Lesions Atypical for NASH/NASH Resolution in EOT Biopsies noted by EMB/CG

Liver Forum Histology Webinar Series #3:
The Role of Liver Biopsy as part of Causality Assessment for Suspected DILI in NASH Clinical Trials

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EOT Slide Review

- Two liver pathologists; **blinded** review of EOT biopsies
  - No knowledge of clinical history, BL biopsy findings, drug dose
  - Grade for NAS (steatosis, lob infl, ballooning), portal infl (HE)
  - Stage fibrosis (trichrome)
  - Assign diagnostic category: NASH/Not NASH
  - Evidence of other signif liver disease: Y/N; if Y, describe:
• Portal inflammation with plasma cells +/- eos and interface hepatitis
  • Some with bile duct injury
  • Rarely with zone 3 drop-out/fibrosis

• Bile duct injury/infiltration

• Granulomatous cholangitis

• Vascular lesions suggestive of porto-sinusoidal vascular disease
• Portal inflammation with plasma cells +/- eos and interface hepatitis
  • Some with bile duct injury
  • Rarely with zone 3 drop-out/fibrosis

• Bile duct injury/infiltration

• Granulomatous cholangitis

• Vascular lesions suggestive of porto-sinusoidal vascular disease

• 42/152 (27.6%)

<table>
<thead>
<tr>
<th>PLACEBO (N=25)</th>
<th>SELADELPAR 10 mg (N=39)</th>
<th>SELADELPAR 20 mg (N=42)</th>
<th>SELADELPAR 50 mg (N=46)</th>
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<tbody>
<tr>
<td>6/25 (24%)</td>
<td>8/39 (20.5%)</td>
<td>10/42 (23.8%)</td>
<td>18/46 (39.1%)</td>
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Marked portal CI with plasma cells, and eos
Endophlebitis
Interface hepatitis
Bile duct infiltration
Marked portal CI with plasma cells; endophlebitis; interface hepatitis; bile duct infiltration

Seladelpar 10mg
Perivenular necrosis and dropout and fibrosis

Seladelpar 20mg
Granulomatous Cholangitis

Seladelpar 10mg
Bile duct injury: 2 different cases

Seladelpar 20mg

Seladelpar placebo
Cholestatic Rosettes

Bile duct injury present, not shown in photo
PSVD-like portal vein alterations
Cholate-stasis noted in photo on right

Seladelpar 50mg
Porto-sinusoidal vascular disease-like alterations of portal veins; Interface hepatitis

Seladelpar 20mg
- Portal vein endothelia touching hepatocytes
- Right-angle entry of venule