PTH-093 INCREASING AZATHIOPRINE DOSE WITH METABOLITE MONITORING IN AIH

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Introduction Initial treatment of AIH, involves prednisolone plus azathioprine (AZA) 1 mg/kg/day. Blood levels of active AZA 6-thioguanine (6-TGN) and 6-methyl-mercaptopurine (6-MMP) metabolites are determined by activity of thiopurine methyl transferase (TPMT). High metabolite levels are associated with efficacy (6-TGN) and toxicity (6-TGN and 6-MMP) (Dhaliwal Hepatology, 2012. 56:1401-8).

Aim To see if AZA metabolite monitoring could optimise AZA dose and improve histological remission rates.

Methods In 26 patients with AIH (1999 International Group Criteria, presenting 2013–2016), we aimed to increase AZA dose from 1 to 2 mg/kg after 3 months, with metabolite monitoring, to achieve 6-TGN levels between 250–500 pmol/8 × 10⁸ RBCs and 6-MMP levels <5000 pmol/8 × 10⁸ RBCs. 13 patients underwent repeat liver biopsy after two years treatment.

Results 5 patients did not achieve a dose of 2 mg/kg/day AZA (raised 6-TGN (n=3), nausea (n=1), metabolites in target range on lower dose (n=1)). In 15 of the other 21 patients, AZA was initially increased to 2 mg/kg/day but had been reduced by the end of follow-up, with corresponding rises and then falls in 6-TGN and 6-MMP land in mean cell volume (MCV) (table 1). Reasons for dose reduction included: metabolite levels above target range (6-MMP: n=4, 6-TGN: n=4, both: n=1), nausea (n=3), malignancy (n=1) and leucopenia (n=1). In 4 patients who developed nausea on AZA, 6-TGN levels were (601, 4 34 528 and 434). No patients developed hepatotoxicity.

Serum ALT normalised in 23 and 25 patients within 6 and 12 months respectively. However, only 7 out of 13 patients who had follow up biopsy achieved histological remission (similar to our previous experience (Dhaliwal, Am J Gastroenterol, 2015; 110 993–999)). 6-TGN levels did not differ between those who did and did not attain remission (median 345 v 275; p=0.295).

Abstract PTH-093 Table 1

	Dose AZA (mg/kg)	6-TGN (pmol/8 × 10 ⁸ RBCs)	6-MMP (pmol/8 × 10 ⁸ RBCs)	MCV fL (80–98)
Initial dose (1 mg/kg)	0.94 (0.62–1.08)	223 (119–785)	427 (100–1960)	92.5 (66.4–105.8)
After dose increase	1.84 (0.89–2.14)	350 (143–802)*	3661 (100–15960)*	96.9 (67.2–112.1)**
End of follow-up	1.3 (0.59–2.14)	322 (123–482)+	900 (100–3753)++	94.15 (66.3–111.9)+++

*,**p=0.002 and p=0.004 vs. initial dose.

+, ++, +++p=0.002, 0.004 and 0.110 respectively vs. after dose increase

Conclusions Increasing AZA dose from 1 to 2 mg/kg/day after 3 months, with metabolite monitoring was (a) limited by high metabolite levels and side effects and (b) did not Result in higher rates of remission, compared to standard therapy.

PTH-094 ROLE OF MYCOPHENOLATE MOFETIL (MMF) IN PATIENTS SWITCHING FROM AZATHIOPRINE DUE TO INTOLERANCE IN AIH

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Introduction Mycophenolate mofetil (MMF) is an alternative steroid-sparing agent in patients with AIH who either respond inadequately to, or are intolerant of azathioprine (AZA). Short-term Results seem better in AZA intolerant than in AZA sub-responsive patients (Hennes 2008 Am. J. Gastro. 103:3063, Sharzei 2010 Can. J. Gastro. 24: 588). There are few data regarding histological response and longer-term outcome in patients switched to MMF.

Methods Study of consecutively recruited patients with AIH (1999 International Group Criteria) managed 1987–2016. Patients also received prednisolone and were followed for >6 months from diagnosis. Results in AZA intolerant patients who switched to MMF within 6 months (23) were compared to those who continued AZA (196), including those who switched to alternative immunosuppression (including MMF) due to AZA unresponsiveness but not intolerance.

Abstract PTH-094 Table 1

	Switched to MMF due to AZA intolerance (23)	AZA continued/changed due to unresponsiveness (196)	p
Men (number (%))	3 (13%)	39 (20%)	0.401
Age at diagnosis*	63 (19.4–80.4)	57 (2.5–85.2)	0.089
Follow-up (years)*	4.0 (1.0–17)	9.8 (0.5–29)	
Presentation:	4/22	60/192	0.858
cirrhosis	2 (9%)	26/193 (13.5%)	0.383
decompensation			
Serum ALT normal by 1 year	21/22 (95%)	179/185 (96%)	0.095
Biopsy 1: Necro-inflammatory (NI) score*	10 (2–16) n=23	12 (1–18) n=173	0.376
Fibrosis stage*	2 (1–6) n=23	3 (0–6) n=148	0.235
Biopsy 2: NI score*	4 (0–12) n=18	4 (0–14) n=122	0.327
Fibrosis stage*	2.5 (0–5) n=18	3 (0–6) n=120	0.190
% Histological remission on FU biopsy	9/18 (50%)	85/178 (48%)	0.746
All-cause death/transplant: 5 year	9%±9%	14%±2%; 25%±3%	ns.
10 year	9%±9%		ns.
Liver death/transplant: 5 year	0%	7%±2%; 11%±2%	ns.
10 year	0%		

*Median (95% CI) ns.=not significant

Compared to those continuing AZA, patients switching to MMF due to AZA intolerance had a trend towards lower all cause death/transplant (p=0.11) and liver death/transplant (p=0.18) rates. Cox regression analysis (including age,

cirrhosis and decompensation at presentation as covariates) showed similar outcomes in both groups. Seventeen of the 23 patients continued MMF to end of follow-up and 6 discontinued MMF (lack of efficacy 4, successfully restarting of AZA 1 and cause unknown 1).

Conclusions Patients switching to MMF because of AZA intolerance do not differ from those continuing AZA in regard to: (a) normalisation of serum ALT (b) necro-inflammatory and fibrosis scores on follow-up biopsy and (c) 5- and 10 year mortality. This supports use of MMF as a steroid sparing agent in AZA intolerant patients.

PTH-095 MINIMISING NON-HEPATIC COMPLICATIONS FOLLOWING LIVER TRANSPLANT: EVALUATION OF PRACTICE FROM A SINGLE REFERRAL CENTRE

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Introduction Non-hepatic complications of liver transplant are common and associated with significant morbidity and mortality. The American Association for the Study of Liver Diseases (AASLD) practice guideline on the long-term management of liver transplant recipients aims to assist with modifying the risk of these complications. There is currently no equivalent European guideline. We analysed clinical records from a large UK centre to ascertain whether post-transplant care was comparable to the AASLD standards of care.

Methods Consecutive patients who had been transplanted at two UK centres following referral from a single UK centre between 1988 and 2016 were analysed retrospectively. All clinical documentation and test Results over a 12 month period were analysed. Outcome measures were aligned with AASLD guidelines, including; screening for diabetes, chronic kidney disease, hypertension, dyslipidaemia and osteopenia.

Results 48 patients (29 female/19 male) were included in analysis. Mean age was 57 (SD 13.4). Median time since transplantation was six years (IQR 3–13). 10/17 (58.8%) diabetic patients met the recommendation of having their HbA1c measured in the preceding 3 months. Of non-diabetic patients, 15/29 (51.7%) underwent annual fasting glucose (or HbA1c) during the study period. 48/48 (100%) of patients had evidence of renal function monitoring within the last 12 months. Yearly urine albumin-creatinine ratio testing was performed in 10/48 (20.8%). Blood pressure was measured in 13/48 (27%) of patients. Of those, 7/13 (53.8%) had a satisfactory blood pressure of <130/80 mmHg. The recommendation of annual blood lipid measurement took place in 30/48 (62.5%) and annual Vitamin D in 20/48 (41.7%). 8/18 (44.4%) of patients transplanted between 2005 and 2012 underwent a Dual Energy X-ray Absorptiometry (DEXA) scan within 5 years. 12/14 (85.7%) of osteopenic patients were receiving the recommended calcium supplementation, while 2/14 (14.3%) of them were receiving annual Bone Mineral Density testing.

Conclusion Liver transplant recipients in this study did not receive a consistent approach to screening for common non-hepatic complications. Although there was often evidence that these complications were appropriately considered, there was wide variability between patients. The level of monitoring for patients, who are high risk for cardiovascular and metabolic disease, was insufficient overall. Consideration should be made to adoption of models of care which provide standardised recommendations for patients in the post-transplant phase. This

may lead to a more rigorous and robust approach to patients' long-term management, which in turn may reduce late morbidity and mortality.

PTH-096 ANTIBIOTIC USE IN PRIMARY AND SECONDARY PROPHYLAXIS OF SPONTANEOUS BACTERIAL PERITONITIS FOR LIVER CIRRHOSIS PATIENTS

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Introduction Spontaneous Bacterial Peritonitis (SBP) is associated with 30%–50% mortality within 1 year and 70% chance of recurrence. EASL guidelines state prophylactic antibiotics should be given to patients with proven SBP (secondary prophylaxis) and patients with low total protein count (<15 g/L) in ascitic fluid with no prior history of SBP (primary prophylaxis). We audited whether these guidelines were followed and the associated mortality risk.

Methods Data on all ascitic taps for patients with confirmed liver cirrhosis were collected retrospectively over a 12 month period.

SBP patients were assessed as to whether secondary prophylactic antibiotics were commenced. The same investigations were carried for bacterascites (BA) patients, including whether BA was treated. Previous ascitic taps were analysed for low total protein count (<15 g/L).

Cirrhotic patients without SBP or BA had their ascitic total protein count measured. If less than 15 g/L we assessed whether primary prophylactic antibiotics were started. We assessed mortality rate for all patients.

Results Data collection period was from 15/10/2016 to 15/10/2017 yielding 860 ascitic taps. Of the 89 patients with liver cirrhosis; infection was identified in 33 patients; 16 patients with SBP and 17 patients with BA.

Gram negative organisms were identified in 4/7 with SBP and 7/17 with bacterascites.

Secondary prophylaxis was started in 10 of 16 (62.5%) patients with SBP. Of the patients where secondary prophylaxis was not started 3 of 6 (50%) died within 12 months. All 16 patients had a previous tap within 12 months (mean 3.4 months) with ascitic protein count less than 15 g/L. Primary prophylaxis was not started for any patients.

10 of 17 (58%) BA patients received intravenous antibiotic treatment. From this group 6 of 10 (60%) received secondary prophylaxis. 6 of 17 (35%) patients died within 12 months and none of these patient commenced secondary prophylaxis. All 17 patients had a previous tap within 12 months (mean 4.2 month) with ascitic protein count less than 15 g/L.

Of the 56 patients without SBP or BA 33 (58.9%) had an ascitic protein count of less than 15 g/L. No patients were started on primary prophylactic antibiotics. 6 of 33 (18.1%) patients with low protein ascites subsequently developed SBP when reviewed prospectively. No patients with ascitic protein count greater than 15 g/L have developed SBP or BA. 16 of 33 (48.4%) patients with low protein ascites died over the next 12 months.

Conclusion 66 of 89 (74%) patients had low protein ascites and 50% (33 of 66) subsequently developed either SBP or BA within 12 months. This highlights the importance of primary prophylactic antibiotics for patients with low protein ascites in the prevention of SBP and BA.