Phase I trial of the programmed death receptor 1 (PD-1) inhibitor, BI 754091, in patients with advanced solid tumors

**INTRODUCTION**

Mechanism of BI 754091 Activity

- Tumors may achieve immune evasion by expressing PD-1 ligand (PD-L1) to PD-1 receptor (PD-1) in order to suppress effector function of T cells. The receptor PD-L1 is expressed on antigen presenting cells within the microenvironment.
- PD-1 pathway inhibition may restore the anti-tumor activity seen in patients with advanced solid tumors.

Here we present the preliminary results of a Phase I trial of the programmed death receptor 1 (PD-1) inhibitor, BI 754091, in patients with advanced solid tumors.

**EXCLUSION CRITERIA**

- History of hypersensitivity reactions to other mAbs
- Untreated brain metastasis considered to be active
- Exhausted standard treatment options
- Inadequate organ function
- Dose escalation: any tumor type
- Dose expansion: anti-PD-1 naïve non-small-cell lung cancer (NSCLC), bladder cancer, head/neck cancer, breast cancer, pancreatic cancer, stroke, breast cancer, and renal cell carcinoma (RCC)
- Stable disease     2 (67)     2 (67)     2 (67)       8 (40)     14 (48)
- Relapsed disease    5 (17)    10 (33)    3 (10)       14 (48)     23 (75)
- Progressive disease 1 (3)    1 (3)    1 (3)         0 (0)       2 (7)
- Stable disease     2 (67)     2 (67)     2 (67)       8 (40)     14 (48)
- Relapsed disease    5 (17)    10 (33)    3 (10)       14 (48)     23 (75)
- Progressive disease 1 (3)    1 (3)    1 (3)         0 (0)       2 (7)

**PHARMACOKINETICS**

- **Nadir concentration (ng/mL)**: 3 5 (1.0-15.0) 3 360 (10.0-120.0) 3 520 (17.0-152.0)
- **AUC (max)**: 3 25300 (32.7) 3 737000 (9.93) 3 1280000 (27.1)
- **Tmax**: 3 4640000 (28.0) 3 14300000 (19.6) 3 1800000 (24.4)
- **Cmax**: 3 25000 (27.7) 3 7737000 (27.1) 3 1280000 (27.1)
- **Tmin**: 3 316 (80.7) 3 307 (80.8) 3 321 (27.1)

**STUDY DESIGN**

Cycle 1 Cycle 2

**Cycle 1: 240 mg or 400 mg BI 754091 to cancer patients (linear scale).**

**Cycle 2: Continued treatment for up to 1 year.**

**REDUCTION OF TOXICITY AND SERIOUS ADVERSE EVENTS**

- There were no dose-limiting toxicities
- There were no treatment-related serious adverse events
- 1 patient in the dose expansion discontinued treatment due to an unrelated AE of minor pain in the context of disease progression with intestinal obstruction

Based on the available BI 754091 safety, PK, receptor occupancy data, and taking into consideration published data for registered PD-1 inhibitors, the dose of 240 mg q3w was selected for testing in Phase Ib expansion cohorts.

**DOSE-RESPONSE ASSESSMENT**

Table 4. Response per RECIST v 1.1*

<table>
<thead>
<tr>
<th>Response</th>
<th>Cycle 1</th>
<th>Cycle 2</th>
<th>Expansion</th>
<th>All Cohorts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stable disease</td>
<td>2 (67)</td>
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</tr>
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</tr>
<tr>
<td>Progressive disease</td>
<td>1 (3)</td>
<td>1 (3)</td>
<td>1 (3)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

**CONCLUSIONS**

- BI 754091 is safe and well-tolerated across all dose levels tested in advanced solid tumors, with preliminary evidence of anti-tumor activity.
- Adverse events were mild and included fatigue, decreased appetite, nausea, rash, and arthralgia.
- A dose of 240 mg q3w was selected for dose expansion cohorts.

**REFERENCES**

3. There were no dose-limiting toxicities
4. There were no treatment-related serious adverse events
5. 1 patient in the dose expansion discontinued treatment due to an unrelated AE of minor pain in the context of disease progression with intestinal obstruction

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