GFR of 61 ml/min and showed an improvement of kidney function at year 1 (mean GFR 69 ml/min), which was maintained over the 3 years. Comparing baseline characteristics of the respective groups, short cold ischemia time, lower age and short ICU stay were associated with a better development of kidney function. In a multivariable clinical prediction model we found predicted probabilities for GFR very close to observed probabilities for development of CKD 3 or worse. However, prediction of CKD 4 or 5 was less accurate.

Conclusions: Imputing the classical risk factors in a prediction model leads to a good prediction of loss of kidney function, but cannot predict whether a patient will later require dialysis. The recognized patterns further underline that liver recipients are a very heterogeneous group and that even a deterioration of kidney function in the first post transplant year does not predict if it later recovers or not.

188

THE MODE OF DEATH OF THE LIVER DONOR IMPRINTS DISTINCT IMMUNE ADAPTIVE RESPONSES ON THE HEPATIC RESIDENT LYMPHOCYTES

E. Xystrakis[1], X. Huang[1], S. Fuggle[2], N. Heaton[1], Y. Ma[1], W. Jassem[1]. [1]*Institute of Liver Studies, School of Medicine, King's College London, London,* [2]*Nuffield Dept of Surgical Sciences, University of Oxford, Oxford, UK*
E-mail: emmanuel.xystrakis@kcl.ac.uk

Background: Experimental liver transplantation studies have shown that brain death in the donor induces a systemic inflammatory response which affects allograft's quality and increases their immunogenicity. It is currently unclear which systemic events preceding the retrieval of the organ have damaging effects to the graft. We hypothesise that brain death in otherwise hemodynamically stable donors influence the differentiation of immune cells resident in the liver hence, predisposing their response to post-transplantation events.

Aim: To test whether the mode of death of the donor alters the phenotype and function of the adaptive immune cells of liver allografts prior to transplantation.

Methods: Liver resident lymphocytes (LRL) were isolated from liver perfusates obtained before implantation, to assess their phenotype and function after ex vivo polyclonal stimulation by anti-CD3 and anti-CD28 antibodies. We compared the LRL from brain dead donors (DBD n≥22), from donors after cardiac death (DCD n≥10) and from living donors (LD n≥10) as control.

Results: We found that LRL from DCD livers preferentially produce IL-17 (IL-17 positive cells being 4.5% in DCD, 0.9% in DBD and 0.8 in LD $p < 0.01$). This IL-17 secretion is attributed to CD4 T (mean at 3.3% in DCD, 1.6% in DBD and 1.2% in LD $p < 0.05$) and CD8 T cells (mean at 1.07% in DBD, 2.7% in DCD and 1.2% in LD $p < 0.05$).

In contrast to DCD, LRL from DBD livers were enriched in CD8 T cells which exhibit an activated phenotype (mean of CD8+CD69+ cells at 60% in DBD, 38% in DCD and 37% in LD, $p < 0.05$). Assessment of cytokine production shows a significant increase in IFN-gamma production by CD8 T cells of DBD grafts (mean at 32% in DBD, 15% in DCD, $p < 0.01$ and 18% in LD livers, $p < 0.05$).

Conclusion: Our data show that the inflammatory environment of DBD promotes activation of potentially cytotoxic IFN-gamma producing CD8 T cells, whereas DCD livers stimulate IL-17 secretion from both CD4 and CD8 T cells. They suggest that the mode of death of the donor leads to distinct adaptive immune responses in the graft, which may influence the transplant outcome.

02b. CIRRHOSIS AND ITS COMPLICATIONS: CLINICAL ASPECTS

189

THE PRESENCE OF HEMOLYTIC SPUR CELL-ANEMIA STRONGLY AFFECTS SURVIVAL IN PATIENTS WITH LIVER CIRRHOSIS

L. Vasilieva, A. Alexopoulou, T. Kanellopoulou, S. Pouriki, A. Soultati, S.P. Dourakis. *2nd Department of Internal Medicine, Medical School, University of Athens, Athens, Greece*
E-mail: alexopou@ath.forthnet.gr

Background and Aims: Hemolytic spur cell-anemia (HSCA) is due to lipid disturbances of the erythrocyte membrane and may develop in patients with advanced liver cirrhosis. Spur cells have spike-like projections which alter the shape of the cells and makes them more susceptible to trapping and destruction by the spleen. HSCA has been associated with poor survival in the past. However, the accurate diagnostic value of HSCA for predicting survival has not been clarified.

Methods: We prospectively evaluated clinical and laboratory parameters including MELD, MELD-Na and survival in cirrhotics with or without HSCA during the period 2008–2011. Patients who had at induction renal failure, other causes of haemolytic anemia, hepatocellular carcinoma, sepsis and/or active bleeding, were excluded. One hundred sixteen cirrhotics were included. HSCA was diagnosed in peripheral blood smear by light microscopy. Assessments of demographics, liver dysfunction and laboratory parameters were recorded. Patients were followed-up for a median of 6.5 months (0.5–46). HSCA (percentage of spur cells >5%) was diagnosed in 36 (31%) patients.

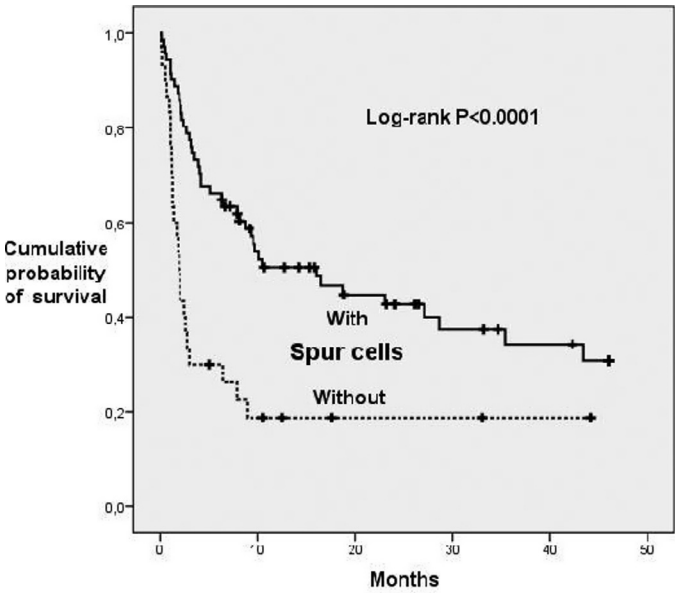

Figure 1. Probability of survival in patients with and without spur cells.

Results: Patients with compared to those without HSCA had more advanced liver disease (higher MELD and MELD-Na, both $P = 0.001$), lower hemoglobin ($P = 0.024$), higher total bilirubin ($P < 0.0001$), INR ($P < 0.0001$) and ferritin levels ($P = 0.015$). There was no difference in age, causes of liver disease, total cholesterol and albumin. Patients with HSCA had a worse survival (log rank $P < 0.0001$). In particular, at the first, second and third year of follow-up, the survival of patients with compared to those without HSCA was 23%, 23% and 19% in the former and 52%, 42% and 41% in the latter, respectively. It

is noteworthy that survival of patients with HSCA at the first, second and third month was 77%, 45% and 33%, respectively. A multivariate analysis showed that age ($P = 0.001$), MELD-Na ($P < 0.0001$) and presence of HSCA ($P = 0.009$) were independent predictive factors of death.
Conclusions: HSCA is prevalent in advanced cirrhosis. Mortality in liver cirrhosis seems to be strongly affected by the presence of HSCA.

190
AST-120 (SPHERICAL CARBON ADSORBENT) IN COVERT HEPATIC ENCEPHALOPATHY: RESULTS OF THE ASTUTE TRIAL
J.S. Bajaj[1], M.Y. Sheikh[2], M. Chojkier[3], L. Balart[4], A.H. Sherker[5], R. Vemuru[6], N.L. Sussman[7], J. Vierling[7], G. Morelli[8], K.E. Anderson[9], M.S. Harris[10], K.D. Mullen[11]. *[1]McGuire DVAMC, Richmond, VA, [2]UCSF, Fresno Community Regional Medical Center, Fresno, [3]Veterans Medical Center, San Diego, CA, [4]Tulane University Health Sciences Center, New Orleans, LA, [5]National Institute for Health, NIDDK, Bethesda, MD, [6]Permian Research Foundation, Odessa, [7]Baylor College of Medicine, Houston, TX, [8]University of Florida, Gainesville, FL, [9]Ocera Therapeutics Inc., San Diego, CA, [10]Georgetown University School of Medicine, Georgetown, DC, [11]Case Western Reserve MetroHealth Medical Center, Cleveland, OH, USA*
E-mail: jasmohan.bajaj@va.gov

Covert hepatic encephalopathy (CHE = minimal and/or ≤ grade 1 HE) adversely affects cirrhotic patients, but no standard-of-care is yet established. AST-120 has demonstrated efficient binding capacity for NH_3 and other gut-based toxins.
Aim: To provide proof-of-concept and safety/tolerability for AST-120 treatment of CHE.
Methods: A multi-center, double-blind, randomized, placebo-controlled, dose-ranging study of AST-120 was conducted over 8 weeks. Compensated cirrhotic patients with MELD Score ≤25 were eligible. CHE was defined as a global summary score on Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) below 10th percentile at screening and/or ≤1 HE by West-Haven criteria. The primary endpoint was neurocognitive improvement, defined as change in global RBANS at 8-weeks compared to baseline. Secondary endpoints included Psychometric HE-Score (PHES), clinical global assessment of HE (CGA-HE), and frequency of occurrences of overt HE and hospitalization. RBANS testing was performed at screening, baseline (+1 week), and 4 and 8-weeks after assigned intervention.
Results: 148 patients (mean 55 yrs, MELD 10, 53% HCV) were randomized to AST-120 12 g (n = 50), AST-120 6 g (n = 50), or placebo (n = 48). No significant changes were noted in the RBANS global-summary scores at week 8 (3.27±7.97 p = 0.2584, 4.51±7.72 p = 0.7812, and 4.57±9.50, Δ vs, baseline; AST-120 12 g, AST-120 6 g, and placebo respectively). A strong learning effect on RBANS ($p < 0.0001$) was apparent between screening and baseline visits in all groups. No differences in PHES, CGA-HE or overt HE/hospitalization events between groups were observed. Over 8 weeks, venous NH_3 significantly decreased from baseline in both treatment groups but increased in the placebo group: Δ ammonia: −17, −14 and +5 μg/dL (AST-120 12 g, AST-120 6 g, and placebo, respectively). The frequencies of treatment-emergent adverse events were similar for all groups (32%, 26% and 37.5%; AST-120 12 g, AST-120 6 g, and placebo, respectively, p = NS).
Conclusion: This was the largest controlled trial yet conducted in CHE or Minimal HE. AST-120 was well tolerated but did not achieve its primary endpoint of RBANS improvement. Results were confounded by study design that allowed for an improvement in neurocognitive measures before drug randomization. NH_3 improved significantly but independently of neurocognitive change.

191
EIGHT QUESTIONS OF THE PATIENT-REPORTED SICKNESS IMPACT PROFILE CAN EFFECTIVELY SCREEN FOR MINIMAL HEPATIC ENCEPHALOPATHY
E. Nabi[1], L.R. Thacker[2], D.M. Heuman[1], A.J. Sanyal[1], R.K. Sterling[1], R.T. Stravitz[1], V. Luketic[1], M. Fuchs[1], I. Bouneva[1], M.S. Siddiqui[1], M.B. White[1], P. Monteith[1], N.N. Jones[1], J.S. Bajaj[1]. *[1]Virginia Commonwealth University and McGuire VAMC, [2]Biostatistics, Virginia Commonwealth University and McGuire VAMC, Richmond, VA, USA*
E-mail: jasmohan@gmail.com

Background: Minimal hepatic encephalopathy (MHE), which impairs quality of life (QOL), is difficult to diagnose using curent cognitive tests by non-specialists. The detection rates could potentially improve with easier, patient-administered methods that do not require specialized testing or equipment.
Aim: To detect MHE using a validated QOL questionnaire, Sickness Impact Profile (SIP).
Methods: 170 cirrhotics (55yrs, 13 yr education, MELD 9, 50%HCV, 11%alcohol) without prior overt HE were administered a standard cognitive battery (NCT-A/B, Digit Symbol and Blocks) as the gold standard for MHE diagnosis along with SIP. SIP consists of 136 questions across 12 QOL domains (body care and movements, mobility, ambulation, emotional behavior, social interactions, alertness, communication, work, sleep and rest, eating, home management and recreation/pastime) that requires a yes/no answer over the past day. Proportion of patients that responded 'yes' to each question was compared between MHE and no-MHE groups. Variables independent of cognitive testing; demographics (age, education, gender, alcoholic etiology) and SIP questions differentiating between groups were analyzed using logistic regression and ROC analysis for MHE diagnosis.
Results: 93 (55%) patients had MHE on standard tests. On SIP, a 'yes' response was found in a higher proportion of MHE patients on 54 questions across all QOL domains. On regression age, male gender and eight questions '*I stay away from home only for brief periods of time*', '*I do not maintain balance*', '*I react slowly to things said or done*', '*I do not keep my attention on any activity for long*', '*I act irritable or impatient with myself*', '*I am not doing any of the shopping that I would usually do*', '*I am not doing any of my usual physical recreation or activities*' and '*I am eating much less than usual*' differentiated between MHE/no-MHE groups. These questions spanned domains of alertness, eating, recreation/pastimes, emotional behaviour, body care, mobility and home management. The AUC on ROC for MHE diagnosis was 0.90 with 81% sensitivity and 78% specificity with all 8 statements, age and male gender.
Conclusions: Eight patient-reported questions on SIP can effectively screen for MHE in outpatient cirrhotic patients. MHE screening strategies that do not include specialized testing could increase detection rates and therapy.

192
RIFAXIMIN IMPROVES COGNITION AND ENDOTOXEMIA IN MINIMAL HEPATIC ENCEPHALOPATHY BY SHIFTING GUT MICROBIAL FUNCTIONALITY WITHOUT ALTERING THEIR ABUNDANCE
J.S. Bajaj[1], D. Heuman[2], A. Sanyal[2], P. Hylemon[3], R.K. Sterling[2], R.T. Stravitz[2], M. Fuchs[2], J.M. Ridlon[3], K. Daita[3], P. Monteith[2], M. White[2], N.A. Noble[2], A. Fisher[4], M. Sikaroodi[4], H. Rangwala[4], P.M. Gillevet[4]. *[1]Gastroenterology, Hepatology and Nutrition, [2]Virginia Commonwealth University and McGuire VAMC, [3]Microbiology, Virginia Commonwealth University and McGuire VAMC, Richmond, [4]Microbiome Analysis Center, George Mason University, Manassas, VA, USA*
E-mail: jasmohan@gmail.com

Minimal hepatic encephalopathy (MHE) has a presumed gut-based pathophysiology. Rifaximin, a gut-specific antibiotic, is effective in