Industry Partnership in Pediatric HIV Cure Research

Daria Hazuda

towards an HIV cure
people focused
science driven

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What are important considerations in pediatric HIV cure research for the industry?

Engagement of industry in pediatric HIV cure research: when and how this should be done?

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Similar (but different) issues as adults

- Understanding what and where is the reservoir
- Measuring affect(s) of intervention(s)
  - Pharmacodynamic (mechanism based) endpoints
  - “Eradication” relevant endpoints
  - Affects in tissue vs plasma
- Pharmacology
  - Dose
  - Drug interactions

Interventional Studies in Pediatrics

Traditional paradigm: Safety and efficacy is established first in adults

- PK and DDI potential is understood
- PK optimized for different pediatric populations, starting with adolescents
- Pilot studies conducted in different age cohorts, staged from older to younger

Note: Regulatory agencies are reluctant to do studies healthy children. All this must be established in HIV infected populations

Alternate Pediatric Paradigm

If scientifically justified; requires rationale that the pediatric population is unique vis-à-vis the intervention

- **Establish as much safety and PK in adults** as makes sense including potential for DDIs
- Initiate efficacy studies in adolescents, stage younger cohorts based on establishing PK targets

Note: May require additional safety studies in juvenal animals, eg immunological interventions

Perinatal vs adult HIV infection

- There are differences in the size, activation and immune response vs adults, at least in infants those who initiate therapy early.
- Infants have fewer long lived memory T-cells than adults. However, there are resting CD4 T-cells in cord blood and given the absence of T-follicular helper cells, follicular dendritic cells or germinal center cells the reservoirs may not be may not be the same as adults.
- The adaptive immune response is only fully mature around 2 years of age.

These biological differences could lead to a differential response and/or distinct approaches for pediatrics..but there is limited data.

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Opportunities for Industry Engagement

Now: Industry can help in providing interventions to assess activity in models and ex vivo studies

- Understanding potential differences in perinatal vs adult infection is critical for designing and justifying interventional studies

Future: May depend on the above…