**Phase Ib study of BI 836880, a VEGF/Ang2-blocking nanobody®, in combination with BI 754091, an anti-PD-1 antibody: initial results in patients with solid tumours**

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## Disclosure of conflicts of interest

| Nicolas Girard | • Advisory/consultancy (Roche, Lilly, Boehringer Ingelheim, AstraZeneca, Novartis, Pfizer, Bristol-Myers Squibb, Merck Sharp and Dohme, Takeda, GlaxoSmithKline, Abbvie, Pharmamar)  
|                | • Research grant/funding (institution; Roche, AstraZeneca, Boehringer Ingelheim)  
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**Introduction and methodology**

- Preclinically, combination of anti-VEGF/Ang2 with anti-PD-1 therapy promotes an immunopermissive state supportive of T-cell-mediated tumour cell killing\(^1\).
- BI 836880 is a humanised bispecific nanobody\(^\circ\) that targets VEGF and Ang2, and BI 754091 is an anti-PD-1 antibody.
- BI 836880 and BI 754091 have shown safety and preliminary antitumour activity as monotherapies in Phase I studies; RP2D: 720 mg IV Q3W for BI 836880\(^2\); RP2D: 240 mg IV Q3W for BI 754091\(^3\).
- Here, we report results from a Phase Ib study assessing BI 836880 in combination with BI 754091.

\[^{3}\text{Johnson ML, et al. Phase I trial of the programmed death receptor 1 (PD-1) inhibitor, BI 754091, in patients (pts) with advanced solid tumors. J Clin Oncol 2018;36(5_suppl):212}}\]
Patient demographics and characteristics (N=50)*

**Sex**
- Male (n=34): 68%
- Female (n=16): 32%

**Prior CPI use**
- Yes (n=30): 60%
- No (n=20): 40%

**Tumour types**
- NSCLC (n=21): 42%
- HCC (n=7): 12%
- GBM (n=5): 10%
- Melanoma (n=11): 22%
- SCLC (n=6): 14%

**Median age (years)**: 61.5

**ECOG PS at baseline**
- 0 (n=17): 34%
- 1 (n=32): 64%
- Missing (n=1): 2%

*14 patients from part 1, 36 patients from part 2; data cut-off: July 13, 2020
ECOG PS, Eastern Cooperative Oncology Group performance status
### Safety overview (N=50)

<table>
<thead>
<tr>
<th>Number of patients with:</th>
<th>All grades n (%)</th>
<th>Grade 1 n (%)</th>
<th>Grade 2 n (%)</th>
<th>Grade 3 n (%)</th>
<th>Grade 4 n (%)</th>
<th>Grade 5 n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any AE</td>
<td>32 (64.0)</td>
<td>7 (14.0)</td>
<td>12 (24.0)</td>
<td>10 (20.0)</td>
<td>1 (2.0)</td>
<td>2 (4.0)</td>
</tr>
<tr>
<td>Asthenia</td>
<td>11 (22.0)</td>
<td>5 (10.0)</td>
<td>4 (8.0)</td>
<td>2 (4.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>10 (20.0)</td>
<td>0 (0.0)</td>
<td>4 (8.0)</td>
<td>6 (12.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Nausea</td>
<td>9 (18.0)</td>
<td>5 (10.0)</td>
<td>4 (8.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Cough</td>
<td>7 (14.0)</td>
<td>5 (10.0)</td>
<td>2 (4.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Dyspnoea*</td>
<td>6 (12.0)</td>
<td>3 (6.0)</td>
<td>1 (2.0)</td>
<td>1 (2.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>6 (12.0)</td>
<td>4 (8.0)</td>
<td>2 (4.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>5 (10.0)</td>
<td>4 (8.0)</td>
<td>1 (2.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Any irAE†</td>
<td>9 (18.0)</td>
<td>3 (6.0)</td>
<td>5 (10.0)</td>
<td>1 (2.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Any DRAE†</td>
<td>25 (50.0)</td>
<td>6 (12.0)</td>
<td>9 (18.0)</td>
<td>8 (16.0)</td>
<td>1 (2.0)</td>
<td>1 (2.0)</td>
</tr>
<tr>
<td>Any AE leading to drug discontinuation</td>
<td>3 (6.0)</td>
<td>0 (0.0)</td>
<td>1 (2.0)</td>
<td>1 (2.0)</td>
<td>0 (0.0)</td>
<td>1 (2.0)</td>
</tr>
<tr>
<td>Any SAE</td>
<td>12 (24.0)</td>
<td>1 (2.0)</td>
<td>3 (6.0)</td>
<td>5 (10.0)</td>
<td>1 (2.0)</td>
<td>2 (4.0)</td>
</tr>
</tbody>
</table>

*AEs with missing CTCAE grades will be counted in the All grades column; †Investigator defined

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CTCAE, Common Terminology Criteria for Adverse Events; DRAE, drug-related AE; ILD, interstitial lung disease; irAE, immune-related AE; SAE, serious AE

**One patient with grade 4 AEs reported:**
Anaphylactic reaction and laryngospasm

**Two patients with grade 5 AEs reported:**
General physical health deterioration and tracheal haemorrhage

**Nine patients had irAEs†:**
Three patients had hypothyroidism, one patient had arthralgia and myalgia, one patient had an increase in ALT, AST and blood lactate dehydrogenase, and one patient each had ILD, vomiting, pruritus or papular rash
Efficacy overview (N=18*)

Best overall response (regardless of confirmation) and tumour size change from baseline

*32 of the total 50 patients were not evaluable due to response data not being available at the time of data cut-off;
†One patient with melanoma had a tumour change from baseline of 0.0%.

Patients 6, 7, 15, and 16 were from the cohort expansion; the remaining patients were from the dose escalation cohort.

PD, progressive disease; PR, partial response; SD, stable disease
Summary and conclusions

- Preliminary antitumour activity was observed
  - 15 of 18 evaluable patients had confirmed best overall response of PR or SD
  - Notably, responses were also observed in patients who had previously progressed on CPIs

- The combination of BI 836880 and BI 754091 had a manageable safety profile
  - The most common AEs were asthenia and hypertension

- Expansion cohorts are ongoing
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