References


Abstracts

OTU-11 NON-SEVERE ALCOHOLIC HEPATITIS IS NOT A BENIGN CONDITION: SYSTEMATIC REVIEW AND META-ANALYSIS OF MORTALITY DATA

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Introduction Alcohol hepatitis (AH) is a serious complication of alcohol misuse characterised by recent-onset jaundice and coagulopathy in long-term heavy alcohol consumers. To date, clinical and academic interest has almost exclusively focused on severe AH (SAH), which has a very high short- and long-term mortality. AH that does not meet SAH criteria, termed ‘non-severe alcoholic hepatitis’ (N-SAH) is at least as common as SAH but is less well characterised and mortality in this group of patients is unknown. We conducted a systematic review and meta-analysis to determine the 28-day, 90-day and 1-year mortality of patients with N-SAH.

Methods The study protocol was registered prospectively on the PROSPERO database. Embase, Medline and Cochrane Central databases were searched until July 2018. Abstracts from international liver conferences and reference lists of identified manuscripts were also reviewed. All study designs reporting survival data in patients with N-SAH in any language were eligible for inclusion. Studies reporting on identical cohorts and those with missing data were excluded. N-SAH was defined as discriminant function <32, Age Bilirubin INR Creatinine (ABIC) <6.71, Model for End-stage Liver Disease (MELD) <15 or bilirubin <85 μmol/L. Mortality data were extracted and meta-analysis performed using a random effects model. Sensitivity or subgroup analyses were performed to determine whether the definition of N-SAH, method of diagnosis (histological vs clinical) or study design influenced the mortality.

Results Twenty-five studies (n=1372 patients) were eligible (12 prospective studies including 5 intervention trials) of which, 17 reported 28-day mortality (n=993), 15, 90-day mortality (n=755) and 5, 1-year mortality (n=234). Mortality was 6% (95% CI 91-97%) and 28 days, 7% (89-96%), I²=67%; p=0.001) at 28 days, 7% (69-96%), I²=64%; p<0.001) at 90 days and 13% (76-96%; I²=72%; p=0.006) at 1 year. Sensitivity analysis demonstrated that the criteria used to define N-SAH did not affect mortality. Subgroup analyses did not find differences in mortality proportion depending on method of diagnosis (histological vs clinical) or study design (retrospective vs prospective).

Conclusions This meta-analysis demonstrates that ‘N-SAH’ is poorly named and not a benign condition as previously assumed. The 28-day mortality of 6% is comparable to that of acute myocardial infarction. Whilst this meta-analysis is limited to some extent by the heterogeneity of studies in terms of design, sample size and population, it shows that there is a paucity of high-quality studies reporting outcomes in this group. N-SAH warrants further study to better define outcomes and develop new strategies to improve survival.
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Introduction Obeticholic acid (OCA), an FXR agonist, improved both fibrosis and histologic features of nonalcoholic steatohepatitis (NASH) in the Ph2 FLINT study. This Month 18 pre-specified interim analysis of the ongoing Ph3 REGENERATE study evaluated the effect of OCA on liver histology in patients (pts) with biopsy-confirmed NASH.

Methods Pts with NASH and fibrosis stages F2–3 (ITT), and an exploratory group of F1 pts with metabolic syndrome, were randomized to placebo (PBO), OCA 10 mg, or OCA 25 mg QD. Primary endpoints were fibrosis improvement (≥1 stage) with no worsening of NASH, or NASH resolution with no worsening of liver fibrosis. The safety population included all randomized and dosed pts (F1–3, N=1968). Clinical outcomes will be evaluated at the end-of-study.

Results The ITT population included 931 pts (PBO [n=311], OCA 10 mg [n=312] or OCA 25 mg [n=308], comprised of 44% F2 and 56% F3). Baseline characteristics were well-balanced across groups. Results in table 1. The primary fibrosis endpoint was met by 11.9% PBO, 17.6% OCA 10 mg (p=0.0446), and 23.1% OCA 25 mg (p=0.0002) pts (ITT). The primary NASH endpoint was not statistically significant (ITT); however, in a pre-specified analysis that included F1–F3 pts (N=1218), more OCA 25 mg pts achieved NASH. Pruritus was the most common AE (19% PBO, 28% OCA 10 mg, 51% OCA 25 mg) and was predominantly mild to moderate in severity (severe: <1% PBO, <1% OCA 10 mg, 5% OCA 25 mg). More OCA 25 mg pts discontinued due to pruritus (<1% PBO, <1% OCA 10 mg, 9% OCA 25 mg). SAEs occurred in 11% PBO, 11% OCA 10 mg and 14% OCA 25 mg pts. Increases in LDLc with OCA were observed by Wk 4, but approached baseline by M18 (OCA 25 mg: LS mean change Wk4 +22.6 mg/dL, M18 +4.0 mg/dL). Three deaths occurred; none were considered treatment-related (PBO n=2; OCA 25 mg n=1).

Conclusion Treatment with OCA 25 mg improved liver fibrosis, key histologic features of steatohepatitis and liver biochemistry, demonstrating consistent efficacy with an overall AE profile similar to previous studies.