

Complications & Co-morbidities Scientific Committee Update

IMPAACT Community and Science Meeting
23 June 2022

Committee Membership

Acting Chair: Jackie Hoare

At Large Members:

Linda Aurbibul*

Sandy Burchett[⊥]

Steve Innes*

Suad Kapetanovic

MacPherson Mallewa*

Evans Mpabalwani*

Savita Pahwa

Adriana Weinberg

NICHD Rep: Jack Moye

NIAID Rep: Ellen Townley, Hans Spiegel

NIMH Rep: Pim Brouwers

PHACS Rep: Kunjal Patel[⊥]

DMC Rep: Madison Cooper

SDAC: Jane Lindsey, Meredith Warshaw

ICAB Rep: Gwyneth Hendricks*; Angie Partap

LC Rep: Dale Dayton

Ops Center Coordinator: Jen Libous, Rachael Jeffrey, Sarah Buisson

SLG Liaison: Grace John-Stewart

*International; [⊥] PHACS

Committee Priorities

- ▶ Investigating potential neuroprotective and neurotoxic effects of ART to preserve neurocognitive development and mental health in infants, children, and adolescents
- ▶ Refining and optimizing the evaluation and treatment of neurocognitive and mental health disorders, particularly executive dysfunction, depression and PTSD
- ▶ Evaluating novel preventive and/or therapeutic approaches to high-priority diseases among pediatric populations with or affected by HIV, including respiratory syncytial virus (RSV), working with NIAID and other partners
- ▶ Evaluating other co-morbidities and complications of importance for pediatric, adolescent and pregnant populations with HIV, with other partners and NIH institutes

Studies Planned for Development

IMPAACT HIV Complications and Comorbidities

IMPAACT 2038 & 2041

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)

anticipated for approval with deferred development

Ongoing Studies

IMPAACT HIV Complications and Comorbidities

IMPAACT 2016 - Overview

- ▶ **Study Title:** Evaluating a Group-Based Intervention to Improve Mental Health and ART Adherence Among Youth Living with HIV in Low Resource Settings
- ▶ **Study Design:**
 - ▶ Two-arm, individually randomized controlled trial preceded by Focus Groups and Pilot Testing to adapt intervention to local context
 - ▶ Eligible participants include 15–19-year-old youth living with HIV and mental health distress, and their caregivers (if available and agreed to by youth participant).
- ▶ **Purpose:** To evaluate whether an Indigenous Leader Outreach Model (ILOM) of trauma informed cognitive behavioral therapy (TI-CBT) [referred to as TI-CBT delivered by Indigenous Youth Leaders (IYL)] is associated with improved mental health outcomes and ART adherence among youth living with HIV.



IMPAACT 2016 – Study Updates

- ▶ Study expected to resume under an amended protocol this year after pause due to COVID-19
- ▶ **To-date:**
 - ▶ Finalized and translated the TI-CBT intervention manuals used to facilitate the TI-CBT intervention
 - ▶ All sites completed community stakeholder engagements
 - ▶ 2 of 5 planned focus groups completed prior to the pause for adaptation feedback; remaining focus groups projected to be completed this year
 - ▶ Intensive two-week training held January 2020 for IYL at the South Africa site



IMPAACT 2018/2021 - Overview

▶ Study Design:

- ▶ Phase I (IMPAACT 2018) and Phase I/II (IMPAACT 2021), double-blind, randomized studies looking at vaccine candidates for Respiratory Syncytial Virus (RSV) compared to placebo
- ▶ Eligible participants include healthy 6 to 24-month-old children, who are exposed to HIV or not living with HIV (as per prior IMPAACT RSV vaccine studies)
- ▶ IMPAACT 2021: 3 lead vaccine candidates from each attenuation strategy are being studied

▶ Vaccines:

- ▶ RSV 276 (IMPAACT 2018/2021): Expected to have attenuation and increased immunogenicity
- ▶ RSV Δ NS2/ Δ 1313/I1314L (IMPAACT 2018/2021): Expected to have attenuation, temperature sensitivity, and increased immunogenicity
- ▶ RSV 6120/ Δ NS2/1030s (IMPAACT 2021): Expected to have slightly less attenuation than RSV Δ NS2/ Δ 1313/I1314L, temperature sensitivity, and increased immunogenicity

IMPAACT 2018/2021 - Study Updates

▶ IMPAACT 2018:

- ◆ Closed to accrual with n=65
- ◆ RSV Δ NS2/ Δ 1313/I1314L and RSV 276 were well tolerated and had excellent infectivity, but RSV 276 had excess cough
- ◆ Primary manuscript accepted for publication

▶ IMPAACT 2021:

- ◆ Study resumed in April 2022 after pause due to COVID-19
- ◆ RSV 276 arm closed due to higher rate of solicited AEs in IMPAACT 2018 (specifically, cough)
- ◆ Protocol Version 3.0 to be implemented to allow year-round enrollment when RSV levels in communities are low and to eliminate requirement for COVID testing
- ◆ **Goal:** candidates will be safe, and result in at least 70% of vaccine recipients having a \geq 4-fold rise in serum RSV-neutralizing antibody titers

Update/Main Findings from Studies Closed to Follow-up

IMPAACT HIV Complications and Comorbidities

12 IMPAACT 2002 - Overview

- ▶ **Study Title:** Combined Cognitive Behavioral Therapy & Medication Management Algorithm for Treatment of Depression among Youth Living with HIV in the US
- ▶ **Purpose:** To examine if a Health and Wellness Cognitive Behavioral Therapy and Medication Management (COMB-R) intervention for depression demonstrates improved outcomes for HIV-infected youth in the United States
- ▶ **Study Design:** Multi-site, two-arm, cluster-randomized study
- ▶ **Study Population:** Approximately 130 youth living with HIV, ages 14-24 with depression
- ▶ **Study Status:** Participants off Study and Primary Analysis Completed

IMPAACT 2002 - Updates

▶ **Primary Manuscript Results:**

- ▶ At Week 24, youth living with HIV (YLWH) at COMB-R sites, compared with enhanced standard of care sites, reported significantly fewer depressive symptoms on the Quick Inventory for Depression Symptomatology Self-Report (QIDS-SR score 6.7 vs. 10.6, $P = 0.01$) and a greater proportion in remission (QIDS-SR score ≤ 5 ; 47.9% vs. 17.0%, $P = 0.01$).
- ▶ A manualized, measurement-guided psychotherapy and medication management algorithm tailored for YLWH significantly reduced depressive symptoms compared with standard care at HIV clinics.

RSV Studies (IMPAACT 2011, 2012, 2013) - Overview

▶ Study Design:

- ▶ Phase I, double-blind, randomized studies looking at vaccine candidates for Respiratory Syncytial Virus (RSV) compared to placebo
- ▶ Eligible participants include healthy 6 to 24-month-old children, who are exposed to HIV or not living with HIV (as per prior IMPAACT RSV vaccine studies)

▶ Vaccines:

- ▶ LID DM2-2/1030s (IMPAACT 2011): 1030s: temperature sensitivity, genetically stabilized
- ▶ LID cp/DM2-2 (IMPAACT 2012): Cold passage “cp” mutations – five amino acid point substitutions in nucleoprotein, fusion protein, and polymerase protein
- ▶ D46 NS2/N/DM2-2 (IMPAACT 2013): Lower replication due to containing the SH noncoding region that is deleted in the other LID Δ M2-2 candidates, one point mutation each in the NS2 and N proteins, a modified version of the M2-2 deletion

RSV Studies (IMPAACT 2011, 2012, 2013) - Updates

▶ Results:

- ▶ All three vaccines had good safety profiles.
- ▶ Attenuation with a deletion in M2-2 gene is highly promising approach.
- ▶ LID DM2-2/1030s (IMPAACT 2011)
 - ◆ More attenuated than parental LID DM2-2
 - ◆ Excellent infectivity and antibody response
 - ◆ Potentially a candidate for further development
- ▶ LID cp/DM2-2 (IMPAACT 2012)
 - ◆ Overattenuated with insufficient infectivity and antibody response
- ▶ D46 NS2/N/DM2-2 (IMPAACT 2013)
 - ◆ Attenuation similar to parental LID DM2-2
 - ◆ Excellent infectivity and antibody response

THANKS!

Any questions?