

Case Examples of DILI Superimposed on NASH

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Liver Forum Histology Series Session 5

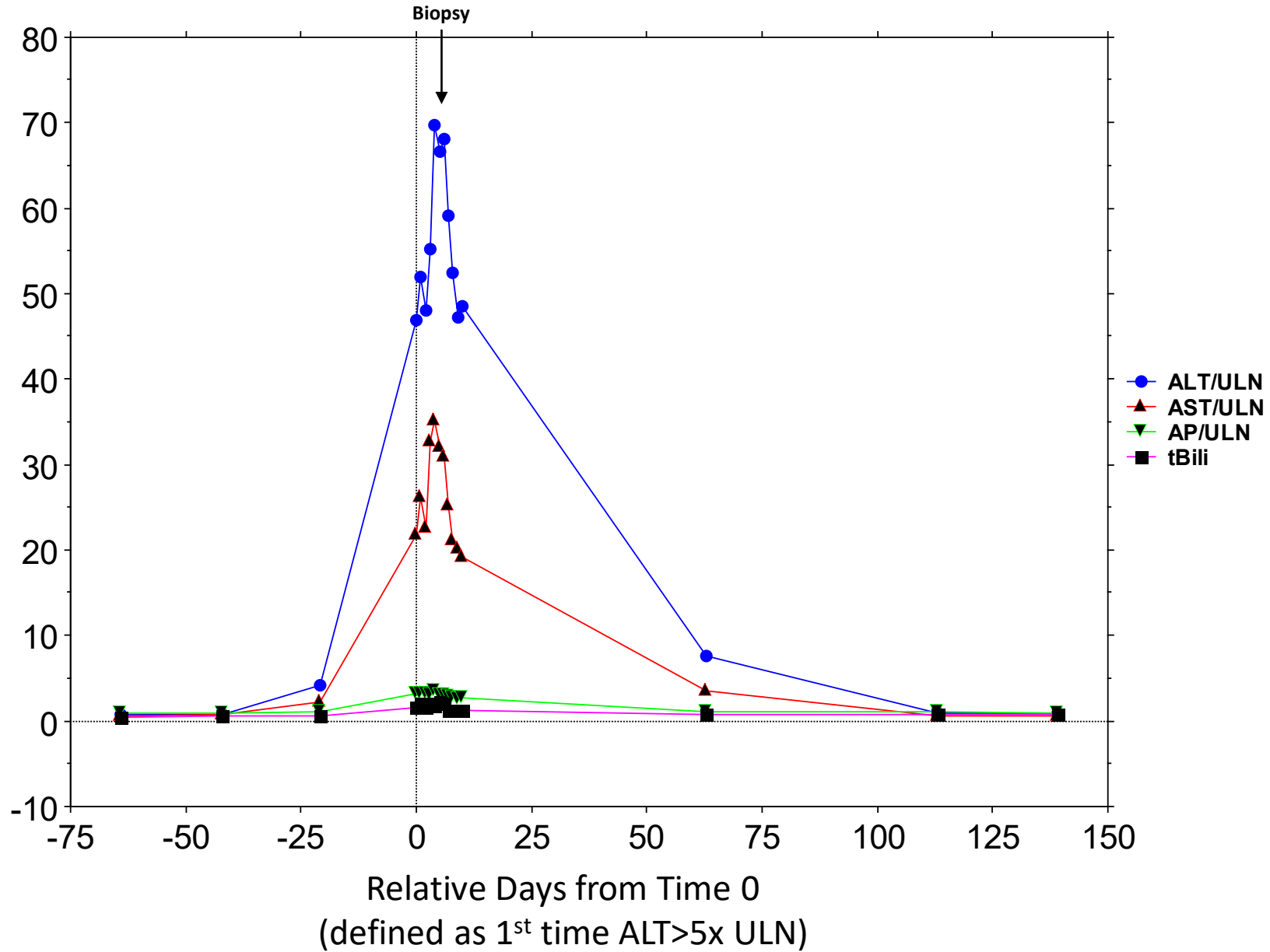
Causality Assessment and the Role of Liver Biopsy as Part of the
Evaluation of Suspected DILI in NASH Clinical Trials

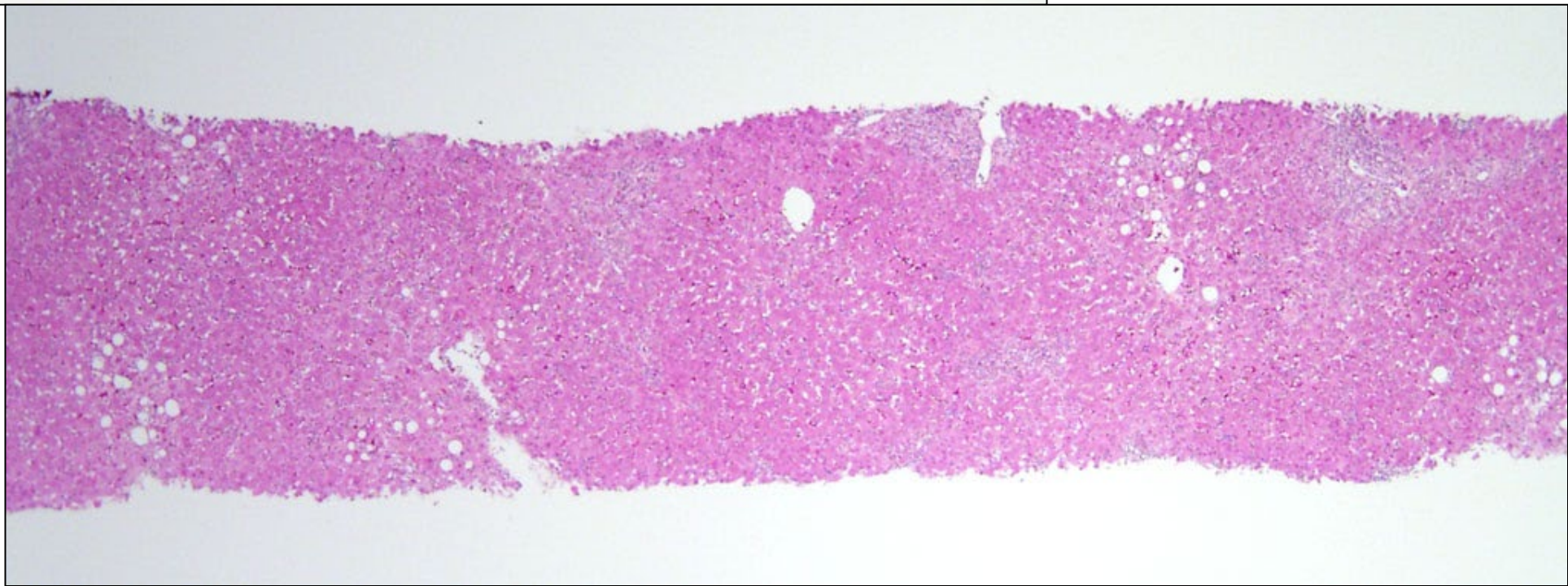
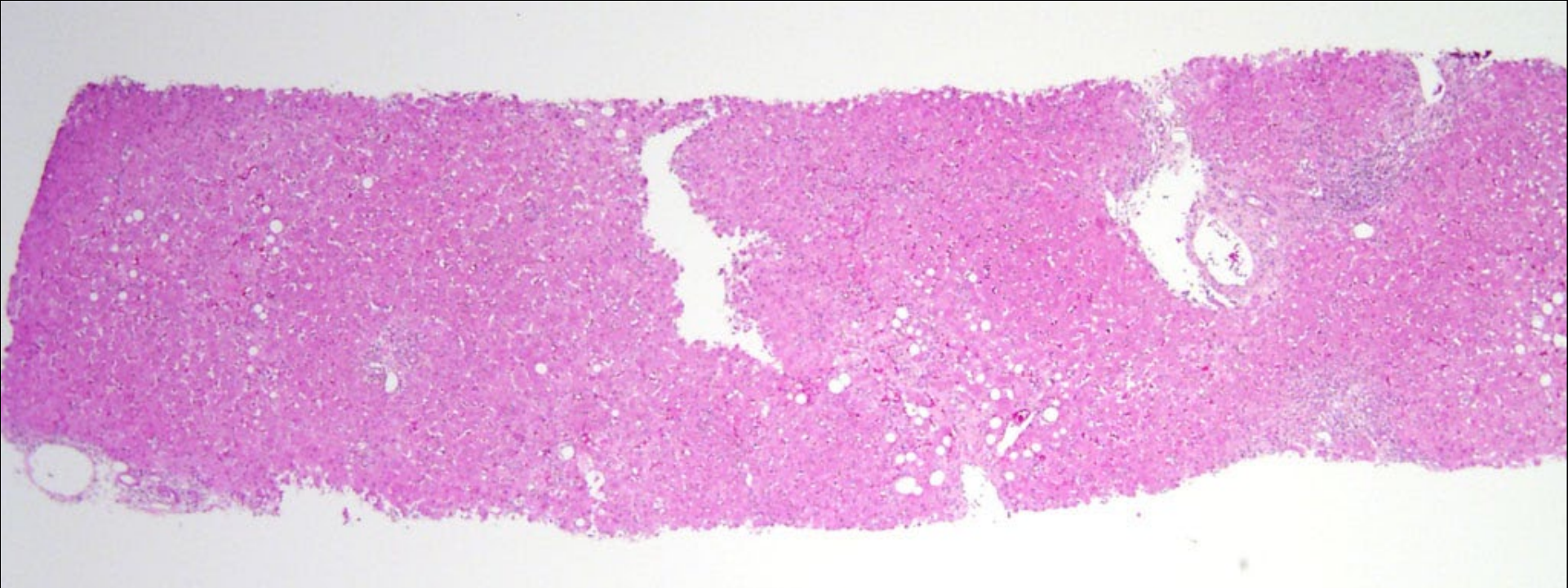
Friday, January 28, 2022

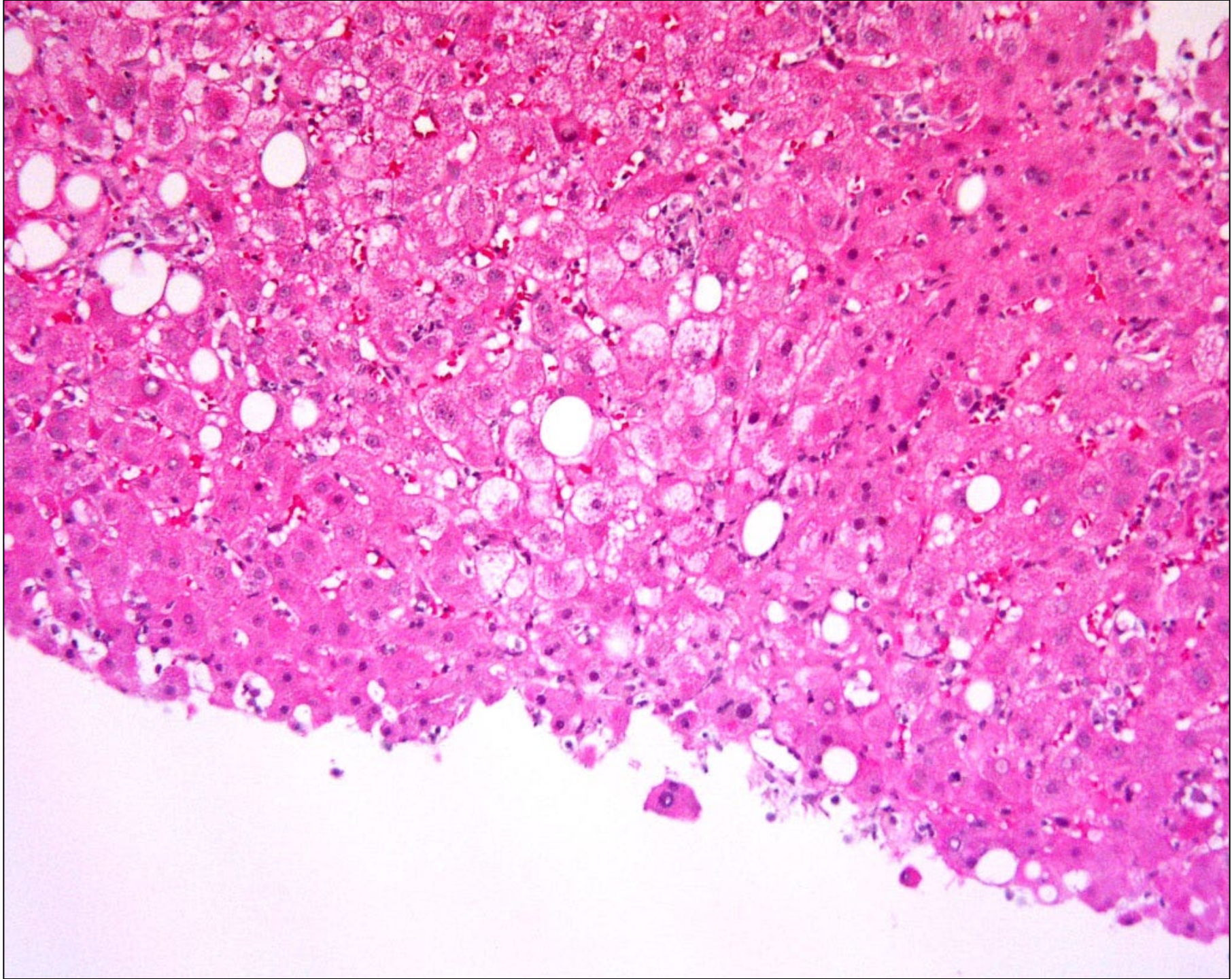
Case 1

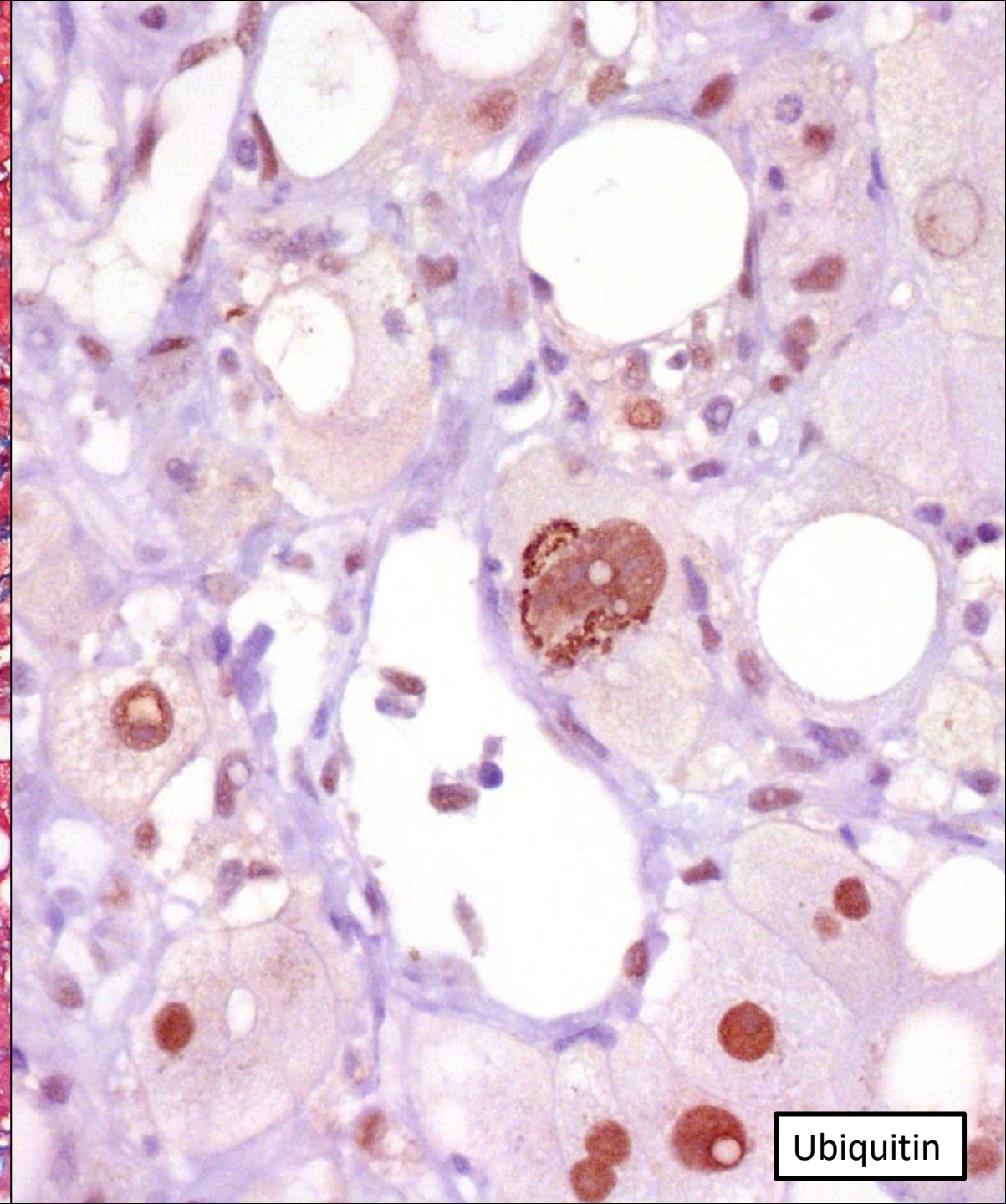
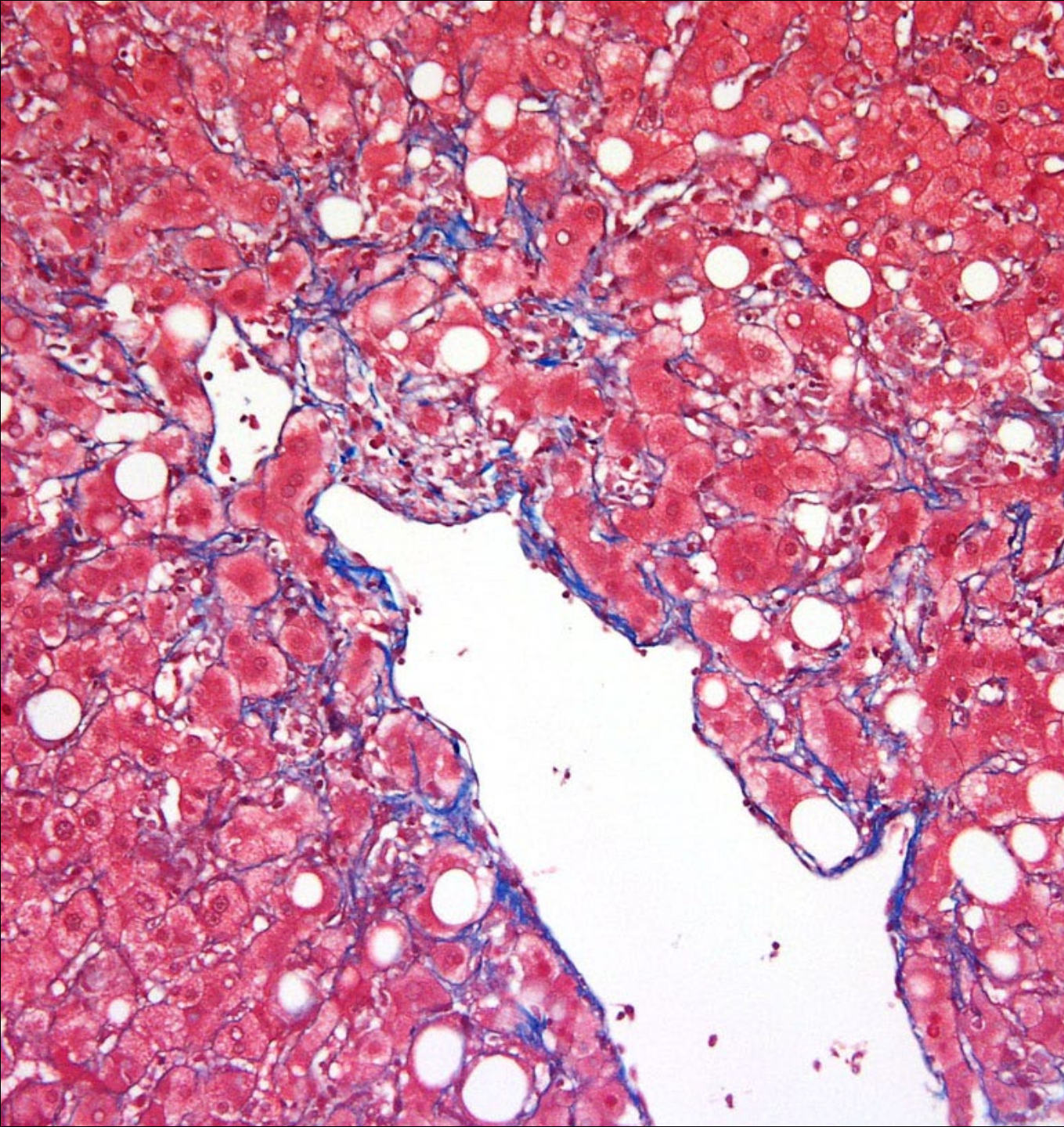
- 43 Male with melanoma, previously treated with IFN alpha and surgery
- Received 3 cycles of a novel, first-in-human, monoclonal anti-CTLA4 (yet to be named ipilimumab)
- Virology and serology at event:
 - Anti HAV-IgM (-), anti-HCV (-), anti-HBsAg (-)
 - ANA 2.4EU (+), ASMA, AMA and anti-LKM (-)
- Obesity, diabetes

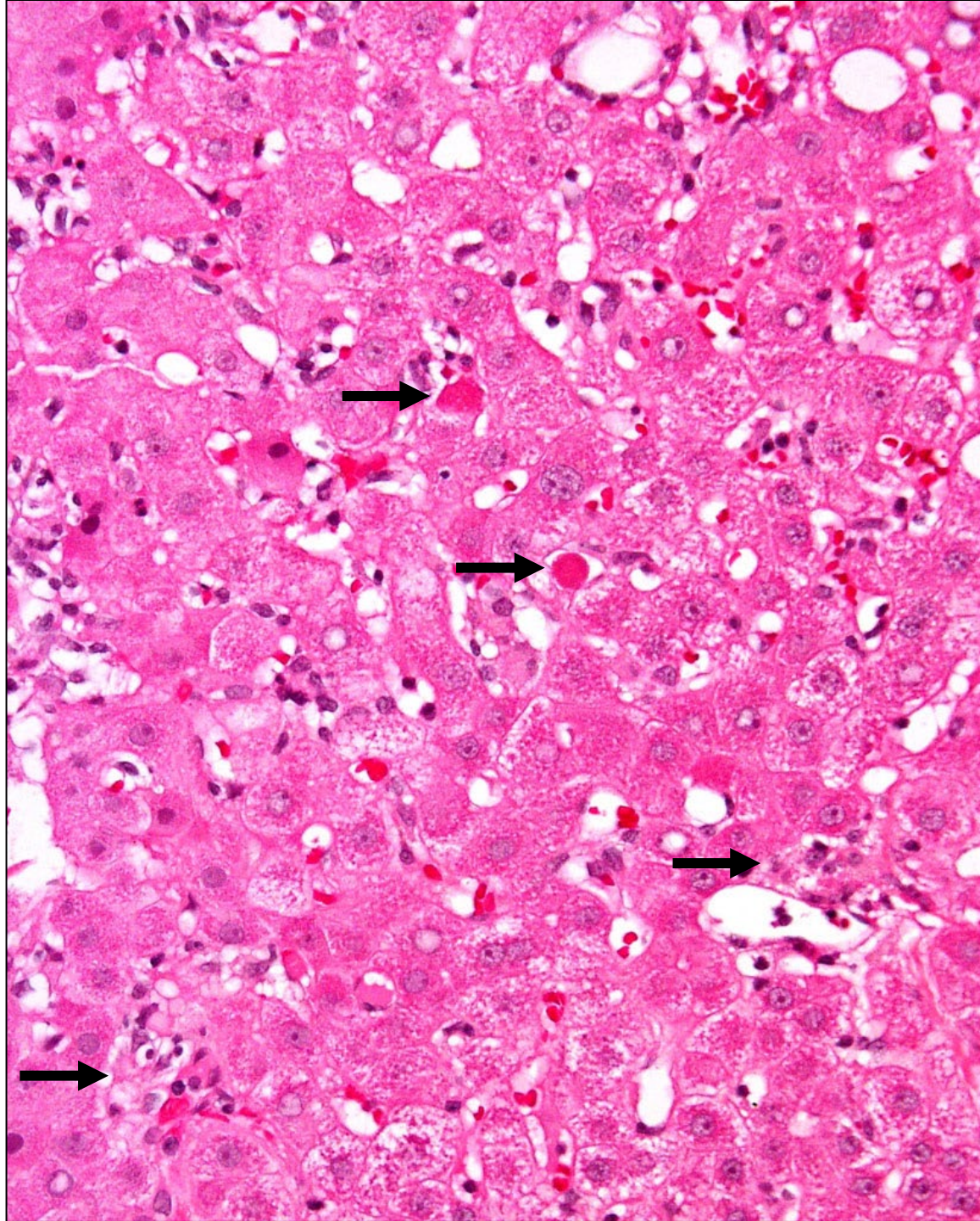
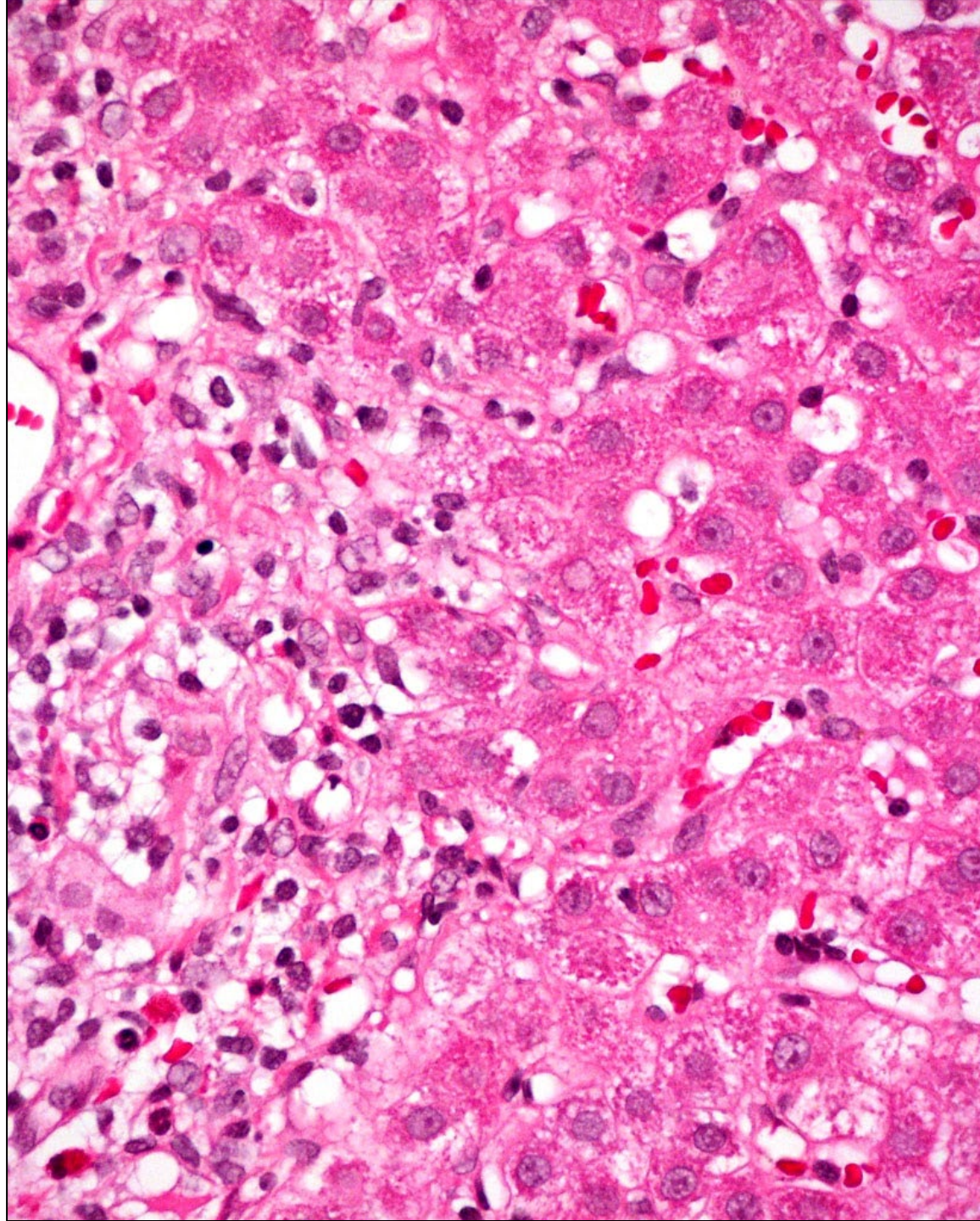
Biochemical Data at Time of Event







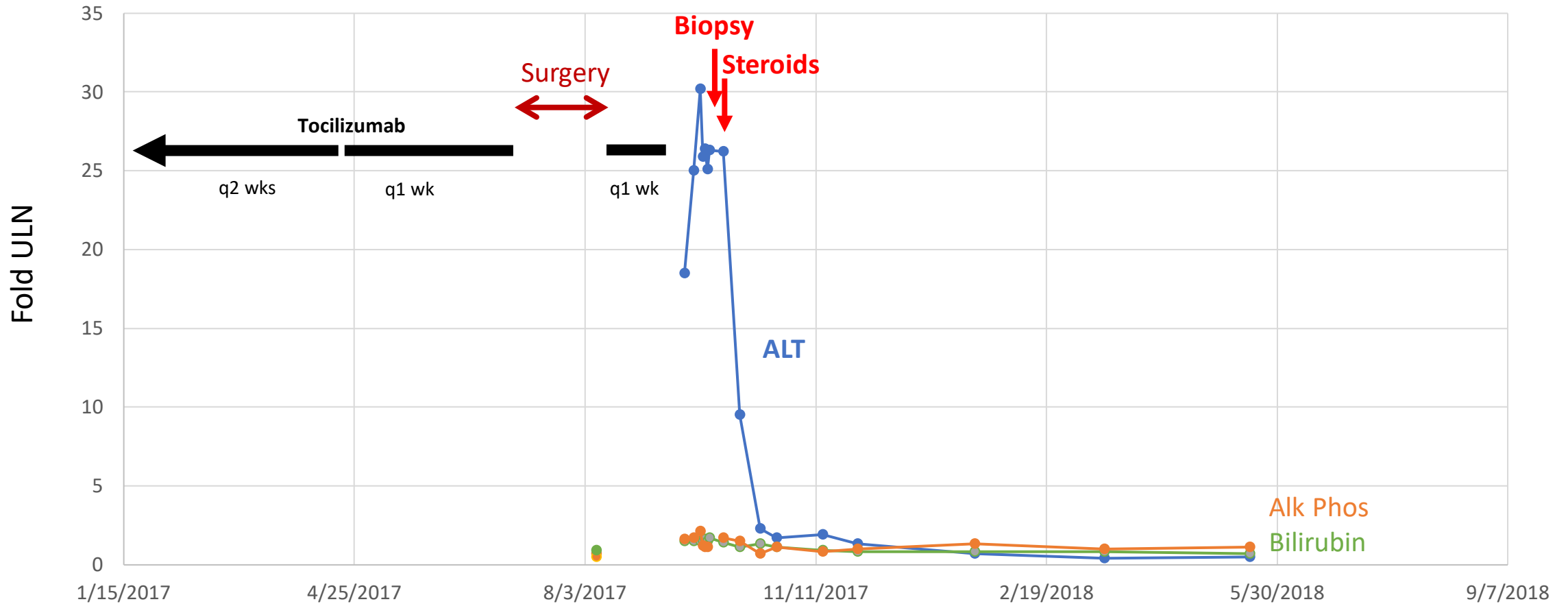


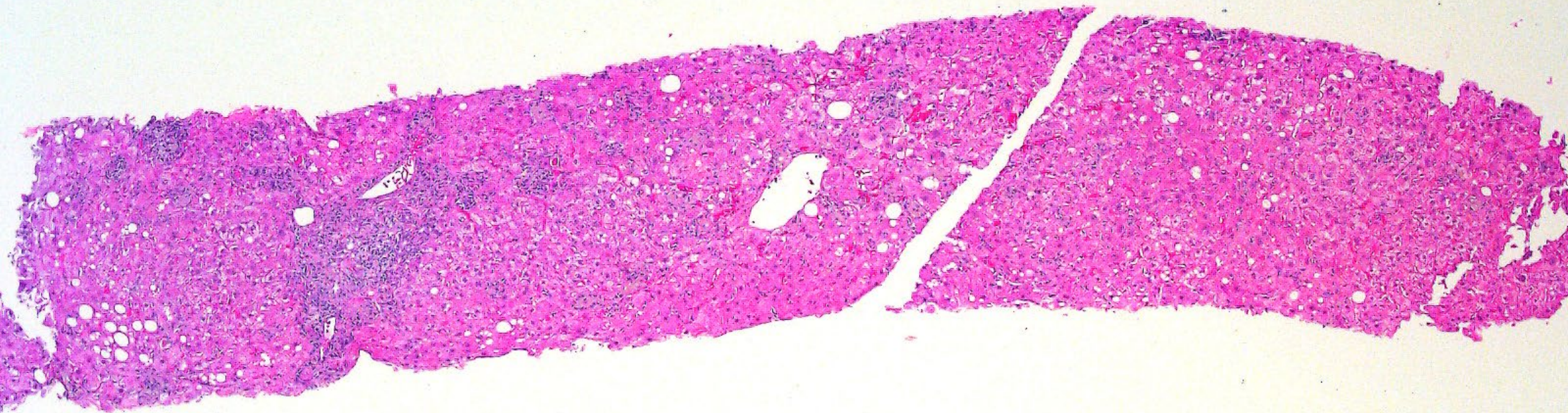
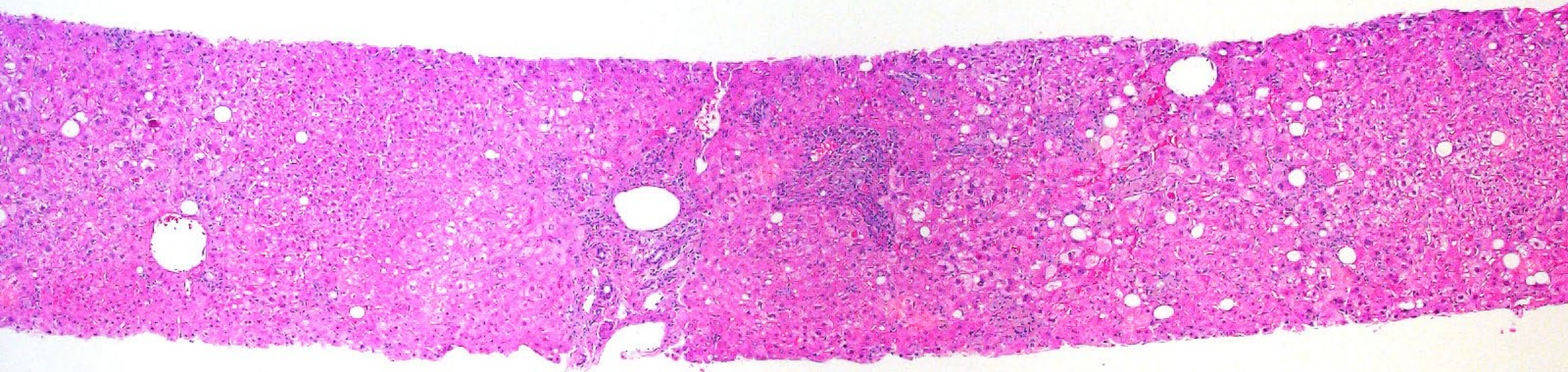


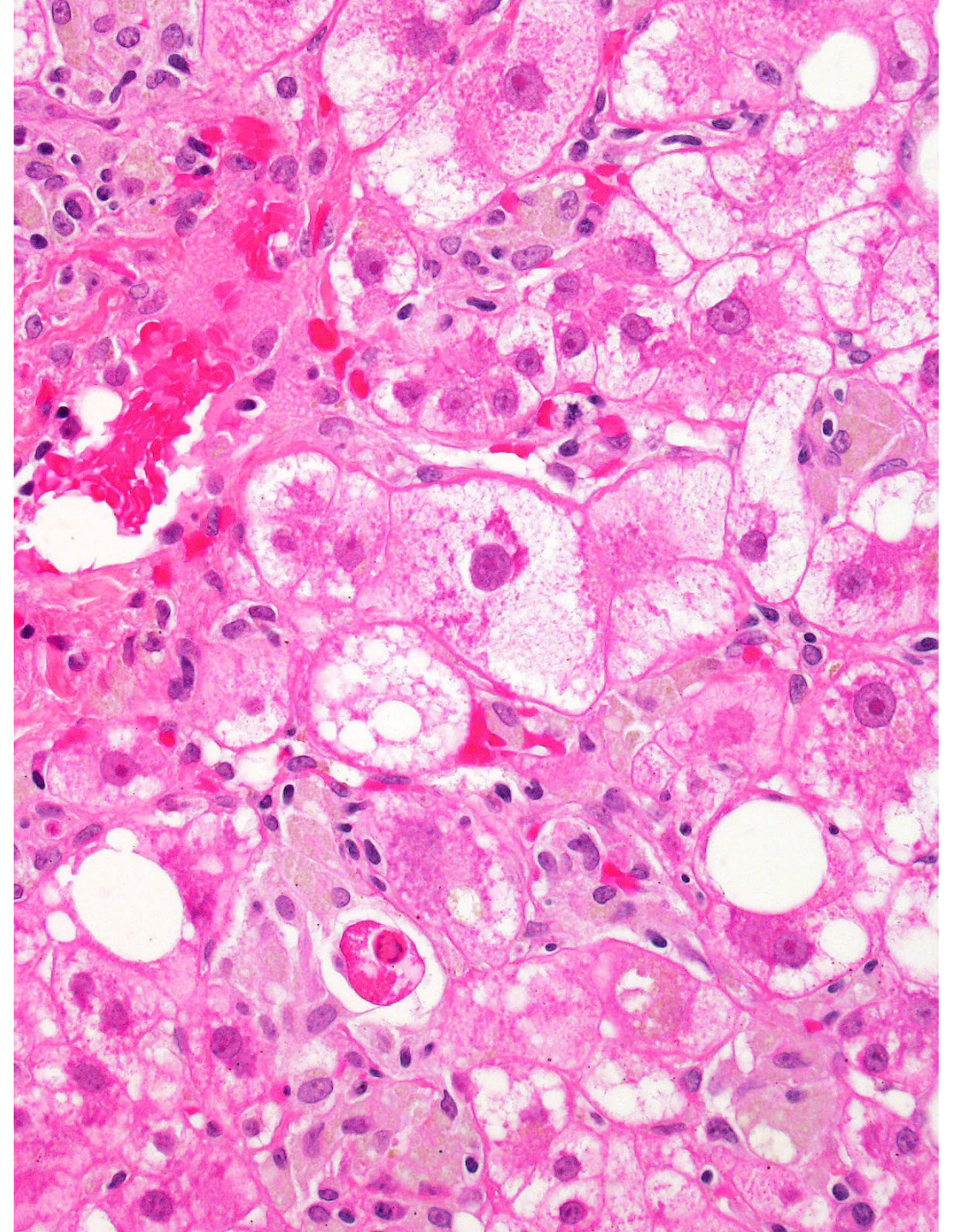
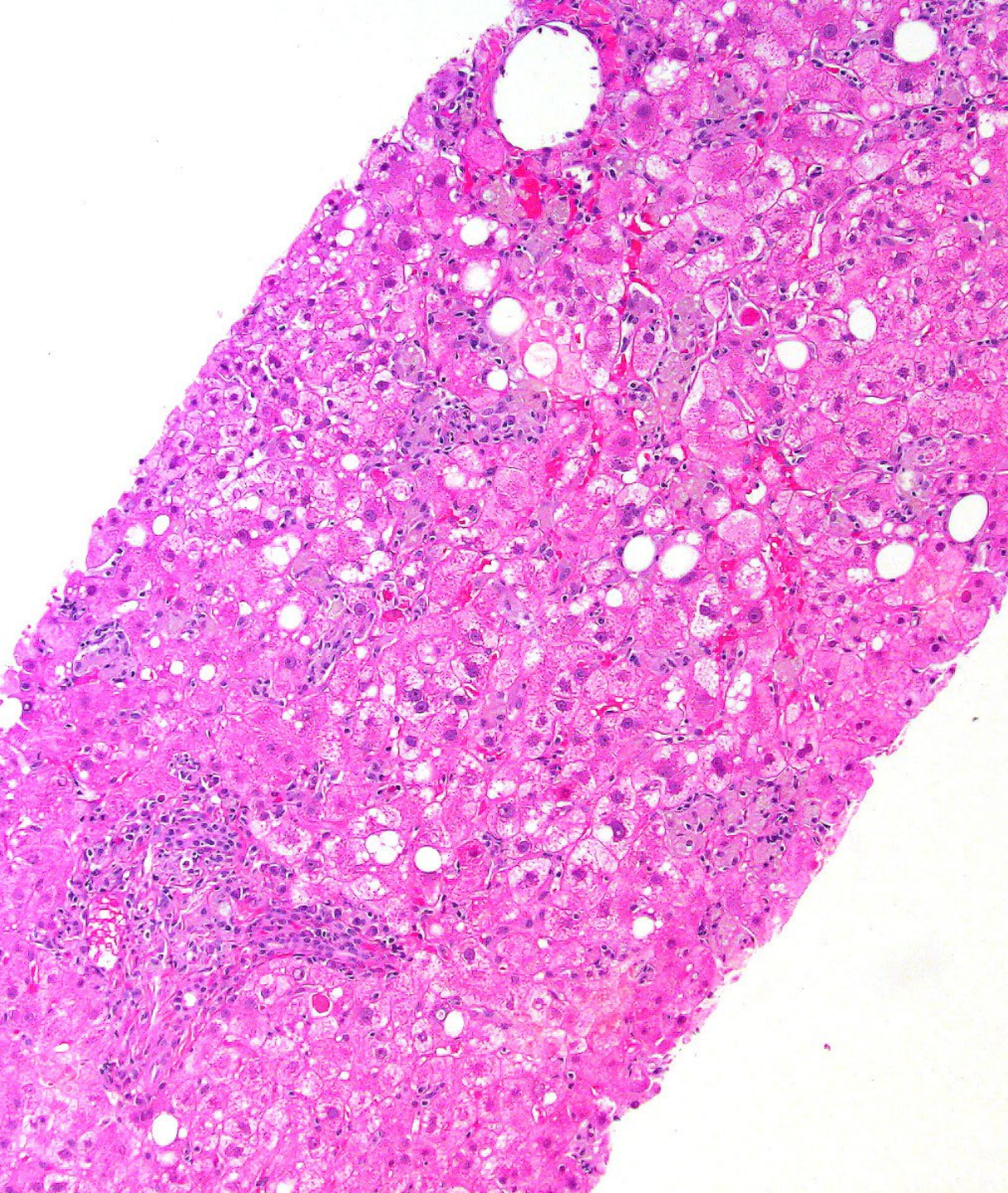
Case 2

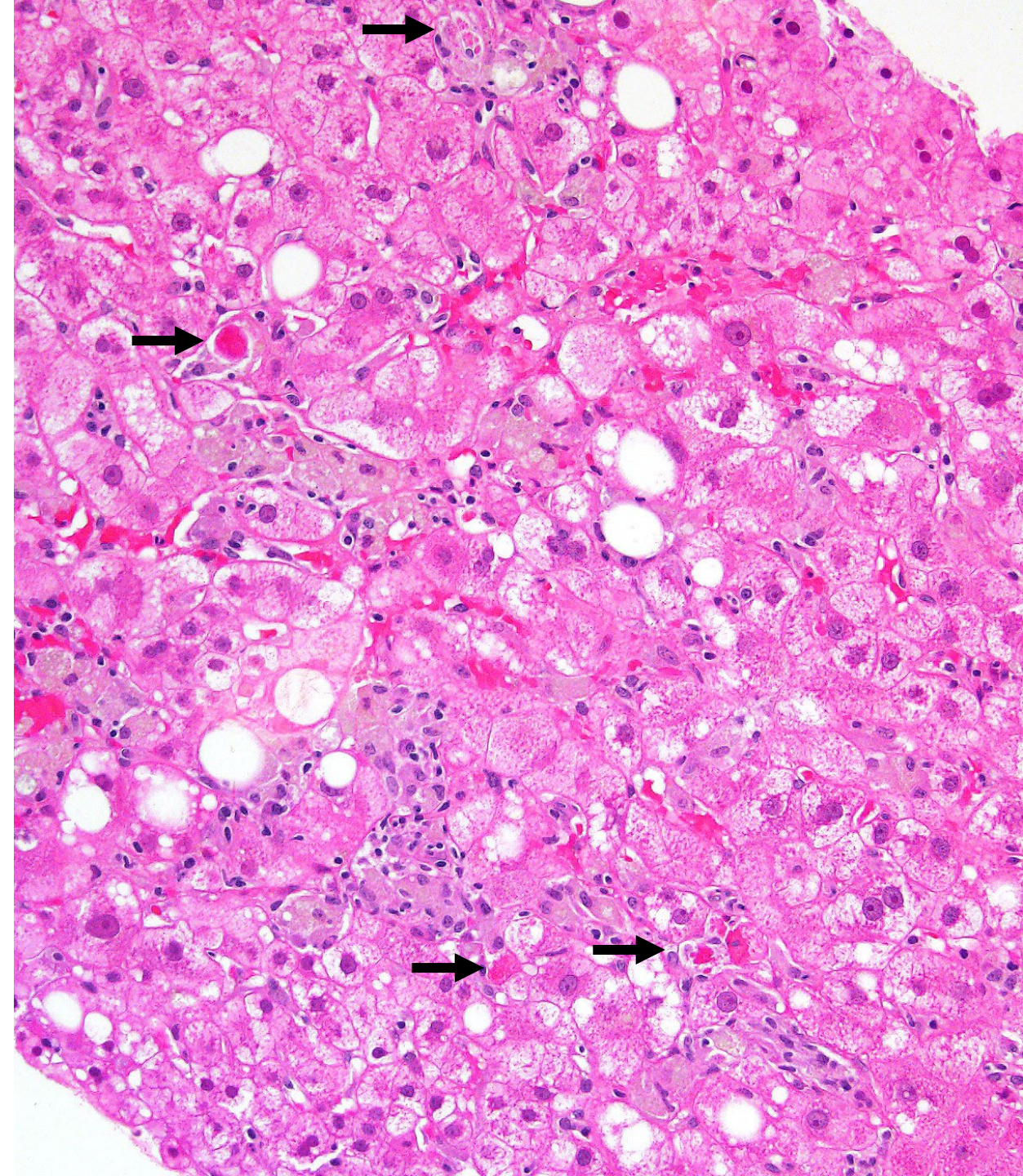
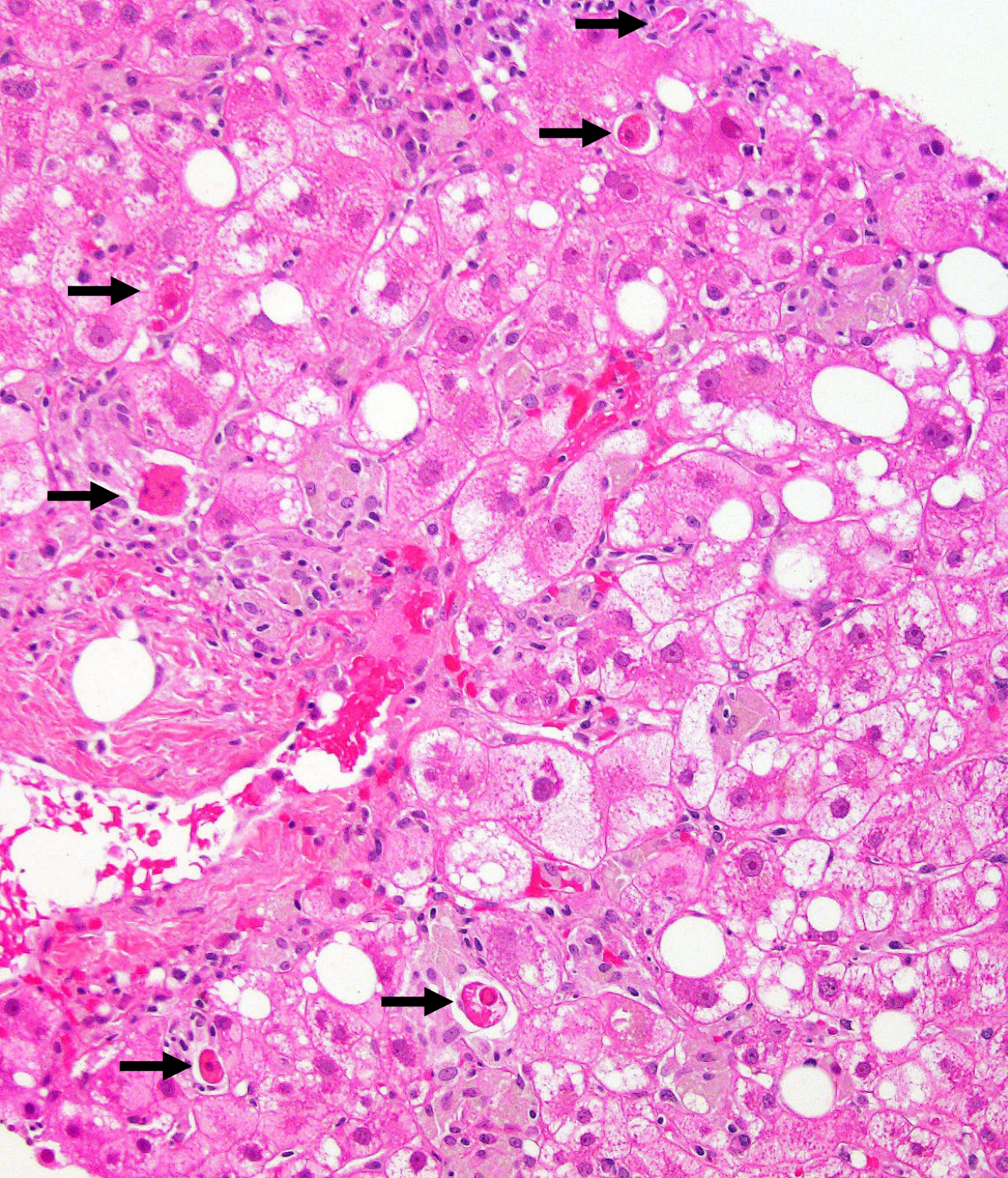
- 62 F with juvenile rheumatoid arthritis with a long and varied medication history for controlling symptoms, currently on tocilizumab and methotrexate (4-5 years on this regimen)
- Diabetic, not obese (BMI 23)
- Stopped tocilizumab prior to shoulder surgery, after restarting, aminotransferases rose (next slide)
- ANA (+) at 1:160, ASMA, AMA negative, IgG normal

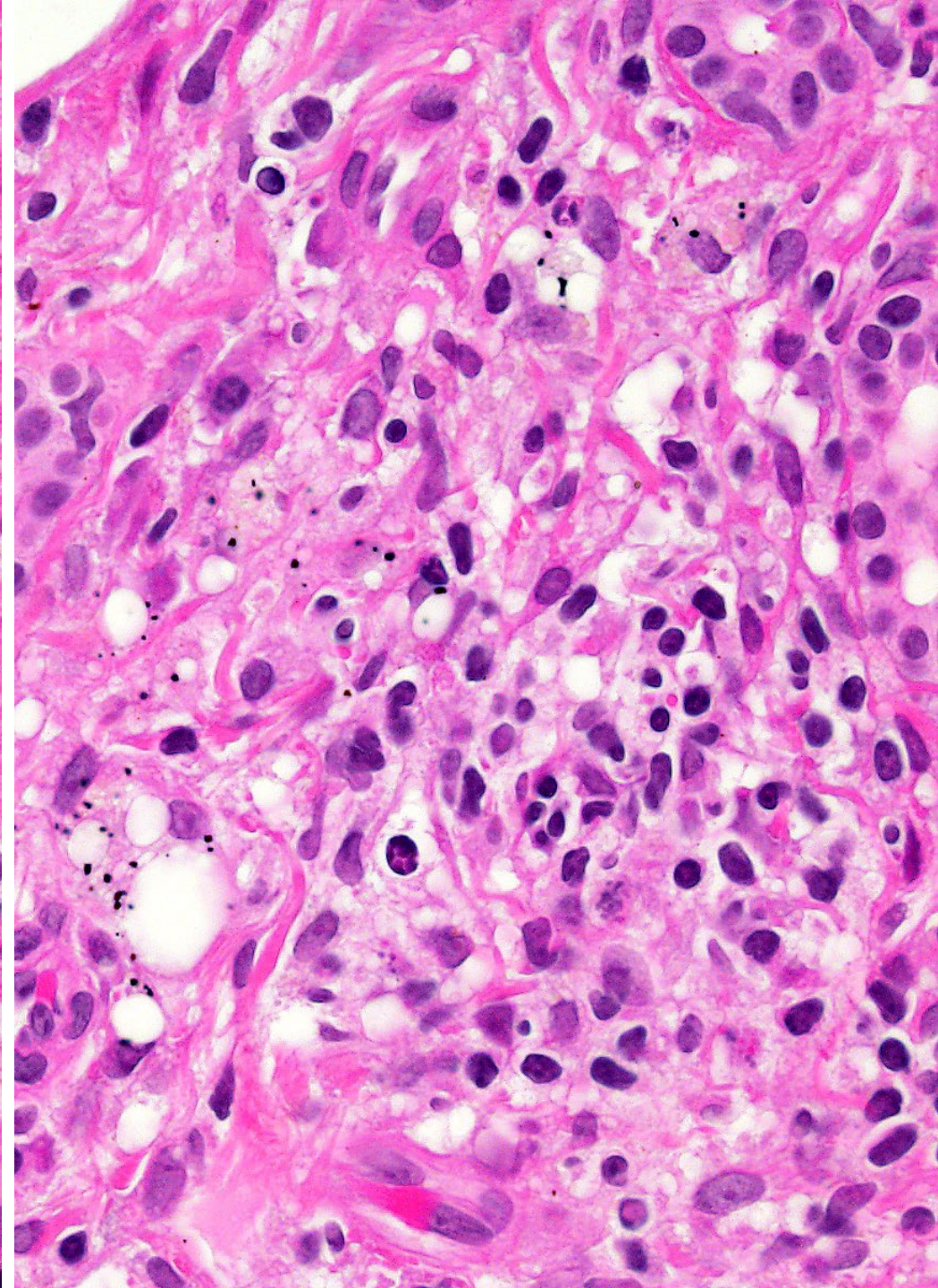
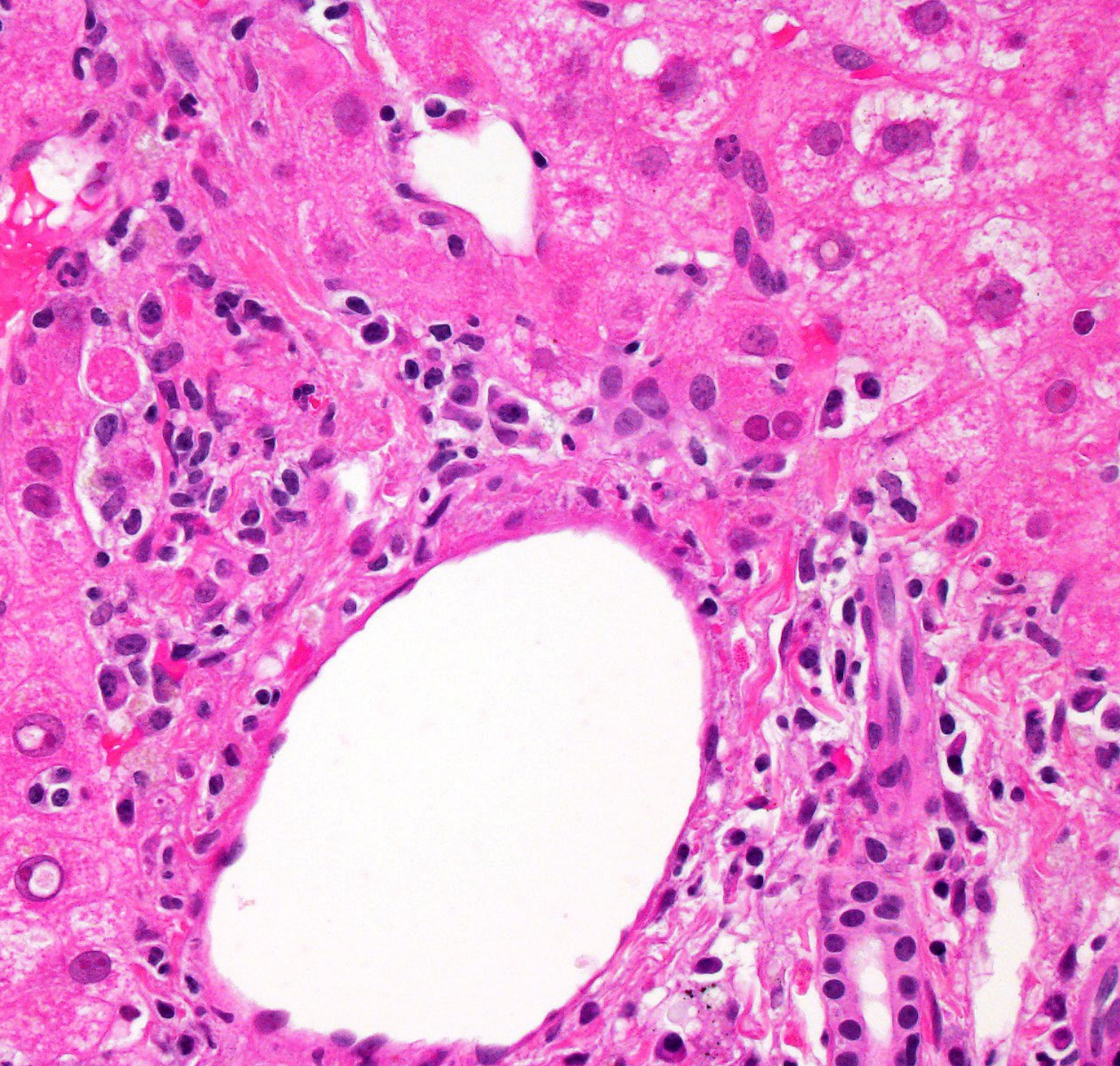
Time course of liver tests, interventions





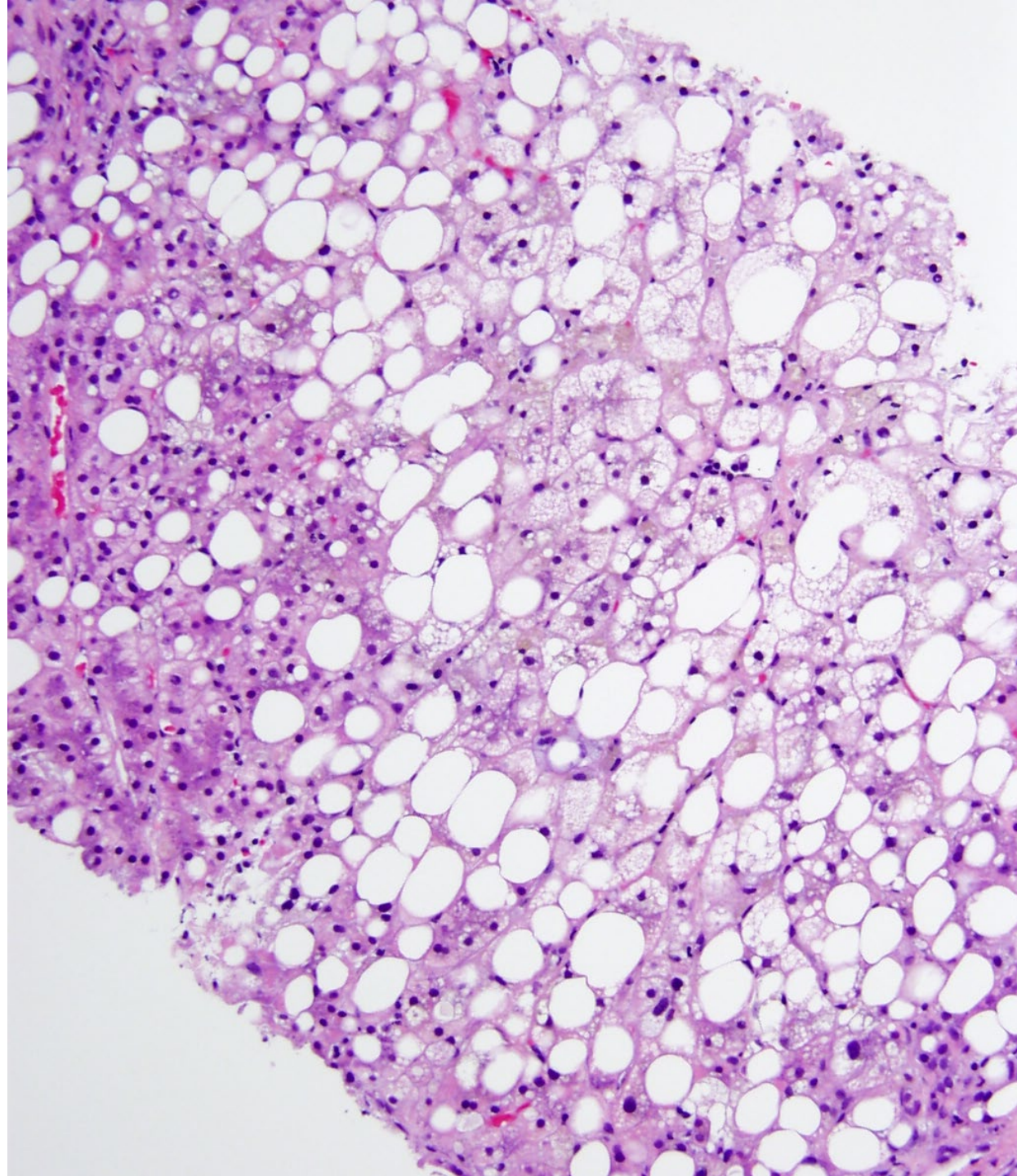
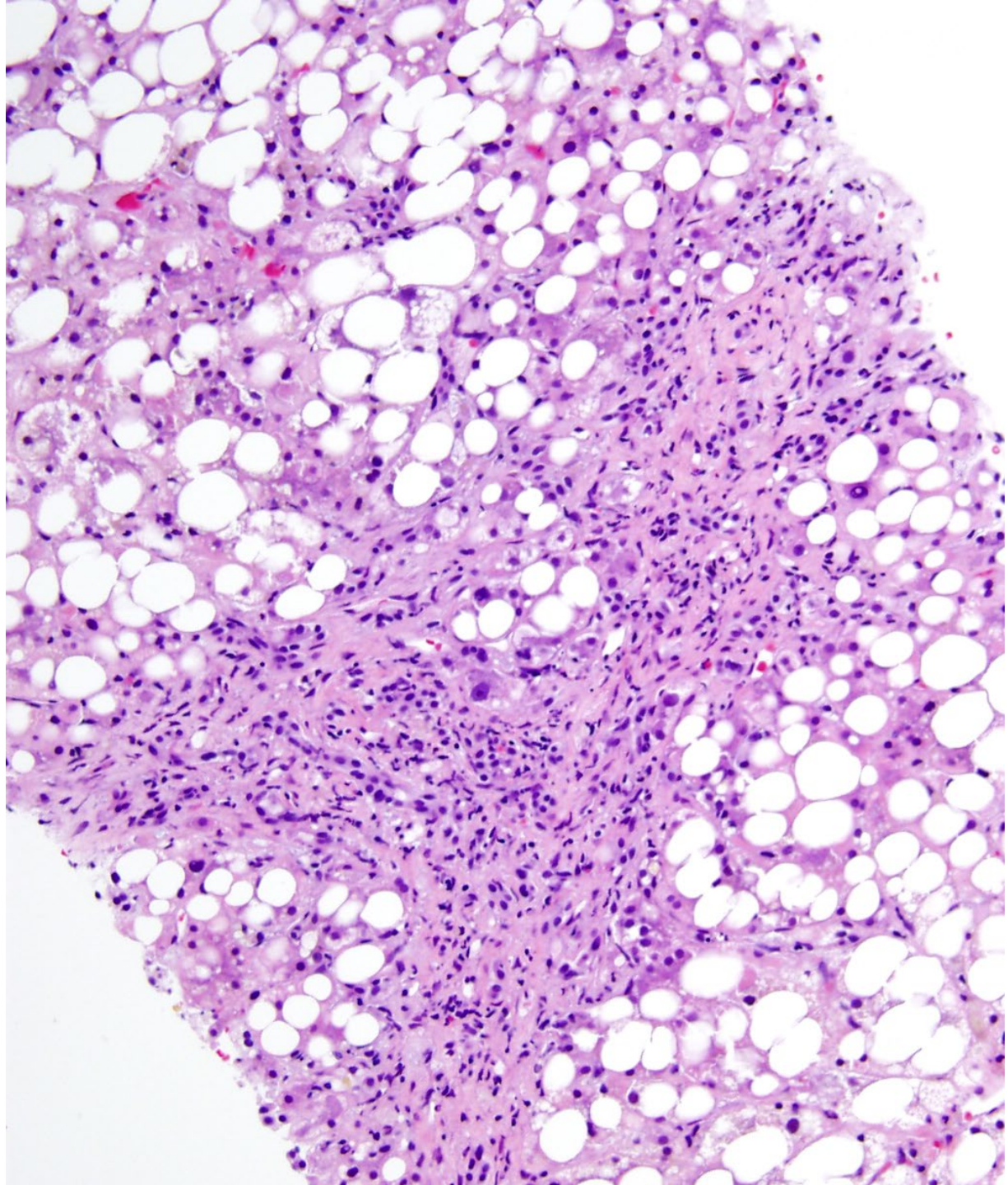


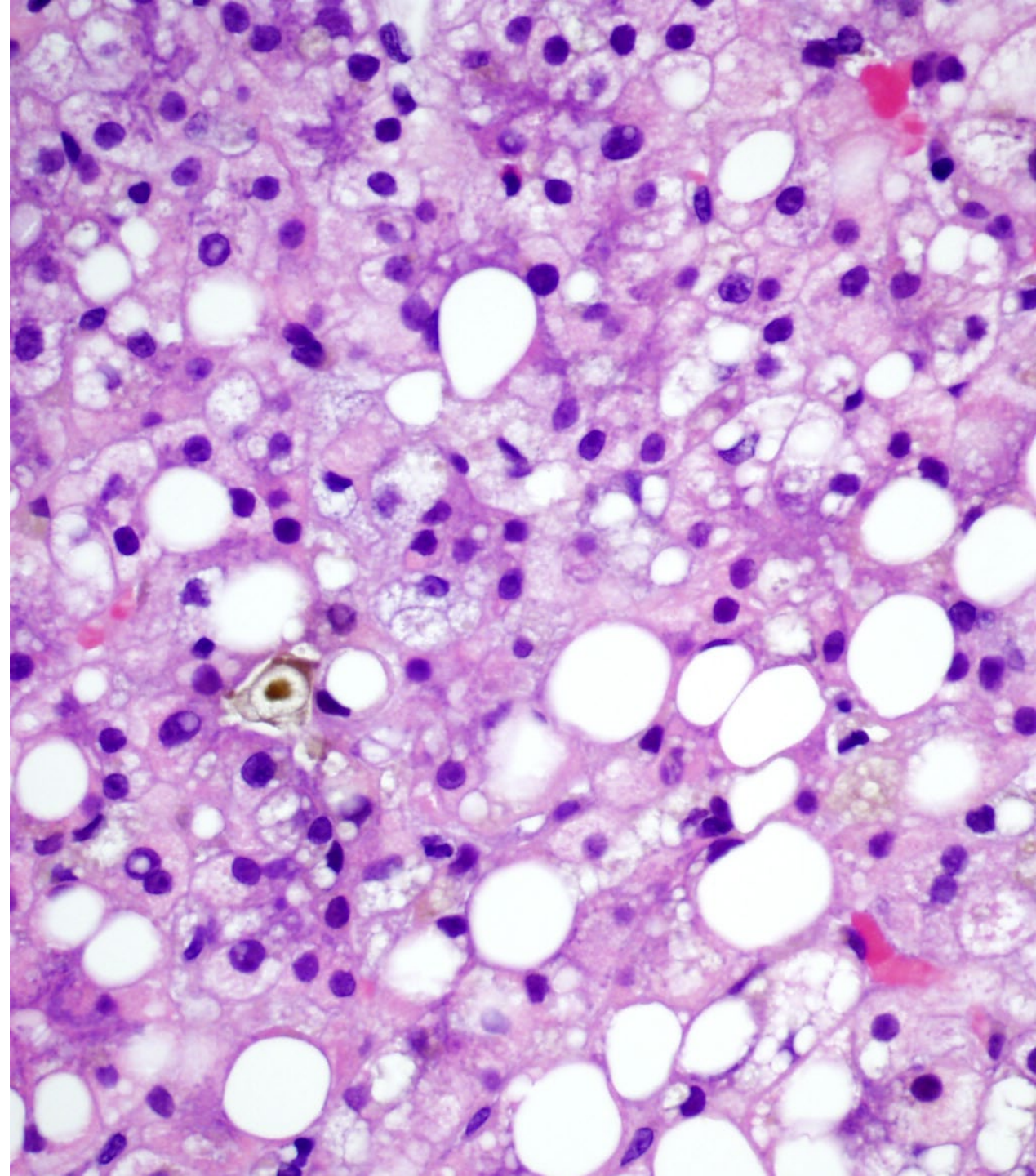
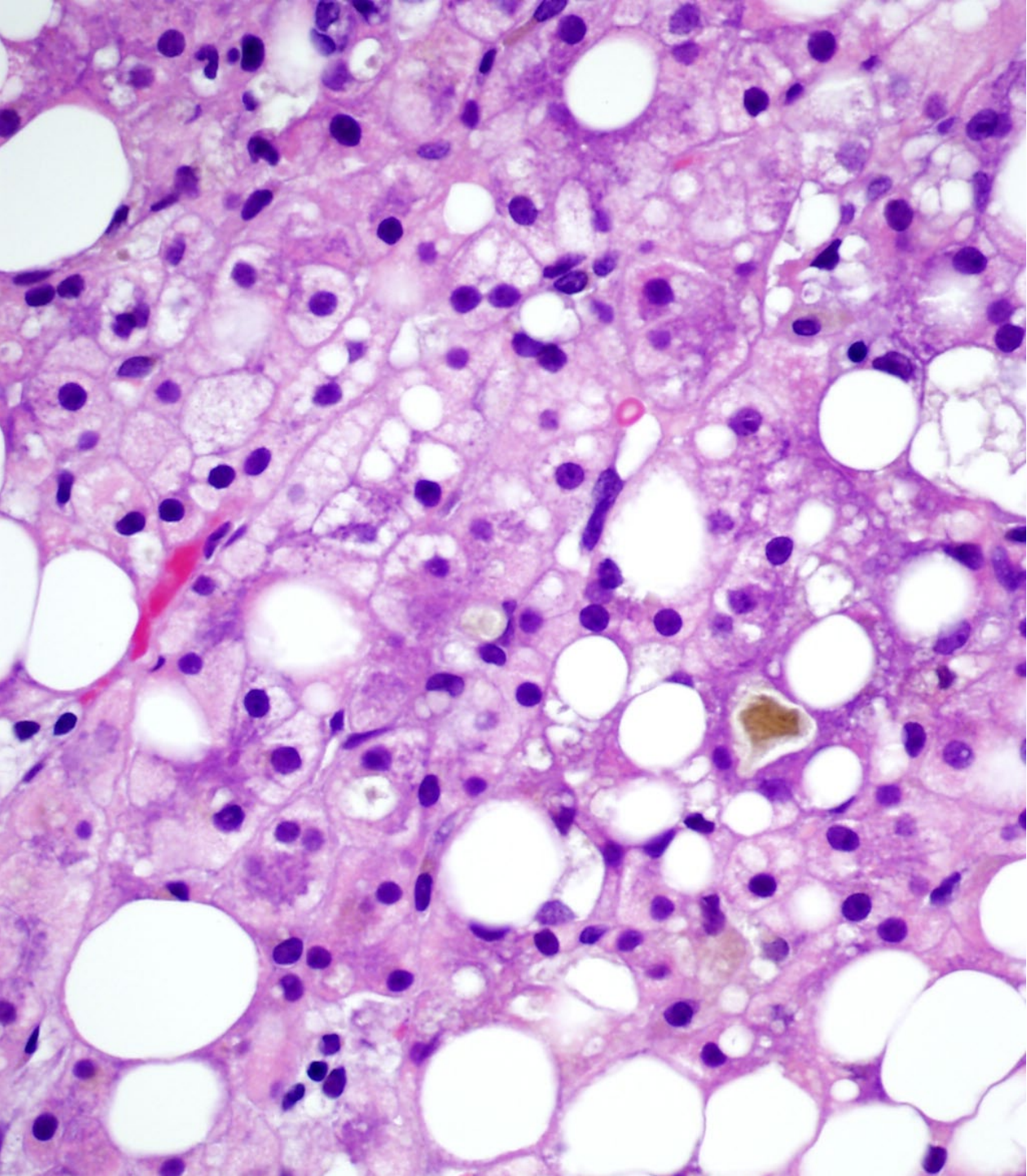




Case 3

- 46 F, morbid obesity, s/p gastric bypass 2 yrs prior
- Initially weight, but regained 50-75 lbs
- Took supplements marketed for weight loss, including Kava Kava
- Developed cholestatic elevations in liver enzymes, with jaundice
- Stopped supplements and recovered, but restarted Kava Kava about 2 months later, with recurrence of jaundice
- Biopsies after both events





Take Home Points

- It is possible to diagnose DILI in the presence of underlying steatohepatitis
- Pathologist should have a good understanding of the spectrum of expected injury in NASH
- If pre-treatment biopsies are available, they should be reviewed at the same time
- The pathologist should take advantage of all of the information known at the time of the biopsy