

# LIVERHOPE

**HORIZON 2020 EU Program funded- 5.6M Euro**

**Concept: Multi-centre, double-blind, placebo RCT**

**-To act in the liver-gut axis and in systemic inflammatory response with a combined rifaximin-simvastatin treatment to prevent cirrhosis progression and ACLF development**

**Safety study WP completed 2018; Efficacy study through regulatory/contracts**

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# LIVERHOPE Efficacy study: to recruit 240 pts across 7 centres- 1 in the UK: RFH

- **Primary Endpoint:** To evaluate the efficacy of oral administration of simvastatin plus rifaximin over 12m in halting the progression of decompensated cirrhosis as assessed by the time to first incidence of ACLF during treatment period
- **Key Secondary Endpoints:**
  - Time to Tx Free survival; Severity of ACLF and/or frequency of hospital admissions secondary to decompensation events
  - Biological markers incl. microbiome changes, neurohormones and SIRS/cytokines
  - QALY and HE and Frailty scores



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# Ancillary Study- Haemodynamics

## ***Background:***

- Cirrhosis decompensation: linked with increased systemic inflammatory response, neurohormonal activation and aggravation of haemodynamic derangements
- Rifaxamin and Statins have anti-inflammatory actions and may decrease sympathetic activation or/and endothelial dysfunction
- Recent published data has not clarified the position on sytemic haemodynamics and cardiac function in relation to statins or rifaxamin in decompensated patients



# Proposed Non-invasive haemodynamics at baseline and after 12 months

- ***Systemic Haemodynamics:***

- U/S doppler of forearm blood flow (distal to ante-cubital fossa): Arterial diameter, flow volume and velocity

- ***Liver Non-invasive Haemodynamics:***

- *Fibroscan and splenic stiffness; ADMA and VWF antigen*

- ***Cardiac Dysfunction:***

- ECHO or cMRI: LAVI, cardiac output, cardiac strain
- Holter or similar device: Heart Rate Variability (+/- QTc)



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# Discussion:

- To optimize recruitment (currently efficacy trial has started late)
- Only 1 UK site- RFH (PI: RM)
  - Seek help from partnership trusts to ensure adequate numbers are assessed for eligibility



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