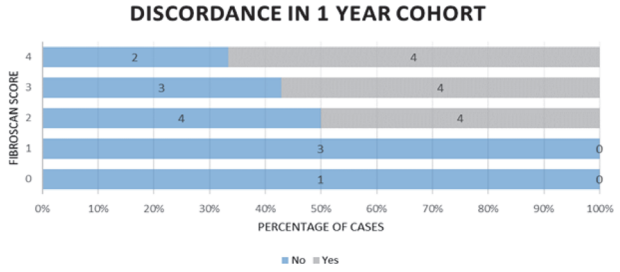
give the Metavir fibrosis score. Where necessary, the Ishak score of the histology samples was converted to a Metavir equivalent. Discordance was defined as a difference of $\geq$ 2 stages between the two modalities of staging fibrosis and was analysed using the Chi square test. We analysed the data within a one year duration between the fibroscan and liver biopsy.

Results During the study period, an overall total of 199 liver biopsies and 1218 fibroscans were undertaken. Twenty-five patients had both a fibroscan and a liver biopsy performed within a one year interval. The mean and median interval between fibroscan and biopsy was 42 and 28 days respectively. The median fibroscan stage was F3 (range 0–4) and the median liver biopsy stage was F1 (range 0–4). When compared to the liver biopsy, an identical fibroscan based fibrosis score was obtained in 4 (16%) cases. Fibroscan had understaged 2 (8%) and over staged 19 (76%) cases while discordance was noted in 12 (48%) cases (figure 1). Discordance was not statistically different for F0-1 in comparison to F2-4 scores (p=0.311), however, fibroscan score of F0-1 was significantly more likely to have identical value of Metavir score for both fibroscan and liver biopsy (p=0.009) (figure 1).



Abstract P200 Figure 1

Conclusion Fibroscan with lower fibrosis scores (F0-1) had higher concordance to the liver biopsy based histological staging and therefore can be used safely to exclude significant fibrosis. Moderate to severe fibrosis staging (F2-4) showed increased disparity between the biopsies and the fibroscan scores, with the latter usually over-staging the level of fibrosis. We therefore feel fibroscan in isolation may not be suitable to diagnose advanced liver fibrosis.

P201 BEZAFIBRATE AS SECOND LINE TREATMENT IN PATIENTS WITH PRIMARY BILIARY CHOLANGITIS: A REAL WORLD EXPERIENCE

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Introduction Failure to improve alkaline phosphatase (ALP) with treatment with Ursodeoxycholic acid (UDCA) is associated with reduced transplant-free survival in primary biliary cholangitis (PBC). Bezafibrate (BZ), as second line treatment, has been shown to be effective in improving ALP in patients with PBC in a recent randomised controlled trial[1] but 'real world' data is limited.

Aim and Method The aim of this study was to retrospectively assess the effectiveness of BZ as second line treatment in patients intolerant of, or non-responsive to UDCA in a single tertiary referral centre.

ALP was recorded at six and twelve months of treatment and compared to baseline. Biochemical response was defined by the Toronto criteria of ALP less than 1.67 times the upper limit of normal. Results are expressed as median (range).

Results 36 patients were identified as treated with BZ. Eight have been excluded as lost to follow-up (n=1) or had been taking BZ less than six months (n=7).

Of the remaining 28 (5 UDCA intolerant, 23 UCDA incomplete response), 23 were female, median age was 54 (32–85) at the start of treatment and 11 patients (40%) had cirrhosis.

Three (10.7%) patients stopped treatment due to intolerance (deteriorating renal function n=1; cramps n=1 and gastrointestinal symptoms n=1). The latter were both also intolerant to UDCA.

In the remaining 25, ALP fell from 279 (125–782) to 154 (74 – 415) at six months, with 76% achieving biochemical response by Toronto criteria.

16 patients have completed 12 months of treatment, with 12 patients (75%) achieving biochemical response. ALP fell from 281 (125 – 720) to 138.5 (90–326) at 12 months. 7 (44%) patients normalised ALP.

20 patients were asked about pruritis before and after treatment. 6 patients (30%) reported no itch either before or after treatment, 2 (10%) reported no change in severity and 12 patients (60%) reported improvement in pruritis.

Conclusion We have found that BZ is an effective second-line treatment, with 75% of those who tolerated it achieving biochemical response at 12 months. It was well tolerated and was also associated with improvement in pruritus in the majority of patients. Further research is required to assess the long-term outcome in these patients.

REFERENCE

1. Corpechot C, *et al*. A Placebo-Controlled Trial of Bezafibrate in PBC. *NEJM* 2018;**378**;23:2171–81.

P202 CHECKPOINT INHIBITOR IMMUNOTHERAPY INDUCED HEPATOTOXICITY IN PATIENTS WITH METASTATIC MELANOMA: THE NORTHERN IRELAND EXPERIENCE

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Introduction The emergence of checkpoint inhibitor immunotherapy (IO) has revolutionised outcomes for patients with metastatic melanoma, with significantly improved response rates and survival shown in clinical trials. This treatment modality is however associated with unique toxicities including hepatotoxicity.

We aimed to determine if the clinical outcomes and hepatotoxicity rates in our routine clinical practice were comparable to those in existing literature.

Methods Patients receiving combination IO (Ipilimumab and Nivolumab) at the Northern Ireland Cancer Centre for metastatic melanoma between 1st September 2016 and 1st January 2020 were identified from an electronic database. Clinical characteristics of the disease, type and grade of hepatotoxicity (maximal rise of ALT or AST), treatment required and time to

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

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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

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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