April 2021, 60 patients have been treated and 46 (77%) patients have experienced adverse events, including nausea (27%), fatigue (23%), and hypertension (20%)
- Of 33 patients evaluable for response, one had confirmed PR (Cohort 5) and 21 had SD
- These preliminary data suggest that ezabenlimab in combination with BI 836880 has a manageable safety profile. Cohorts are continuing to recruit

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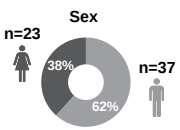
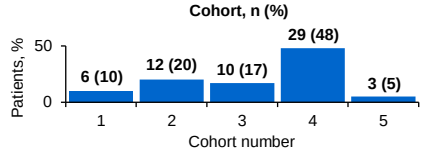
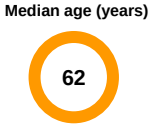
Results

- As of April 2021, 60 patients have been treated. Median duration of treatment is 70 days (range 12–160 days)







Safety

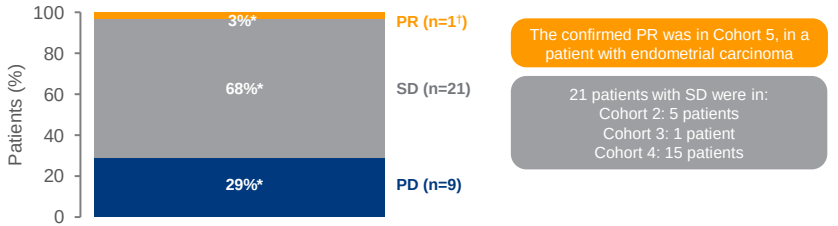
Patients with:	All Grades n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)
Any adverse event*	46 (77)	10 (17)	15 (25)	19 (32)	0	2 (3)
Nausea	16 (27)	8 (13)	7 (12)	1 (2)	0	0
Fatigue	14 (23)	8 (13)	5 (8)	1 (2)	0	0
Hypertension	12 (20)	0	4 (7)	8 (13)	0	0
Diarrhea	7 (12)	5 (8)	1 (2)	1 (2)	0	0
Arthralgia	7 (12)	5 (8)	1 (2)	1 (2)	0	0
Treatment-related adverse events	28 (47)	10 (17)	7 (12)	11 (18)	0	0
Immune-related adverse events	4 (7)	2 (3)	1 (2)	1 (2)	0	0
Serious adverse events	12 (20)	0	3 (5)	7 (12)	0	2 (3)

- The two Grade 5 adverse events were aspiration pneumonia (Cohort 3) and cardiac arrest (Cohort 2) which were not related to treatment
- Immune-related adverse events included: Grade 1 rash (Cohort 4) and arthralgia (Cohort 2), Grade 2 hypothyroidism (Cohort 4) and Grade 3 blood creatine phosphokinase increased (Cohort 2)
- Five patients had infusion-related reactions (Grade 1, n=2; Grade 2, n=3)
- Two patients had adverse events that led to treatment discontinuation (Grade 3 bile duct stone and Grade 2 pain)

*Maximum Common Terminology Criteria for Adverse Events Grade

Efficacy

- As of April 2021, 33 patients are evaluable for response:



*Percentages based on confirmed responses (n=31). †Confirmed PR, n=1; unconfirmed PR, n=2 (Cohorts 1 and 4); PR partial response

References

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