Phase I, first-in-human trial evaluating BI 1387446 (STING agonist) alone and combined with BI 754091 (anti-PD-1) in solid tumors

#P408

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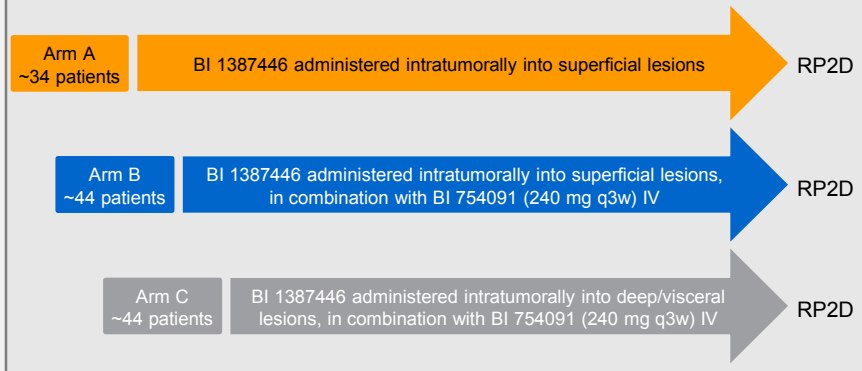
Introduction

- Activation of the STING pathway in intratumoral immune cells leads to increased type I interferon production, promoting recruitment and priming of T cells against tumor antigens, and providing anti-tumor activity[1]
- BI 1387446 potently and highly selectively activates the STING pathway[2] (Figure 1)
- Intratumoral administration of STING agonists has resulted in notable therapeutic activity in animal models[1]
- Intratumoral administration of BI 1387446 resulted in dose-dependent local tumor control and induction of immunological memory[2]
  - Delay in tumor growth was seen in non-injected lesions, indicative of an abscopal effect
  - Systemic anti-tumor effect was further enhanced with PD-1 inhibition
- BI 754091 is a humanized IgG4 anti-PD-1 monoclonal antibody

IgG4, immunoglobulin G4; PD-1, programmed cell death protein-1; STING, stimulator of interferon genes

Study design

- First-in-human, Phase I, open-label, multicenter trial (NCT04147234)
- The study will consist of two arms: Arm A and Arm B (with a potential third arm: Arm C)
- Arm B will open at the starting dose level once the starting dose level in Arm A is considered safe by the SMC; Arm C may open at the starting dose level once this dose level is considered safe in Arm B
- The study uses a Bayesian logistic regression model with overdose control to investigate a range of dose levels



IV, intravenously; q3w, every three weeks; RP2D, recommended Phase II dose; SMC, Safety Monitoring Committee

Key points

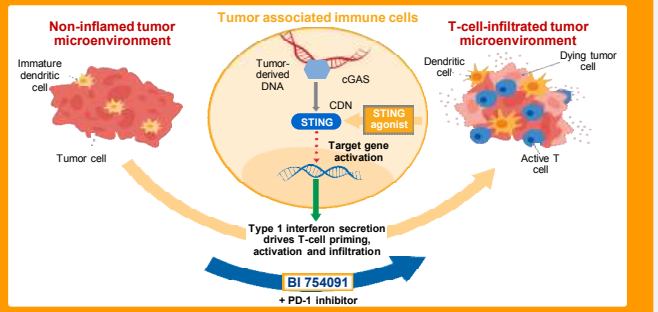


Figure 1 immuno-modulatory mechanism of action of BI 1387446
CDN, cyclic dinucleotide; cGAS, cyclic GMP-AMP synthase

Objectives

- To characterize safety and determine the MTD for BI 1387446 ± BI 754091

Study design

- First-in-human, Phase I, open-label, multicenter trial (NCT04147234)
- Two confirmed arms and a potential third arm:
  - BI 1387446 administered intratumorally into superficial lesions
  - BI 1387446 administered intratumorally into superficial lesions, in combination with BI 754091 IV
  - BI 1387446 administered intratumorally into deep/visceral lesions, in combination with BI 754091 IV

Current status

- As of October 2020, recruitment for the trial has started, and two patients have been treated

References

1. Corrales L, et al. J Clin Invest 2016;126:2404–11
2. Gremel G, et al. Cancer Res 2020;80:(16 Suppl): abstract 4522

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Objectives and inclusion/exclusion criteria

- To characterize safety and determine the MTD for BI 1387446 ± BI 754091

Key inclusion criteria
Adult patients (≥18 years of age)
Diagnosis of advanced, unresectable and/or metastatic malignant solid tumor and indication for treatment
Patient must have exhausted established treatment options known to meaningfully prolong survival
≥1 tumor lesion suitable for injection
≥1 additional tumor lesion amenable to biopsy
ECOG PS 0/1

Key exclusion criteria
Any investigational or anti-tumor treatment within 4 weeks or 5 half-life periods (whichever is longest) prior to the first treatment with BI 1387446 or BI 754091
History or evidence of active, non-treatment-related autoimmune disease, except for endocrinopathies
History or evidence of pneumonitis related to prior immunotherapy
Presence of other active invasive cancers other than the one treated in this trial within 5 years prior to screening

ECOG PS, Eastern Cooperative Oncology Group performance status; MTD, maximum tolerated dose

Endpoints and assessments

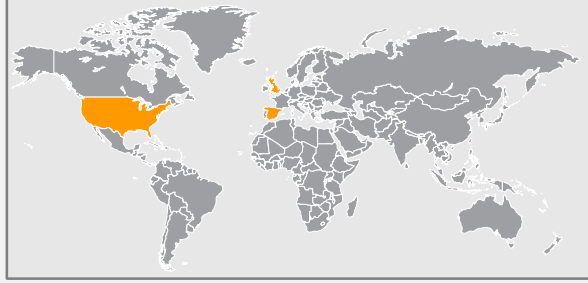
Primary endpoints
MTD based on number of DLTs
Number of patients with DLTs in the MTD evaluation period

Secondary endpoints
OR based on RECIST 1.1 criteria
Best percentage change from baseline in size of target lesions
Best percentage change from baseline in size of injected lesions

- The study of biomarkers (in plasma, blood and tumor samples) will be hypothesis-generating and will substantially contribute to the understanding of the BI 1387446 mode of action

DLT, dose-limiting toxicity; OR, objective response; RECIST, Response Evaluation Criteria in Solid Tumors

Study status



The trial is currently open for recruitment in six sites in Europe and the USA

As of October 2020, two patients have been treated

Presented at the Society for Immunotherapy of Cancer (SITC) 35th Anniversary Annual Meeting & Pre-Conference Programs Virtual Congress, November 9–14, 2020

This study was funded by Boehringer Ingelheim. The authors were fully responsible for all content and editorial decisions, were involved at all stages of poster development and have approved the final version.
Medical writing assistance, supported financially by Boehringer Ingelheim, was provided by Steven Kirkham, of GeoMed, an Ashfield company, part of UDG Healthcare plc, during the development of this poster