treatment. 72 patients (65%) attained histological remission. Comparing these with the 37 patients not in histological remission, there were no significant differences in age, gender, presenting serum ALT, or in NIS or fibrosis stage at diagnostic biopsy. Neither were there differences in either (a) starting or cumulative dose of prednisolone or azathioprine (either absolute or corrected for body weight) or (b) time to achieve normal serum ALT. Only serum globulin at presentation was lower in those who achieved histological remission (42 vs 49 g/l, p = 0.01). On multivariate analysis, NIS at follow-up biopsy was independently associated with serum ALT at time of biopsy (p = 0.001) but with none of above baseline, treatment or early response-related variables.

Conclusion We could not identify baseline or treatment-related variables associated with (and thus, potentially predictive of) histological remission. Specifically, we could not establish that histological remission was related to either time to serum ALT normalisation or to starting or cumulative dose of prednisolone.

Competing interests None declared.

REFERENCES

PTU-035 AZATHIOPRINE METABOLITE CONCENTRATIONS IN AUTOIMMUNE HEPATITIS: RELATIONSHIP TO DISEASE REMISSION

doi:10.1136/gutjnl-2012-302514c.35

Introduction Azathioprine (AZA) is used to maintain remission in AIH but is sometimes ineffective. AZA is a pro-drug and formation of active thioguanine nucleotide (TGN) metabolites varies widely. Competing with TGN formation is drug methylation, catalysed by thiopurine methyltransferase (TPMT). The methylated drug is inactive, but the methyl-mercaptopurine nucleotide metabolites (MeMPs) may not be. Previous studies, based mainly on single measurements, have not shown a relationship between TGN levels and clinical efficacy. We assessed the relationship between mean of several metabolite levels (TGNs and MeMPs), and therapeutic response in AIH patients prescribed a constant dose of AZA for remission maintenance.

Methods Erythrocyte TGNs and MeMPs were measured on serial blood samples by established techniques over 2 years. Average TGNs (avTGNs) and MeMPs (avMeMPs) concentrations for each patient at a constant AZA dose were analysed. Therapeutic response was defined as maintenance of remission on a given dose of AZA. Relapse was defined by the IAIHG criteria (ALT > 2 × ULN or symptoms + ALT > ULN).

Results 349 samples from 68 patients (median 5, range 2–9, per patient) were analysed. Median avTGN concentration was 220 pmol/8×10^6 RBC (range 66–888) at a median dose of 1.9 mg/kg/day. AZA dose (mg/kg/day) correlated positively with avMeMPs (r = −0.38, p = 0.001) but not with avTGN (r = −0.06, p = 0.6). Patients in whom remission was maintained compared to those who relapsed had higher avTGN concentrations (Abstract PTU-035 table 1) but avMeMPs concentrations were not significantly different. Mean ALT (both over the metabolite monitoring period and over the time on the constant AZA dose) correlated negatively with avTGN (r = −0.322, p = 0.007 and r = −0.542, p = 0.004) but not with avMeMPs. Patients who maintained a normal ALT had higher avTGN concentration compared to those who did not (median 287 vs 177 pmol/8×10^6 RBC).

Conclusion In patients with AIH maintained on AZA, lower average TGN concentrations are related to development of relapse and to higher ALT.

Abstract PTU-035 Table 1

<table>
<thead>
<tr>
<th>Group 1: Remission maintained, median (range) n = 53</th>
<th>Group 2: Relapse while on treatment, median (range) n = 15</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZA dose, mg/kg/day</td>
<td>1.8 (0.4–2.7)</td>
<td>2.0 (0.9–3.2)</td>
</tr>
<tr>
<td>Time of Dose, months</td>
<td>41 (1–208)</td>
<td>11 (2–216)</td>
</tr>
<tr>
<td>avTGN pmol/8×10^6 RBC</td>
<td>238 (66–888)</td>
<td>177 (67–400)</td>
</tr>
<tr>
<td>avMeMP pmol/8×10^6 RBC</td>
<td>1428 (189–23 798)</td>
<td>1041 (175–18 679)</td>
</tr>
</tbody>
</table>

Competing interests None declared.

PTU-036 MYCOPHENOLATE MOFETIL IN PATIENTS WITH AUTOIMMUNE HEPATITIS AND AZATHIOPRINE INTOLERANCE: HISTOLOGICAL RESPONSE COMPARED TO THAT IN AZATHIOPRINE-TREATED PATIENTS

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Introduction Prednisolone (PRED) in combination with azathioprine (AZA) is commonly used to induce remission in autoimmune hepatitis (AIH). Up to 20% of patients are intolerant of AZA and mycophenolate mofetil (MMF) is often used as an alternative. However there are few data on its ability to induce histological remission and prevent relapse. Therefore, we aimed to evaluate the efficacy of MMF, compared to AZA, in inducing and maintaining remission.

Methods 58 patients with AIH presenting since 2003 were retrospectively studied. All initially received PRED+AZA. Those who developed intolerance to AZA (n = 13, after 1–6 weeks) were switched to MMF (1 (1–2) g/day). Follow-up liver biopsy, obtained after median 25 (12–41) months was assessed in 11 of these patients (MMF group) and 44 patients in whom AZA was continued (AZA group).

Results The two groups were similar with regards to (a) serum ALT at 0, 3, 6, 12, 24 and 36 months, and (b) Ishak necroinflammatory grade at baseline (11 vs 10 in AZA and MMF group respectively, p = 0.6) and follow-up (4 vs 3, p = 0.9) biopsy. 48% of the AZA group and 64% of the MMF group achieved histological remission (p = 0.5). Fibrosis regressed in both groups but regression was greater in the MMF group (Ishak stage 3.2 to 1.7, p = 0.002) compared to the AZA group (3.5 to 2.8, p = 0.02). When attempted, PRED was successfully withdrawn in 7/10 patients in the MMF group, and in 32/37 patients in the AZA group (p = 0.3). After PRED withdrawal, 4/7 patients in the MMF group and 11/32 patients in the AZA group relapsed (p = 0.4). Up to the end of follow-up (71 months for AZA vs 65 months for MMF, p = 0.6) PRED requirement (median 0 vs 2.5 mg, p = 0.8) and relapse rate (median 0 vs 0, p = 0.5) were similar in the two groups.

Conclusion MMF is as effective as AZA, at inducing and maintaining biochemical and histological remission in AIH. It may lead to more regression of fibrosis but this requires further evaluation.

Competing interests None declared.