Effect of NGM282, an FGF19 Analogue, on Pruritus in Patients with Primary Sclerosing Cholangitis: Analysis of a Phase 2, Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial

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BACKGROUND AND AIMS

- NGM282 is an engineered, non-tumorigenic analogue of human FGF19.
- Administration of NGM282 resulted in improvements in ALT, AST, and serum markers of fibrogenesis (ELF and Pro-C3), without reducing alkaline phosphatase (ALP), in 12 weeks in patients with primary sclerosing cholangitis (PSC).
- Approximately 50% of PSC patients experience pruritus, a symptom that can reduce quality of life; however, several drugs in development for PSC further increased pruritus.1
- We report here the effect of NGM282 on pruritus after 12 weeks of treatment.

METHODS

- Sixty-two PSC patients received NGM282 1 mg (n=21), 3 mg (n=22) or placebo (n=20) once daily for 12 weeks, with a follow-up at week 15.
- Key inclusion criteria included PSC by EASL criteria and an elevated ALP>2xULN.
- The primary endpoint was the change in AUP from baseline (A1) to Week 12 (W12).
- ID-itch pruritus questionnaires (scores range from 5 to 25, with higher scores indicating worse itch) were collected.
- Patients also recorded pruritus intensity on a numeric rating scale (NRS) ranging from 0 to 10, with higher numbers indicating more severe itch.
- An analysis of covariance (ANCOVA) model was used to compare the NGM282 groups with the placebo group.

RESULTS

- In particular, patients treated with NGM282 3 mg showed a trend of improvement in pruritus disability domain score as early as Week 2, and at repeated assessments at Weeks 4, 8 and 12 (end of treatment).
- Pruritus disability domain assess the impact of pruritus on the following activities:
  - Sleep
  - Leisure/Social
  - Housework/Errands
  - Work/School
- Pruritus direction, which assess the location of pruritus in various parts of the body
- Pruritus distribution, which assess the location of pruritus in various parts of the body
- Patients treated with NGM282 3 mg showed a trend of improvement in pruritus distribution, which assess the location of pruritus in various parts of the body

CONCLUSION

- In this population of patients with PSC, treatment with NGM282 was not associated with drug-induced pruritus, but was associated with a trend of improvement in pruritus, especially in the 3 mg group.
- Levels of ALP did not correlate with ID-itch total score or its five domains.
- Changes from baseline to week 12 in ELF correlate with changes in pruritus distribution, degree and direction, revealing an unexpected connection between collagen turnover and pruritus.
- These patient experience data may provide important additional information about the clinical benefit of NGM282.
- Clinically relevant, patient-reported outcome measures should be evaluated in future PSC trials.

Acknowledgments

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