cases and controls, and to determine its role in development of cardiac fibrosis and dysfunction associated with heart failure (HF).

Methods Through a HORIZON 2020 collaboration, 54 symptomatic patients were recruited from St Michael’s Hospital, Dublin and University Hospital of Ioannina (Greece), over a 6-month period. The recruited cohort consisted of 20 hypertensive or obese non-HF patients with symptoms of breathlessness, and 34 patients diagnosed with acute HF. Plasma samples were collected and CLEC3B was quantified using ELISA. As the primary cell type contributing to cardiac fibrosis is the fibroblast, parallel in vitro studies were carried out using primary human cardiac fibroblast cells (HCF). Both CLEC3B gene over-expression and gene knock-down studies were carried out in HCFs, in the presence or absence of stimulation with the pro-fibrotic growth factor TGFβ. The impact of modulating endogenous CLEC3B levels on gene and protein expression was studied, including by RNA sequencing, to identify the potential role of CLEC3B in fibroblast cells. An in vivo model of angiotensin II knock out mice was also conducted to study the impact of CLEC3B on cardiac function and remodelling (echocardiography, histology, gene and protein analysis).

Results Within a breathless cohort, circulating CLEC3B levels were significantly reduced by approximately 30% in acute HF patients compared to non-HF patients (P<0.0001). Receiver operating characteristic (ROC) predictive modelling of plasma CLEC3B in non-HF vs. acute HF patients showed area under the curve, AUC=0.92. RNA sequencing analysis of HCF cells showed significant changes in over 2000 genes following both CLEC3B over-expression and knockdown, with different genes being modulated depending on activation status of the HCF cells. Our mouse model of angiotensin II induced HF showed that there was an impact of global CLEC3B knockout on the expression of genes related to fibrotic processes.

Conclusions/Implications These data show that CLEC3B shows promise as a diagnostic tool that could help identify HF patients within a symptomatic breathless population. It also highlights that CLEC3B may have an important role in the development and progression of fibrosis associated with cardiac remodelling in heart failure, due to the impact on function of activated cardiac fibroblasts in both in vitro and in vivo experimental models. This aspect opens up the possibility of CLEC3B being a potential novel therapeutic target in diseases associated with cardiac fibrosis and remodelling.

57 PATIENT TOLERANCE AND THE CLINICAL EFFECT OF SGLT2 INHIBITORS IN A ROUTINE COMMUNITY HEART FAILURE POPULATION

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Aims Sodium-glucose Cotransporter-2 (SGLT2) Inhibitors are now advised as standard front line therapy for heart failure reduced ejection fraction (HFrEF) patients irrespective of whether diabetes is present or not. There has now been a multitude of positive trials in favour of SGLT2 inhibitor use with little information on how routine community HFrEF populations respond to this intervention in the setting of already taking maximum tolerated conventional disease modifying therapies. We therefore set out to assess the clinical response (using NYHA and NT-proBNP change) and tolerability of SGLT2 inhibitors in patients attending our outpatient heart failure unit.

Methods All patients commenced on SGLT2 inhibitors as additional medical therapy for HFrEF in a twelve-month period were included in the study. SGLT2 inhibitor therapy was initiated once patients were fully optimised on conventional medical therapy and stable from a heart failure perspective. For all patients commenced on an SGLT2 inhibitor as part of their HFrEF pharmacotherapy we then studied what effect this had on each patients NYHA functional class and NT-proBNP levels before and after initiation of SGLT2 inhibitor. For all patients we recorded whether a not a patient was still taking their SGLT2 inhibitor at most recent follow up appointment at our heart failure unit. Where patients were no longer prescribed SGLT2 inhibitors at follow-up, we analysed the reasons documented for this in the patients electronic patient record.

Results There were 184 patients commenced on SGLT2 in the 12-month period studied of which 78% (144 patients) were male and 26% (48 patients) were diabetic. The average age was 69 years old. Out of the 184 patients, 158 patients (86%) had their initial NYHA class documented in their patient record. The average NYHA functional class at time of commencing SGLT2 inhibitor for these patients was 1.9. At a subsequent follow-up review, 120 patients had a repeat NYHA documented and the average NYHA functional class at this time was 1.7 (with a mean time interval of 4.2months). 86 patients (72%) were in the same NYHA functional class, 28 patients (23%) were now in a lower NYHA functional class while 6 patients (5%) were in a higher NYHA functional class. The mean NT-proBNP was 1610pg/mL at initiation of SGLT2 inhibitor and it was 1830pg/mL at the follow-up visit with a mean time interval of 4months. The difference in NT-proBNP was not meeting statistical difference. 166 patients (90%) were still prescribed their SGLT2 inhibitor at most recent follow up. The most common reasons patients had stopped their SGLT2 inhibitors during follow-up was due to urinary tract infections (3% of total patients) and symptomatic hypotension (3% of total patients).

Conclusion For the majority of patients there was no significant change in their reported NYHA class or NT-proBNP levels at follow-up. Overall, we found SGLT2 inhibitors to be a well-tolerated with high adherence rates (90%) at follow up and relatively few side effects warranting discontinuation.

58 STRATEGIES TO OPTIMISE GUIDELINE-DIRECTED MEDICAL THERAPY IN HEART FAILURE PATIENTS WITH REDUCED EJECTION FRACTION BY IMPROVING SGLT2 INITIATION RATES IN NURSE-LED OUTPATIENT HEART FAILURE CLINICS

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Background Heart failure with reduced ejection fraction (HFrEF) is a complex disease, with multiple comorbidities, making management with guideline-directed medical therapy (GDMT) a challenging feat. Nurse-led outpatient HF clinics