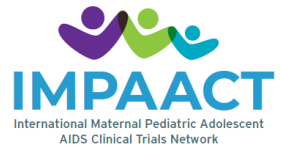




State of the Network

Sharon Nachman, MD
IMPAACT Network Chair
22 June 2021

IMPAACT Annual **Meeting** 2021





William "Bill" Borkowsky
1947-2021

State of the Network: A Snapshot



- ▶ IMPAACT in the context of COVID-19
- ▶ Network activities and achievements in the past two years
- ▶ Study updates and achievements
- ▶ Continued and new partnerships

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IMPAACT's Goals

To improve health outcomes for infants, children, adolescents and pregnant/postpartum women who are impacted by or living with HIV by evaluating novel treatments and interventions for HIV and its complications and for tuberculosis and other HIV-related conditions.

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IMPAACT in the context of HIV and COVID-19

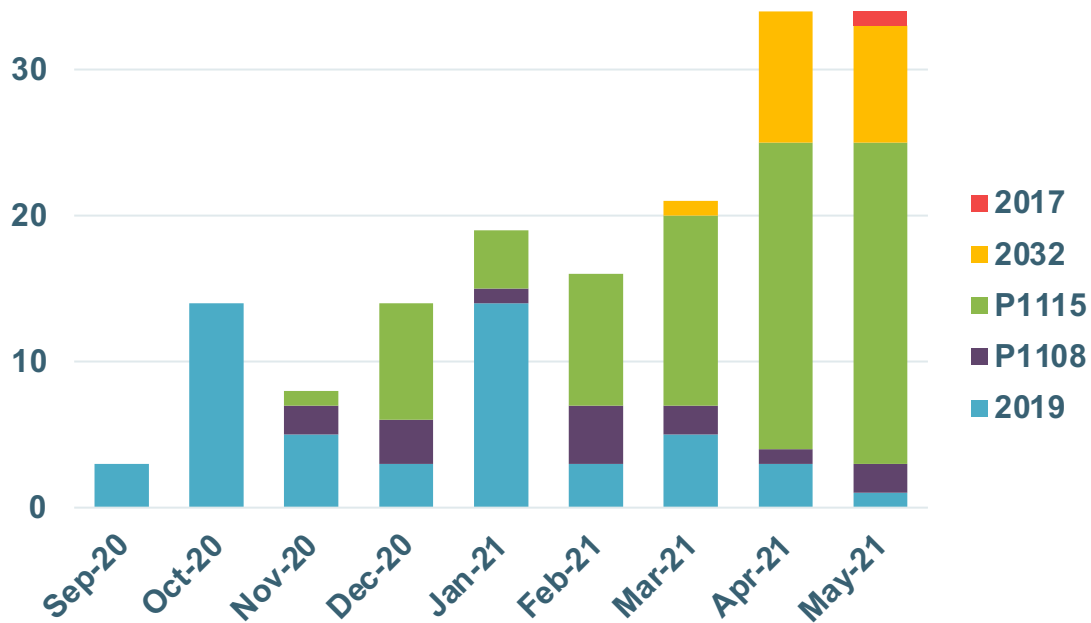
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Response to COVID-19

- ▶ Accrual into all IMPAACT studies was paused in March 2020 and resumed in most studies beginning in July 2020, with careful consideration of study conduct in the context of the pandemic and detailed guidance issued for participating sites
- ▶ Ongoing studies continued with high rates of visit completion and protocol compliance and minimal disruption thanks to the awesome diligence and dedication of site staff!!
- ▶ The safety and well-being of participants, study staff and their communities remains of utmost importance

Response to COVID-19

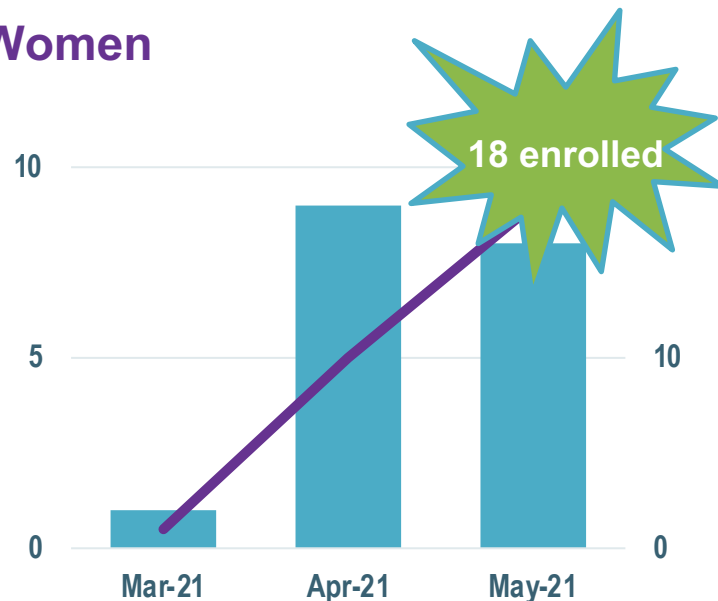
In addition to implementing ongoing studies in the context of COVID-19, accrual has been initiated or resumed in five studies



Study Highlight: IMPAACT 2032

Remdesivir in Pregnant and Non-Pregnant Women

- ▶ Rapidly developed with separate funding through the RADx-UP Initiative (Rapid Acceleration of Diagnostics for Underserved Populations)
- ▶ First participant enrolled on 31 March 2021 at JHU site (5092)
- ▶ 18 participants enrolled at 4 sites in the US through 31 May 2021



Anticipate complete accrual
by September 2021

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IMPAACT Activities and Achievements in the Past Two Years

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Successful Re-Competitions!

- ▶ The IMPAACT Network was awarded the grant for another seven years of support by the National Institutes of Health
- ▶ Clinical Research Sites continuing, with the same overall number in the same locations (26 international sites; 19 in the US)

NIH Announces Restructured HIV
Clinical Trials Networks

Grant Awards Set Stage for Next Seven Years of Science-
Driven HIV Clinical Research

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Contributions to Expanded Treatment Options

- ▶ Three studies have had recent regulatory submissions (P1090/ETV, P1093/DTG, IMPAACT 2007/MVC)
- ▶ Two additional studies (IMPAACT 2014/DOR, 2017/CAB+RPV) are anticipated to be submitted within the next year
- ▶ Over the course of the last grant cycle and moving forward: 12 licensure studies, some with multiple regulatory submissions (RAL, DTG, ETV, MVC, DOR, CAB/RPV, DTG/ABC/3TC, DTG/RPV, remdesivir)

Current Portfolio

includes evaluation of the following interventions/agents

Treatment

- DTG/RPV in Children
- DTG in Neonates, Infants, Children and Adolescents
- Selected ARV and TB drugs in Pregnant/ Postpartum Women
- ABC/DTG/3TC in Children
- LA CAB/RPV in Children
- DOR/3TC/TDF in Children
- Oral PrEP (TDF/FTC) in Pregnant & Postpartum Women
- bNAbs in Infants

Tuberculosis

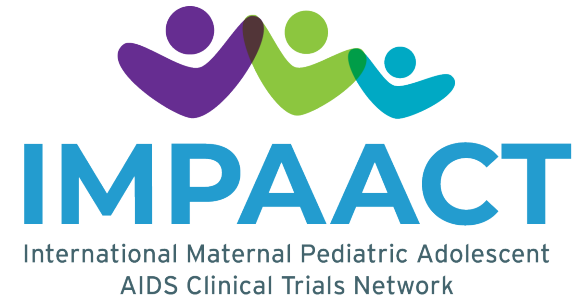
- VPM1002/BCG in Pre-Adolescents
- Pretomanid in Children
- RPT/INH in Children
- BDQ in Children
- DLM in Children
- RPT/INH in Pregnant/ Postpartum Women

Complications

- RSV vaccines in children
- Group-based counseling intervention in treatment non-adherent Adolescents

Cure

- LPV and NVP containing early intensive treatment, RAL and NVP containing early intensive treatment, and VRC01 in Infants
- Cord Blood Transplantation with CCR5Δ32 Donor Cells



Current Portfolio

30 active studies

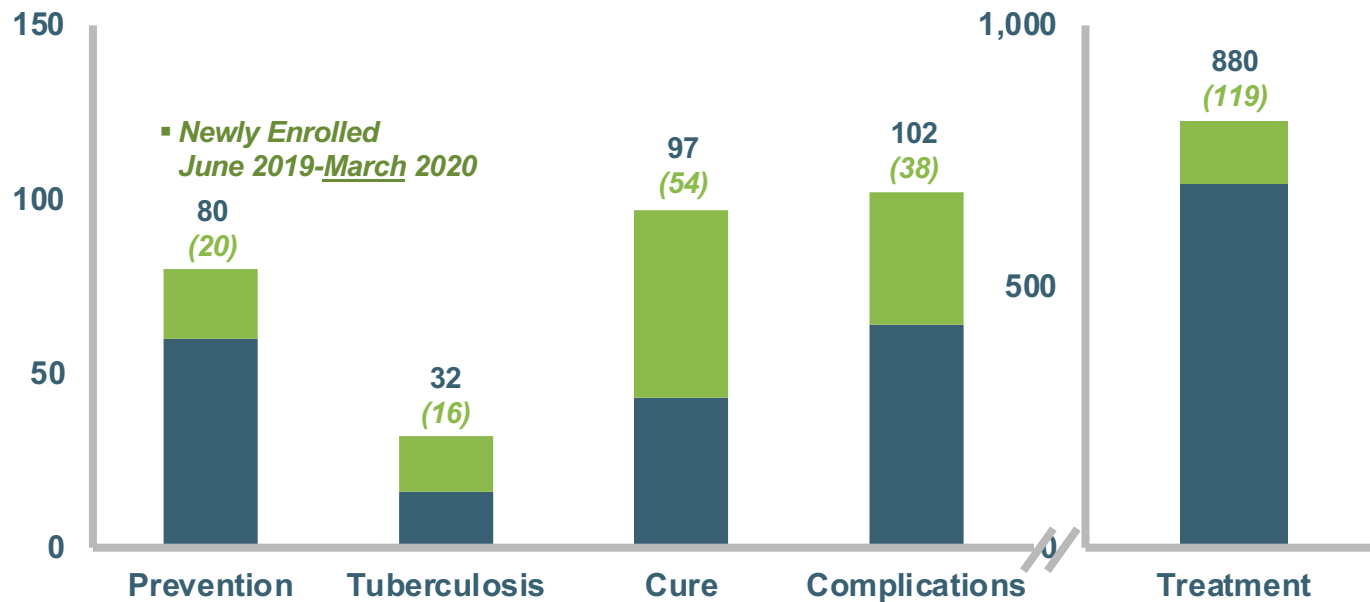
	9 Protocols in Development	3 Pending and Open	9 Enrolling	5 in Follow-Up	4 Closed to Follow-Up*
Treatment	2036, 2029, 2023, 2022	2026	2019, 2017, 2009	2014, P1112, P1102, P1093	2010, P1026s
Tuberculosis	2035, 2034, 2025, 2024, 2020		2003B/A5300B, 2005, P1108		
Complications		2016	2021		2018
Cure		2028	P1115	P1107	2008
COVID-19			2032		

Approximately 30 additional studies and ancillary studies (NWCS, DACS, DR) in analysis and manuscript writing phase

*closed to follow-up in the last year

IMPAACT Participants on Study

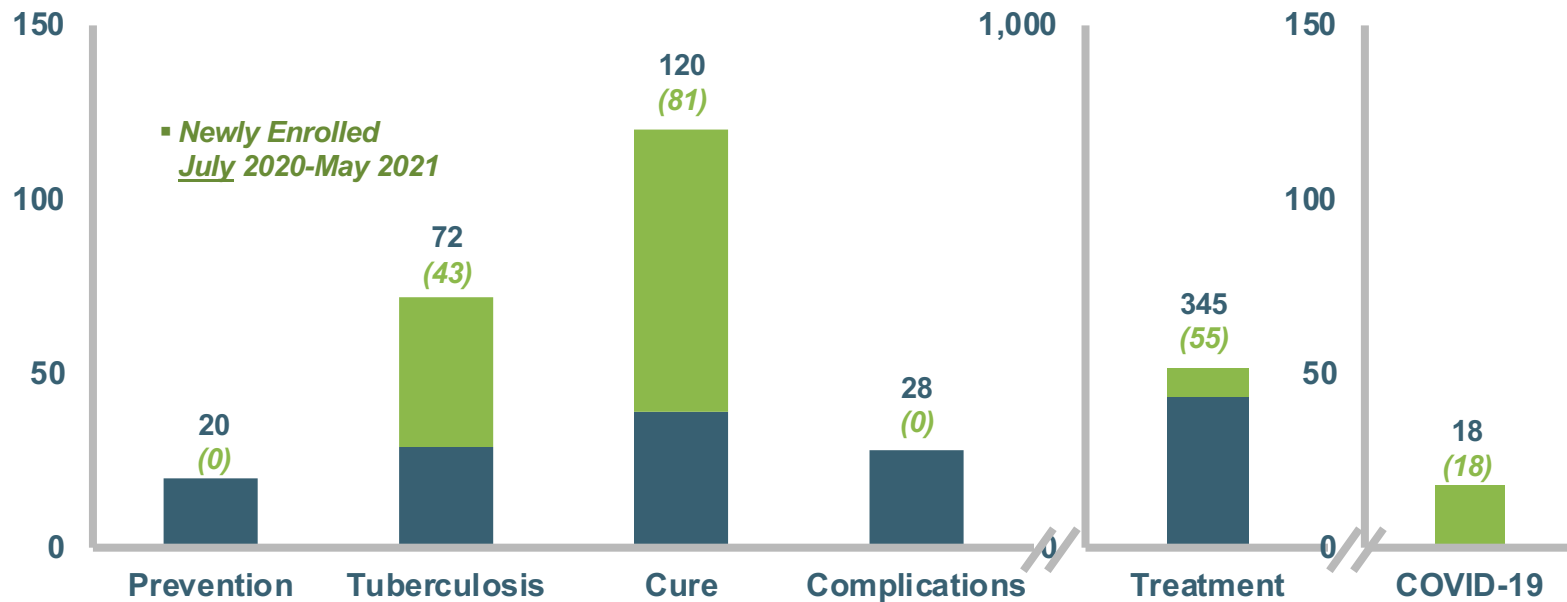
June 2019 to May 2020



Total On Study = 1,191 participants
Newly Enrolled = 247 participants

IMPAACT Participants on Study

June 2020 to May 2021 *(during pandemic)*



Total On Study = 603 participants
Newly Enrolled = 197 participants

Study Updates and Achievements

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Study Highlight: P1093

PK, Safety, & Antiviral Activity of Dolutegravir

- ▶ Landmark study of child-friendly dolutegravir formulations in children that continues to contribute to FDA and EMA approvals, with ODYSSEY study
- ▶ Completed accrual with 181 participants enrolled at 35 sites in Botswana, Brazil, Kenya, South Africa, Tanzania, Thailand, Uganda, the United States, and Zimbabwe

Drug Topics

FDA Approves Dolutegravir Tablets for Oral Suspension for ...

Officials with the FDA have approved dolutegravir (Tivicay PD, Viiv ... The new approval is based on data from the ongoing P1093 and ...

Jun 12, 2020

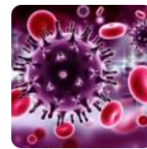


PharmaTimes

EU approval for Viiv's Tivicay for children living with HIV

... formulation of its HIV-1 treatment Tivicay (dolutegravir) in paediatric patients ... The approval is based on data from the ongoing P1093 and ...

Jan 14, 2021

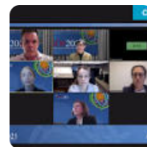


Aidsmap

Dolutegravir superior to standard-of-care treatment in children ...

Dr Anna Turkova of the United Kingdom Medical Research Council presented the 96-week results of the ODYSSEY study at the 2021 virtual ...

Mar 12, 2021



MPR

Tivicay Labeling Updated to Include More Pediatric HIV Patients

... open-label, non-comparative, P1093 IMPAACT study that evaluated dolutegravir in combination regimens in HIV-1 infected infants, children, ...

Jun 10, 2016



IMPAACT Annual Meeting

Study Highlight: P1108

PK and Safety of Bedaquiline in Infants, Children, and Adolescents with MDR-TB Disease and with or without HIV

- ▶ Addressing critical need for better medications to treat children with MDR-TB
- ▶ All five sites approved to resume accrual during the COVID-19 pandemic
- ▶ 15 participants enrolled in the past year with 30 evaluable enrolled overall



Anticipate Version 2 issued by July with accrual completion by September 2022

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Study Highlight: P1112

Safety and PK Parameters of Potent Anti-HIV Neutralizing Monoclonal Antibodies

- ▶ First of its kind monoclonal antibody study of potential early intervention among infants exposed to HIV
- ▶ 83 participants enrolled at sites in South Africa, the United States, and Zimbabwe
- ▶ Results from Dose Group 4 recently published in *JID*



Anticipate completing follow-up by February 2022

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Study Highlight: P1115

Very Early Intensive Treatment of Infants with HIV to Achieve HIV Remission

- ▶ Network's flagship proof-of-concept study for HIV remission in infants
- ▶ 76 mother-infant pairs have enrolled since accrual was approved to resume
- ▶ 18 sites have met requirements to resume accrual during pandemic
 - Accrual into Steps 1 and 2 approved to resume in July 2020
 - Entry into Step 3 approved on a site-by-site basis in May 2021

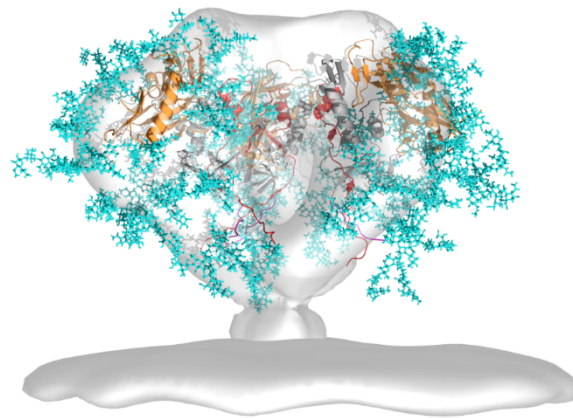
Anticipate enrollment completion
by December 2023

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Study Highlight: IMPAACT 2008

Study of Monoclonal Antibody Combined with ART

- ▶ First to evaluate monoclonal antibodies for treatment (and potential remission) in infants living with HIV
- ▶ 61 infants enrolled in Botswana, Brazil, Malawi, and Zimbabwe



Successfully completed follow-up
as of 11 February 2021

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Study Highlight: IMPAACT 2014

Doravirine as Fixed-Dose Combination for Adolescents

- ▶ New fixed-dose, one-pill/once-a-day combination for adolescents
- ▶ 10 participants enrolled at 4 sites in the US in Cohort 1
- ▶ 45 participants enrolled at 5 sites in South Africa, Thailand, and the US in Cohort 2

Anticipate completing follow-up
by December 2021



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Study Highlight: IMPAACT 2017

PK & Safety of Long-Acting Injectable Cabotegravir & Rilpivirine

- ▶ First study of long-acting injectable regimens in adolescents with HIV
- ▶ 24 adolescents and 10 parents/caregivers enrolled at 8 sites in the United States
- ▶ International sites working on approvals to start enrolling

Anticipate completing accrual
by July 2022

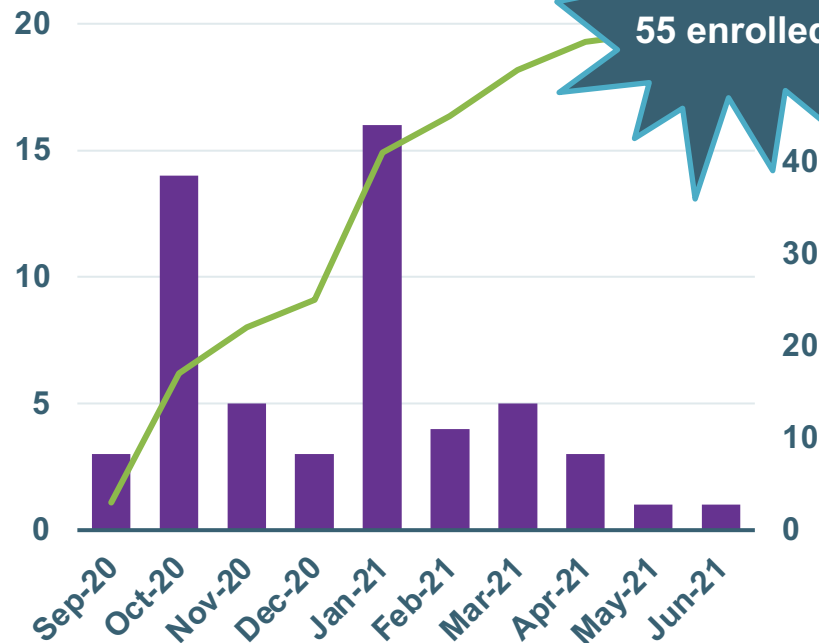


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Study Highlight: IMPAACT 2019

ABC/DTG/3TC as Fixed-Dose Combination for Children

- ▶ New fixed-dose, dispersible, once-a-day combination for young children
- ▶ Fully enrolled but pending confirmation of evaluability for lowest weight band
- ▶ Participants enrolled at 15 sites in Botswana, Thailand, South Africa, and United States



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Study Highlight: IMPAACT 2021

RSV Candidate Vaccine Study

- ▶ Randomized, Phase I/II placebo-controlled study among healthy RSV-seronegative children 6-24 months of age to assess safety and immunogenicity of candidate vaccines
- ▶ 30 of 160 participants enrolled at 10 sites in the US prior to accrual pause due to COVID-19
- ▶ Team, Network leadership, and sites in discussion on appropriate timeline to resume accrual in the United States (anticipated soon)

Anticipate issuance of Protocol
Version 2 by Q3 2021

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Community Engagement

- ▶ Community representation and input on all network groups and levels – clinical research sites, leadership groups, scientific and other committees, protocol teams, cross-network activities
- ▶ ICAB ensures that the principles of community participation and partnership are at the foundation of all community engagement activities and provides community input throughout the research process (concept development, study implementation, and results dissemination)



Successful IMPAACT Community Advisory Board Leadership Transition

- ▶ Emanuelli Msuya transitioned from Vice Chair of the ICAB Leadership Group to Chair
- ▶ Jayshawnda Arrington voted by ICAB members as Vice Chair
- ▶ New leadership group representatives voted by ICAB members

Publications

- ▶ **65** publications submitted for IMPAACT review in past 12 months
- ▶ **35** manuscripts published in JAIDS, AIDS, JAMA, PLoS One, Lancet, Lancet HIV, Journal of Clinical Pharmacology, PIDJ, CID, among others

Tenofovir Diphosphate Concentrations in Dried Blood Spots From Pregnant and Postpartum Adolescent and Young Women Receiving Daily Observed Pre-exposure Prophylaxis in Sub-Saharan Africa

Lynda Stranix-Chibanda,^{1,2,*} Peter L. Anderson,³ Clemensia Nakabiito,⁴ Maysebole Masenyi,⁵ K. Rivet Amico,⁶ James F. Rooney,⁷ Nahid

THE LANCET

ARTICLES | VOLUME 397, ISSUE 10281, P1276-1292, APRIL 03, 2021

Efficacy and safety of dolutegravir with emtricitabine and tenofovir alafenamide fumarate or tenofovir disoproxil fumarate, and efavirenz, emtricitabine, and tenofovir disoproxil fumarate HIV antiretroviral therapy regimens started in pregnancy (IMPAACT 2010/VESTED): a multicentre, open-label, randomised, controlled, phase 3 trial

Shahin Lockman, MD, ¹ Sean S Brummel, PhD, ² Lauren Ziemba, MS, ³ Lynda Stranix-Chibanda, MBChB, ⁴

HIV REPORTS

OPEN

Pharmacokinetics and Safety of Zidovudine, Lamivudine, and Lopinavir/Ritonavir in HIV-infected Children With Severe Acute Malnutrition in Sub-Saharan Africa: IMPAACT Protocol P1092

Maxensia Owor, MMed,¹ Camlin Tierney, PhD,² Lauren Ziemba, MS,³ Renee Browning, MSN,⁴ John Moye, MD,⁵ Bobbie Graham, BS,⁶ Christina Reding, MPH,⁷ Diane Castello, BS,⁸ Jennifer Norman, MS,⁹ Lubbe Wiesner, PhD,¹⁰ Emma Hughes, BS,¹¹ Meghan E. Whalen, PharmD,¹² Lynette Purdue, PharmD,¹³ Blandina Theophil Mmbaga, PhD,¹⁴ Portia Kamthunzi, MBBS, MSc,¹⁵ Rachel Kavvalazira, MBBS,¹⁶ Kusum Nathoo, MRCP,¹⁷ Sarah Bradford, MPH,¹⁸ Anne Coletti, MS,¹⁹ Francesca Aweka, PhD,²⁰ and Philippa Musoke, PhD,²¹

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The Pediatric Infectious Disease Journal • Volume 40, Number 5, May 2021

IMPAACT Annual Meeting 2021

Abstracts

14 at CROI 2020, **7** at AIDS 2020, **8** at CROI 2021

- 3 abstracts from IMPAACT 2010/VESTED
- 2 abstracts from PROMISE and 2 abstracts from P1106
- Additional results from P1026s, P1078, P1101, P1112, 2001, 2003, 2007, 2009, 2014, among others!

IMPAACT 2014 24-week PK and
Safety of Doravirine/3TC/TDF in
Adolescents with HIV-1

Ann J Melvin, Brooke Best, Petronella Muresan, Sarah Pasyar, Hedy Teppler, Kelly Yee, Katie McCarthy, Rachel Scheckter, Hong Wan, Lina de Montigny, Linda Aupibul, Pradthana Ounchanum, Avy Violari, Nicole Tobin, and Ellen Townley

Safety/Efficacy of DTG vs EFV,
TDF vs TAF in Pregnancy/Postpartum:
IMPAACT 2010

Lameck Chinula, Sean Brummel, Lauren Ziemba, Katie McCarthy, Benjamin Johnston, Nahida Chakhtoura, Patrick Jean-Philippe, Lynda Stranix-Chibanda, Violet Korutaro, Haseena Cassim, Lee Fairlie, Gaerolwe Masheto, Paul Sax, Judith S. Currier, Shahin Lockman

Optimizing Dolutegravir Initiation in
Neonates using Population Pharmacokinetic
Modeling

Joseph Piscitelli PharmD¹, Mina Nikanjam MD PhD¹, Jeremiah Momper PharmD PhD¹, Brooke Best PharmD¹, Edward Acosta PharmD², Mark Mirochnick MD³, Diana Clarke PharmD⁴, Edmund Capparelli PharmD¹

¹Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California San Diego, La Jolla, CA

²Department of Pharmacology, University of Alabama Birmingham, Birmingham, AL

³Department of Pediatrics, Boston University School of Medicine, Boston, MA

⁴Section of Pediatrics Infectious Diseases, Boston Medical Center, Boston, MA

***Additional abstracts accepted to upcoming meetings
at IAS 2021 and the HIV Pediatrics Workshop***

Cross Network Study Initiatives



- ▶ Pregnancy Studies (IMPAACT 2026)
- ▶ MDR-TB Prevention (PHOENIx)
- ▶ TB Vaccine Studies (IMPAACT 2036)
- ▶ Dolutegravir (P1093/ODYSSEY)
- ▶ RSV and VRC Studies (IMPAACT 2011/2012/2013, IMPAACT 2018, IMPAACT 2021; P1112, IMPAACT 2008)



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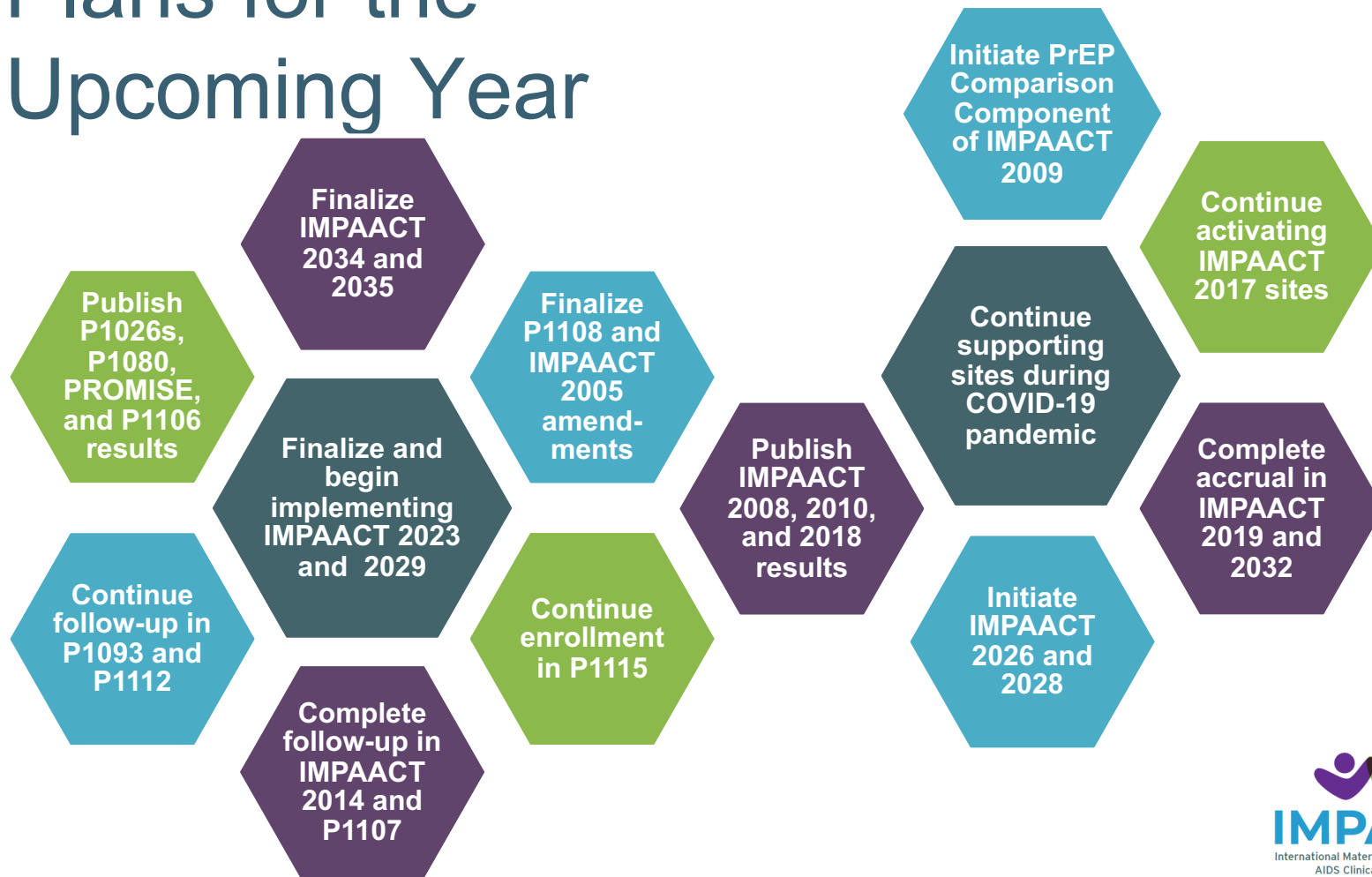
Pharma and Other Collaborations



IMPAACT Annual **Meeting** 2021



Plans for the Upcoming Year



Thank you to site staff, to the communities,
and to all of the individuals and families
engaged in clinical research!

Let's continue to move the science forward!



THANKS!

Any questions?

IMPAACT Annual Meeting 2021