A Phase I, open-label, dose-escalation, confirmation, and expansion trial of BI 1810631, a HER2 inhibitor, as monotherapy in patients with advanced or metastatic solid tumours with HER2 aberrations

Frans Opdam,¹ ¹John Heymach, ¹Minal Barve, ¹Neil Gibson, ¹Behbod Sadrohlfazli, ¹Josep Serra, ²Noboru Yamamoto
¹Department of Clinical Pharmacology, The Netherlands Cancer Institute, Amsterdam, The Netherlands; ²Department of Thoracic-Head and Neck Medical Oncology, Division of Cancer Medicine, MD Anderson Cancer Center, University of Texas, Houston, TX, USA; ³Mary Crowley Cancer Research, Dallas, TX, USA; ⁴Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany; ⁵Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA; ⁶Boehringer Ingelheim España S.A., Barcelona, Spain; ⁷National Cancer Center Hospital, Tokyo, Japan

Introduction

• Activating mutations in the HER2-gene have frequently been reported to occur in many solid cancers, with a low to moderate prevalence.
• There is currently an unmet need for effective targeted therapy against HER2 mutations in solid tumours, particularly in NSCLC, where HER2 mutations are present in 2–4% of NSCLC tumours; of these, ~50% are ex20ins mutations
• Historically, HER2 ex20ins mutations have responded poorly to TKIs. Moreover, TKIs that inhibit both EGFR and HER2 are typically limited by toxicities associated with inhibition of wild-type EGFR
• BI 1810631 is a HER2-selective TKI currently undergoing clinical investigation in a Phase I study (NCT04886804) as monotherapy in patients with advanced/metastatic solid tumours harbouring HER2 aberrations (Phase la) and HER2-ex20ins mutation-positive advanced/metastatic NSCLC (Phase lb).

Phase Ia primary objectives are to investigate safety, tolerability, and PK of BI 1810631 in patients with advanced solid tumours.

Phase Ib objectives will be to further investigate the safety and treatment efficacy of BI 1810631 monotherapy in patients with advanced/metastatic NSCLC.

Key inclusion criteria (overall)

Patients with histologically/pathologically confirmed diagnosis of an advanced, unresectable and/or metastatic solid tumour, who are refractory after standard therapy for the disease, or for whom standard therapy is not suitable:

• HER2 positive NSCLC (≥1% HER2 IHC and/or HER2 FISH)$
• HER2 positive advanced/metastatic solid tumours (≥1% HER2 FISH)

Inclusion criteria

• Breast cancer (3–4%)
• Lung cancer (2–4%)
• Skin cancer (2–3%)
• Oesophageal cancer (2–4%)
• Cervical cancer (3–4%)
• Bladder cancer (13–18%)
• Head and neck cancer (2–4%)
• Colorectal cancer (5–6%)

Key inclusion criteria for Phase la and lb

• Adult patients (≥18 years old)
• ECOG PS of 0/1
• Recurrent/severe comorbidities able to be managed
• For Phase la, DLTs are defined as any treatment-emergent grade ≥ 3 adverse event (AE) or serious AE (SAE) associated with BI 1810631
• For Phase Ib, DLTs are defined as any treatment-emergent grade ≥ 3 AE, SAE or grade ≥ 3 AE that results in death

Key exclusion criteria

• Patients receiving concomitant investigational agents during the study
• Patients receiving concomitant investigational TKIs or HER2 inhibitors during the study
• Patients with brain metastases or other active (> 1 month), uncontrolled, symptomatic metastatic disease
• Patients with any previous treatment with a TKI in the HER2-ex20ins mutational context

Study status

As of February 2022, study is ongoing. Two solid tumours with HER2 ex20ins mutations are enrolled in the first two dose levels of escalation

References