Table 1: Change from baseline to week 24 in key endpoints

| | PBO (n = 25) | Aldafermin 1 mg (n = 52) |
|---|---|---|
| *Primary Endpoint* | | |
| Δ Absolute MRI-PDFF, % | −2.7 (1.3) | −7.7 (0.8) P = 0.002 vs PBO |
| *% subjects with ↓5% absolute* | *24%* | *68%* P < 0.001 vs PBO |
| Δ Relative MRI-PDFF | −13.1% | −38.8% P = 0.008 vs PBO |
| *% subjects with ↓30% relative* | *29%* | *66%* P = 0.004 vs PBO |
| *Secondary Endpoints* | | |
| % Subjects achieving fibrosis improvement (≥1-stage) with no worsening of NASH | *18%* | *38%* |
| % Subjects achieving resolution of NASH with no worsening of fibrosis | *9%* | *24%* |
| % Subjects achieving fibrosis improvement (≥1-stage) with no worsening of NASH AND resolution of NASH with no worsening of fibrosis | *0%* | *22%* |
| Δ Absolute ALT, U/L | −15.9 (3.5) | −36.6 (2.4) |
| Δ Absolute AST, U/L | −8.5 (3.6) | −19.0 (2.4) |
| Δ Pro-C3, ng/mL | −0.9 (1.1) | −5.5 (0.7) |

Shown are LS mean (SE) or %subjects.

**Conclusion:** In patients with NASH, aldafermin therapy resulted in statistically significant reduction in LFC and robust improvement in fibrosis and NASH histology compared with PBO. A greater proportion of patients treated with aldafermin achieved both histological endpoints of fibrosis improvement and NASH resolution compared to PBO. Aldafermin 1 mg maintained a durable response for 24 weeks with a favorable tolerability and safety profile.

## LBO02

### ATTIRE: Albumin to prevent infection in chronic liver failure: an interventional randomised controlled trial

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**Background and aims:** Acutely decompensated cirrhosis patients are highly prone to infection. Multiple experimental studies support an anti-inflammatory role for Albumin in addition to its oncotic properties. Evidence supports the use of weight-based infusions of 20% Human Albumin Solution (HAS) for Spontaneous Bacterial Peritonitis and Hepato-renal syndrome, but albumin is also widely used for other indications where there is an absence of trial data. Recent albumin trials in outpatients with ascites support the notion that regimens that aim to normalise serum albumin concentrations might improve mortality. The ATTIRE trial aimed to determine if targeting a serum albumin level ≥35 g/L in decompensated cirrhosis inpatients using repeated daily HAS infusions reduced incidence of infection, renal dysfunction and mortality compared to standard care.
**Method:** ATTIRE was a multicentre, open label trial in hospitalised decompensated cirrhosis patients with serum albumin <30 g/L at enrollment at 35 UK sites (January 2016–June 2019). Treatment commenced within 3 days of admission with patients randomised to targeted 20% HAS for up to 14 days (or discharge) or standard care. The composite primary endpoint was new infection, renal dysfunction or mortality from day 3–15 of treatment.
**Results:** 828 patients were recruited with no baseline differences between groups with respect to median(IQR): creatinine 68(54–90) μmol/L, bilirubin 94(46–171) μmol/L, INR 2(1–2) and albumin 23(4) g/L. 70% were male, 79% reported alcohol misuse, 28% had infection and 53% were prescribed antibiotics. The median(IQR) volume of HAS infused to patients in the treatment versus standard care arm was 1000(700–1500) ml vs 100(0–600) ml ($p < 0.0001$). There was no difference in composite primary endpoint between targeted albumin (n = 125/414; 30.2%) and standard care (n = 128/414, 30.9%, OR 0.968 (95%CI 0.716–1.307, p = 0.830). There was no difference when the endpoint window was extended to day 1, in individual components, length of stay or mortality at 3/6 months. There was no treatment effect in subgroup analyses that included baseline organ dysfunction, infection, MELD score, albumin level or reason for admission. The mean increase in cost associated with intervention was £573.26 (95% CI −1,247.54–101.01). There were more serious adverse events in the HAS arm (95 vs 74).
**Conclusion:** The ATTIRE trial does not support targeted HAS over current UK standard care for hospitalised decompensated cirrhosis patients.

## LBO03

### Early liver transplantation for severe alcoholic hepatitis not responding to medical treatment: results of the French-Belgian prospective study QuickTrans

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Table: (abstract: LBO02)

| | | Albumin | Standard Care | Adjusted OR (95% CI) | p |
|---|---|---|---|---|---|
| | | n = 414 | n = 414 | | |
| Primary outcome | n (%) | 125 (30.2%) | 128 (30.9%) | 0.968 (0.716–1.307) | 0.830 |
| Composite endpoint components (day 3–15): | | | | | |
| New infection | | 87 (21.0%) | 76 (18.4%) | 1.196 (0.845–1.693) | 0.313 |
| Renal dysfunction | | 45 (10.9%) | 62 (15.0%) | 0.674 (0.445–1.022) | 0.063 |
| Death | | 32 (7.7%) | 34 (8.2%) | 0.936 (0.566–1.550) | 0.798 |
| 3-month mortality | | 84 (20.3%) | 80 (19.3%) | 1.084 (0.761–1.544) | 0.6548 |

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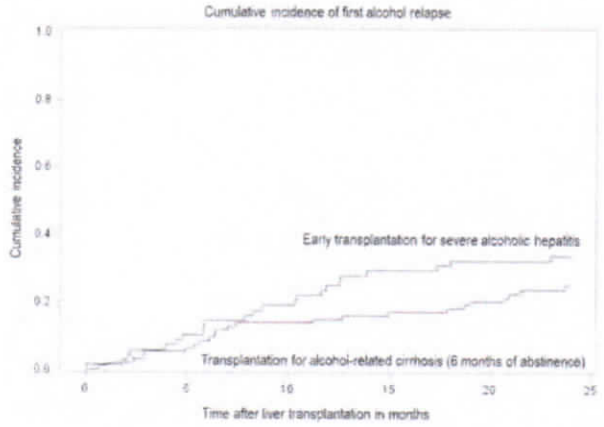
**Background and aims:** Early liver transplantation (eLT) for severe alcoholic hepatitis (SAH) is an emerging therapy that must be evaluated in prospective controlled studies with a rigorous study design to bring reliable data to experts.
**Method:** this prospective controlled trial (NCT01756794) compared 3 groups: A: patients with SAH not responding to medical treatment selected for eLT using a dedicated score (≥220/250), based on social and addiction parameters; B: patients candidates for transplantation for alcohol-related cirrhosis with at least 6 months of abstinence; C: patients with SAH not responding to medical treatment denied for eLT (score <220). Primary analysis was restricted to transplanted patients, to assess the non-inferiority of A versus B on 2-year alcohol relapse after LT using the alcohol timeline follow back (ATLFB) method and a pre-specified margin of 10%. Secondary outcomes were pattern of alcohol relapse and survival after LT. A secondary analysis was restricted to all patients of groups A and C to assess the benefit of eLT in SAH on 2-year survival.
**Results:** We included 155 patients with SAH: 78 selected for eLT (group A, median Lille score = 0.86), 77 denied for eLT (group C, median Lille score = 0.81). 129 patients were included in group B. Primary analysis: 68 (A) and 93 patients (B) were transplanted and included. MELD score at inclusion in groups A and B were 30.6 vs. 22.3, $p < 0.001$. The non-inferiority of A versus B was not demonstrated with a 2-year alcohol relapse of 33.8 (A) and 24.7% (B, figure), absolute difference of 9.1, one-sided 95% confidence interval, $-\infty$ to 21.1%. Regarding secondary outcomes, 2-year heaving drinking relapse rate was higher in group A (22.1 vs. 5.4%, $p < 0.001$). In heavy drinking relapsers, median percentage of time spent to drink during the follow-up was 10 (A) vs. 5.9% (B). Two-year survival in groups A and B was similar (89.7 vs. 88.1%). Secondary analysis: 2-year survival was higher in group A (patients transplanted or not, n = 78) than in group C (n = 77): 82.8 vs. 28.2%, $p < 0.001$.




**Conclusion:** In the first controlled study in this field, relapse rate is of 33.8% in patients early transplanted for SAH as compared to 24.7% in patients with alcohol-related cirrhosis. Using a pre-specified non-inferiority margin of 10%, we cannot conclude to non-inferiority. Heavy drinking is more frequently seen after eLT. Early liver transplantation induces a drastic improvement of survival in patients with SAH not responding to medical therapy.

## LBO04

## Safety and efficacy of combination therapies including cilofexor/firsocostat in patients with bridging fibrosis and cirrhosis due to NASH: Results of the phase 2b ATLAS trial

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**Background and aims:** Patients with advanced fibrosis due to NASH are at increased risk of end-stage liver disease, hepatocellular carcinoma, and mortality. We evaluated the safety and efficacy of an ACC inhibitor, FXR agonist, and ASK1 inhibitor, as monotherapy and in combination, in patients with advanced fibrosis due to NASH.
**Method:** In this phase 2b trial, 392 patients with advanced fibrosis (F3-F4) due to NASH were randomized to receive placebo, selonsertib 18 mg (SEL), cilofexor 30 mg (CILO), or firsocostat 20 mg (FIR), alone or in two-drug combinations, once daily for 48 weeks (W48). Biopsies from baseline (BL) and W48 were read by a central reader and digital images of biopsies were evaluated using a machine learning (ML) approach (PathAI, Boston, MA). The primary endpoint was the proportion of patients with a ≥1-stage improvement in fibrosis without worsening of NASH. Secondary endpoints included changes in NAFLD Activity Score (NAS), liver biochemistry, and noninvasive fibrosis markers.
**Results:** The majority of patients had cirrhosis (56%), diabetes (72%), and NAS ≥5 (83%). More patients treated with combination therapy achieved a ≥1-stage improvement in fibrosis without worsening of NASH compared to placebo: CILO/FIR (21%, p = 0.17), CILO/SEL (19%, p = 0.26), FIR/SEL (15%, p = 0.62), FIR (12%, p = 0.94), CILO (12%, p = 0.96), and placebo (11%). Based on a ML approach, CILO/FIR led to a significant decrease in NASH CRN fibrosis score (difference in LSmeans from BL to W48: −0.42 vs. −0.16 for placebo; p = 0.040) and a shift in biopsy proportionate area from F3-F4 to ≤F2 fibrosis. Compared to placebo, CILO/FIR led to significantly increased proportions of patients with a ≥2-pt reduction in NAS and ≥1-grade improvements in steatosis, lobular inflammation, and ballooning (all $p < 0.05$; Figure). Fibrosis improvement without worsening of NASH with CILO/FIR was more frequent in patients with ≥2-pt NAS response (35% vs 14%, p = 0.060). CILO/FIR also led to significant improvements