POSTER PRESENTATIONS

Conclusion: Delaying of azathioprine therapy does not decrease the likelihood of biochemical remission in AIH and might be associated with lower discontinuation rates of the drug.

THU-214

The risk predictive values of UK-PBC and GLOBE scoring system and performance of biochemical response criteria in Chinese patients with primary biliary cholangitis (PBC) on ursodeoxycholic acid

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Background and Aims: The biochemical response to ursodeoxycholic acid (UDCA) in primary biliary cholangitis (PBC) is a strong predictor of long-term outcome and thus facilitates the rapid identification of patients needing new therapeutic approaches. Numerous criteria for predicting outcome of treatment have been studied based on biochemical response to UDCA at 1 year. We sought to determine whether biochemical response based on these criteria could identify Chinese patients with PBC at risk of clinical adverse outcome, as defined by liver-related death, liver transplantation, and complications of cirrhosis.

Method: 119 consecutive patients (median age 46, female sex 83.2, median follow-up of 3.8 [range: 1.1–9.1]) all with biopsy-proved PBC treated with UDCA from one of the biggest tertiary hospitals in China (Beijing 302 hospital) were included. Clinical characteristics and liver biochemistry were collected at every 6-month interval. Death, liver transplantation (LT) and complications of cirrhosis were used as clinical adverse outcome. Cox proportional hazards regression analysis was used to identify the risk factors for progression after a year of UDCA treatment. The prognostic ability of UK-PBC score and GLOBE score were evaluated alongside those of the Barcelona, Paris-I, Rotterdam, and Paris-II criteria. The Area-Under-the-Receiver-Operating-Curve (AUROC) for survival analysis (c-statistics) was used to determine the performance of each prognostic method.

Results: The survival rates without adverse clinical outcome at 2, 5 and 8 years were 95.8% and 78.7% and 61.8% respectively. Under UDCA therapy, laboratory liver parameters experienced the most prominent improvement at 1st year (all $p < 0.05$). The Paris I and Paris II, but not the Rotterdam and Barcelona definition applied at 1st year after UDCA therapy significantly discriminated the patients in terms of long-term clinical outcome. Paris I was the most powerful predictor among four criteria (HR: 3.6, 95%CI: 1.5–8.3, AUROC 0.65) for non-responders versus responders. According to Paris I criteria 8-yr survival was 79.6% for responders and 43.6% for non-responders. The AUROC was 0.78 for GLOBE scoring system (HR: 2.9, 95%CI: 1.9–4.4). Patients with a GLOBE score > 0.3 (non-responders) had a significantly diminished survival compared with those with a score ≤ 0.3 (responders), and the 3-, 5- and 8-year clinical adverse outcome free survival rates were 95% vs. 74%, 91% vs. 64%, and 87% vs. 35%, respectively. The AUROC was 0.739, 0.738 and 0.738 for 3-, 5-, 8-year UK-PBC risk score.

Conclusion: This analysis confirms the prognostic value of previously proposed response criteria and scoring systems. Paris I was the most powerful predictor among all the criteria while GLOBE score predicted more accurate than UK-PBC score in Chinese cohort.

THU-215

Biochemical response to ursodeoxycholic acid predicts histologic primary biliary cholangitis progression

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Background and Aims: The prognosis and natural history of primary biliary cholangitis (PBC) have improved; its clinical endpoint needs to be discovered. We aimed to identify the surrogate markers for predicting histologic PBC progression.

Method: We enrolled the 99 patients to evaluate the potential correlation between biochemical response to ursodeoxycholic acid (UDCA) and histological stage at baseline according to both Scheuer (SC) and Nakanuma (NA) systems. We then conducted sequential biopsies in 35 patients with PBC treated with UDCA. They were divided into UDCA responders (R; $n = 14$) and non-responders (N; $n = 21$) based on reductions in γ -glutamyl transpeptidase levels at 1 year post UDCA therapy initiation (Nara criteria). We analyzed correlations between magnitude of biochemical response to UDCA and progression of histological changes of PBC. The Nakanuma system grades liver fibrosis (fibrosis score) and bile duct loss (BDL score).

Results: The proportion of R to N was significantly higher among patients in Scheuer and Nakanuma stages 1–3 and those with BDL scores of 0–2 compared with those in Scheuer and Nakanuma stages 4 and those with BDL score of 3, respectively ($P < 0.05$ for all). The number of stage 1, 2, 3, or 4 cases according to the SC was 6, 12, 17, and 0, respectively; according to the NA, it was 4, 18, 11, and 2, respectively. As per the SC, 1 patients had improved histological findings (I), 21 had stable histological findings (S), and 13 had histological progression (P); the NA categorized 4, 23, and 8 patients as I, S, and P, respectively. The fibrosis score progressed in 13 patients, while 1 showed improvement and 21 showed no progression; 4 patients exhibited improved BDL scores, while 23 showed no change and 8 showed worsening. In R ($n = 14$), proportions of patients with I, S, or P according to the SC were 0% (0/14), 78.5% (11/14), and 21.4% (3/14), respectively; this proportion per the NA was 14.3% (2/14), 57.1% (8/14), and 14.3% (4/14), respectively. Proportions of patients with improved, stable, or worsened fibrosis score were 0% (0/14), 64.3% (9/14), and 35.7% (5/14), respectively; as per BDL scores, it was 14.3% (2/14), 71.4% (10/14), and 14.3% (2/14), respectively. In N ($n = 21$), this proportion according to the SC was 4.8% (1/21), 47.6% (10/21), and 47.6% (10/21), respectively; per the NA, it was 9.5% (2/21), 71.4% (15/21), and 19.1% (4/21), respectively. The proportion for fibrosis score was 4.8% (1/21), 57.1% (12/21), and 38.1% (8/21), respectively; for the BDL score, it was 9.5% (2/21), 61.9% (13/21), and 28.6% (6/21), respectively. Histological progression rate per the SC and deterioration rate of BDL score was significantly higher in N than in R ($p < 0.01$ and $p < 0.05$, respectively).

Conclusion: The biochemical response to UDCA according to Nara criteria predicts the histological progression of PBC.

THU-216

Durable response in the markers of cholestasis through 36 months of open-label extension study of obeticholic acid in primary biliary cholangitis

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Background and Aims: Obeticholic Acid (OCA) is a selective and potent farnesoid X receptor agonist indicated for treatment of primary biliary cholangitis (PBC). POISE is a 12-month double-blind (DB), placebo (PBO)-controlled, Phase 3 PBC study including an open-label extension (OLE). The purpose of the OLE is to assess safety and durability of the OCA effect on serum markers of cholestasis.

Method: Key POISE inclusion criteria: PBC diagnosis, ALP $\geq 1.67 \times$ ULN and/or total bilirubin (TB) $>ULN$ to $<2 \times$ ULN, stable UDCA dose or unable to tolerate UDCA. During the DB phase, 216 patients were randomized and dosed to: daily PBO, $n = 73$; OCA 5–10 mg (titration after 6 months based on response and tolerability), $n = 70$; or OCA 10 mg, $n = 73$. In the OLE, all patients were initially treated with OCA 5 mg regardless of DB treatment with the option to increase after 3 months based on response and tolerability.

Results: 193 of 198 (97%) patients completing the DB phase of the study enrolled in the OLE; 165 reached 36 months of the OLE: PBO, $n = 49$; OCA 5–10 mg, $n = 59$; OCA 10 mg, $n = 57$. At the end of the DB phase, patients on OCA had significant reductions in ALP and patients on PBO did not (Table 1). ALP reduction observed in OCA-treated patients was durable through 36 months OLE. PBO-treated patients experienced a significant reduction in ALP after switching to OCA, which was durable through 36 months OLE. Similar durable improvements were seen for GGT, ALT, and AST (data not shown). For OCA-treated patients, mean TB remained below BL through 36 months OLE. For PBO-treated patients, mean TB increased at 12 months DB, but trended back toward baseline (BL) with 36 months of OCA during OLE. During the OLE, 28 (15%) patients discontinued treatment, 7 (4%) patients for pruritus.

Table 1: ALP and TB mean change from BL through 36 month OLE

DB Phase Treatment Group	PBO	OCA 5–10 mg	OCA 10 mg
ALP (U/L)			
DB BL	327 (115)	326 (116)	316 (104)
Δ DB 12 mo [†]	–8 (88)	–104 (87)***	–118 (73)***
Δ OLE 24 mo [‡]	–101 (87)***	–121 (97)***	–103 (79)***
Δ OLE 36 mo [‡]	–113 (90)***	–101 (110)***	–85 (137)***
TB (μmol/L)			
DB BL	11.8 (7.2)	10.2 (5.5)	11.3 (6.6)
Δ DB 12 mo [†]	1.5 (4.1)	–0.5 (3.4)**	–1.2 (4.3)***
Δ OLE 24 mo [‡]	1.9 (7.6)	–0.4 (3.6)	–0.6 (4.8)
Δ OLE 36 mo [‡]	0.5 (3.6)	–0.5 (3.4)	–0.9 (4.1)

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.0001$. Values are Mean (SD).

[†]P-value for comparing active treatments to PBO is obtained using an ANCOVA model with Baseline value as a covariate and fixed effects for treatment and randomization strata factor.

[‡]P-value for the within treatment comparisons are obtained using the Student's t -test.

Conclusion: OCA treatment results in improvement in liver biochemistry; this improvement is shown to be durable in this analysis. For patients initially treated with PBO, switching to OCA is also associated with a durable biochemical response. Consistent with the DB phase, pruritus was the most common side effect of OCA, but discontinuation due to pruritus continues to be infrequent.

THU-217

Quantification of biliary phosphatidylcholine by non-invasive ³¹P magnetic resonance spectroscopy imaging suggests differences in cholangiopathies: A pilot study

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Background and Aims: Changes of bile composition play a role in the pathogenesis and progression of cholangiopathies. Phosphatidylcholine (PtdCh) is the major biliary phospholipid counteracting bile acid toxicity and may be targeted by novel therapeutic strategies. However studies on bile composition in patients are scarce due to invasive nature of bile sampling. PtdCh concentration can be assessed with ³¹P MR spectroscopy (MRS) in human bile. Therefore, our aim was to investigate this non-invasive method for detection of the PtdCh concentration in the gall bladder of healthy controls in comparison with primary sclerosing cholangitis (PSC) and primary biliary cholangitis (PBC) patients.

Method: Biliary PC concentrations were studied in 4 healthy volunteers (3m/1f), 6 PBC (2m/4f) and 4 PSC (2m/2f) patients using ³¹P MR spectroscopic imaging on a 7T Magnetom System (Siemens Healthineers, Erlangen, Germany) with a double-tuned ¹H/³¹P surface coil. All PSC and PBC patient were treated with ursodeoxycholic acid. The signal quantification was based on a 3D sequence covering the liver and gall bladder of patients. The signal distribution of PtdC was then referenced to the corresponding localizer images and calibrated to mean γ -resonance of adenosine triphosphate concentration.

Results: Typical spectral from gall bladder region and homogeneous hepatic tissue was obtained in all included subjects. Calculated PtdCh concentration of the healthy volunteers was 11.77 ± 1.18 mmol/l ($n = 4$) comparable with previously published concentrations. In PSC patients, PtdCh content was much lower with 6.92 ± 0.80 mmol/l ($n = 4$) compared to controls ($p < 0.001$), whereas its concentration in PBC patients averaged at 12.81 ± 11.22 mmol/l ($n = 6$) and did not differ from control s. Interestingly, lowered PtdCh concentration (7.05 ± 1.76 mmol/l) was observed in all 4 female PBC patients ($p < 0.01$).

Conclusion: This pilot study confirmed that ³¹P MRSI can be used to quantify the biliary PC concentration in non-invasive manner. Low biliary PtdCh concentration in PSC and female PBC patients strengthens the hypothesis that biliary composition may be an important pathogenetic factor. Further investigations are needed to validate ³¹P MRS as a novel non-invasive method for addressing the role of PtdCh in cholangiopathies.

THU-218

Pre-treatment risk stratification in primary biliary cholangitis: a predictive model to guide first-line combination therapy

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