A Phase 1, Randomized, Single-Blind, Placebo-Controlled Pharmacokinetic Study Evaluating Oral BX002-A Bacteriophage Therapy for Inflammatory Bowel Disease / Primary Sclerosing Cholangitis

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DIGITAL EXPERIENCE

INTRODUCTION

Role of *Klebsiella* in Inflammatory Bowel Disease (IBD) and Primary Sclerosing Cholangitis (PSC)

A *Klebsiella pneumoniae* strain isolated from IBD and PSC patients

- Induced moderate-severe colitis in IL-10-/- mice[1]
- Gut pathobiont of PSC that plays etiologic role in pathogenesis of PSC, causing intestinal barrier dysfunction[2]
- *K. pneumoniae* potential therapeutic target in IBD and PSC

AIM

First-in-human study

- Evaluated safety and tolerability of orally administered BX002-A cocktail of bacteriophages (phages) targeting a pathogenic *K. pneumoniae* strain
- Assessed phage viability after oral BX002-A

METHODS

Randomized, single-blind, placebo-controlled study

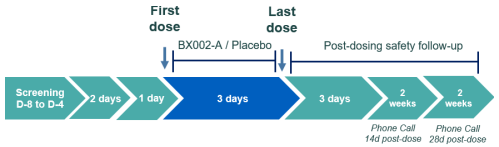
- N=18 healthy adults
  - BX002-A: 14 subjects
  - Placebo: 4 subjects

Treatment regimen

- Twice daily x 3 days, oral administration (Figure 1)
- Stool collected D-1 to D6
- Phage viability after oral BX002-A assessed in stool by analysis of phage forming units (PFU)

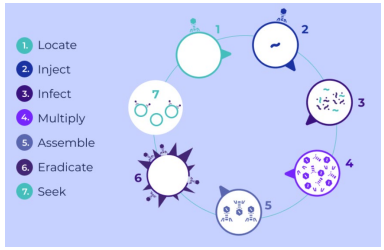
METHODS (con'd)

Figure 1. Study Design



- Bacteriophages (phage): Viruses that target specific bacterial strains, without disrupting potentially beneficial bacteria (Figure 2)
  - Inert to mammalian cells
  - Natural predators of bacteria, found wherever bacteria exist
- Phages rapidly kill their bacterial targets
  - Amplify inside bacteria
  - Release new phage to infect and selectively kill nearby bacterial targets
- BX002-A
  - Cocktail of naturally-occurring bacteriophages that selectively target *Klebsiella pneumoniae* strains thought to be pathogenic in IBD

Figure 2. Mechanism of action of phage



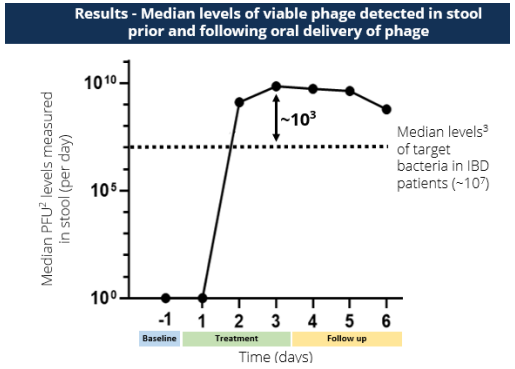
RESULTS

BX002-A: well-tolerated

- Similar rates of treatment-emergent AEs (TEAEs) between BX002-A (42.9%) and placebo (50.0%)
- No treatment-related TEAEs in BX002-A group
- One (25.0%) subject in placebo group had a treatment-related TEAE
- No serious AEs or TEAEs that led to discontinuation of study drug or study
- No clinically concerning changes in vital signs or laboratory values

- Phage detected in stool of all subjects (Figure 3)
- All subjects with samples at D4, 5, and 6 had phages detected, even after dosing completed at D3

Figure 3. Median levels of viable phage detected in stool



Viable phage was detected at concentrations several log higher compared to expected bacterial burden of *K. pneumoniae* in IBD and PSC patients

(1) Study conducted with BX002-A, a phage cocktail for oral administration targeting *K. pneumoniae*

(2) PFU – Plaque forming units

(3) Value based on median levels of *K. pneumoniae* measured in clinical stool samples collected by BiomX from IBD and PSC patients

CONCLUSIONS

Orally administered BX002-A in first-in-human study

- Safe and well-tolerated in healthy adults
- PK analysis showed high levels of viable phages in stool at sufficient levels to interact with target bacteria after passage through gastrointestinal tract
- Oral phage therapy should be further explored for its ability to reduce pathogenic *Klebsiella pneumoniae* bacteria in the gut and serve as a potential therapeutic in IBD and PSC patients

ACKNOWLEDGEMENTS

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REFERENCES

1. Atarashi et al. Science 2017;358(6361):359-365.
2. Nakamoto et al. Nat Microbiol. 2019 Mar;4(3):492-503.

DISCLOSURES

All authors are employees of BiomX and may own stock

CONTACT INFORMATION

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