Implementing Long-Acting Studies in Adolescents: lessons from the field

Overview

- **Recruitment lessons learned (5 minutes)**
- What the patients and their families are telling us (15 minutes)

IMPAACT
International Maternal Pediatric Adolescent AIDS Clinical Trials Network

MOCHA: Study Design

Cohort 1

(Add on to background cART)

n=15 CAB

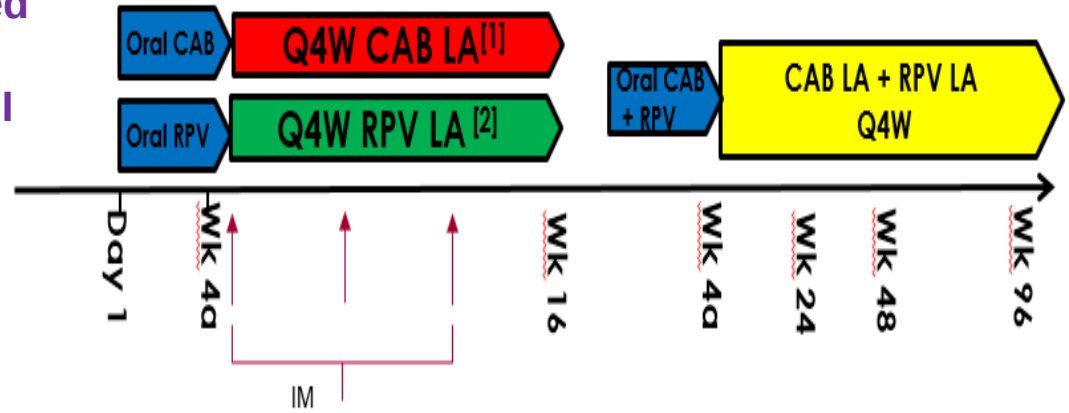
n=15 RPV

Cohort 2

(No background cART)

n=100

Protocol version 3.0 changed Q4W to Q8W dosing
Version 4.0 includes O.O.L.I



- Population at entry: HIV-infected, virologically suppressed adolescents (12 to <18 years old) on stable cART consisting of 2 or more drugs from 2 or more classes of ARV drugs.
- Cohort 1 participants are assigned to **Cohort 1C** (receive CAB + cART) or **Cohort 1R** (receive RPV + cART) based on their pre-study cART regimen.

[1] PI/NNRTI based cART [2] INI based cART.

IMPAACT
International Maternal Pediatric Adolescent AIDS Clinical Trials Network

Recruitment expereince

IMPAACT
International Maternal Pediatric Adolescent AIDS Clinical Trials Network

Enrollment overview

- IMPAACT 2017 was opened to accrual on March 19, 2019 and the first participant enrolled April 3, 2019
- Cohort 1 closed to enrollment Nov 25, 2021 after 30 participants enrolled in Cohort 1C and 25 in Cohort 1R.
- Of note, accrual was paused from March 2020 through February 2021 due to the COVID-19 pandemic, as directed by the network.
- Cohort 2 opened to enrollment of Cohort 1 naïve participants May 2nd, 2022
- Taking a look at the enrollment experience of Cohort 1 and Cohort 2

IMPAACT
International Maternal Pediatric Adolescent AIDS Clinical Trials Network

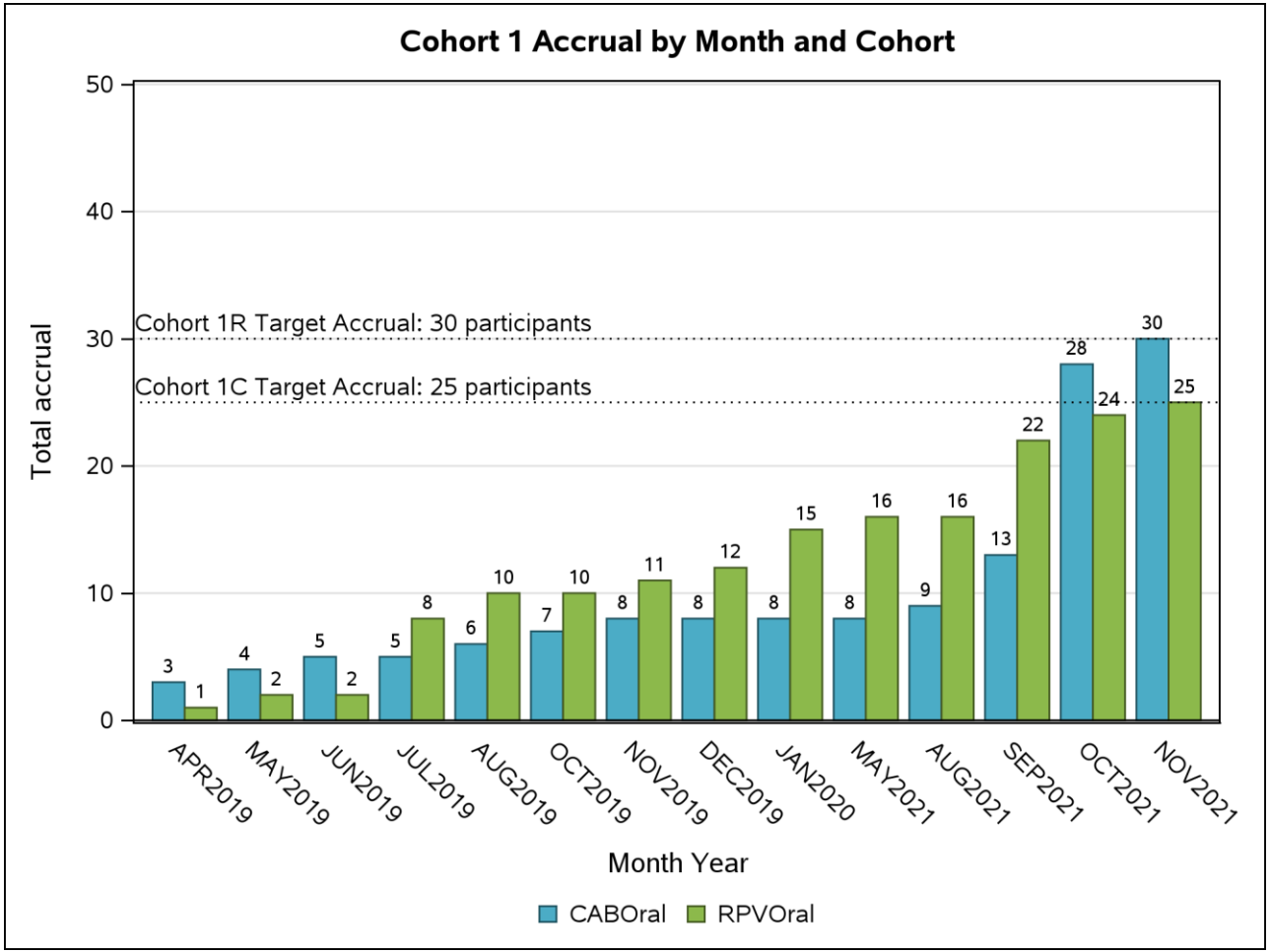


Figure credit to Ryan Milligan at SDAC

IMPAACT
International Maternal Pediatric Adolescent AIDS Clinical Trials Network

Assessing challenges to recruitment in the US

- Teleconferences with sites were scheduled in two rounds in late 2019.
  - Round 1 of calls was held with 15 sites that had projected at least one Cohort 1 enrollment per the July 2019 updated accrual projections but had not yet met their projections.
  - Round 2 of calls was with the remaining 5 sites that had either met their enrollment projection or had projected zero enrollments for Cohort 1.

Feedback from sites

Pre-Screen Failure Reason	Number of Sites Reporting	Suggested Action Item for Sites	Suggested Action Item for Protocol Team Consideration
Potential participant declines due to time commitment/visit burden/visit frequency	7	Parent-to-parent discussion; peer-to-peer discussion; Sites to reconsider incentives, as appropriate	Amend protocol; develop a video and other audio/visual media describing the benefits of research
Increase in viral load (note: this does not separate out multiple "blips" within the 6-month timeframe from significant elevations)	6	using the study as an incentive for maintaining low VL	Amend protocol to be more lenient to allow for blips
Potential participant declines due to fear of injections	5	Peer-to-peer discussions	Develop a video or other audio/visual media depicting an enrolled participant receiving the injection and sharing their experience

Note: Patients on Boosted elvitegravir regimen were not eligible for Cohort 1

IMPAACT
International Maternal Pediatric Adolescent AIDS Clinical Trials Network

Virologic Suppression Criteria - Implementation

<table>
<tr><th colspan="5">From plasma HIV-1 RNA testing:</th></tr>
<tr><th>12-18 months prior to entry (365-545 days)</th><th>6-12 months prior to entry (180-365 days)</th><th colspan="2">Within 6 months prior to entry (within 179 days)</th><th>At Screening</th><th>Eligible</th></tr>
<tr><td>At least 1 test result less than lower limit of detection of the assay – Inclusion 4.1.8</td><td></td><td>At least 1 test result less than lower limit of detection of the assay – Inclusion 4.1.8</td><td rowspan="2">Does <u>NOT</u> have two consecutive documented HIV-1 RNA values greater than the lower limit of detection of the assay – Exclusion 4.2.1</td><td rowspan="2">< 50 copies/mL – Inclusion 4.1.11</td><td>Eligible</td></tr>
<tr><td></td><td>At least 1 test result less than lower limit of detection of the assay – Inclusion 4.1.8</td><td></td><td>Eligible</td></tr>
</table>

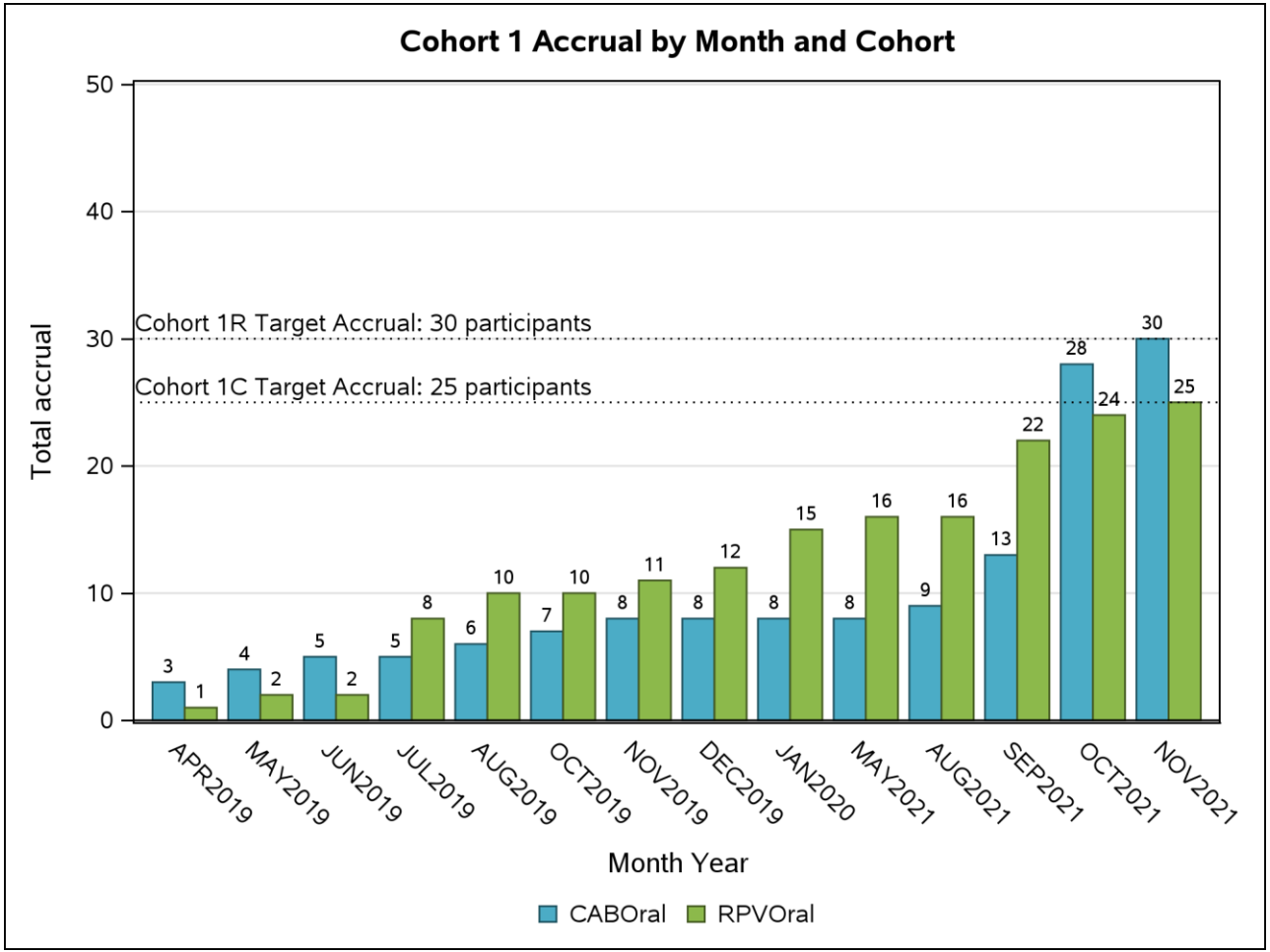


Figure credit to Ryan Milligan at SDAC

IMPAACT
International Maternal Pediatric Adolescent AIDS Clinical Trials Network

IMPAACT 2017 Cohort 1 enrollment

- Enrollment was likely impacted by regional differences in background cART regimen of potential participant cohorts
- Domestic enrolments:
  - 25 participants were enrolled across 8 sites in the United States (USA)
- International enrolments:
  - Five participants were enrolled across 2 sites in Botswana (BWA), 8 participants were enrolled across 2 sites in Thailand (THA), and 17 participants were enrolled across 3 sites in South Africa (ZAF)
- Enrollment by collaborating sites in South Africa and Thailand was critical to timely completion of enrollment in Cohort 1

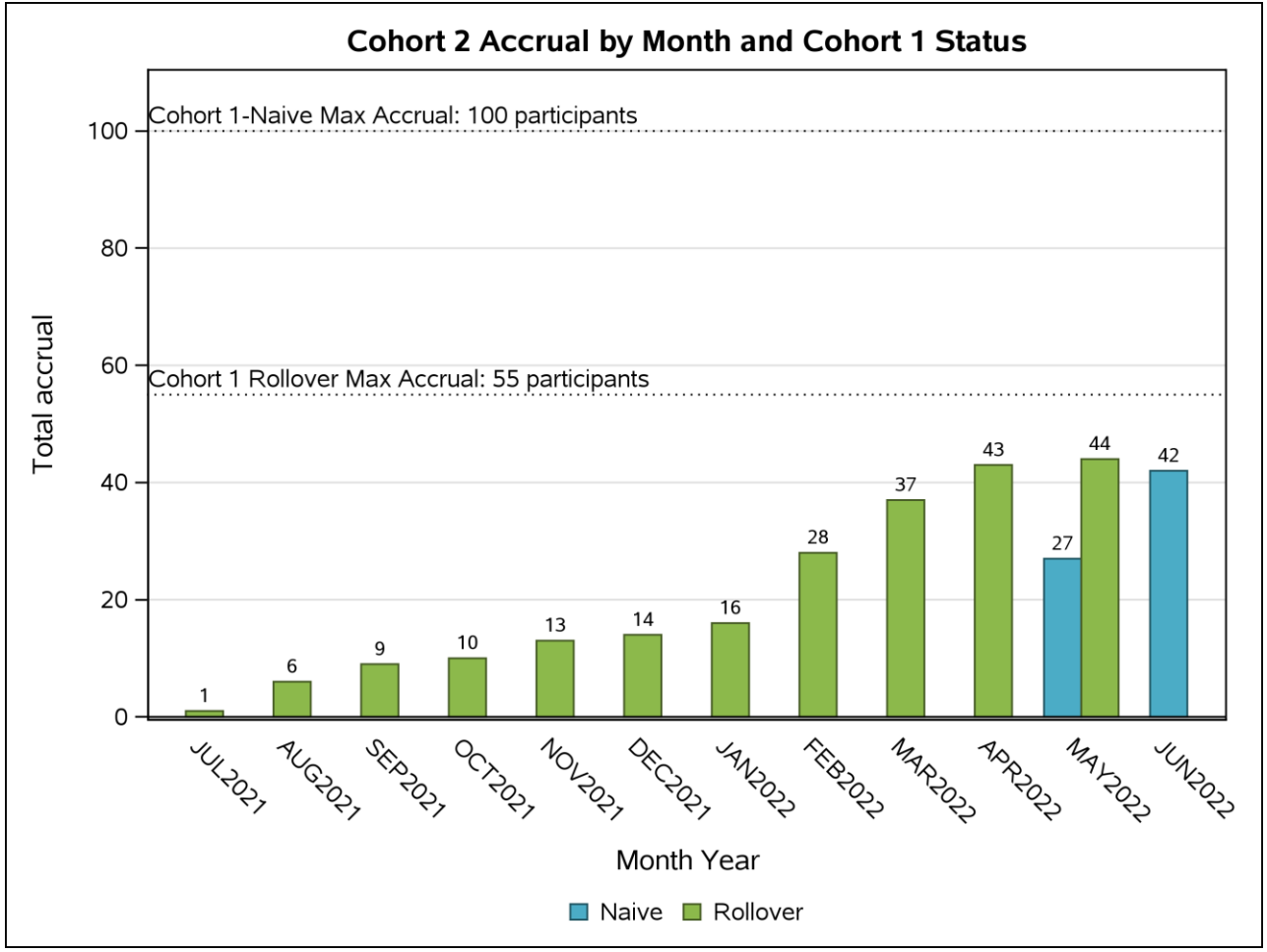


Figure credit to Ryan Milligan at SDAC

IMPAACT
International Maternal Pediatric Adolescent AIDS Clinical Trials Network

IMPAACT 2017 Cohort 2 enrollment

- Enrollment at a remarkable pace and majority at non-US sites – we look forward to learning from the enrolling sites what they are seeing….hearing from potential participant approaches
- Highlights the strength of the IMPAACT Network and most importantly some of the member sites
- Understanding what worked and what can be improved from the experience with this all long-acting antiretroviral regimen protocol maybe informative for other long-acting injectable studies to follow

IMPAACT
International Maternal Pediatric Adolescent AIDS Clinical Trials Network

Acknowledgments

FHI 360: Kat Calabrese, MPH, Sarah Buisson, MSW, MPH and Michael Whitton, BA
DAIDS: Ellen Townley, MSN, FNP, Dwight Yin, MD, MPH
NICHD: Jack Moye, MD
SDAC: Kristen Baltrusaitis, MS, Shawn Ward, MS, Ryan Milligan, MB
PAB: Cindy Parker, PharmD, RPh
UCSD: Edmund Capparelli, PharmD and Brookie Best, PharmD, MAS
CHOP & JHU: Jennifer Chapman, MPH, Elizabeth Lowenthal, MD, and Sharon Nachman, MD
FSTRF: Barbara Heckman, BS, Jared Kneebone, MPH, Andi Ace, and Kyle Whitson, MA
ILC: Sara Zabih, Emma Duffy
LT: Chiraphorn Kaewkosaba, MSc
Westat: Scott Watson, BS, RN
ViiV Healthcare: Cindy McCoig, MD, Conn Harrington, Susan Ford, Jenny Huang
Janssen: Herta Crauwels, PhD, Rodica Van Solingen-Ristea, MD, Kati Vandermeulen
Site investigators from US and International sites
Protocol Chairs: Carolyn Bolton Moore, MSc, MBBCh, and Aditya H. Gaur, MD

We appreciate the contributions of the study participants and their families

Overall support for the International Maternal Pediatric Adolescent AIDS Clinical Trials Network (IMPAACT) was provided by the National Institute of Allergy and Infectious Diseases (NIAID) with co-funding from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) and the National Institute of Mental Health (NIMH), all components of the National Institutes of Health (NIH), under Award Numbers UM1AI068632-15 (IMPAACT LOC), UM1AI068616-15 (IMPAACT SDMC) and UM1AI106716-09 (IMPAACT LC), and by NICHD contract number HHSN275201800001I. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

IMPAACT
International Maternal Pediatric Adolescent AIDS Clinical Trials Network