Clinical summary for novel oral polio vaccine type 2 (nOPV2)

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Background

To better address the evolving risk of type 2 circulating vaccine-derived poliovirus (cVDPV2), GPEI partners are working to deploy an additional innovative tool – novel oral polio vaccine type 2 (nOPV2). The vaccine is a modified version 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 into a form which can cause paralysis in low immunity settings. The vaccine's increased genetic stability means there is a reduced risk of seeding new cVDPV2 outbreaks compared to mOPV2 and reduced risk of vaccine-associated paralytic polio (VAPP).

Human clinical trials for two nOPV2 vaccine candidates began in 2017. In late 2019, after a careful review of available clinical data and manufacturing considerations, candidate 1 was prioritized for assessment under the WHO Emergency Use Listing (EUL) procedure – a mechanism which enables early, targeted use of unlicensed vaccines, therapeutics and in-vitro diagnostic products during a Public Health Emergency of International Concern.

A summary of key clinical data findings for nOPV2 candidate 1 can be found below, for both high dose and low dose potencies.

Clinical Studies

Clinical studies have been conducted in Belgium and Panama in both adults and children. Prior to the global withdrawal of Sabin OPV2 from routine use in 2016, mOPV2 clinical trials were carried out in both of these countries to provide data for comparison. The first in-human nOPV2 study was conducted in Belgium in adults under physical and biological containment, with findings published in *The Lancet* [1]. Further studies in Belgium, again in adults, and Panama, in 18-22-week-old infants and children aged 1-5 years, were completed. Preliminary results from the nOPV2 Panama study are available.

Summary of Clinical Data

Safety*:*

Data from the clinical studies show nOPV2 to be well-tolerated in adults, young children, and infants, with no indication of any increase in general safety risk compared to mOPV2. There have been no serious adverse events identified that are considered to be related to vaccination with nOPV2.

Immunogenicity:

The most important immunogenicity evaluation was the seroprotection rate and seroconversion rate, 28 days following a single dose, in 18-22-week-old infants.

- Non-inferiority (in comparison to mOPV2) for seroprotection was established for both low dose and high dose potencies of nOPV2.
- There was no significant difference in seroconversion rates between nOPV2 and mOPV2.
- Following a second vaccine dose, both seroprotection and seroconversion rates were uniformly high for both groups.

Viral excretion:

- An exclusively IPV-vaccinated (no history of OPV vaccination) cohort of adults who received a second dose of nOPV2, provided an opportunity for indirect assessment of intestinal immunogenicity to type 2 poliovirus, induced by a dose of nOPV2. There was a substantial decrease in proportion of subjects shedding the vaccine virus following second dose compared to shedding positivity following the first dose. This is comparable to prior experience with Sabin OPVs, and is encouraging.
- In infants, the rate of nOPV2 shedding was comparable to mOPV2 at the peak of shedding (first 2 weeks). However, the proportion of infants that shed nOPV2 was significantly lower than mOPV2 historic controls by week 4, indicating a likely shorter duration of shedding.

Genetic stability:

Using the standard method to evaluate the neurovirulence of polioviruses (i.e. to measure paralysis rates in transgenic mice after intraspinal administration of the virus), the vaccine viruses isolated from the stool of participants after vaccination with mOPV2 or nOPV2 could be compared. In participants who receive mOPV2, the shed vaccine virus causes high paralysis rates in the mouse model after approximately 7 days. In contrast, nOPV2 shows low to no paralysis associated across the studies, regardless of the age of study participants (adults and children).

Conclusions

Overall, the pre-clinical and clinical data continue to be supportive of further clinical development, initial EUL submission and at-risk stockpile production of nOPV2. The candidate demonstrated non-inferior immunogenicity to the historical mOPV2 control groups in the pivotal evaluation among infants. 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 following vaccination in infants. While there is 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 mOPV2.

Acknowledgements

Clinical trial sponsors for phase I and II studies – University of Antwerp, FIDEC; Bio Farma; GPEI and other global partners involved in the development program, for early access to the preliminary, unpublished data for program use.

References

[1] Van Damme, Pierre, et al. "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."

The Lancet 394.10193 (2019): 148-158.

Further information

For further scientific publications on nOPV2: http://polioeradication.org/nopv2/ (see 'Publications')

For further information on nOPV2 seroprotection and seroconversion rates, and shedding, please see below links to clinical data presentations.*

WHO Strategic Advisory Group of Experts on immunization (SAGE) meeting April 2020

WHO Strategic Advisory Group of Experts on immunization (SAGE) meeting October 2019

* Presentations may display outdated timelines for nOPV2 introduction. Please refer to polioeradication.org/nopv2 for more recent information.