Open-label, Phase I dose escalation/expansion trial of the anti-SIRPα monoclonal antibody BI 770371 in patients with advanced solid tumours, alone or in combination with the anti-PD-1 monoclonal antibody ezabenlimab

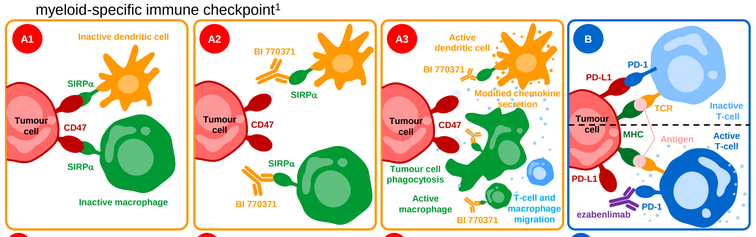
#697P

Martin E. Gutierrez[1]*, Rahima Jamal[2], Noboru Yamamoto[3], Toshihiko Doi[4], Gunther Kretschmar[5], Javier Ferrada[5], Stephan Wojciekowski[6], Manish R. Patel[7]

[1]Hackensack University Medical Center at Hackensack Meridian Health, Hackensack, NJ, USA; [2]Centre Hospitalier de l'Université de Montréal (CHUM), Centre de recherche du CHUM, Montreal, QC, Canada; [3]National Cancer Center Hospital, Tokyo, Japan; [4]National Cancer Center Hospital East, Kashiwa, Japan; [5]Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT, USA; [6]Boehringer Ingelheim Pharma GmbH & Co KG, Biberach an der Riss, Germany; [7]Florida Cancer Specialists/Sarah Cannon Research Institute, Sarasota, FL, USA

Introduction

- The SIRPα (CD172)/CD47 axis is a critical regulator of myeloid cell activation and serves as a myeloid-specific immune checkpoint[1]



A1 The SIRPα-CD47 interaction promotes immune suppression in the tumour microenvironment, by inhibition of phagocytosis, downregulation of antigen-presenting cells and maintenance of myeloid-derived suppressor cells[1,2]

A2 BI 770371 is an anti-SIRPα (anti-CD172) IgG1 mAb that binds to human SIRPα and blocks its interaction with its ligand CD47[3]

A3 By blocking the interaction between SIRPα and CD47, BI 770371 inhibits SIRPα-mediated suppression of the innate immune system and restores the immune functions of myeloid cells in the tumour microenvironment[4]

B Ezabenlimab (BI 754091) is a humanised PD-1-targeting mAb that blocks the interaction between PD-1 and its ligands. This blocks PD-1 signalling, thereby restoring T-cell anti-tumour activity[5,6]

- BI 770371 is currently undergoing investigation as monotherapy and in combination with ezabenlimab, a PD-1 inhibitor, in a Phase I, open-label, dose escalation/dose expansion trial (NCT05327946) in patients with advanced solid tumours

CD, cluster of differentiation; IgG1, immunoglobulin G1; mAb, monoclonal antibody; MHC, major histocompatibility complex; PD-1, programmed death-1 receptor; PD-L1, programmed death-1 receptor ligand; SIRPα, signal regulatory protein α; TCR, T-cell receptor

Objectives

- The primary objective is to determine the MTDs for BI 770371 monotherapy and in combination with ezabenlimab
- To determine an RDE based on all available data, including safety, preliminary efficacy and pharmacokinetics/pharmacodynamics

MTD, maximum tolerated dose; RDE, recommended dose for expansion

Methods

Primary endpoint: Occurrence of DLTs during the MTD evaluation period (first 21 days of study treatment)

Secondary endpoints: Occurrence of AEs and DLTs during the on-treatment period, and efficacy (RECIST v1.1, investigator's assessment)

Inclusion criteria
- Adults aged ≥18 years
- Advanced, unresectable and/or metastatic solid tumours
- Presence of ≥1 measurable lesion per RECIST v1.1
- ECOG PS 0–1
- Life expectancy ≥3 months
- No further treatment options/not eligible for standard treatment

- BLRM with overdose control is being used to guide dose escalation
- Dose escalation will continue until the MTD is reached or until a maximum BI 770371 dose has been confirmed safe by the DEC

*Escalating doses of BI 770371 and a fixed dose of ezabenlimab given as IV infusion q3w
AE, adverse event; BLRM, Bayesian logistic regression model; DEC, Dose Escalation Committee; DLT, dose-limiting toxicity; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; RECIST, Response Evaluation Criteria In Solid Tumours; q3w, once every three weeks

Key findings and conclusions

- In this Phase I, open-label, dose escalation/dose expansion trial (NCT05327946) in patients with advanced solid tumours, BI 770371 ± ezabenlimab was well tolerated
- There were no DLTs during the MTD evaluation period. One DLT (encephalitis) occurred during the on-treatment period
- AEs were manageable during the on-treatment period
- BI 770371 exhibited disease control
- MTD has not been reached. The trial is ongoing

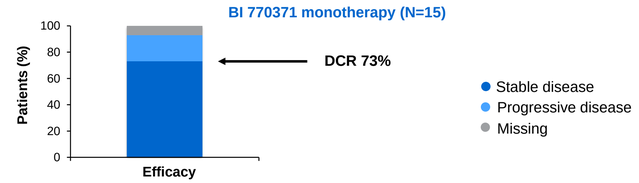
Patients

- As of 31 March 2023, a total of 18 patients (BI 770371 group, N=15; BI 770371 + ezabenlimab group, N=3) have been treated in Canada, Japan, and the USA
- The most common tumours were colorectal, ovarian, and prostate (n=2, each) in the BI 770371 group and pancreas (n=2) and bladder (n=1) in the BI 770371 + ezabenlimab group

Baseline characteristics	BI 770371 (N=15)	BI 770371 + ezabenlimab (N=3)
Median age, years (range)	64 (26–77)	67 (61–70)
Male, n (%)	8 (53)	1 (33)
Race, n (%)		
White	10 (67)	2 (67)
Asian	4 (27)	1 (33)
Black or African American	1 (7)	0 (0)
ECOG PS at baseline, n (%)		
0	8 (53)	2 (67)
1	7 (47)	1 (33)
Number of prior lines of systemic therapies >2 , n (%)	15 (100)	2 (67)

Efficacy

- In 14 evaluable patients in the monotherapy group (N=15), 11 (73%) achieved a best response of stable disease
- In the combination therapy group (N=3), two patients evaluated (50%) achieved a best response of progressive disease; data were missing for one patient



DCR, disease control rate

Safety

- AEs in the BI 770371 group were manageable
- The MTD has not been reached; dose escalation is ongoing

BI 770371 (N=15)
Primary endpoints: MTD evaluation period

0% DLTs n=0 — Grade ≥3: none

BI 770371 + ezabenlimab (N=3)

0% DLTs n=0 — Grade ≥3: none

Secondary endpoints: on-treatment period

80% Any AE n=12
- Most commonly: pruritus (n=5); anaemia (n=3); peripheral oedema (n=3)
- Grade ≥3: anaemia (n=1); atrial fibrillation (n=1)

67% TRAEs n=10
- Most commonly: pruritus (n=5); peripheral oedema (n=2)
- Grade ≥3: none

27% SAEs n=4
- Most commonly: atrial fibrillation (n=1); decreased appetite (n=1); disease progression (n=1); encephalitis (n=1); hypoxia (n=1)
- Grade ≥3: atrial fibrillation (n=1)

7% AEs leading to treatment discontinuation n=1
- Most commonly: encephalitis (n=1)
- Grade ≥3: none

0% AEs leading to dose reduction n=0
- Most commonly: none
- Grade ≥3: none

7% DLTs n=1
- Most commonly: encephalitis (n=1)
- Grade ≥3: none

SAE, serious AE; TRAE, treatment-related AE

References

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*Corresponding author email address: martin.gutierrez@hmhn.org

Presented at the European Society for Medical Oncology (ESMO) Congress, Madrid, Spain, 20–24 October 2023

This study was funded by Boehringer Ingelheim. The authors were fully responsible for all content and editorial decisions, were involved at all stages of poster development and have approved the final version. The authors did not receive payment related to the development of the poster. Medical writing support for the development of this poster, under the direction of the authors, was provided by Frans Everson PhD, of Ashfield MedComms, an Inizio Company, and funded by Boehringer Ingelheim

MG reports: invited speaker: Guardant; advisory board: Sanofi, Bristol Meyers Squibb; consulting: Celularity, Merck