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Efficacy and safety of inhaled ENaC inhibitor BI 1265162 in patients with cystic fibrosis: BALANCE-CF 1, a randomised, phase II study

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Phase I trials showed that single and multiple doses of the inhaled ENaC inhibitor BI 1265162 are safe. In this phase II trial in patients with CF, BI 1265162 was safe, but did not demonstrate clinically relevant efficacy. The trial was terminated. https://bit.ly/3CiB8uM

Cite this article as: Goss CH, Fajac I, Jain R, *et al*. Efficacy and safety of inhaled ENaC inhibitor BI 1265162 in patients with cystic fibrosis: BALANCE-CF 1, a randomised, phase II study. *Eur Respir J* 2022; 59: 2100746 [DOI: 10.1183/13993003.00746-2021].

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Received: 12 March 2021
Accepted: 19 June 2021

Abstract

Background Inhibition of the epithelial sodium channel (ENaC) in cystic fibrosis (CF) airways provides a mutation-agnostic approach that could improve mucociliary clearance in all CF patients. BI 1265162 is an ENaC inhibitor with demonstrated pre-clinical efficacy and safety already demonstrated in humans.

Objective We present results from BALANCE-CF™ 1, a phase II, placebo-controlled, randomised, double-blind study of four dose levels of BI 1265162 *versus* placebo for 4 weeks on top of standard of care in adults and adolescents with CF.

Results Initially, 28 randomised subjects (BI 1265162 200 µg twice daily n=14, placebo twice daily n=14) were assessed at an interim futility analysis. Compared with placebo, numerical changes of –0.8% (95% CI –6.6 to 4.9%) in percentage predicted forced expiratory volume in 1s ($ppFEV_1$) and +2.1 units (95% CI –2.4 to 6.5 units) in lung clearance index (LCI) were observed in the active group, meeting a pre-defined stopping rule; accordingly, the study was terminated. Recruitment had continued during the interim analysis and pending results; 24 patients were added across three dose levels and placebo. The final results including these patients (+1.5% $ppFEV_1$, 200 µg twice-daily dose *versus* placebo) were not supportive of relevant clinical effect. Furthermore, LCI change was not supportive, although interpretation was limited due to insufficient traces meeting quality criteria. A 9.4-point improvement in the Cystic Fibrosis Questionnaire – Revised Respiratory Domain was observed in the 200 µg twice daily dose group *versus* placebo. BI 1265162 up to 200 µg twice daily was safe and well-tolerated. Pharmacokinetics were similar to those in healthy volunteers.

Conclusion BI 1265162 was safe, but did not demonstrate a potential for clinical benefit. Development has been terminated.