

State of the Network

Sharon Nachman, MD
IMPAACT Network Chair
28 June 2022



ANNUAL MEETING
2022

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2 State of the Network: A Snapshot



- ▶ Research agenda
- ▶ Network activities and achievements
- ▶ Study updates and achievements
- ▶ Upcoming studies and protocols in development
- ▶ Continued and new partnerships



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IMPAACT's Goal

To improve health outcomes for infants, children, adolescents, and pregnant and postpartum people 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



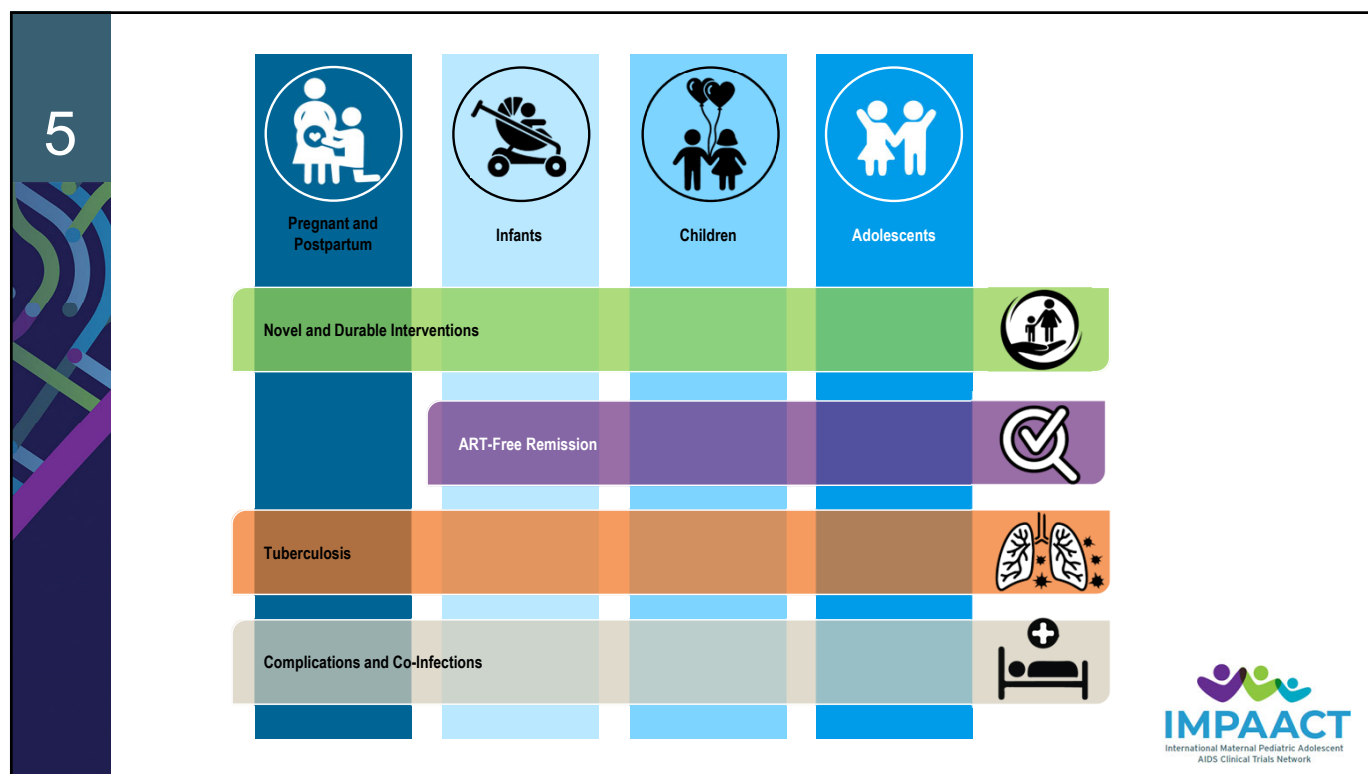
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IMPAACT Research Agenda

2022 - 2027



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Current Portfolio

includes evaluation of the following interventions/agents

Treatment <ul style="list-style-type: none"> • DTG in Neonates, Infants, Children and Adolescents • Selected ARV and TB drugs in Pregnant/ Postpartum People • ABC/DTG/3TC in Children • LA CAB/RPV in Children & Adolescents and in Pregnancy • DOR/3TC/TDF in Children • Oral PrEP (TDF/FTC) in Pregnancy & Postpartum • bNAbs in Infants 	Complications <ul style="list-style-type: none"> • RSV Vaccines in Children • Group-based Counseling Intervention in Treatment Non-adherent Adolescents • GLE/PIB for Hepatitis C in Pregnancy 	Tuberculosis <ul style="list-style-type: none"> • VPM1002/BCG in Pre-Adolescents • Pretomanid in Children • RPT/INH in Children • BDQ in Children • DLM in Children
Cure <ul style="list-style-type: none"> • 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 • HIVconsvX Vaccines and bNAbs in Children 		

IMPAACT
International Maternal Pediatric Adolescent
AIDS Clinical Trials Network

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Current Portfolio

26 active studies

	2 Proposals Recently Approved	7 Protocols in Development	2 Pending and Open	9 Enrolling	3 in Follow-Up	3 Closed to Follow-Up*
Treatment		2040, 2037, 2036	2023	2026, 2017, 2009	P1093, 2019	2014, P1112
Tuberculosis		2035, 2034, 2024		2005, 2003B, P1108		
Complications	2041, 2038		2016	2021		2032 (COVID-19)
Cure		2039		2028, P1115	P1107	

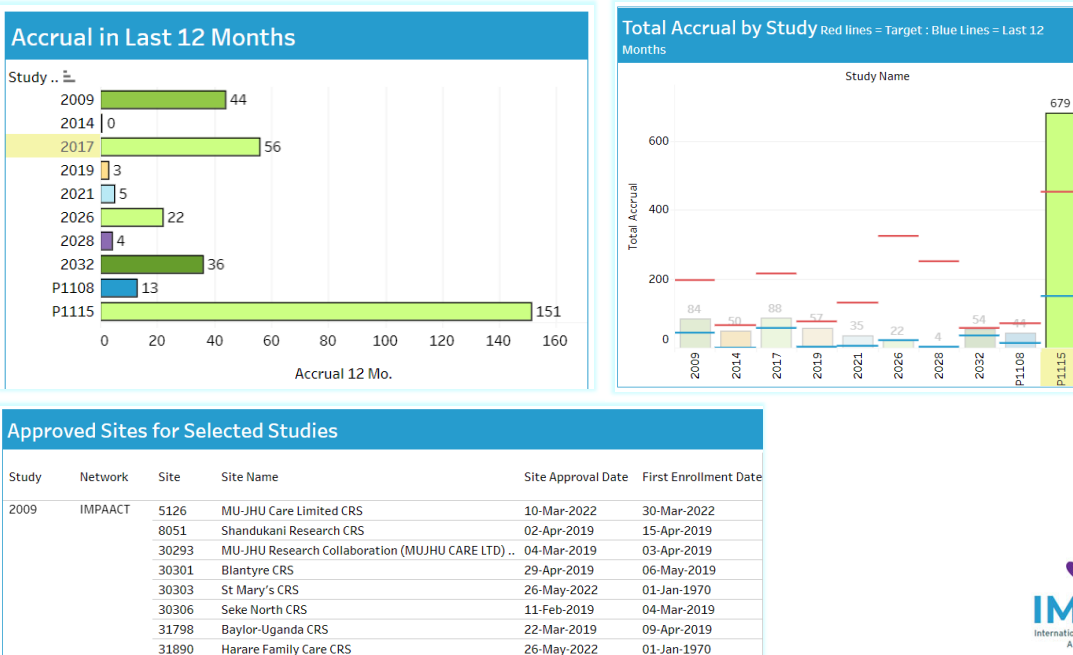
Approximately 30 additional studies and ancillary studies (NWCS, DACS, DR) in analysis and manuscript writing phase

*closed to follow-up in the last year

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Data Dashboards

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Seven Protocols Currently in Development

Three within the Treatment Research Area

2040	Phase I/II Pharmacokinetics and Safety of Long-Acting Injectable Cabotegravir and Rilpivirine in People with Virally Suppressed HIV-1 during Pregnancy and Postpartum
2037	Open-Label, Phase I Study of the Safety and Pharmacokinetics of PGT121.414LS alone and in combination with VRC07-523LS in Infants Exposed to HIV-1
2036	Phase I/II Study of the Safety, Tolerability, Pharmacokinetics, and Antiviral Activity of Oral and Long-Acting Injectable Cabotegravir and Rilpivirine in Virologically Suppressed Children with HIV >2 to <12 years of age and weighing >10 kg and <40 kg



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Seven Protocols Currently in Development

Three within the Tuberculosis Research Area

2035	Phase I/II Study of the Safety and Immunogenicity of VPM1002 Vaccination or BCG Re-Vaccination against Tuberculosis in South African Pre-Adolescents Living with and without HIV
2034	Phase I Study of PK, Safety, & Acceptability of Pretomanid in Children with Rifampicin-Resistant TB
2024	Phase I/II Dose Finding, Safety, and Tolerability Study of Daily Rifapentine Combined with Isoniazid (1HP) for Tuberculosis Prevention in Children 2 to <13 years of age with and without HIV



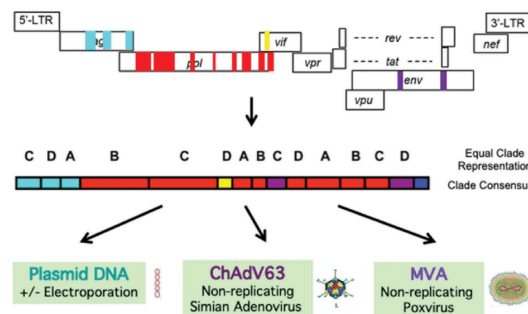
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Seven Protocols Currently in Development *One within the Cure Research Area*

2039

Phase I/II Study of the Safety, Immunogenicity, and Efficacy of **HIVconsvX Vaccines and Broadly Neutralizing Antibodies** in Children Living with HIV



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Protocols Planned for Development *Two within the Complications Research Area*

2038

Phase I Study of the Infectivity, Safety and Immunogenicity of two **Recombinant, Live-Attenuated B/HPIV3 Vector Vaccines** Expressing the Fusion Glycoprotein of **RSV** Engineered for Increased Immunogenicity, Delivered in Single Doses as **Nose Drops** to HPIV3-Seronegative Infants and Children 6 to 18 Months of Age (CAP 554)

2041

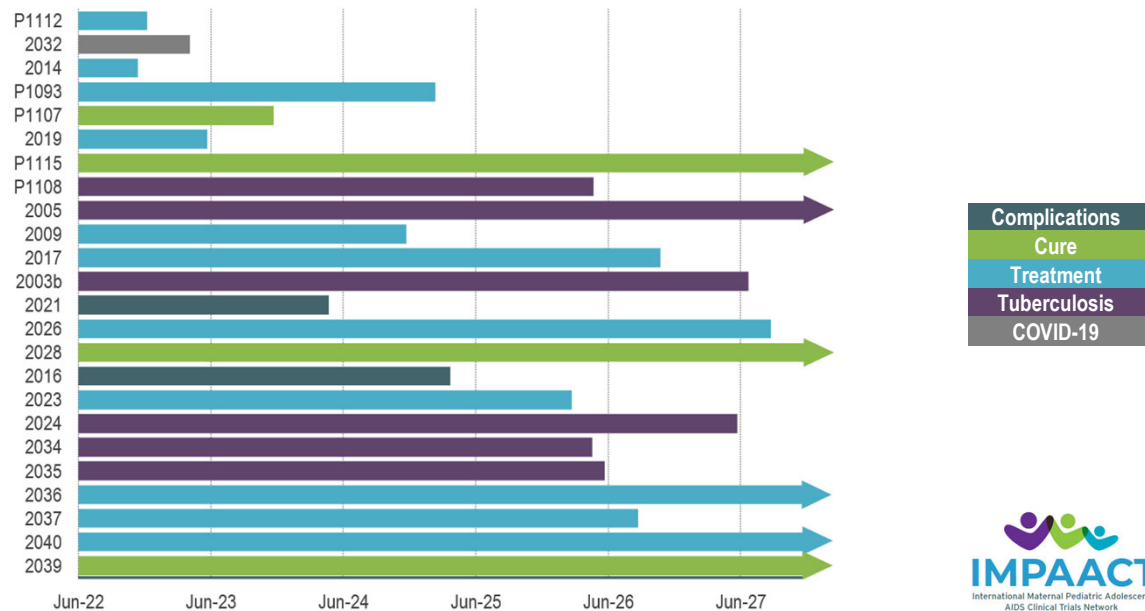
Safety and Pharmacokinetics of **GLE/PIB** in **Pregnant Persons with Hepatitis C** with or without HIV (CS 5032)



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The Network has a robust and growing portfolio of current studies and new proposals in the pipeline



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Network Activities and Achievements

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Contributions to Expanded Treatment Options – *In the Past Year*

Data from three studies informed recent US FDA decisions for ART in children living with HIV

- ✓ **P1093/DTG:** expanded approval of *Triumeq* and *Triumeq PD* for children 10-25 kg
- ✓ **IMPAACT 2014/DOR and DOR/3TC/TDF:** expanded approval of *Destrigo* and *Pifeltro* for children 35 kg and more
- ✓ **IMPAACT 2017/CAB/RPV:** expanded approval of *Cabenuva* for children aged 12 years and older, 25 kg and more



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IMPAACT 2017 (MOCHA) Data Informs U.S. FDA Approval of Cabenuva for HIV Treatment in Virologically Suppressed Adolescents

MARCH 2022

ANNOUNCEMENTS

SHARE

The IMPAACT Network is pleased to announce that interim data from **IMPAACT 2017/MOCHA** (More Options for Children and Adolescents) has informed the U.S. Food and Drug Administration's (FDA) decision to approve Cabenuva (cabotegravir, CAB; rilpivirine, RPV) for the treatment of HIV-1 in adolescents who are virologically suppressed, 12 years of age or older, and weigh at least 25 kg. Adolescents must be on a stable antiretroviral regimen with no history of treatment failure, and with no known or suspected resistance to either



First time a long-acting HIV treatment is available for adolescents

ViiV HEALTHCARE ANNOUNCES US FDA APPROVAL OF *CABENUVA* (CABOTEGRAVIR, RILPIVIRINE) FOR VIROLOGICALLY SUPPRESSED ADOLESCENTS LIVING WITH HIV WHO ARE 12 YEARS OF AGE OR OLDER AND WEIGH AT LEAST 35 KG

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Contributions to Expanded Treatment Options – *Looking Forward*

Additional data from four studies anticipated to be submitted to regulatory authorities:

- ▶ IMPAACT 2014 – DOR and DOR/3TC/TDF
- ▶ IMPAACT 2017 – CAB/RPV
- ▶ IMPAACT 2019 – ABC/DTG/3TC
- ▶ IMPAACT 2032 – RDV



Group of children, Getty Images



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IMPAACT P1107 Team Presents First Known Case of a Woman with HIV Remission

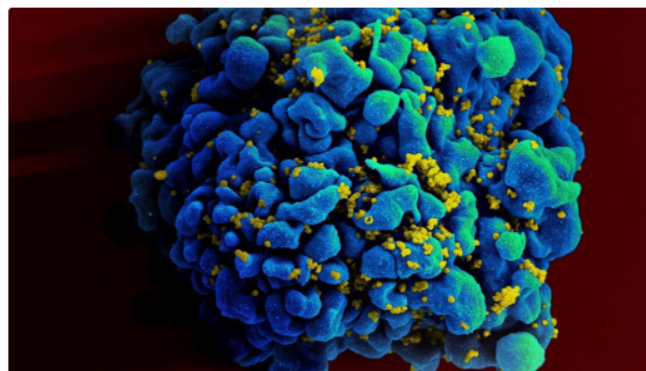
FEBRUARY 2022

STUDY RESULTS

SHARE

The [IMPAACT P1107](#) protocol team presented the **first known case of a woman with HIV remission** following a stem cell transplant for treatment of acute myelogenous leukemia (AML) at CROI 2022 on 15 February. The transplant consisted of cord blood stem cells with the CCR5 Δ 32 genetic mutation and haploidentical peripheral blood stem cells from a relative. Since having the stem cell transplant, the participant has been in remission for AML.

>> [See Latest Press Coverage](#)

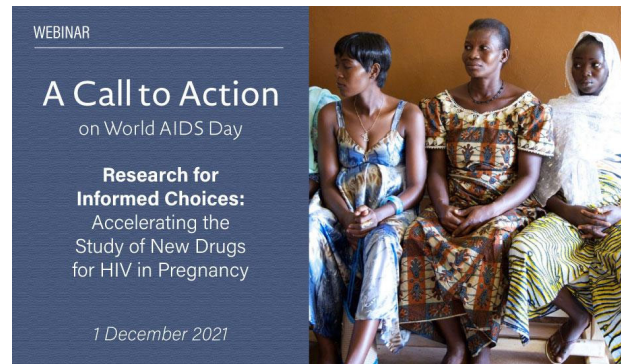


HIV-infected T cell, NIAID

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Call to Action: Accelerating Study of New Drugs for HIV in Pregnancy



Three major conceptual shifts that will facilitate inclusion of pregnant people in research:

- ✓ Considering pregnant individuals as a **complex population** rather than a vulnerable population
- ✓ Moving from protecting from research to **protecting through research**
- ✓ **Promoting fair inclusion in**, rather than presumptive exclusion from, clinical drug trials

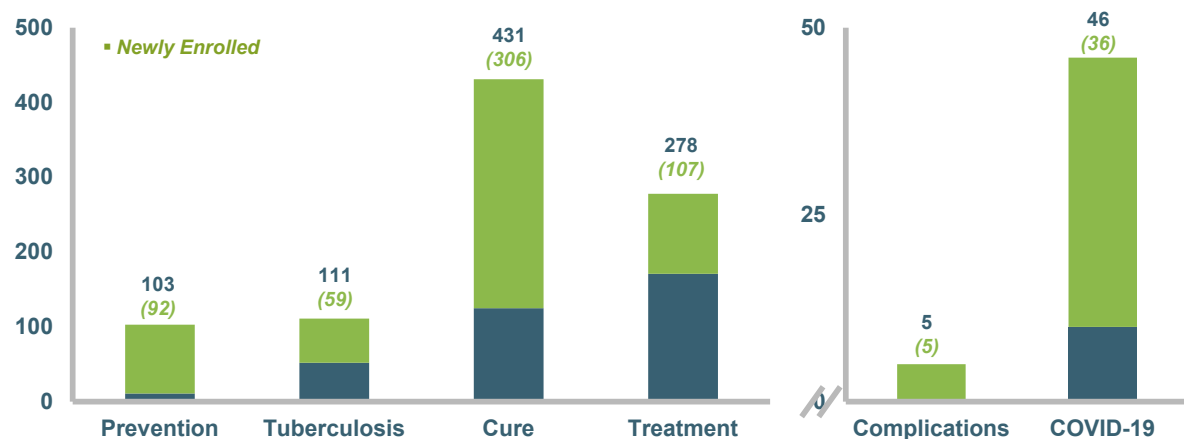
Source: WHO and IMPAACT: A Call to Action Webinar on World AIDS Day. 1 December 2021.
<https://www.impaactnetwork.org/who-and-impaact-call-action-webinar-world-aids-day>. Accessed 08 June 2022.



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IMPAACT Participants on Study June 2021 to May 2022



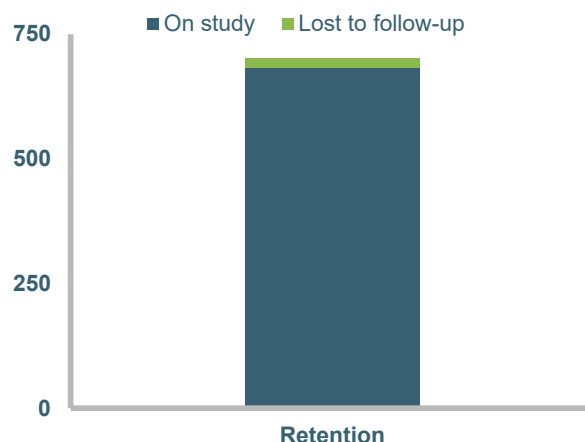
Total On Study = 974 participants
Newly Enrolled = 605 participants

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Overall Retention Across Ongoing IMPAACT Studies

- ▶ Sites have maintained excellent retention throughout the COVID-19 pandemic!
- ▶ 97% retention rate with 702 participants on study and only 19 participants lost to follow-up in the past 12 months



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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)



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23 Early Career Investigators Program

Overall goal: to prepare the next generation of health care professionals with skills to maintain and strengthen HIV programs for IMPAACT's populations of interest, experience the collaborative nature of network research, hone presentation skills, and develop a scholarly work that is suitable for publication.

More
details
to come
soon!

Key Dates:

- ▶ July 2022: Application announcement
- ▶ 1 October 2022: submission deadline
- ▶ 1 December 2022: funding initiated



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Study Updates and Achievements



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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
- ▶ Interim study data informed 2022 WHO consolidated guidelines on tuberculosis, Module 5: management of tuberculosis in children and adolescents
- ▶ 43 evaluable participants enrolled of 54 total at sites in Haiti and South Africa



Child with mask, Getty Images

Anticipate Version 2.0 issued
by August 2022

TB Research Agenda



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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
- ▶ 55 participants enrolled at 8 sites in South Africa, Thailand, and the US in Cohort 2
- ▶ Data informed recent US FDA and EMA decisions to approve DOR and fixed-dose combination of DOR/3TC/TDF in adolescents living with HIV



Group of adolescents inside, Getty Images



Treatment Research Agenda

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Closed to
follow-up and
POS/PAC
25 May 2022

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Study Highlight: IMPAACT 2021

RSV Vaccine Candidate 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
- ▶ 5 participants enrolled since accrual resumed at 2 sites!



Babies holding hands, Getty Images

Resumed
Accrual
01 Apr 2022

Complications Research Agenda



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Study Highlight: IMPAACT 2028

Long-Term Clinical, Immunologic, and Virologic Profiles of Children who Received Early Treatment for HIV

- ▶ Enable long-term follow-up of infants who received early or very early treatment for HIV in other cure-related studies
- ▶ Establish a biorepository for investigations related to the clinical, immunologic, and virologic effects of early treatment with priority for early career investigators
- ▶ Six of 35 sites activated, with four participants enrolled at sites in the US

Opened to accrual
(8 Nov 2021) with
first enrollment
2 February 2022

Cure Research Agenda



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More to come at tomorrow's plenary!

IMPAACT 2032	Remdesivir for COVID-19 Treatment in Pregnancy	Kristina Brooks
IMPAACT 2017/ MOCHA	Long-Acting CAB & RPV in Adolescents Living with HIV	Carolyn Bolton & Aditya Gaur
IMPAACT 2010/ VESTED	ARV Regimens for Pregnant People Living with HIV and Their Infants	Lameck Chinula
IMPAACT 2019	Fixed-Dose Combination of ABC/DTG/3TC in Children Living with HIV	Pat Flynn
IMPAACT P1115	Very Early ART Treatment for Neonates Exposed to HIV	Ellen Chadwick



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Publications

- ▶ **59** publications submitted for IMPAACT review in past 12 months
- ▶ **41** manuscripts published in Lancet HIV, CID, JID, Antimicrobial Agents and Chemotherapy, AIDS, JAIDS, Journal of Clinical Pharmacology, among others



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Abstracts

17 at CROI 2022, **3** at IAS 2021, **5** at HIV Peds 2021

- ▶ 6 abstracts from IMPAACT 2010/VESTED
- ▶ 4 abstracts from P1078/TB APPRISE, 3 from IMPAACT 2019, and 3 from PROMISE 1077BF/1077FF/P1084s
- ▶ Additional results from P1041/P1106, NICHD P1081, P1107, P1112, P1115, IMPAACT 2017/MOCHA, IMPAACT 2032 among others!

HIV-1 REMISSION WITH CCR5Δ32Δ32
HAPLO-CORD TRANSPLANT IN A U.S.
WOMAN: IMPAACT P1107

Yvonne Bryson, MD

David Geffen School of Medicine at UCLA and Mattel
Children's Hospital, Los Angeles, California, USA

<https://www.impaactnetwork.org/abstracts/1107>
Oral presentation at CROI 2022, 12-16 February 2022



Growth of infants with perinatal exposure
to maternal DTG vs EFV and TDF vs TAF:
the randomized IMPAACT 2010 trial

Lynda Stranix-Chibanda, Lauren Ziemba, Sean Brummel,
Benjamin Johnston, Tapwa Mbengeramwa, Haseenda Cassim,
Gerhard Theron, Sherika Hanley, Maxensia Owor, Katie McCarthy,
Nahida Chakhtoura, Patrick Jean-Philippe, Lameck Chinula,
Shahin Lockman, for the IMPAACT 2010/VESTED study team and investigators

<https://www.impaactnetwork.org/abstracts/2010>
Oral presentation at CROI 2022, 12-16 February 2022



TWO YEAR VIROLOGIC OUTCOMES
OF VERY EARLY ART FOR INFANTS
IN THE IMPAACT P1115 STUDY

Deborah Persaud, MD

Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

<https://www.impaactnetwork.org/abstracts/1115>
Oral presentation at CROI 2022, 12-16 February 2022



*Additional abstracts accepted to upcoming meetings
at AIDS 2022 and the HIV Pediatrics Workshop*

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Looking Forward



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Study Highlight: IMPAACT 2023

Safety & PK of Dolutegravir in Neonates Exposed to HIV

Version 2.0
to sites
30 March 2022

- ▶ Study to determine DTG dosing for children from birth through the first 4-6 weeks of life
- ▶ Planned at 17 sites in Brazil, South Africa, Thailand, and the US



Baby feet, Getty Images

Anticipate open to accrual
by July 2022

Treatment Research Agenda



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Study in Development: IMPAACT 2034

PK and Safety of Pretomanid in Infants, Children, and Adolescents with RR-TB with or without HIV

- ▶ Addressing critical need for better medications to treat children with drug resistant tuberculosis
- ▶ Collaborative study with TB Alliance
- ▶ Planned at 7 sites in India, South Africa, Tanzania, and Thailand



Child with mask, Getty Images

Anticipate Version 1.0
by July 2022

TB Research Agenda



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Study in Development: IMPAACT 2035

Safety and Immunogenicity of VPM1002 Vaccination or BCG Revaccination against TB in Pre-Adolescents with and without HIV

- ▶ Addressing critical need for vaccinations against tuberculosis
- ▶ Collaborative study with HVTN

Anticipate Version 1.0
within the next few weeks!



Adolescent with mask getting vaccinated, Getty Images

TB Research Agenda



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Study in Development: IMPAACT 2036

Safety & PK of Oral and Long-Acting Injectable Cabotegravir and Rilpivirine in Virologically Suppressed Children with HIV

- ▶ Continued successful collaboration from IMPAACT 2017 with ViiV/Janssen to study long-acting, injectable regimens in children
- ▶ Children will be two to less than 12 years old
- ▶ Planned at 12 sites in Brazil, Botswana, South Africa, Thailand, Uganda, and the US

Anticipate protocol to sites
by September 2022



Child with celebratory soccer/football gear, Getty Images

Treatment Research Agenda



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Study in Development: IMPAACT 2037

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

- ▶ Building on work from IMPAACT P1112, evaluating two potent anti-HIV neutralizing monoclonal antibodies
- ▶ Will be administered soon after birth to infants at high risk for peripartum or breastfeeding HIV transmission

Anticipate protocol to sites by Q4 2022



Clinician administering shot to infant on lap, Getty Images



Treatment Research Agenda

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Study in Development: IMPAACT 2040

PK & Safety of Long-Acting Injectable Cabotegravir and Rilpivirine in People with Virally Suppressed HIV-1 during Pregnancy and Postpartum

- ▶ Continued successful collaboration from IMPAACT 2017 and 2036 with ViiV/Janssen to study long-acting, injectable regimens
- ▶ Enrolling participants who are pregnant and living with HIV (and their infants)

Anticipate protocol to sites by May 2023



Group of people who are pregnant, Getty Images

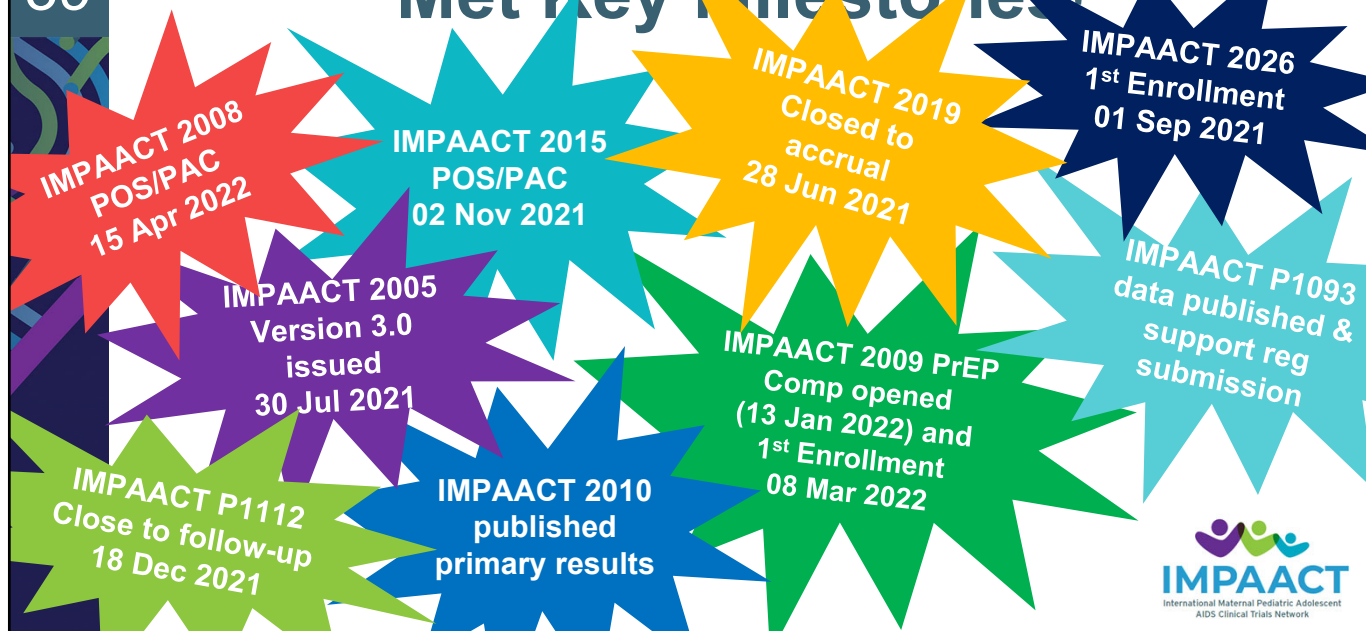


Treatment Research Agenda

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And Many Other Studies Met Key Milestones!



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Cross Network Study Initiatives



- ▶ 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, IMPAACT 2037)



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Pharma and Other Collaborations

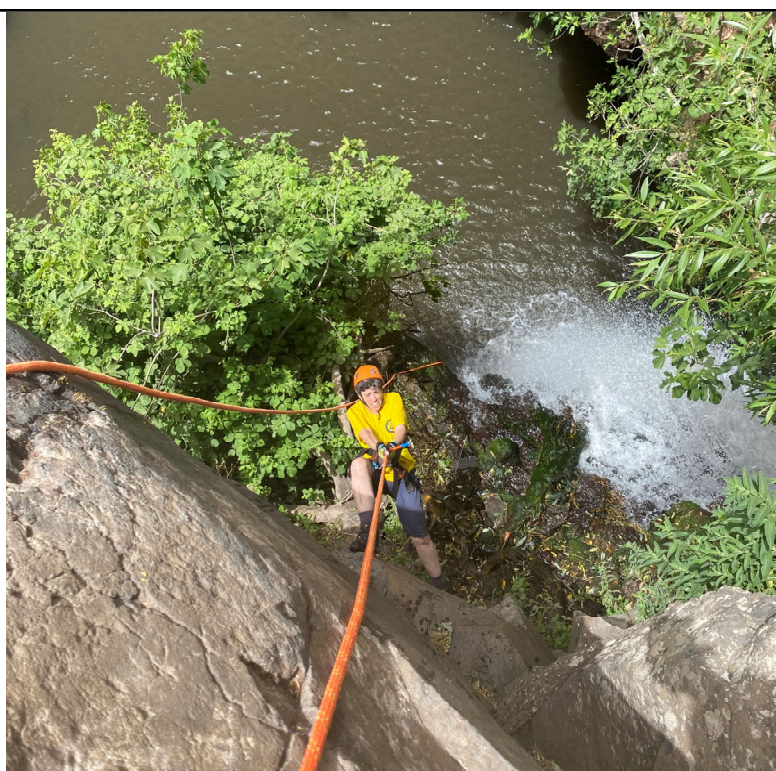


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We have had a great year with excellent work and significant accomplishments!

Let's prepare for the coming year of IMPAACT work and keep climbing to greater heights!



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THANKS!



Children smiling on a playground, Getty Images

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!

