Virological Outcomes, Safety and Acceptability of LPV/r Pellets-Based ART in Young Children: 48-Week Interim Analysis of the LIVING Study.

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Background

- There are limited options for first line ARVs in infants and young children.
- The current tablet and syrup formulations of LPV/r are not suitable for use for very young children and their caregivers.
- DND*i* has worked with CIPLA to develop a new pellet formulation of LPV/r which is palatable, heat-stable, taste-masked and easy-to-administer.

Pic 1:LPV/r Pellets (DND*i* 2016)

- The pellets formulation has been approved for use in infants and young children. However, there is limited clinical data on its effectiveness and safety in routine care.

Study Objectives

The LIVING study aims to evaluate the effectiveness, safety, PK and acceptability of LPV/r pellets + standard NRTIs in HIV+ children unable to swallow tablets.

Methods

Inclusion criteria

- HIV infected children
- ARV naïve, or already on first line liquid lopinavir-based treatment, or failing first line, NNRTI based therapy
- weight ≥3 and <25 kg at the time of enrolment (age is not an inclusion criterion)
- Unable to swallow tablets

Exclusion criteria

- Treatment failure with the presence or strong suspicion of a PI resistance mutation
- Current treatment with a drug that interacts significantly with LPV/r
- Clinically significant disease in the investigator's opinion, which would compromise participation in the study
- Treatment with experimental drugs for any indication within 30 days prior to study entry
- Anticipated transfer to non study treatment site.

Study Design

- Single-arm phase IIIb implementation study
- open-label
- prospective
- non-randomized
- non-comparative
- multicentre, multi-country

- Dosing of LPV/r pellets followed WHO weight bands
- Observation of pellets administration performed at clinic
- Enrolment completed across 12 sites in Kenya, Uganda and Tanzania

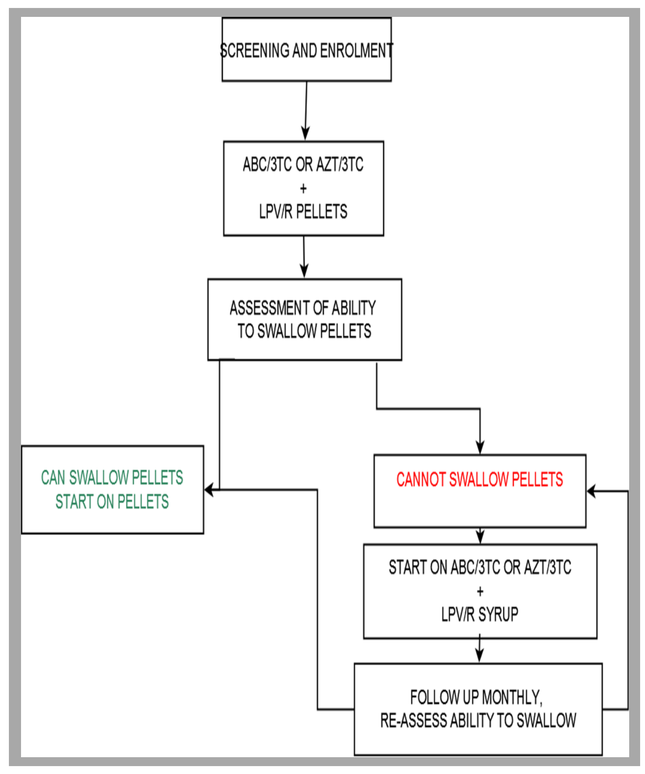

Fig 1: patient flow

Results

1. Patient disposition

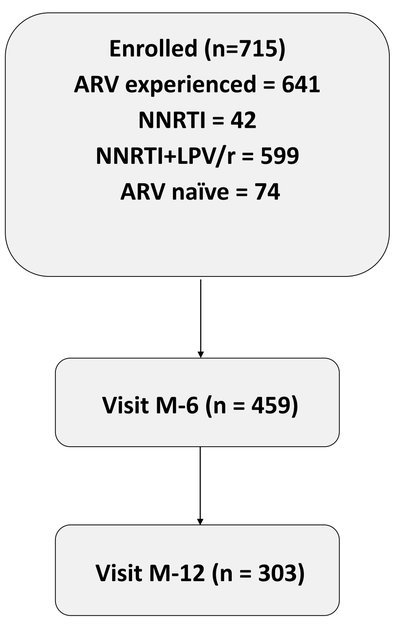

Fig 2: patient disposition

Complete VL results available for n=266, data as of 31/10/2017

Table 1: baseline characteristics

	n	%
Sex		
Male	130	48.9
Female	136	51.1
Treatment exposure		
ART naïve	25	9.4
Lopinavir	229	86.1
NNRTI	12	4.5

2. Baseline characteristics

	ART naive			NNRTI+LPV/rr			NNRTI			Total		
	median	95% CI		median	95% CI		median	95% CI		median	95% CI	
ART duration (mths)	0.0	0.0	0.0	26.8	10.6	45.8	32.6	14.2	39.5	27.1	11.4	45.7
Age (mths)	20.0	11.0	38.0	44.0	28.0	63.0	52.5	43.5	62.5	43.0	25.0	62.0
Weight (kg)	9.0	6.2	11.7	14.0	11.0	16.0	14.8	11.6	16.8	13.8	10.7	16.0
VL log10 copies/ml	5.5	4.9	5.7	2.0	1.6	3.8	4.6	3.5	5.1	2.4	1.6	4.6

Table 2: baseline characteristics

3. Virological outcome

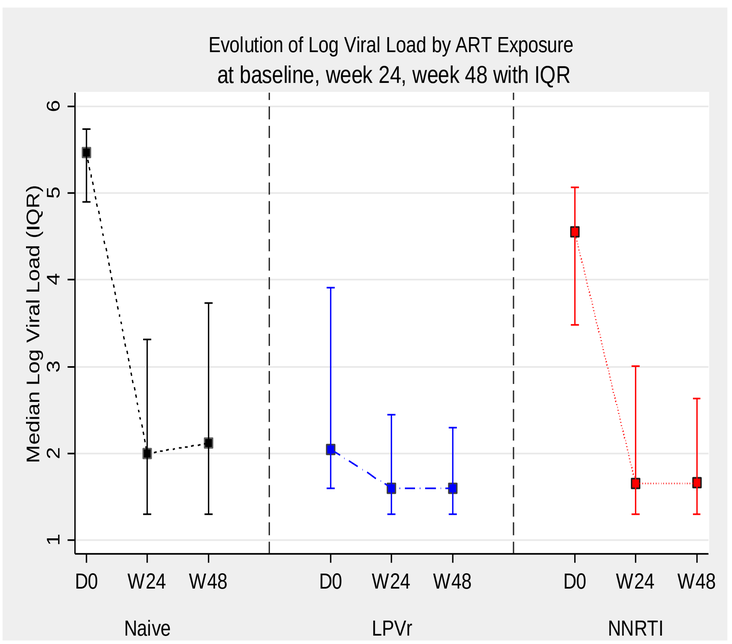

Fig 3: Median log VL at baseline, M6 and M12 stratified by prior ART exposure

		n	Median Log 10 cp/ml	IQR		≤50 copies	≤*400 cp/ml	≤'1000 cp/ml	>1000 cp/ml
Baseline	ART naïve	25	5.5	4.9	5.7	1(4.0%)	1(4.0%)	1(4.0%)	24(96.0%)
	NNRTI+Lopinavir	229	2.0	1.6	3.9	77(33.6%)	138 (60.3%)	153 (66.8%)	76(33.2%)
	NNRTI	12	4.6	3.5	5.1	1(8.3%)	2 (16.7%)	2(16.7%)	10(83.3%)
	Overall	**266**	**2.4**	**1.6**	**4.7**	**79(29.7%)**	**141(53.0%)**	**156(58.7%)**	**110(41.4%)**
Month 6	ART naïve	25	2.0	1.3	3.3	9(36.0%)	15(60.0%)	16(64.0%)	9(36.0%)
	NNRTI+Lopinavir	229	1.6	1.3	2.4	121(52.8%)	177(77.3%)	186(81.2%)	43(18.8%)
	NNRTI	12	1.7	1.3	3.0	6(50.0%)	8(66.7%)	9(75.0%)	3(25.0%)
	Overall	**266**	**1.7**	**1.3**	**2.6**	**136(51.1%)**	**200(75.2%)**	**211(79.3%)**	**55(20.7%)**
Month 12	ART naïve	25	2.1	1.3	3.7	12(48.0%)	16(64.0%)	17(68.0%)	8(32.0%)
	NNRTI+Lopinavir	229	1.6	1.3	2.3	127(55.5%)	182(79.5%)	187(81.7%)	42(18.3%)
	NNRTI	12	1.7	1.3	2.6	6(50.0%)	9(75.0%)	10(83.3%)	2(16.7%)
	Overall	**266**	**1.6**	**1.3**	**2.5**	**145(54.5%)**	**207(77.8%)**	**214(80.5)**	**52(19.6%)**

Table 3: viral suppression

* Includes patients<50 cp/ml, ' includes <50 and <400 cp/ml

4. Ease of administration of pellets

Response from caregiver	Month 3, n=548*	Month 6, n=454*	Month 12, n=297*
Very easy, n (%)	246 (44.9%)	216 (47.6%)	154 (51.9%)
Easy, n (%)	194 (35.4%)	149 (32.8%)	94 (31.6%)
Average, n (%)	63 (11.5%)	48 (10.6%)	29 (9.8%)
Difficult, n (%)	21 (3.8%)	24 (5.3%)	11 (3.7%)
Most difficult, n (%)	5 (0.9%)	4 (0.9%)	0%
Pending, n (%)	19 (3.5%)	13 (2.9%)	9 (3%)

Table 4: acceptability

* Acceptability questionnaires administered to mothers at scheduled study visits

5. Adverse events

- 36 children had 74 grade 3/4 AEs.
- 2 AEs led to treatment discontinuation.

Conclusion

Naïve children failing NVP, as well as those switching from LPV/r syrup were well suppressed at week 48. LPV/r pellets were well accepted with minimal safety concerns.

Acknowledgements

This project has been made possible thanks to the support of Unitaid, the French Development Agency (AFD), and Médecins Sans Frontières. We also acknowledge here all study participants, site teams, DND*i* staff, and partners.