Poster

Safety, tolerability and pharmacokinetics of BI 1015550 in patients with IPF

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Safety, tolerability and pharmacokinetics of BI 1015550 in patients with IPF

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INTRODUCTION

- IPF is a rare lung disease characterized by progressive decline in lung function.[1,2]
- PDE4 inhibition may reduce inflammation and fibrotic remodeling. [3–5]
- In a Phase I trial, BI 1015550, an oral preferential inhibitor of PDE4B, appeared to be well tolerated in healthy adult males: see ATS P5217.

AIM

- To investigate the safety, tolerability and pharmacokinetics of BI 1015550 in patients with IPF.

METHODS

- This was a Phase Ic trial with a randomized, double-blind, placebo-controlled design (NCT03422068) conducted between April 2018 and July 2019 at 11 sites in 7 European countries:
  - Denmark: Odense
  - Finland: Helsinki, Turku
  - Germany: Heidelberg, Hannover
  - Italy: Rome
  - Netherlands: Rotterdam, Nieuwegein
  - Spain: Barcelona
  - UK: London, Southampton
- Male and female patients with a diagnosis of IPF based on the American Thoracic Society/European Respiratory Society/Japanese Respiratory Society/Latin American Thoracic Association 2011 Guidelines, aged ≥40 years, who were not receiving antifibrotic treatment, were eligible for participation.
- Participants were treated with 18 mg BID BI 1015550 or matching placebo for up to 12 weeks.
- The primary endpoint was the number of participants with drug-related AEs.
- Secondary endpoints were pharmacokinetic parameters.

CONCLUSIONS

- 18 mg BI 1015550 BID appears to have an acceptable safety and tolerability profile in patients with IPF.
- 95% of the steady-state concentration is reached after ~five administrations.
- A Phase II trial (NCT04419506) investigating the efficacy, safety and tolerability of BI 1015550 in patients with IPF with and without antifibrotic treatment has recently completed: see ATS P11301.

RESULTS

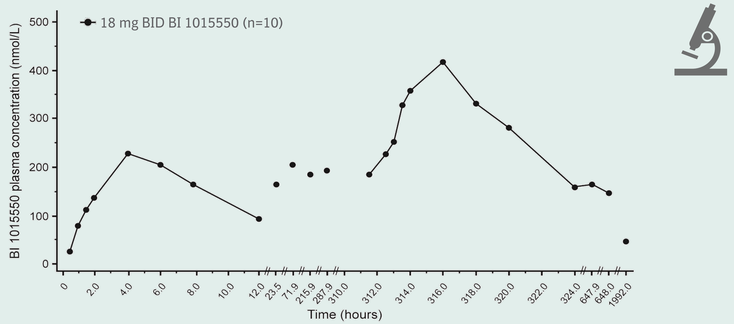
Baseline characteristics

- Participants comprised 15 patients with a mean age of 69.7 years (SD=8.3), mean weight of 82.5 kg (SD=11.1), and median time since diagnosis of 412 days.
- All patients were White; 13 (86.7%) were male.
- Ten patients were treated with BI 1015550 and five patients with placebo for a median duration of 53.5 and 84.0 days, respectively.
- Baseline lung function was comparable between the treatment groups.

Placebo (n=5)	18 mg BID (n=10)
FVC (% pred): 91.1 (SD=17.1)	FVC (% pred): 92.0 (SD=15.3)
FEV_1 (% pred): 94.5 (SD=12.7)	FEV_1 (% pred): 97.4 (SD=10.7)
DL_{co} Hb corr (% pred): 62.4 (SD=18.8)	DL_{co} Hb corr (% pred): 61.6 (SD=30.2)

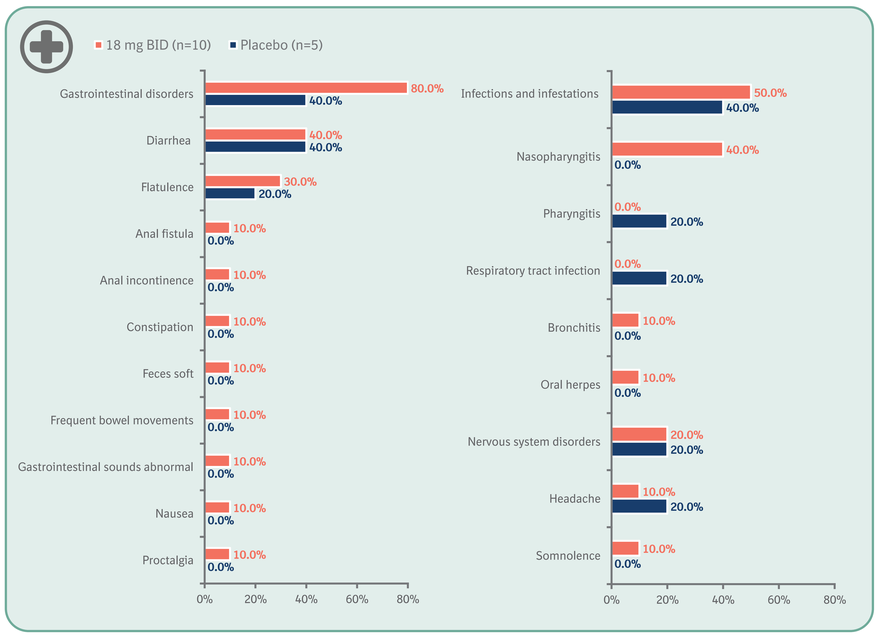
Pharmacokinetic parameters

- The geometric means for C_{max} and $AUC_{τ,1}$ were higher after multiple administrations than after administration of a single dose.
- After approximately five administrations of BI 1015550 at 18 mg BID, 95% of the steady-state concentration was reached.



Adverse events

- Drug-related AEs were reported more frequently in patients treated with BI 1015550 versus placebo (90.0% vs 60.0%).
- The most frequent AEs were GI disorders (80.0% for BI 1015550 vs 40.0% for placebo).
- There was one severe AE of insomnia in a patient treated with BI 1015550, which was considered drug related, and this was the only AE leading to discontinuation in the trial.
- All other AEs were mild or moderate in intensity.
- One patient treated with BI 1015550 experienced two serious AEs (anal fistula and anal incontinence) that were mild in intensity and not considered drug related.



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ABBREVIATIONS

AE, adverse event; AUCτ,1, area under the curve of the analyte in plasma over a uniform dosing interval τ after administration of the first dose; BID, twice daily; C_{max}, maximum measured concentration of the analyte in plasma; DL_{co} Hb corr, diffusing capacity of the lung for carbon monoxide corrected for hemoglobin; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; GI, gastrointestinal; IPF, idiopathic pulmonary fibrosis; PDE4B, phosphodiesterase 4B; pred, predicted; SD, standard deviation.

DISCLOSURES

TMM has received consulting fees from Boehringer Ingelheim, Roche/Genentech, AstraZeneca, Bayer, Blade Therapeutics, Bristol-Myers Squibb, Galapagos, Galecto, GlaxoSmithKline, IQVIA, Pliant, Respivant, Theravance, and Veracyte. He has also received speaker fees from Boehringer Ingelheim and Roche/Genentech. SB, MEM, DFZ and DL are employees of Boehringer Ingelheim.

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