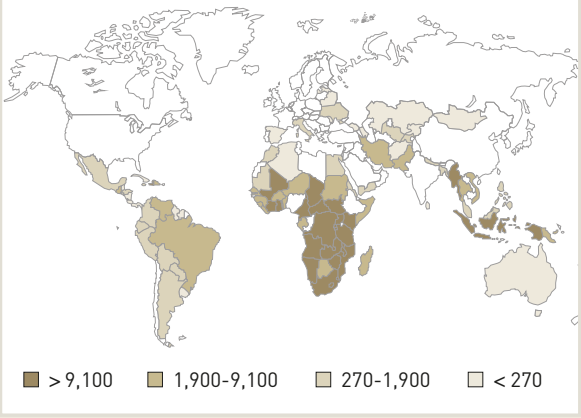
PAEDIATRIC HIV

- 90% of infected infants acquire HIV from their mothers, during pregnancy, delivery, or through breast-feeding
- Without treatment, 1 in 3 children die in their first year of life; and half before they reach their second birthday
- Fewer than half of children (<15 years) living with HIV are on antiretroviral medication
- Opportunistic infections such as tuberculosis (TB) are common

1.8
million children living with HIV in 2015

150,000
children newly infected with HIV in 2015

▼ Children (<15 years) living with HIV in 2015



Nearly **90%**
of cases are in sub-Saharan Africa

300
child deaths every day

Infants and young children need treatments that are safe, efficacious, and easy to swallow, to ensure their best chance of survival to adulthood. Because children are frequently co-infected with TB, any paediatric HIV treatment also needs to be TB treatment-compatible. In 2016, based on the interim results of a DND*i*-sponsored study (see p. 9), the WHO revised its guidelines to recommend the 'superboosting' of ritonavir in treatment of children co-infected with HIV and TB.

Today, the only approved protease inhibitor for young children is a foul-tasting lopinavir/ritonavir solution with a high alcohol content that requires refrigeration and is difficult to store, making it unsuitable for use in resource-poor settings. A taste-masked, oral formulation is needed.

Ultimately, it would be combined with other antiretrovirals into a single 4-in-1 capsule, thus radically simplifying treatment of HIV in children.

"I face a lot of difficulties with the medicine. I really have to battle in order for my baby to take them. It's heart-breaking to give a child four medicines at a time."

Sani Nojiyeza
23-year-old mother to baby Mel. Sani and Mel are both HIV positive, Mel is also co-infected with TB. Durban, South Africa

DND*i* aims to deliver:

- **Develop a solid taste-masked first-line LPV/r-based fixed-dose formulations** in combination with two NRTIs, 3TC and prioritizing ABC as the second NRTI.
- **Immediate introduction of the recently US FDA approved LPV/r-pellets**, before the availability of better-adapted 4-in-1 products

Comparison of the current treatment, lopinavir/ritonavir pellets plus the 2 NRTIs dispersible tablets which need to be taken dispersed in water (on the left), vs the future treatment, the granules of lopinavir/ritonavir mixed with the granules of NRTIs as the '4-in-1' treatment (on the right)

TRANSLATION

4-in-1' fixed-dose combination with LPV/r

OBJECTIVE: Develop and register a solid taste-masked first-line LPV/r-based fixed-dose formulation with two NRTIs, 3TC and prioritizing ABC as the second NRTI.

Background: The objective is to combine the four drugs needed for the treatment of paediatric HIV into an easy-to-use single unit, or fixed-dose combination, which is heat-stable, taste-masked, solid, does not contain alcohol or inappropriate solvents.

2016 Following preliminary studies, the best formulation candidates in terms of bioavailability and taste-masking have been chosen – out of the 30 formulations evaluated since 2014 – for testing in healthy human volunteers in on-going Phase I studies.

DEVELOPMENT

LPV/r pellets with dual NRTI

OBJECTIVE: Evaluate the effectiveness of LPV/r pellets in addition to AZT/3TC (or ABC/3TC) paediatric fixed-dose combination tablet in an implementation study in HIV-infected infants and young children who cannot swallow tablets.

Background: Cipla Inc has developed LPV/r pellets in capsules which can be opened and administered orally to small children; they are alcohol-free, do not require a cold chain and are less costly to transport. However, they must be given with two other antiretrovirals which come in dispersible tablet form.

The DND*i* project includes large-scale implementation studies (known as the LIVING study) to provide supportive clinical data on the acceptability, feasibility, efficacy, safety, and pharmacokinetics of LPV-based therapies in routine treatment settings and to provide early access to better formulations and facilitate registration in the countries concerned.

388 patients recruited at 9 sites

2016 Patients were recruited in Kenya (221 patients out of a target 350) and Uganda (167 patients out of a target 350) for the implementation study. Clinical trials will also be initiated in South Africa, Tanzania, Zambia in 2017.

Access: Rolling out LPV/r pellets in Uganda

In 2016, Uganda announced its intention to begin using lopinavir/ritonavir (LPV/r) pellets to treat children living with HIV, starting from January 2017.

Until the development of the pellets in 2015, the only available version of LPV/r for kids was a harsh-tasting syrup that requires refrigeration and contains 40% alcohol. Through the LIVING study being conducted in Kenya and Uganda, DND*i* has developed extensive experience in understanding the use of the pellets and was asked to help strengthen the capacity of health workers to help patients and caregivers in using them. Information, education, and communication materials developed for use in the LIVING study sites were shared with ministries of health for translation and adaptation as training materials.

Uganda joins Kenya in including pellets in national treatment guidelines, with Cameroon, Nigeria, Zimbabwe, and the Democratic Republic of Congo all expressing interest in adopting pellets for use from 2017 ■

Dr Cordelia Katureebe
National coordinator, Paediatric and adolescent care and treatment, AIDS Control Programme, Ministry of Health, Uganda

"The pellets will provide an opportunity for our children to have better and simpler treatment formulations. We are happy to introduce them in 2017 here in Uganda and believe that the study currently being conducted by DND*i* will provide important lessons towards a seamless launch."