

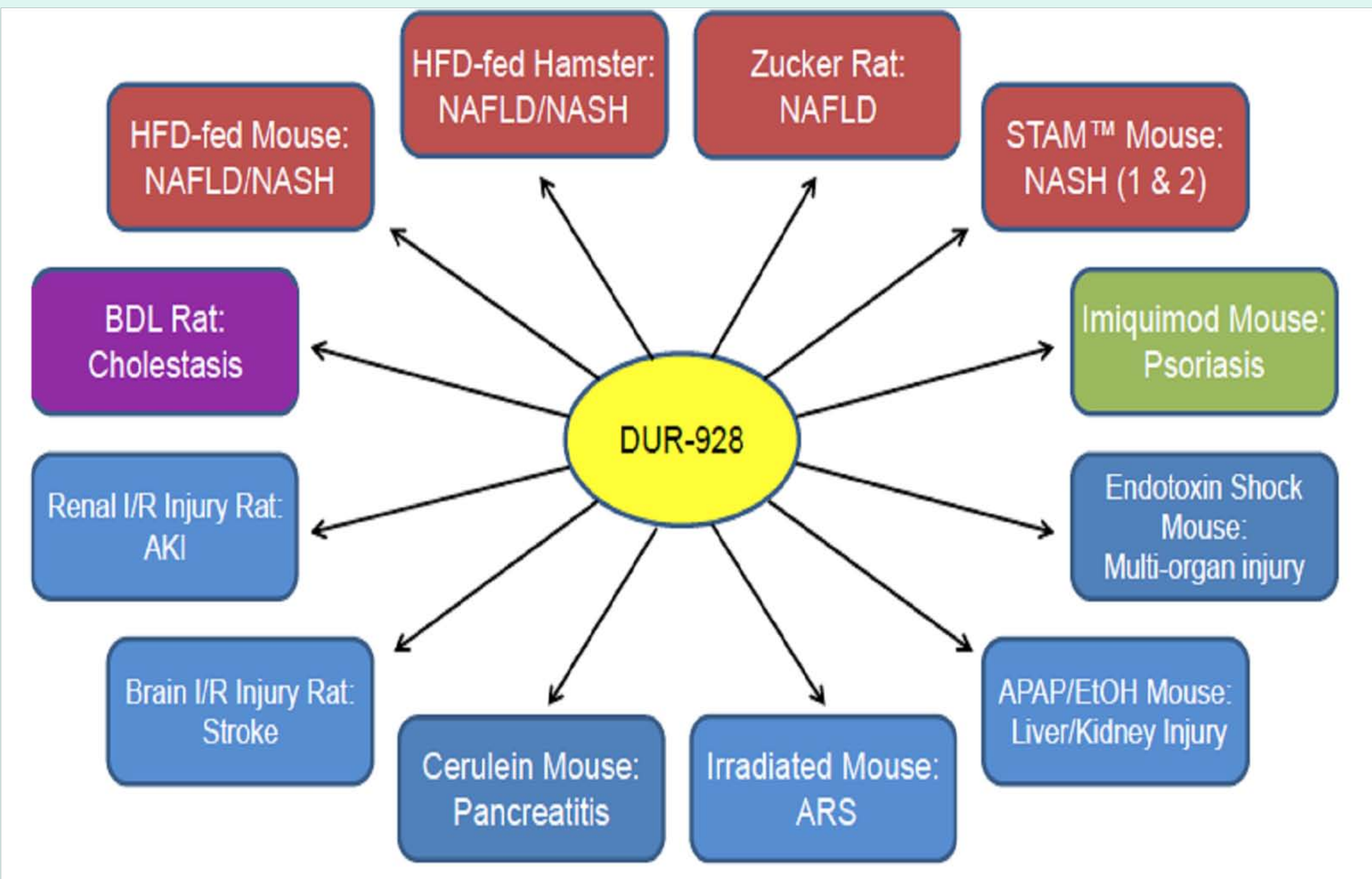
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## Introduction

Severe Acute Alcoholic Hepatitis (AAH) remains an important cause of liver-related morbidity and mortality, with no FDA approved therapy. Corticosteroids are generally considered to be the standard of care (SOC) for severe AAH. However, corticosteroid applicability in clinical practice is limited, and this therapy does not improve the outcome beyond one month. Despite the enormous public health burden, no new drugs for AAH have been successfully developed since the introduction of corticosteroids as a treatment in the early 1970s. DUR-928, a novel sulfated oxysterol (25-hydroxycholesterol-3-sulfate-25HC3S), has recently been identified as an important regulatory molecule in the liver.



DUR-928 has multiple beneficial hepatic effects including reduction in lipid synthesis, inhibition of inflammation and cell death, and stimulation of hepatic regeneration which make it an excellent potential therapeutic agent in AAH .

## Design and Methods

This is an ongoing open-label, dose-escalation Phase 2a trial assessing the safety/pharmacokinetics (PK) and pharmacodynamics of DUR-928 in AAH. Sixteen AAH patients (8 severe and 8 moderate) received one or two doses of DUR-928 via 2-hour IV infusions on Day1 and Day4 (if still hospitalized), and patients are followed for 28-days All severe patients had an admission 20<MELD≤30. A disease control group consisted of 13 patients with similar MELD scores who were entered into an NIH-funded trial on AAH and who received SOC corticosteroids for 28 days. PK data was performed on both the reported eight severe AH patients as well as a group of moderate AH patients (MELD<20). Between group/s analyses were performed for the frontline clinical markers at baseline; and longitudinally at day 7 and day 28. The primary endpoint of efficacy assessment was a decrease in the 7-day Lille score.

## Results

### Demographics

	Severe AAH on Steroid (n=13)	Severe AAH on DUR-928 (n=8)	p-value <sup>o</sup>
Sex (Female, n)	F=3, M=10	F=5, M=3	NA
Age	44.67±10.86	43.75±6.76	NS
MELD	24.46±3.382	24.50±2.77	NS
Maddrey	62.98±25.39	61.25±12.88	NS
Total Bilirubin (mg/dl)	14.469±8.7713	16.81±8.19	NS
Albumin (g/dL)	2.315±.4413	2.89±0.46	0.011
AST (U/L)	249.69±365.571	94.13±30.51	NS
ALT (U/L)	64.00±70.362	34.25±12.64	NS
AST:ALT^	6.1±3.616	3.00±1.50	NS
Creatinine (mg/dL)	.84±0.38	0.86±0.34	NS
INR	2.1±0.47	1.91±0.26	NS

Table 1: Description of baseline demographics, and clinical presentation of the severe AAH patients receiving treatment as standard of care (corticosteroid), and DUR-928. Data are presented as Mean±SD (standard deviation). <sup>o</sup>P-value shows statistical difference between the corticosteroid and DUR-928 group. NA = not applicable; NS = not significant.

### Biomarkers of AAH Severity in SOC and DUR-928 treated Patients

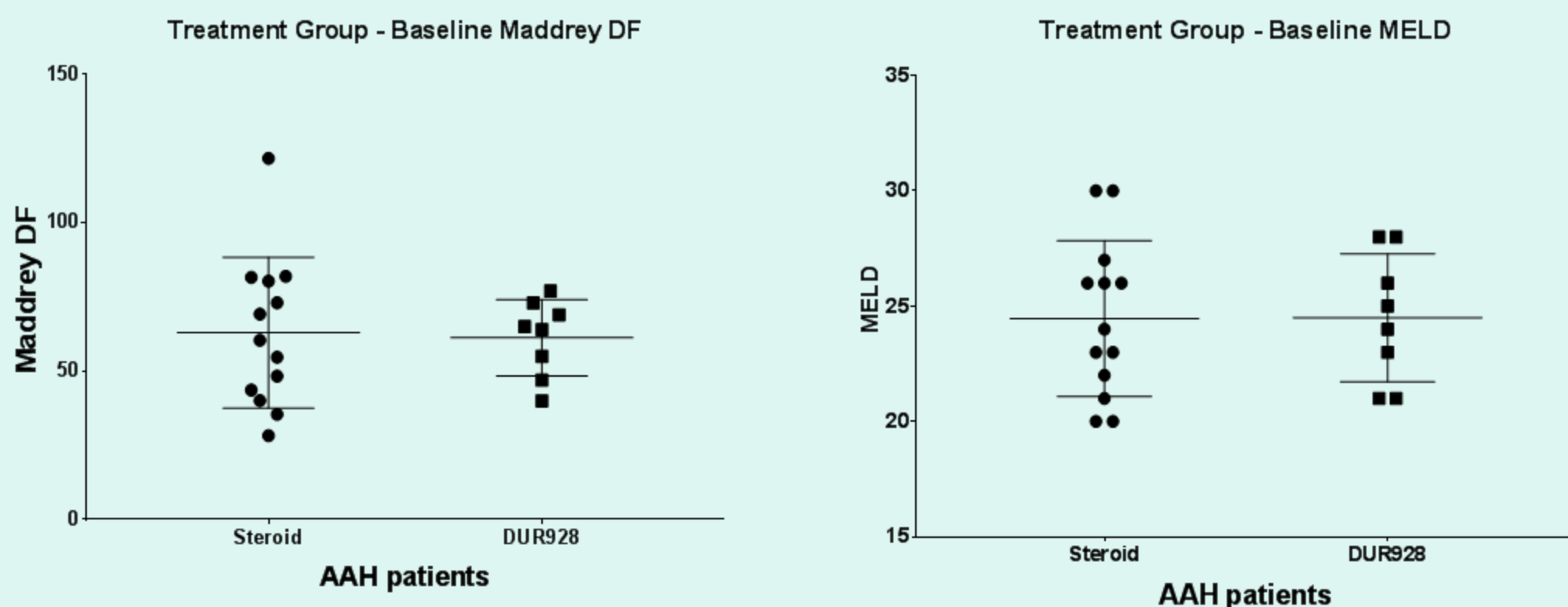


Figure 1: Well-matched severe AAH patients in the two treatment arms: corticosteroid and DUR-928.

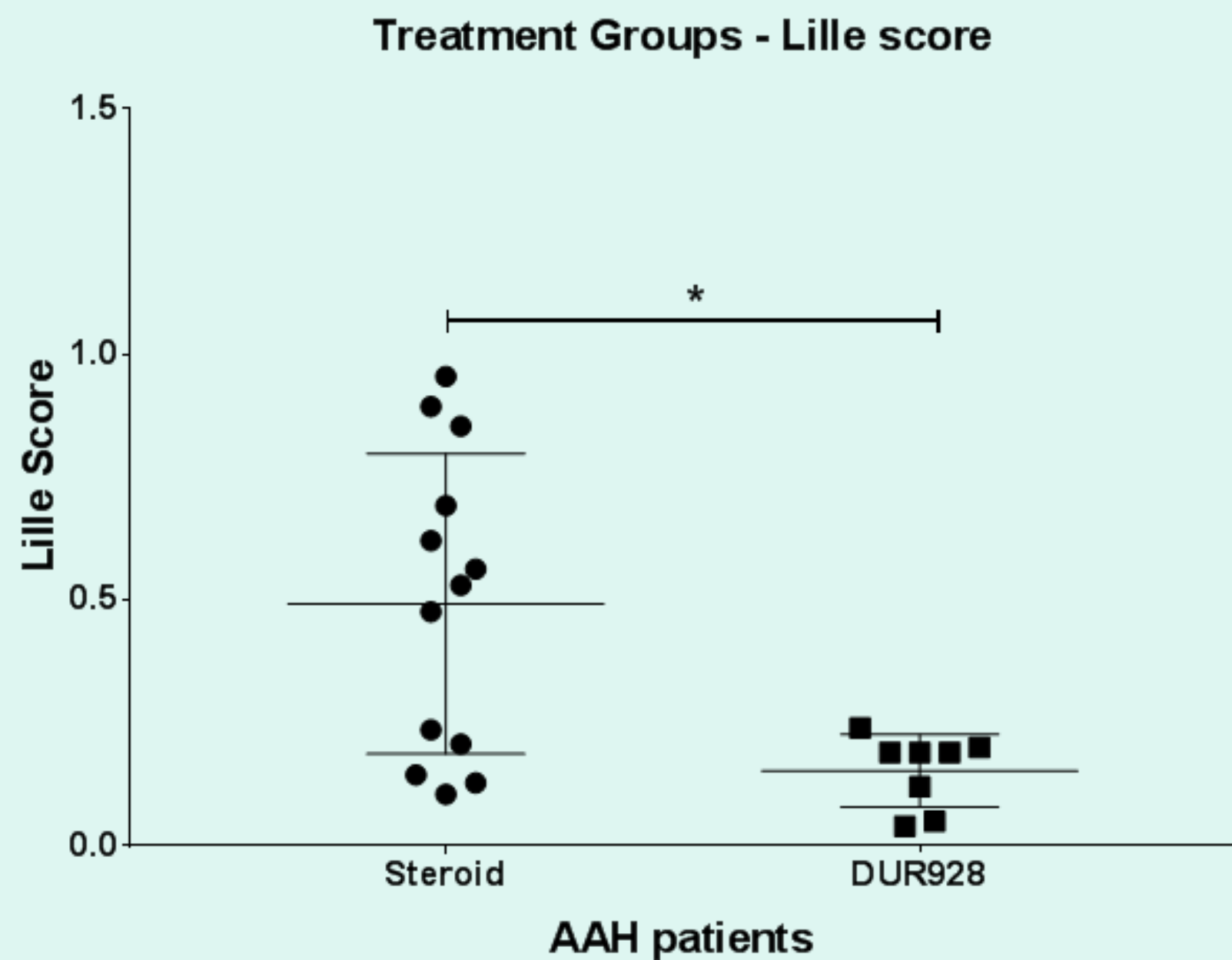


Figure 2: Significant difference in Lille score between corticosteroid and DUR-928 treated severe AAH patients.

### Assessment of Clinical Markers of AAH patients in the Corticosteroid and DUR-928 treated groups over 28-day period

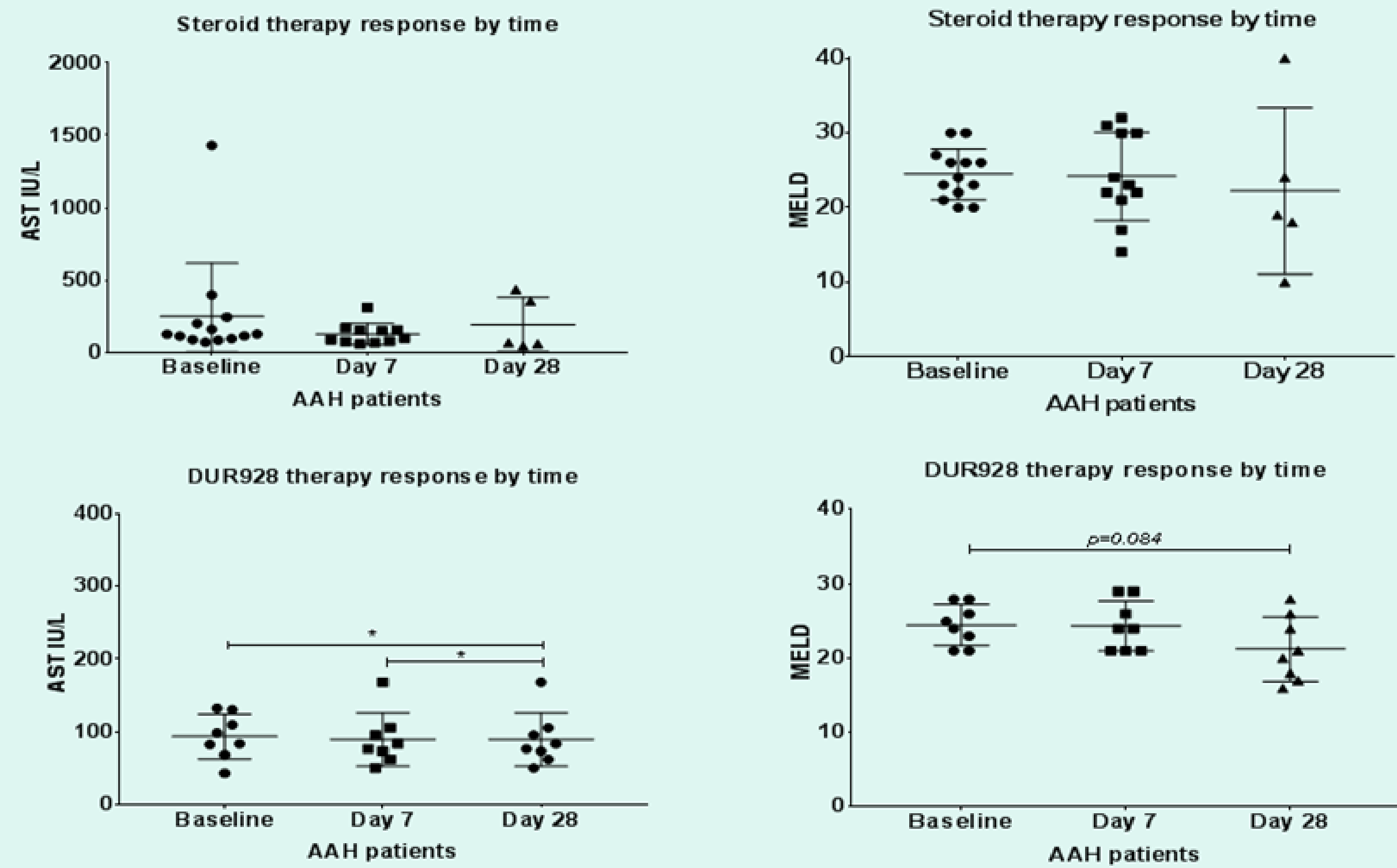


Figure 3: 28-day longitudinal response change in the liver injury and severity markers in AAH patients treated with corticosteroid ~ and DUR-928.

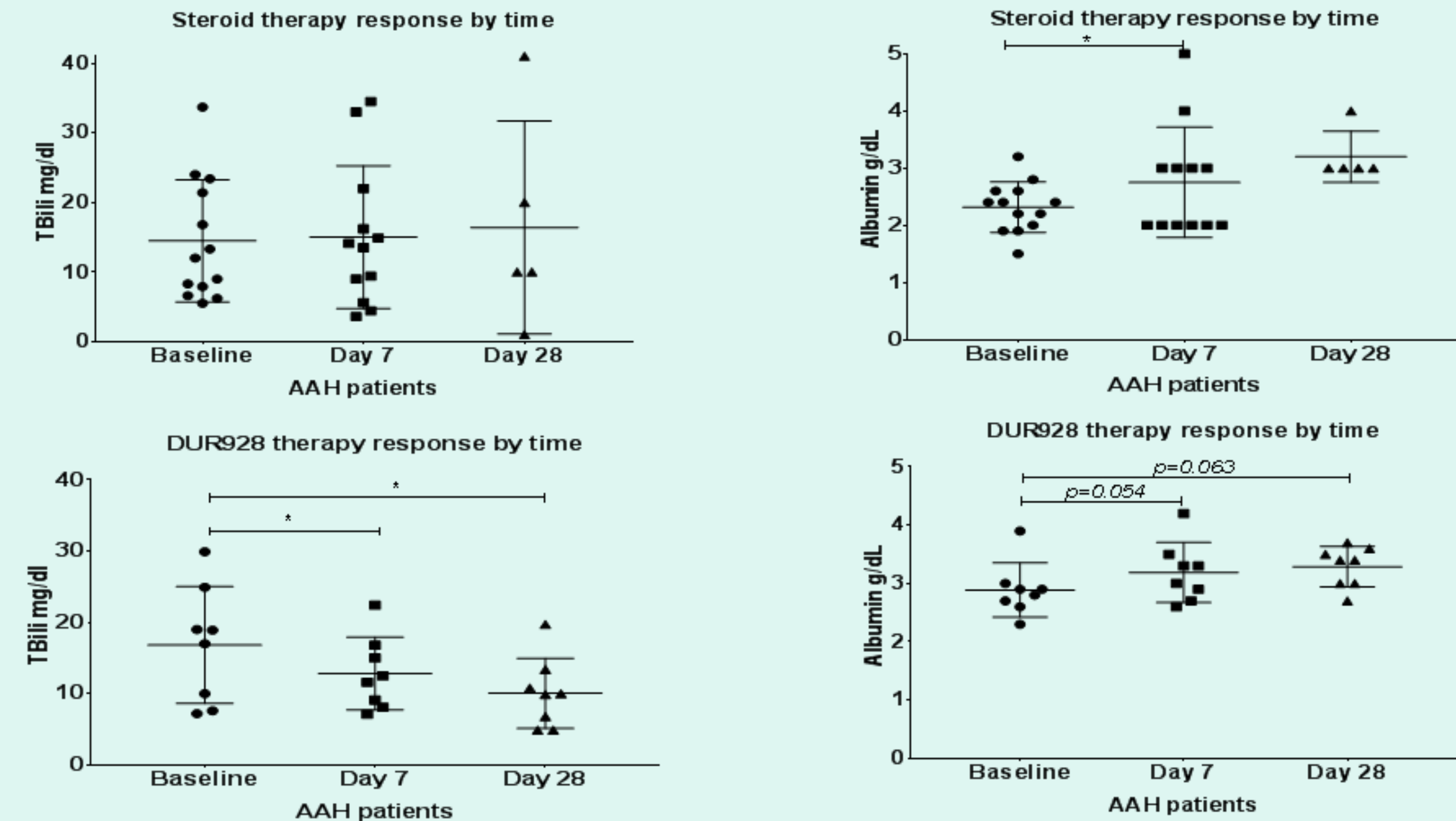


Figure 4: 28-day longitudinal response change in the liver function markers in AAH patients treated with corticosteroid ~ and DUR-928.

## Conclusions

- DUR-928 was well-tolerated in severe AAH patients.
- Prominent drop in Lille Score in DUR-928 treated cohort, in comparison to the corticosteroid treated group.
- Longer duration of DUR-928 therapy (outpatient) in Severe AAH might increase the efficacy of treatment in terms of survival and recovery.