Poliovirus vaccine options: another step forward


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Now, more than 20 years after the initial target for polio eradication, the Global Polio Eradication Initiative (GPEI) remains off track in its mission to stop and prevent the transmission of all three types of wild-type polioviruses.[1] The GPEI successfully certified global eradication of type 2 polioviruses in September, 2015,[2] and type 3 in October, 2019,[3] with the remaining most transmissible and virulent type 1 confined to Afghanistan and Pakistan. In April and May, 2016, the GPEI coordinated global cessation of type 2 oral poliovirus vaccine (OPV2) use. However, this effort did not lead to the end of all type 2 live poliovirus transmission, with the annual reported cases caused by these vaccine-derived polioviruses increasing from 71 in 2018, to 366 in 2019, and 739 in 2020 (as of Dec 3).[4] Monovalent OPV2 remains the primary defence against type 2 circulating vaccine-derived poliovirus outbreaks. Increased demand and limited supplies in 2020 led the GPEI to procure the production of more monovalent OPV2 and trivalent OPV (containing all three OPV types), which both carry the risk of reversion that could seed the creation of new type 2 circulating vaccine-derived polioviruses.[5,6] To mitigate these risks, the GPEI accelerated the development and production of novel OPV2 strains, and issued an addendum to its 2019–23 strategic plan.[7]

In *The Lancet*, Ilse De Coster and colleagues[8] report the results of a phase 2 clinical trial comparing the safety and efficacy of two novel OPV2 strains with monovalent OPV2 in adults. Anticipating global OPV2 cessation, they did a phase 4 historical control study using monovalent OPV2 in Antwerp, Belgium (Jan 25 to March 18, 2016; for study population and baseline characteristics, see table 1 in Article). After the completion of the novel OPV2 phase 1 trial,[9] a novel OPV2 phase 2 trial was done at two sites in Belgium, Antwerp and Ghent (Oct 15, 2018, to Feb 27, 2019).[8] Confirming the phase 1 trial results,[9] they report non-inferiority with respect to safety, tolerability, and immunogenicity for both novel OPV2 strains compared with monovalent OPV2 (100% [95% CI 96–100] seroprotection after one dose for both novel OPV2 candidates compared with 97% [92–99] after one dose of monovalent OPV2 and 98% [89–100] after two doses of monovalent OPV2).[8] Analysis of viruses shed by participants suggested improved genetic stability of the novel OPV2 candidates.[8]

Also in *The Lancet*, Xavier Sáez-Llorens and colleagues[10] report the results of two phase 2 clinical trials that assessed the safety and efficacy of the two novel type 2 OPV candidates (OPV2-c1 and OPV2-c2)[9] in infants (aged 18–22 weeks) and young children (aged 1–4 years; Sept 19, 2018, to Sept 30, 2019), and a phase 4 historical control trial using monovalent OPV2 (Oct 23, 2015, to April 29, 2016).[10] For further information on study population and baseline characteristics, see table 1 in Article. The infant trial, which escalated from a low dose to the same high-dose given to children, showed non-inferiority for both doses of OPV2-c1 and the high dose for OPV2-c2 compared with monovalent OPV2.[10] The results showed non-inferiority with respect to safety, tolerability, and immunogenicity for both novel OPV2 strains compared with monovalent OPV2 for infants. The day 28 seroprotection rate was 94% (95% CI 87–98) for monovalent OPV2; 93% (87–97) for low-dose OPV2-c1 and 94% (88–97) for high-dose OPV2-c1; and 91% (84–95) for low-dose OPV2-c2 and 95% (90–98) for high-dose OPV2-c2. For children, the day 28 seroprotection rate was 100% for monovalent OPV2 and both novel OPV2 candidates.[10] The preliminary results of this study[10] helped to support the selection of OPV2-c1 for WHO's Emergency Use Listing for type 2 circulating vaccine-derived poliovirus outbreaks.[11]

Both studies used the best possible methods to compare novel and monovalent OPV2 given global OPV2 containment constraints. Both are limited by the small numbers of trial participants (eg, observations of reversion and rare events like vaccine-associated paralytic polio would require use in millions of people, similar to OPV[5]), different participant immunity profiles, and the potential for secondary monovalent OPV2 exposure for the historical controls but not the novel OPV2 trials. The results from these two studies and the Emergency Use Listing represent exciting next steps for a world that already needed more OPV2 before the COVID-19 pandemic.[12,13] This progress will allow for broader use of novel OPV2 and the observation of evidence related

to its actual performance in the field. Initial modelling of the potential effects of use of novel OPV2 instead of monovalent OPV2 for outbreak response suggests that novel OPV2 could help to reduce the cases caused by type 2 circulating vaccine-derived poliovirus outbreaks.[14] However, less than ideal novel OPV2 performance could counterintuitively lead to more cases in the short term than continued use of monovalent OPV2.[14] In addition, only using OPV2 reactively after outbreaks occur is not likely to shut down the broadening global transmission given current levels of national and GPEI programme performance.[14]

By early 2020, the point passed at which the best case scenario was possible of stopping all type 2 poliovirus transmission using vaccine supplies produced before OPV2 cessation.[15] This situation puts the world into a new and much more challenging phase that will require careful deliberation of long-term poliovirus vaccine options and management of some insufficient poliovirus vaccine supplies. The disruption in immunisation caused by the COVID-19 pandemic further exacerbates the situation.

Meanwhile, the costs of maintaining very high control of poliovirus to keep cases low continue to increase. Countries that currently use OPV will need to pay (or seek donor support) for national immunisation schedules that include a minimum of five poliovirus vaccine doses (ie, three doses of bivalent OPV [containing types 1 and 3 OPV], two doses of inactivated poliovirus vaccine[16]), plus additional doses of OPV used in supplementary immunisation activities. The supplementary immunisation activities include preventively using bivalent OPV to increase population immunity to pre-empt outbreaks or reactively in response to type 1 or 3 outbreaks; or reactively using trivalent OPV (in Afghanistan and Pakistan), monovalent OPV2, or novel OPV2 for outbreak response. Future studies will reveal the true value of novel OPV2, as well as similar efforts to develop novel OPV strains for types 1 and 3. Ultimately, the development of novel OPVs could lead to an easier-to-deliver and more cost-effective poliovirus vaccine option than inactivated poliovirus vaccine for countries that rely on OPV. The studies by De Coster and colleagues[8] and Sáez-Llorens and colleagues[10] represent promising next steps towards the future of global poliovirus control and eradication using better performing OPV strains.

I declare no competing interests.

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