

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

Kevin Harrington,¹ Eileen Parkes,² Jared Weiss,³ Mathew Ingham,⁴
Andrés Cervantes,⁵ Emiliano Calvo,⁶ Matthew Riese,⁷ Ute Klinkhardt,⁸
Patricia Sikken,⁹ Michael Schmohl,⁹ Elena Garralda¹⁰

¹The Institute of Cancer Research, Division of Radiotherapy and Imaging, The Royal Marsden NHS Foundation Trust, London, United Kingdom; ²Department of Oncology, Medical Sciences Division, University of Oxford, Oxford, United Kingdom; ³Division of Hematology/Oncology, UNC School of Medicine, Chapel Hill, NC, USA; ⁴Division of Hematology and Oncology, New York Presbyterian Hospital/Columbia University Medical Center, New York, NY, USA; ⁵Department of Medical Oncology, Biomedical Research Institute INCLIVA, University of Valencia, Valencia, Spain; ⁶START Madrid-CIOCC, Centro Integral Oncológico Clara Campal, Madrid, Spain; ⁷Division of Hematology and Oncology, Department of Medicine, Medical College of Wisconsin, Milwaukee, WI, USA; ⁸Boehringer Ingelheim International GmbH, Ingelheim, Germany; ⁹Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach an der Riß, Germany; ¹⁰Medical Oncology Department, Vall d'Hebron University Hospital and Institute of Oncology, Universitat Autònoma de Barcelona, Barcelona, Spain

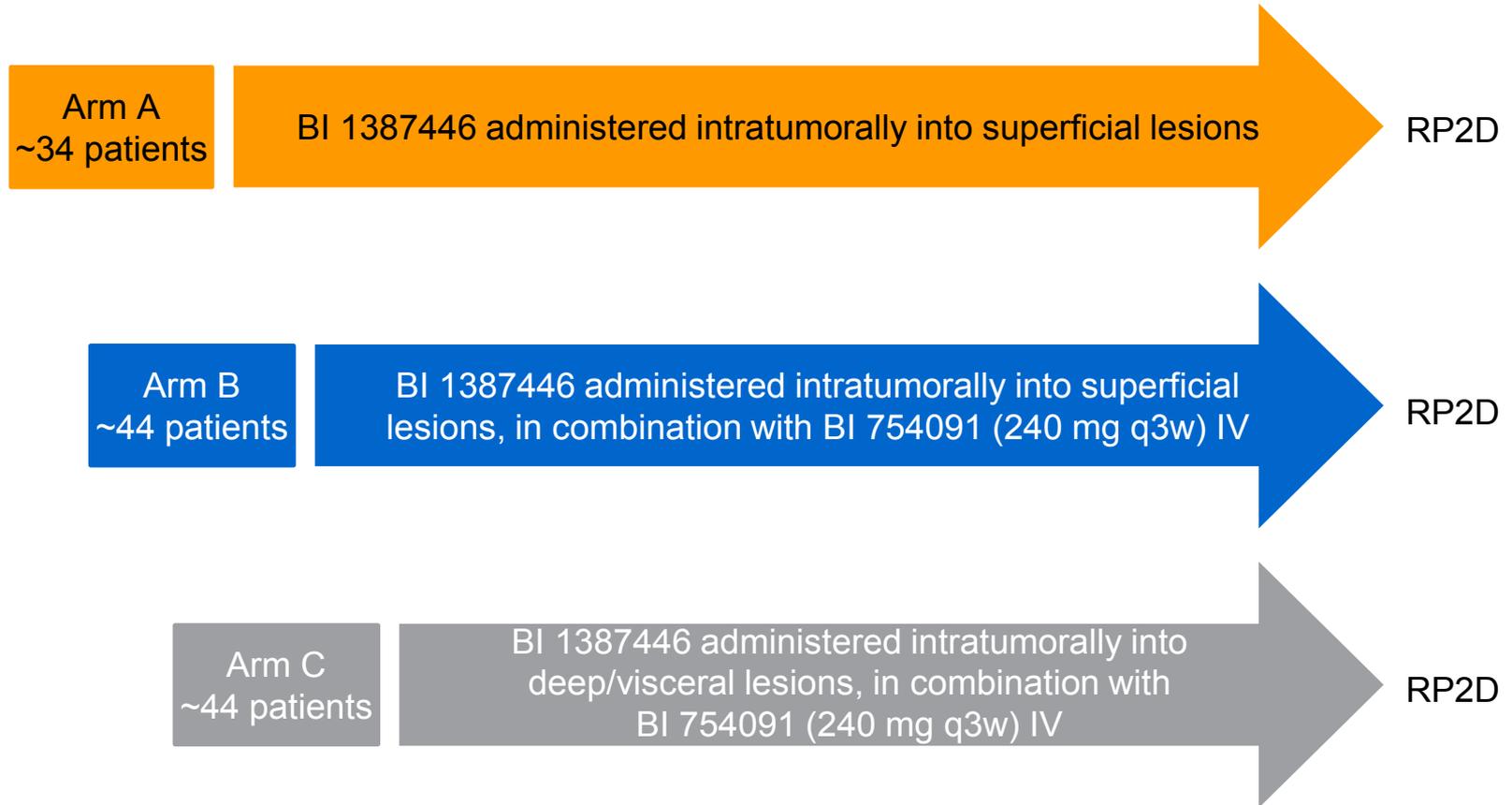
Introduction

- 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 activity¹
- BI 1387446 potently and highly selectively activates the STING pathway² (Figure 1)
- Intratumoral administration of STING agonists has resulted in notable therapeutic activity in animal models¹
- Intratumoral administration of BI 1387446 resulted in dose-dependent local tumor control and induction of immunological memory²
 - 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

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

Study design (cont'd)



IV, intravenously; q3w, every three weeks; RP2D, recommended Phase II dose

Objectives and inclusion/exclusion criteria

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

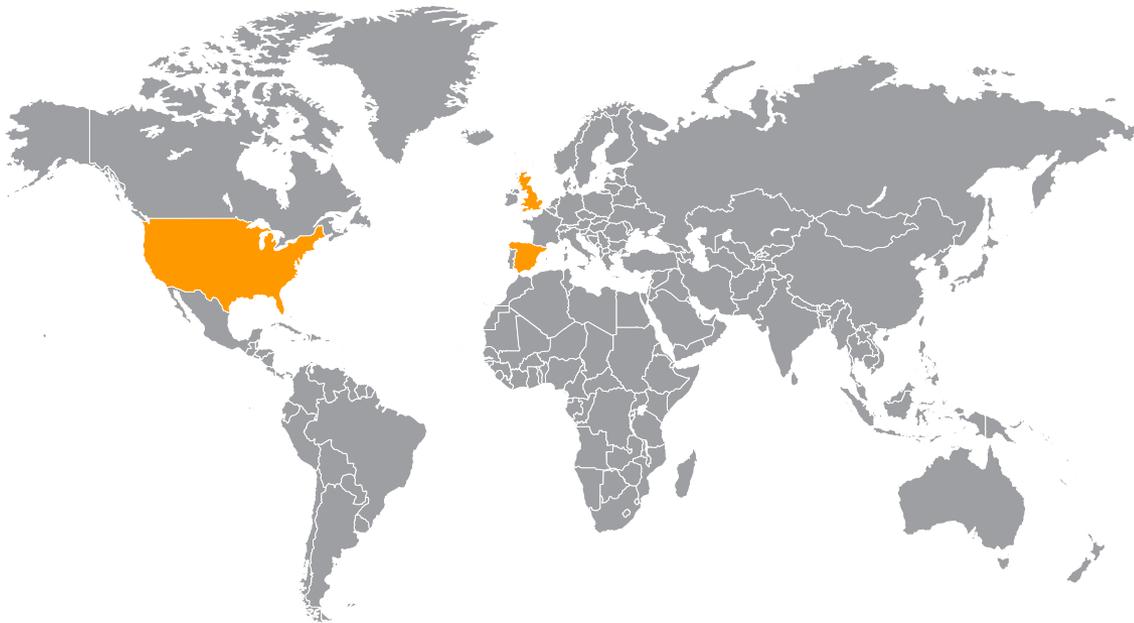
Key inclusion criteria	Key exclusion criteria
Adult patients (≥18 years of age)	Any investigational or anti-tumor treatment within 4 weeks or 5 half-life periods (whichever is longest) prior to the first treatment with BI 1387446 or BI 754091
Diagnosis of advanced, unresectable and/or metastatic malignant solid tumor and indication for treatment	History or evidence of active, non-treatment-related autoimmune disease, except for endocrinopathies
Patient must have exhausted established treatment options known to meaningfully prolong survival	History or evidence of pneumonitis related to prior immunotherapy
≥1 tumor lesion suitable for injection	Presence of other active invasive cancers other than the one treated in this trial within 5 years prior to screening
≥1 additional tumor lesion amenable to biopsy	
ECOG PS 0/1	

Endpoints and assessments

- 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

Primary endpoints	Secondary endpoints
MTD based on number of DLTs	OR based on RECIST 1.1 criteria
Number of patients with DLTs in the MTD evaluation period	Best percentage change from baseline in size of target lesions
	Best percentage change from baseline in size of injected lesions

Study status

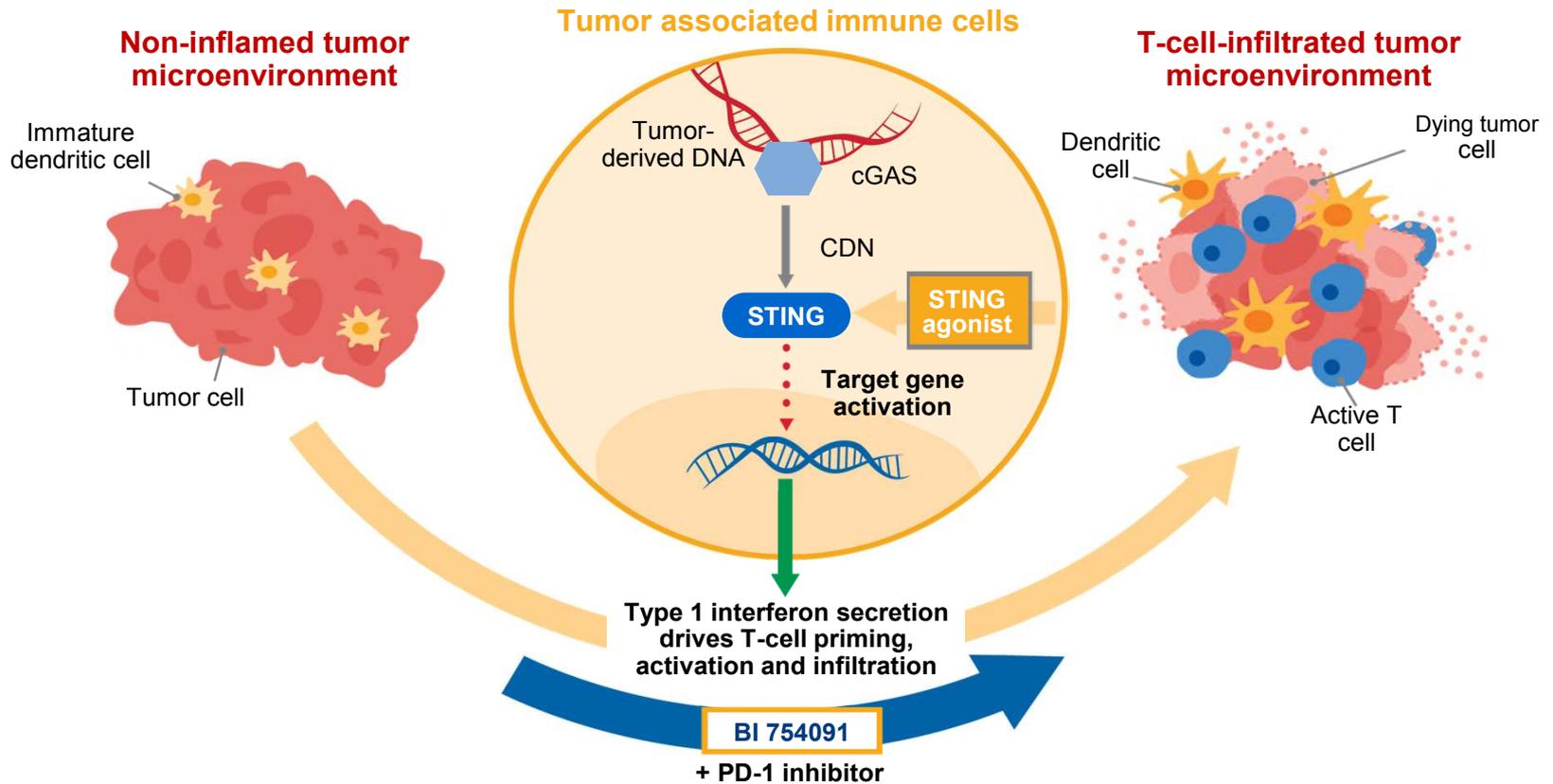


The trial is currently open for recruitment in six sites in Europe and the USA

As of October 2020, two patients have been treated

Key points

Figure 1 immuno-modulatory mechanism of action of BI 1387446



CDN, cyclic dinucleotide; cGAS, cyclic GMP-AMP synthase

Key points (cont'd)

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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