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## IMPROVEMENT IN NASH HISTOLOGICAL ACTIVITY HIGHLY CORRELATES WITH FIBROSIS REGRESSION

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**Background:** A NASH treatment should protect from long-term progression to cirrhosis and its complications by suppressing the underlying cause of fibrogenesis. Whether changes in individual histological features of NASH alter fibrosis progression remains to be determined.

**Methods:** All completers of the 1-year GOLDEN-505, elafibranor vs. placebo trial (N=237) were analyzed. Biopsies were scored by the NASH-CRN classification at baseline and end-of-treatment (EOT). At inclusion all pts had scores  $\geq 1$  for steatosis, lobular inflammation and hepatocyte ballooning. Pts were grouped by changes between EOT and inclusion for steatosis (from -3 to +2), lobular inflammation (from -2 to +2) or ballooning (from -2 to +1) scores. For each group, the percentage of patients experiencing an improvement or a worsening ( $>1$  stage) in fibrosis stage was calculated. Associations between changes in scores and fibrosis evolution were assessed by the Fisher exact test.

**Results:** Changes in both lobular inflammation and ballooning were highly and positively correlated with changes in fibrosis ( $p < 0.001$  and  $p = 0.04$ , respectively). Among pts with a 2 point score reduction in inflammation, 67% improved fibrosis (0% worsened); in contrast, if inflammation progressed by  $>1$  point, 56% of pts worsened fibrosis and only 6% improved. For ballooning changes, a 2 point reduction in score resulted in 71% fibrosis improvement (0% worsening); conversely, a 1 point increase resulted in 35% fibrosis worsening and only 26% improvement. In contrast, there was no association between changes in steatosis scores and changes in fibrosis: 25% improved and 0% worsened for a change  $\leq -2$ ; 45% improved and 18% worsened for a change  $\geq 1$ . An activity index defined as the sum of lobular inflammation and ballooning scores shows a positive linear relationship with mean changes in fibrosis score ( $R^2 = 0.95$ ). Similar results were obtained when considering placebo and elafibranor-treated patients separately or when considering only patients with  $NAS \geq 4$  and  $F \geq 2$  at inclusion.

**Conclusion:** Improvement in NASH activity and regression of fibrosis are highly

correlated supporting the concept that resolution of NASH can reverse fibrosis progression and is reasonably likely to predict long term clinical benefit. (no table selected).

**Disclosure:**

*Employee:* GENFIT