Poster

Safety, Tolerability and Pharmacokinetics of BI 1015550 in Healthy Adult Males

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Safety, tolerability and pharmacokinetics of BI 1015550 in healthy adult males

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INTRODUCTION

- There is an unmet need for additional treatments for patients with idiopathic pulmonary fibrosis.[1]
- BI 1015550 is an oral preferential inhibitor of PDE4B that has shown anti-inflammatory and antifibrotic effects in preclinical studies.[2]

AIM

- To investigate the safety, tolerability and pharmacokinetics of single (SRD) and multiple (MRD) rising doses of BI 1015550 in healthy males.

METHODS

- This was a Phase I trial with a partially randomized, parallel-group design (NCT03230487) conducted between August 2017 and January 2018 in Mannheim, Germany.
- Healthy males aged 18–45 years received BI 1015550 or placebo:
  - as a single dose of 36 mg or 48 mg under fasted conditions (SRD part, single-blind); or
  - BID at a dose of 6 mg or 12 mg under fed conditions over 14 days* (MRD part, double-blind).
- Participants were partially randomized within each dose group.
  - The first block of each dose group was treated in a fixed sequence, whereas the other block was randomized in a 2:1 ratio reflecting the ratio of subjects receiving BI 1015550 to placebo.
- The primary endpoint was the number of participants with drug-related AEs.
- Secondary endpoints were pharmacokinetic parameters.

CONCLUSIONS

- All AEs were mild or moderate in intensity, providing preliminary evidence that BI 1015550 has an acceptable safety and tolerability profile in healthy adult males.
- Based on the results from this trial, a Phase Ic trial investigated the safety, tolerability and pharmacokinetics of BI 1015550 in patients with IPF: see ATS P5220.

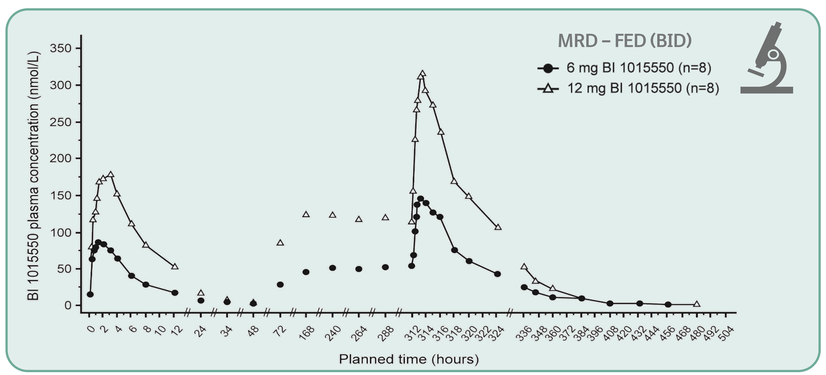
RESULTS

Baseline characteristics

- Participants comprised 42 healthy adult males (39 White, 2 Black, 1 Asian) with a mean age of 34.6 years (SD=7.0) and a mean BMI of 25.0 kg/m2 (SD=2.7).
- Demographics were similar across dosing schedules and treatment groups.

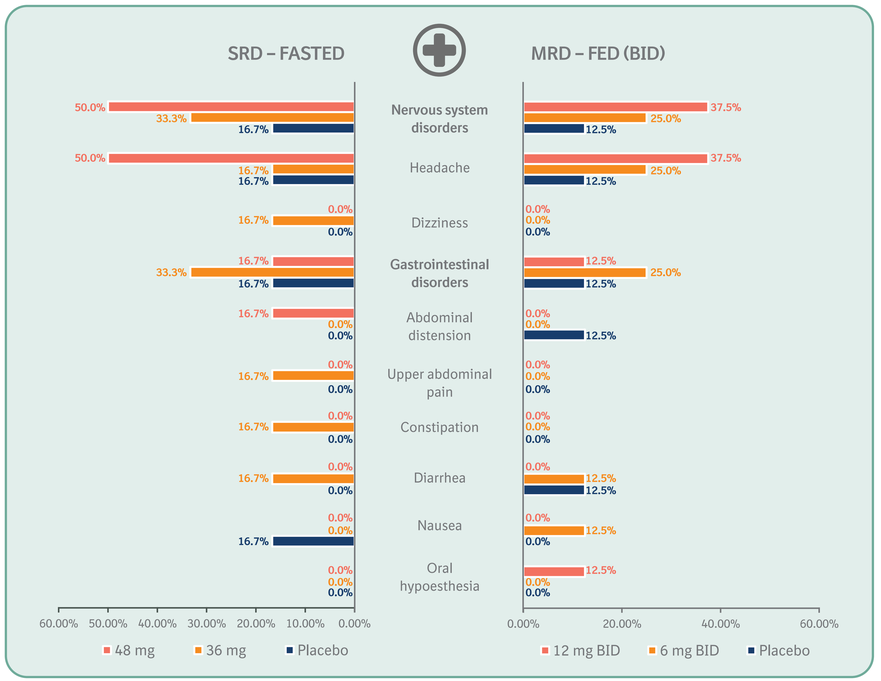
Pharmacokinetic parameters

- Overall, the total exposure to BI 1015550 appeared to increase proportionally with dose over the range tested.
- Plasma concentrations increased quickly, before declining with terminal half-lives of 16 hours to 27 hours.
- Linear pharmacokinetics with a dose-proportional increase in the AUC of the analyte in plasma were observed for the dose ranges tested.
- Steady state was reached by Day 6, with a slight accumulation after multiple BID administrations.



Adverse events

- Drug-related AEs were reported more frequently in participants treated with BI 1015550 versus placebo in the SRD part (50.0% vs 16.7%) and the MRD part (37.5% vs 12.5%).
- One participant (48 mg) prematurely discontinued due to an AE (ligament sprain) that was not considered drug related.
- There were no reported deaths, severe AEs, serious AEs, protocol-specified AEs of special interest or other significant AEs.



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REFERENCES

1. Sisson TH, et al. Physiol Rep 2018; 6:e13753;
2. Herrmann FE, et al. Front Pharmacol 2022; 13:838449.

ABBREVIATIONS

AE, adverse event; AUC, area under the curve; BID, twice daily; BMI, body mass index; IPF, idiopathic pulmonary fibrosis; MRD, multiple rising dose; PDE4B, phosphodiesterase 4B; SD, standard deviation; SRD, single rising dose.

*Participants were treated over 14 days and received a single morning dose on Day 1, followed by 11 days of treatment (i.e. 6 mg BID, 12 mg BID or matching placebo on Days 3 to 13), and a single morning dose on Day 14. No treatments were administered on Day 2 to allow 34-hour pharmacokinetic sampling after a single dose.

DISCLOSURES

CS, DL, and CC are employees of Boehringer Ingelheim International GmbH.
AS is an employee of Clinical Research Services Mannheim GmbH.

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