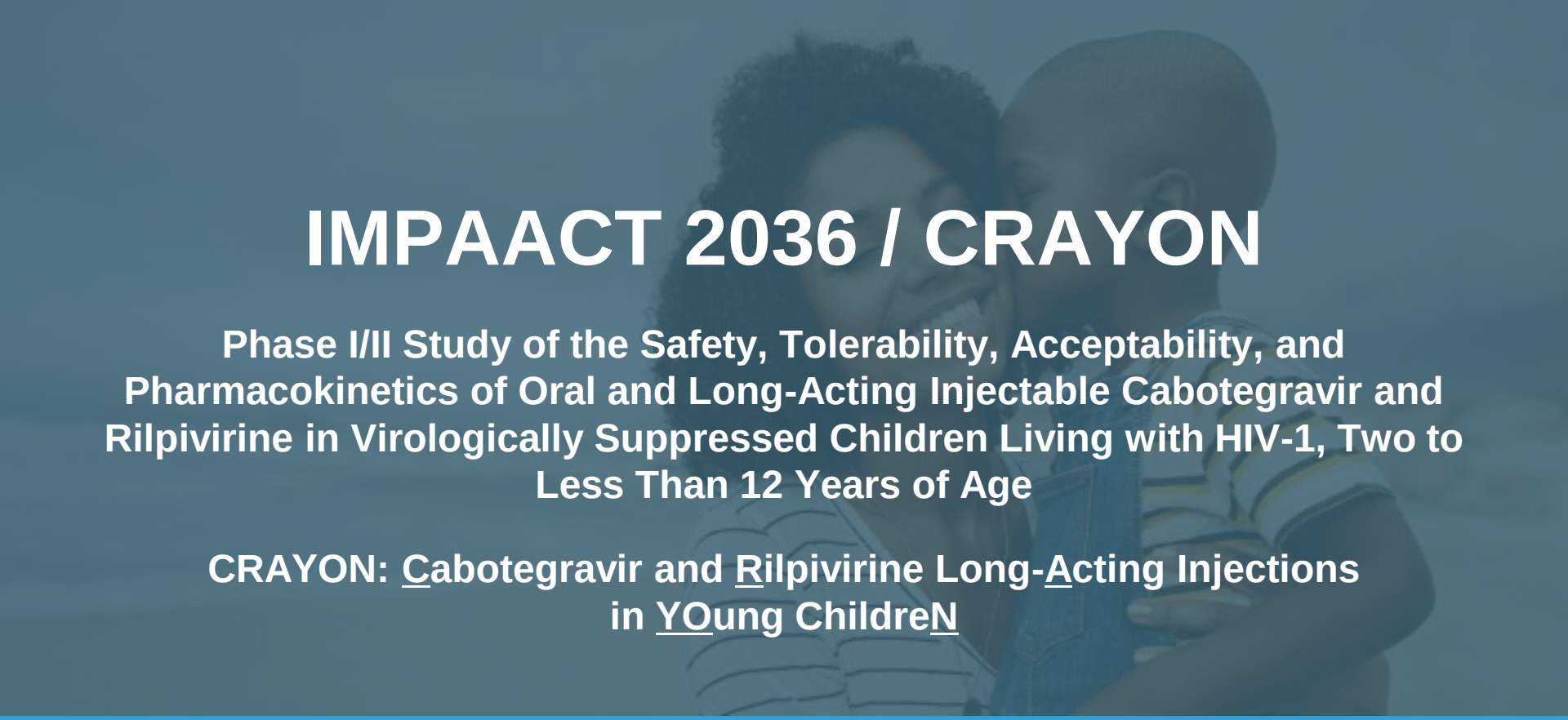

# IMPAACT 2036 / CRAYON

## Phase I/II Study of the Safety, Tolerability, Acceptability, and Pharmacokinetics of Oral and Long-Acting Injectable Cabotegravir and Rilpivirine in Virologically Suppressed Children Living with HIV-1, Two to Less Than 12 Years of Age

## CRAYON: Cabotegravir and Rilpivirine Long-Acting Injections in YOung ChildreN

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# Introduction

## Background

- Long-acting (LA) injectable antiretrovirals are promising new therapies both for HIV treatment and HIV prevention that may change the treatment paradigm, although present unique implementation challenges.
- This study aims to build on the experience to date with CAB LA and RPV LA in adults living with HIV-and an ongoing study among adolescents living with HIV (IMPAACT 2017; ClinicalTrials.gov Identifier: NCT03497676).

## Purpose

- To propose the weight band dosing of oral cabotegravir (CAB) + oral rilpivirine (RPV) followed by long-acting injectable CAB (CAB LA) + long-acting injectable RPV (RPV LA) in children living with HIV-1, and to describe participant choice and experience with the regimen with or without an oral lead-in period.

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# Study Schema

## Cohort 1

Enroll up to 70 children (50 evaluable) → Discontinue pre-study ART → CAB + RPV PO (4 weeks) → CAB LA + RPV LA IMI (Q4W/Q8W) through Week 72

## Cohort 2

20-40 children

(at least 4 in Cohort 2a and 4 in Cohort 2b)

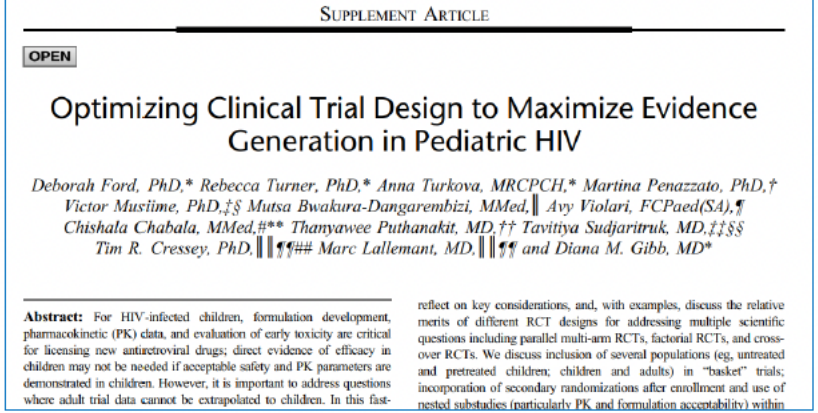
### Cohort 2a (with oral dosing)

Discontinue pre-study ART → CAB + RPV PO (4 weeks) → CAB LA + RPV LA IMI (Q4W/Q8W) through Week 48

### Cohort 2b (direct to inject)

Discontinue pre-study ART → CAB LA + RPV LA IMI (Q4W/Q8W) through Week 44

- WHO weight-band dosing
- PK modelling methods for better prediction of dosing, particularly in neonates
- Simultaneous enrolment across different weight bands for younger children
- Enrolling adolescents in adult clinical trials
- Extrapolation of efficacy data from adult trials for regulatory approvals
- The use of innovative paediatric trial designs to maximise the use of available data
- Wide collaboration across different stakeholders



SUPPLEMENT ARTICLE

OPEN

Optimizing Clinical Trial Design to Maximize Evidence Generation in Pediatric HIV

*Deborah Ford, PhD,* Rebecca Turner, PhD,* Anna Turkova, MRCPCH,* Martina Penazzato, PhD,† Victor Musiime, PhD,‡§ Mutsa Bwakura-Dangarembizi, MMed,‖ Avy Violari, FCPaed(SA),¶ Chishala Chabala, MMed,#** Thanyawee Puthanakit, MD,†† Tavitiya Sudjaritruk, MD,‡‡§§ Tim R. Cressey, PhD,‖‖¶¶## Marc Lallemant, MD,‖‖¶¶ and Diana M. Gibb, MD**

**Abstract:** For HIV-infected children, formulation development, pharmacokinetic (PK) data, and evaluation of early toxicity are critical for licensing new antiretroviral drugs; direct evidence of efficacy in children may not be needed if acceptable safety and PK parameters are demonstrated in children. However, it is important to address questions where adult trial data cannot be extrapolated to children. In this fast-reflect on key considerations, and, with examples, discuss the relative merits of different RCT designs for addressing multiple scientific questions including parallel multi-arm RCTs, factorial RCTs, and cross-over RCTs. We discuss inclusion of several populations (eg, untreated and pretreated children; children and adults) in "basket" trials; incorporation of secondary randomizations after enrollment and use of nested substudies (particularly PK and formulation acceptability) within


*Clinical Infectious Diseases*

VIEWPOINTS

IDSA Infectious Diseases Society of America

hivma hiv medicine association

Optimizing Research to Speed Up Availability of Pediatric Antiretroviral Drugs and Formulations

**Martina Penazzato,[1] Devasena Gnanashanmugam,[2] Pablo Rojo,[2,4] Marc Lallemant,[5] Linda L. Lewis,[6] Francesca Rocchi,[4] Agnes Saint Raymond,[7] Nathan Ford,[1] Rohan Hazra,[8] Carlo Giaquinto,[9] Yodit Belew,[10] Diana M. Gibb,[11] and Elaine J. Abrams[12,13]; for the Paediatric Antiretroviral Working Group (PAWG)**

[1]HIV Department, World Health Organization, Geneva, Switzerland; [2]Division of AIDS, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland; [3]Hospital 12 de Octubre, Facultad de Medicina, Universidad Complutense, Madrid, Spain; [4]Paediatric European Network for Treatment of AIDS, Padua, Italy; [5]Drugs for Neglected Diseases Initiative, Geneva, Switzerland; [6]Clinton Health Access Initiative, Bethesda, Maryland; [7]European Medicines Agency, London, United Kingdom; [8]Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, Maryland; [9]Department of Woman and Child Health, University of Padua, Italy; [10]Center for Drug Evaluation and Research, US Food and Drug Administration, Silver Spring, Maryland; [11]Medical Research Council Clinical Trials Unit, University College London, United Kingdom; and [12]ICAP, Mailman School of Public Health and [13]College of Physicians and Surgeons, Columbia University, New York

Globally 1.8 million children are living with human immunodeficiency virus (HIV), yet only 51% of those eligible actually start treatment. Research and development (R&D) for pediatric antiretrovirals (ARVs) is a lengthy process and lags considerably behind drug development in adults. Providing safe, effective, and well-tolerated drugs for children remains critical to ensuring scale-up globally.

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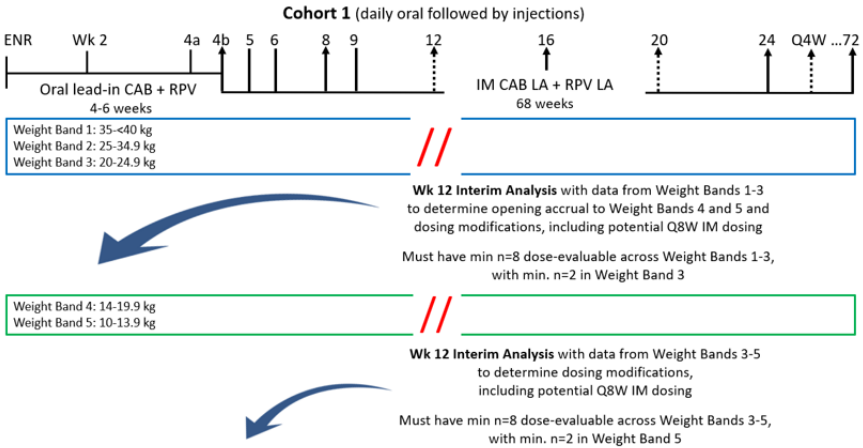
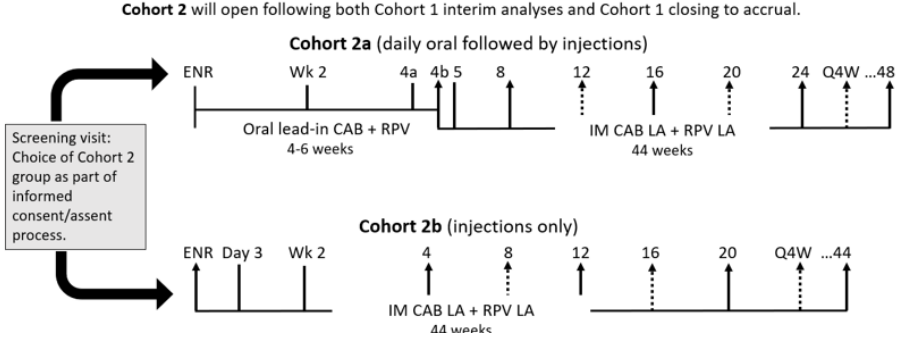
# Weight-band dosing

| | Weight Bands (minimum accrual per weight band) | Total Minimum Accrual Across Weight Bands |
|---|---|---|
| 1. | 35-<40 kg (min n=6) | Minimum of n =18 across Weight Band 1 and 2 |
| 2. | 25-34.9 kg (min n=6) | |
| 3. | 20-24.9 kg (min n=6) | Minimum of n=32 across Weight Band 3,4, and 5 |
| 4. | 14-19.9 kg (min n=6) | |
| 5. | 10-13.9 kg (min n=10) | |




## Limiting staggered opening of weight-bands

## Innovative paediatric trial designs

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# Study Duration

- Approximately three and a half years in total, from the time of the first participant enrollment.
- Accrual into Cohort 1 is expected to require approximately 12 months. Accrual into Cohort 2 will continue for a maximum of six months.
- Participants will be followed approximately 18 months on study product in Cohort 1 and approximately 12 months in Cohort 2.

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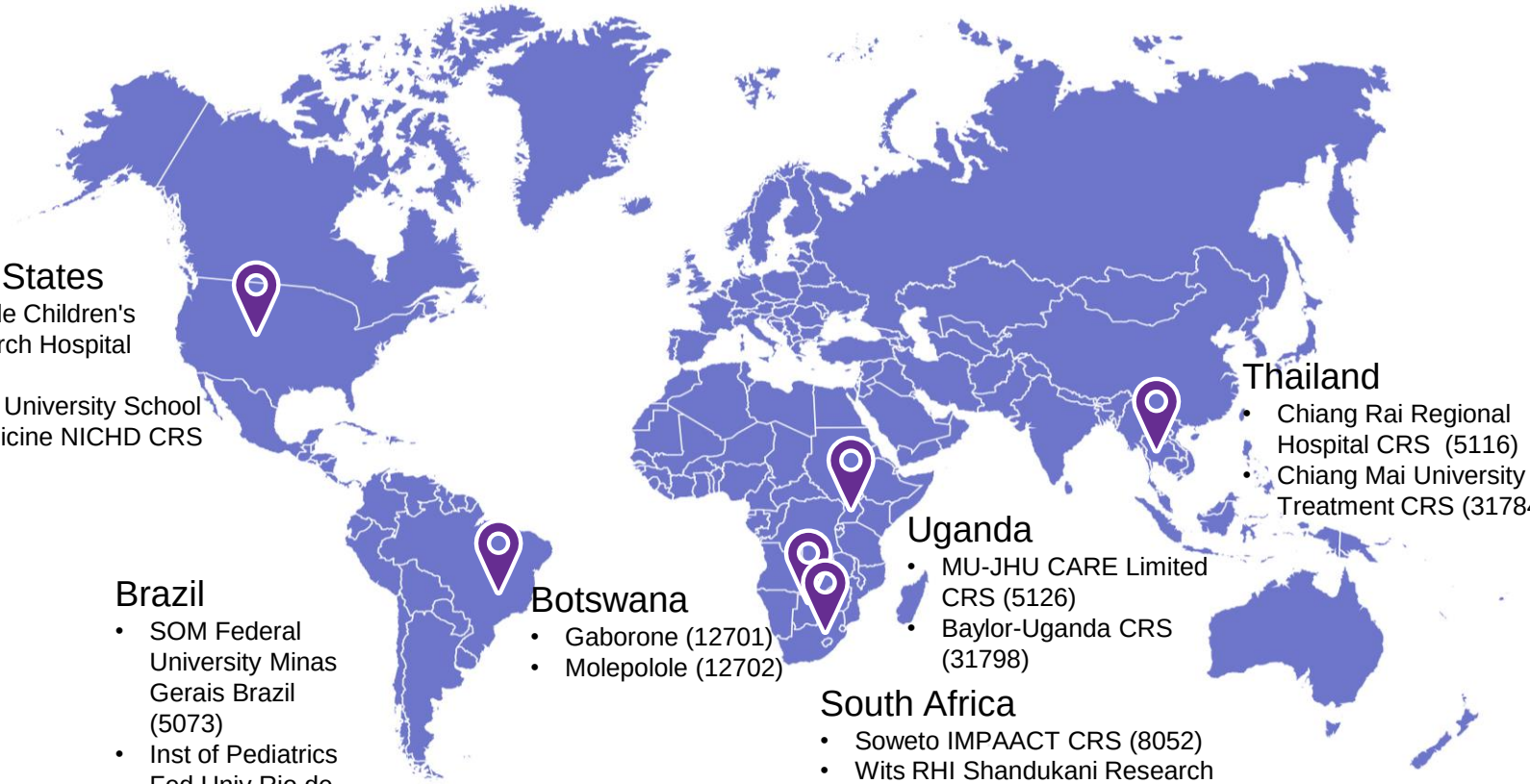

## United States

- St. Jude Children's Research Hospital (6501)
- Emory University School of Medicine NICHD CRS (5030)

## Brazil

- SOM Federal University Minas Gerais Brazil (5073)
- Inst of Pediatrics Fed Univ Rio de Janeiro NICHD CRS (5071)

## Botswana

- Gaborone (12701)
- Molepolole (12702)

## Uganda

- MU-JHU CARE Limited CRS (5126)
- Baylor-Uganda CRS (31798)

## South Africa

- Soweto IMPAACT CRS (8052)
- Wits RHI Shandukani Research Centre CRS (8051)

## Thailand

- Chiang Rai Regional Hospital CRS (5116)
- Chiang Mai University HIV Treatment CRS (31784)

# THANKS!

## Any questions?

Impaact.team2036@fstrf.org