



Management of acute alcoholic hepatitis

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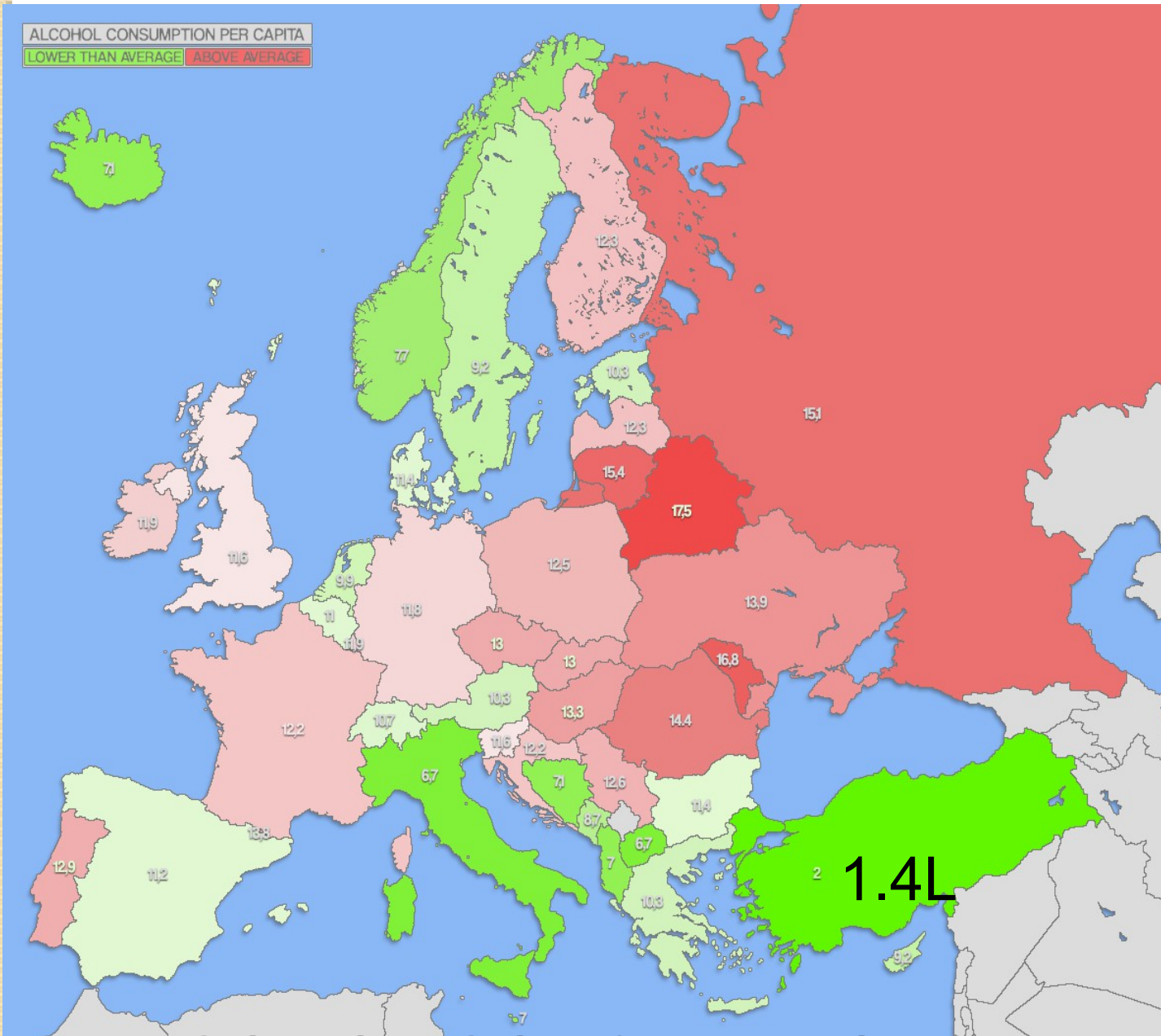
Marmara University Hospital, Istanbul/TURKEY

5 th European Young Hepatologists Workshop

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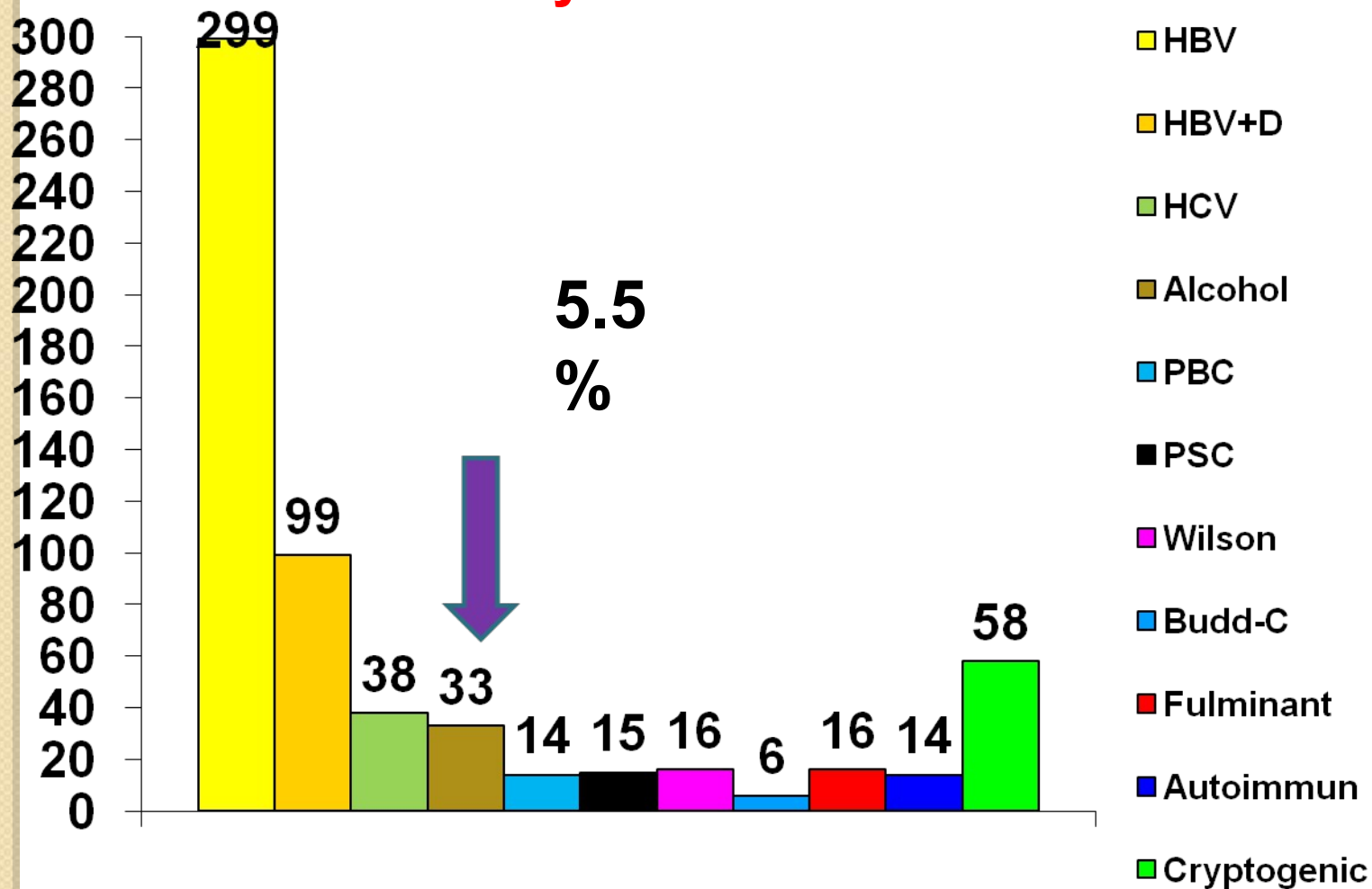
ALCOHOL CONSUMPTION PER CAPITA

LOWER THAN AVERAGE ABOVE AVERAGE





ALCOHOL CONSUMPTION PER CAPITA IN EUROPE


Etiology of liver disease in a transplant centre in Turkey





Alcohol 33 cases over 606


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- A 32 year old man, worker at shipyard
 - Admitted to hospital with one week history of nausea, vomiting, mild abdominal pain, and jaundice


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- No significant chronic disease
 - 80-100g/day alcohol consumption since 15 years
 - Nonsmoker, living alone

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- Denies any use of medication or herbal medicine or IV drug or mushroom ingestion
 - He has been in prison for 20 months
 - Family history irrelevant


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- In 2012 he applied to a state hospital with same complaints
 - **AST:583 U/L**
 - **ALT:494 U/L**
 - **ALP:143 U/L**
 - **GGT:88 U/L**

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- In 2012;
 - Viral serology
 - AntiHbs positive, others negative
 - Autoimmune markers were negative
 - Hepatobiliary USG: normal
 - Upper abdominal MRI:liver paranchyme is heterogenous
 - Lost for follow-up


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- On current physical exam, he appears quite ill,
 - BMI:21.2
 - Fully oriented, alert and cooperated
 - No flapping tremor
 - The sclerae are icteric
 - No spider anjioma
 - No clubbing


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- No fever
 - Pulse: 80/min BP: 110/70 mmHg
 - The lung, heart exam unremarkable
 - Abdominal exam; soft, mild tenderness on right upper quadrant
 - No hepatomegaly or splenomegaly
 - Neurological exam unremarkable


- At the last admission;
 - **AST:1781 U/L ALT:2758 U/L**
 - **ALP:149 U/L GGT:449 U/L (7-49)**
 - **LDH:560 U/L**
 - **Total bilirubin:17.11mg/dl D.**
bil:9.05mg/dl
 - **Total protein:6.71 g/dl Albumin:4.15**
g/dl


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- PT/INR: 16/ **1.38**
 - WBC: 7100 / μ L
 - Hb: 15.8 g/dL
 - MCV: 101.1 fL
 - Plt: 148000 / μ L


- Viral serology;
 - HbsAg negative
 - AntiHbs **positive**
 - AntiHCV negative
 - AntiHAV IgM negative
 - AntiHAV IgG **positive**
 - Anti HIV negative
 - Anti Hep E igG negative
 - Anti Hep E IgM negative


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- Seruloplasmin N
 - ANA, ASMA, AMA, LKM are negative
 - Transferrin saturation is normal


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- Blood and urine cultures negative
 - Renal functions N

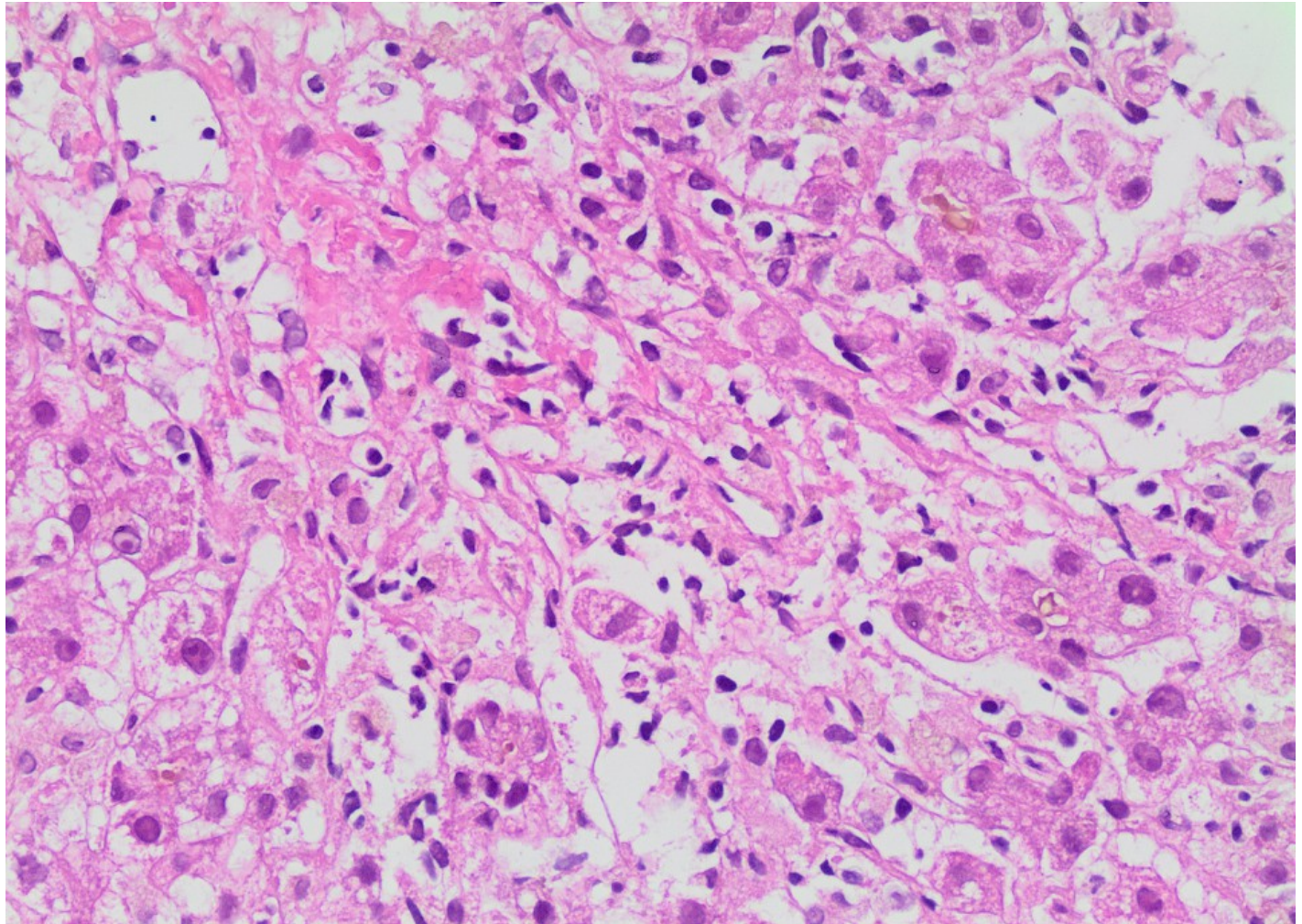
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- Hepatobiliary USG : liver total span 14cm
Paranchyme is homogenous No biliary duct dilatation
 - Portal Doppler USG: Portal vein and splenic vein diameter N and patent

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- Would you ask for any further investigation?
 - Any advice?
 - Any question?

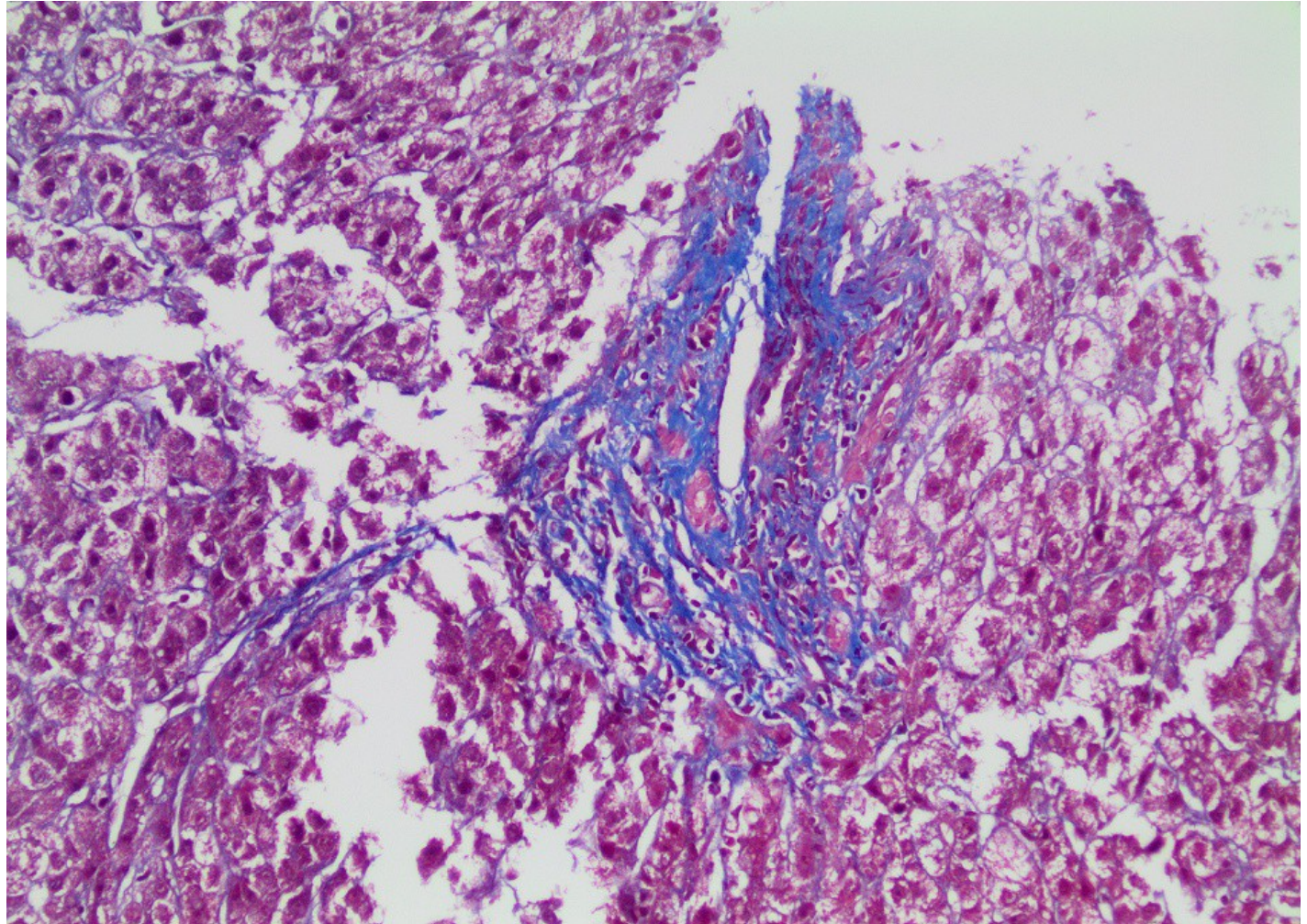
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- **Summary**
 - Excessive alcohol use
 - Elevated transaminases and GGT
 - Jaundice
 - No other causes of liver injury

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- Our pre-diagnosis was alcoholic hepatitis
 - Maddrey's Discriminant Function=35.4
 - Performed liver biopsy

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- **Acute event**
 - Pericentral necrosis
 - Biliary canalicular stasis
 - Mild inflammatory infiltration at portal region
 - Microsteatosis
 - Ballooning degeneration
 - **Chronic damage**
 - Periportal fibrosis

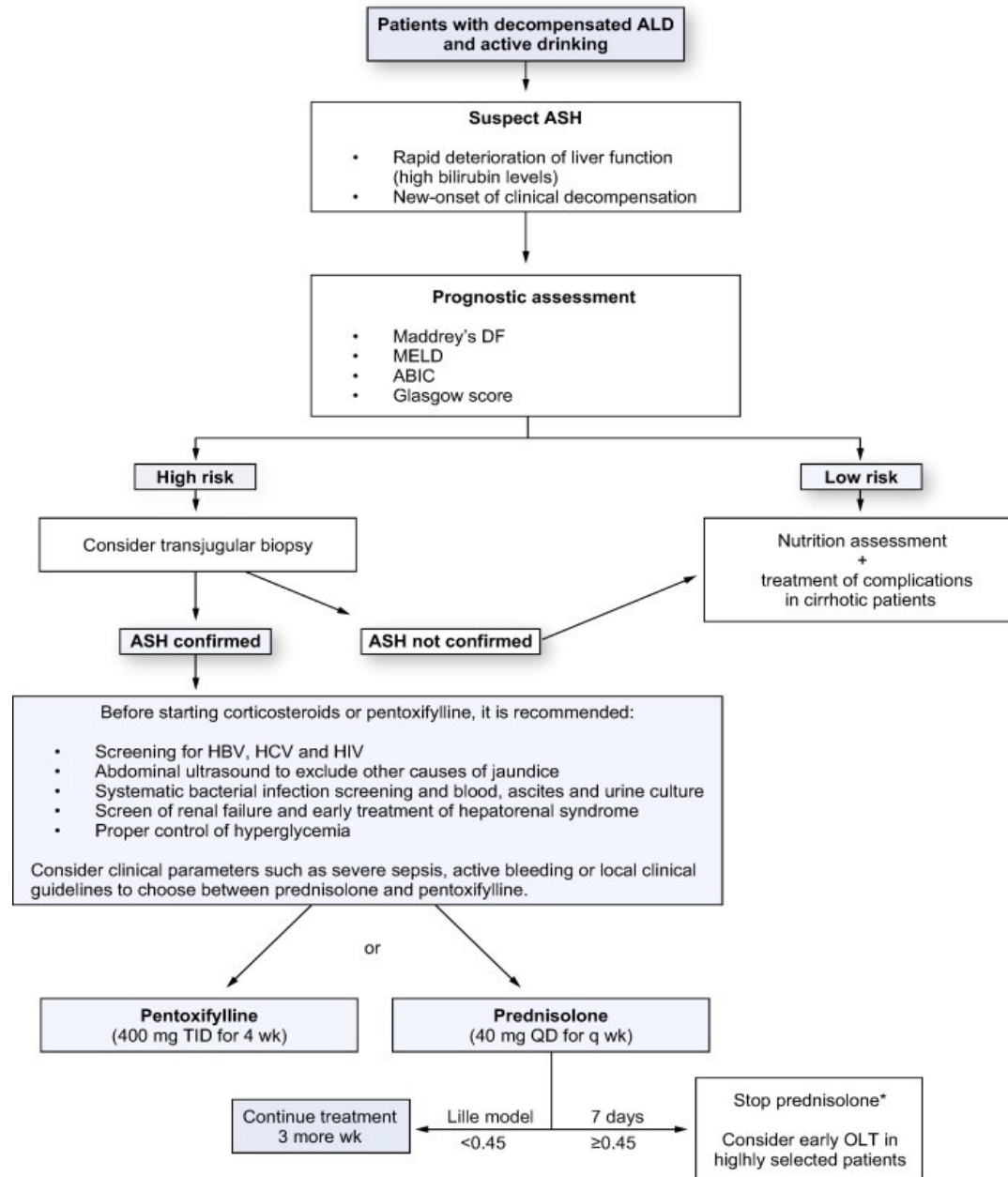


Necrosis around central vein and biliary canicular stasis




Trichrome stain- periportal fibrosis

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- What should be the next step?



- Started prednisolone 40mg/day

- 7 days later
 - ALT:270 U/L
 - AST:104 U/L
 - GGT:191
 - T. Bil: 4.33 mg/dL
 - PT:12.9 sec INR:1.04
 - Lille score:0.3982 (<0.45)

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- He was well and discharged after 2 weeks of treatment
 - After 4 weeks prednisolone tapered

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- **Is our management correct??**

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- According EASL and AASLD guideline

- **YES**

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- **BUT...**

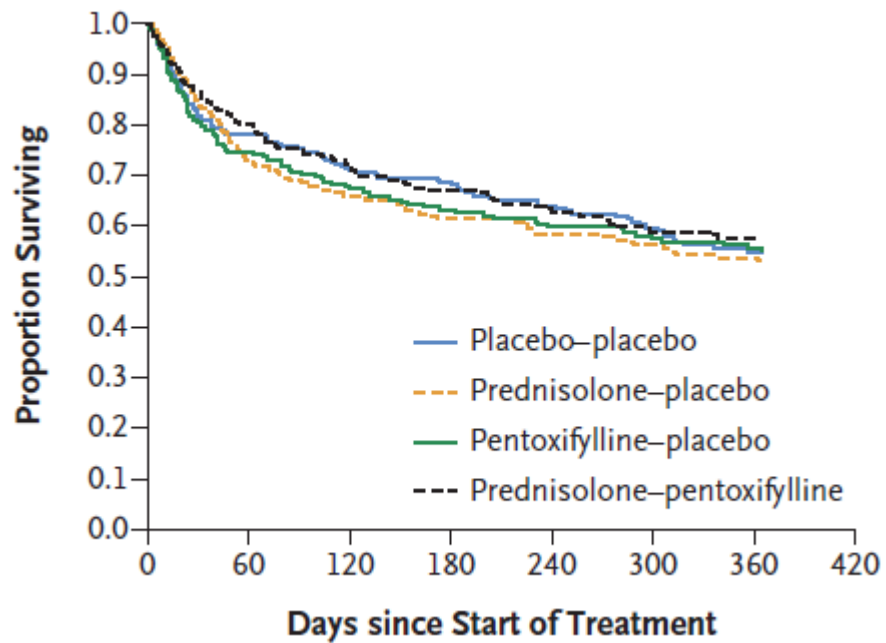
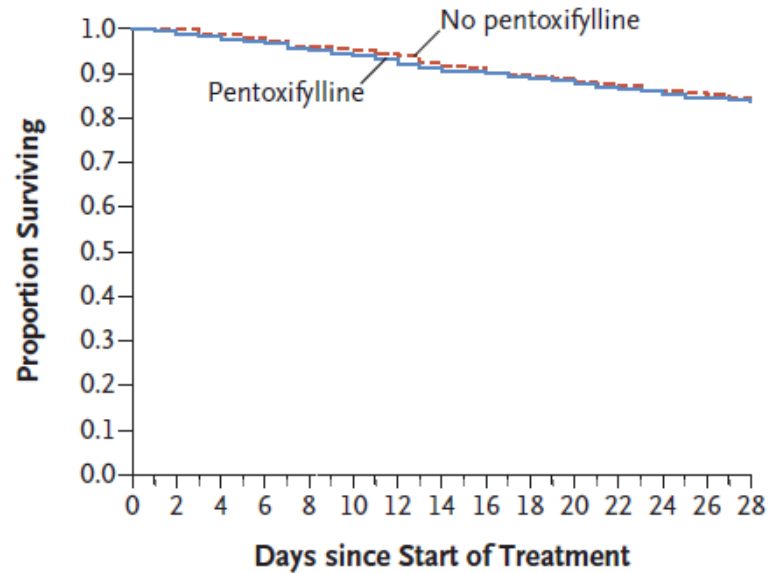
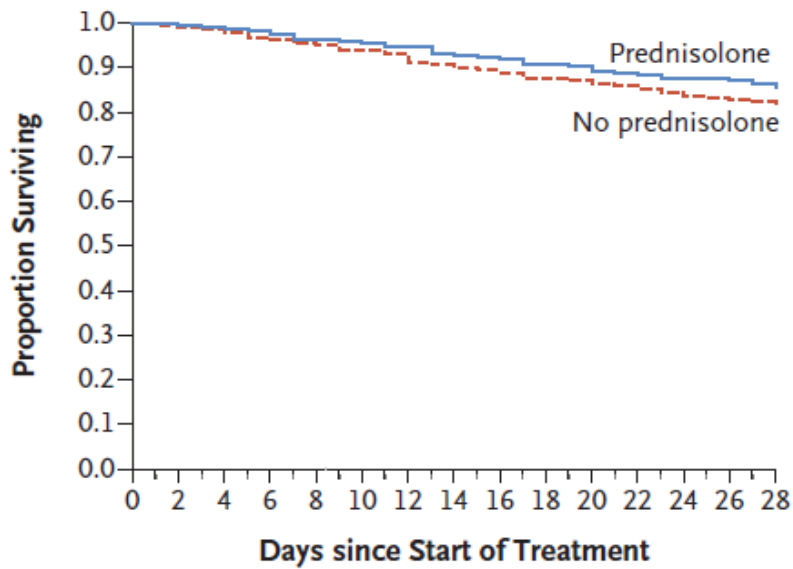
STOPAH STUDY


- Prednisolone and pentoxifylline are both recommended for the treatment of severe alcoholic hepatitis, but uncertainty about their benefit persists
 - Thursz MR, Richardson P, Allison M, et al. Prednisolone or pentoxifylline for alcoholic hepatitis. N Engl J Med 2015;372:1619-1628


Table 2. Mortality at 28 Days, 90 Days, and 1 Year.*


End Point	Prednisolone	No Prednisolone	Pentoxifylline	No Pentoxifylline	Prednisolone		Pentoxifylline	
					Odds Ratio (95% CI)	P Value	Odds Ratio (95% CI)	P Value
28-Day mortality — no./total no. (%)	73/526 (14)	95/527 (18)	85/518 (16)	83/535 (16)	0.72 (0.52–1.01)	0.06	1.07 (0.77–1.49)	0.69
90-Day mortality or liver transplantation — no./total no. (%)	144/484 (30)	141/484 (29)	139/478 (29)	146/490 (30)	1.02 (0.77–1.35)	0.87	0.97 (0.73–1.28)	0.81
1-Year mortality or liver transplantation — no./total no. (%)	210/371 (57)	211/376 (56)	205/365 (56)	216/382 (57)	1.01 (0.76–1.35)	0.94	0.99 (0.74–1.33)	0.97

* The interaction between interventions was investigated as a secondary analysis.



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- Pentoxifylline did not improve survival in patients with alcoholic hepatitis.
 - Prednisolone was associated with a reduction in 28-day mortality that did not reach significance and with no improvement in outcomes at 90 days or 1 year

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- **Meta-analysis (including 22 randomized controlled trials)**
 - Singh S, Murad Mhet al. Comparative Effectiveness of Pharmacological Interventions for Severe Alcoholic Hepatitis:A Systematic Review and Network Meta-analysis. *Gastroenterology*. 2015 Jun 16.

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- In patients with severe AH corticosteroids can reduce short-term mortality.
 - The addition of NAC, but not pentoxifylline may be superior to corticosteroids alone for reducing short term mortality
 - Low quality evidence showed that pentoxifylline also decreased short-term mortality
 - No treatment decreases risk of medium-term mortality.



Thanks for your attention