Research Gaps
### PAD3 RESEARCH PRIORITIES

#### Newborns

**A. Neonatal Prophylaxis**
- PMTCT risk on maternal DTG – Transmission risk and risk of transmission of DR virus
- PMTCT in low risk infants: No ART vs Standard of care
- Duration of infant prophylaxis in unsuppressed BF mother
- AZT prophylaxis dose older than 6 week

**B. Newborn Treatment:**
- Long acting agents in neonates – PK and safety, muscle bulk issues
- Monoclonal antibodies – long acting formulations,
- Novel delivery systems
- ABC down to <3M
- Safety in HIV exposed uninfected

**C. Remission research:**
- IMPAACT P1115, EPIICAL (novel agents, vaccines

#### Sequencing

**A. Dosing and formulations**
- TB-HIV trials: nest PK studies in ongoing trials to gather data in children that acquire TB while on studies
- Taste masking and Bioequivalence of crushed tablets
- LATs -injectables/patches: 1mo vs 2 mo
- Collection of more toxicity data (ie. in children < 3 years and bone/renal effect of TAF)

**B. Alternative agents**
- INSTIs vs bPIs (i.e. DTG vs bPIs) in NNRTI resistance
- Future third line : DTG/Ril and DTG/DRV

**C. Innovative strategies**
- Dual therapy : DTG/3TC, DRV/r/3TC, DRV/r/DTG in a **non-inferiority trial** including naïve and experienced
- Weekend off with DTG/EFV (?)

#### Novel antivirals
- Broadly neutralizing antibodies (VRC01 in phase II in adults; Vedolizumab (anti- a4b7 integrin) in phase I
- Adnectins = molecules that target CD4 and gp41
  - Combinectin (SC): anti-CD4, anti-gp41,fusion inhibitor, HAS
- Nano- formulations & role in pediatric HIV

*Many questions are still unanswered*
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NEW:

- Need to better define renal toxicity of TDF 300 mg in children 25-30 kg
- PK data for dose reduction of DRVr
- Efficacy of DTG in second line for failures on RAL-based first-line ART
- PK data to support the use of TAF and DRVr in children on TB treatment
- Efficacy and safety of alternative regimens for PNP
Global research agendas

- Paediatric and Adolescent briefs
- In English and French
- Available online: https://www.iasociety.org/CIPHER
Methods

- Child Health and Nutrition Research Initiative (CHNRI, [www.chnri.org](http://www.chnri.org)) systematic method for setting priorities in health research

CHNRI process:
- **BROAD CALL FOR RESEARCH QUESTIONS**
  - 264 respondents
- **CONSOLIDATION**
  - 749 questions were cleaned and consolidated into 52 questions after merging
- **SCORING OF THE RESEARCH QUESTIONS**
  - 134 respondents scored the consolidated questions
- **EXPERT CONSULTATION**
  - 5 themes per research area included in the prioritized research agenda

Putting CHNRI into context:
Ongoing research, published scientific literature and current WHO guidance were considered
Top 5: Treatment

Children

- Safety, efficacy, acceptability, pharmacokinetics and optimal dosing of existing and new antiretroviral drugs and formulations, particularly with novel drug delivery systems
- Strategies or interventions to improve adherence and factors that affect success
- Optimal prevention and clinical management of co-infections, particularly tuberculosis
- Impact of HIV infection and ART on short- and long-term outcomes, in particular non-communicable disease
- Short- and long-term virologic and immunologic outcomes of starting very early treatment in infants living with HIV (impact on functional cure)
Top 5: Treatment

Adolescents

- Effective monitoring approaches and strategies to improve adherence among adolescents and factors that impact success
- Safety, efficacy and acceptability of novel drug delivery systems
- Prevention and clinical management of co-infections, particularly tuberculosis
- Optimal sequencing of ART in adolescents
- Impact of HIV infection and ART on short- and long-term outcomes in particular non-communicable diseases