Scottish Society of Gastroenterology SSG

SUMMER MEETING 2022

Abstract Submission Form

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ABSTRACT SUBMISSION
Note: Abstracts should be no more than **500 words in total**.

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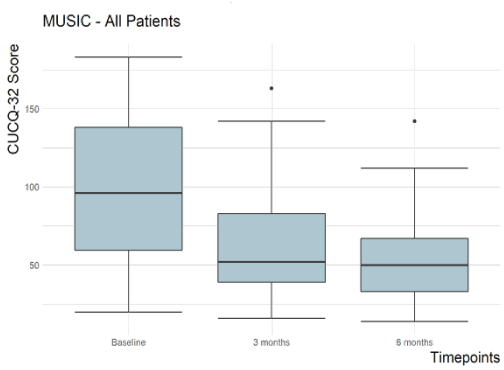
ABSTRACT DETAILS:	
Background:	The MUSIC study[1] is a 12-month prospective longitudinal study (from 2020-2025) built into the 'real world' NHS clinical setting to translate the clinical utility of mitochondrial damage-associated molecular patterns (DAMPs) as a new inflammatory signal in IBD. We set up this collaborative study in Edinburgh, Glasgow and Dundee in the midst of the Covid19 pandemic; and present the initial data from our first 58 patients and the development of key infrastructural and data-pipeline processes to build an integrated Precision Medicine-enabled study in Scotland.
Method:	We prospectively capture clinical (HBI, SCCAI), biomarker (calprotectin, CRP), TDMs, patient-reported outcome measures (PROMs), endoscopic and histology (~350 data fields) in conjunction with scientific (proteomics, transcriptomics, genetics, microbiome) data in active IBD patients over 5 defined time-points with total 30 000 biological sampling points over 12-months follow-up (Cohort 1; target n=250). GI-DAMPs is a parallel cross-sectional study capturing *ad hoc* clinical activity and mucosal inflammation with optional serial sampling; and non-IBD controls (Cohort 2; targets n=1000 and 250 respectively). In both Cohorts, we aim to combine blood mitochondrial DAMPs analysis and carry out modelling with clinical and multi-omic metadata across time to predict mucosal healing in IBD.
Results:	**In Cohort 1**, we recruited n=58 subjects from February 20-March 2021, (F/M=20/38; UC/CD=21/37; Edinburgh/Glasgow/Dundee =34/21/3; Age=18-68 years) with 5 completed 12 months' data. Preliminary analyses show improving clinical IBD clinical activity in response to treatment: Median CD HBI score 4→2.5→3→0 →0.5; UC SCCAI 3→2 →2 →1→0 per 3 months F/U. PROMs using CUCQ-32 reduced from 96 (IQR 60-138) →50 (IQR 33-67) at baseline to 6 months FU respectively (p=0.001). Serial paired endoscopic and histologic mucosal healing data at 0 vs. 3-6 months have been completed in 17/58 (29%) subjects (with Mayo/UCEIS/SES-CD and associated raw digital imaging) of which only 6 (35%) achieved complete mucosal healing on FU. **In Cohort 2,** from

	January 2019-March 2022, we recruited n=493 subjects, (F/M=262/230, UC/CD/IBD-U/non-IBD/pending diagnosis =182/137/28/132/13; Age=17-75 years; 69 [14%] with serial data). 108 (22%) subjects were recorded as 'highly active' (requiring in-patient IV steroids; CRP = median 11.5 mg/L IQR 3.8-29.0, calprotectin = median 1122 ug/g IQR 883-1250). In Cohort 2, initial interim analysis of circulating cell-free DNA and mitochondrial DNA confirms association with highly active disease ([plasma cfDNA : 0.66ng/uL vs. 0.22ng/uL; p=0.002) and mitochondrial genes *COXIII* (1134 copies/uL vs. 183 copies/uL)/*ND2* copy numbers (1297 copies/uL vs. 197 copies/uL); both p=0.01).  **Interim MUSIC longitudinal PROMs follow-up data.**
Conclusions:	We present the initial dataset to demonstrate the organic set-up and feasibility of the MUSIC/GI-DAMPs study, a complex integrated multi-centre Precision Medicine-enabled study with novel features to capture dynamic evolution of IBD from mucosal healing to patient-centred outputs. This ensuing framework will incorporate paediatric IBD (Mini-MUSIC) and 2 biomarker-enabled phase 2b RCTs (MARVEL and Mini-MARVEL) in 2022[2]; and deliver long term gains in translational IBD science in Scotland.
References:	[1]Mitochondrial DAMPs as mechanistic biomarkers of mucosal inflammation in Crohn's disease and Ulcerative Colitis (MUSIC). https://doi.org/10.1101/2022.03.21.22270313; ClinicalTrials.gov Registration NCT04760964 and www.musicstudy.uk [2]www.marvelstudy.uk; ClinicalTrials.gov Registration: NCT04276740

ABSTRACT SUMMARY

The full abstract will be available on the SSG website for one month following the meeting.

Please summarise the details of the abstract below in no more than **100 words**:

Precision Medicine to deliver tangible clinical benefits remains an aspiration in IBD. The MUSIC/GI-DAMPs is a 12-month prospective longitudinal study combined with a parallel cross-sectional arm, built into the 'real world' NHS clinical setting (target ~1500 subjects, 350 clinical metadata points, 30 000 biological sampling points with multi-omic data to features to capture the dynamic evolution of IBD with outputs from mucosal healing to patient-centred outputs. On this platform, we aim to translate the clinical utility of mitochondrial DAMPs as a new inflammatory signal in IBD. We set up this collaborative study

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in Edinburgh, Glasgow and Dundee in the midst of the Covid19 pandemic; and present the initial data from our first 58 patients and the development of key infrastructural and data-pipeline processes to build an integrated and organic Precision Medicine enabled study in Scotland. We also demonstrated how our bespoke framework will incorporate paediatric IBD (Mini-MUSIC) and two Phase 2b clinical trials (MARVEL and Mini-MARVEL) with PROMs, clinical activity outcomes, mucosal healing and scientific data that can integrate across adult/children with IBD with projected collective total of >2000 participants; and provide a robust platform to enable future translational IBD scientific studies in Scotland.

Do you give your consent for the abstract to be posted on a private area of the SSG website for one month following the meeting?
YES/ * *delete as applicable*