Global transition to Dolutegravir-based ART in children and adolescents 0-19 years living with HIV

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Sophie Desmonde[1], Kim Anderson[2], Joyeux Bwami[1], Quy Tuan Du[3], Winstone Nyandiko[4], Christella Twizere[5], Marco Tulio[6], Renee De Waal[2], Vohith Khol[7], Patricia Lelo[8], Vanessa Rouzier[9], Frankie Odhaimbo[10], Valériane Leroy[1] on behalf of IeDEA

[1]Inserm U1295, University of Toulouse 3, France; [2]University Cape Town, South Africa; [3]Children's Hospital 1, Ho Chi Minh City, Vietnam; [4]Academic Model Providing Access to Healthcare (AMPATH), Moi University, Eldoret Kenya; [5]Centre National de Reference en Matière de VIH/SIDA (CNR), Bujumbura, Burundi.

[6]Instituto Hondureño de Seguridad Social and Hospital Escuela Universitario, Tegucigalpa, Honduras; [7]National Center for HIV/AIDS, Dermatology and STD, Phnom Penh, Cambodia; [8]Kalembelembe Pediatric Hospital, Kinshasa, Democratic Republic of Congo.; [9]Les Centres GHESKIO, Port-au-Prince, Haiti; [10]Kenya Medical Research Institute, Kisumu Kenya

BACKGROUND

Dolutegravir (DTG)-based regimens are recommended as first-line antiretroviral therapy (ART) for all children and adolescents living with HIV (CALHIV).

We describe transition to DTG in the multiregional International epidemiology Database to Evaluate AIDS (IeDEA) cohort.

METHODS

- Population: all ART-treated CALHIV in IeDEA sites where DTG was available, from 6 regions (Figure 1)
- Study period: January 2018 – March 2023
- Patient baseline: date DTG was first prescribed at the patient's site (or ART initiation, whichever occurred later)
- Endpoint: DTG initiation (or database closure, death or lost-to-follow-up [LTFU])
- LTFU: last clinical contact > 7 months at database closure

Statistical analyses:

- Regional cumulative incidence functions (CIF) for DTG initiation
- Factors associated with DTG initiation:
  - Cox proportional hazard model with calendar time scale
  - Adjusted for sex, baseline age, baseline ART regimen and baseline viral load (VL), stratified by region

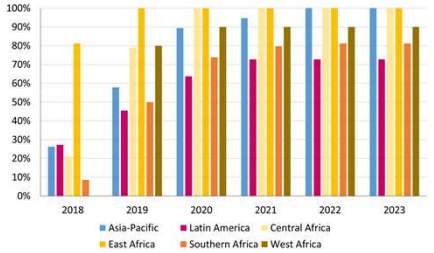

Figure 1 – Cumulative proportion of pediatric IeDEA sites prescribing DTG by region, 2018-2023

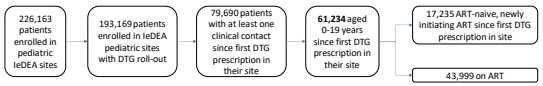

Figure 2 – Flow diagram

Table 1 – Baseline characteristics of the 61,234 patients 0-19 years followed up in IeDEA sites rolling out DTG

	Asia-Pacific	Latin America	Central Africa	East Africa	Southern Africa	West Africa	p
	n=3166	n=1400	n=2839	n=13844	n=36895	n=3180	
Male sex, %	53	47	47	44	43	52	*<0.0001*
Age (years), %							*<0.0001*
<5	12	15	16	13	19	11	
5-9	19	18	15	22	21	24	
10-14	41	18	27	32	28	38	
≥ 15	28	49	41	34	33	27	
On NNRTIs, %	63	39	67	55	40	62	*<0.0001*
Viral load, %	44	56	30	43	33	53	*<0.0001*
Among those with available viral load							
Suppressed*, %	77	48	66	49	47	56	*<0.0001*

** Viral load < 50 copies*

Successful DTG scale-up among patients0-19 years, but with unequal access.

Girls and those with detectable viral load are least likely to access DTG. There is a need to promote transitioning to DTG-based ART regardless of sex and VL

RESULTS

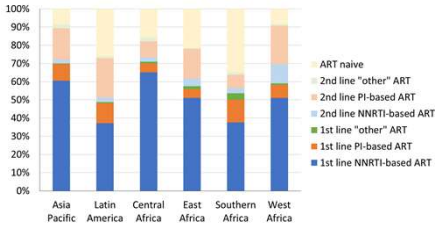

Figure 3– Distribution of baseline ART regimen, by region

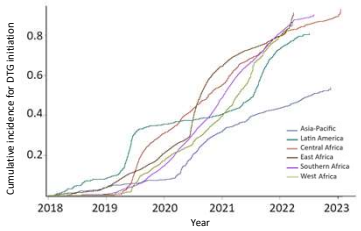

Figure 4 – Cumulative incidence functions for initiating DTG 2018-2023 by region

Table 3 – Factors associated with DTG initiation in IeDEA cohorts; Multivariate Cox proportional Hazard model, stratified by region

	Asia Pacific		Latin America		Central Africa		East Africa		Southern Africa		West Africa	
	aHR*	95%CI**	aHR*	95%CI**	aHR*	95%CI**	aHR*	95%CI**	aHR*	95%CI**	aHR*	95%CI**
Female vs Male	0,89	[0,79 - 1,01]	1,05	[0,92 - 1,2]	0,67	[0,61 - 0,73]	0,72	[0,69 - 0,75]	0,93	[0,91 - 0,96]	0,61	[0,55 - 0,68]
Age (ref: < 5 years)												
5-9 years	1,34	[0,92 - 1,97]	2,48	[1,95 - 3,16]	3,32	[2,66 - 4,14]	3,37	[3,08 - 3,69]	3,87	[3,66 - 4,09]	2,46	[1,84 - 3,28]
10-14 years	7,14	[5,06 - 10,08]	2,70	[2,09 - 3,5]	5,03	[4,07 - 6,2]	4,30	[3,93 - 4,7]	6,68	[6,32 - 7,05]	5,62	[4,25 - 7,43]
15-19 years	9,28	[6,52 - 13,2]	3,05	[2,43 - 3,82]	4,31	[3,52 - 5,26]	4,73	[4,33 - 5,17]	8,06	[7,63 - 8,51]	6,78	[5,10 – 9,00]
Baseline ART regimen (ref: PI-based ART)												
NNRTI-based ART	2,68	[2,22 - 3,25]	1,53	[1,29 - 1,81]	3,13	[2,69 - 3,64]	3,79	[3,57 - 4,03]	1,77	[1,69 - 1,85]	1,11	[0,99 - 1,24]
Other ART	3,11	[1,92 - 5,05]	0,42	[0,17 - 1,03]	4,78	[3,62 - 6,3]	9,95	[8,66 - 11,43]	3,00	[2,8 - 3,23]	2,41	[1,65 - 3,51]
ART naive	5,76	[4,32 - 7,68]	6,41	[5,3 - 7,76]	6,09	[5,04 - 7,35]	4,72	[4,37 - 5,09]	3,78	[3,6 - 3,96]	1,52	[1,17 - 1,98]
Baseline viral status (ref: undetectable; VL < 50 copies)												
Detectable VL	1,06	[0,84 - 1,34]	1,20	[0,99 - 1,45]	0,75	[0,64 - 0,89]	0,49	[0,46 - 0,52]	0,69	[0,66 - 0,73]	0,77	[0,68 - 0,88]
Unavailable VL	0,67	[0,59 - 0,77]	1,18	[0,98 - 1,43]	1,10	[0,98 - 1,23]	0,75	[0,71 - 0,79]	0,95	[0,91 - 0,99]	0,74	[0,66 - 0,83]

** Adjusted hazard ratio; ** 95% Confidence interval*

CONCLUSIONS

- **In sites where DTG was available**, scale-up was successful. Access to DTG, however, was unequal:
- Delayed access in the Asia-Pacific compared to sub-Saharan Africa
- Girls are less likely to access DTG compared to male counterparts in sub-Saharan Africa. This could be explained by DTG transition conditioned on contraception, or the lack of sexual and reproductive health services in these settings.
- Access to DTG was associated with older age, mainly explained by availability of only the DTG 50mg oral tablet formulation for children > 20 kgs in the earlier years of the study.
- Those on PI-based ART were less likely to initiate DTG; of note, those PI-based ART were mostly part of a 2nd line regimen in our cohort.
- Access to DTG was associated with undetectable viral load at baseline. These observations could be explained by the reluctance to switch failing and/or unstable CALHIV.

Our results highlight the need to promote equitable use of DTG regardless of sex and viral load. As new pediatric formulations for DTG become available, continued documentation of treatment practices is required to ensure universal access to DTG for all CALHIV.

CORRESPONDING AUTHOR

Sophie Desmonde, PhD
Centre for Epidemiology and Research in POPulation Health (CERPOP)
UMR1295, joint Inserm - Toulouse III Paul Sabatier University research unit. France
sophie.desmonde-phillips@inserm.fr

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