Τυχαιοποιημένη, ελεγχόμενη δοκιμή του αναλόγου FGF21 Pegozafermin στη NASH

Randomized, Controlled Trial of the FGF21 Analogue Pegozafermin in NASH

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Background

Pegozafermin is a long-acting glycopegylated (pegylated with the use of site-specific glycosyltransferases) fibroblast growth factor 21 (FGF21) analogue in development for the treatment of nonalcoholic steatohepatitis (NASH) and severe hypertriglyceridemia. The efficacy and safety of pegozafermin in patients with biopsy-proven noncirrhotic NASH are not well established.

Methods

In this phase 2b, multicenter, double-blind, 24-week, randomized, placebo-controlled trial, we randomly assigned patients with biopsy-confirmed NASH and stage F2 or F3 (moderate or severe) fibrosis to receive subcutaneous pegozafermin at a dose of 15 mg or 30 mg weekly or 44 mg once every 2 weeks or placebo weekly or every 2 weeks. The two primary end points were an improvement in fibrosis (defined as reduction by ≥1 stage, on a scale from 0 to 4, with higher stages indicating greater severity), with no worsening of NASH, at 24 weeks and NASH resolution without worsening of fibrosis at 24 weeks. Safety was also assessed.

Results

Among the 222 patients who underwent randomization, 219 received pegozafermin or placebo. The percentage of patients who met the criteria for fibrosis improvement was 7% in the pooled placebo group, 22% in the 15-mg pegozafermin group (difference vs. placebo, 14 percentage points; 95% confidence interval [CI], −9 to 38), 26% in the 30-mg pegozafermin group (difference, 19 percentage points; 95% CI, 5 to 32; P=0.009), and 27% in the 44-mg pegozafermin group (difference, 20 percentage points; 95% CI, 5 to 35; P=0.008). The percentage of patients who met the criteria for NASH resolution was 2% in the placebo group, 37% in the 15-mg pegozafermin group (difference vs. placebo, 35 percentage points; 95% CI, 10 to 59), 23% in the 30-mg pegozafermin group (difference, 21 percentage points; 95% CI, 9 to 33), and 26% in the 44-mg pegozafermin group (difference, 24 percentage points; 95% CI, 10 to 37). The most common adverse events associated with pegozafermin therapy were nausea and diarrhea.

Conclusions

In this phase 2b trial, treatment with pegozafermin led to improvements in fibrosis. These results support the advancement of pegozafermin into phase 3 development. (Funded by 89bio, NCT04929483)

ΣΧΟΛΙΟ

Ο αυξητικός παράγοντας των ινοβλαστών 21 (FGF21) συμμετέχει στη ρύθμιση του μεταβολισμού

των λιπιδίων και της γλυκόζης. Το Pegozafermin, ένα μακράς δράσης ανάλογο του FGF21, έδωσε ελπιδοφόρα στοιχεία όσον αφορά στη βελτίωση της ηπατικής στεάτωσης, φλεγμονής και ίνωσης μετά από 24 εβδομάδες αγωγής σε αυτή τη φάσης 2b μελέτη. Μένει να φανεί αν αυτά τα αποτελέσματα θα επαληθευτούν σε μελέτες φάσης 3, οι οποίες ενδεχομένως να πρέπει να διαρκέσουν μεγαλύτερο χρονικό διάστημα. Ένα επιπλέον όφελος αυτής της ουσίας φαίνεται να είναι η βελτίωση των τιμών των τριγλυκεριδίων και της HDL, κάτι, που δυνητικά θα μπορούσε να είναι ωφέλιμο όσον αφορά στην αυξημένη καρδιαγγειακή νοσηρότητα των ασθενών με NASH.