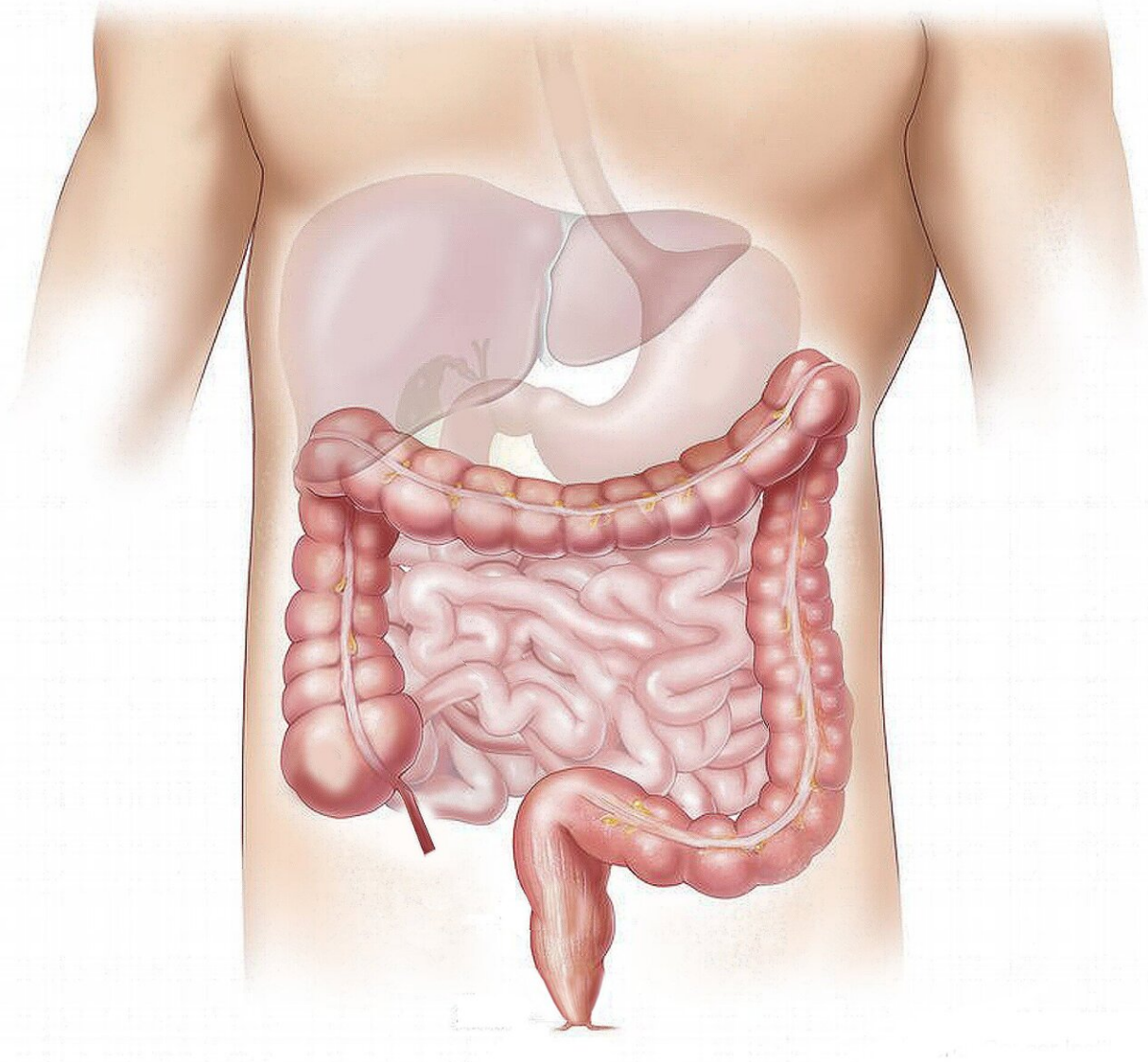


Obeticholic acid improves liver fibrosis and other histological features of NASH

April 11 2019



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A prespecified interim analysis of the ongoing Phase 3 REGENERATE study has confirmed that obeticholic acid (OCA) is effective in the treatment of nonalcoholic steatohepatitis (NASH) with liver fibrosis. The 18-month analysis, which was reported today at The International Liver Congress 2019 in Vienna, Austria, demonstrated that the 25 mg dose of OCA studied improved fibrosis in almost one-quarter of recipients, with significant improvements also reported in other histological markers of NASH.

Nonalcoholic steatohepatitis is a severe form of nonalcoholic fatty liver disease (NAFLD) and is characterized by the presence of steatosis, hepatocellular ballooning, and lobular inflammation. The condition is associated with rapid progression of fibrosis, which can eventually lead to the development of cirrhosis and hepatocellular carcinoma. The global prevalence of NASH has been estimated to range from 1.50% to 6.45%, with almost 60% of individuals with NAFLD who undergo biopsy found to have NASH. There are currently no medications approved in Europe or the USA specifically for the treatment of NASH.^{2,4}

Obeticholic acid is a potent activator of the farnesoid X nuclear receptor that was shown to improve liver histology and fibrosis in a Phase 2 clinical trial (FLINT) published in 2015. The Phase 3 trial reported today is the first study in NASH to be designed in conjunction with [regulatory authorities](#), with the aim of achieving approval for OCA in NASH with fibrosis.

In the analysis reported today, 931 individuals with biopsy-confirmed NASH and significant or severe fibrosis (stages F2 or F3) were randomized to receive OCA 10 mg/day (n=312), OCA 25 mg/day (n=308), or placebo (n=311). The primary endpoints of the study were either fibrosis improvement (greater than or equal to 1 stage) with no

worsening of NASH or NASH resolution with no worsening of [liver fibrosis](#) on liver biopsy. The most pronounced benefits were observed in the OCA 25 mg treatment group. Once daily OCA 25 mg met the primary endpoint of fibrosis improvement (greater than or equal to 11 stage) with no worsening of NASH in 23.1% of patients ($p=0.0002$ vs placebo). Although the NASH resolution primary endpoint was not met, 35.1% of patients receiving OCA 25 mg showed improvements in hepatocellular ballooning ($p=0.0011$ vs placebo), and 44.2% of patients had lobular inflammation ($p=0.0322$ vs placebo). Dose-dependent reductions in [liver enzymes](#) were also observed.

Pruritus, the most commonly-reported adverse event (AE), affected 51% of the OCA 25 mg/day treatment group, 28% of the OCA 10 mg/day treatment group, and 19% of the placebo group. More participants withdrew from the study due to pruritus in the OCA 25 mg/day group (9%) than in the OCA 10 mg/day (

Citation: Obeticholic acid improves liver fibrosis and other histological features of NASH (2019, April 11) retrieved 7 May 2024 from <https://medicalxpress.com/news/2019-04-obeticholic-acid-liver-fibrosis-histological.html>

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