STOP-HCV-1
Stratified Treatment OPtimisation for HCV-1

An open-label randomised controlled trial (RCT) testing biomarker-stratified short-course first-line and re-treatment direct-acting antiviral (DAA) oral treatment regimens to cure mild chronic Hepatitis C (HCV) disease.

For Adults (≥18 years) infected with HCV genotype 1a/1b or 4 for ≥6 months, with detectable plasma HCV RNA and mild liver disease (Fibroscan score F0-F1 or biopsy proven minimal fibrosis), HCV viral load <10 million IU/ml, no previous DAA exposure (previous pegylated-interferon/ribavirin allowed) and not pregnant. Patients co-infected with HIV are eligible if HIV viral load has been <50 copies/ml for >24 weeks on anti-HIV drugs.

PATIENT INCLUSION CRITERIA
1. Aged ≥18 years
2. Infected with HCV genotype 1a or 1b or 4 with access to first-line treatment appropriate for their genotype (ombitasvir/paritaprevir/(dasabuvir)/ritonavir or glecaprevir/pibrentasvir)
3. At least one detectable viremia 6 months prior to randomisation (by quantitative HCV RNA, qualitative assay or HCV genotype), with no intervening undetectable results
4. Plasma HCV RNA >LLOQ at screening
5. No evidence of significant liver fibrosis resulting from any aetiology (defined as Fibroscan* score ≤7.1kPa, equivalent to F0-F140, within 180 days prior to planned randomisation or biopsy consistent with mild fibrosis (Ishak score <=2/6) within 180 days prior to planned randomisation)
6. BMI >=18kg/m2
7. Laboratory tests: platelets >=60x109/l, haemoglobin >12g/dl (male) or >11g/dl (female), creatinine clearance (estimated using Cockcroft-Gault) >=60ml/min, international normalised ratio (INR) <1.5
8. Screening HCV viral load <10,000,000IU/ml
9. Written informed consent obtained from the patient.
If HIV infected, then an additional eligibility criteria is:
10. On antiretroviral therapy with HIV viral load <50 copies/ml for >24 weeks at the screening visit.

*Fibroscan must be a valid result (based on at least 10 readings) performed by an experienced technician and conducted as described in the Manual of Operations.
3.2 PATIENT EXCLUSION CRITERIA

1. Previous DAA exposure for this infection (previous treatment with pegylated-interferon and/or ribavirin allowed. DAA treatment for a previously cured infection allowed).

2. FEMALES ONLY: Lactating, or pregnant, or planning to become pregnant, or not willing to use effective contraception, during the study and for four months after last dose of study medication.

3. FEMALES ONLY: currently taking ethinyl-oestradiol-containing medicinal products such as those contained in most combined oral contraceptives or contraceptive vaginal rings.

4. MALES only: planning pregnancy with female partner, or not willing to use effective contraception, during the study and for seven months after last dose of study medication.

5. Malignancy within 5 years prior to screening

6. Any condition in the judgement of the investigator which might limit the patient’s life expectancy

7. Currently receiving medication known to interact with study medication (ombitasvir, paritaprevir, dasabuvir, ritonavir, sofosbuvir, ledipasvir, ribavirin, glecaprevir, pibrentasvir; see relevant prescribing information. (www.hep-druginteractions.org)

8. Disorder which may cause ongoing liver disease including, but not limited to, active hepatitis B, ongoing alcohol misuse

9. Any disorder which in the opinion of the investigator may have a significant negative impact on the ability of the patient to adhere to the trial regimen

10. Use of other investigational products within 60 days of screening

11. Known hypersensitivity to any active ingredient and/or excipients of the study medicines, namely Microcrystalline cellulose, Lactose monohydrate, Croscarmellose sodium, Magnesium stearate, Gelatine, Shellac, Propylene glycol, Polyethylene glycol, Ammonium hydroxide, Pregelatinised maize starch, Sodium starch glycinate (type A), Maize starch, Hypromellose, Talc, Ethylcellulose aqueous dispersion, Triacetin, Copovidone, Colloidal anhydrous silica, vitamin E (tocopherol) polyethylene glycol succinate, sodium stearyl fumarate, Polyvinyl alcohol, Macrogol 3350, Sunset yellow FCF aluminium lake (E110), Colouring agent (E132), Titanium dioxide (E171), Yellow iron oxide (E172), Red iron oxide (E172), Black iron oxide (E172).

12. History of severe pre-existing cardiac disease, including unstable or uncontrolled cardiac disease, in the previous six months

13. Haemoglobinopathies (e.g., thalassemia, sickle-cell anaemia).