Forum for
Collaborative HIV Research

EMEA Perspective on HCV Clinical Trials

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And

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Draft EU guideline on the development of DAA in HCV

- End of the consultation period
- About to be adopted
- Input of this meeting to consider the need for revising some items
- Some key issues developed in the EU guideline

Risk of resistance

- Should be the leading issue when designing clinical trials (from exploratory monotherapy trial to phase III)
- Need to avoid functional monotherapy
- Importance of virological stopping criteria
- Need to substantiate the risk of resistance before targeting difficult-to-treat populations (notably non responders to SoC)

Patients population

- Naïve to HCV therapy

- Treatment experienced
  - Responder-relapser
  - Non responder: two distinct sub-populations:
    - Null responder (<2 log10 reduction in HCV RNA at week 12)
    - Partial responder (≥2 log10 reduction in HCV RNA at week 12 but detectable at the end of treatment with SoC)

- *Stepwise approach in the clinical development:*
  - First, HCV genotype 1, naïve to HCV therapy or relapse after SoC treatment, do not have advanced fibrosis and are not co-infected with HIV
  - *Later , answering a medical need, but minimizing the risk of being potentially harmful: non responders, HIV-HCV, patients with fibrosis/cirrhosis, liver transplant* …and genotype 2/3

Objectives/endpoints

- As compared to SoC : increased SVR (shorter treatment duration)

- Endpoints:
  - SVR 24 weeks after end of treatment
  - Long term follow-up : up to 72 weeks
  - RVR, EVR to be defined prospectively

- Resistance analysis: pre-existing, emerging, reversion to WT, long term persistence

- Safety

Some points for discussion…

- Level of reassurance before targeting difficult-to-treat populations
- SoC sparing regimen with DAA combinations: interesting concept, challenging development, risk of multiple resistance
- Once a DAA will be registered=> Superiority/Non inferiority trial versus the registered DAA