Clinical trials in special patient populations

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HIV and HBV co-infected patients

- HIV:
  - Major issue will be managing the potential for drug-drug interactions with antiretrovirals
    - Ritonavir: inhibition 3A4, PgP
    - Efavirenz: induction 3A4
  - May be less of an issue with nucleoside polymerase inhibitors
  - HIV treatment with raltegravir-NRTI may be an elegant alternative
- HBV:
  - Less risk for DDI's given the different metabolic pathways

Compensated and decompensted cirrhosis

- Compensated Cirrhosis
  - Progressively include these patients into primary development if safety data permit.
  - Potential impact on efficacy will become less important over time when more effective treatment combinations will be available
- Decompensated cirrhosis
  - Is there a role for IFN or should this be IFN-free treatment?
  - Is there a role for maintenance therapy aimed at delaying disease progression?

Pre- and Post-transplantation

- Pre-transplantation:
  - Would it be possible to design a short peri-transplant treatment regimen with highly active drugs that could prevent re-infection?
- Post-transplantation:
  - Issues of DDI with immunosuppressive drugs and other co-medication
  - Would it help to have an IFN-free treatment?

Paediatric Patients

- When to treat children?
  - Chances of spontaneous conversion before the age of 3
  - Risk of growth retardation with IFN, which increases the risk for permanent impact on final height if treatment is just before or during puberty (less time to catch up).
  - Choice of SOC comparator given that paediatric development will lag several years behind adult development
  - What about genotype 2-3? Virtually 100% SVR with current treatment and very accepatable safety profile.

Racial and Ethnic groups

- Impact of racial and ethnic origin is likely to become less prominent with more effective treatments.

- It is probably more important to identify the factors that are at the origin of a positive or negative treatment response and drive ethnic differences, rather than make an epidemiological inventory of treatment response and safety

Other genotypes

- What do we aim for?
  - Genotype 3:
    - Superiority on SVR for a triple therapy may be feasible, but is it ethical to expose te 70% of patients to triple therapy that do not need it.
    - Non-inferiority with shorter triple therapy or better tolerated dual therapy including 1 or 2 new compounds?
    - Triple therapy for non-responders-relapsers
  - Genotype 2:
    - Only the second and third option seem realistic
  - Genotype 4,5 and 6:
    - Specific development needed or can they be pooled with GT1?