Abstract P202 Table 1 Severity of IO hepatotoxicity and time to resolution

Severity of IO Hepatotoxicity (Grade)	No of Patients (%)	Mean time to Resolution (Days)
1	7 (22%)	16
2	8 (25%)	38
3	14 (44%)	51
4	3 (9%)	49

resolution were evaluated, and compared with clinical outcomes using inferential statistics.

Results 58 evaluable patients were identified, of which 54% had an elevated LDH indicative of a poor prognosis patient population. IO toxicity occurred in 84.7% of the group, with hepatotoxicity being the most common (64%). All patients were treated in accordance with regional guidance, with full resolution of all cases, and no treatment related deaths.

Grade 1 hepatotoxicity did not require treatment. Grade 2 toxicity generally resolved with oral prednisolone (88%). In Grade 3 hepatotoxicity, 29% settled with oral prednisolone alone, with 71% receiving IV methylprednisolone. 21% required escalation to mycophenolate mofetil (MMF). All Grade 4 toxicities required IV methylprednisolone and escalation to MMF, with one refractory case requiring tacrolimus.

Median duration of follow up was 8.6 months (mo) (1.2 – 38.8 mo). 70% of patients with $\geq$ grade 2 hepatotoxicity had a tumour response to IO treatment compared with 34% of those with grade 0 or 1. Median progression-free survival was also significantly longer in this group (not reached vs 2.7 mo, P = 0.003) and a trend towards improved overall survival was seen (not reached vs 12.6 mo, P = 0.053).

Conclusion Our study shows that hepatotoxicity is common in metastatic melanoma patients treated with combination IO, but is associated with a favourable response to treatment and survival, even in this poor prognostic cohort. This is consistent with the literature, which has shown a correlation between IO-related adverse events and better clinical outcomes. Our data highlights the frequency of hepatotoxicity in this population, and the need for vigilance and prompt management to optimise their potentially enhanced clinical outcomes.

P203 ANGIOTENSIN CONVERTING ENZYME INHIBITORS AND THE RISK OF HEPATOCELLULAR CANCER: A NESTED COHORT ANALYSIS

Shyam Menon*, Ray Mathew. *The Royal Wolverhampton Nhs Trust, Wolverhampton, UK*

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Introduction Angiotensin Converting Enzyme Inhibitors (ACEI), Angiotensin Receptor Blockers (ARB), Calcium Channel Blocker (CCB) are used widely in the management of hypertension. Hypertension is a constituent of the diagnosis of metabolic syndrome, which is characterized by Obesity, Diabetes Mellitus, Insulin resistance and Dyslipidemia. We have previously demonstrated an association between metabolic syndrome and risk of hepatocellular cancer. There is conflicting data on the chemopreventative effects of ACEI, ARB and CCBs on solid organ cancers.

Aim To examine the association of ACEI, ARB and CCB use and risk of hepatocellular cancer using a primary care database.

Methods The THIN (The Health Improvement Network) database (UK) was interrogated to identify patients with a diagnosis of hepatocellular cancer and were matched with controls in a 1:2 fashion. Data on ACEI, ARB and CCB use was examined. Statin, Aspirin, Proton Pump Inhibitors (PPI) use were also additionally evaluated. A nested cohort analysis was performed and each case and corresponding control subject was followed longitudinally in the database to understand the temporal impact of ACEI, ARB and CCB use using time-dependent covariates.

Results 2998 patients (63% male, mean age 75 years) with hepatocellular cancer were age and gender-matched with 5996 controls. On univariate analysis, CCB use (Hazard ratio (HR) 0.89 (95% Confidence Intervals (CI) 0.82–0.97), p=0.005) was inversely associated with risk of hepatocellular cancer. ACEI (0.93 (0.86–1.01), p=0.085) and ARB (0.90 (0.796–1.027), p=0.12) did not demonstrate any association. CCB use was examined as a time-dependent covariate and duration of CCB use (1.60 (1.33–1.91), p<0.001) was associated its overall inverse association with hepatocellular cancer. This effect was not seen with ACEI (1.07 (0.95–1.20), p=0.25) or ARB (0.84 (0.64–1.105), p=0.211) use.

Statin use (0.74 (0.68–0.81), p<0.001) and aspirin use (0.88 (0.81–0.94), p<0.001 were inversely associated with hepatocellular cancer on univariate analysis. PPI use (2.02 (1.86–2.19), p<0.001) was also strongly associated with risk of hepatocellular cancer.

On multivariate analysis, CCB use was not associated with risk of hepatocellular cancer. Statin use (0.68 (0.62–0.74), p<0.001) demonstrated an inverse association whilst PPI use (1.92 (1.77–2.09), p<0.001) was associated with hepatocellular cancer risk. On modelling statin as a time-dependent covariate, longer duration of use (0.65 (0.46–0.81), p=0.001) was associated with its protective effect on hepatocellular cancer.

Conclusions ACEI, ARB and CCBs are not associated with risk of hepatocellular cancer. Longer duration of statin use has a potential protective effect against hepatocellular cancer. PPI use seems to be strongly associated with risk of hepatocellular cancer.

P204 MITOCHONDRIAL DYSFUNCTION MAY EXPLAIN INNATE IMMUNOPARESIS AND SUSCEPTIBILITY TO INFECTION OF PATIENTS WITH ALCOHOLIC HEPATITIS

Paul Middleton*, Mark Thursz, Nikhil Vergis, Trial Management Group MIMAH. *Imperial College London, London, UK*

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Background Alcoholic hepatitis (AH) is the most florid form of alcohol related liver disease. Infection develops in 50% of patients and is strongly associated with mortality. Innate immune paresis is recognised in this condition, but mechanisms have been elusive. Mitochondrial damage within hepatocytes in AH is a strong prognostic finding however mitochondrial defects in immune cells have not been investigated. We therefore sought to explain innate immune defects