

**Anti-retroviral therapy (ART) outcomes in
children < 13 years of age in resource-limited
countries (RLCs):
a Médecins Sans Frontières (MSF) cohort**

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Some Challenges Facing Children

■ Prevention

- Limited maternal/child access to PMTCT interventions
- Breast-feeding risks and benefits



Challenges Facing Children (2)

- Access to diagnosis, particularly for infants < 18 months
- Identifying and maintaining medical follow-up for “at risk” children



Challenges Facing Children (3)

- Appropriate array of anti-retrovirals in pediatric formulations, adapted to the growing child, and adherence-friendly, at fair cost

HIV - DRUG DOSES expressed in BODY WEIGHT									
Drug	Product	Name	Strength	5-9 kg	10-14 kg	15-19 kg	20-24 kg	25-29 kg	30-39 kg
Co-trimoxazole Prophylaxis									
TMP-SMX	Cotrimoxazole	Bactrim	TMP 80/SMX 400mg	1/2 tab OD	1 tab OD	1 tab OD	1 tab OD	2 tab OD	2 tab OD
			TMP 40mg/5mL	5 mL OD	10 mL OD	15 mL OD	15 mL OD		
Fluconazole Prophylaxis									
Primary	Fluconazole	Diflucan	50, 100, 200mg caps		50mg OD	100mg OD	100mg OD	100mg OD	400mg/week
Secondary	Fluconazole		50, 100, 200mg caps		50mg OD	100mg OD	100mg OD	100mg OD	150mg OD
NRTI (Nucleoside analogues)									
AZT	Zidovudine (ZDV)	Retrovir	100mg caps			1 caps TID	1 caps TID	2 caps BID	
			250mg caps					1 caps BID	1 caps BID
			300mg tab						
			10mg/mL	7.5 mL BID	12.5 mL BID	17.5 mL BID			
3TC	Lamivudine	Epivir	150mg tab		1/2 tab BID	1/2 tab BID	1 tab BID	1 tab BID	1 tab BID
			10mg/mL	2.5 mL BID	5 mL BID	7.5 mL BID	10 mL BID	12.5 mL BID	
AZT + 3TC		Combivir	300+150mg tab						
ddI	Didanosine	Videx (caps) Videx EC (tab)	25 mg tab	1 tab OD +					
			50 mg tab	1 tab OD					
			100 mg tab						
			125 mg caps		1 caps OD				
			150 mg tab			1 tablet OD			
			200 mg tab / caps				1 tab/caps OD	1 tab/caps OD	
			250 mg caps						1 caps OD
			400 mg caps						
d4T	Stavudine	Zerit	15mg caps			1 caps BID			
			20mg caps				1 caps BID		
			30mg caps					1 caps BID	
			40mg caps						1 caps BID
			1mg/mL	7.5 mL BID	12.5 mL BID	17.5 mL BID			
ABC	Abacavir	Ziagen	300mg tab		1/2 tab BID	1/2 tab BID	1 tab BID	1 tab BID	1 tab BID
			20mg/mL	2.5 mL BID	5 mL BID	7.5 mL BID	10 mL BID	12.5 mL BID	
NNRTI (Non-nucleoside Reverse Transcriptase inhibitors)									
NVP	Nevirapine	Viramune	200mg tab		1/2 tab BID	1/2 tab BID	1 tab BID	1 tab BID	1 tab BID
			10mg/mL	7.5 mL BID	10 mL BID	15 mL BID	17.5 mL BID		
EFV	Efavirenz	Stocrin	50mg caps			1 caps OD +	2 caps OD +	3 caps OD +	
			200mg caps			1 caps OD	1 caps OD	1 caps OD	2 caps OD
PI (Protease inhibitors)									
RTV	Ritonavir	Norvir	100mg caps		2 caps BID	3 caps BID	3 caps BID	4 caps BID	4 caps BID
			80mg/mL	2 mL BID	2.5 mL BID	3.5 mL BID	4 mL BID	5 mL BID	5 mL BID
IDV	Indinavir	Crixivan	200mg caps		1 caps BID		1 caps BID +	1 caps BID +	2 caps BID
			400mg caps		1 caps BID	1 caps BID	1 caps BID	1 caps BID	2 caps BID
NFV	Nelfinavir	Viracept	250mg tab		2 tab BID	3 tab BID	4 tab BID	5 tab BID	5 tab BID
SQV SGC	Saquinavir	Fortovase	200mg SGC		2 caps TID	3 caps TID	4 caps TID	5 caps TID	6 caps TID
Booster RTV + SQV			100mg caps RTV + 200mg SGC/HGC						
Booster RTV + SQV			100mg caps RTV + 200mg SGC						
Booster RTV + IDV			100mg RTV						
			400mg caps IDV						

MSF Pediatric Cohort

- FUCHIA (Follow Up Care of HIV-AIDS, *Epicentre*) database analysis as of May 2006
- Children < 13 years old
- 28 projects in 14 countries with at least 25 children under ART
 - Africa: 85% of individuals in cohort
 - Asia: 13%
 - Latin America: 1%

MSF ART Program

- WHO guidelines for initiating ART, via clinical and/or immunologic staging
- Adherence counseling
 - Parent or guardian at initiation and monthly
- Nutritional support for acute/chronic malnutrition determined by weight-height deviations (Z-score)

Cohort Anti-retroviral Regimens

- 99% received combination of:
 - Stavudine or zidovudine
 - Lamivudine
 - Nevirapine or efavirenz
- Formulations:
 - Syrups
 - Scored adult triple fixed-dose combination
 - Pediatric dose tablets (i.e., AZT 100mg)

Baseline Characteristics: Epidemiology

N° in cohort	3,754
Female (%)	1,765 (47.2)
Median age [IQR]	5.7 [3.2-8.4]
Age distribution (%)	
0-17 months	4.7
18-35 months	16.2
36-59 months	20.8
≥ 60 months	58.4

Baseline Characteristics: Clinical

Weight to height Z-score **n: 1,728**

WHZ < -3 **4.3 %**

-3 ≤ WHZ < -2 **11.5 %**

CDC clinical stage (%) **n: 3465**

N **6.5**

A **13.5**

B **36.7**

C **43.4**

Baseline Characteristics: Immunological

Age < 60 months	n: 887 (57%)
Median CD4% [IQR]	11 [7.0 - 14.9]
Percentage < 15%	75.3
15-24%	20.0
≥ 25%	4.7
Age 5-12 years	n: 1174 (54%)
Median absolute CD4 [IQR]	208 (73 - 364)
Percentage < 50	20.6
50-199	27.7
200-499	38.8
≥ 500	12.9

ART History

ARV naïve, n (%)	3,641 (97.0)
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Follow-up time on ART	
Median, m [IQR]	10.0 [3.9-17.6]
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Distribution (%)	
< 6 months	34.1
6-12 months	23.3
12-24 months	32.4
24-36 months	8.9
≥ 36 months	1.2

Global Treatment Outcomes

n: 3,754

Followed, on ART (%)	80.4
Death (%)	6.6
Median time on ART before death, <i>m</i> [IQR]	2.2 [0.9-5.9]
Lost to follow-up > 2 months (%)	7.2
Median time on ART before lost, <i>m</i> [IQR]	3.9 [0.9-9.0]
Transferred (%)	3.9
Unknown (%)	0.8

Treatment Outcomes (2)

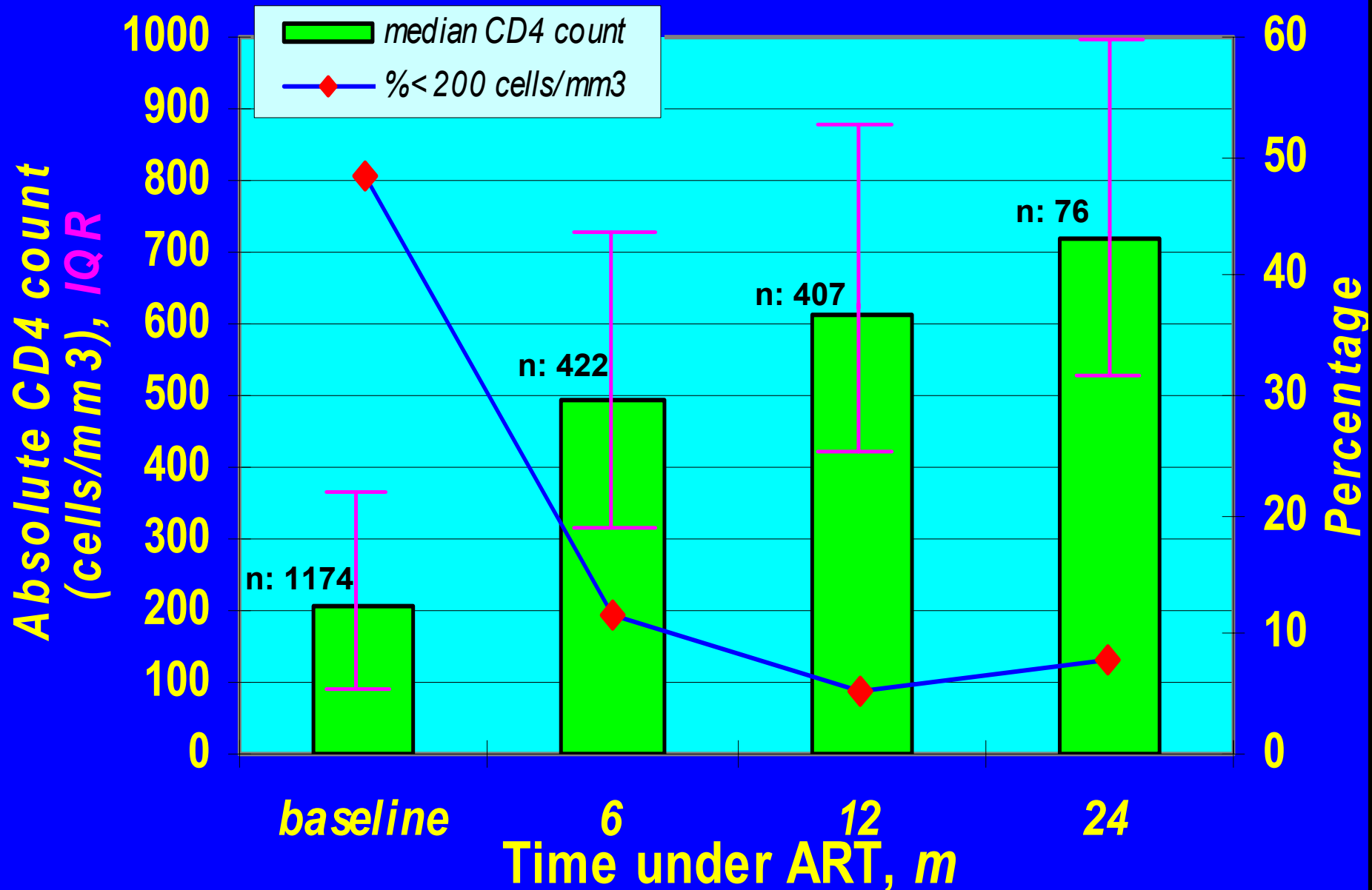
■ Tolerance:

- 3.5% (132 / 3754) had at least one drug stopped due to side effects
- Median time to stop (months, IQR): 1.3 [0.7-5.4]
 - NVP: 66%, 0.9 m [0.5-4.7]
 - d4T: 20%, 2.0 m [0.9-11.5]
 - AZT: 14%, 3.2 m [0.7-6.4]

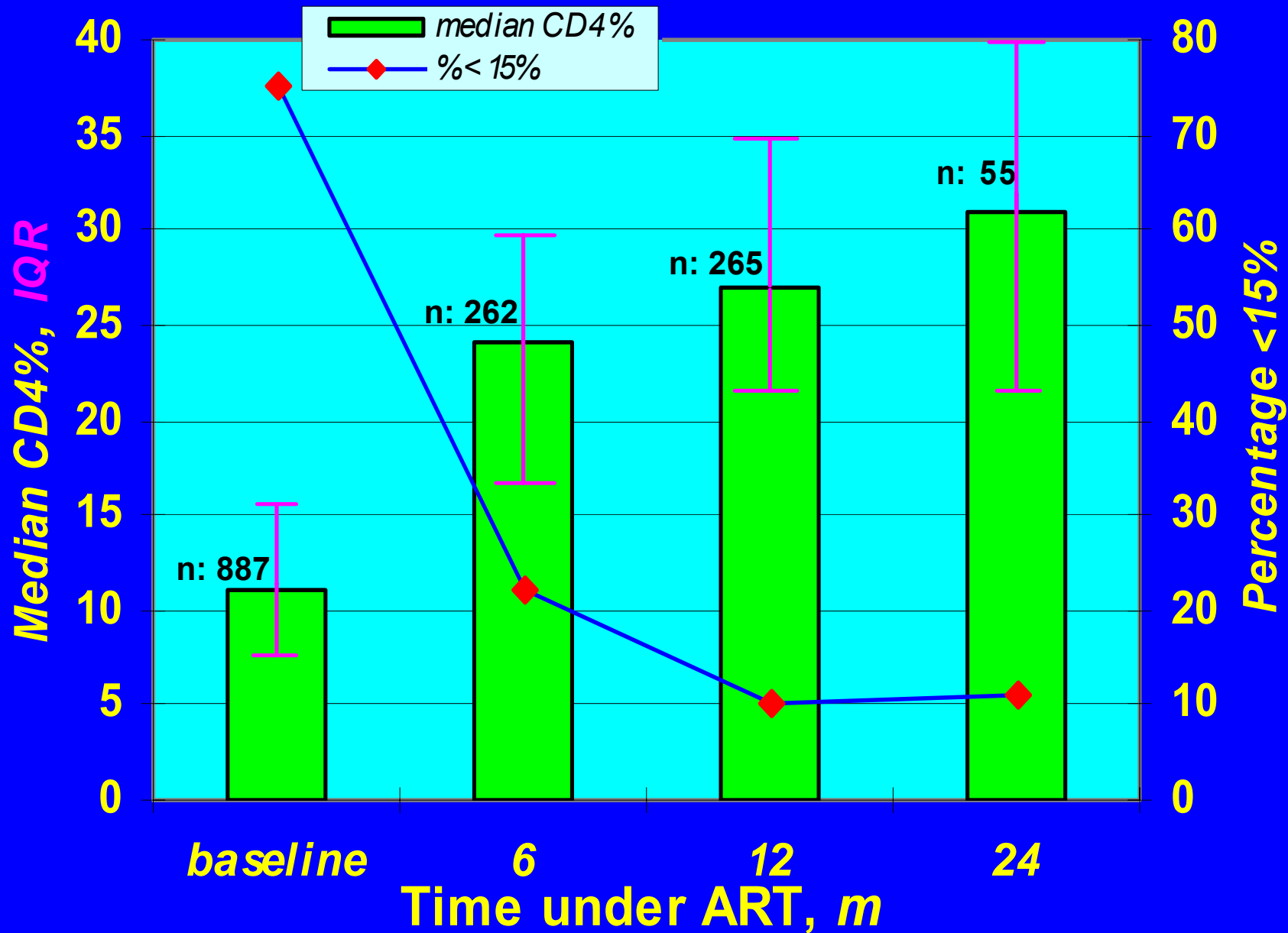
■ Second Line

- Only 5 patients (0.13%) reported to have switched
- Median time to switch (months, IQR) 16.3 [13.7-18.6]

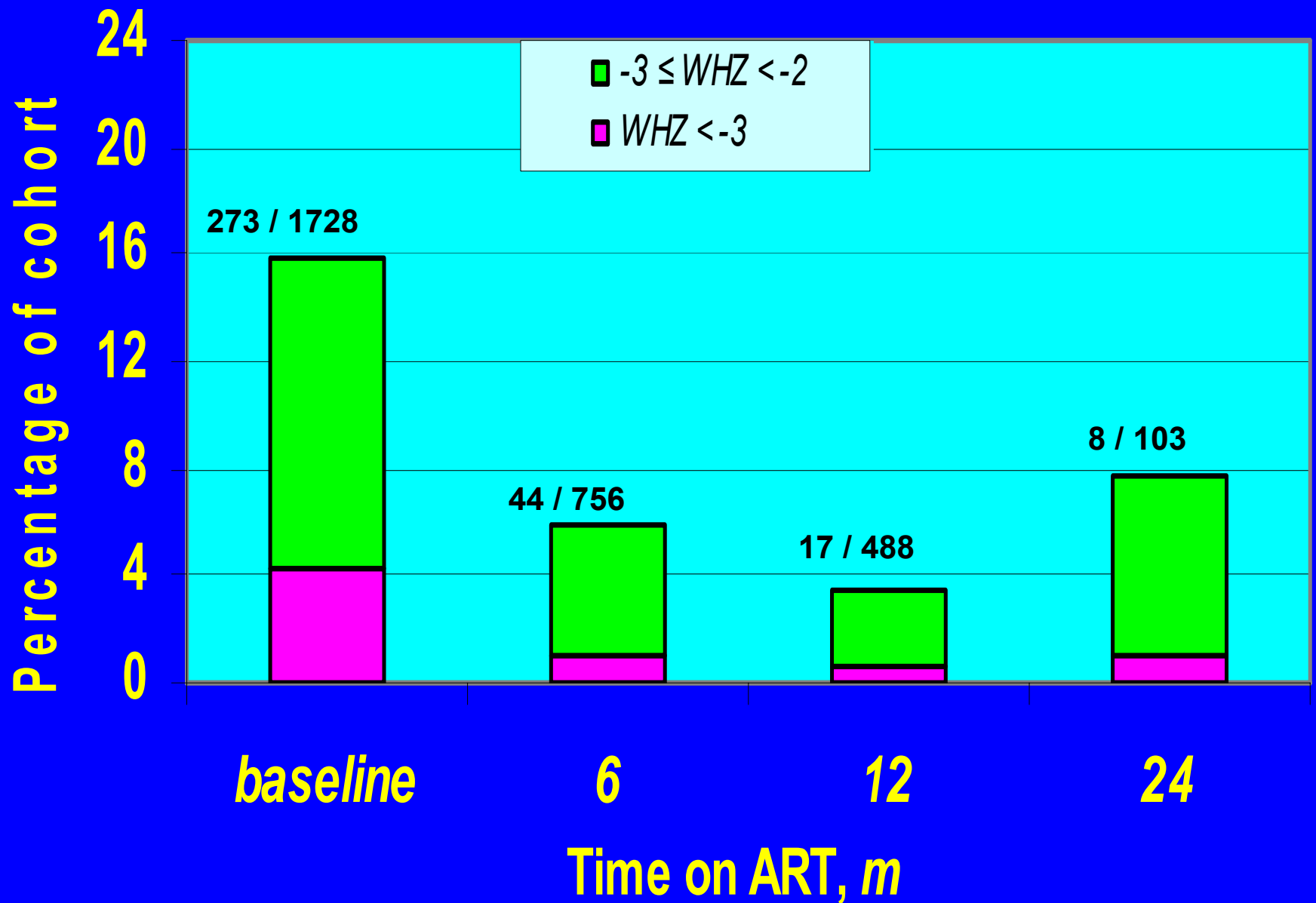
CD4 Evolution: Children 5-13 years



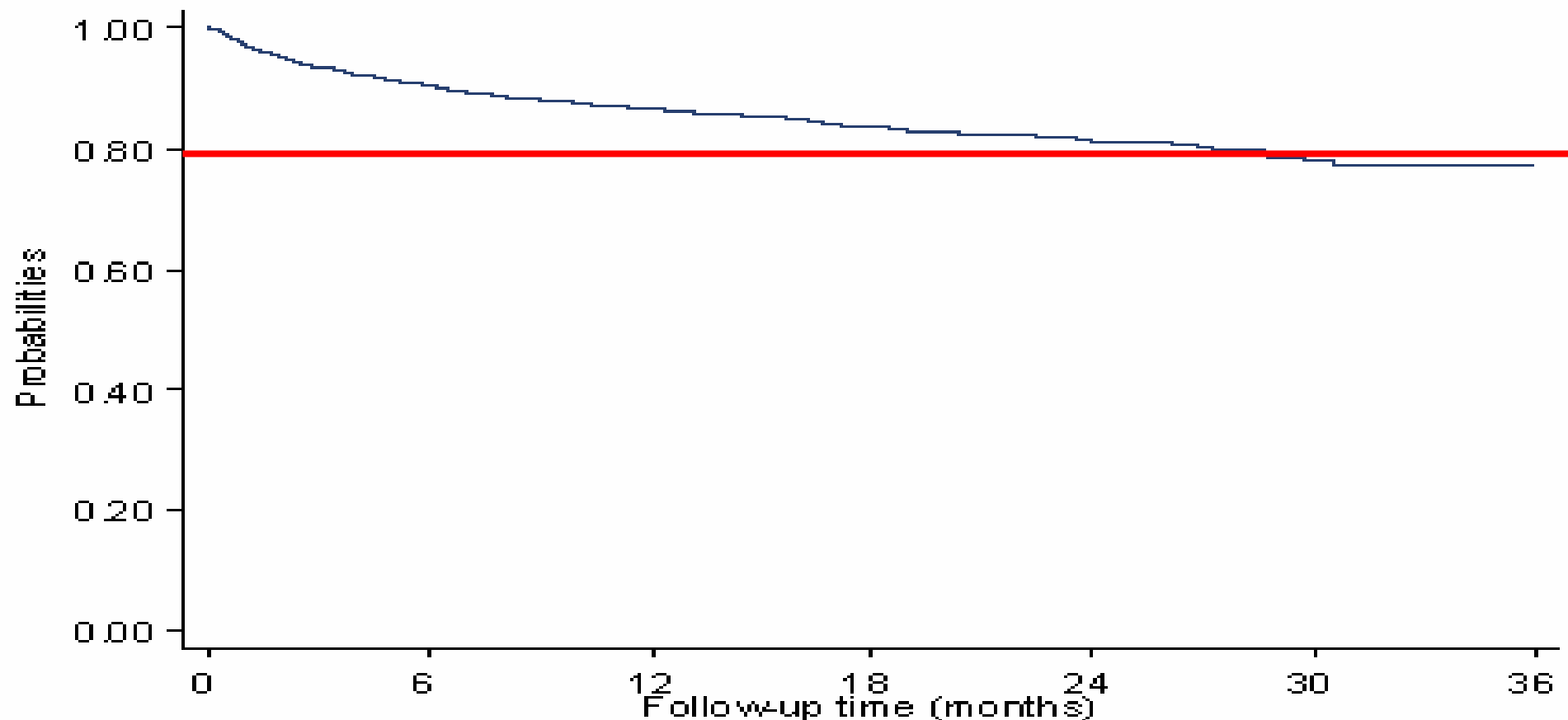
CD4% Evolution: Children < 60 months old



Evolution of Weight-Height Z-score

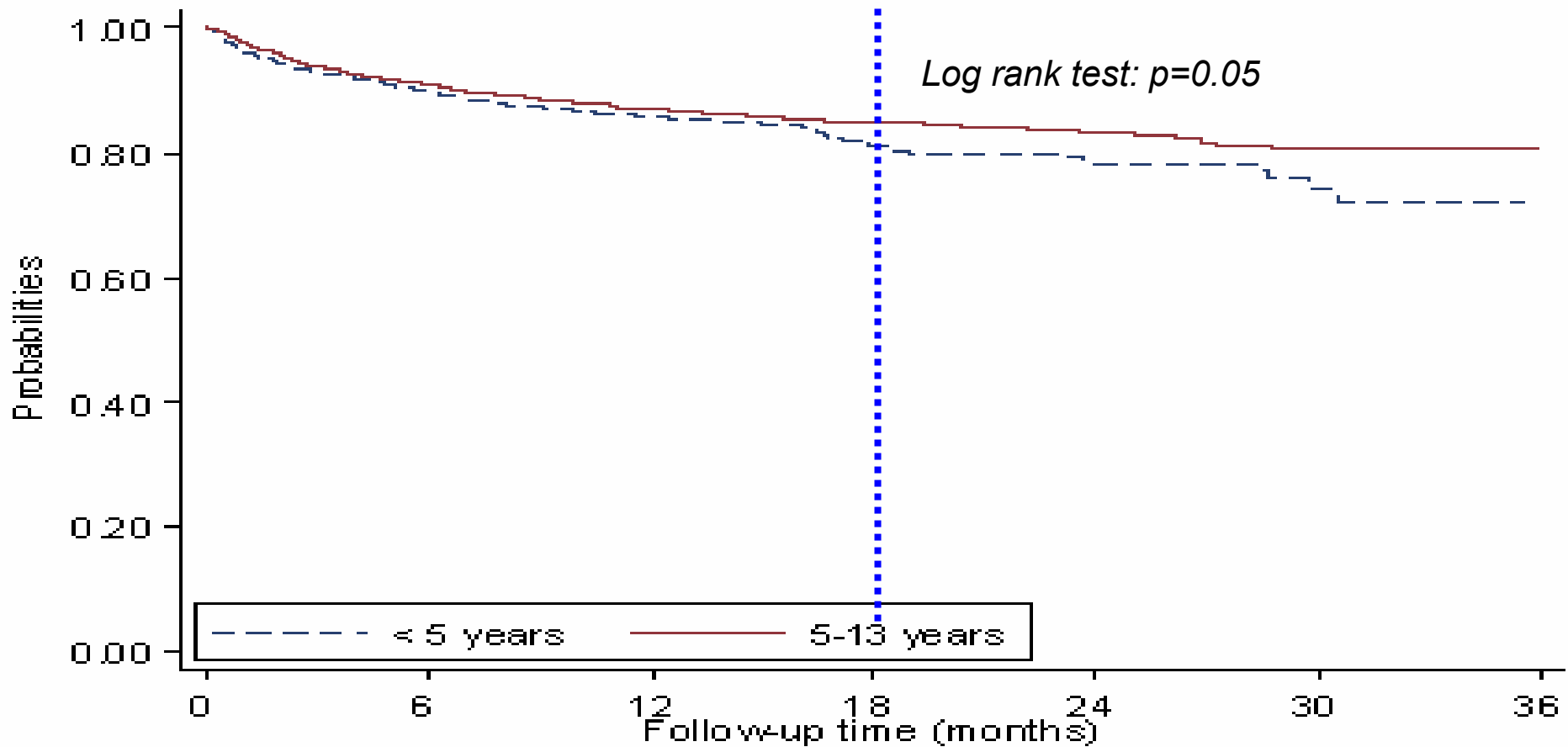


Probability of success of ART: (failure: death + lost to f/u)



<i>N° at risk</i>	2499	1604	382	47
<i>Probability</i>	0.90	0.87	0.81	0.77
<i>95% CI</i>	0.89-0.91	0.85-0.88	0.79-0.83	0.74-0.80

Probability of success of ART: by age at ART initiation



N° at risk:

< 5 years

975

627

136

25

5-13 years

1524

977

246

22

Conclusions (1)

- NNRTI-based HAART can be administered to children over a wide array of settings in RLCs
- More than 80% of children are alive and continuing therapy after 24 months in this multi-centric cohort
- As with adults, the majority of mortality is seen within the first 6 months under ART

Conclusions (2)

- Survival is accompanied by a marked gain in CD4 counts at least through 24 months
- After 18 months of ART, a smaller (but significant) proportion of children under 60 months of age remain on treatment
- Prevalence of malnutrition may be reduced when enrolled in an ART program (drug and nutritional support effects)

Study Limitations

- Retrospective cohort multi-centric analysis
- Relatively short median follow-up time (< 1 year)
- No viral load data
- Under-representation of infants < 18 months

Thank You!

- Children and parents represented in this cohort
- All MSF staff in HIV treatment programs
- *Epicentre*
- Members of the MSF AIDS Working Group

