Forum for Collaborative HIV Research

FDA-Perspective on HCV Clinical Trials

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Resistance Concerns/Objectives

- Learn lessons from past drug development including HIV
- Avoid a paradigm of sequential “monotherapy”
- Reduce risks for clinical trial participants with respect to future therapeutic options
- Remain aware that HCV is NOT HIV and that we need to base decisions from data generated in HCV studies

Specific Clinical Trial/Resistance Issues

- Duration of monotherapy in initial proof-of-concept studies
- Appropriate sequence of development in patient populations: naïve-relapsers-null responders
- Impact of selection of drug resistance on use of subsequent regimens: cross-resistance and persistence
- Mutational barrier needed for non-interferon based regimens

Definitions of Treatment Experienced Populations

- Naïve: received no prior therapy for HCV
- Null Responder: <2 $\log_{10}$ reduction in HCV RNA at Wk 12 on a PEG-IFN/RBV regimen
- Partial Responder: ≥ 2 $\log_{10}$ reduction in HCV RNA at Week 12, but not achieving HCV RNA undetectable at end of treatment with a PEG-IFN/RBV regimen
- Responder Relapser: HCV RNA undetectable at end of treatment with a PEG-IFN/RBV regimen, but HCV RNA detectable within 24 weeks of treatment follow-up

Concerns:

- Adding one drug to PEG-INF/RBV in previous null responders
- “Functional monotherapy”? Is this a useful term for combinations with PEG-IFN/RBV.
  - RBV has no antiviral activity alone—but increases antiviral effect of INF
- How much data (SVR and resistance data) is needed before studying treatment-experienced patients
- How much data (SVR and resistance data) is needed before combination therapy