

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:

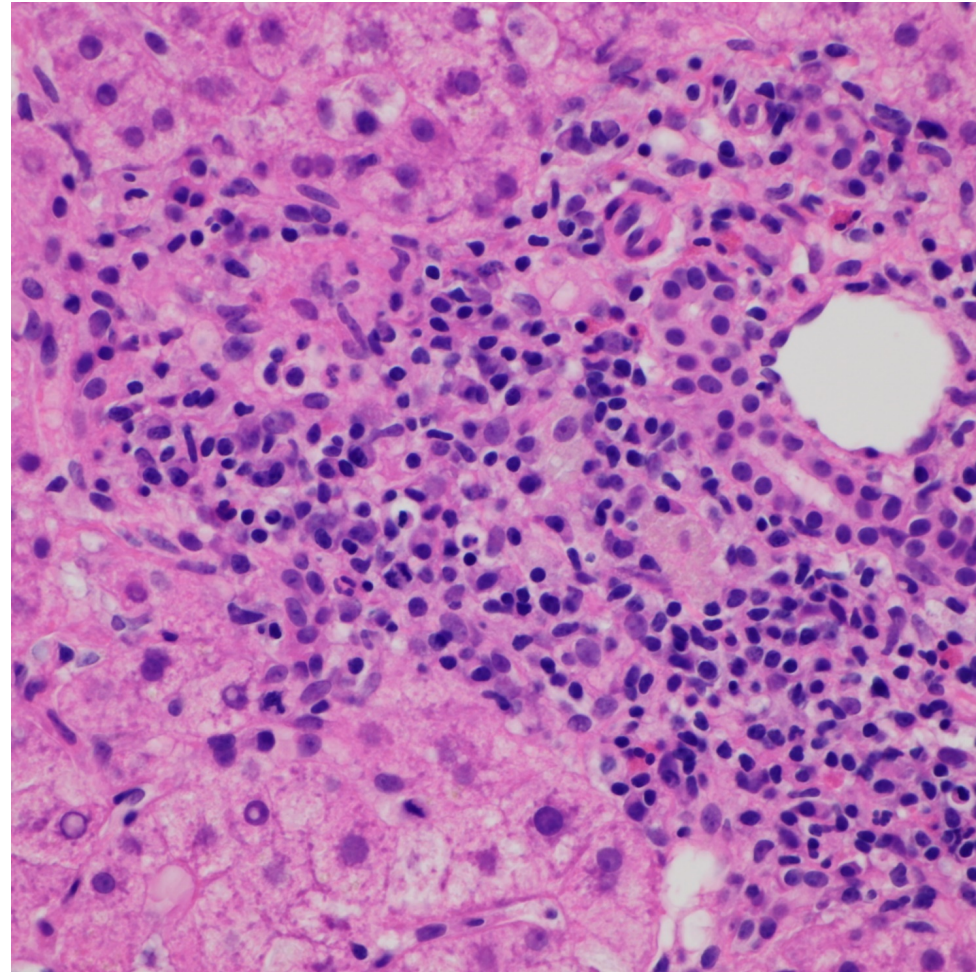
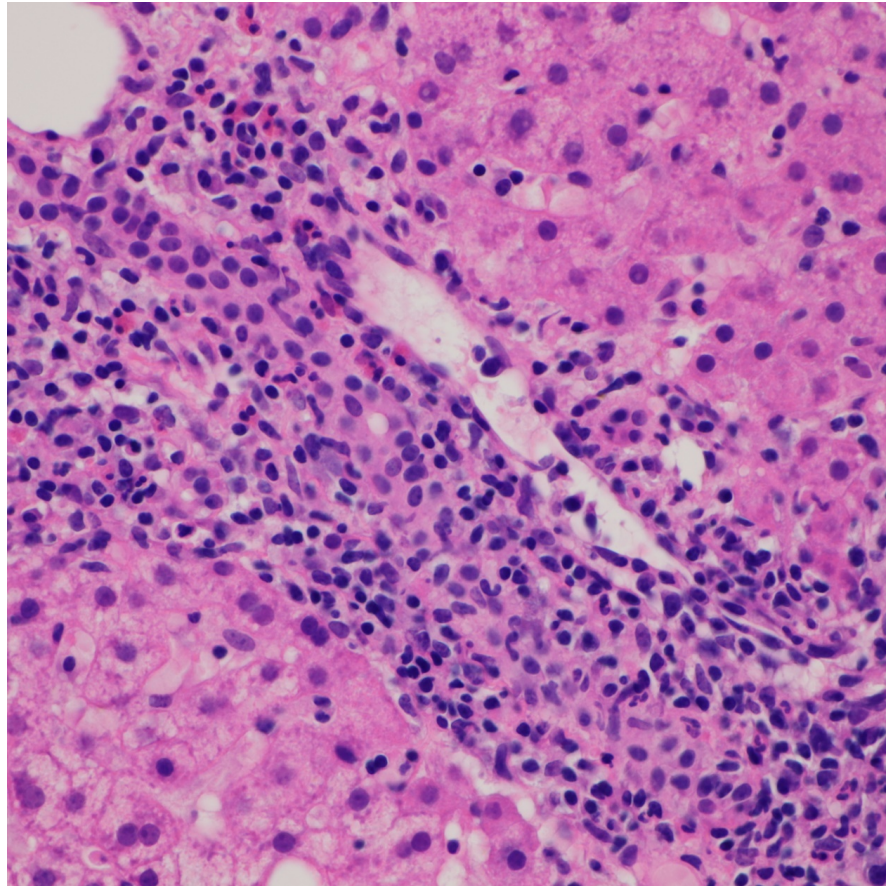
- Portal inflammation with plasma cells +/- eos and interface hepatitis
 - Some with bile duct injury
 - Rarely with zone 3 drop-out/fibrosis
- Bile duct injury/infiltration
- Granulomatous cholangitis
- Vascular lesions suggestive of porto-sinusoidal vascular disease

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- 42/152 (27.6%)

PLACEBO (N=25)	SELADELPAR 10 mg (N=39)	SELADELPAR 20 mg (N=42)	SELADELPAR 50 mg (N=46)
6/25 (24%)	8/39 (20.5%)	10/42 (23.8%)	18/46 (39.1%)

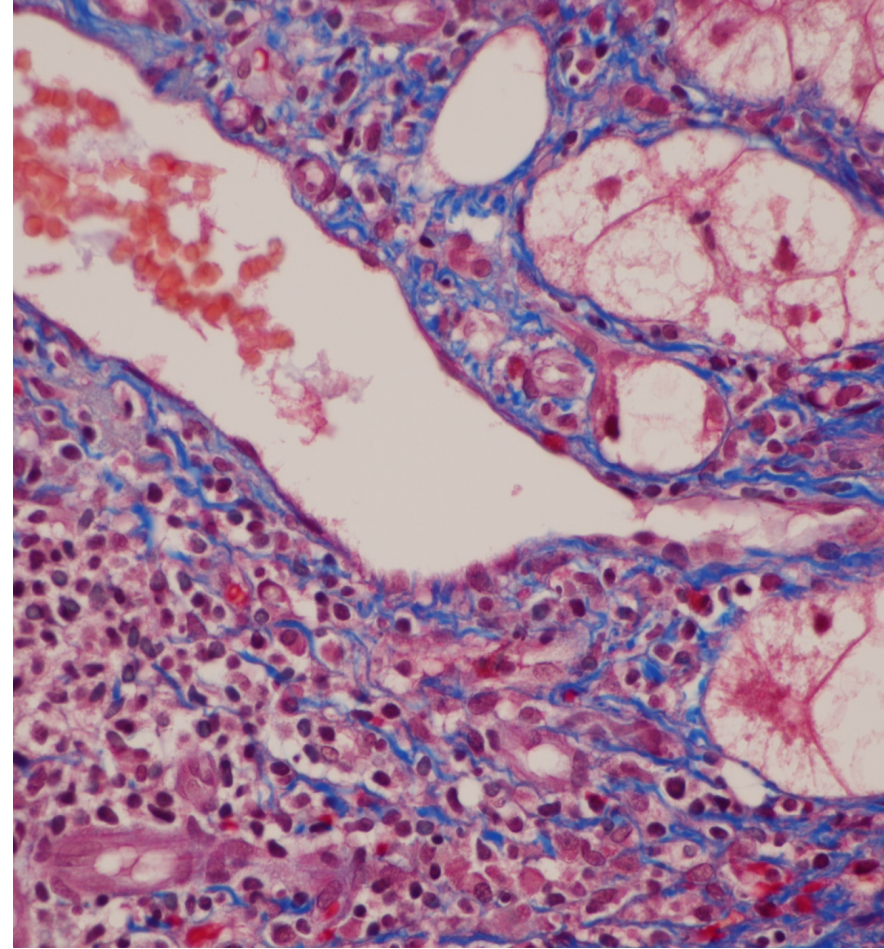
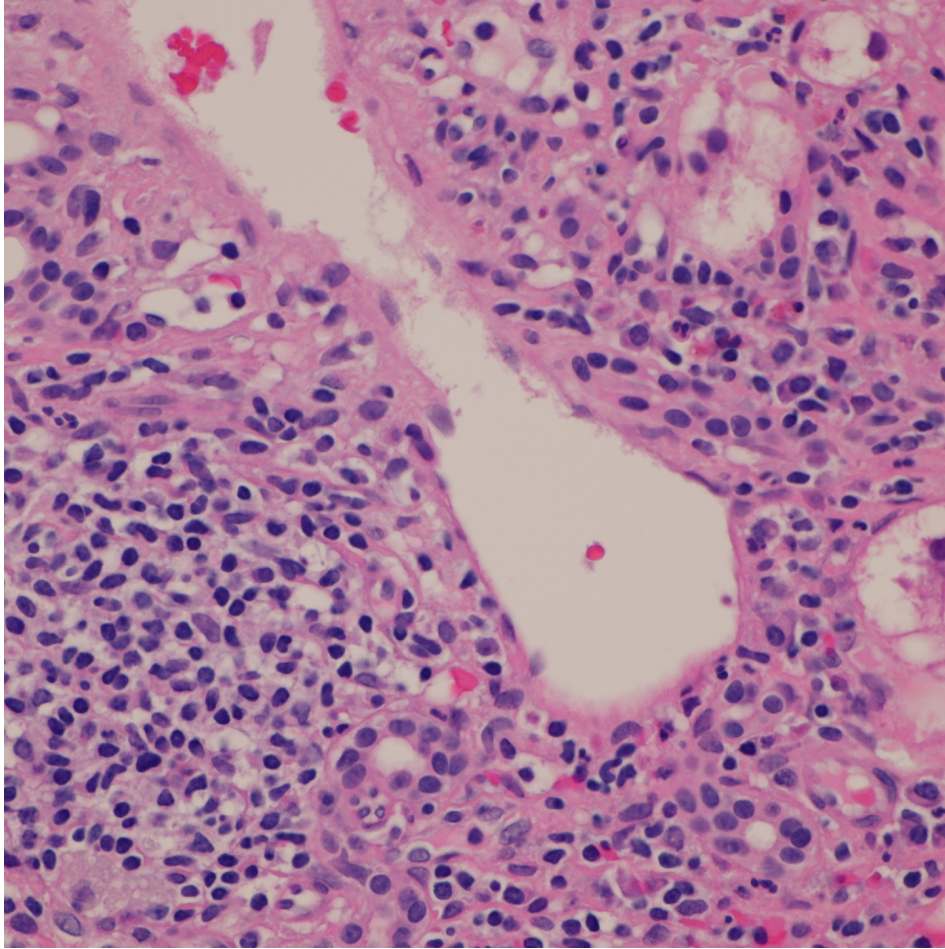
Marked portal CI with plasma cells, and eos
Endophlebitis
Interface hepatitis
Bile duct infiltration

Seladelpar 50mg



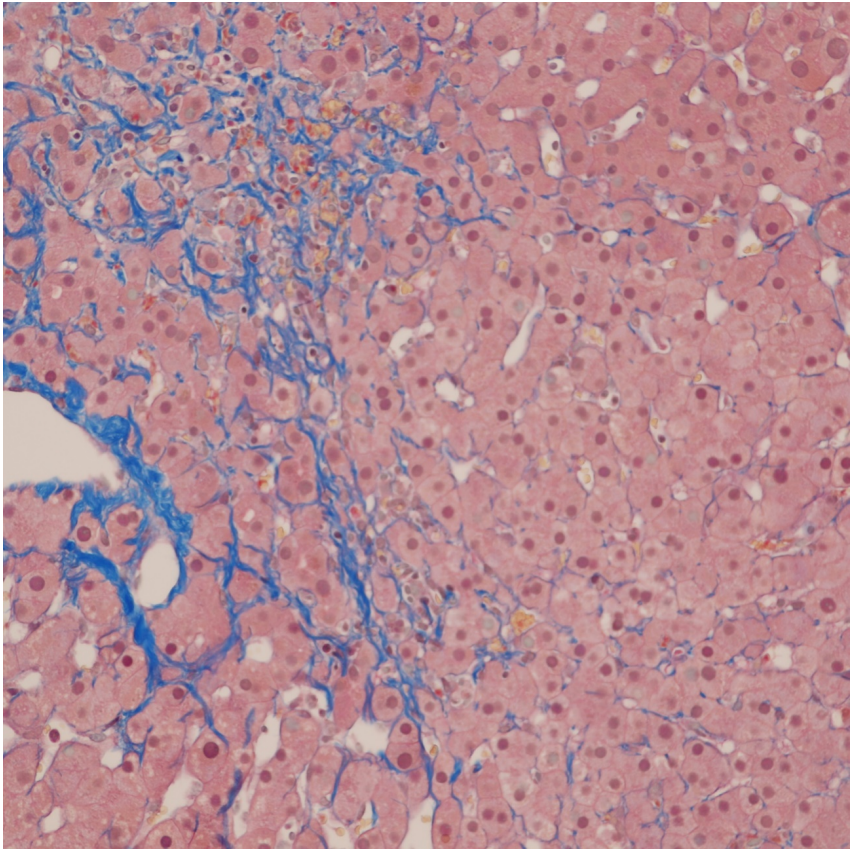
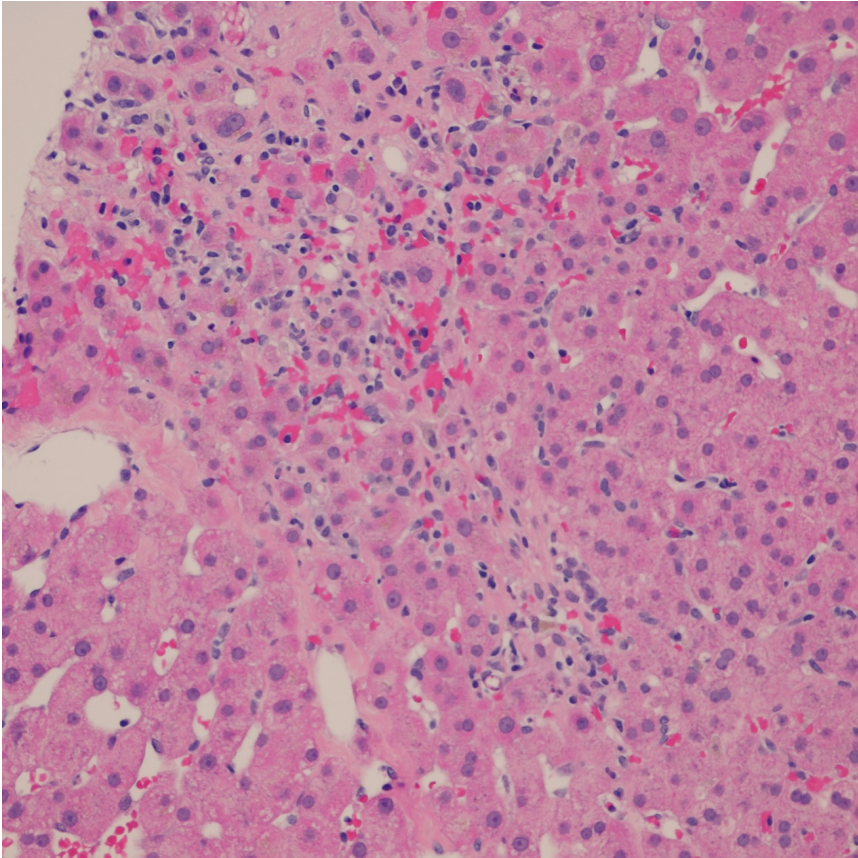
Marked portal CI with plasma cells;
endophlebitis; interface hepatitis;
bile duct infiltration

Seladelpar 10mg

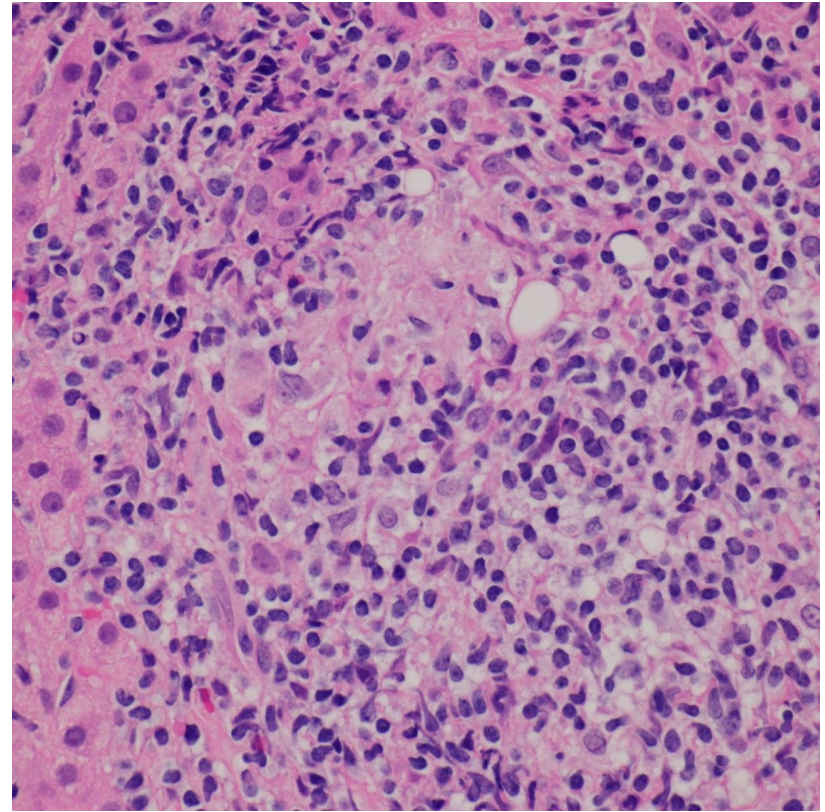
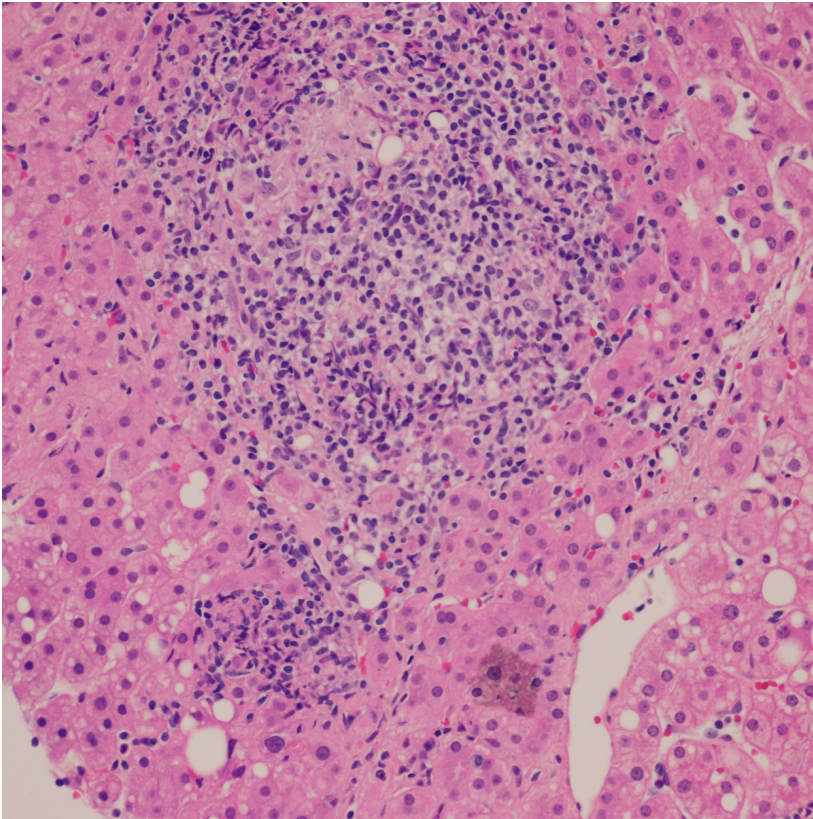


Perivenular necrosis and dropout and fibrosis

Seladelpar 20mg



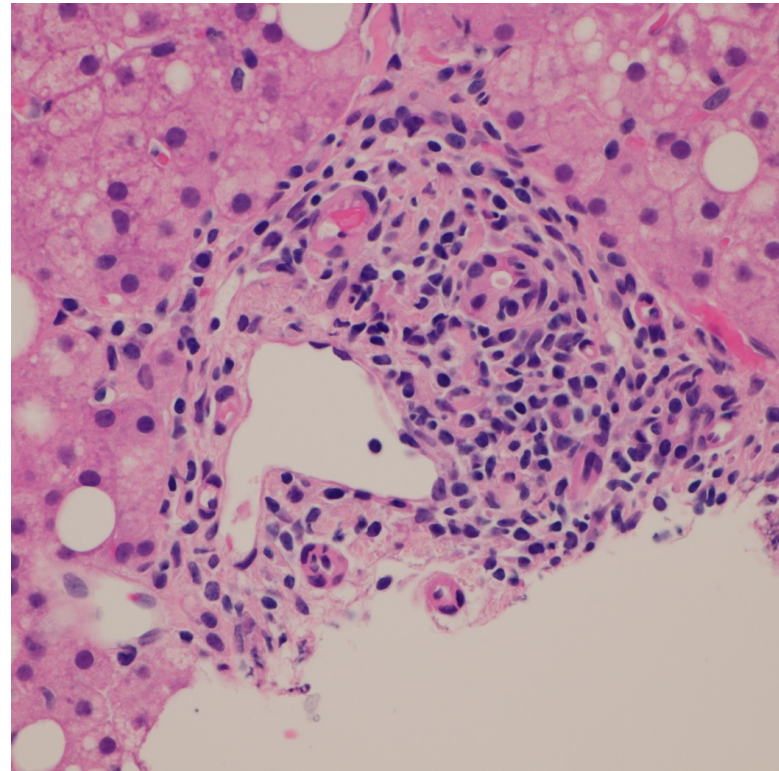
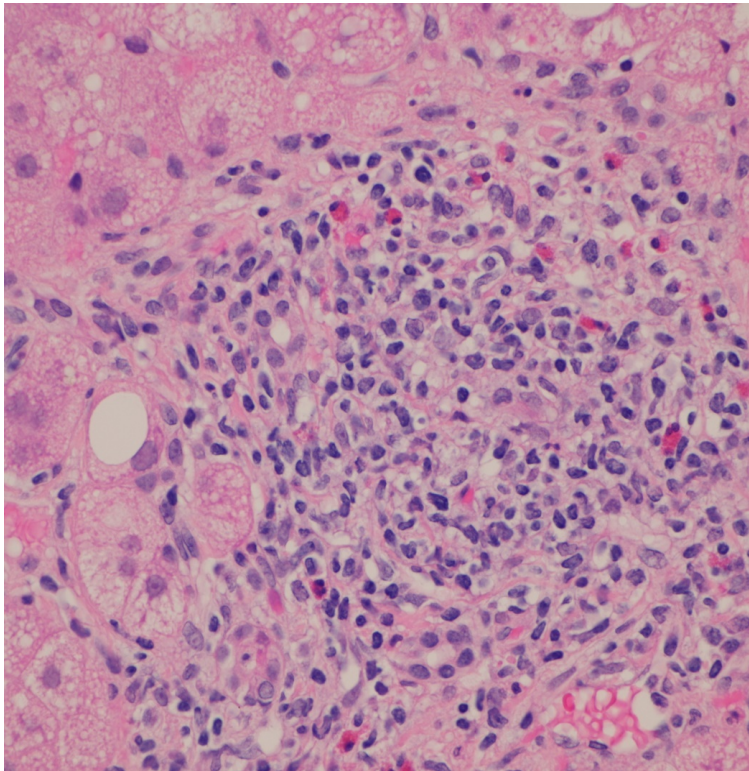
Granulomatous Cholangitis



Bile duct injury: 2 different cases

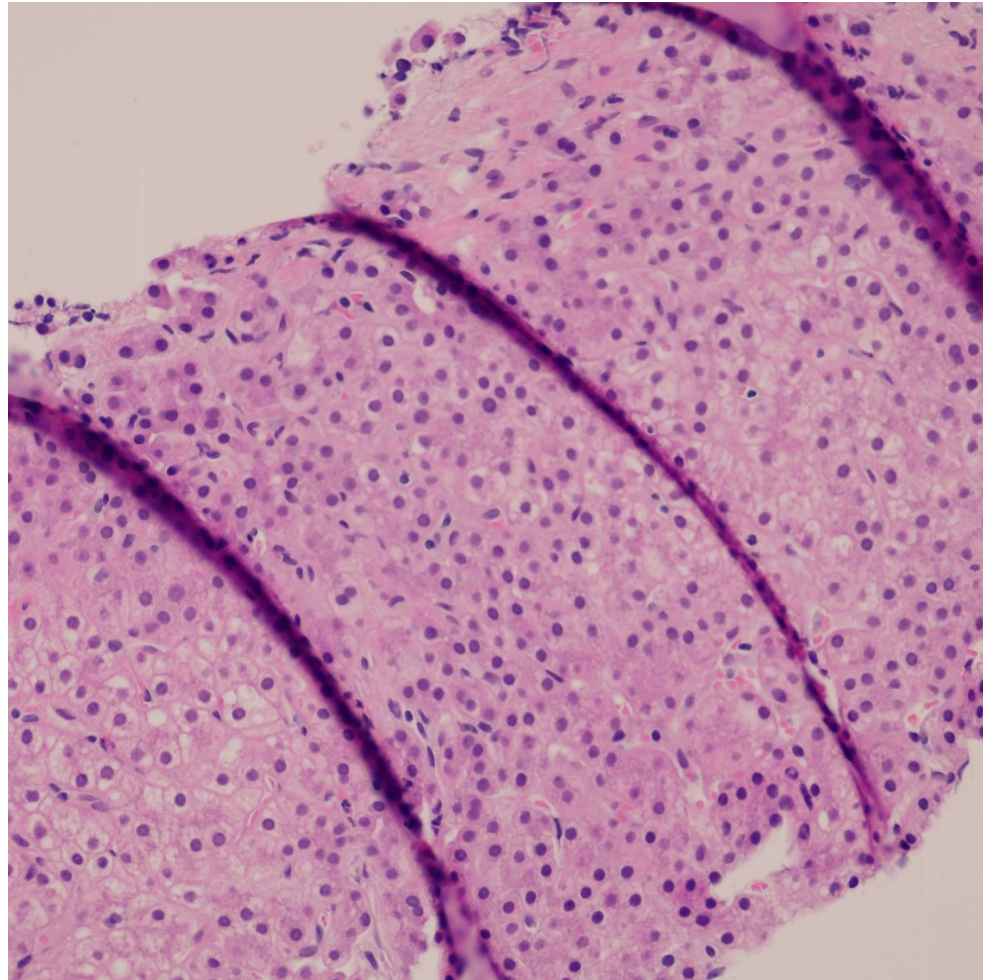
Seladelpar 20mg

Seladelpar placebo

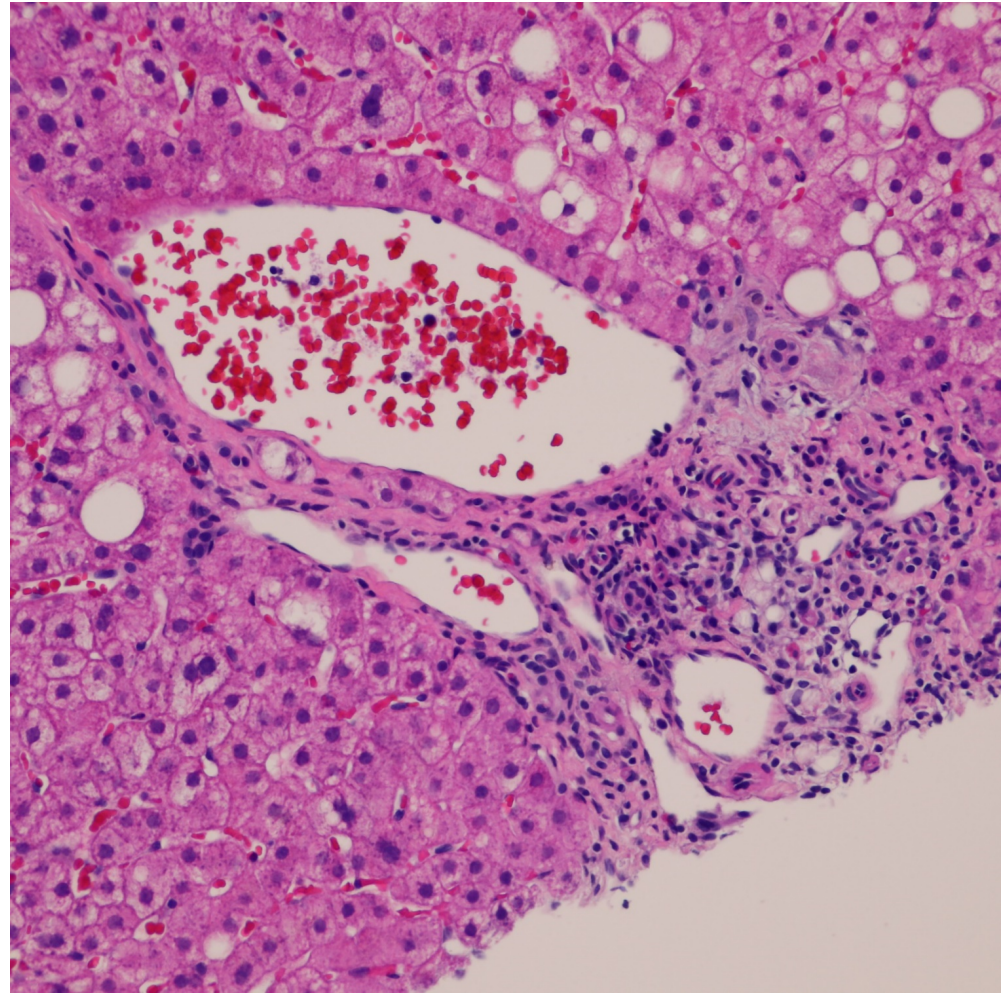
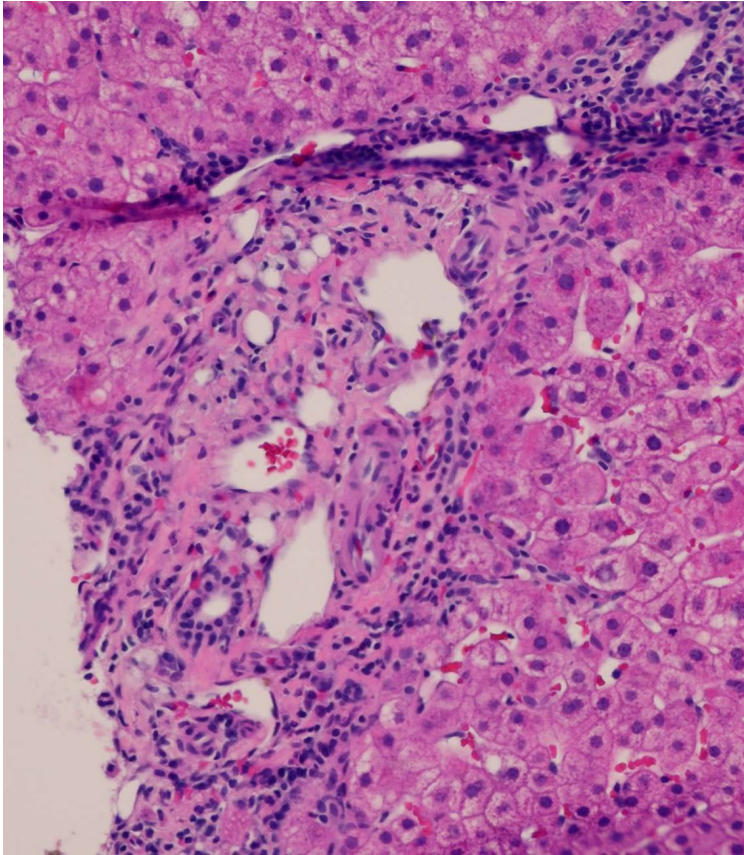


Cholestatic
Rosettes

Bile duct injury
present, not
shown in photo

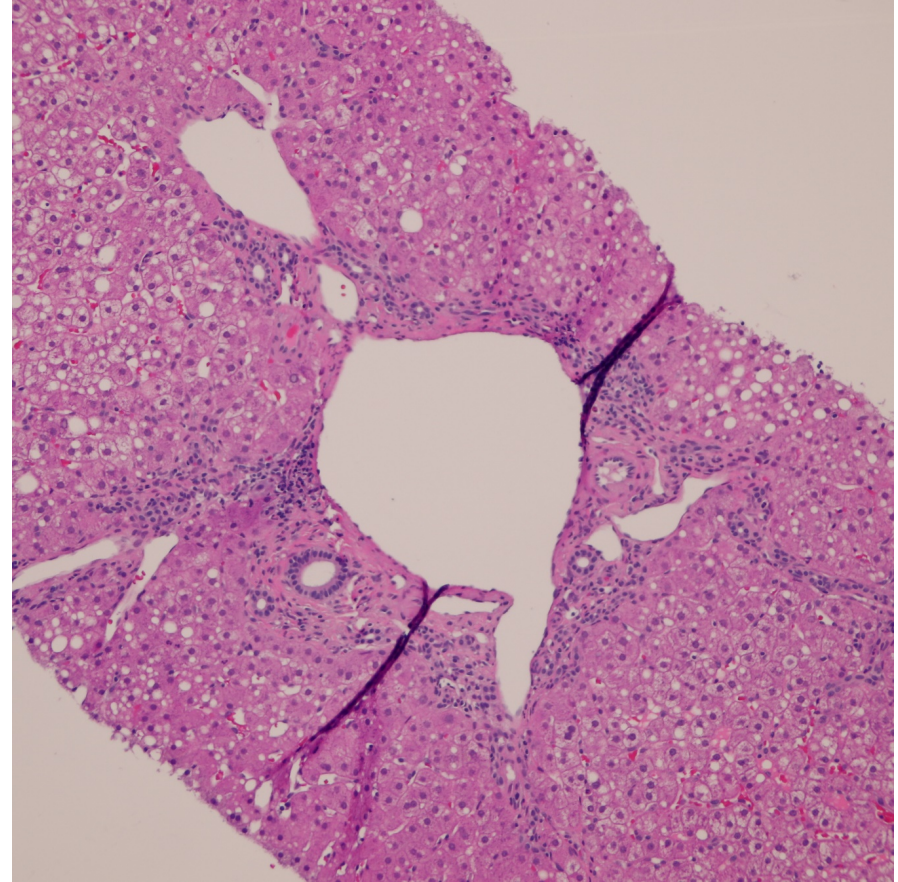
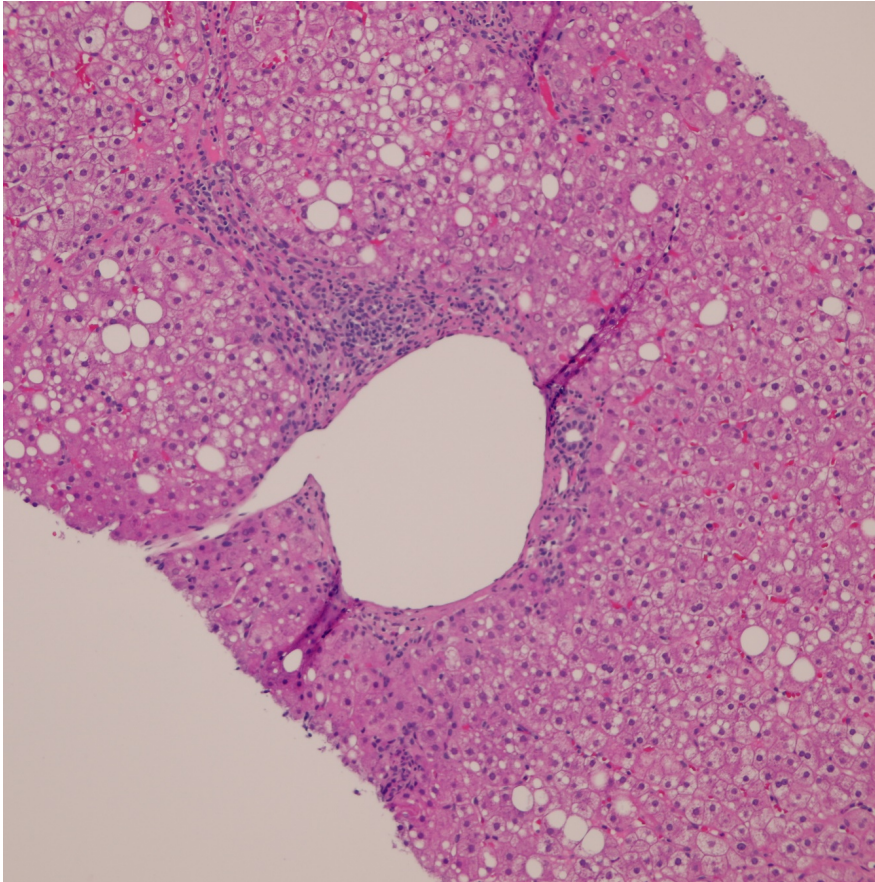


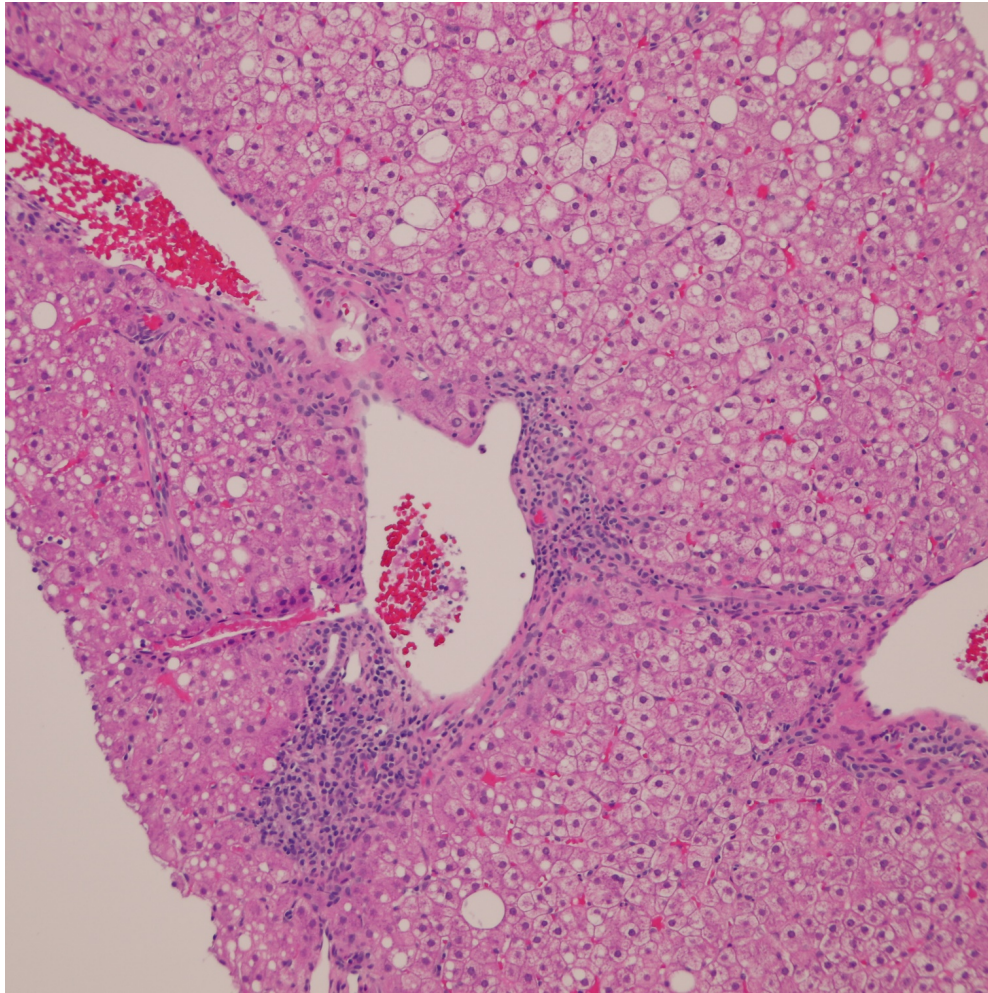
PSVD-like portal vein alterations
Cholate-stasis noted in photo on right



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

Seladelpar 20mg





- Portal vein endothelia touching hepatocytes
- Right-angle entry of venule