The Oral Factor D Inhibitor BCX10013 Inhibits the Complement Alternative Pathway in Healthy Participants

Poster 106

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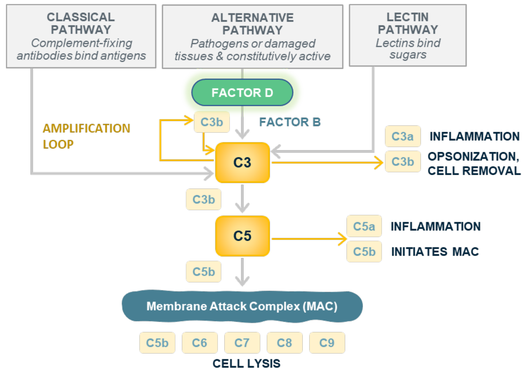
Introduction

- BCX10013 is a potent and selective oral inhibitor of Factor D, the rate-limiting enzyme of the complement alternative pathway (AP)[1]
- Factor D inhibition may effectively control complement dysregulation for treatment of complement-mediated diseases

Figure 1. Factor D in the AP



Methods

- Study BCX10013-101 was a randomized, double-blind, placebo-controlled clinical trial in healthy volunteers

Dose levels:

- Single doses from 1–200 mg
  - Planned n = 6 BCX10013 and n = 2 placebo per cohort
- Multiple doses from 20-160 mg once daily (QD) for 7-14 days
  - Planned n = 10 BCX10013 and n = 2 placebo per cohort

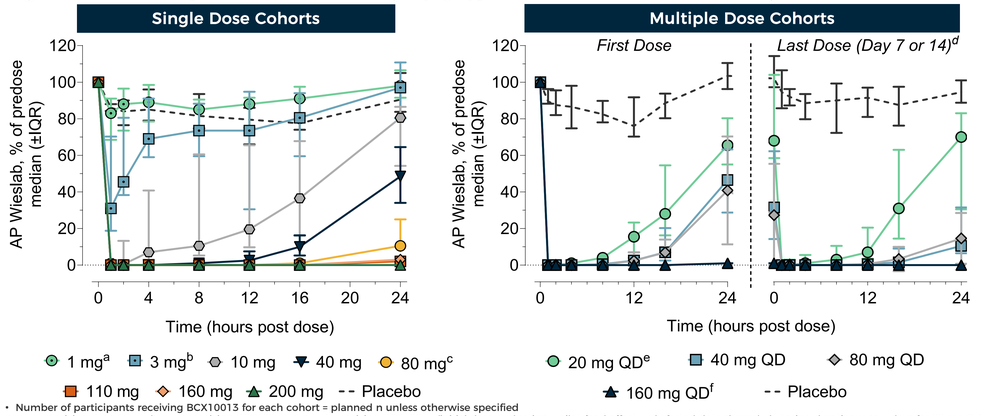
Key Outcome Measures:

- **Pharmacodynamic effects** of complement suppression: ex vivo activated C5b-9 (AP Wieslab)
- **Pharmacokinetics** (PK) using validated LC/MS/MS assay
- **Safety and Tolerability**

Reference: 1. Barratt J, Weitz I. *Front Immunol.* 2021;12:712572.

Results

Figure 2. Median [±Interquartile Range (IQR)] AP Wieslab Suppression by BCX10013



• Number of participants receiving BCX10013 for each cohort = planned n unless otherwise specified
a. n = 5 receiving BCX10013; b. n = 4 receiving BCX10013; c. n = 12 receiving BCX10013 (initial dose evaluation + pilot food effect; only fasted data shown); d. Dosing duration was 7 days for 20 mg QD cohort and 14 days for 40, 80, and 160 mg cohorts; e. n = 10 and n =9 receiving BCX10013 on Day 1 and Day 7, respectively; f. n = 9 and n = 8 receiving BCX10013 on Day 1 and Day 14, respectively.

AP Suppression (via AP Wieslab) by BCX10013 was:

Rapid	Onset of effect ≤1 hour from first dose
Potent	≥99% suppression for all participants receiving >10 mg
Sustained	at 24 hours post (last) dose for highest single and multiple doses

Table 1. Incidence of TEAEs by Treatment
(number and % of participants)

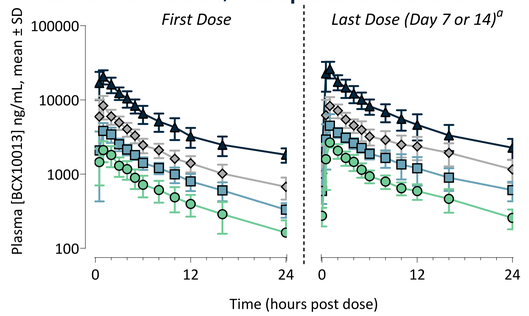
Category	Single Dose Cohorts		Multiple Dose Cohorts	
	BCX10013 *(n = 51)*	Placebo *(n = 16)*	BCX10013 *(n = 39)*	Placebo *(n = 8)*
Any TEAE	17 (33.3)	7 (43.8)	23 (59.0)	5 (62.5)
Grade 3 or 4 TEAE	0 (0)	0 (0)	0 (0)	0 (0)
TESAE	0 (0)	0 (0)	0 (0)	0 (0)
TEAEs occurring in >10% of participants				
Headache	5 (9.8)	4 (25)	6 (15.4)	1 (12.5)

BCX10013 was safe and generally well tolerated

There were no dose-related tolerability or safety findings

TEAE = treatment-emergent adverse event; TESAE = treatment-emergent serious adverse event

Figure 3. Mean [±Standard Deviation (SD)] BCX10013 Plasma Concentration; Multiple Dose Cohorts



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BCX10013 PK profile was characterized by…

- **Rapid absorption** following oral dosing
- **Dose-proportional exposure** across the evaluated range
- **Low accumulation** (30-40%) following 7-14 days of dosing[a]
- Median terminal half-life of approximately 14-16 hours

• Similar trends were observed following single doses (data not shown).
a. Based on median ratio of area under the concentration vs. time curve from 0-24 hours (AUC_{0-24}) on the last dosing day vs. Day 1

Conclusions

1. BCX10013 rapidly, potently, and durably suppressed the AP via Factor D inhibition
2. BCX10013 demonstrated a favorable PK profile following oral dosing
3. BCX10013 was safe and generally well tolerated in this first in human study
4. Results support further evaluation of the therapeutic potential of BCX10013 in complement-mediated diseases

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