Pediatric HIV Cure Research Hypothetical Case Studies

Purpose/Objective: Participants can apply and reflect the data learned in the presentation

Materials:
- Markers
- Flipchart
- Printed case studies

Method: Group discussion

To conduct this activity:
First
- Explain the purpose of the activity to the learners
- If necessary, review and answer any questions related to key concepts of pediatric HIV cure research
- Explain that the case studies are **fictional**. They do NOT represent current research being planned or currently ongoing in children.

Second
- Divide the participants into three groups
- Give the groups some allotted time to read and discuss their case study
- Be available in case groups have questions

Third
- Wrap up the session by asking a group leader to share the discussions and main conclusions of the group
- Write conclusions on the flipchart
- Ask other participants whether they understand and agree with the considerations
- Have members add additions or corrections until all of the major conclusions have been raised
Scenario 1

A mother in labor comes into the hospital testing positive for HIV during the time of delivery. She had received very little prenatal care. During the first trimester of her pregnancy she did have an HIV test and the results were negative. The baby was delivered and a blood test was taken immediately to determine if the child was HIV-positive. Within 72 hours the results came back positive and the child was started on 3 drug combination therapy. Mother and child both achieved viral suppression shortly after starting treatment and remain virally suppressed.

After six months of viral suppression the opportunity to participate in a pediatric clinical trial arises. The mother consents, and the child is given a single dose of a latency reversing agent known as romidepsin. The child experienced no symptoms other than a rash at the infusion site. After the single dose of romidepsin, there is a small but detectable number of viral copies in the child’s blood. The child remained on suppressive ART throughout the course of the trial. Once romidepsin was no longer detectable in the child’s blood (48 hours later) virus levels in the blood also returned to undetectable.

Following the latency reversing study, the mother is approached about entering her child into a follow-on clinical trial where the child would have a scheduled treatment interruption of ART to determine if the single dose of romidepsin was enough to clear the reservoir. Given the child’s young age only blood samples would be collected to test for viral rebound.

Questions
1. What are the scientific considerations for enrolling the child into this study?
2. What are the ethical considerations?
Scenario 2

A mother in Cape Town, South Africa comes into the hospital during labor having received no prenatal care. She tests positive for HIV during the time of delivery and no prophylaxis was given. The baby was delivered and a blood test was taken immediately to determine if the child was HIV-positive. In the two-week interim between finding out the results the child was put on a standard twice daily zidovudine in combination with nevirapine. Within two weeks the results came back positive and the child was started on a standard three-drug combination therapy. Mother and child both achieved viral suppression shortly after starting treatment and remain virally suppressed.

After four months of undetectable HIV and immune responses to HIV in blood the opportunity to participate in a pediatric clinical trial arises. The mother is approached to join by the child’s primary care physician. She consents and the child is given three doses of a therapeutic vaccine to try and boost the child’s immune system to kill residual virus. During the administration of the therapeutic vaccine, the child remains on ART. The child experienced no side effects related to the therapeutic vaccine. After the third dose of the therapeutic vaccine a scheduled treatment interruption is planned.

Questions
1. What are the scientific considerations for enrolling the child into this study?
2. What are the ethical considerations?
A mother in labor comes into the hospital testing positive for HIV during the time of delivery. She had received no prenatal care. The baby was delivered and a blood test was taken immediately after birth to determine if the child was HIV-positive. Within 48 hours the results come back positive. The child, as a precaution was started on three drug combination therapy six hours after birth. Mother and child both achieved viral suppression shortly after starting treatment and remain virally suppressed.

After twelve years of viral suppression on the original combination therapy the mother is approached by her child’s physician to enroll the child in a clinical trial. After a conversation with her child the mother consents, and the child is given a single dose of a latency reversing agent known as romidepsin. The child experienced no symptoms other than a rash at the infusion site. After the single dose of romidepsin, there is a small but detectable number of viral copies in the child’s blood. The child remained on suppressive ART throughout the course of the trial. Once romidepsin was no longer detectable in the child’s blood (48 hours later) virus levels in the blood also returned to undetectable.

Following the latency reversing study, the mother is approached about entering her child into a follow-on clinical trial. The child would undergo several biopsies to determine if there is latent reservoir in the tissue. If the biopsies return with undetectable virus the child would have a scheduled treatment interruption of ART to determine if the single dose of romidepsin was enough to clear the reservoir.

Questions
1. What are the potential scientific considerations for enrolling the child into this study?
2. What are the ethical considerations for enrolling the child into this study?
Discussion Guide

Scenario 1

Scientific considerations
- No way to measure if ALL of the reservoir is gone
- Known infant exposure to high viral load
- Inability to collect large blood draws and tissue samples
- No biomarkers for HIV remission

Ethical considerations
- Risk of drug resistance from treatment interruption
- Risk of increased viral reservoir from treatment interruption
- Risk from long term drug exposure

Scenario 2

Scientific considerations
- Potential for a high viral load
- Lack of ultra-sensitive diagnostic equipment
- Inability to collect large blood and tissue samples
- No biomarkers to measure for HIV remission
- Treatment interruption may not reactive the entire reservoir

Ethical considerations
- Risks from long term drug exposure
- Risks of drug resistance
- Mother was approached by physician so potential issues with consent
- The trial is taking place is the developing world so potential language or comprehension barriers
- Unknown benefits
- Risk of increased viral reservoir from treatment interruption

Scenario 3

Scientific considerations
- No biomarkers to measure for HIV remission
- No way conclusive measurement to determine if the child has any additional reservoir

Ethical considerations
- Risks for long term drug exposure
- Risks of drug resistance
- Potential issues with comprehension of risk. Child may just have drug fatigue
- Risk of biopsies

If learners have additional questions please refer them to the resources available on www.avac.org/cure-curriculum.