# 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†

https://bit.ly/2TzZZ8o

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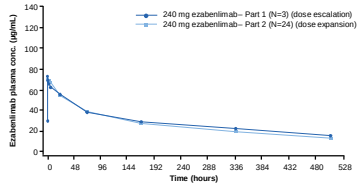
## References

1. Zettl M, et al. Cancer Res 2018;78(Suppl13):abstract 4558; 2. Johnson ML, et al. J Clin Oncol 2018;36 (Suppl5):abstract 212; 3. Brahmer JR, et al. J Clin Oncol 2010;28:3167–75; 4. Patnaik A, et al. Clin Cancer Res 2015;21:4286–93; 5. Russell BL, et al. Front Oncol 2021;11:641428

## 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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