



Instituts
thématiques



Inserm

Institut national
de la santé et de la recherche médicale



UNIVERSITÉ
PARIS DESCARTES



Management of autoimmune hepatitis

Pierre-Emmanuel RAUTOU

Inserm U970, PARCC@HEGP, Paris

Service d'hépatologie, Hôpital Beaujon, Clichy, France

41 year-old woman, coming to emergency department for fatigue and jaundice

- **Medical history**

- Delivery of a healthy boy 10 weeks before
- No medication or substance abuse
 - No alcohol

- **Physical examination**

- 55 kg; 1.65 m
- Jaundice

Laboratory results

	28/07/2013
AST (IU/L) (< 31)	1191
ALT (IU/L) (<34)	1444
ALK (IU/L) (<100)	108
GGT (IU/L) (<38)	167
Bilirubin ($\mu\text{mol/L}$)	73
INR	1.2
Platelet count	376

- **Ultrasound**

- Normal liver aspect
- No hepatic vein thrombosis
- No ascites

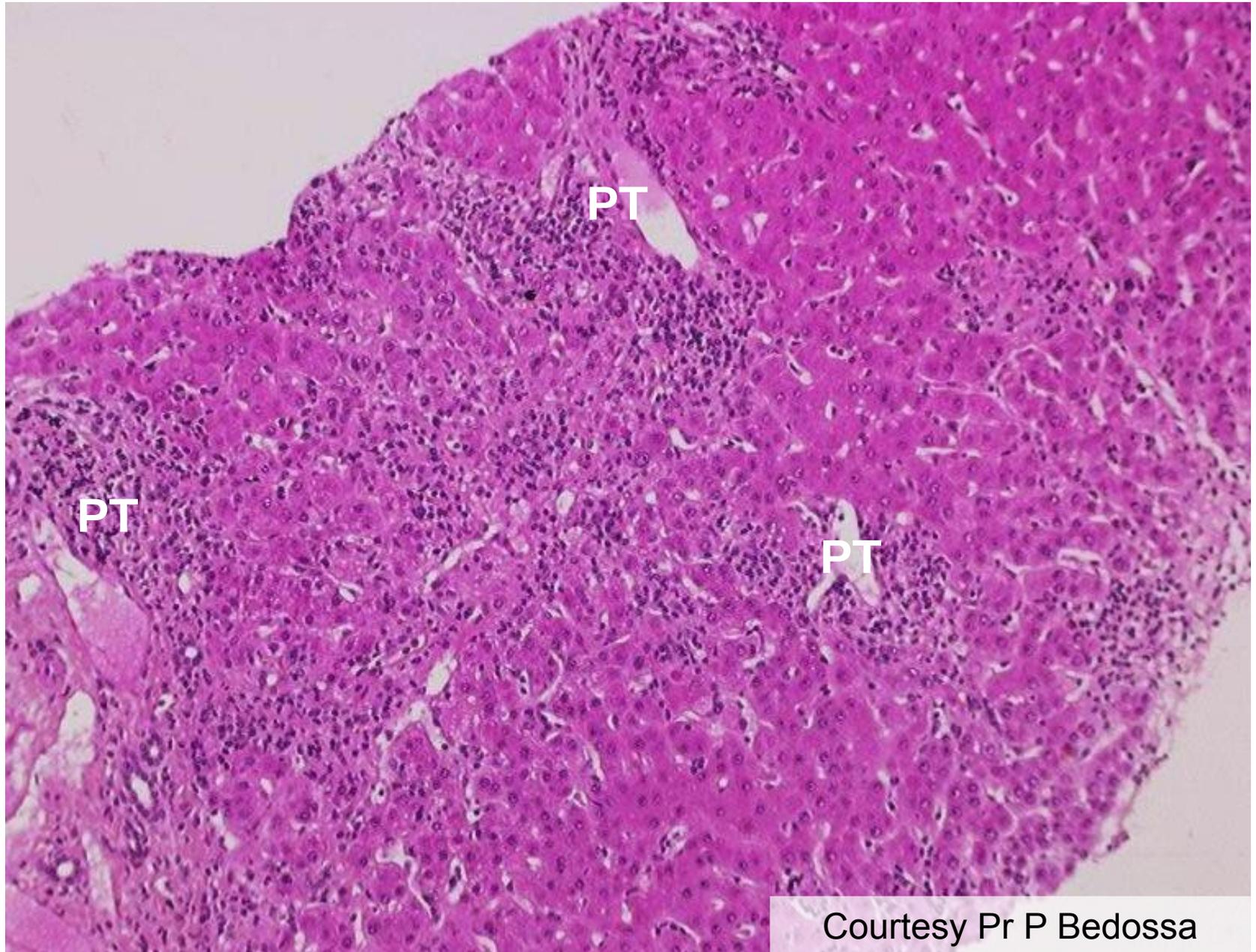
- **Work-up for causes:**

- HBs Ag undetectable
- Anti-HCV Ab undetectable
- Anti-HEV IgM undetectable
- Anti-HAV IgM undetectable
- Ceruloplasmin level normal
- Copper level normal
- IgG 36 g/L (<16g/L)
- Auto-antibodies waiting

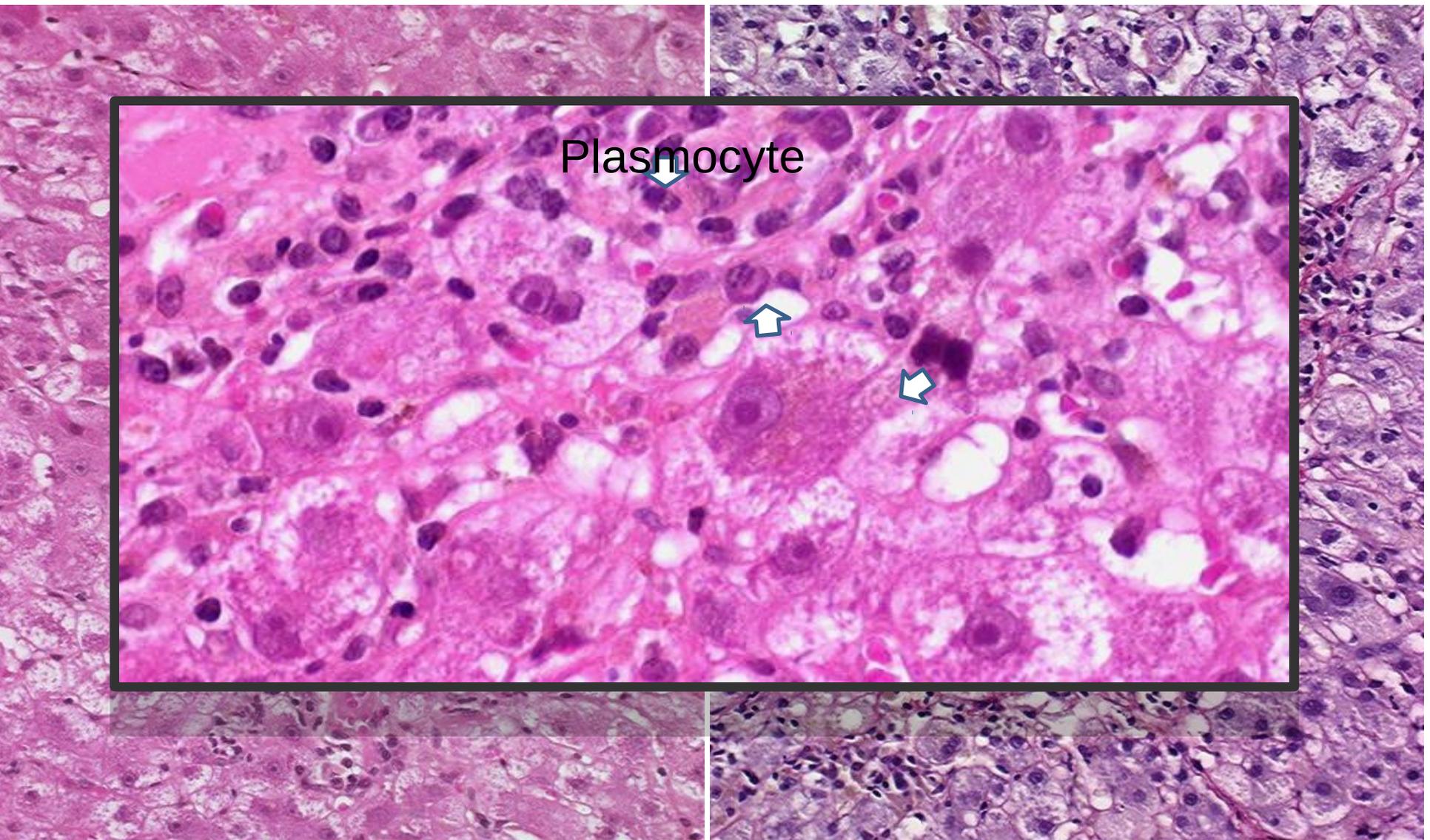
Question

What would you do at that stage?

Liver biopsy



Courtesy Pr P Bedossa



Plasmocyte



- **Work-up for causes:**

- Anti-HAV IgM undetectable
- HBs Ag undetectable
- Anti-HCV Ab undetectable
- Anti-HEV IgM undetectable
- Ceruloplasmin level normal
- Copper level normal
- **IgG 36 g/L (<12 g/L)**
- **Auto-antibodies anti-SMA 1/80**

Question

What treatment would you propose?

Prednisolone 30 mg/day
Azathioprine 50 mg/day



	28/07/2013	26/08/2016
AST (IU/L) (< 31)	1191	30
ALT (IU/L) (<34)	1444	29
ALK (IU/L) (<100)	108	80
GGT (IU/L) (<38)	167	50
Bilirubin ($\mu\text{mol/L}$)	73	17
INR	1.2	1.0
Platelet count	376	290

1 year later:

- Normal AST and ALT levels
- Normal IgG levels
- Azathioprine 100 mg/day
- **Desires a new pregnancy**

Question

Is pregnancy contraindicated?

Question

Regarding therapy, what would you suggest?

1. Interrupt Azathioprine → no treatment
2. Interrupt Azathioprine → give prednisolone
3. Interrupt Azathioprine → give MMF
4. Maintain Azathioprine at the same dose

Question

Regarding therapy, what would you suggest?

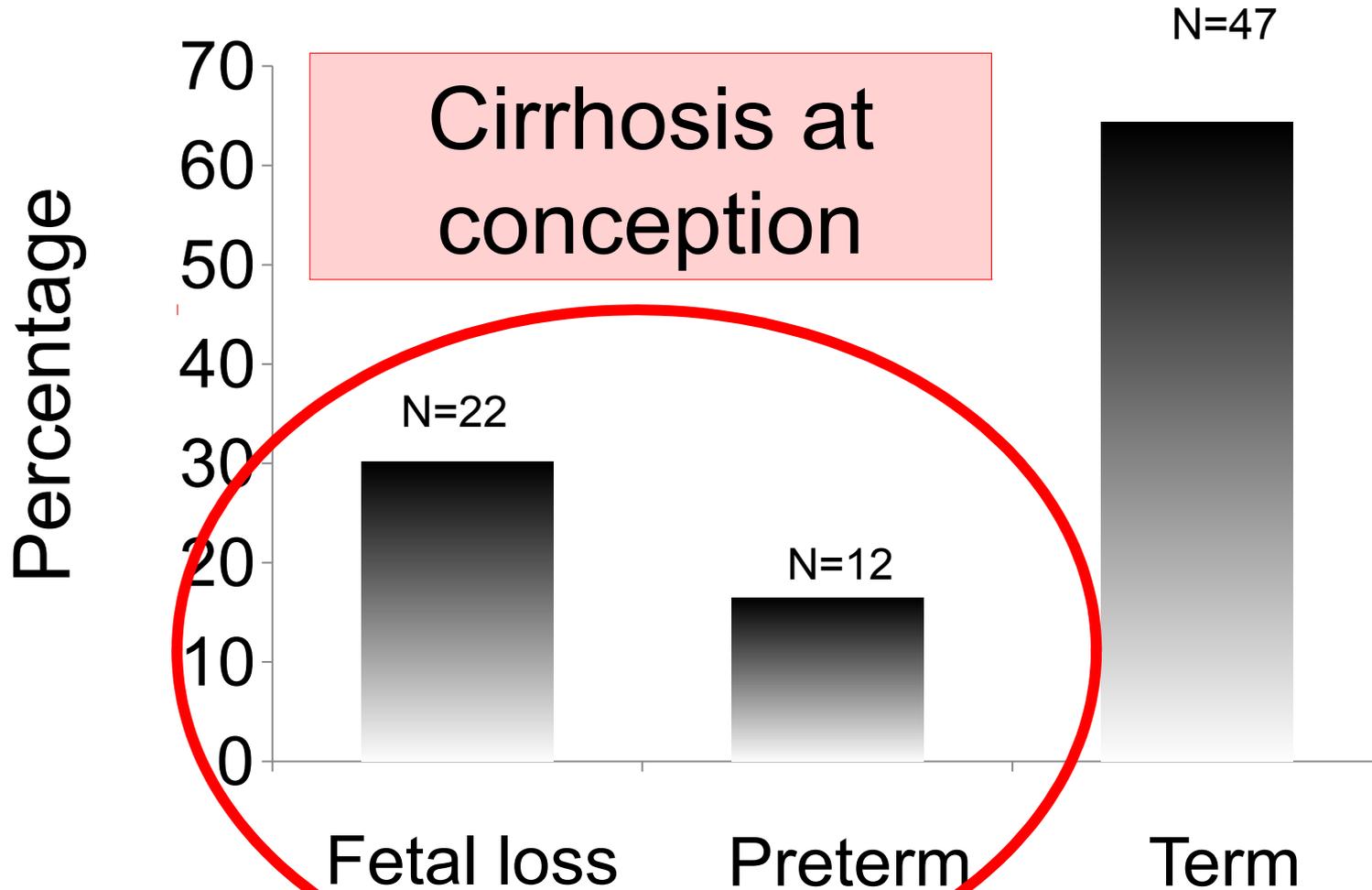
- ~~1. Interrupt Azathioprine \Rightarrow no treatment~~
2. Interrupt Azathioprine \rightarrow give prednisolone
- ~~3. Interrupt Azathioprine \Rightarrow give MMF~~
- 4. Maintain Azathioprine at the same dose**

Question

**The patient wants to know the expected maternal and foetal outcome.
What do you tell her?**

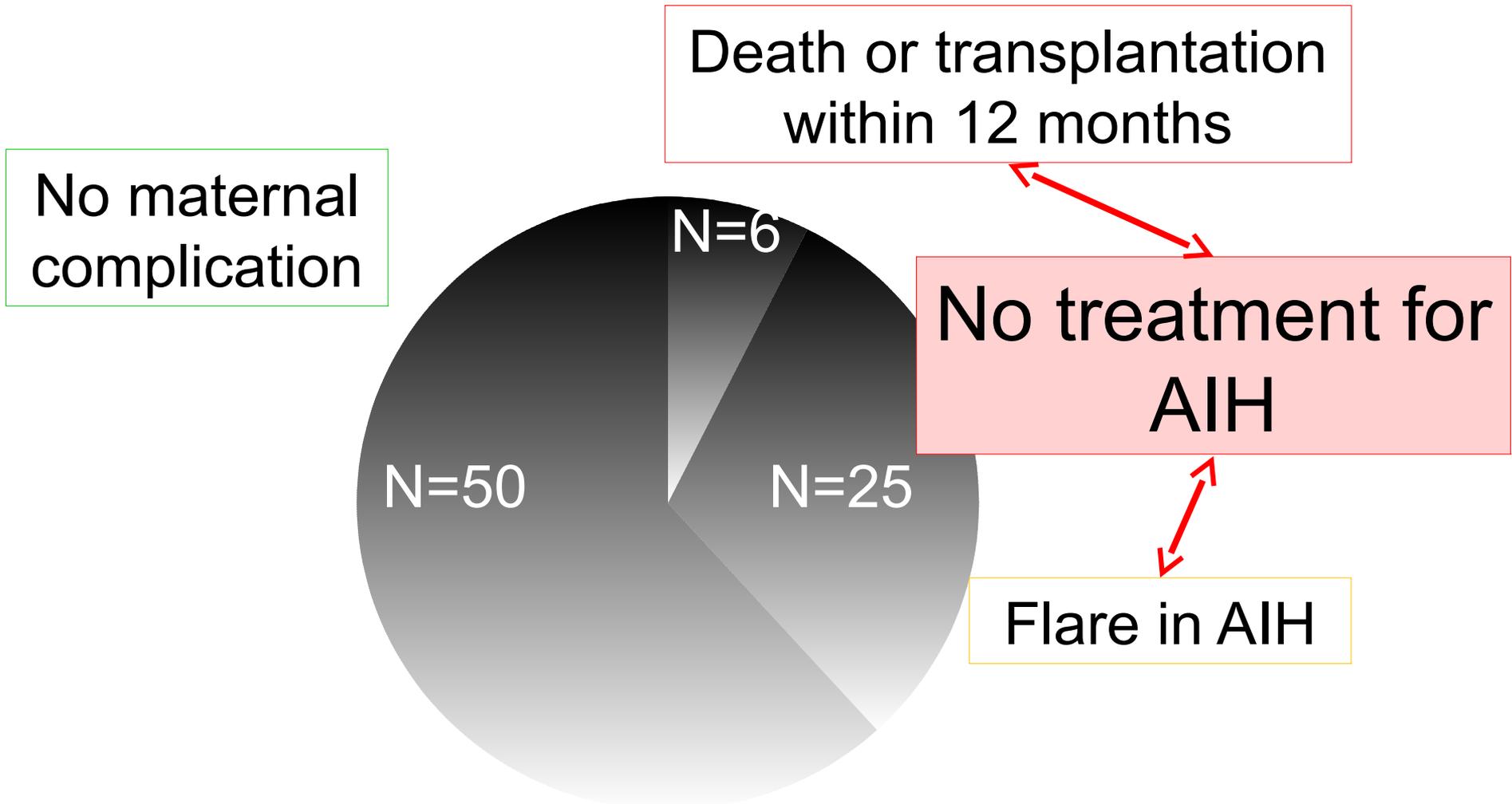
Fetal outcome

81 pregnancies at King's college (1982-2009)



Maternal outcome

81 pregnancies at King's college (1982-2009)



Question

Is breastfeeding possible in this patient with aziathioprine?

Breastfeeding in AIH

- Data derived from use for other conditions
- Considered safe for breastfeeding (small amounts of metabolite detected in breastmilk)

Take home messages

- Controlled AIH is neither a contraindication to pregnancy nor to breastfeeding
- Maintenance of azathioprine +/- predniso(lo)ne
- Mild flares can occur in the 1st trimester and in particular after delivery and may require transient increase in immunosuppression
- MMF is contraindicated in pregnancy

Case 2

57 year-old woman, coming to emergency department for jaundice

- **Medical history**

- Lupus erythematosus
- No medication or substance abuse
 - No alcohol

- **Physical examination**

- 61kg; 1.68 m
- Jaundice; no hepatic encephalopathy

Laboratory results

	05/03/2009
AST (IU/L) (< 31)	2981
ALT (IU/L) (<34)	3685
ALK (IU/L) (<100)	339
GGT (IU/L) (<38)	565
Bilirubin ($\mu\text{mol/L}$)	292
INR	2.2
Platelet count	165

- **Ultrasound:** irregular liver surface; No ascites
- **No hepatitis A, B, C or E virus infection**
- **Anti-antinuclear Ab: 1/320**
- **γ -globulin level: 9 g/L (normal < 12)**
- **Liver biopsy:**
 - Massive hepatocellular necrosis
 - Mild inflammatory infiltrate
 - No cirrhosis

Question

What do you propose?

Prednisolone 30 mg/day
Azathioprine 50 mg/day



	05/03/2009	20/03/2009
AST (IU/L) (< 31)	2981	297
ALT (IU/L) (<34)	3685	509
ALK (IU/L) (<100)	339	347
GGT (IU/L) (<38)	565	402
Bilirubin ($\mu\text{mol/L}$)	292	614
INR	2.2	2.4
Platelet count	165	150



Prednisolone 30 mg/day
Azathioprine 50 mg/day

	05/03/2009	20/03/2009
AST (IU/L) (< 31)	2981	295
ALT (IU/L) (<34)	3685	50
ALK (IU/L) (<100)	339	342
GGT (IU/L) (<38)	565	32
Bilirubin (μmol/L)	292	321
INR	2.2	2.1
Platelet count	165	15

Emergency liver transplantation

↑ Metabolic encephalopathy

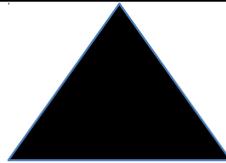
Severe forms of AIH

Can respond and
be controlled

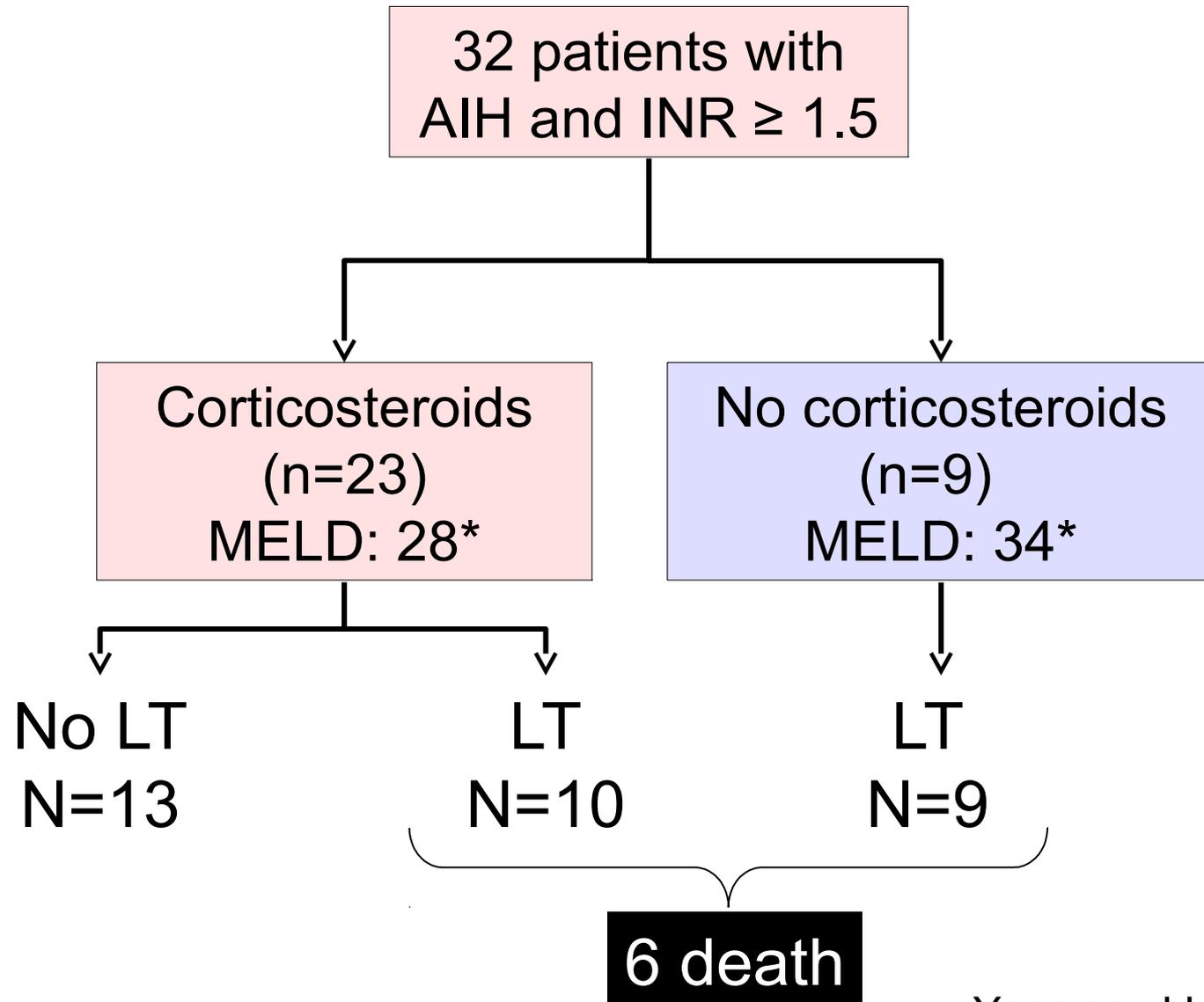
Risk of severe
sepsis

In favor of steroids

Against steroids



Severe forms of AIH



Severe forms of AIH

- All patients should be considered for a trial of corticosteroids at the earliest
- Failure to improve serum bilirubin or MELD-Na within 7 days: strong negative prognostic value → consider LT

- The patient improved and was discharged from hospital 1 month later
- You see the patient 4 mo after transplantation
- Liver blood tests are normal

Question

**How do you manage
immunosuppressive therapy?**

AIH following liver transplantation

- Recurrent AIH: 20–25% of cases
- Usually managed by ↑ or re-instituting corticosteroids

Case 3

61 year-old woman, referred by a gastroenterologist for abnormal liver blood tests

- **Medical history**

- Crohn's disease treated with Azathioprine (not tolerated), then Infliximab
- No medication or substance abuse
 - No alcohol

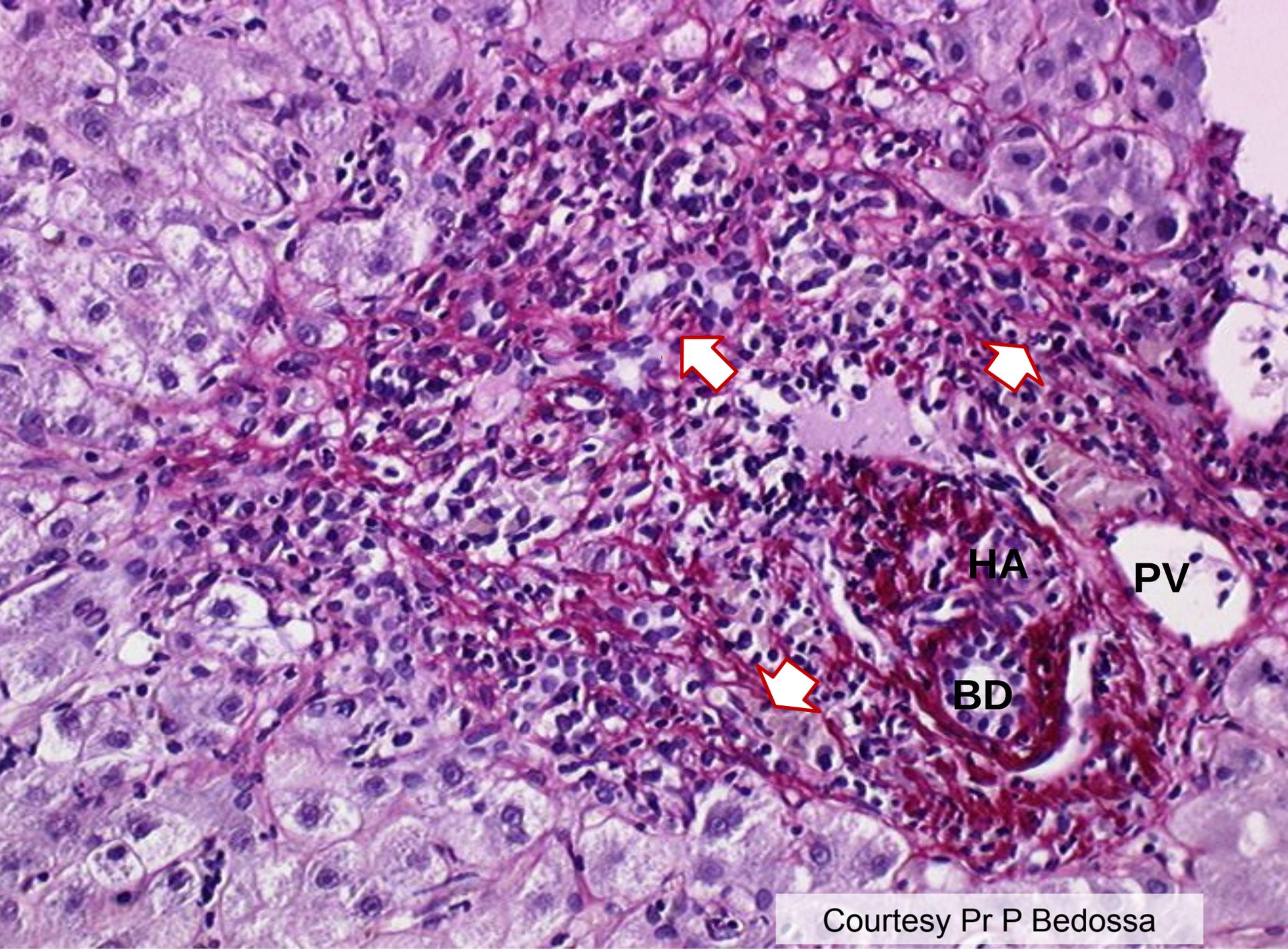
- **Physical examination**

- Normal

	25/08/2016
AST (IU/L) (< 31)	56
ALT (IU/L) (<34)	28
ALK (IU/L) (<100)	127
GGT (IU/L) (<38)	68
Bilirubin ($\mu\text{mol/L}$)	14
INR	1.63
Platelet count	125



- **No hepatitis A, B, C or E virus infection**
- Anti-antinuclear Ab: 1/160
- γ -globulin level 24,5 g/L (normal < 12)
- **Transjugular liver biopsy:**
 - Hepatic venous pressure gradient: 22 mm Hg
 - Advanced fibrosis
 - Dense plasma cell-rich lymphoplasmocytic infiltrates



HA

PV

BD

Courtesy Pr P Bedossa

Question

What do you propose to this patient not tolerating azathioprine?

- No treatment since ALT levels normal
- Budesonide
- Prednisolone
- MMF
- Tacrolimus

Should AIH be systematically treated?

Mild disease

- ALT <3x ULN
- Mild histological activity
- No advanced fibrosis



Treatment can optional, taking into account:

- age
- co-morbidity
- patient preference