Ezabenlimab (BI 754091) monotherapy in patients with advanced solid tumours

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Introduction and objectives

- Ezabenlimab (BI 754091) is a PD-1 targeting monoclonal antibody,[1] which is being investigated as monotherapy and in combination with other anti-cancer agents (see QR code for posters reporting data with ezabenlimab in combination with BI 836880 [VEGF/Ang2 inhibitor] and BI 765063 [SIRPα antagonist])
- The RP2D for ezabenlimab monotherapy was previously reported to be 240 mg q3w.[2] Here, we report safety and efficacy data in patients who received ezabenlimab at the RP2D, as well as preliminary pharmacokinetic data

Ang2, angiopoietin-2; PD-1, programmed cell death protein-1; q3w, every 3 weeks; RP2D, recommended Phase II dose; SIRPα, signal regulatory protein alpha; VEGF, vascular endothelial growth factor

Methods

- Data from patients treated in two Phase I dose escalation/expansion trials and a Phase I imaging trial are presented; all received intravenous infusions of ezabenlimab 240 mg q3w
- Tumour response was evaluated as per RECIST 1.1. Safety was assessed by incidence and severity of AEs

Study 1381.1 (NCT02952248)

Dose escalation (80/240/400 mg)
Patients with any advanced/metastatic tumours (prior anti-PD-1 therapy permitted)

Dose expansion of ezabenlimab 240 mg in four cohorts (anti-PD-1-naïve) in patients with:
1. Advanced tumours (NSCLC, bladder cancer, melanoma, gastric cancer, ovarian cancer, TNBC, and RCC)
2. Tumours that are TMB-high (≥10 mutations/Mb), excluding those that are MSI-high
3. Squamous cell cervical, anal, and skin tumours
4. Recurrent vaginal or vulvar squamous cell carcinoma (HPV-positive or -negative) not amenable to surgery

Study 1381.4 (NCT03433898)

Dose confirmation of ezabenlimab 240 mg in Japanese patients
Patients with any advanced/metastatic tumours (prior anti-PD-1 therapy permitted)

Study 1381.3 (NCT03780725)

PET imaging study
Patients with advanced NSCLC (with ≥3 months SD on prior anti-PD-1 therapy) and HNSCC (prior anti-PD-1 permitted)

AE, adverse event; HNSCC, head and neck squamous cell carcinoma; HPV, human papilloma virus; MSI, microsatellite instability; NSCLC, non-small cell lung cancer; PET, positron emission tomography; q3w, every 3 weeks; RCC, renal cell carcinoma; RECIST, Response Evaluation Criteria In Solid Tumors; SD, stable disease; TMB, tumour mutational burden; TNBC, triple negative breast cancer

Patients

- A total of 111 patients received ezabenlimab 240 mg q3w across the three Phase I studies
- At data cut-off (Nov 2020), enrolment was complete and 98 (88%) patients had discontinued treatment
  - The most common reason for discontinuation was progressive disease (78 [70%] patients)
- Final analyses of each trial will be performed when all patients have completed the trials
- At data cut-off, median treatment duration was 94 days (range 20–655 days)

	N=111
Female, n (%)	83 (75)
Median (range) age, years	62 (25–85)
Race, n (%)	
Asian	8 (7)
Black or African American	10 (9)
White	89 (80)
Other	4 (4)
ECOG PS, n (%)	
0	34 (31)
1	77 (69)
Median (range) number of prior systemic therapies	2 (1–10)

ECOG PS, Eastern Cooperative Oncology Group performance status

Key findings and conclusions

- Ezabenlimab, a PD-1 targeting monoclonal antibody, showed clinical activity in a heterogeneous and heavily pre-treated patient population
- The observed response rate is consistent with other PD-1 inhibitors in similar populations[3–5]
- Ezabenlimab was well tolerated, with a similar safety profile to other PD-1 inhibitors[3,4]
  - Treatment-related grade 3 AEs occurred in 6% of patients
- Ezabenlimab is being assessed in combination with other anti-cancer therapies (see QR code for posters reporting ezabenlimab combination data)

https://bit.ly/3y5orkv

Scan this QR code or visit the URL for an electronic copy of the poster and supplementary content†

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References

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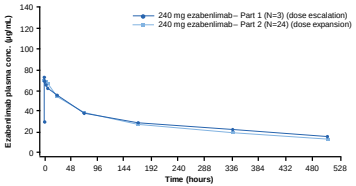
Pharmacokinetics

Please scan the QR code for additional pharmacokinetic data

- Geometric mean ezabenlimab plasma concentration-time profiles showed a rapid distribution phase followed by a slower elimination phase
- Profiles for the 240 mg dose escalation and dose expansion cohorts were very similar
- There were no apparent differences observed in Japanese and Caucasian patients (see Table in supplemental content)



Conc, concentration

Safety

Patients (N=111) with:	All grades n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)
Any AE*	107 (96)	10 (9)	40 (36)	54 (49)	3 (3)	0
Fatigue	43 (39)	24 (22)	15 (14)	4 (4)	0	0
Nausea	32 (29)	23 (21)	9 (8)	0	0	0
Anaemia	24 (22)	5 (5)	7 (6)	12 (11)	0	0
Decreased appetite	22 (20)	16 (14)	4 (4)	2 (2)	0	0
Treatment-related AE	64 (58)	25 (23)	32 (29)	7 (6)†	0	0
Fatigue	20 (18)	13 (12)	7 (6)	0	0	0
Nausea	11 (10)	9 (8)	2 (2)	0	0	0

AEs are those reported during the on-treatment and residual period. *Maximum Common Terminology Criteria for Adverse Events grade; †Events were decreased appetite, arthralgia, rash, aspartate aminotransferase increased, weight increased, allergic dermatitis and rash, stomatitis and diarrhoea

- Serious AEs were reported in 38 patients (34%); two of these events were considered treatment-related (grade 2 pyrexia and grade 3 rash)
- Immune-related AEs (during the entire study) were reported in 33 patients (30%); most commonly hypothyroidism (7 patients [6%]). Five patients (5%) had grade 3 immune-related AEs
- Anti-drug antibodies occurred infrequently and did not affect the pharmacokinetic profile of ezabenlimab

Efficacy

	Dose escalation/imaging trial* (n=10)	Dose expansion cohorts			
		Advanced (n=30)	TMB-high (n=27)	Cervical/ anal/skin (n=31)	Vaginal/ vulvar (n=13)
Objective response	2 (20)†	4 (13)‡	3 (11)	5 (16)	2 (15)
Complete response	0	0	0	1 (13)	1 (8)
Partial response	2 (20)	4 (13)	3 (11)	4 (13)	1 (8)
Stable disease	5 (50)	11 (37)	12 (44)	12 (39)	5 (38)
Progressive disease	2 (20)	13 (43)	8 (30)	13 (42)	5 (38)
Disease control	7 (70)	15 (50)	15 (56)	17 (55)	7 (54)
No post-baseline assessment	1 (10)	2 (7)	4 (15)	1 (3)	1 (8)

Table shows best overall confirmed response in patients receiving ezabenlimab 240 mg q3w. *Includes patients from dose escalation/confirmation in Studies 1381.1 (n=3), 1381.4 (n=6), and 1381.3 (n=1); †Tumour types: oesophageal, mesothelial; ‡Tumour types: breast cancer (n=2), fallopian tube, RCC

- Duration of confirmed response ranged from 43 to 570 days at data cut-off

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