Best Treatment Options for Children with HIV

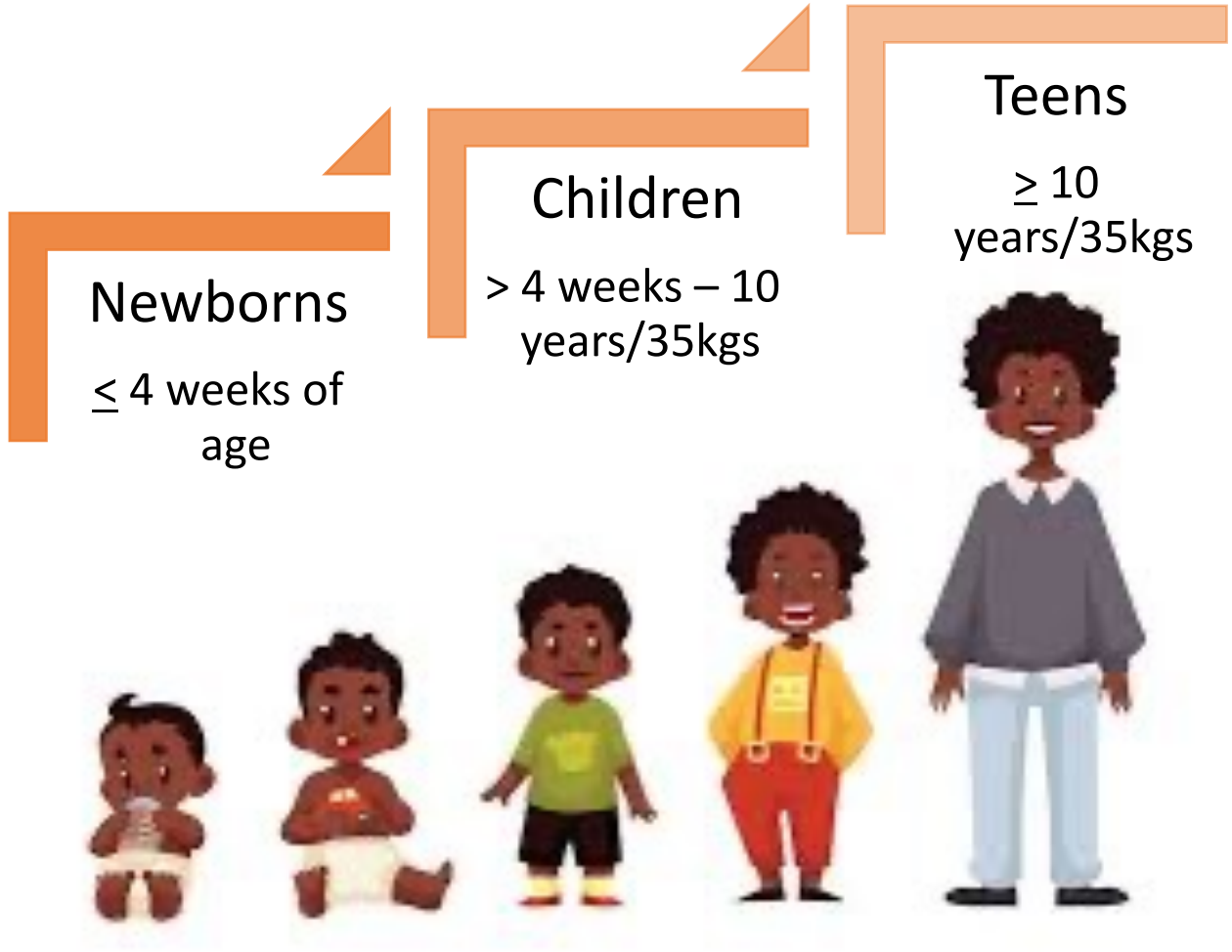
Prof Mo Archary

Paediatric Infectious diseases unit

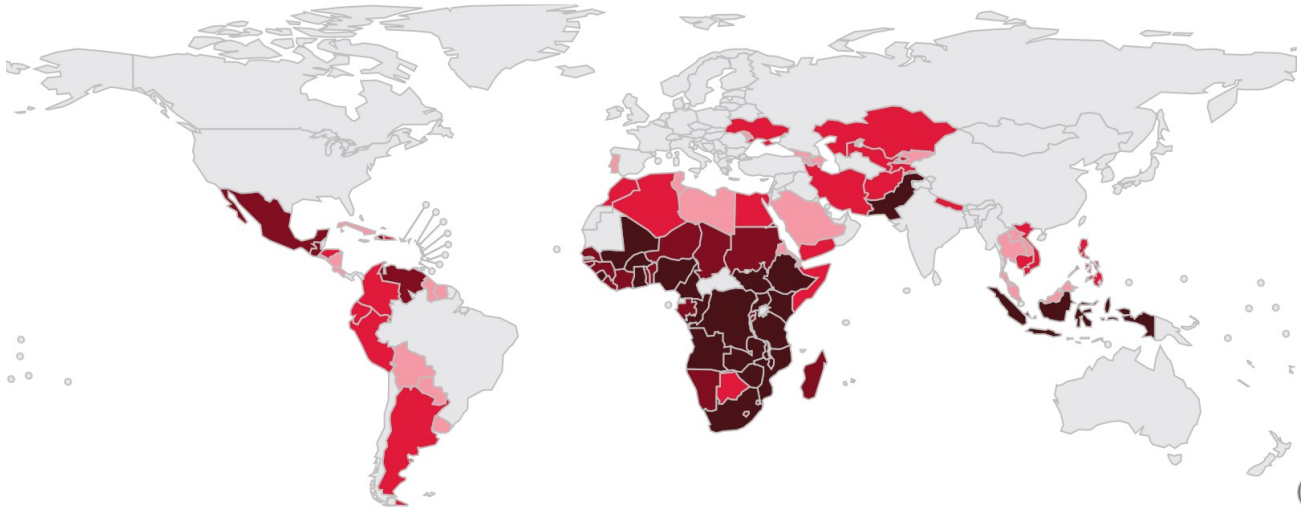
King Edward VIII Hospital / University of KwaZulu-Natal

Overview

- Paediatric HIV Landscape
- Gaps in the HIV Treatment Cascade
- Current state of Paediatric ART
- Treatment across the age spectrum
- Options for treatment
- Long-term landscape
- Conclusion



Paediatric HIV Landscape in 2022

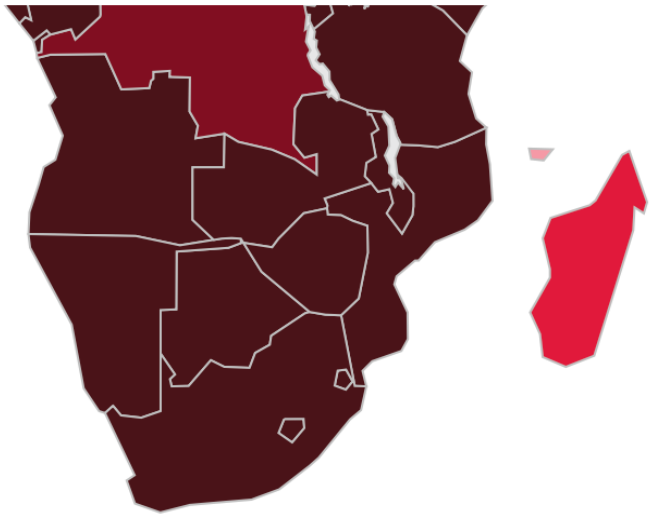


New Pediatric HIV infections

Eastern/Southern Africa	50%
Western/Central Africa	37%
Asia/Pacific	9%

- Despite falling incidence rates - approximately 150 000 children become newly infected with HIV
- Approximately 95 000 AIDS-related deaths in children
- Approximately 1.7 million children (<14 years) living with HIV

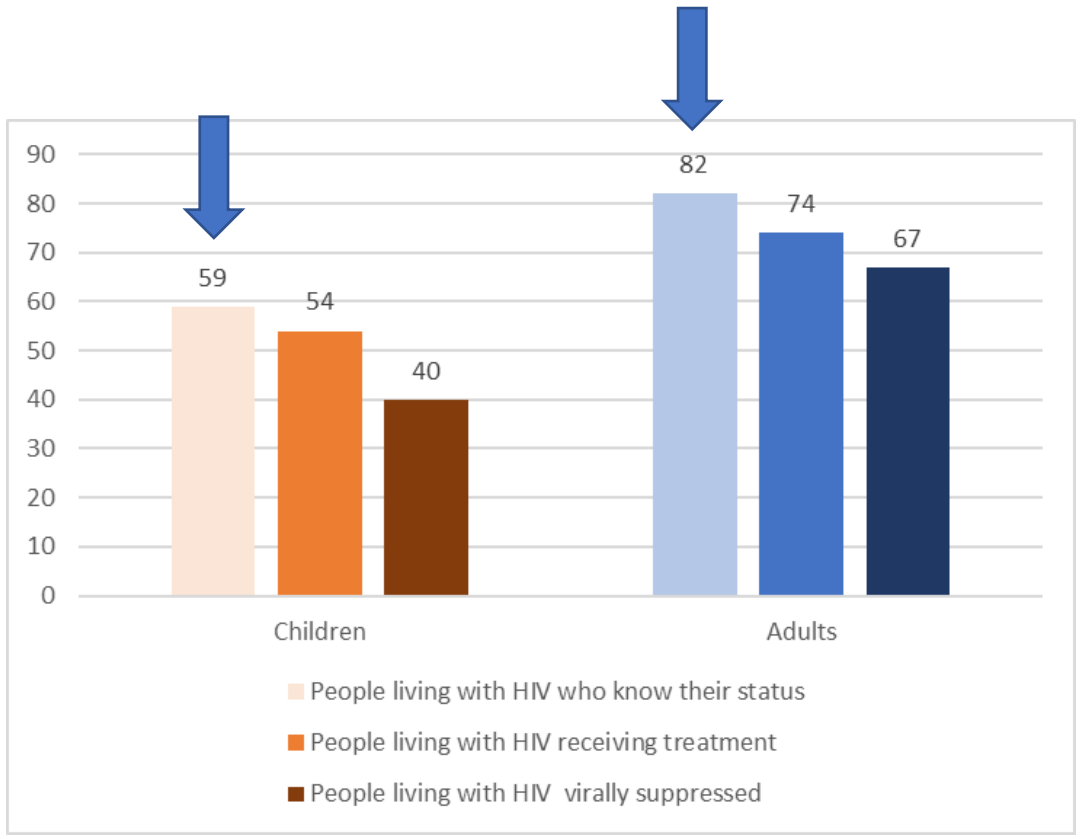
Paediatric HIV Landscape – South Africa



- **New HIV infections in 2020**
- Children (<15 years): 12 000 (6900 – 31 000)
- Adolescents (10-19 years): 38 000 (5 400 - 77 000)
- All Ages: 230 000 (150 000 – 310 000)

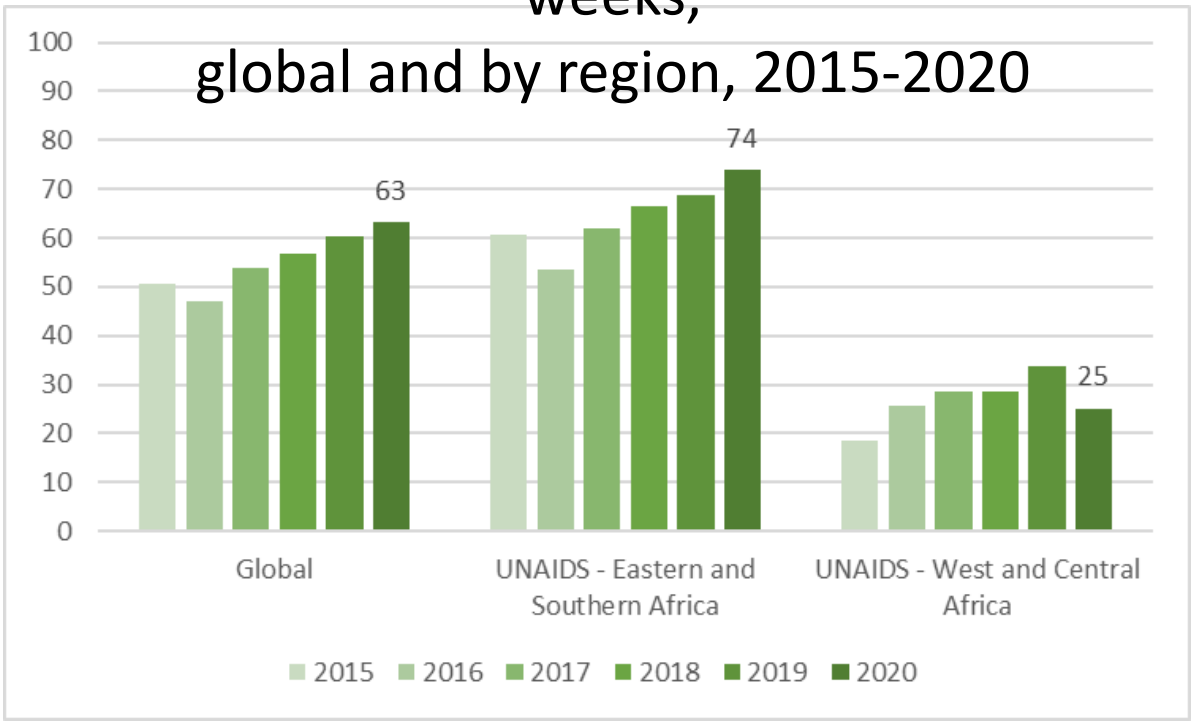
- **People living with HIV**
- Children (<15 years): 310 000 (200 000 – 540 000)
- Adolescents (10-19 years): 370 000 (190 000 - 550 000)
- All Ages: 7 800 000 (5 200 000 – 10 000 000) – Prevalence 17.7 (11.7 – 22.5)

Paediatric HIV Treatment Cascade: 95:95:95



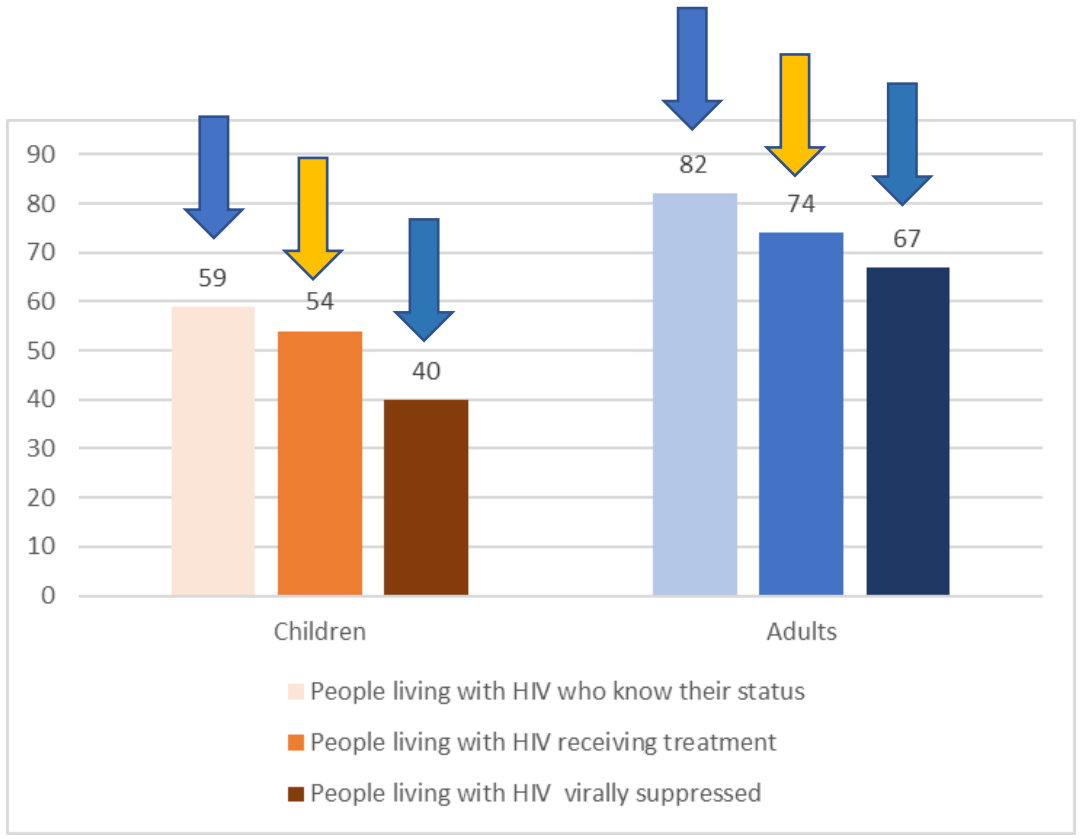
Treatment cascade for children and adults, global, 2020

Percent of HIV exposed children tested by 8 weeks,
global and by region, 2015-2020



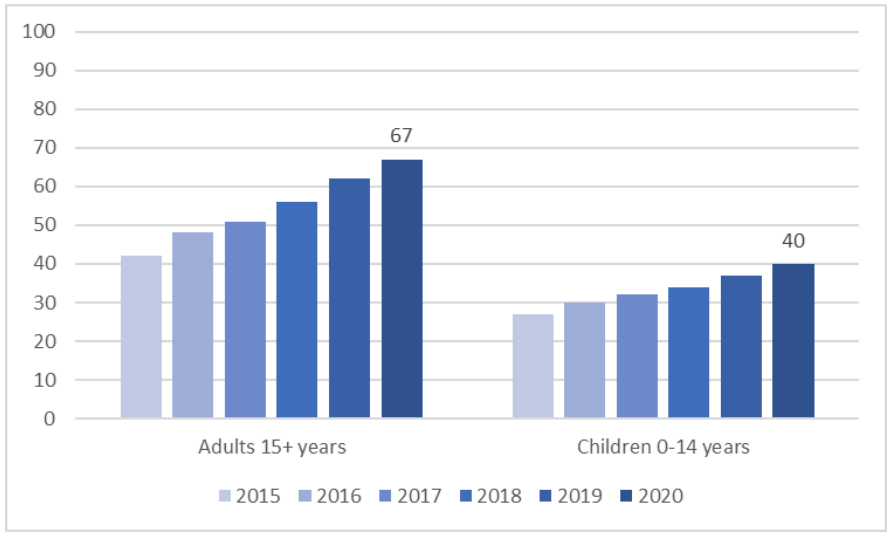
Source: UNAIDS 2021 epidemiological estimates
Slide courtesy of Mary Mahy

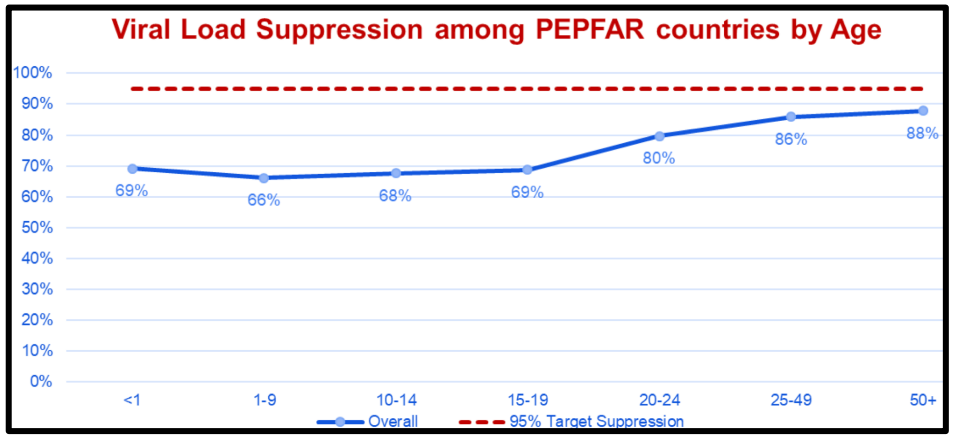
Paediatric Treatment Cascade: Viral Suppression



Treatment cascade for children and adults, global, 2020

Percentage of people living with HIV with suppressed viral load, by age, Global, 2015-2020





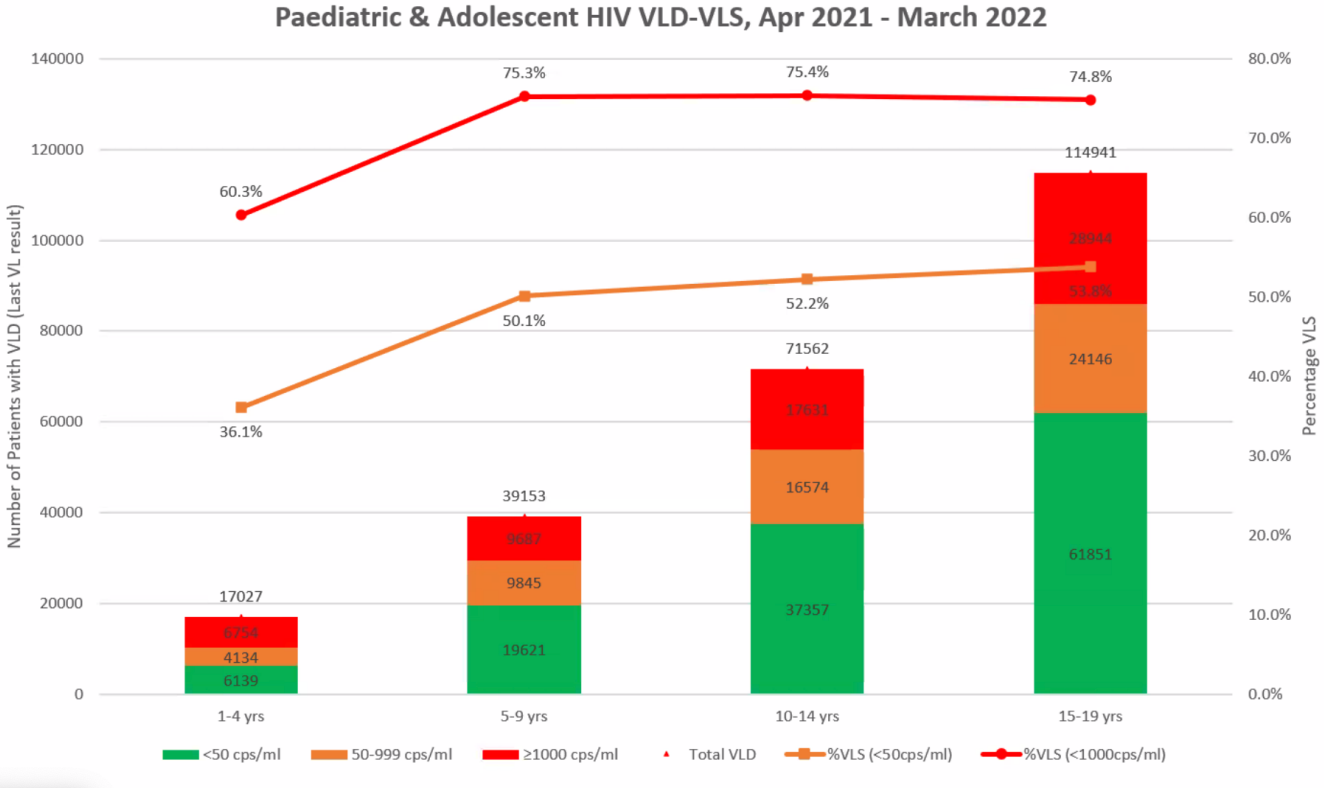
Source: UNAIDS 2021 epidemiological estimates.

Cascade - South Africa

Adults: 93:78:89

Children: 80:59:63

In patients where VL were performed children <5 are the most vulnerable



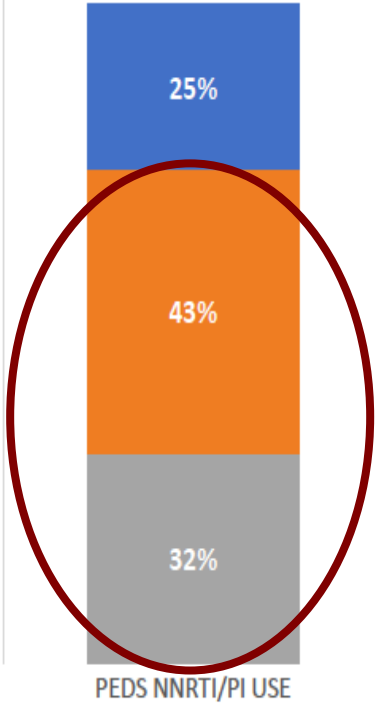
Adult - Paediatric Treatment Divide

Context

Unique Adherence Issues

Adult - Paediatric Treatment Divide

VS

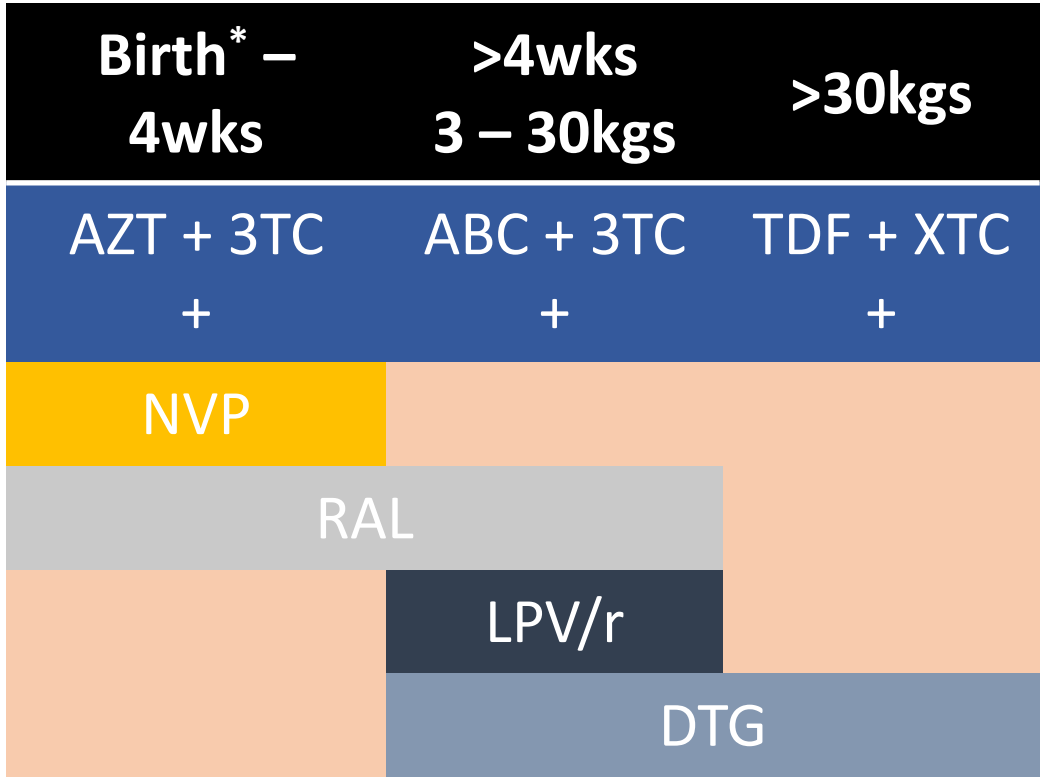


SIMPLICITY
Highly potent Fixed Dose Combination ART

COMPLEXITY
Less potent/ Individual formulations

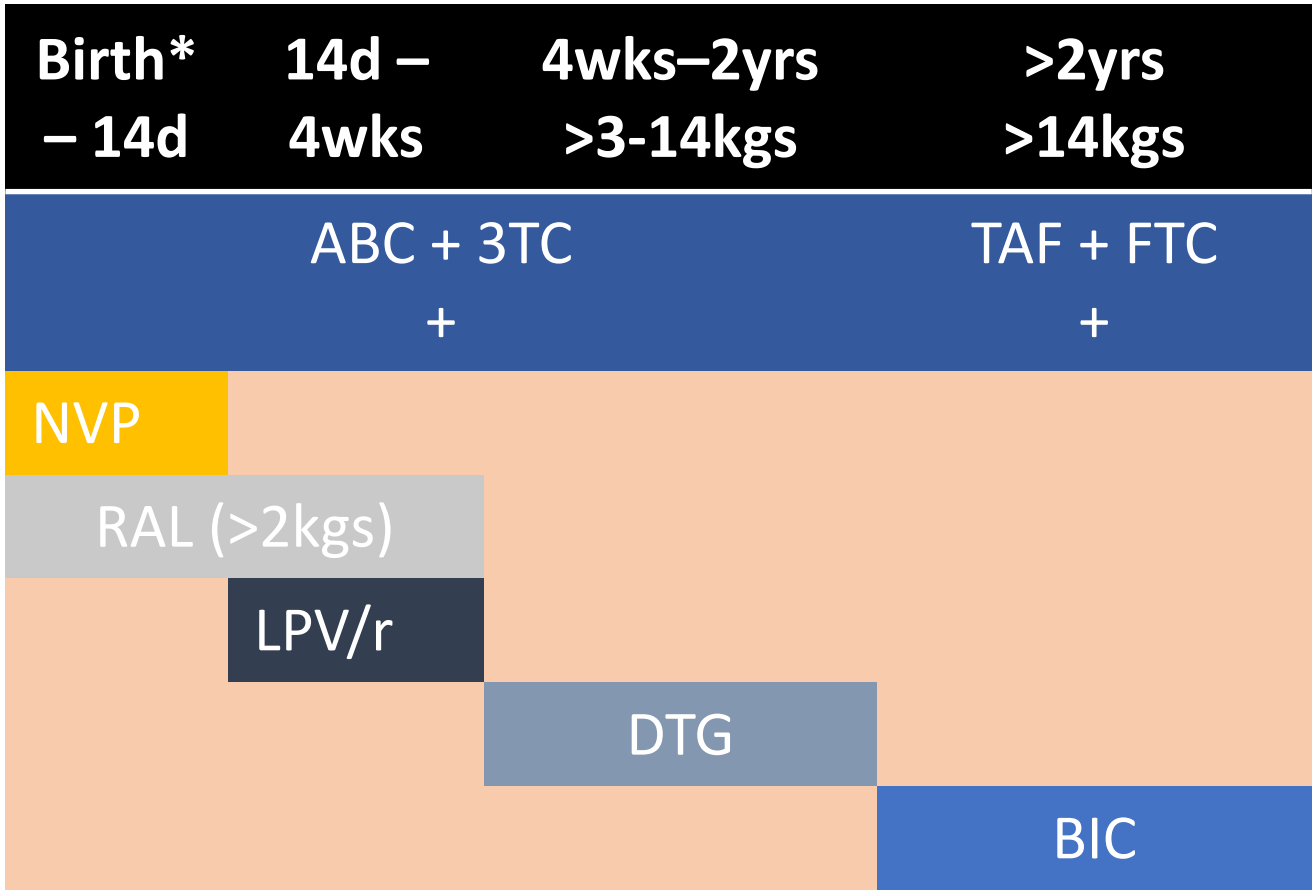
75% on NNRTI-based regimens

Status of current ART Recommendations



WHO RECOMMENDATIONS

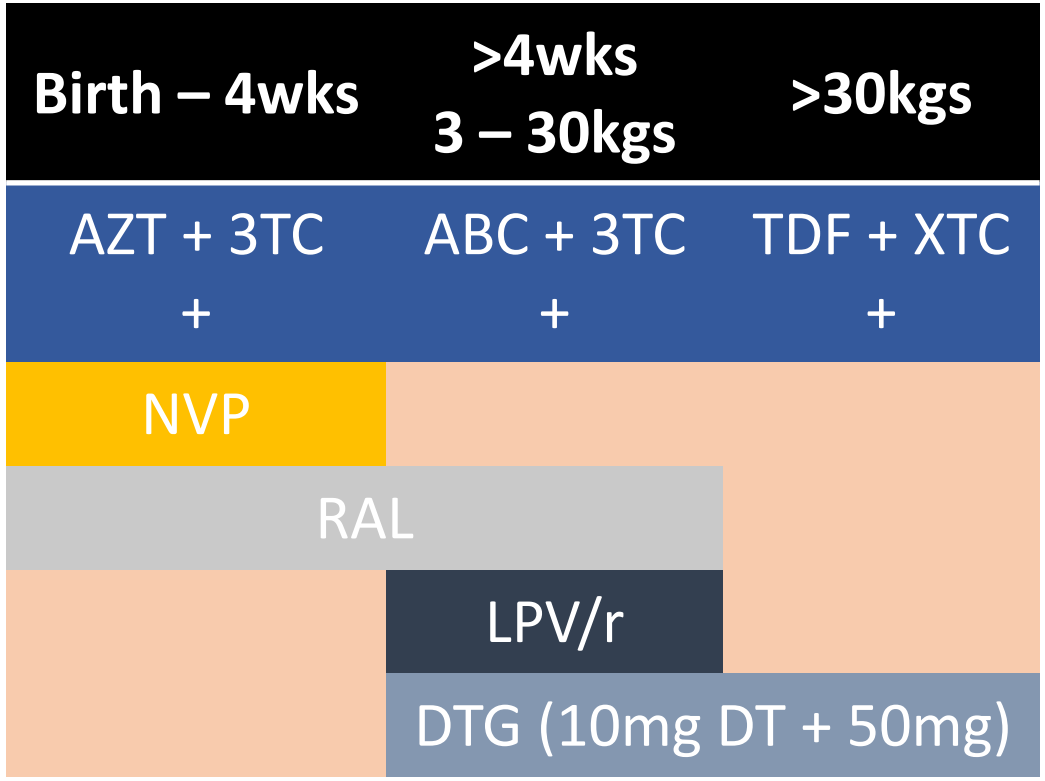
* Term neonates



DHHS RECOMMENDATIONS

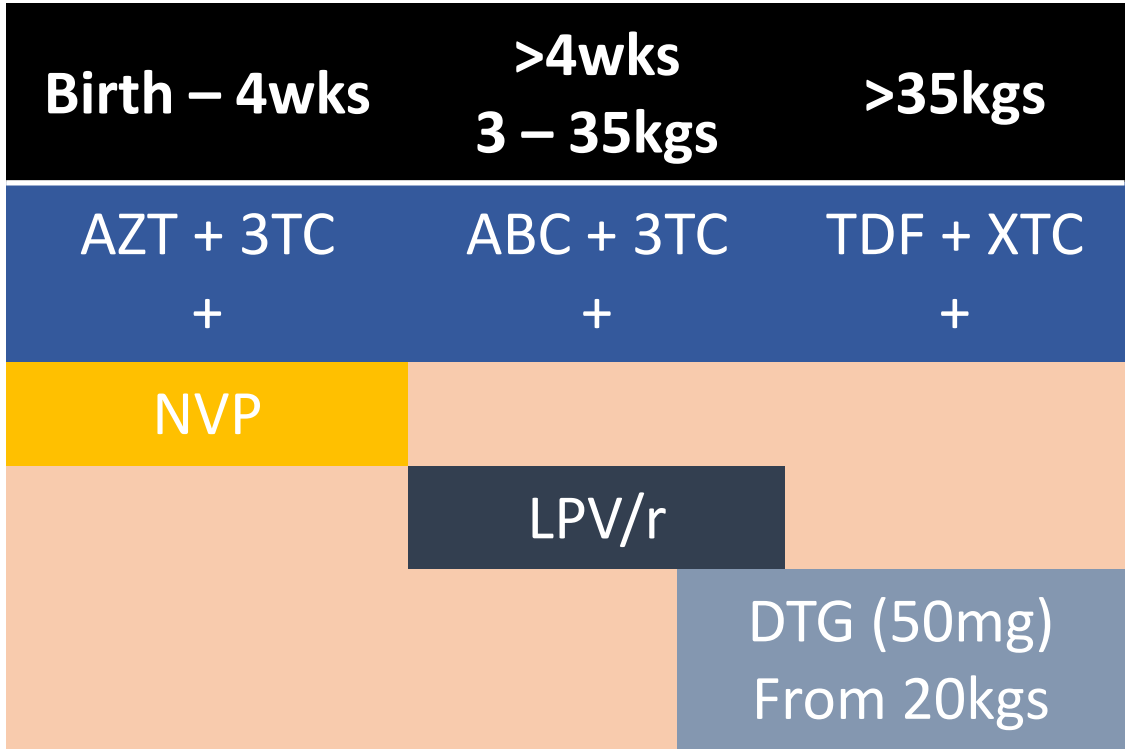
Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. Available at https://clinicalinfo.hiv.gov/en/guidelines/pediatric-arv/regimens-recommended-initial-therapy-antiretroviral-naive-children?view=full

Status of current ART Recommendations



WHO RECOMMENDATIONS

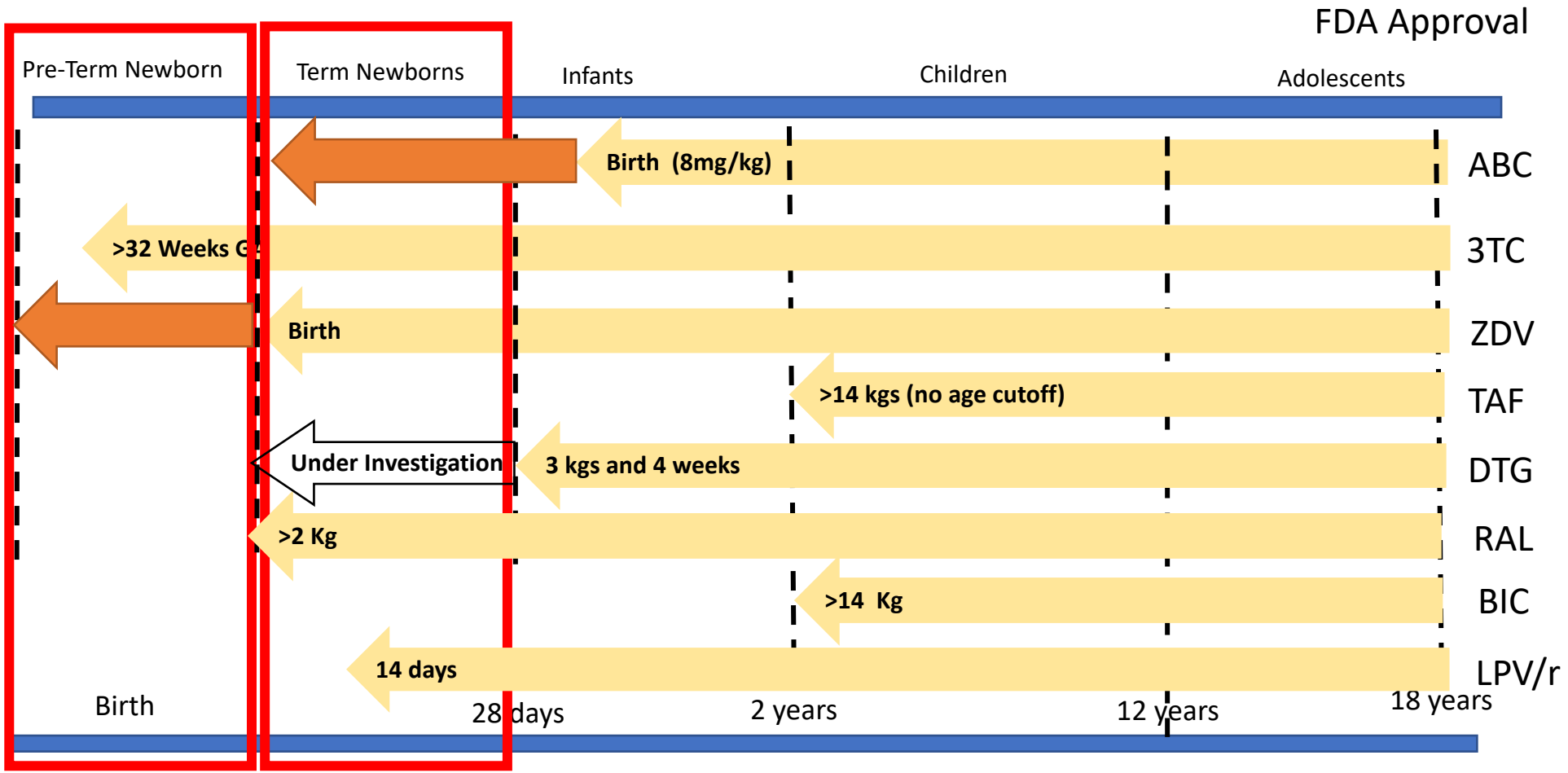
* Absence of guidance for pre-term neonates



SA NDOH RECOMMENDATIONS 2019

Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. Available at https://clinicalinfo.hiv.gov/sites/default/files/inline-files/pediatricguidelines.pdf.

Closing the Gap – Towards Optimized Regimens

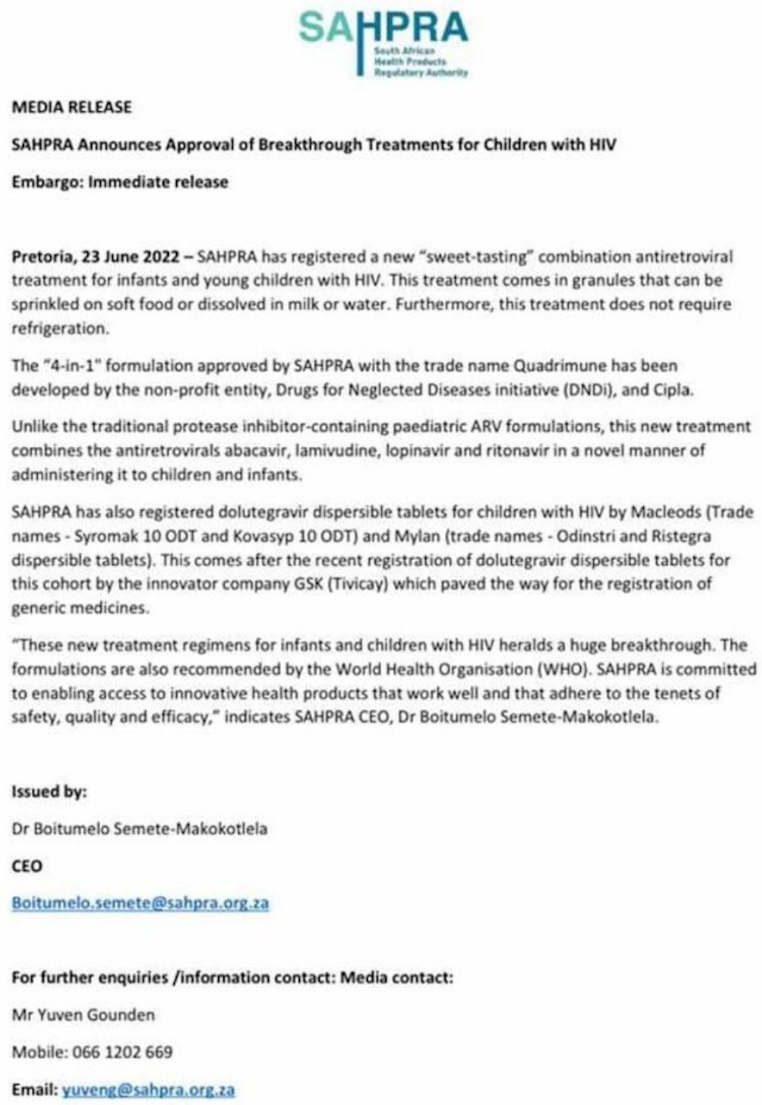


Off-label use: Data available

Source: Drug Package Inserts

Improving Access

- Reducing regulatory barriers delaying access to optimized paediatric formulations
  - 4-in-1 ABC/3TC/LPV/r Granules
  - DTG 10mg Dispersible Tablets (DT)



SAHPRA
South African Health Products Regulatory Authority

MEDIA RELEASE

SAHPRA Announces Approval of Breakthrough Treatments for Children with HIV

Embargo: Immediate release

Pretoria, 23 June 2022 – SAHPRA has registered a new "sweet-tasting" combination antiretroviral treatment for infants and young children with HIV. This treatment comes in granules that can be sprinkled on soft food or dissolved in milk or water. Furthermore, this treatment does not require refrigeration.

The "4-in-1" formulation approved by SAHPRA with the trade name Quadrimune has been developed by the non-profit entity, Drugs for Neglected Diseases initiative (DNDi), and Cipla.

Unlike the traditional protease inhibitor-containing paediatric ARV formulations, this new treatment combines the antiretrovirals abacavir, lamivudine, lopinavir and ritonavir in a novel manner of administering it to children and infants.

SAHPRA has also registered dolutegravir dispersible tablets for children with HIV by Macleods (Trade names - Syromak 10 ODT and Kovasyp 10 ODT) and Mylan (trade names - Odinstri and Ristegra dispersible tablets). This comes after the recent registration of dolutegravir dispersible tablets for this cohort by the innovator company GSK (Tivicay) which paved the way for the registration of generic medicines.

"These new treatment regimens for infants and children with HIV heralds a huge breakthrough. The formulations are also recommended by the World Health Organisation (WHO). SAHPRA is committed to enabling access to innovative health products that work well and that adhere to the tenets of safety, quality and efficacy," indicates SAHPRA CEO, Dr Boitumelo Semete-Makokotlela.

Issued by:

Dr Boitumelo Semete-Makokotlela

CEO

Boitumelo.semete@sahpra.org.za

For further enquiries /information contact: Media contact:

Mr Yuven Gounden

Mobile: 066 1202 669

Email: yuveng@sahpra.org.za

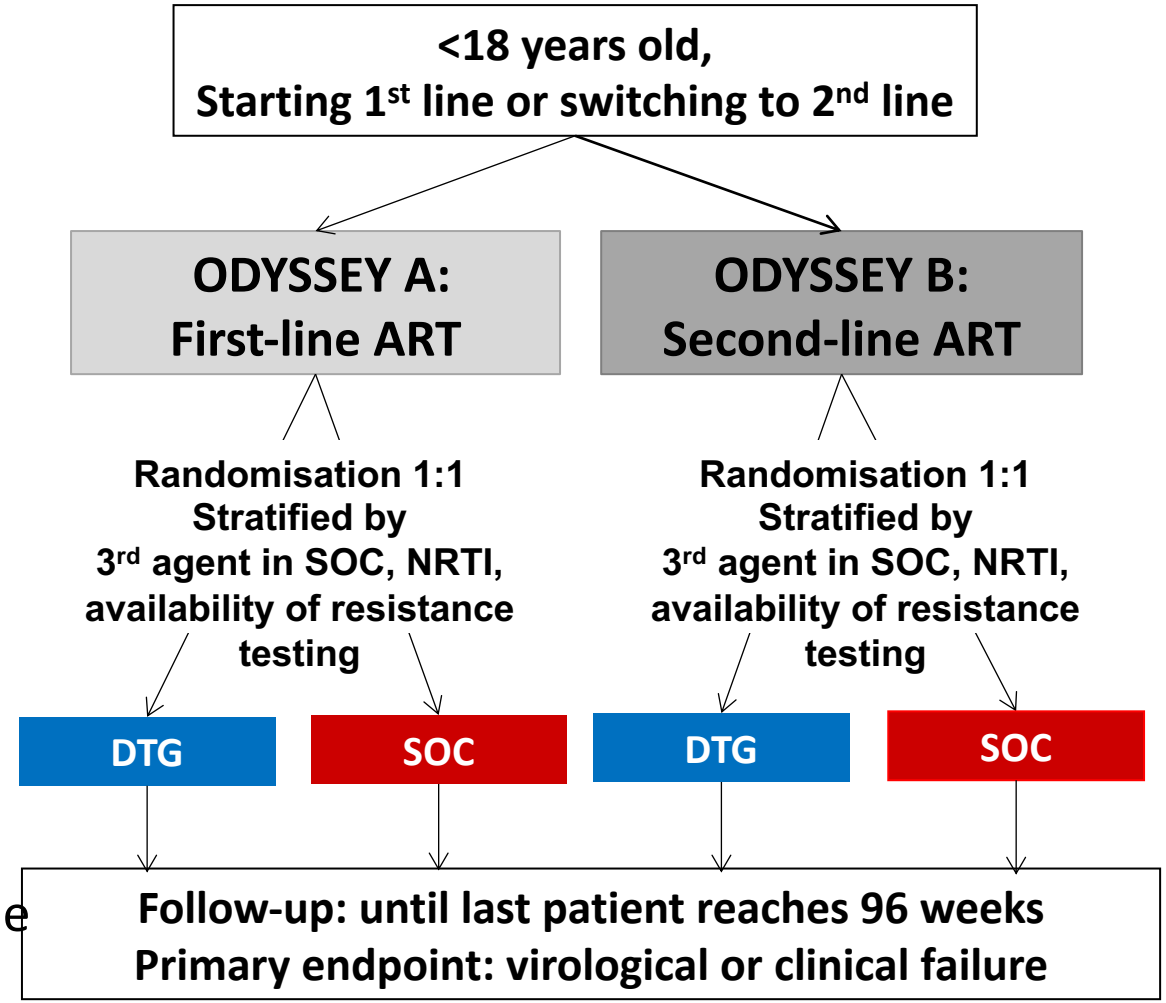
Adolescents (>10 years and >35kgs)

- Significant advantages for alignment with adult regimens

- **Preferred Option:**
- Tenofovir/Lamivudine/Dolutegravir (TLD FDC 300/300/50mg)
  - Monitoring requirements: Calculated Creatinine Clearance - >80 mL/min
  - Other concerns include weight gain and neuropsychiatric symptoms

ODYSSEY

- International multi-centre, randomised 96-week non-inferiority trial
- We aimed to compare **efficacy and safety** of DTG-based ART with standard-of-care in children and adolescents starting **first-line ART (ODYSSEY A)** or **second-line (ODYSSEY B)**
- **Main trial enrolled children ≥14 kg**
  - Aim to enrol ≥700 children: 310 ODYSSEY A, 390 ODYSSEY B
  - Powered for efficacy (total population and A&B separately)
  - Once enrolment in the main trial was completed, the trial was opened for 'under 14kg cohort'



Penta

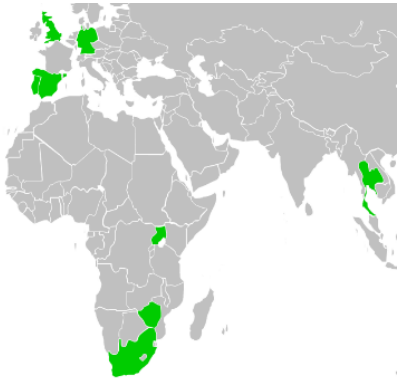
SOC= standard of care

Trial population

Main trial ≥14 kg, n=707

Baseline characteristics

- Median age 12.2 (range 2.9-18.0), 96% ≥6 years
- 49% female; 88% African
- 27% WHO stage 3/4
  22% CD4 <200 cells/mm^3
- **44% started first-line and**
  56% second-line (by design)



Baseline ART from randomisation

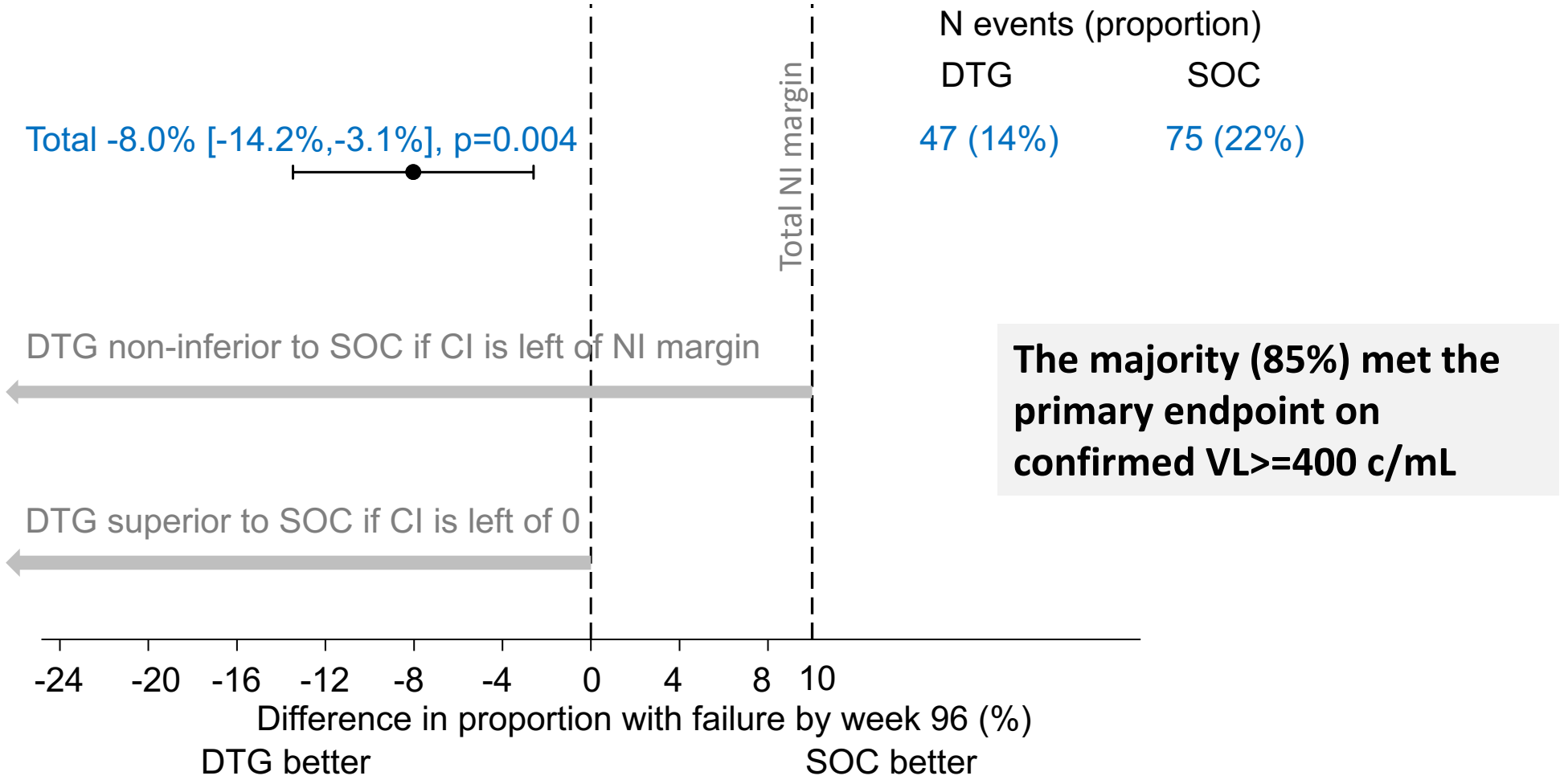
- NRTI: 65% ABC+3TC, 23% TDF+XTC, 11% ZDV+3TC
- Third agent in SOC: **first-line 92% EFV**;
  second-line 72% LPVr, 25% ATVr

Follow-up

- Median follow-up 142 weeks (IQR 124, 159)
- 37 (5%) lost to follow-up

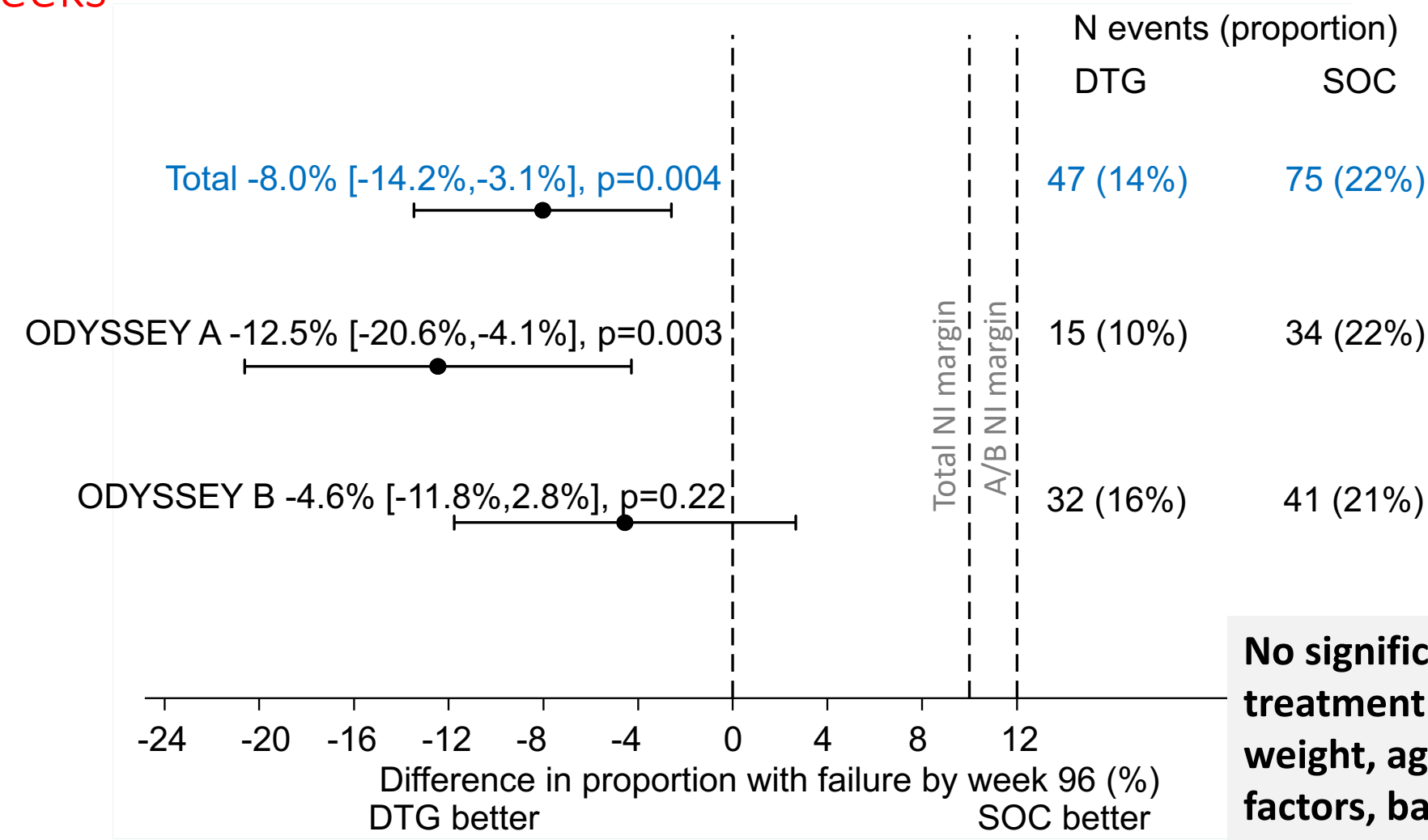
ODYSSEY A – first-line	ODYSSEY B – second-line
NRTI backbone	
80% ABC+3TC	54% ABC+3TC
19% TDF+XTC	26% TDF+XTC
	19% ZDV+3TC
Third agent in SOC	
92% EFV	72% LPVr, 25% ATVr

Primary outcome in the main trial (≥14kg): virological or clinical failure by 96 weeks



The majority (85%) met the primary endpoint on confirmed VL>=400 c/mL

Primary outcome in the main trial (≥14kg): virological or clinical failure by 96 weeks

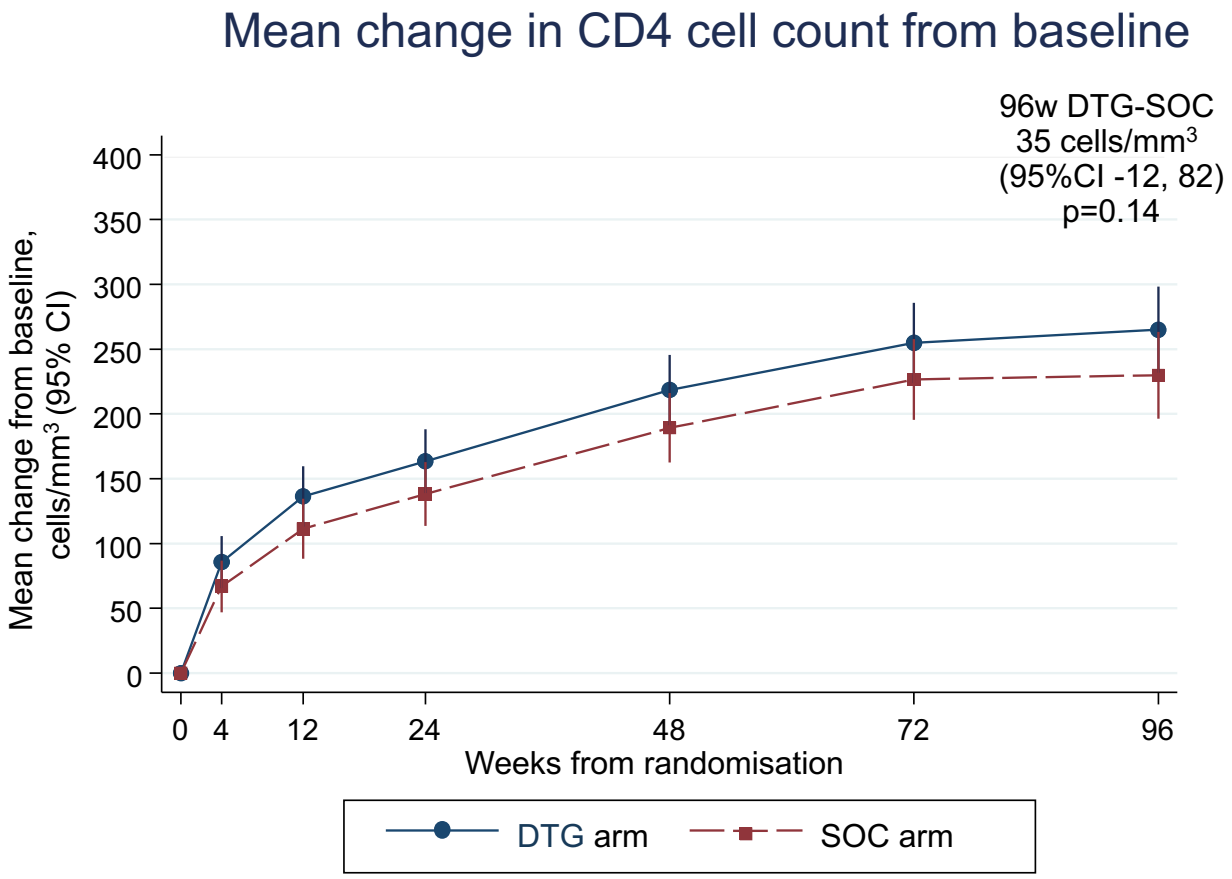


Test of heterogeneity of treatment effect between A & B p=0.16

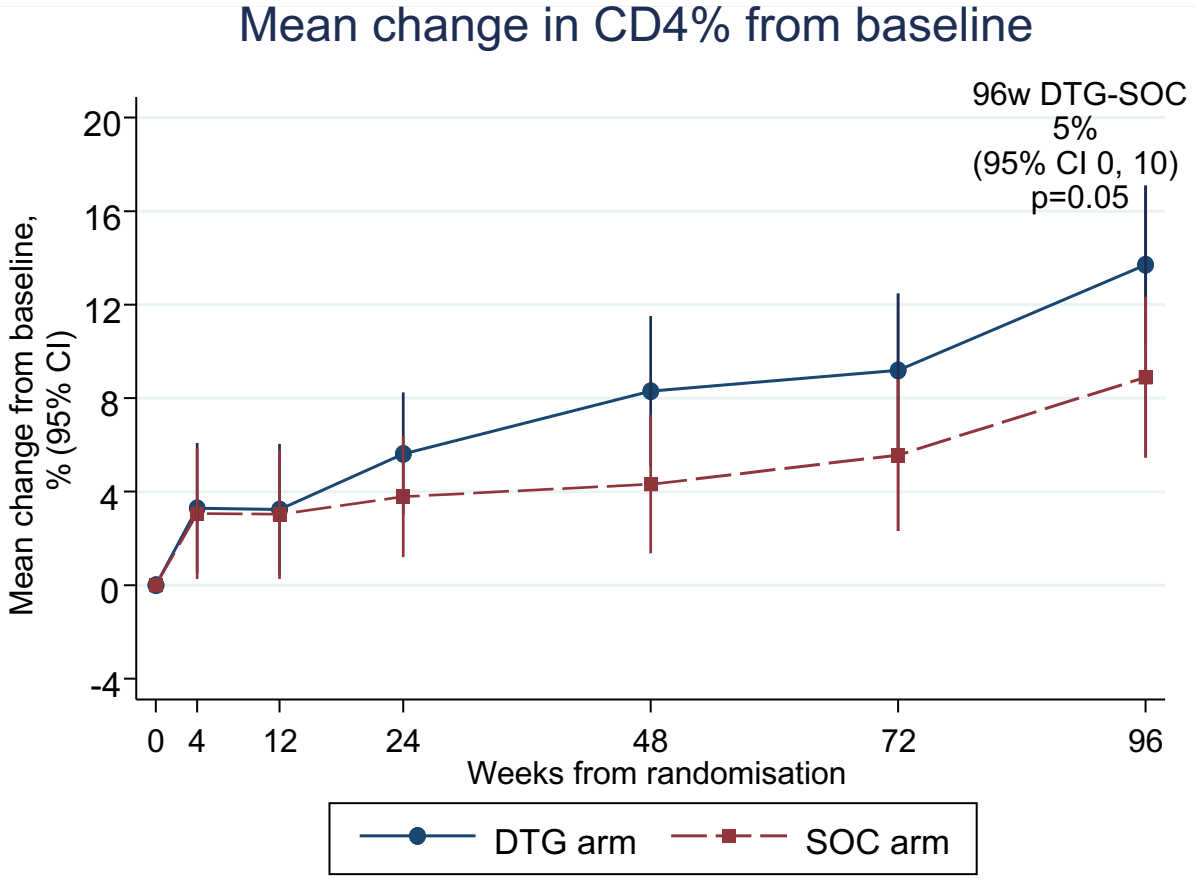
No significant difference in treatment effects by sex, weight, age, stratification factors, baseline VL or baseline CD4

CD4 count: change from baseline

Main trial (≥14kg), 96% ≥6years

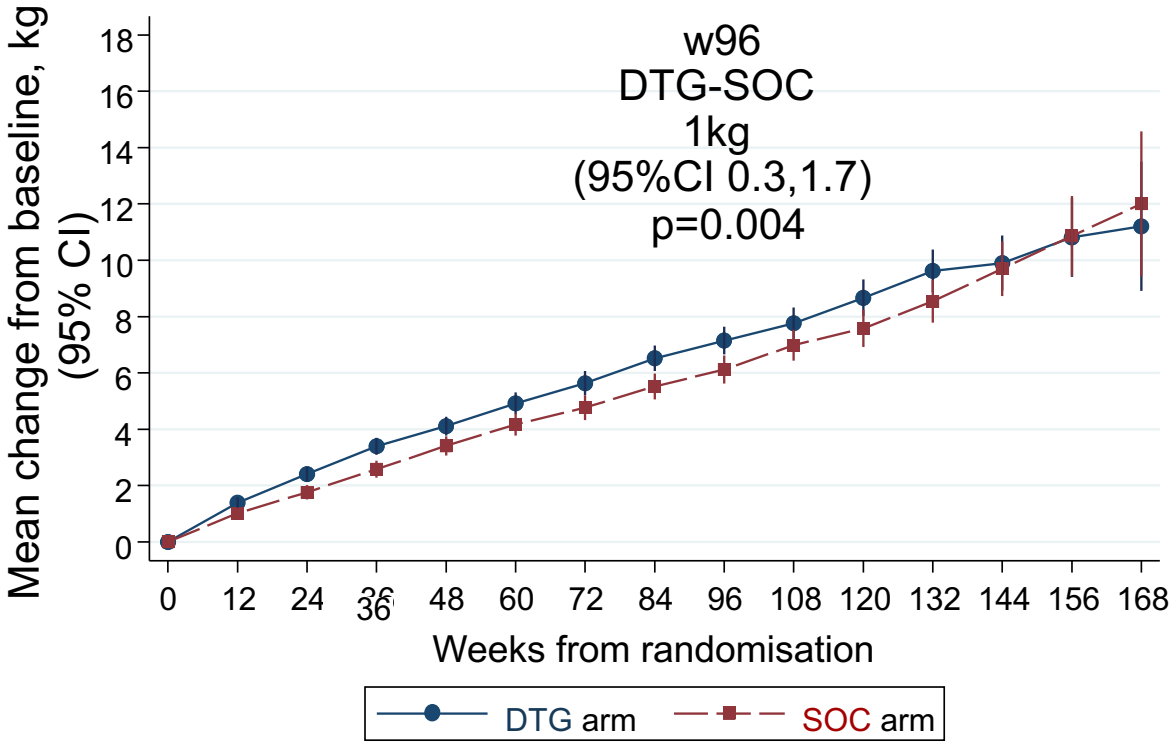


'Under 14kg' cohort, 100% <6 years

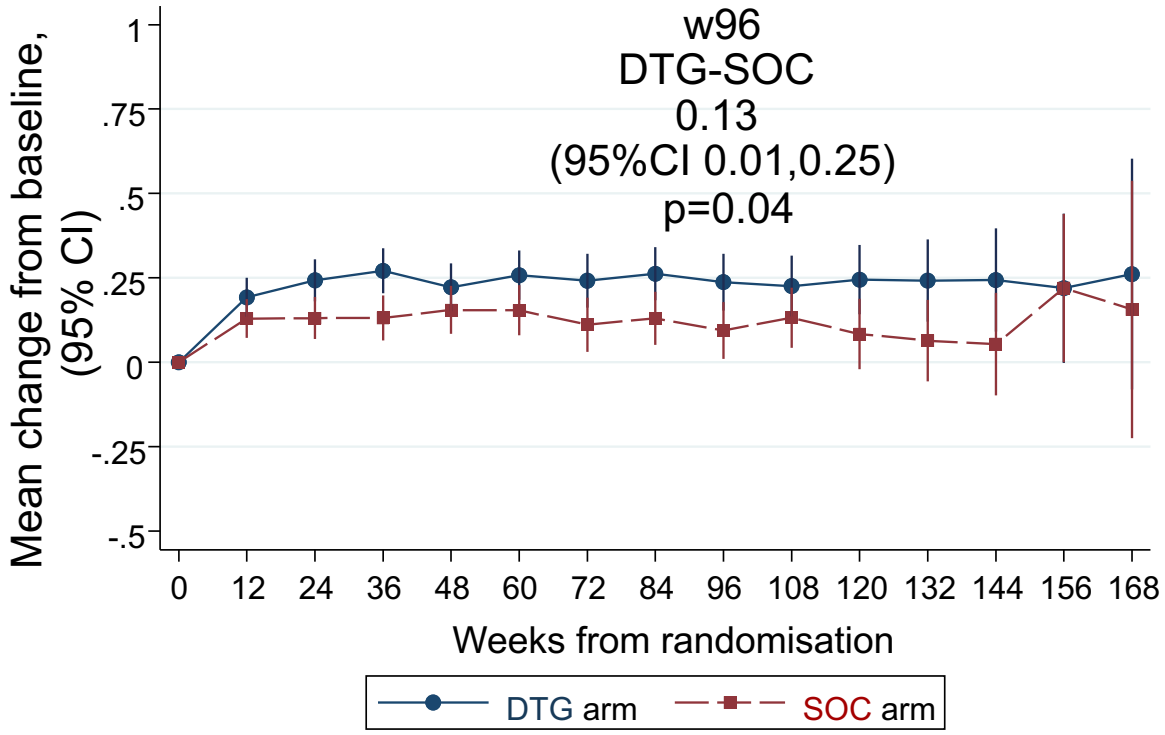


Summary of anthropometric measurements (main trial, ≥14kg)

Weight: change from baseline



BMI-for-age: change from baseline



- Over 96 weeks mean additional gain in weight was ~1kg, and in height 0.8cm in DTG vs SOC
- The differences occurred early and the gap between arms did not increase with time
- Differences in BMI-for-age between arms were similar by: first- or second-line, sex, age and TDF use
- Overall, 25 (4%) were newly overweight or obese at 96 weeks: 14 (4%) DTG vs 11 (3%) SOC (p=0.55)

Psychiatric adverse events (PAEs): ≥14 kg

	DTG		SOC		Total		P-value
	N=350		N=357		N=707		
Psychiatric AEs, N [N participants]	**12**	**[10]**	**7**	**[4]**	**19**	**[14]**	**0.097***
Suicidal ideation/behaviour	8	[8¥]	7	[4]			
Depression	2	[2¥]	0	0			
Insomnia	1	[1¤]	0	0			
Psychosis	1	[1¤]	0	0			
Serious Adverse Events	**3**	**[2]**	**2**	**[1]**			
ART-modifying AEsΨ	**2**	**[2]**	**1**	**[1]**			
Hazard Ratio for time to first PAE§ (95% CI)	**2.48 (0.78, 7.90)**		**1(ref)**				**0.125**

*Comparing number of participants with at least 1 event; ¥ Two events: parasuicide and depression occurred in the same patient; ¤ Events occurred in the same patient; Ψ One additional participant in the DTG arm changed ART due to an ongoing NPAE post trial censoring date; §Adjusted for ODYSSEY A and B

Mood questions (reports across follow-up): ≥14 kg

- No difference between treatment arms in “low mood or feeling sad often”, “feeling worried often” and “feeling angry or aggressive often”
- More participants/carers reported symptoms of self-harm, “life was not worth living” or suicidal thoughts in DTG vs SOC:

N Reports, N [N participants]	**TOTAL**						
	DTG		SOC		Total		P-value*
Self-harm	8	[8]	1	[1]	9	[9]	0.038
Life not worth living	20	[17]	5	[5]	25	[22]	0.009
Suicidal thoughts	13	[13]	0	[0]	13	[13]	<0.001
Life not worth living or suicidal thoughts combined	27	[23]	5	[5]	32	[28]	0.001

* Comparison between participants ever reporting (carer or participant or both)

- Most reported symptoms were transient and did not lead to treatment change
  - Only 4/23 patients in DTG arm and none in SOC reported “life was not worth living” or suicidal thoughts more than once

Adolescents (>10 years and >35kgs)

- **Alternative Options (SA):**
- Tenofovir Alafenamide/Emtricitabine/Dolutegravir (TAF/LD FDC 25/200/50mg)
- Tenofovir/Emtricitabine/Rilpivirine (TER FDC 300/200/50mg)
- Tenofovir/Emtricitabine/Efavirenz (TEE FDC 300/200/600mg
- Abacavir/Lamivudine/Dolutegravir (ALD FDC 600/300/50mg)

Adolescents
(>10 years and >35kgs)

- **Alternative Options (Global):**
- Tenofovir Alafenamide/Emtricitabine/Bictegravir (TAF/FTC/BIC FDC 25/200/50mg - ≥25kgs and 15/120/30mg - 14 – 25kgs)

- CAB/RPV LA injectable (>12 yrs and > 35Kgs) – given every 2 months – Stable switch in virally suppressed adolescents without prior evidence NNRTI or INSTi resistance)

Infant and Child (4 weeks/3kgs and above)

- **Preferred Option:**
- Abacavir/Lamivudine (120/60mg DT) + Dolutegravir (10mg scored DT)

There are multiple ABC and 3TC single formulations with varying dosing frequencies across the weight bands; ABC/3TC dispersible, scored tablets greatly simplify the regimen dosing across multiple weight bands

CURRENT PAEDIATRIC SINGLE FORMULATION REGIMENS DOSING CHART

Product	3-4.9kg	5-6.9kg	7-9.9kg	10-13.9kg	14-19.9kg	20-24.9kg
ABC (20 mg/ml) Oral Solution	2 ml bd	3 ml bd	4 ml bd	6 ml bd OR 12 ml od	8 ml bd OR 15 ml od	10 ml bd
ABC (60 mg) Dispersible Tablet	*Not recommended for children <10kg*			2 tablets bd OR 4 tablets od	2.5 tablets bd OR 5 tablets od	3 tablets bd
3TC (10mg/ml) Oral Solution	2 ml bd	3 ml bd	4 ml bd	6 ml bd OR 12 ml od	8 ml bd OR 15 ml od	15 ml bd OR 30 ml od

Please note the table above has been simplified and does not include combinations of paediatric formulations with adult formulations, kindly refer to the Republic of South Africa: ARV Drug Dosing Chart for Children 2021, to access the comprehensive dosing chart.

ABC/3TC dispersible, scored tablets only need to be given **once a day.** This **greatly simplifies the dosing schedule** across multiple weight bands.

ABC/3TC DISPERSIBLE, SCORED TABLETS DOSING CHART

Product	3-5.9kg	6-9.9kg	10-13.9kg	14-19.9kg	20-24.9kg
ABC/3TC (120/60 mg) Dispersible, Scored Tablet	1 tablet od	1.5 tablets od	2 tablets od	2.5 tablets od	3 tablets od

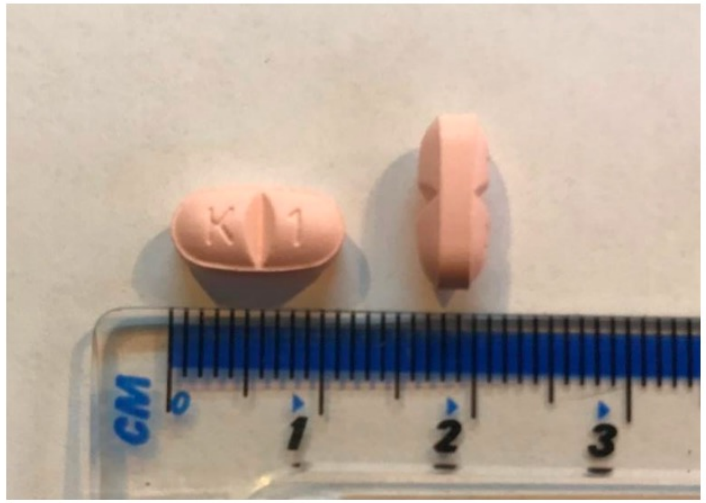
health
Department:
Health
REPUBLIC OF SOUTH AFRICA

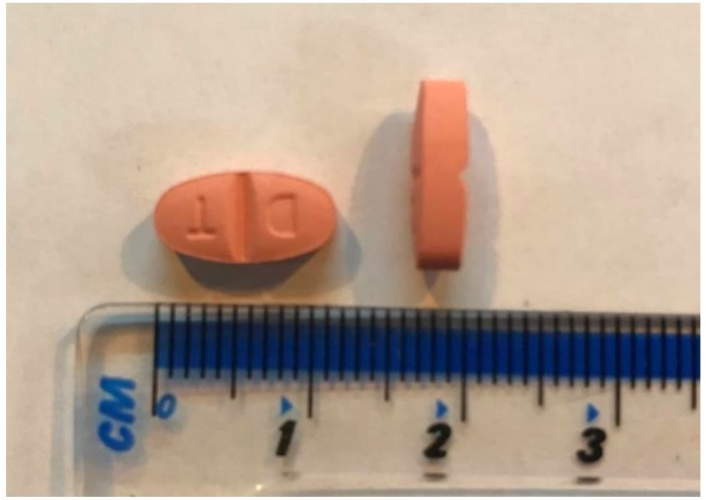
*Note: As soon as a child is developmentally **able to swallow tablets**, and is **above 25kg, they should switch to ABC/3TC 600/300mg** tablets once a day*

2030 NDP

DTG 10mg Dispersible

Suppliers	Dosage
Mylan MacLeods	10mg





Dispersible tablets:

- Dispersed in liquid and consumed
- Chewed and swallow
- Swallowed whole

	3.0-3.9kg		4.0-5.9kg		6.0-9.9kg		10.0-13.9kg		14.0-19.9kg		20.0-24.9kg	
	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
ABC/3TC 120/60mg dispersible tablet												
DTG 10mg dispersible tablet												
Or DTG 50mg film coated tablet				Cost: $4.50/pack of 90 tablets Anticipated annual cost for a 10 kg child is R1840/year Current annual cost (LPV/rtv) R7360/year								

Supply Update

Supplier: Mylan and MacLeods

- Mylan FDA t-approval November 2020. Second supplier approval expected Q1 2021.
- The CHAI estimated price is **~$4.50 per pack of 90 tablets*.**

CHAI new product introduction toolkit: https://www.newhivdrugs.org/

Courtesy of Caroline Middlecote (CHAI)

1

Add the correct number of DTG10 and ABC/3TC tablets to a clean, empty glass based on your child's weight. (See Dosing Table).

Weight	No. of DTG Daily Tablets	No. of ABC/3TC 120/60 mg Daily Tablets
3 to < 6 kg	0.5	1
6 to < 10 kg	1.5	1.5
10 to < 14 kg	2	2
14 to < 20 kg	2.5	2.5

2

Add 10-20 mL (2-4 teaspoons) of clean water into the glass and stir until the tablets dissolve. If the tablets do not dissolve completely (i.e., they lump together), stir and slowly add a small amount of extra water until the tablets fully dissolve.

3

Give the medicine to your child to drink. Make sure they drink all the medicine right away or within a maximum of 30 minutes.

4

If any medicine remains in the glass, add a little more water to the glass and give to your child. Repeat until no medicine remains in the glass.

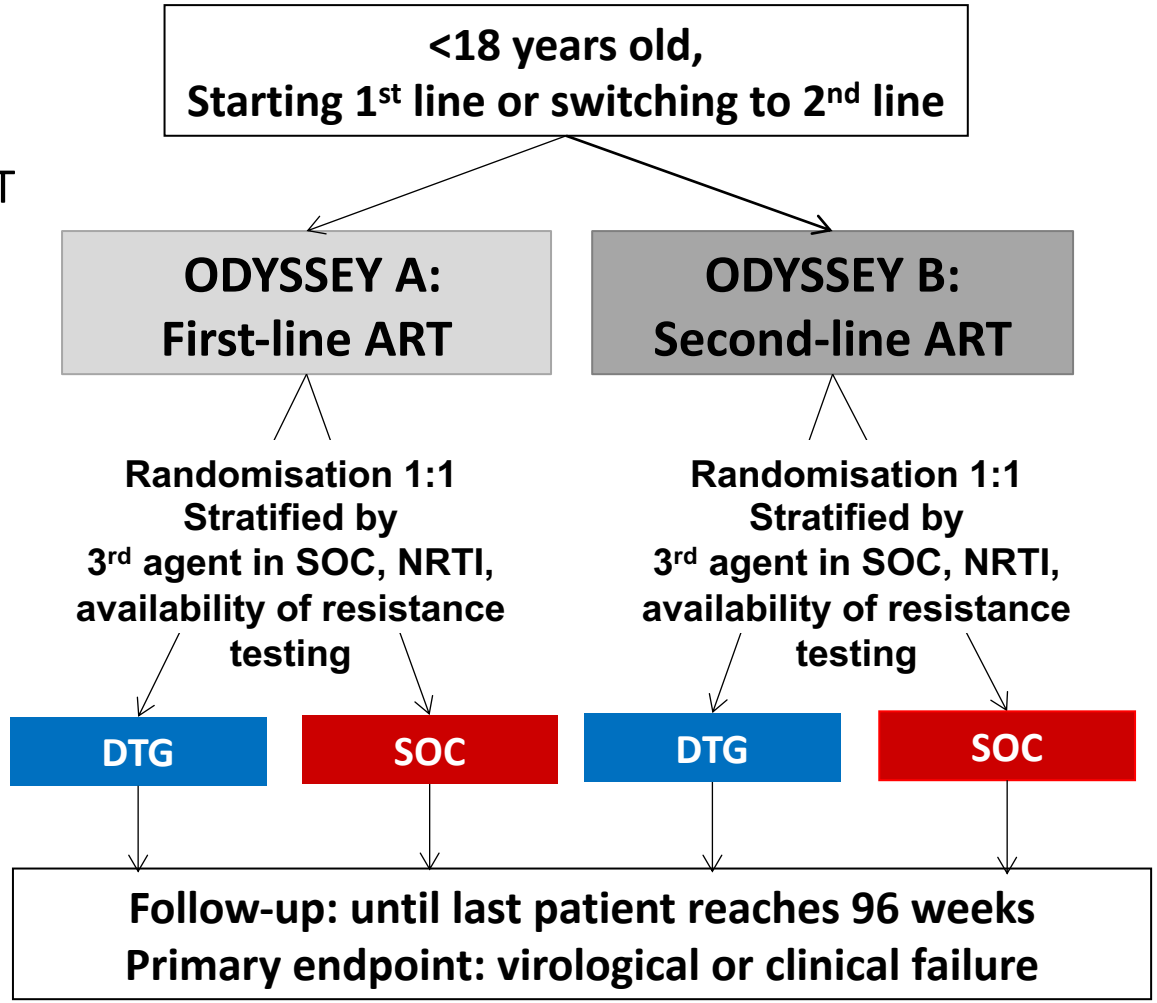
Reminders

- Remember to give Paediatric DTG 10 mg (and other ARVs) at the same time everyday.
- Use other liquids or foods for mixing if your child is unable to take the tablets in water. Follow the same volume recommendations as above to avoid spills and to ensure the child takes the full dose.
- Crushing, chewing, or mixing with other foods or liquids can be considered as long as the entire tablet is ingested.
- Give the child another full dose of Paediatric DTG 10 mg if they vomit within 30 minutes of taking their initial dose. If they vomit after 30 minutes, you do not need to give them another dose.

Weight (kg)	Abacavir (ABC)		Lamivudine (3TC)		Abacavir + Lamivudine (ABC + 3TC	Dolutegravir (DTG)	Dolutegravir when on rifampicin
Target dose	8 mg/kg **TWICE daily** **OR** ≥ 10 kg: 16 mg/kg **ONCE daily**		4 mg/kg **TWICE daily** **OR** ≥ 10 kg: 8 mg/kg **ONCE daily**		As for individual medications ONCE daily	By weight band **ONCE daily**	By weight band **TWICE daily**
Available formulations	Sol. 20 mg/mL Tabs 60 mg (scored, dispersible), 300 mg (not scored),		Sol. 10 mg/mL Tabs 150 mg (scored),		Dispersible tablets: 120/60 mg DT Tablet: 600/300 mg	Dispersible Tabs 10mg Tabs 50 mg (not scored) TDF/3TC/DTG 300/300/50 mg	Dispersible Tabs 10mg Tabs 50 mg
	Currently available tablet formulations of abacavir (except 60 mg), dolutegravir, LPV/r and AZT must be swallowed whole and **not** chewed, divided or crushed.						
	< 3 kg: See section 9.1.2: The HIV infected neonate (< 1 month of age).						
3–4.9	2 mL 12 hourly		2 mL 12 hourly		1 x 120/60 mg DT daily	0.5 X 10mg DT daily	0.5 X 10mg DT 12 hourly
5–5.9	3 mL 12 hourly		3 mL 12 hourly				
6-6.9					1.5 x 120/60 mg DT daily	1.5 x 10mg DT daily	1.5 x 10mg DT 12 hourly
7–9.9	4 mL 12 hourly		4 mL 12 hourly				
	Choose only one option:		Choose only one option:				
10–13.9	6 mL **OR** 2 x 60 mg tabs 12 hourly	12 mL **OR** 4 x 60 mg tabs daily	6 mL 12 hourly	12 mL daily	2 x 10mg DT daily	2 x 10mg DT daily	2 x 10mg DT 12 hourly
	Choose only one option.		Choose only one option.				
14–19.9	8 mL **OR** 2.5 x 60 mg tabs 12 hourly	1 x 300 mg tab **OR** 15 ml daily	8 mL **OR** ½ x 150 mg tab 12 hourly	15 mL **OR** 1 x 150 mg tab daily	2.5 x 120/60 mg DT daily	2.5 x 10mg DT daily	2.5 x 10mg DT 12 hourly
20–22.9	10 mL 12 hourly **OR** 3 x 60 mg tabs 12 hourly	1 x 300 mg tab + 1 x 60 mg tab daily	15 mL **OR** 1 x 150 mg tab 12 hourly	30 mL **OR** 1 x 300 mg tab **OR** 2 x 150 mg tabs daily	3 x 120/60 mg DT daily	50 mg tab daily	50 mg tab 12 hourly
23–24.9		1 x 300 mg tab + 2 x 60 mg tabs daily					
25–29.9	1 x 300 mg tab 12 hourly	2 x 300 mg tabs daily	1 x 150 mg tab 12 hourly	2 x 150 mg tabs daily **OR** 1 x 300 mg tab daily	1 x ABC/3TC 600/300 mg tab daily	50 mg tab daily **OR** 1 x TDF/3TC/DTG 300/300/50 mg tab daily	50 mg tab 12 hourly **OR** 1 x TDF/3TC/DTG 300/300/50 mg tab daily + 50 mg 12 hours after TLD dose
30–34.9							
35–39.9							
> 40							

ODYSSEY

- International multi-centre, randomised 96-week non-inferiority trial
- We aimed to compare **efficacy and safety** of DTG-based ART with standard-of-care in children and adolescents starting **first-line ART (ODYSSEY A)** or **second-line (ODYSSEY B)**
- **Main trial enrolled children ≥14 kg**
  - Aim to enrol ≥700 children: 310 ODYSSEY A, 390 ODYSSEY B
  - Powered for efficacy (total population and A&B separately)
  - Once enrolment in the main trial was completed, the trial was opened for 'under 14kg cohort'
- **'Under 14kg' cohort**
  - Aim to enrol ≥20 children in each of the three lower WHO weight bands: 3-<6kg, 6-<10kg and 10-<14kg
  - To confirm efficacy, safety and the most practical dosing
  - Proportions of first- and second-line not pre-specified
  - **Children in DTG arm did intensive PK**



Penta

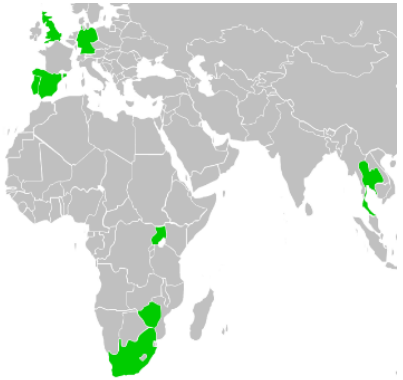
SOC= standard of care

Trial population

Main trial ≥14 kg, n=707

Baseline characteristics

- Median age 12.2 (range 2.9-18.0), 96% ≥6 years
- 49% female; 88% African
- 27% WHO stage 3/4
  22% CD4 <200 cells/mm^3
- **44% started first-line and**
  56% second-line (by design)



Baseline ART from randomisation

- NRTI: 65% ABC+3TC, 23% TDF+XTC, 11% ZDV+3TC
- Third agent in SOC: **first-line 92% EFV**;
  second-line 72% LPVr, 25% ATVr

Follow-up

- Median follow-up 142 weeks (IQR 124, 159)
- 37 (5%) lost to follow-up

<14kg, n=85

Baseline characteristics

- Median age 1.4 years (range 0.1, 5.9)
- All from Africa
- 34% WHO stage 3/4
  22% had CD4 <15%
- **85% started first-line ART**
  15% second-line ART

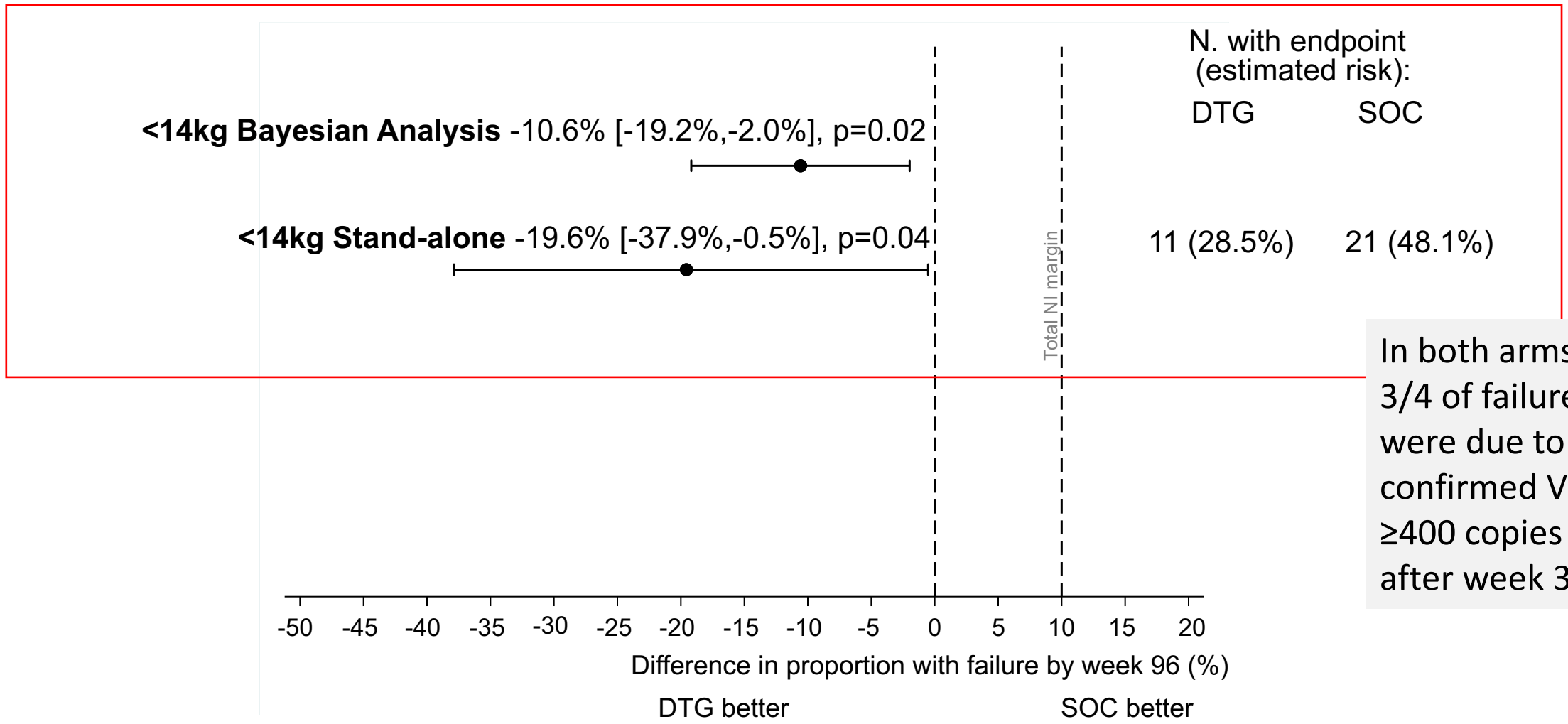
Baseline ART from randomisation

- NRTI mostly **88% ABC+3TC**; 12% ZDV+3TC
- Third agent in SOC **74% LPV/r**; 21% NNRTI,
  5% RAL

Follow-up

- Median follow-up 120 weeks (IQR 97, 132)
- 5 (6%) lost to follow-up

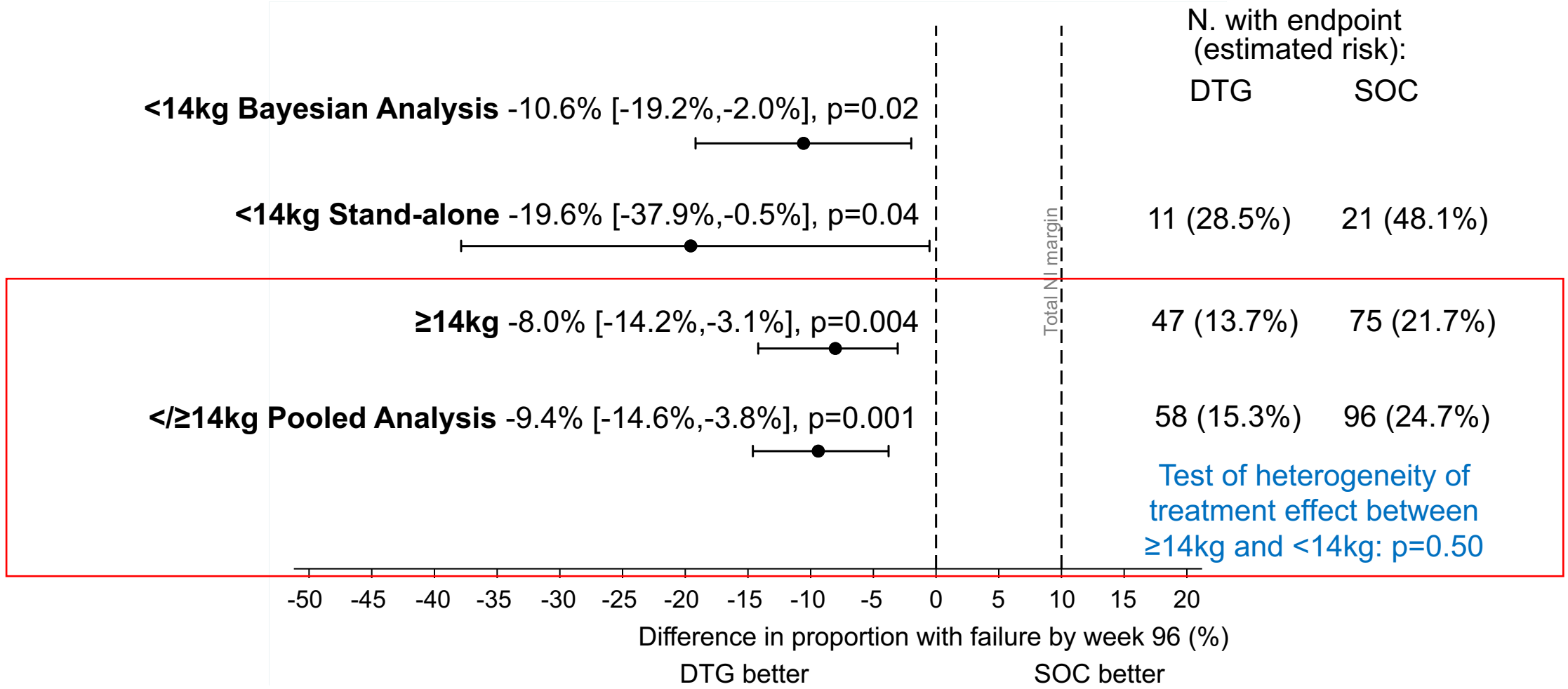
Primary outcome (children <14kg): virological or clinical failure by 96 weeks



In both arms, 3/4 of failures were due to confirmed VL ≥400 copies after week 36

SOC= standard of care

Primary outcome (children <14kg and ≥14kg): virological or clinical failure by 96 weeks



Penta

SOC= standard of care

Infant and Child (4 weeks/3kgs and above)

- **Alternative Options:**
- Abacavir/Lamivudine (120/60mg DT) + LPV/r (Syrup/Pellets/Paediatric Tablet)
- TAF/Emtricitabine (25/200mg) + DTG (50mg) – over 20kgs
- Abacavir/Lamivudine/Lopinavir/ritonavir (FDC granules 30/15/40/10mg)

Infant and Child (4 weeks/3kgs and above)

- **Alternative Options (Global):**
- Abacavir/Lamivudine/Dolutegravir (FDC 60/30/5mg DT)

Pediatric Population Body Weight	Number of Tablets (once daily)	Recommended Daily Dose
	TRIUMEQ PD Tablets (10 kg to <25 kg)	
10 kg to <14 kg	4	240 mg ABC, 20 mg DTG, and 120 mg 3TC
14 kg to <20 kg	5	300 mg ABC, 25 mg DTG, and 150 mg 3TC
20 kg to <25 kg	6	360 mg ABC, 30 mg DTG, and 180 mg 3TC
	TRIUMEQ Tablets (≥25 kg)	
≥25 kg	1	600 mg ABC, 50 mg DTG, and 300 mg 3TC

ABC = abacavir, DTG = dolutegravir, 3TC = lamivudine.

- TAF/Emtricitabine/Bictegravir (FDC 15/120/30mg - 14 – 25kgs)

Infant and Child (4 weeks/3kgs and above)

- **On the Horizon:**
- CAB/RPV LA injectable (>2 yrs and > 10Kgs) – given every 1- 2 months being studied in the CRAYON study – Stable switch in virally suppressed adolescents without prior evidence NNRTI or INSTi resistance)

- TAF/Emtricitabine/Bictegravir (FDC 15/120/30mg) and TAF/Emtricitabine (FDC)

Full-term Neonate (37 – 42 wks at Birth)

- **Recommended options**
- Zidovudine/Lamivudine/Nevirapine (Individual syrups – from D0)
- Abacavir/Lamivudine/Lopinavir/ritonavir (Individual syrups – from D14)

	Lamivudine (3TC)		Abacavir (ABC)		Lopinavir/ritonavir (LPV/rtv)	
Target dose	2 mg/kg/dose TWICE daily		8 mg/kg/dose TWICE daily		300/75 mg/m^2/dose TWICE daily	
Available formulation	10 mg/mL		20 mg/mL		80/20 mg/mL	
Weight (kg)	**Dose in mL**	**Dose in mg**	**Dose in mL**	**Dose in mg**	**Dose in mL**	**Dose in mg**
≥ 3.0–< 4.0	0.8 mL 12 hourly	8 mg 12 hourly	0.5 mL 12 hourly	14 mg 12 hourly	0.8 mL 12 hourly	64/16 mg 12 hourly
≥ 4.0–< 5.0	1 mL 12 hourly	10 mg 12 hourly	0.6 mL 12 hourly	12 mg 12 hourly	1 mL 12 hourly	80/20 mg 12 hourly

Full-term Neonate (0– 4 weeks)

Alternative options

- Abacavir/Lamivudine (Individual syrups from Birth)
- Raltegravir granules – from D0/>2kgs)

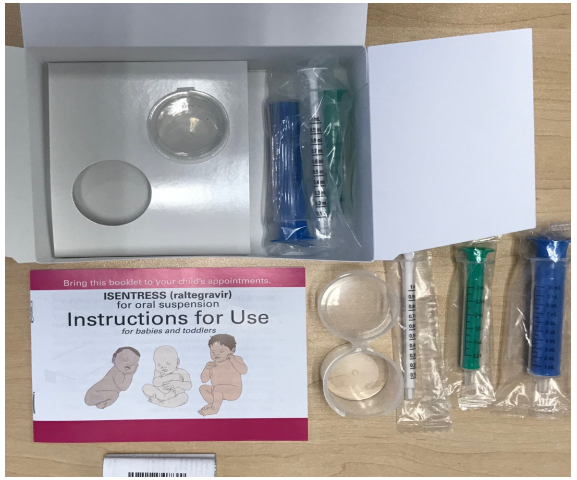


Table A1.4 Drug dosing of liquid formulations for infants younger than four weeks of age[a]

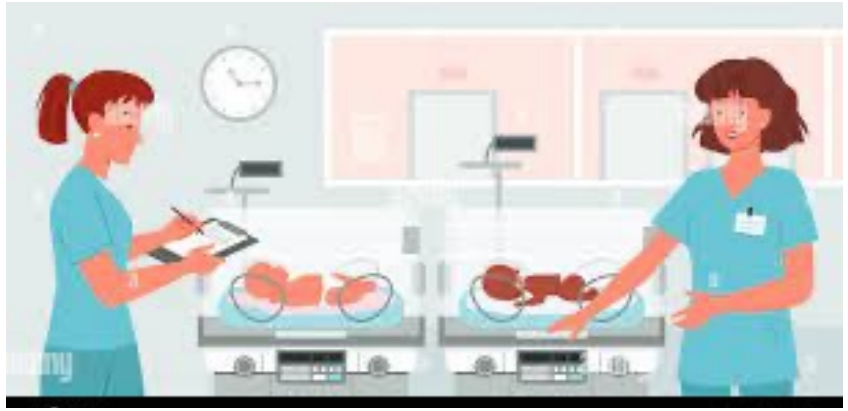
Drug	Strength of oral solution		2–<3 kg		3–<4 kg		4–<5 kg	
			AM	PM	AM	PM	AM	PM
AZT	10 mg/mL		1 mL	1 mL	1.5 mL	1.5 mL	2 mL	2 mL
ABC	20 mg/mL		0.4 mL	0.4 mL	0.5 mL	0.5 mL	0.6 mL	0.6 mL
NVP	10 mg/mL		1.5 mL	1.5 mL	2 mL	2 mL	3 mL	3 mL
3TC	10 mg/mL		0.5 mL	0.5 mL	0.8 mL	0.8 mL	1 mL	1 mL
LPV/r[b]	80 mg/20 mg/mL		0.6 mL	0.6 mL	0.8 mL	0.8 mL	1 mL	1 mL
	Granules 40 mg/10 mg sachet		–	–	2	2	2	2
RAL	10 mg/mL (Oral granules for suspension: 100 mg/ sachet)[c]	<1 week	0.4 mL (once daily)[c]		0.5 mL (once daily)[c]		0.7 mL (once daily)[c]	
		>1 week	0.8 mL	0.8 mL	1 mL	1 mL	1.5 mL	1.5 mL

Full-term Neonate (37 – 42 wks at Birth)

- **On the Horizon**
- Abacavir/Lamivudine (DT 60/30mg - from D0) – PETITE study
- Lopinavir/ritonavir (Granules – from D0) – PETITE study
- Dolutegravir (DT or syrup) – IMPAACT 2040 / PETITE study

Pre-term Neonate (<37wks at Birth)

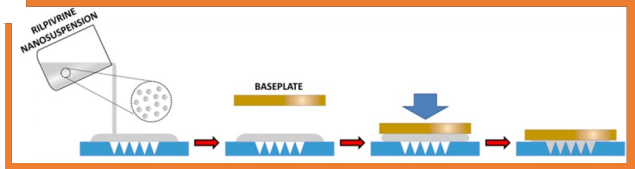
- **Recommended options**
- Zidovudine/Lamivudine/Nevirapine (Individual syrups – from D0)

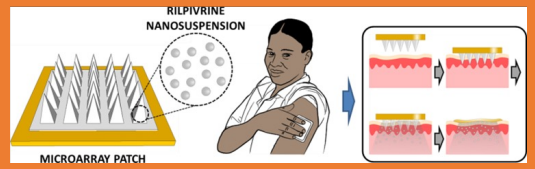


ARV drug dosing chart:
For preterm infants < 42 weeks corrected gestational age

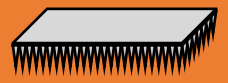
Drugs	Lamivudine (3TC)		Zidovudine (AZT)		Nevirapine (NVP)	
< 30 weeks	2 mg/kg twice daily		2 mg/kg twice daily		2 mg/kg twice daily	
30–35 weeks	2 mg/kg twice daily		Day 0–14	2 mg/kg twice daily	2 mg/kg twice daily	
			Day > 14	3 mg/kg twice daily		
> 35 weeks	2–< 3 kg	0.5 mL twice daily	2–< 3 kg	1 mL twice daily	Day 0–14	4 mg/kg twice daily
	3–< 4 kg	0.8 mL twice daily	3–< 4 kg	1.5 mL twice daily	Day > 14	6 mg/kg twice daily
			4–< 5 kg	2 mL twice daily		

Long-term Landscape





Microarray / microneedle patch (theoretical)

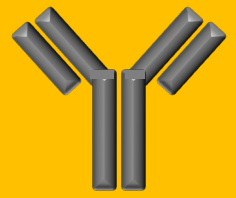


Long-acting formulations

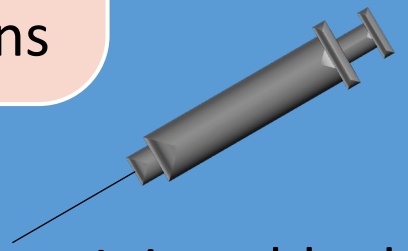
- Islatravir
- Lencapavir

Achieve further simplification of ART regimens through novel delivery mechanisms or long-acting formulations

Broadly neutralizing monoclonal antibodies



- VRCO1
- VRC7-523LS
- CAP256V2LS



Injectable drug

- Cabotegravir/ Rilpivirine LA

McCrudden et al, 2018

McFarland et al, 2017

Conclusion

- Major advances in simplifying child-friendly treatment options for ART across the paediatric age spectrum

- Young children (esp Premature neonates) have the least number of treatment options – need innovative research strategies to close the gap esp wash-out studies

- The priority is to translate improved access to child-friendly ART regimens to tangible improvements in achieving the 95:95:95 targets