Polio Eradication Endgame: A Novel Oral Polio Vaccine On The Horizon

Dr. Ananda S. Bandyopadhyay

ADVAC Webinar; May 26, 2020

OUTLINE

- *Polio Eradication Endgame*
  - The VDPV *conundrum*
- *What is novel OPV2?*
  - Background
- *Does it work ?*
  - Clinical Development Update
- *How would we use it ?*
  - Emergency Use Listing, Country Prioritization
- *Key Takeaways*

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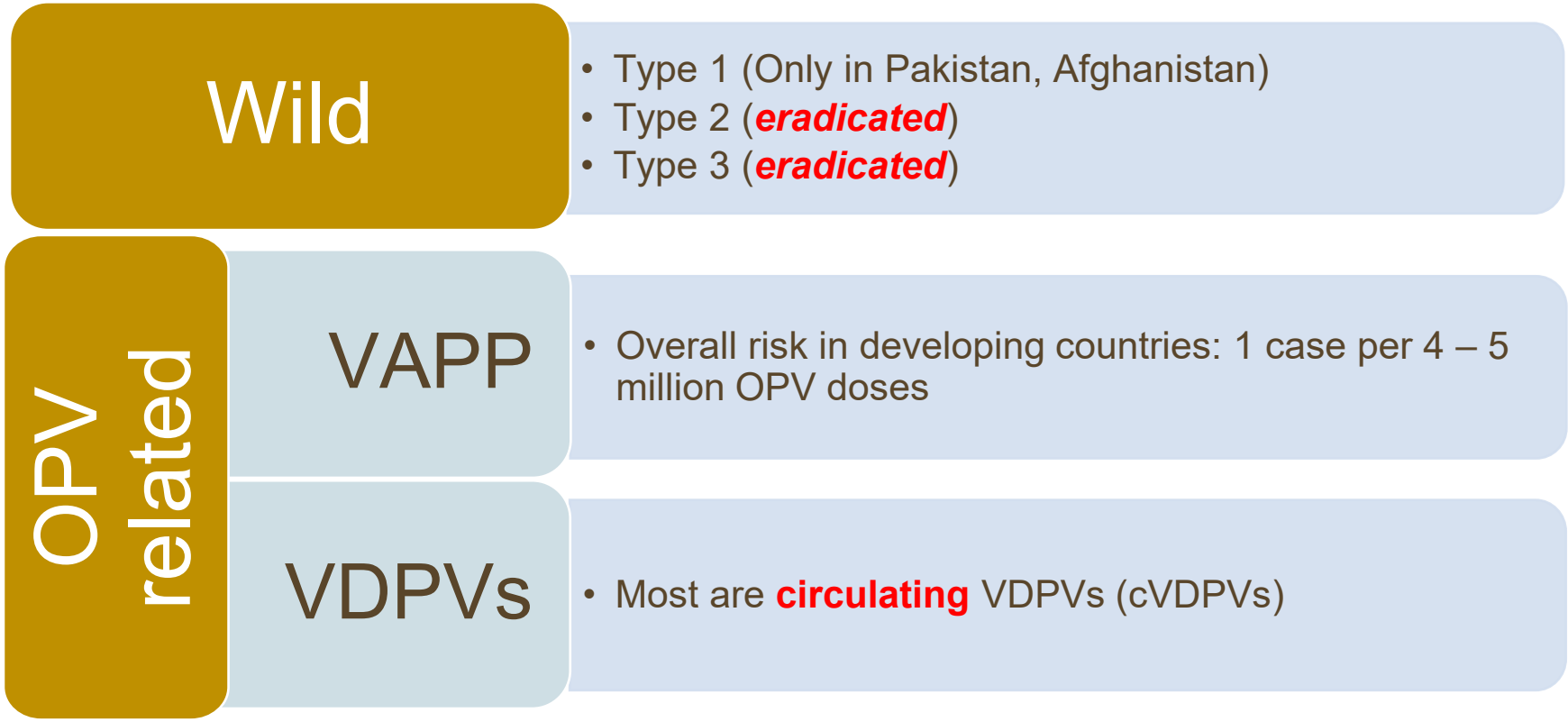
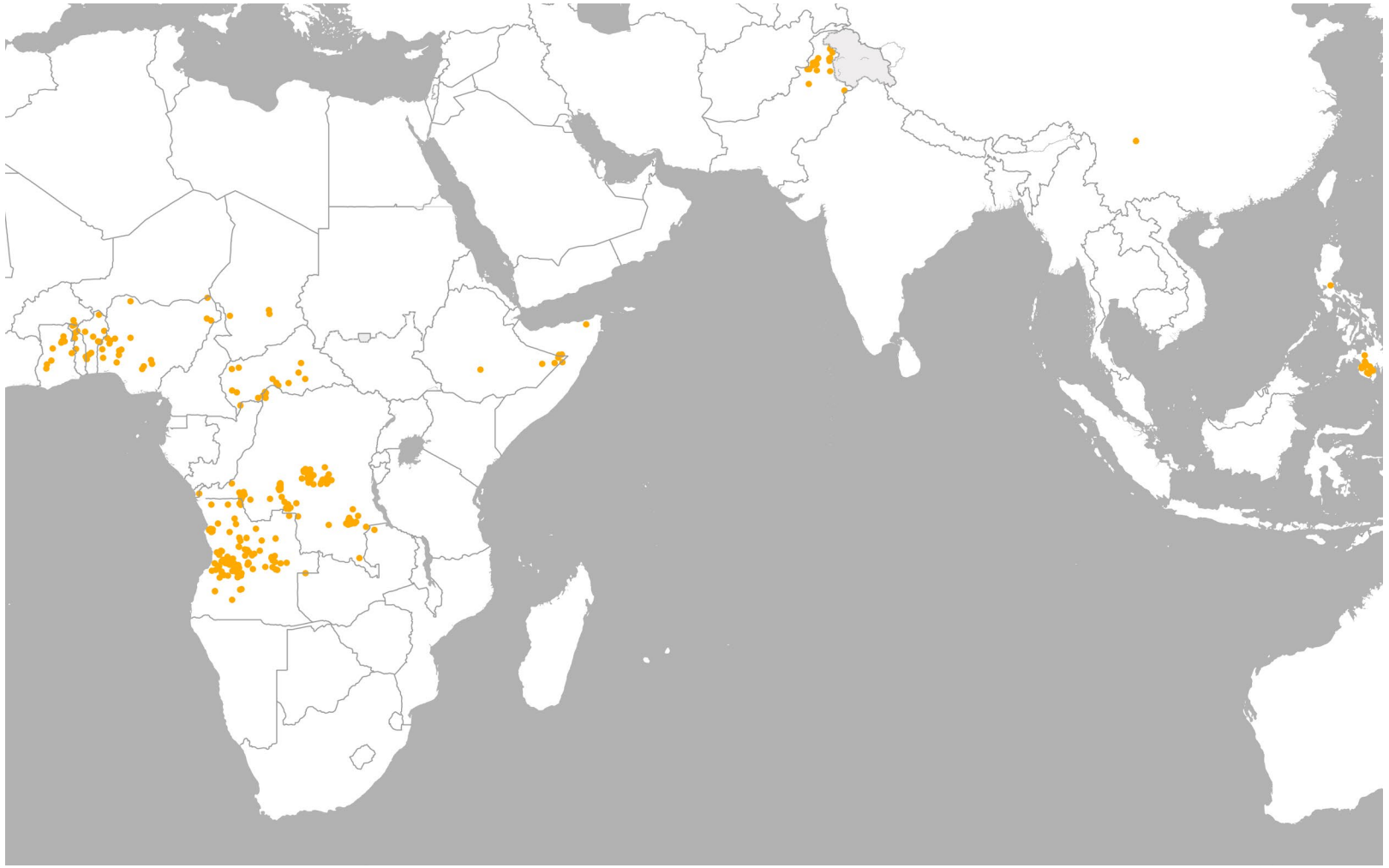
Polio: "*Many* diseases"?



The Challenge of Circulating Vaccine-Derived Polio

Type 2 cVDPVs are the most prevalent form, and their frequency and scope have increased since the removal of type 2 OPV in 2016, with the switch from trivalent OPV to bivalent OPV.

Spread of cVDPV2 Cases, 2019



GPEI Strategy for Control of cVDPV2, 2020-2021

Accelerating the development of nOPV2 is one component of **the GPEI's comprehensive new strategy to stop the spread of cVDPV2,** characterized by improved outbreak response and attention to challenging contexts.

Optimize outbreak response using mOPV2, currently the best available tool for combatting type 2 vaccine-derived polio

Accelerate development of a new vaccine—novel OPV2 (nOPV2)—as a potential alternative for cVDPV2 outbreak response and ultimately as a replacement for mPOV2

Strengthen routine immunization by increasing coverage with inactivated polio vaccine (IPV) in high-risk areas to protect children from paralysis

Ensure sufficient supply of OPV2 is available to reach every at-risk child, utilizing innovative strategies as needed

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nOPV2: An Innovative New Tool

ADDRESSES cVDPV2s and VAPP

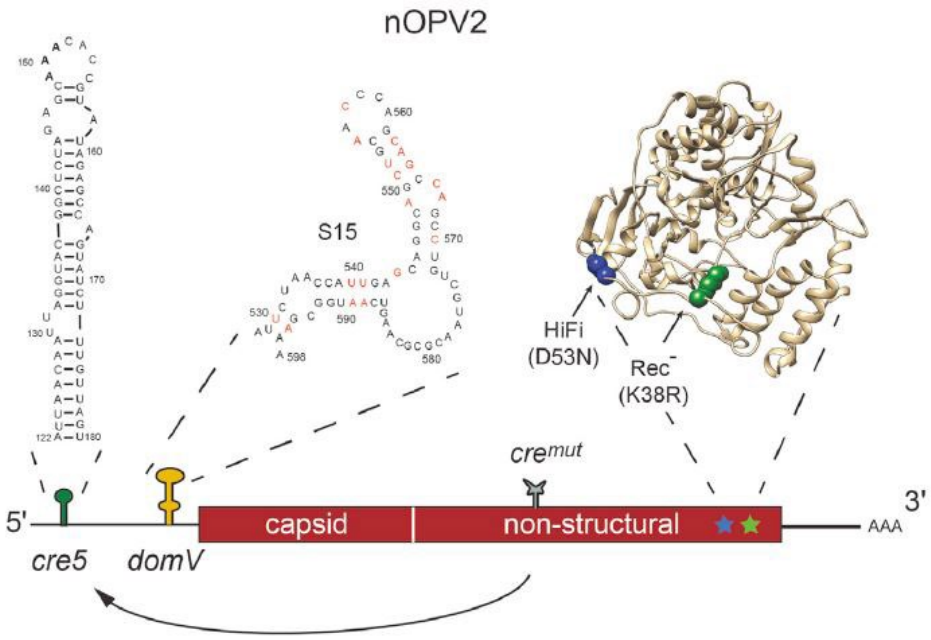
The novel oral polio vaccine type 2 (nOPV2) is a new tool developed to better address the risk of type 2 circulating vaccine-derived poliovirus (cVDPV2) and vaccine-associated paralytic poliomyelitis (VAPP).

MODIFICATION OF mOPV2

nOPV2 is a modification of the existing type 2 monovalent OPV (mOPV2) that clinical trials have shown provides comparable protection against poliovirus while being more genetically stable and less likely to revert to a form that can cause paralysis. The increased genetic stability means there is a reduced risk of seeding new cVDPV2 outbreaks compared to the existing mOPV2.

nOPV2 could eventually be used as a replacement for mOPV2

nOPV2 Genome with modifications



Ming Te Yeh, Erika Bujaki, Patrick T. Dolan, Matthew Smith, Rahnuma Wahid, John Konz, Amy J. Weiner, Ananda S. Bandyopadhyay, Pierre Van Damme, Ilse De Coster, Hilde Revets Andrew Macadam, and Raul Andino. Engineering the Live-Attenuated Polio Vaccine to Prevent Reversion to Virulence. Cell Host and Microbe. 2020.

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Accelerated Clinical Development

A dedicated group of global agencies and vaccine experts have been engaged in developing candidates for nOPV2 for the past nine years, with the first clinical study with nOPV2 implemented in 2017.

nOPV2 Trials	
M4a (Phase I)	2017 (containment) Belgium – 10^6 dose. **First-in-human study.**
M4 (Phase II)	2018/2019 Belgium – adults - 10^6 dose General safety, immunogenicity, shedding, genetic stability.
M5a/M5b (Phase II)	2018/2019 Panama – 18-22 wk infants, 1-5 year old - 10^6 and 10^5 dose; 2018 vaccine lot. General safety, immunogenicity, shedding, genetic stability.
Phase III	**Expanded Safety & Lot-to-lot consistency** Selected vaccine candidate only.

"Historical control" trials with mOPV2	
M1 (Phase IV)	2016 Belgium – OPV-vaccinated adults
M2a/M2b (Phase IV)	2015/2016 Panama, 18-22 wk infants, 1-5 year old - IPV/OPV-vaccinated

KEY

All studies completed for major field activities. Primary end-points have been met.

Completed

Yet to start

Other Studies (Phase II / III) under planning, with selected candidate:

- nOPV2 safety and immunogenicity in polio vaccine naïve, newborn infants
- Safety and immunogenicity when nOPV2 is co-administered with bOPV in infants
- Assessment of nOPV2 administration in a campaign-like setting

NOVEL OPV2 DEVELOPMENT: FIRST-IN-HUMAN STUDY

Pierre Van Damme, Ilse De Coster, Ananda S Bandyopadhyay, Leen Suykens, Patrick Rudelsheim, Pieter Neels, M Steven Oberste, William C Weldon, Ralf Clemens, and Hilde Revets. **Poliopolis**: pushing boundaries of scientific innovations for disease eradication. ***Future Microbiology***. 2019.

June 4, 2019

THE LANCET

Articles

The safety and immunogenicity of two novel live attenuated monovalent (serotype 2) oral poliovirus vaccines in healthy adults: a double-blind, single-centre phase 1 study

Pierre Van Damme, Ilse De Coster*, Ananda S Bandyopadhyay, Hilde Revets, Kanchanamala Withanage, Philippe De Smedt, Leen Suykens, M Steven Oberste, William C Weldon, Sue Ann Costa-Clemens, Ralf Clemens, John Modlin, Amy J Weiner, Andrew J Macadam, Raul Andino, Olen M Kew, Jennifer L Konopka-Anstadt, Cara C Burns, John Konz, Rahnuma Wahid, Christopher Gast*

Summary of Clinical Trial Findings

CONCLUSIONS FROM PRELIMINARY DATA

Favorable general safety / reactogenicity profile of nOPV2

No evidence of any increase in general safety risk compared with **mOPV2**

nOPV2 appears as immunogenic as mOPV2

nOPV2 demonstrated **non-inferior immunogenicity to the historical mOPV2 control groups** among infants

nOPV2 appears to induce lower or comparable shedding as mOPV2

Assessment of viral excretion indicates that **nOPV2 is unlikely to be shed in a greater rate or quantity as compared to mOPV2**, and the cessation of intestinal mucosal viral replication and shedding may actually be earlier in infants

Data available supports view that nOPV2 is likely to have significantly lower risk of paralysis in humans than mOPV2

No direct way to quantitatively extrapolate to reduced risk of paralysis in humans, the available data support **significantly improved genetic and phenotypic stability of shed nOPV2 compared to shed Sabin-2**

Adapted from: Bandyopadhyay, AS. Summary of nOPV2 clinical data. SAGE presentation. Polio Session. April 1, 2020.
Information courtesy: Clinical Trial Sponsors (UW, FIDEC); Bio Farma; PATH; US CDC; and development partners.

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Key Takeaways

Emergency Use Listing (EUL)

WHAT IS WHO'S EUL?

The EUL involves careful and rigorous analysis of available data to enable early, targeted use of unlicensed vaccine, therapeutic and in-vitro diagnostic for a Public Health Emergency of International Concern, which polio has been since 2014. **nOPV2 could be the first vaccine** to be approved through WHO EUL.

SCIENTIFIC DATA REVIEW

Data is submitted for review under WHO's EUL (for nOPV2, the review is ongoing)

POST DEPLOYMENT MONITORING (PDM)

EUL requires enhanced monitoring of the vaccine while it is used under an EUL recommendation to assess safety surveillance, performance, quality complaints, and other relevant factors impacting the validity of the listing

ONGOING REVIEW

If quality or safety issues are identified, WHO may revoke the EUL recommendation for use of nOPV2

Country Groupings for nOPV2 Rollout

If approved, nOPV2 could be deployed as early as Q3 2020

All countries identified at high-risk of VDPV2 transmission should begin preparing for nOPV2 use once an interim EUL recommendation is made.

Countries at Highest Risk of cVPDV2 Outbreak and Meet "Initial Use Criteria"

9* countries

Goal: Ensure countries are fully ready for nOPV2 initial use

GPEI financial support & TA provided as needed, based on country context, to strengthen outbreak response, surveillance, AEFI systems to prepare for initial use/ early use of nOPV2

Countries at High Risk of cVDPV2 Outbreak

30-40 countries

Goal: Support countries to assess readiness for nOPV2 introduction and encourage active preparation

Potential for focused support from GPEI, to be assessed on country-by-country basis

Countries in Regions with cVDPV2 Outbreaks

~80 countries

Goal: Build country awareness for nOPV2; assess feasibility and interest in nOPV2 use

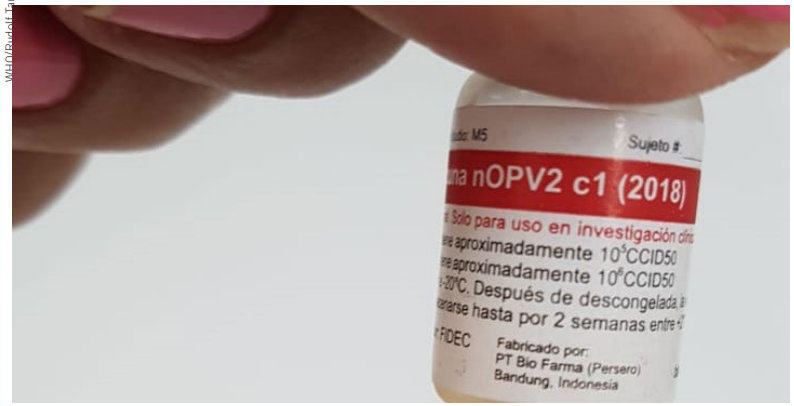
GPEI to provide tools and guidance to build awareness of cVDPV2 risk & nOPV2 use

* Current thinking, may expand in number based on discussions with regions and their ability to support, but targeted to stay around 10- 15 max

"Vaccination"

Inactivated poliovirus vaccine (IPV)

Sabin Oral polio vaccine (OPV)



Novel oral polio vaccine (nOPV)

REACHING EVERY CHILD: A HEROIC FEAT

Photo: Ananda Bandyopadhyay, Bill & Melinda Gates Foundation

KEY TAKEAWAYS

- *Expanding VDPV2 outbreaks in the post-switch era a major challenge.*
- *novel OPV2 could be an effective tool in reducing risk of vaccine-derived transmission.*
- *Phase I and phase II study results supportive of promising safety, immunogenicity and genetic stability.*
- *Streamlining of activities for use of the vaccine in field and strengthening of outbreak response strategies key to interrupt continued spread.*

Acknowledgement

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*and other members of the **novel OPV2 working group** of GPEI*

POLIO GLOBAL ERADICATION INITIATIVE

MERCI

THANK YOU

World Health Organization · unicef · Rotary · CDC Centers for Disease Control and Prevention · Bill & Melinda Gates foundation · Gavi The Vaccine Alliance

EVERY LAST CHILD