**Introduction**

**Background**
- Signaling via the immune checkpoint molecules PD-1 and LAG-3 can lead to T-cell dysfunction and prevent antitumor responses.

**Objectives**
- Assess the safety, tolerability and pharmacokinetics (PK) of BI 754091 with and without BI 754111.
- Determine the maximum tolerated dose (MTD) and/or recommended Phase II dose (RP2D) of BI 754091 monotherapy, and BI 754091 plus BI 754111.
- Assess the efficacy of the RP2D of BI 754091 plus BI 754111 in patients with gastric/esophageal junction cancer (GEJC), esophageal cancer (EC) or hepatocellular cancer (HCC).

**Eligibility criteria**
- Adult patients
- Measurable lesions, according to Response Evaluation Criteria in Solid Tumors (RECIST) v1.1
- Parts 1 and 2: confirmed diagnosis of advanced, unresectable, and/or metastatic solid tumors (any type)
- Part 3 (Cohort 1): status of systemic therapy (including adjuvant), prior anti-PD-1/PD-L1 therapy
- Part 3 (Cohort 4): disease progression or after prior anti-PD-1/PD-L1 therapy

**Study design**

**Endpoints**

**Primary endpoints**
- MTD of BI 754091 and BI 754111 based on dose-limiting toxicities in Cycle 1

**Secondary endpoints**
- BI 754091; BI 754091 + BI 754111 plasma C0 and AUC
- Investigator assessed objective response according to RECIST v1.1

**Key points**

**Key inclusion criteria**
- Adult patients
- Measurable lesions, according to Response Evaluation Criteria in Solid Tumors (RECIST) v1.1
- Parts 1 and 2: confirmed diagnosis of advanced, unresectable, and/or metastatic solid tumors (any type)
- Part 3 (Cohort 1-3): status of systemic therapy (including adjuvant), prior anti-PD-1/PD-L1 therapy
- Part 3 (Cohort 4): disease progression or after prior anti-PD-1/PD-L1 therapy

**Key exclusion criteria**
- Antitumor treatment within 4 weeks or 5 half-lives periods (whichever is shorter)
- Part 2 and 3 only: prior anti-LAG-3 therapy
- Inadequate organ function or bone marrow reserve (based on laboratory values)
- Immunosuppressive corticosteroids (>10 mg/day prednisone, or equivalent) ≤4 weeks prior to first dose of treatment
- History of pneumonitis (in last 5 years), HIV or interstitial lung disease
- Active autoimmune disease
- Active infection requiring systemic treatment

**Presented at 2018 Japanese Society of Medical Oncology Annual Meeting, July 19–21, 2018, Kobe, Japan**
Phase 1 trial of an anti-PD-1 mAb BI 754091 ± an anti-LAG-3 mAb BI 754111 in Asian patients with advanced solid tumors

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Presented at 2018 Japanese Society of Medical Oncology Annual Meeting (JSMO), July 19–21, 2018, Kobe, Japan
Introduction

Background

- Signaling via the immune checkpoint molecules PD-1 and LAG-3 can lead to T-cell dysfunction and prevent antitumor responses\(^1\)
- Dual inhibition of PD-1 and LAG-3 may synergistically restore T-cell activation and enhance antitumor immune responses\(^{1,2}\)
- Combined treatment with an anti-PD-1 monoclonal antibody (mAb) and an anti-LAG-3 mAb may achieve greater rates and durations of response compared with anti-PD-1 mAb monotherapy
- Anti-PD-1/anti-LAG-3 mAb combinations have demonstrated encouraging preclinical\(^3\) and clinical\(^4\) antitumor activity
- Preliminary study results in patients with advanced solid tumors demonstrate that BI 754091 is safe and well-tolerated up to 400 mg, with evidence of antitumor activity\(^5\)
- In this Phase I trial (NCT03433898), the anti-PD-1 mAb BI 754091 will be evaluated in Asian patients with advanced, unresectable, and/or metastatic solid tumors (as monotherapy and together with the anti-LAG-3 mAb, BI 754111)
Introduction (cont’d)

Objectives
• Assess the safety, tolerability and PK of BI 754091 with and without BI 754111
• Determine the MTD and/or RP2D of BI 754091 monotherapy, and BI 754091 plus BI 754111
• Assess the efficacy of the RP2D of BI 754091 plus BI 754111 in patients with G/EJC, EC or HCC

EC, esophageal cancer; G/EJC, gastric/esophagogastric junction cancer; HCC, hepatocellular cancer; MTD, maximum tolerated dose; PK, pharmacokinetics; RP2D, recommended Phase II dose
# Eligibility criteria

## Key inclusion criteria

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Details</th>
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<tbody>
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<tr>
<td>Part 3 (Cohorts 1–3): ≥1 line of systemic therapy (excluding adjuvant), no prior anti-PD-1/PD-L1 mAb therapy</td>
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<tr>
<td>Part 3 (Cohort 4): disease progression on or after prior anti-PD-1/PD-L1 mAb therapy</td>
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mAb, monoclonal antibody; RECIST, Response Evaluation Criteria in Solid Tumors
### Key exclusion criteria

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</table>
Study design

Open-label, single-arm, Phase I trial in patients with advanced solid tumors

Part 1
BI 754091
240 mg via iv infusion; Q3W

Japanese patients with advanced solid tumors of any type

Part 2
BI 754091 + BI 754111
Starting doses: 240 mg from Part 1 and 80 mg via iv infusion; Q3W

Q3W, once every three weeks
Study design (cont’d)

<table>
<thead>
<tr>
<th>Part 3</th>
<th>BI 754091 + BI 754111 (at RP2D)</th>
</tr>
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<tbody>
<tr>
<td>Cohort 1</td>
<td><strong>Gastric/esophagogastric junction cancer</strong></td>
</tr>
<tr>
<td>Cohort 2</td>
<td><strong>Esophageal cancer</strong></td>
</tr>
<tr>
<td>Cohort 3</td>
<td><strong>Hepatocellular cancer</strong></td>
</tr>
<tr>
<td>Cohort 4</td>
<td><strong>Gastric/esophagogastric junction, esophageal, or hepatocellular cancer</strong></td>
</tr>
</tbody>
</table>

- **Cohort 1**
  - Asian patients (including Japan, Taiwan and Korea)
  - No previous anti-PD-1 / PD-L1 mAb therapy
  - ≥1 line of systemic therapy

- **Cohort 4**
  - Asian patients (including Japan, Taiwan and Korea)
  - Failure of previous anti-PD-1 / PD-L1 mAb therapy

mAb, monoclonal antibody; RP2D, recommended Phase II dose
Endpoints

Primary endpoints

Parts 1 and 2
MTD of BI 754091 and BI 754091 + BI 754111, based on dose-limiting toxicities in Cycle 1

Part 3
Investigator assessed objective response according to RECIST v1.1

MTD, maximum tolerated dose; RECIST, Response Evaluation Criteria in Solid Tumors
Endpoints (cont’d)

Secondary endpoints

**Parts 1 and 2**

BI 754091; BI 754091 + BI 754111
plasma $C_{\text{max}}$ and AUC

**Parts 1 and 2**

Investigator assessed objective response according to RECIST v1.1

AUC, area under curve; $C_{\text{max}}$, maximum drug concentration; RECIST, Response Evaluation Criteria in Solid Tumors
Endpoints (cont’d)

Secondary endpoints

Part 3
Duration of response

From
Date of first documented investigator-assessed PR or CR according to RECIST v1.1

To
Date of progressive disease or death

Part 3
Disease control
(investigator-assessed PR, CR or stable disease according to RECIST v1.1)

CR, complete response; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors
Key points

Objectives:
• Parts 1 and 2
  – Determine safety, tolerability, PK, and MTD/RP2D of BI 754091 monotherapy and BI 754091 + BI 754111 combination therapy
• Part 3
  – Explore the efficacy, and further investigate safety, tolerability and PK of BI 754091 + BI 754111 in patients with G/EJC, EC or HCC

Study design:
• Open-label, single-arm, Phase I trial in Asian patients with advanced, unresectable, and/or metastatic solid tumors

EC, esophageal cancer; G/EJC, gastric/esophagogastric junction cancer; HCC, hepatocellular cancer; MTD, maximum tolerated dose; PK, pharmacokinetics; RP2D, recommended Phase II dose
Current status

- Enrollment opened in February, 2018
- Target enrollment is 164 patients from Asian countries including Japan
- Part 1 is complete; no dose limiting toxicities were reported, RP2D of BI 754091 confirmed as 240 mg
- Part 2 opens for recruitment in July 2018
References


Acknowledgments

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