A Phase Ib/la, dose-escalation/expansion study of BI 907828 in combination with immune checkpoint inhibitor(s) in patients with advanced solid tumors

Noboru Yamamoto,1 Navid Hafez,2 Anthony Tolcher,3 Michael Teufel,4 Junxian Geng,5 Liz Svensson,6 Mehdi Lahmar,6 Mirjana Gounder7

1Department of Experimental Therapeutics, National Cancer Center Hospital, Tokyo, Japan; 2Yale Comprehensive Cancer Center, Yale School of Medicine, CT, USA; 3NEXT Oncology, San Antonio, TX, USA; 4Boehringer Ingelheim Pharmaceuticals, Inc, Ridgefield, CT, USA; 5Boehringer Ingelheim ABB, Stockholm, Sweden; 6Boehringer Ingelheim International GmbH, Ingelheim am Rhein, Germany; 7Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA

Introduction

- BI 907828, an MDM2-p53 antagonist, inhibits the interaction between the tumor suppressor p53 and its negative regulator MDM2.1 This leads to stabilization of p53, followed by target gene induction that may result in cell cycle arrest or apoptosis in tumors with TP53 wt status.2
- Preclinical data show that combining an MDM2-p53 antagonist with immune checkpoint inhibitors produces antitumor effects in multiple tumor types.3
- The recommended dose for expansion for BI 907828 monotherapy was previously established at 45 mg qd.4

- In the present trial (NCT03964235), treatment was initiated as a triplet combination of BI 907828 plus ezabenlimab (an anti-PD-1 monoclonal antibody) plus BI 754111 (anti-LAG3).5 During the course of the Phase I part, other studies indicated a lack of added efficacy when BI 754111 was combined with ezabenlimab; therefore, the study design was updated to switch the dose escalation to the doublet combination of BI 907828 plus ezabenlimab.6
- We present results from patients enrolled in the Phase Ia part who received BI 907828 plus ezabenlimab.7

Methods

- Administration: BI 907828 (10, 20, 30 mg); ezabenlimab (200 mg, 400 mg) intravenous (day 1) of 21-day cycles.

Phase Ia

- Primary endpoints: - Number of patients with DLTs during the first treatment cycle
- MTD based on number of DLTs

Phase Ib

- Primary endpoints: - Objective response per RECIST 1.1
- Progression-free survival
- Secondary endpoints: - Objective response per RECIST
- Disease control per RECIST 1.1, RECIST
- Overall survival
- Number of patients with DLTs during the entire treatment period

Key findings and conclusions

- This Phase Ia/la study (NCT03964233) is assessing BI 907828, an MDM2-p53 antagonist, combined with immune checkpoint inhibitor(s) in TP53 wt tumors.
- The double combination of BI 907828 plus ezabenlimab showed a manageable safety profile and early signs of antitumor activity.
- Recruitment is ongoing.

Patients

- In the Phase Ia part, 11 patients received the triplet combination (BI 907828 plus ezabenlimab) with BI 754111 (10) as the suspect dose level (n=3/3, respectively). No DLTs were reported in Cycle 1; the MTD was not reached.
- As of 20 Jan 2022, 15 patients have received the double combination (BI 907828 plus ezabenlimab) at 30/45 mg doses level (n=10/5, respectively).
- Among these, histologies were: biliary duct carcinoma (n=3), PD-L1 positive (n=2), DLPS, endometrial carcinosarcoma, esophageal carcinoma, invasive urothelial carcinoma, neuroendocrine carcinoma, myxoid liposarcoma, myxoid rhabdomyosarcoma, pleomorphic liposarcoma. (n=1 each); other (n=2).

Safety

- Among patients receiving BI 907828 plus ezabenlimab:
  - One patient had a DLT during Cycle 1:
    - G3 neutropenia causing Cycle 2 delay (45 mg)
  - Four DLTs were reported after Cycle 1:
    - G3 anemia (30 mg); G2 thrombocytopenia causing Cycle 2 delay (45 mg); G3 neutropenia and G4 thrombocytopenia (45 mg)
  - Most common Grade 3/4 AEs were: Anemia (n=4); thrombocytopenia (n=4); lymphopenia (n=3).

Efficacy

Best response among response-eligible patients who received BI 907828 plus ezabenlimab (n=9)

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<th>Best response</th>
<th>Patients (n=9)</th>
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| SD | 7 (78%)
| PR | 2 (22%)

 pacientes (%) | Response rate (%) | Progression-free survival (%) | Overall survival (%) | Stable disease (%) | Dying/deterioration (%) | Portal response (%) | Progression disease (%) | Stable disease (%) | Dying/deterioration (%) |
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Best change from baseline among response-eligible patients who received BI 907828 (n=9)

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