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Management of autoimmune hepatitis

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Case 1

52 year-old woman, referred for liver blood tests abnormalities for 2 years

- **Medical history**

- Type 2 diabetes (Metformin)
- Arterial hypertension (Perindopril, Amlodipine)
- No alcohol

- **Physical examination**

- 108 kg; 1.62 m (BMI 41.0 kg/m²)

Laboratory results

	22/01/2013
AST (IU/L) (< 31)	165
ALT (IU/L) (<34)	70
ALK (IU/L) (<100)	94
GGT (IU/L) (<38)	25
Bilirubin ($\mu\text{mol/L}$)	25
Albumin (g/L)	35
Prothrombin time (%)	65%

- **Work-up for causes:**

- HBs Ag undetectable
- Anti-HCV Ab undetectable
- IgG **19 g/L (<16g/L)**
- Anti-antinuclear Ab: **1/320**

- **Ultrasound:** steatosis, no thrombosis

Question

Liver blood tests abnormalities in this patients can be due to:

A- Non alcoholic steatohepatitis

B- Autoimmune hepatitis

Question

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A- Non alcoholic steatohepatitis

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NASH and auto-antibodies

864 patients with
biopsy proven NASH

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graph TD; A[864 patients with biopsy proven NASH] --> B[Significant autoantibodies* N=182 (21%)]; A --> C[No significant autoantibodies N=682 (79%)]; B --- D[No difference in:]; C --- D;
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Significant autoantibodies*
N=182 (21%)

No significant autoantibodies
N=682 (79%)

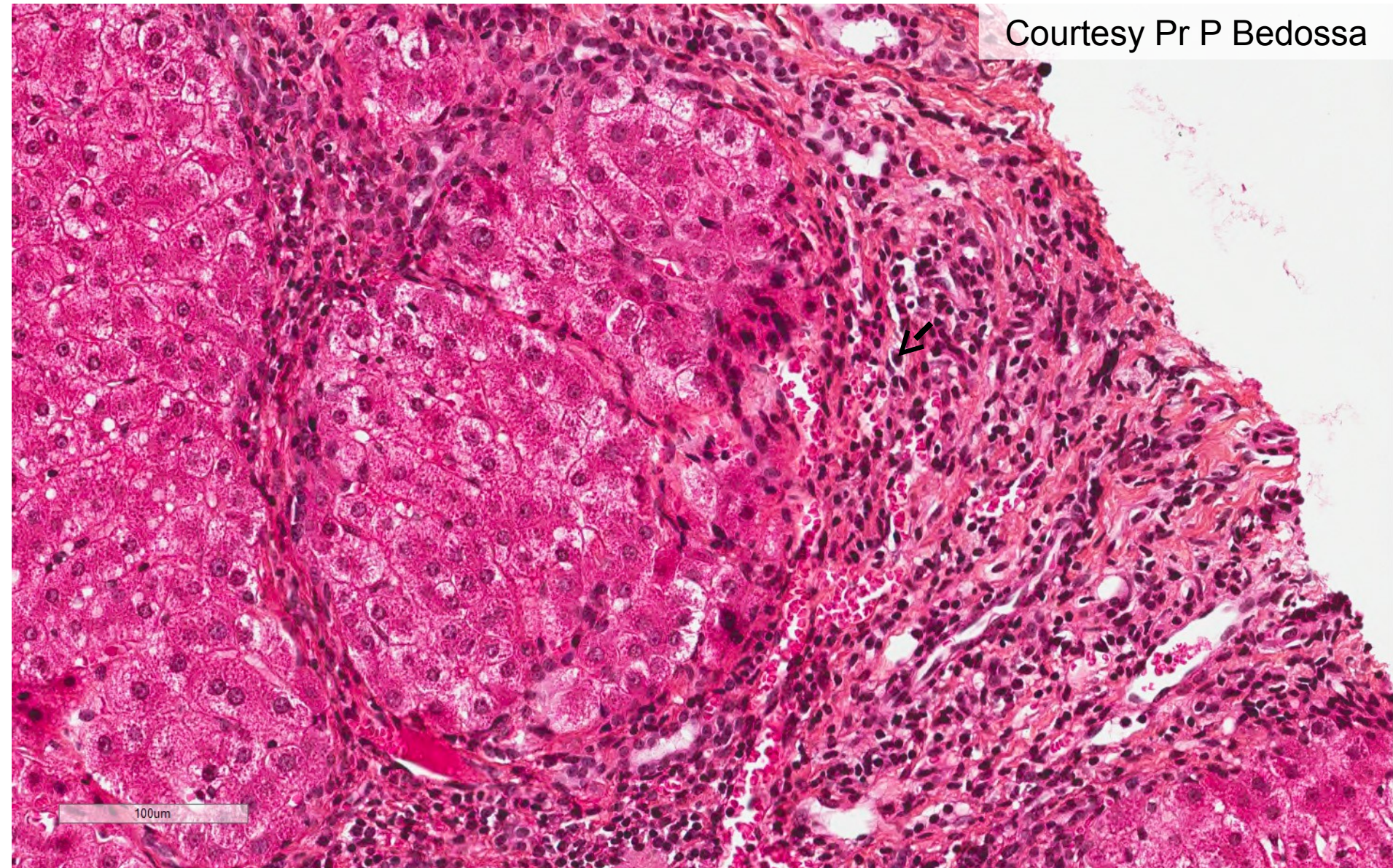
No difference in:

- age, gender, race, BMI, HOMA-IR or history of diabetes
- lobular inflammation, ballooning, advanced fibrosis

Less steatosis

Liver biopsy

Courtesy Pr P Bedossa



Question

How would you manage that patient?

A- No treatment

B- Prednisolone alone

C- Prednisolone + Azathioprine

D- Budesonide alone

E- Budesonide + Azathioprine

Question

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Laboratory results

Prednisolone + Azathioprine



	01/2013	06/2013
AST (IU/L) (< 31)	165	62
ALT (IU/L) (<34)	70	51
ALK (IU/L) (<100)	94	90
GGT (IU/L) (<38)	25	24
Bilirubin (μmol/L)	25	20
Albumin (g/L)	35	36
PT (%)	65%	70
IgG (g/L)	19	16

But, poor diabetes control and intolerance to azathioprine

Question

What would you then propose to this patient?

A- No treatment (stop immunosuppression)

B- Prednisolone alone

C- Mycophenolate mofetil alone

D- Tacrolimus alone

Question

What would you then propose to this patient?

A- No treatment stop (immunosuppression)

B- Prednisolone alone

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Second line for azathioprine-intolerant patients: MMF

	N=	Biochemical remission maintenance
Efe, CGH 2017	74	92%
Roberts, CGH 2017	63	62%

Efe, CGH 2017
Roberts, CGH 2017

Laboratory results

Prednisolone + AZA

MMF 2g/day

	01/2013	06/2013	01/2014
AST (IU/L) (< 31)	165	62	60
ALT (IU/L) (<34)	70	51	53
ALK (IU/L) (<100)	94	90	85
GGT (IU/L) (<38)	25	24	27
Bilirubin (μmol/L)	25	20	19
Albumin (g/L)	35	36	36
PT (%)	65%	70	71
IgG (g/L)	19	16	15

Weight loss, good diabetes control

Laboratory results

Prednisolone + AZA

MMF 2g/day

	01/2013	06/2013	01/2014	12/2014
AST (IU/L) (< 31)	165	62	60	29
ALT (IU/L) (<34)	70	51	53	30
ALK (IU/L) (<100)	94	90	85	70
GGT (IU/L) (<38)	25	24	27	20
Bilirubin (μmol/L)	25	20	19	15
Albumin (g/L)	35	36	36	43
PT (%)	65%	70	71	86
IgG (g/L)	19	16	15	13

Weight loss, good diabetes control

Question

The patient asks you if you will consider stopping MMF. What would you answer?

A- Now, since biochemical remission is obtained

B- After 2 years of normal AST and ALT

C- After 2 years of normal AST, ALT + IgG

D- Never (lifelong treatment)

Question

The patient asks you if you will consider stopping MMF. What would you answer?

A- Now, since biochemical remission is obtained

B- After 2 years of normal AST and ALT

C- After 2 years of normal AST, ALT + IgG

D- Never (lifelong treatment)

But relapse 50%, typically within 12 months

Question

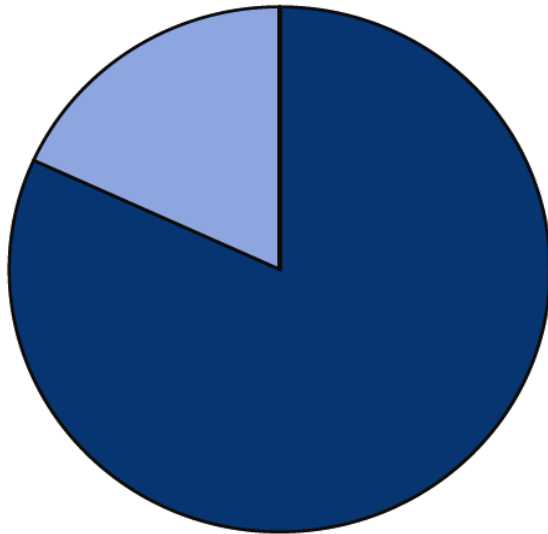
2017: AST, ALT and IgG strictly normal since 2014

You consider interrupting MMF

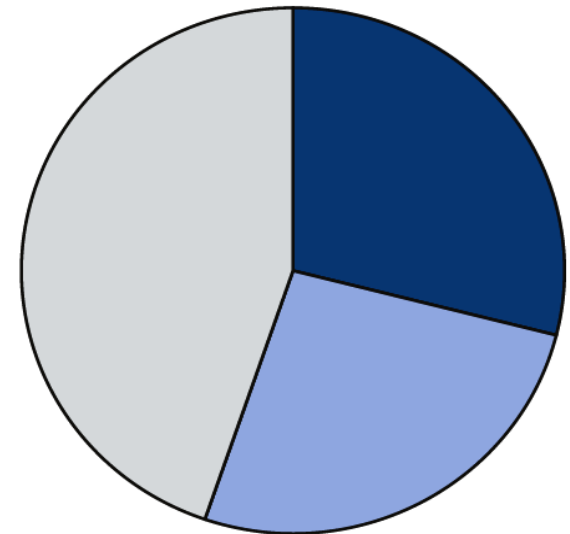
Do you perform a liver biopsy?




Biochemical vs. histological remission

Normal IgG
Normal ALT
N=22

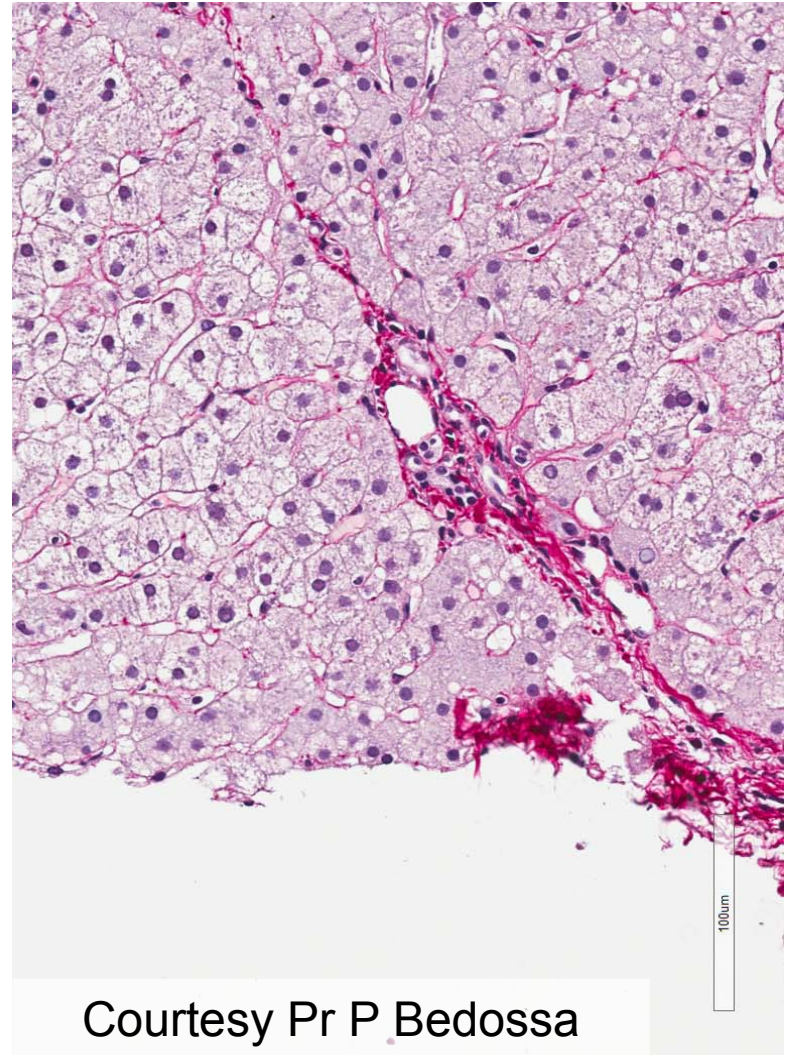
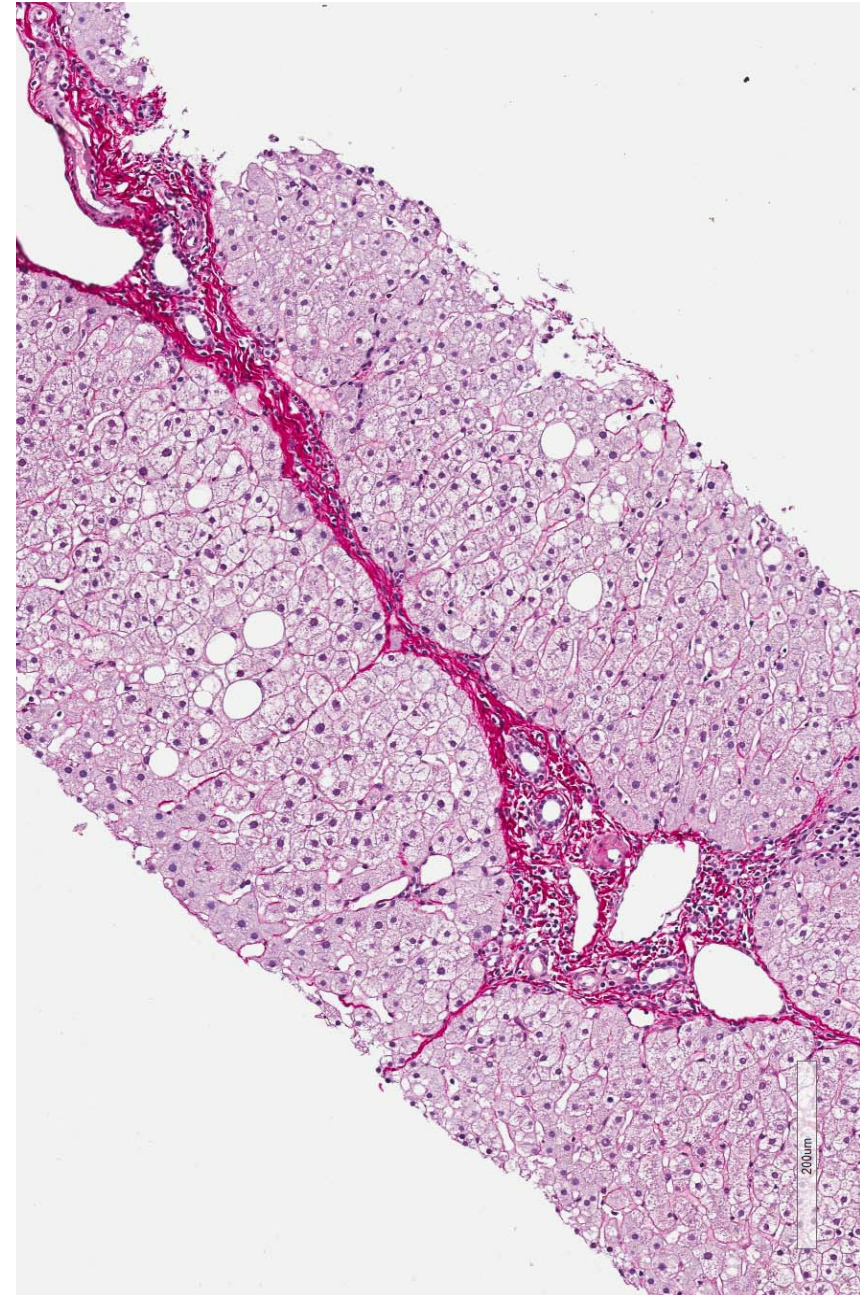


↑ IgG
And/or ↑ ALT
N=38

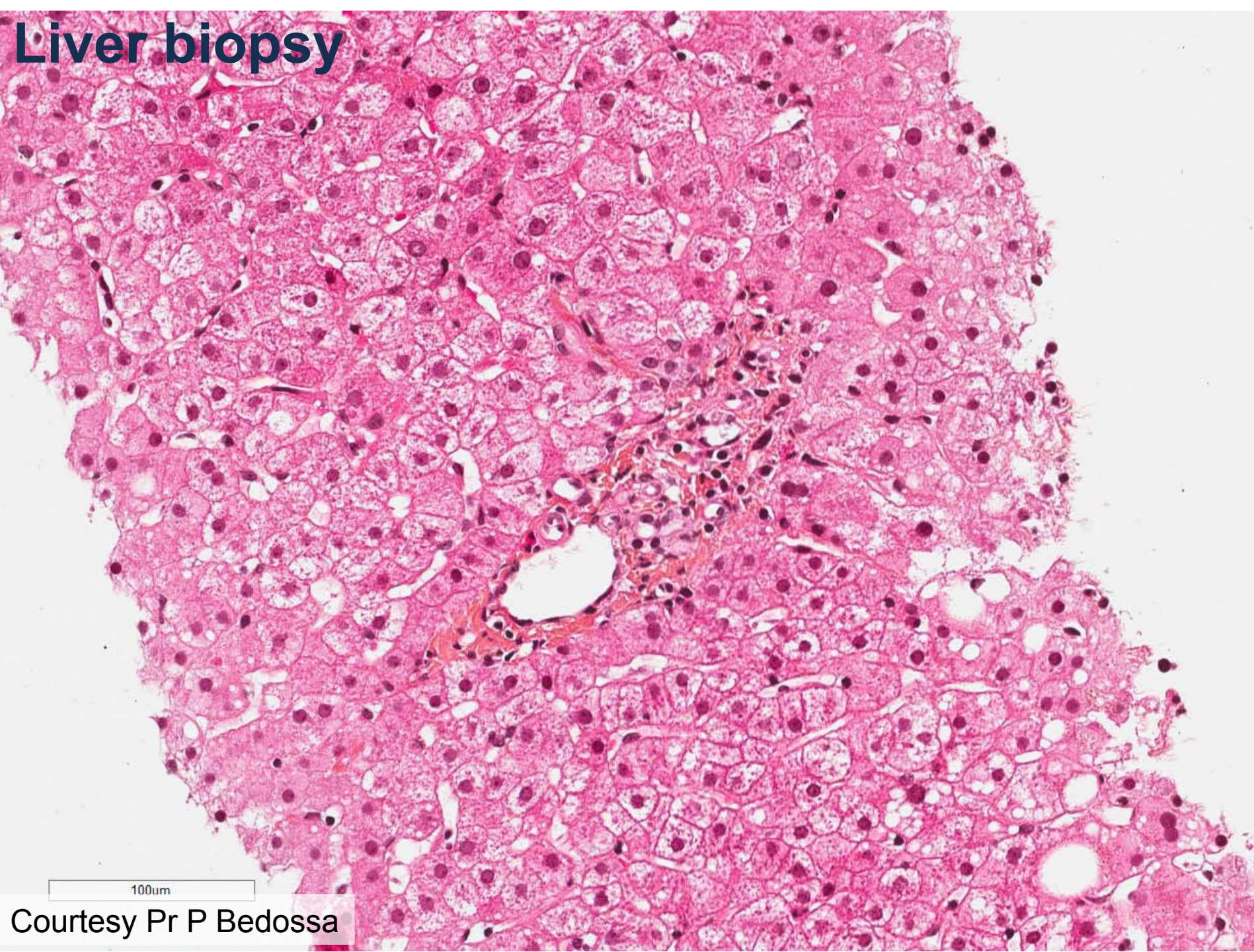


-  Histological remission
-  Mild histological disease activity
-  High histological disease activity

Liver biopsy



Liver biopsy



100um

Courtesy Pr P Bedossa

Question

You propose withdrawal of MMF. How?

A- Complete interruption (biochemical + histo remission)

B- Stepwise reduction every 6-8 weeks

C- Stepwise reduction every year

Question

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B- Stepwise reduction every 6-8 weeks

C- Stepwise reduction every year

Question

How frequently do you perform blood tests during MMF withdrawal?

A- Every week

B- Every 3 weeks

C- Every 3 months

D- Every year

Question

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B- Every 3 weeks

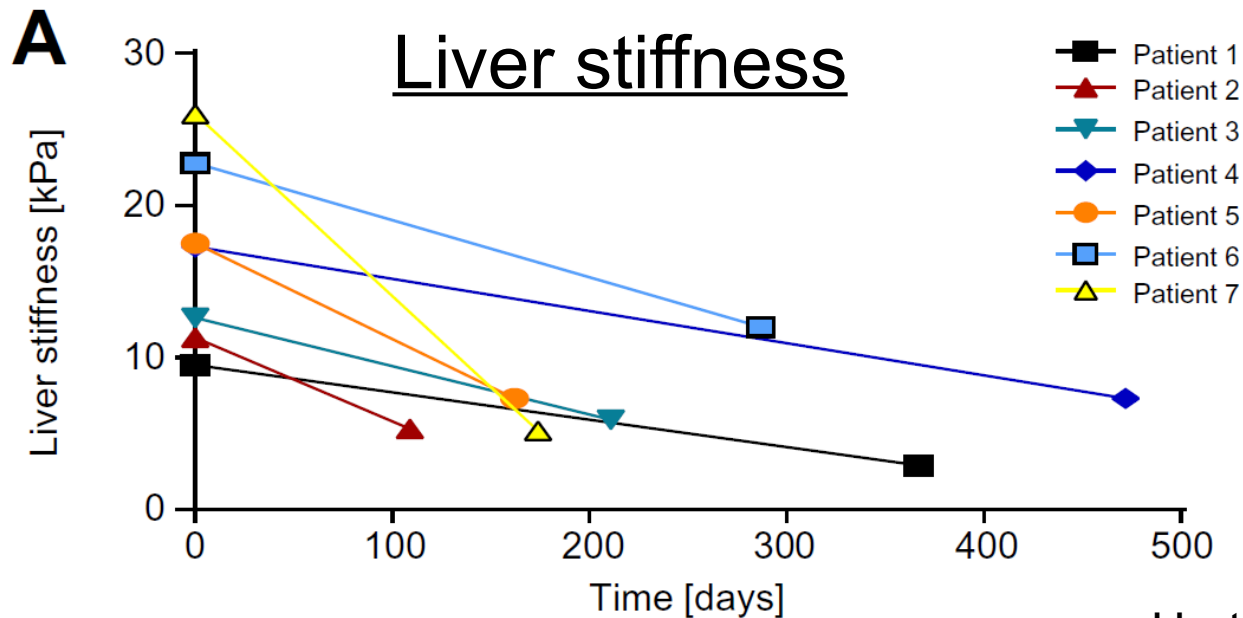
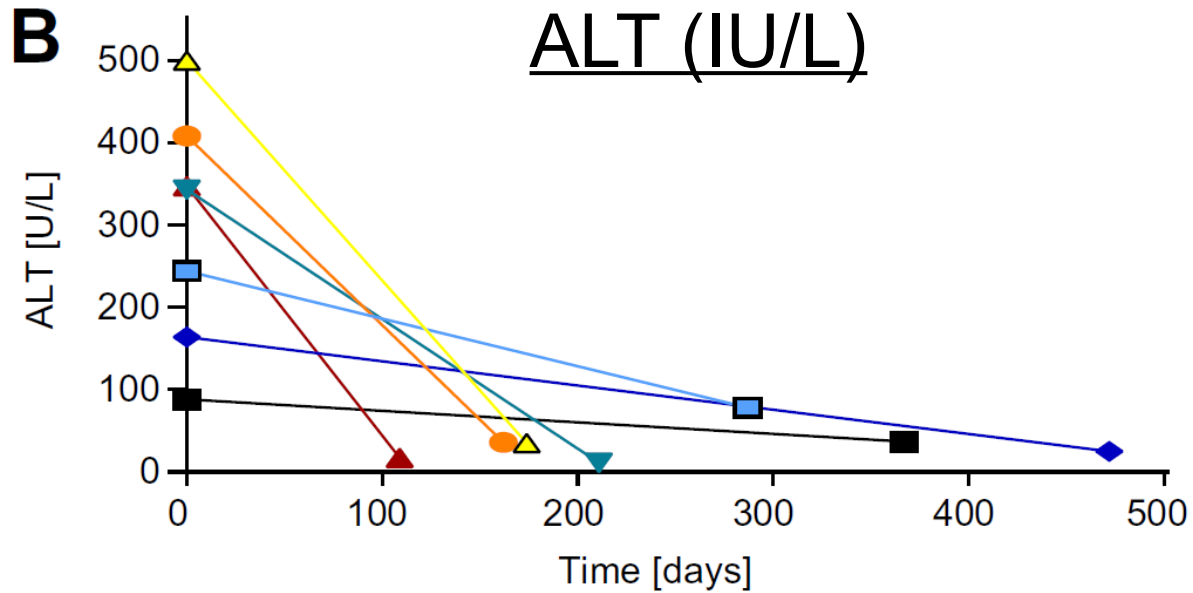
C- Every 3 months

D- Every year

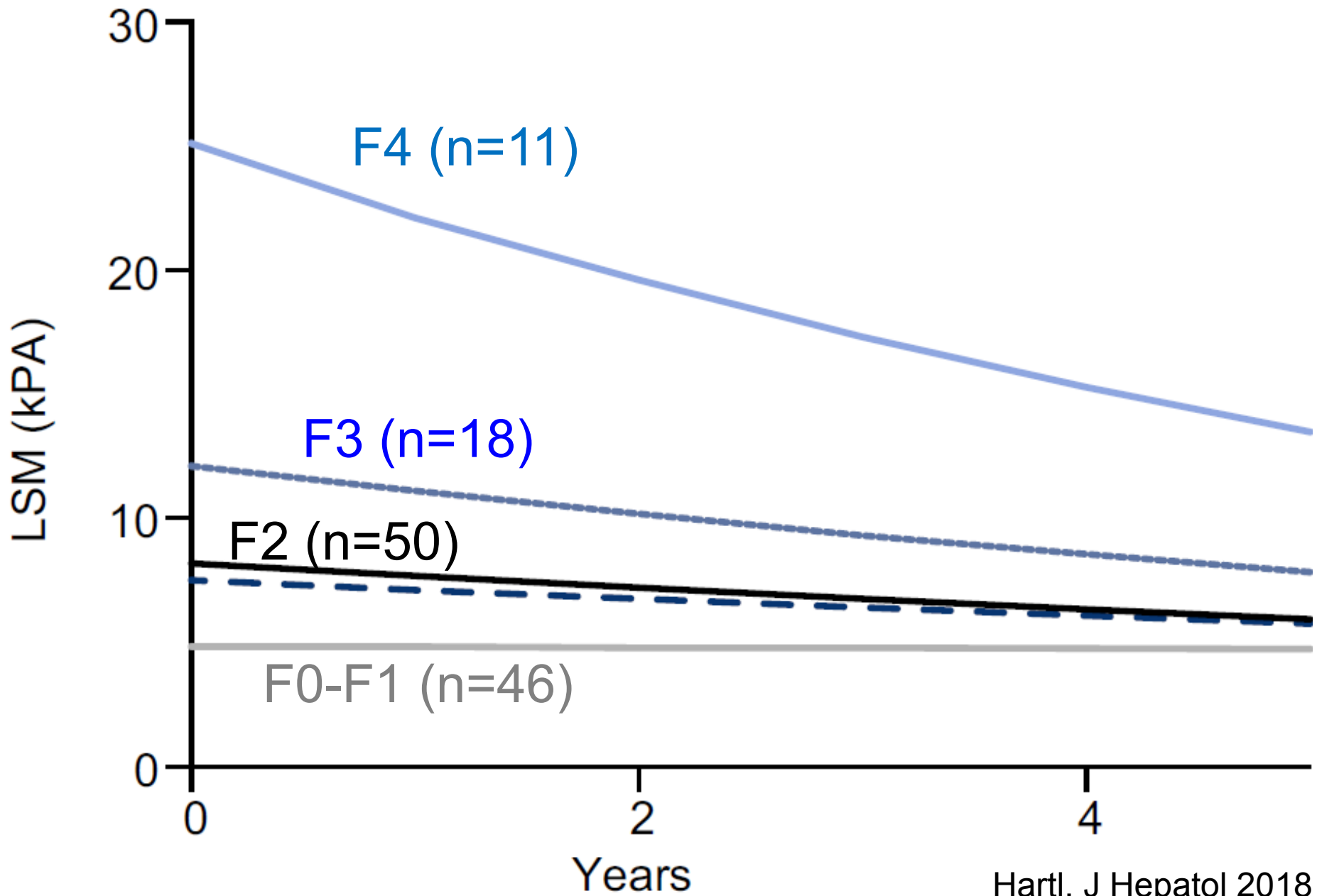
Question

Do you think that liver stiffness could be of interest?

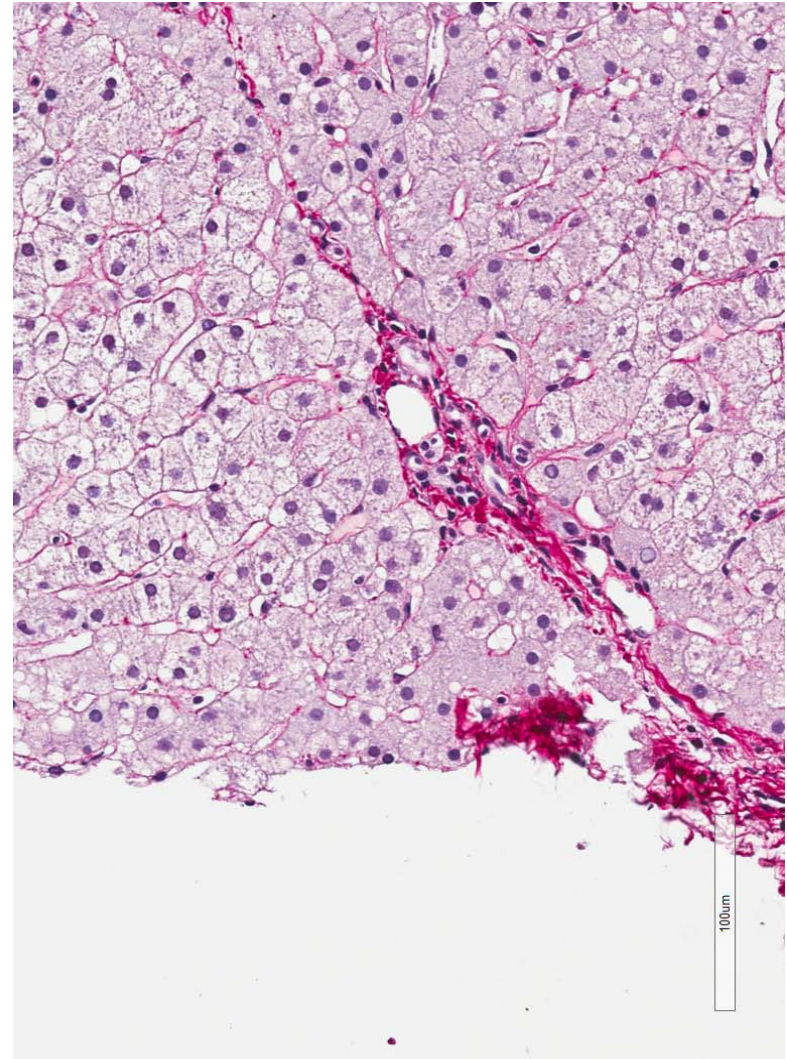
Liver stiffness in AIH: first 6 months



Liver stiffness in ALH: long-term



Liver biopsy vs. liver stiffness



- Liver stiffness: 5.9 kPa
- Hepatic venous pressure gradient: 7 mm Hg

Case 2

15 year-old man, referred for liver blood tests abnormalities discovered at the time of the diagnosis of ulcerative colitis (pancolitis)

- **Medical history**
- none
- **Physical examination**
 - 53 kg; 1.76m

Laboratory results

AST (IU/L) (< 35)	89
ALT (IU/L) (<45)	246
ALK (IU/L) (<150)	235
GGT (IU/L) (<55)	81
Bilirubin ($\mu\text{mol/L}$)	7
Albumin (g/L)	35
Prothrombin time (%)	76

- **Work-up for causes:**

- HBs Ag undetectable
- Anti-HCV Ab undetectable
- IgG **28 g/L (<16g/L)**
- Anti-antinuclear Ab: **1/1280**

Question

This presentation is consistent with:

A- Autoimmune hepatitis (AIH)

B- Primary sclerosing cholangitis (PSC)

C- Overlap syndrome (AIH-PSC)

Question

This presentation is consistent with:

A- Autoimmune hepatitis (AIH)

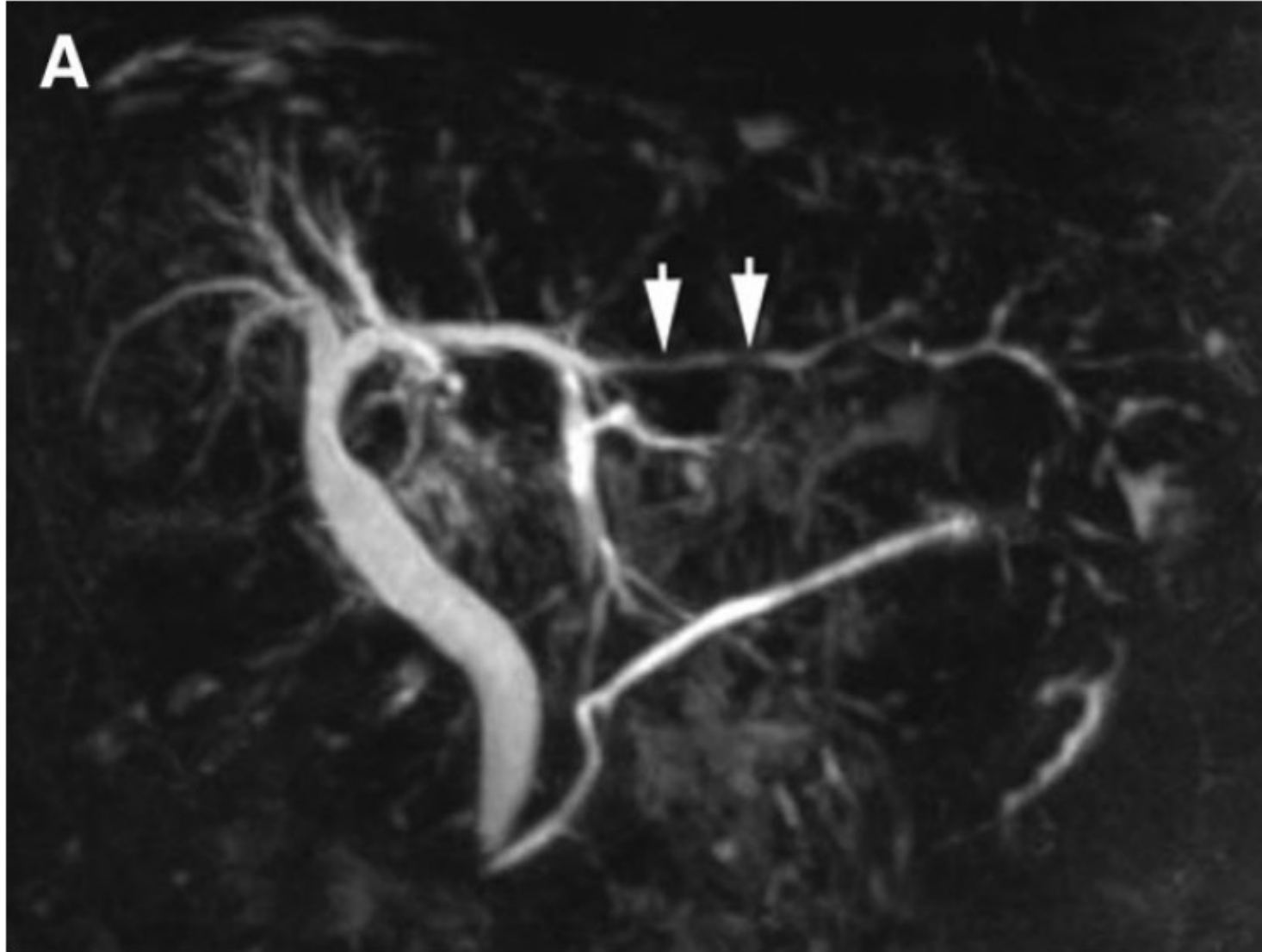
B- Primary sclerosing cholangitis (PSC)

C- Overlap syndrome (AIH-PSC)

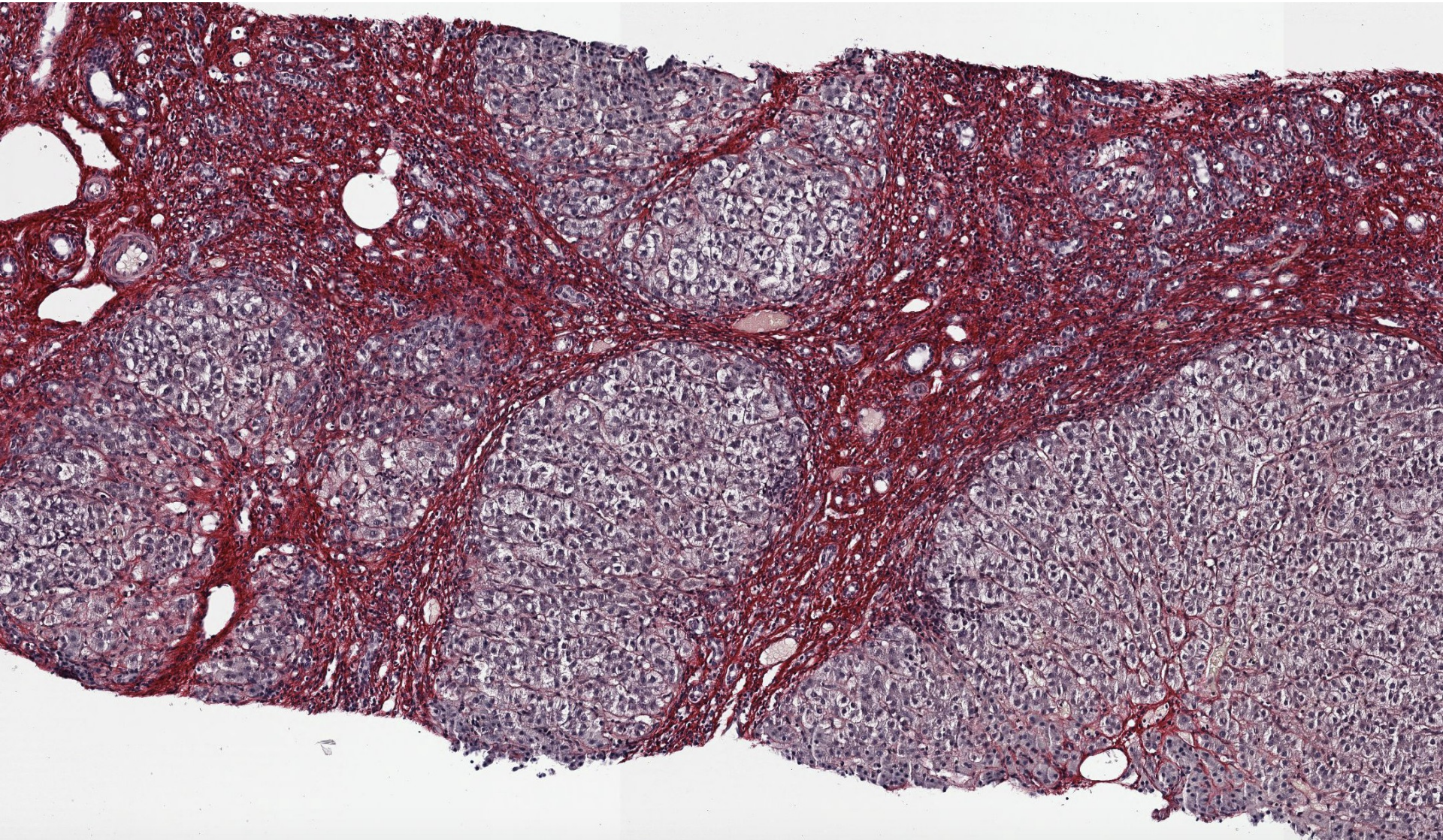
AIH, PSC in children

- **Among children with PSC:**
 - 33% have autoimmune hepatitis
 - 25% have normal ALK levels
- **Overestimation due to fibrosis**

Extensive liver fibrosis induces mild intrahepatic bile duct abnormalities in AIH

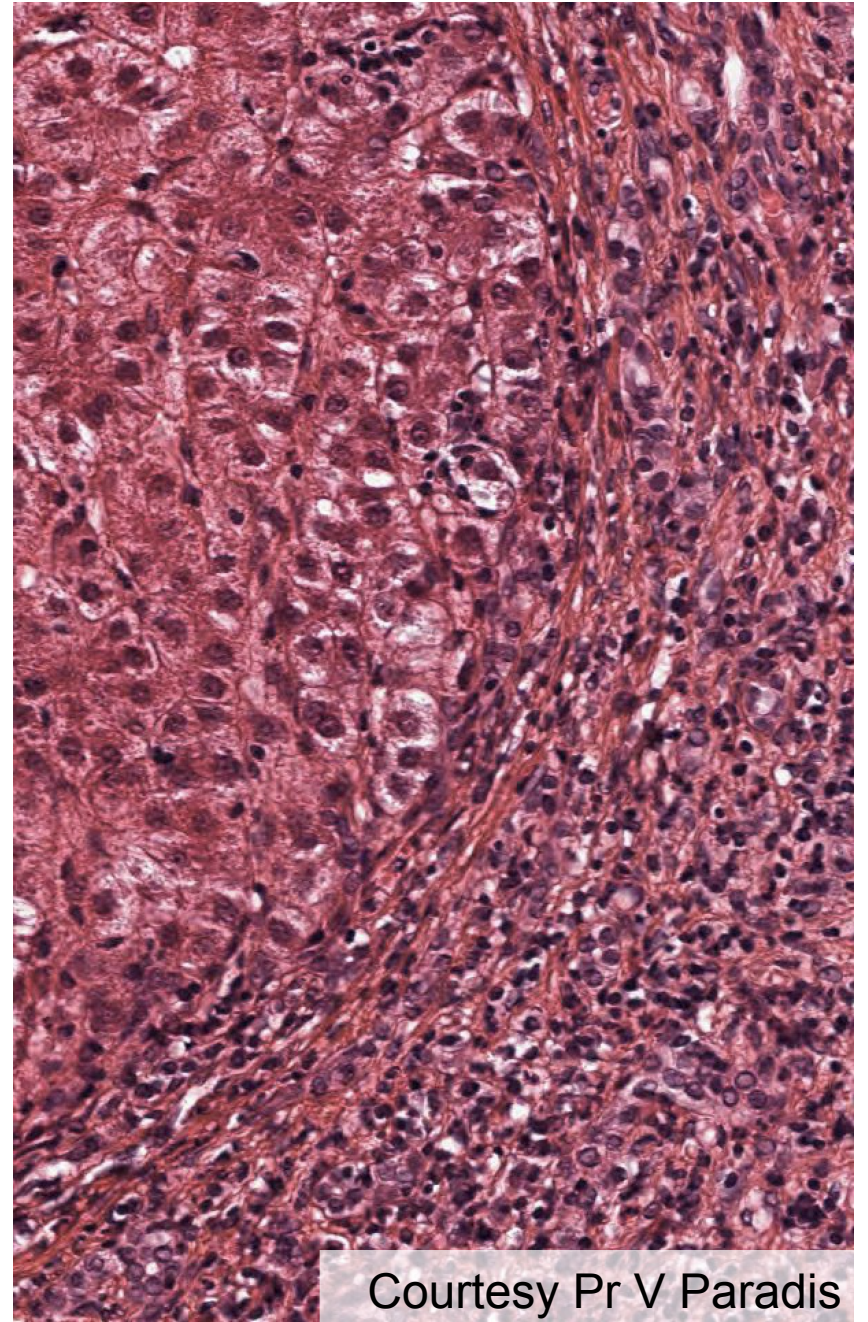
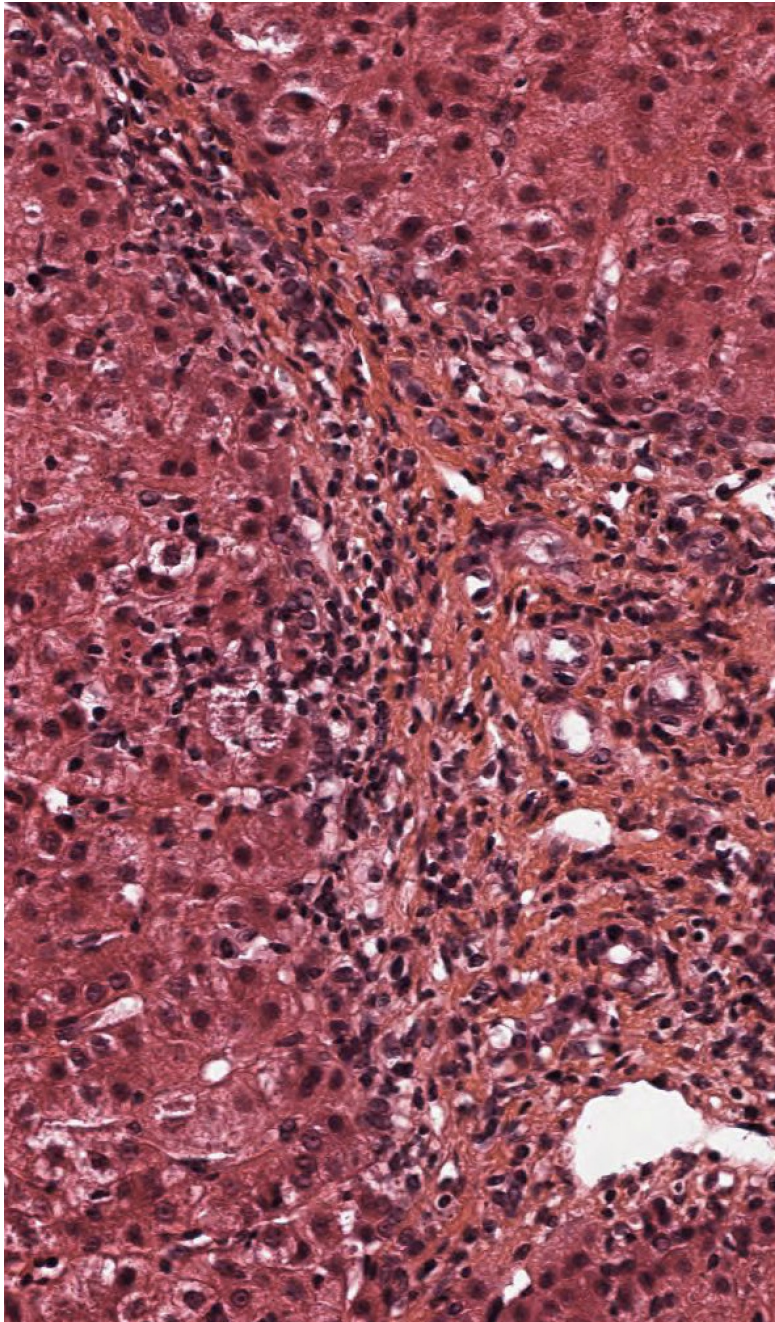


Liver biopsy



Courtesy Pr V Paradis

Liver biopsy



Courtesy Pr V Paradis

Question

Well-controlled liver disease with MMF 2 g/day (relapse when withdrawal tested). He married and wants children. What would you suggest?

A- Maintain MMF

B- Stop all immunosuppressive therapy

C- Low dose prednisolone

Question

Well-controlled liver disease with MMF 2 g/day (relapse when withdrawal tested). He married and wants children. What would you suggest?

A- Maintain MMF

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