Welcome to the IMPAACT Complications & Co-Infections Scientific Committee Open Session

IMPAACT
International Maternal Pediatric Adolescent AIDS Clinical Trials Network

The session will begin shortly

IMPAACT Annual Meeting
30 June 2022

Virtual Attendee Logistics:

All virtual attendees are muted.

Any questions should be sent via the Q&A.

Raise your hand to elaborate on a question sent in the Q&A

Session Agenda

1. Welcome and Committee Introduction Overview
2. Update/Main Findings on Studies Closed to Follow-up
3. Studies Planned for Development
4. RSV Study Updates – IMPAACT 2018 and IMPAACT 2021 **with Q&A**
5. IMPAACT 2016 **with Q&A**
6. Mental Health on the Frontline **with Q&A**
7. Closing Remarks

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Acting Chair: Jackie Hoare

- Clinical work includes - treating mental illness, neurocognitive disorders and adherence in adolescents and adults with chronic illness.
- Clinical experience in managing the mental health consequences of COVID-19.
- Principal Investigator or Co-Investigator of NIH USA federal funded research projects in South Africa focused on mental health, neurocognitive disorders, neuroimaging, epigenetics and developing adherence interventions in adolescents living with HIV.
- Founded and chairs the Adolescent Clinicians Group and Better Together Adolescent service at Groote Schuur Hospital.

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Committee Membership

At Large Members:
Linda Aurpibul*
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

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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

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Update/Main Findings from Studies Closed to Follow-up

Complications & Co-Infections Research Area

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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 Analysis 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).

- **Upcoming Publications and Presentations:**
  - AIDS 2022 Conference Presentations
    - 48 Week outcomes
    - Participant Acceptability and Clinician Satisfaction
  - Planned Secondary Manuscripts:
    - 48 Week Outcomes
    - Inflammatory biomarkers
    - Acceptability
    - Medication management and adherence
    - CBT outcomes

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IMPAACT 2002 - Publications

- **Primary Manuscript:** Brown LK, Chernoff M, Kennard BD, Emslie GJ, Lypen K, Buisson S, Weinberg A, Whiteley LB, Traite S, Krotje C, Harriff L, Townley E, Bunch A, Purswani M, Shaw R, Spector SA, Agwu A, Shapiro DE; IMPAACT 2002 team. **Site-Randomized Controlled Trial of a Combined Cognitive Behavioral Therapy and a Medication Management Algorithm for Treatment of Depression Among Youth Living With HIV in the United States.** J Acquir Immune Defic Syndr. 2021 Dec 15;88(5):497-505. doi: 10.1097/QAI.0000000000002790. PMID: 34483297; PMCID: PMC8585710.

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RSV Studies (IMPAACT 2011, 2012, 2013):

- **Study Design:**
  - Phase 1, double-blind, randomized 2:1 to vaccine or placebo
  - Eligibility- healthy 6 to 24-month-old children, HIV-exposed, uninfected allowed (as per prior IMPAACT RSV vaccine studies)
- **Vaccines:** all derived from parent with deletion mutation in M2-2
  - **LID ΔM2-2/1030s (**IMPAACT 2011**)**: 1030s: temperature sensitivity, genetically stabilized
  - **LID cp/ΔM2-2 (**IMPAACT 2012**)**: Cold passage "cp" mutations – five amino acid point substitutions in nucleoprotein, fusion protein, and polymerase protein
  - **D46 NS2/N/ΔM2-2-HindIII (**IMPAACT 2013**)**: Lower replication due to containing the SH noncoding region that is deleted in the other LID ΔM2-2 candidates, one point mutation each in the NS2 and N proteins, a modified version of the M2-2 deletion

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

- **Conclusions:**
  - All three vaccines had good safety profiles.
  - Attenuation with a deletion in M2-2 gene is highly promising approach.
  - **LID ΔM2-2/1030s** (IMPAACT 2011)
    - More attenuated than parental LID ΔM2-2
    - Excellent infectivity and antibody response
    - Potentially a candidate for further development
  - **LID cp/ΔM2-2** (IMPAACT 2012)
    - Overattenuated with insufficient infectivity and antibody response
  - **D46 NS2/N/ΔM2-2** (IMPAACT 2013)
    - Attenuation similar to parental LID ΔM2-2
    - Excellent infectivity and antibody response

RSV Studies (IMPAACT 2011, 2012, 2013):

- **Publications:**
  - **IMPAACT 2011 Primary Manuscript:** McFarland EJ, Karron RA, Muresan P, Cunningham CK, Libous J, Perlowski C, Thumar B, Gnanashanmugam D, Moye J, Schappell E, Barr E, Rexroad V, Fearn L, Spector SA, Aziz M, Cielo M, Beneri C, Wiznia A, Luongo C, Collins P, Buchholz UJ, the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) 2011 Study Team. Live Respiratory Syncytial Virus Attenuated by M2-2 Deletion and Stabilized Temperature Sensitivity Mutation 1030s Is a Promising Vaccine Candidate in Children. The Journal of Infectious Diseases. 2020 February 15; 221(4): 534–543. https://doi.org/10.1093/infdis/jiz603.
  - **IMPAACT 2012 Primary Manuscript:** Cunningham CK, Karron R, Muresan P, McFarland EJ, Perlowski C, Libous JL, Thumar B, Gnanashanmugam D, Moye J, Schappell E, Barr E, Rexroad V, Aziz M, Deville J, Rutstein R, Yang L, Luongo C, Collins P, Buchholz U, the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) 2012 Study Team. Live-attenuated respiratory syncytial virus vaccine with deletion of RNA synthesis regulatory protein M2-2 and cold passage mutations is over-attenuated. Open Forum Infectious Diseases. 2019; June; 6(6):ofz212. https://doi.org/10.1093/ofid/ofz212
  - **IMPAACT 2013 Primary Manuscript Publication:** McFarland EJ, Karron RA, Muresan P, Cunningham CK, Perlowski C, Libous J, Oliva J, Jean-Philippe P, Moye J, Schappell E, Barr E, Rexroad V, Fearn L, Cielo M, Wiznia A, Deville JG, Yang L, Luongo C, Collins PL Buchholz UJ, International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) 2013 Study Team. Live-attenuated respiratory syncytial virus vaccine with M2-2 deletion and with small hydrophobic non-coding region is highly immunogenic in children. The Journal of Infectious Diseases. 2020 June 15; 221(12): 2050-2059. https://doi.org/10.1093/infdis/jiaa049

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Studies Planned for Development

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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

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