A Phase I, open-label, dose escalation trial of BI 1701963 as monotherapy and in combination with KRAS mutated advanced or metastatic solid tumors

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Objectives

- To determine the MTD and/or RP2D of BI 1701963 as a monotherapy and in combination with trametinib
- To evaluate safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary efficacy

Study design

- Multicenter, open-label, first-in-human dose escalation and expansion trial

Endpoints

- Primary: MTD, DLTs
- Secondary: PK, OR, PFS rate at 6 months, Grade ≥3 TRAEs

Current status

- As of February 11th, 2020, three patients have been treated

Key points

- BI 1701963 is a small-molecule protein–protein interaction inhibitor that prevents the interaction between KRAS and SOS1, thereby inhibiting activation of KRAS proteins
- Preclinical studies demonstrated cytostatic effects for BI 1701963 in cancer cells with an activated KRAS pathway, and combination with a MEK inhibitor resulted in a more pronounced effect
- BI 1701963 dose will be escalated until the MTD, or a max. of 2 mg QD

Previous RAS, MAPK, or KRAS targeted therapies

Retinal vein occlusion

Retinal pigment epithelial detachment

Decreased cardiac function

Endpoints and assessments

<table>
<thead>
<tr>
<th>Key inclusion criteria</th>
<th>Key exclusion criteria</th>
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<tr>
<td>Aged ≥18 years</td>
<td>Previous RAS, MAPK, or KRAS targeted therapies</td>
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<tr>
<td>Tumors with activating KRAS mutations</td>
<td>Retinal vein occlusion</td>
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<td>≥1 evaluable lesion (RECIST v1.1)</td>
<td>Retinal pigment epithelial detachment</td>
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<td>ECOG PS ≤1</td>
<td>Decreased cardiac function</td>
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<td>Adequate organ function</td>
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<td>Parts B and C will be conducted in patients with advanced NSCLC only</td>
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