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THERAPY

Oral *SMAD7* antisense oligonucleotide proves effective for Crohn's disease

A new agent for the treatment of IBD seems to be on the horizon as the results of a phase II trial indicate that mongersen (a *SMAD7*-targeting antisense oligonucleotide) induces remission in patients with active Crohn's disease.

Inflammation during Crohn's disease is characterized by reduced activity of the immunosuppressive cytokine, transforming growth factor β (TGF-β), which is itself regulated by SMAD7. In the new study, SMAD7 was targeted as a means to suppress intestinal inflammation via TGF-β. "Mongersen is a 21-base single-strand phosphorothioate oligonucleotide, which hybridizes to the human *SMAD7* RNA and facilitates RNAse-H-mediated RNA degradation (i.e. acting through a classic antisense mechanism)," explains first author Giovanni Monteleone.

The researchers enrolled 166 patients with moderate-to-severe Crohn's disease (Crohn's Disease Activity Index [CDAI] score ranging 220–400) in the trial. Participants were then randomly assigned to receive either 10 mg, 40 mg or 160 mg mongersen or placebo daily for 2 weeks.

Patients with active Crohn's disease who received mongersen had higher rates of clinical remission (CDAI score <150 at day 15, which was maintained at day 28) than those on placebo: 55% and 65% of those receiving 40 mg and 160 mg mongersen, respectively, compared with only 10% of the placebo group (P <0.001). Moreover, substantially more patients taking mongersen achieved a clinical response (≥100 decrease in CDAI score at day 28) than those on placebo.

Overall, the number of adverse events were similar across the treatment groups and placebo group. Furthermore, serious adverse events (such as abdominal pain) seemed to be related to complications or symptoms of Crohn's disease and were not thought to be due to the treatment itself.

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"The remission rate seen with the two highest doses are unprecedented when compared with those reported in previous induction studies in which biologic agents were tested," says Monteleone, although he acknowledges that no head-to-head comparisons for mongersen versus biologic agents have been conducted. Initiation of a phase III trial of mongersen is planned for later in 2015.

Katrina Ray

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