HCV Studies - Control Arms: community/my perspective

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NATAP

- **www.natap.org**
  - A leading resource for HIV & hepatitis care-treatment-related reporting/conference coverage, news.
  - 'real-time' reporting from conferences
  - 2.5 million monthly hits
  - 20,0000+ on NATAP daily listserve
- **HIV & HCV Treatment Education Program Community-Based in English/Spanish – work with patients directly**
  - Since 1996: 300 events in 25+ cities; NYC-DOH Pt Support Program
  - 17,000 attended; 85% African-American/Latinos
  - 100-700 at an event
  - HCV Speakers: thought leaders. Jules
- **Policy: HCV/HBV language in Ryan White Care Act**

Early Access: these circumstances

- In a Study: controlled environment for safety
- Patients with advanced disease who need therapy & can't wait til approval or they might be too sick to be treated
- Don't qualify for a study
- Usually PR failures so will need at least 2 orals, with or without PR if contraindicated
- FDA must be nice: in terms of tox/label, is that possible? Accelerated Approval for regimen!

No Controls

- I take Cutting Edge Approach (CEA) my acronym
- There is no need for expensive, unethical, difficult to use control arms in US & international trials
- What about re-imbursement/cost-effectiveness, are there implications?
- Cost of multiple orals in developing world, generics?
- PR control; Telaprevir, BOC +PR controls

1 Exception

- Peg-Lambda studies should continue
- What if there are patient populations for whom 2/3 orals without PR does not cure? (1a)
- We should study IFN contraindication with 2 or 3 orals
- Coinfection studies should be fast-tracked

- Unethical to use peg/rbv
- Patients do not want to use it, many patients will not enroll at least in USA with an oral on market unless of course if trial has 2 orals. But in the future when 2 orals are available how can you have PR control
- Is it ethical to have 12-week rollover? I know we are using it now, Very questionable in the near future
- Is there a control in recent announced Pharmasset study, no I believe right?

- Historical controls make sense
- We are planning future studies for many HCV orals
- The landscape is changing very quickly
- The Standard-Of-Care will be a moving target.
- By next year only we don't know where we will be, what study results we will see from INF-free regimens, and from QUAD regimens with 2 orals+peg/rbv(PR):
- Pharmasset 7977/938, BMS/Pharmasset 7977/BMS790052, BMS052+032Tibotec/Pharm 7977/TMC435, DEBO25+telaprevir/BOC, BI335+127+RBV, Vertex222+TLV, RocheDanoprevir+7128, Gilead, Abbott

Hard To Treat Patients

Unethical PR control…..

- African-Americans, Latinos
- Coinfected
- Cirrhotics, advanced disease
- Null responder cirrhotics

International, developing countries: since drug development is slower in developing world can studies use PR when US is using orals, no control? Activists

How do you conduct these expensive mutiple oral studies in developing world…it is not cost effective not to mention the ethics for a control

Telaprevir, BOC + PR Control

- In short term some patients will enroll because they might get potentially better arm, 2 orals+PR
- Expensive & cumbersome, do we need this control
- I say no!
- After BI, Tibotec (Janssen), DEB025…what about Roche/BMS/Abbott Pis which are approaching phase 3…..
- Should we even have a phase 3 of PI+PR??

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- What if double oral, triple orals show high SVR rates in the next 2 years: BMS052+032 100% SVR 1b 9 patients (AASLD), Pharmasset (100% SVR), BMS052/NS5A+7977…what if 90-100% SVR
- Is it ethical, can trials enroll as this data accumulates?

No Controls, When?

- I suggest NO CONTROLS be adopted but at the right time
- Timing is everything, so when?
- At what point do we decide to stop using any control group in trial
- We need to do continual monitoring, Fda/Panel to constantly review this question/decide when & how?
- Every drug should be approved, every combination should be approved, unless of course if SVR or toxicities are inordinately bad…..let market decide
- We don’t need a control to show TLV triple is 5 % points better or worse than another PI+PR

No Controls

- When we have 2/3 orals +/- PR cure rates will be so high to negate utility of SVR comparisons....how can you compare these regimens already showing 100% SVR or close to it
- Even if you compare & there are differences are they real differences, I say NO
- Should we compare for safety? NO

Controls Committee

- Suggest empanel committee for ongoing review of this important question: FDA, industry?, academia, community
- What about insurance coverage, reimbursent implications of not having a control arm….is there a negative consequence & how do we address it
- In the near term there might be a neg implication but not when multiple orals have very high SVR rates

PI TLV/BOC Failures Trials

- Multiple orals +/- PR: if PI is used at this point in time you need 2 additional classes: nucleotide/NS5A/nuke/2nd gen PI