

Ezabenlimab (BI 754091), an anti-PD-1 antibody, in combination with BI 836880, a VEGF/Ang2-blocking nanobody, in patients with previously treated advanced solid tumours

#541P

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Introduction

- The combination of anti-PD-1 antibodies with other immunomodulatory or targeted therapies has the potential for synergistic effects¹
- VEGF and Ang2 play key roles in tumour angiogenesis and have an immunosuppressive effect in the tumour microenvironment. Combining anti-VEGF/Ang2 with an anti-PD-1 therapy promotes an immunopерmissive state supportive of T-cell-mediated tumour cell death.^{1,2} An ongoing Phase Ib trial investigating this therapeutic approach has observed manageable safety and preliminary antitumour activity.^{3,4}
- In this 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 the module assessing ezabenlimab in combination with BI 836880, a humanised bispecific nanobody⁶ that targets VEGF and Ang2

Ang2, angiotensin-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 tumours

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 3 weeks

Cohort 1: Locally advanced/metastatic GEC with ≥1 prior treatment (anti-PD-[L]1 naïve)

Cohort 2: Any advanced/metastatic solid tumour (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 (secondary resistance)

Cohort 3: Advanced/metastatic solid tumours¹ with no benefit from prior anti-PD-(L)1 treatment* (SD <4 months or PD in <4 months; primary resistance)

Cohort 4: Locally advanced/metastatic microsatellite stable colorectal cancer with ≥1 prior treatment (anti-PD-[L]1 naïve) [RECRUITMENT COMPLETE]

Cohort 5: Advanced metastatic microsatellite stable and mismatch repair-proficient endometrial carcinoma, which progressed after one 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	Further endpoints
Objective response per RECIST version 1.1, as assessed by the Investigator	Antitumour activity by iRECIST
Secondary endpoints	Safety and tolerability of ezabenlimab and BI 836880
Duration of response	Safety and biomarker measurements
Disease control	Pharmacokinetics and pharmacodynamics
Progression-free survival	Overall survival

*A maximum of one line of prior anti-PD-(L)1-based therapy permitted. ¹Eligible tumour types: previously treated colorectal cancer; Merkel cell carcinoma; squamous cell skin carcinoma; other squamous cancers (head and neck, cervical, anal, penile, oesophagoesophageal and vulvar); other gastrointestinal cancers (biliary tract, gastric, oesophagoesophageal, gastrointestinal stromal tumour); other thoracic cancers (small cell lung cancer, mesothelioma); urothelial cancers; renal cell carcinoma; neuroendocrine tumours; soft-tissue sarcomas; thyroid cancer; gynaecological tumours (ovary, endometrial, cervical); other tumour 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. GEC, gastroesophageal cancer; RECIST, 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 the module evaluating ezabenlimab plus BI 836880 (a humanised bispecific antibody that targets VEGF and Ang2)
- Ezabenlimab in combination with BI 836880 had a manageable safety profile; most frequently reported AEs were nausea (29%) and fatigue (25%)
- The combination showed preliminary activity; confirmed PRs were observed in the GEC (n=1), secondary resistance (n=1), and endometrial cancer (n=2) cohorts
- The colorectal cancer cohort has completed recruitment; others are continuing to recruit



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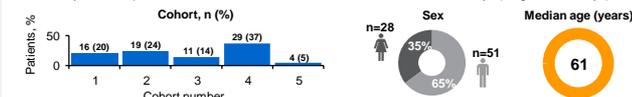
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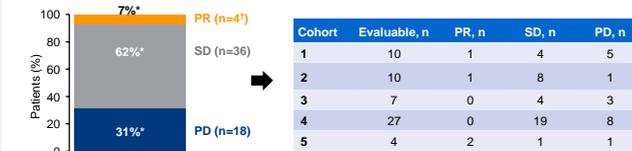
Patients

- As of July 2021, 79 patients have been treated. Median duration of treatment is 99 days (range 16–232 days)



Efficacy

- As of July 2021, 59 patients are evaluable for response:



- The median duration of SD was 90 days (Cohort: 1, 43 days; 2, 107 days; 3, 63 days; 4, 126 days; 5, 83 days)

*Percentages based on confirmed responses (n=58); ¹Confirmed PR, n=4; unconfirmed PR, n=1 (Cohort 2); PR, partial response

Safety

Patients with:	All grades n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)
Any AE ¹	70 (89)	11 (14)	25 (32)	31 (39)	1 (1)	2 (3)
Nausea	23 (29)	13 (17)	8 (10)	2 (3)	0	0
Fatigue	20 (25)	11 (14)	7 (9)	2 (3)	0	0
Hypertension	15 (19)	0	6 (8)	8 (10)	1 (1)	0
Diarrhoea	14 (18)	9 (11)	1 (1)	4 (5)	0	0
Peripheral oedema	14 (18)	7 (9)	7 (9)	0	0	0
Treatment-related AEs	46 (58)	10 (13)	17 (22)	18 (23)	1 (1)	0
Immune-related AEs	8 (10)	2 (3)	5 (6)	1 (1)	0	0
Serious AEs	22 (28)	0	3 (4)	16 (20)	1 (1)	2 (3)

¹Maximum Common Terminology Criteria for Adverse Events grade. AE, adverse event

- The two grade 5 AEs were aspiration pneumonia (Cohort 3) and cardiac arrest (Cohort 2); both were considered non-related

- Seven patients had infusion-related reactions (grade 1, n=1; grade 2, n=6)
- Two patients had adverse events that led to treatment discontinuation (grade 3 bile duct stone and grade 2 pain)

References

- Fukamura D, et al. Nat Rev Clin Oncol 2018;15:325–40; 2. Allen E, et al. Sci Transl Med 2017;9:eak9679; 3. ClinicalTrials.gov identifier: NCT03468426; 4. Girard N, et al. J Clin Oncol 2020;38(Suppl15):9566; 5. Hussein M, et al. J Clin Oncol 2021;39(Suppl):TPS152

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