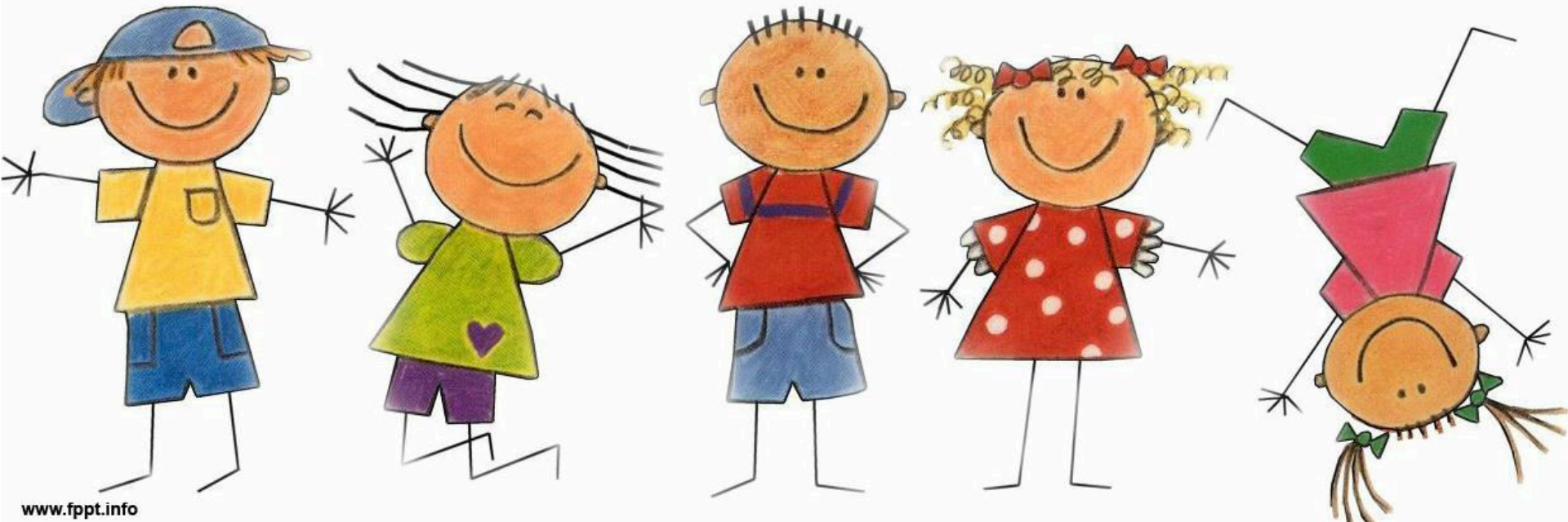


Cases of ART failure in children

Dr M Lawler

Paediatric Infectious Disease unit

King Edward VIII hospital

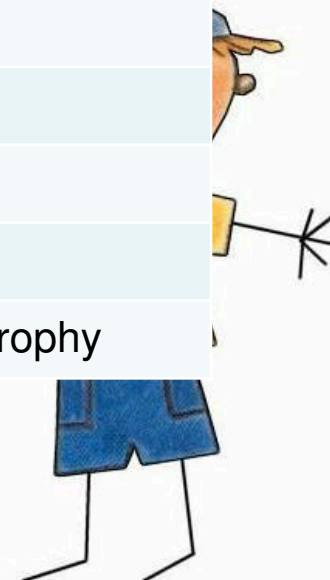


Pt BM

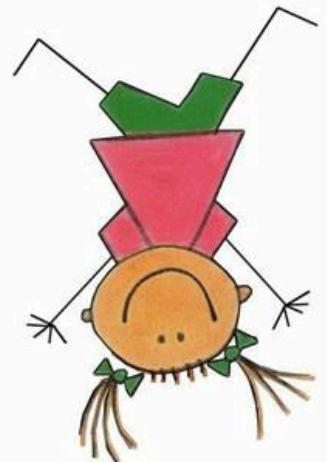
- 7 yr old female
- Unknown PMTCT
- Diagnosed HIV positive at 3 months of age
- Stage 3 Initial CD4 1321 (31%)
VL 3 million
- TB treatment commenced at 5 months of age
- Started ART at 6 months of age
 - D4T,3TC,Ritonavir
 - CD4 571 (17,4%) VL 220 000



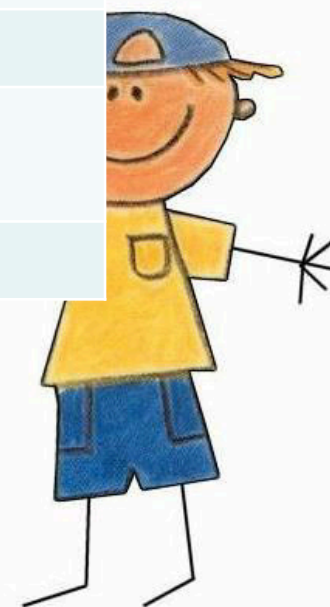
Months on Rx	CD4	VL	Regimen	Diagnosis
0	571 (17.4%)	220 000	D4T+3TC+ Ritonavir	TB
6	813 (25.6%)	4000		
8			D4T+3TC+ Kaletra	Formulary change
9	913 (24.6%)	undetectable		
18	1478 (30.8%)	5300		
24	1003 (25.7%)	3800		
29	1140 (28.4%)	2100		BPN
34	1066 (29.5%)	210 000		
38	1064 (26.7%)	170 000		CSOM
48	1020 (19.8%)	114 624		Lipodystrophy



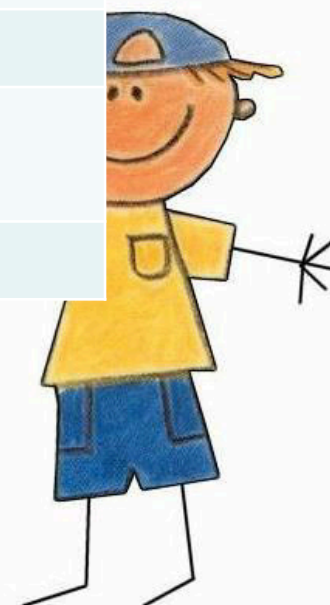
What would you have done?



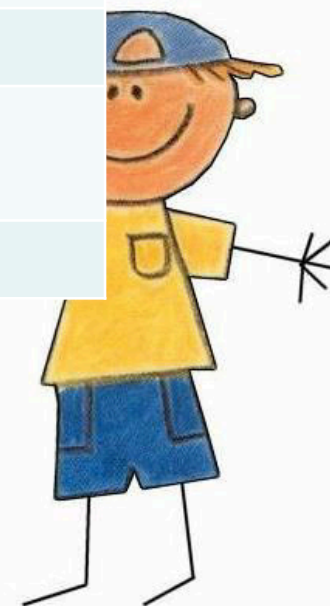
Months on Rx	CD4	VL	Regimen	Diagnosis
53			AZT/DDI/ EFV	
56	771 (26.2%)	1839		
62	499 (16.53%)	93 140		
65	491 (14.76%)	207 815		



Months on Rx	CD4	VL	Regimen	Diagnosis
53			AZT/DDI/ EFV	
56	771 (26.2%)	1839		
62	499 (16.53%)	93 140		
65	491 (14.76%)	207 815	3TC	
68	211 (8.44%)			



Months on Rx	CD4	VL	Regimen	Diagnosis
53			AZT/DDI/ EFV	
56	771 (26.2%)	1839		
62	499 (16.53%)	93 140		
65	491 (14.76%)	207 815	3TC	
68	211 (8.44%)			
70	137 (4.31%)	385 218	ABC/AZT/ 3TC	
78	60 (4.91%)	69 606		

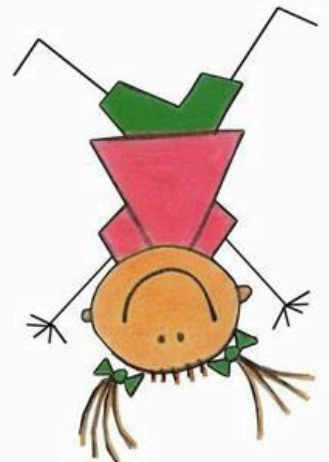


Summary

- Treatment for 6 years
- D4T/3TC/Ritonavir
 - Swapped to Kaletra
- AZT/DDI/EFV
- 3TC monotherapy
- Now 7 yrs old 18.8 kg
 - Holding regimen AZT/3TC/ABC
 - CD4 60 (4.91%) VL 69 606



What is the next step?





STANFORD UNIVERSITY

HIV DRUG RESISTANCE DATABASE

Drug Resistance Interpretation: RT

NRTI Resistance Mutations: D67N, T69D, K70R, M184V, T215F
 NNRTI Resistance Mutations: K103N, V106M
 Other Mutations: A98S

Nucleoside RTI

lamivudine (3TC) High-level resistance
 abacavir (ABC) Intermediate resistance
 zidovudine (AZT) High-level resistance
 stavudine (D4T) High-level resistance
 didanosine (DDI) High-level resistance

Non-Nucleoside RTI

efavirenz (EFV) High-level resistance
 etravirine (ETR) Susceptible
 nevirapine (NVP) High-level resistance
 rilpivirine (RPV) Susceptible

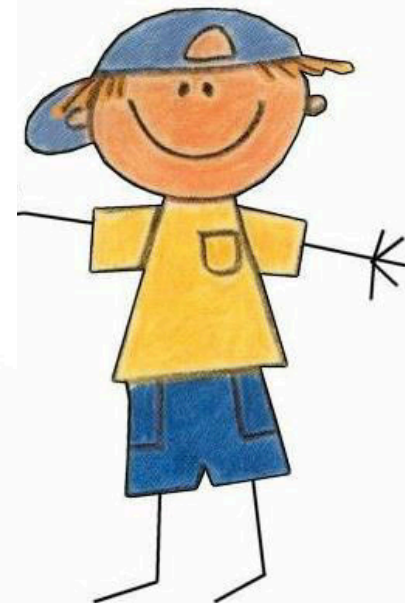
emtricitabine (FTC) High-level resistance
 tenofovir (TDF) Low-level resistance



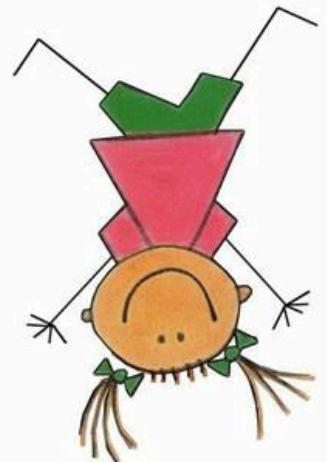
PI Major Resistance Mutations: M46I, I47V, I54V, L76V, V82A
 PI Minor Resistance Mutations: L10V, Q58E, A71V
 Other Mutations: I15V, K20R, M36I, D60E, H69K, L89M

Protease Inhibitors

atazanavir/r (ATV/r)	High-level resistance
darunavir/r (DRV/r)	Intermediate resistance
fosamprenavir/r (FPV/r)	High-level resistance
indinavir/r (IDV/r)	High-level resistance
lopinavir/r (LPV/r)	High-level resistance
nelfinavir (NFV)	High-level resistance
saquinavir/r (SQV/r)	Intermediate resistance
tipranavir/r (TPV/r)	Intermediate resistance



What regimen options do we have?



- Options

- NRTI

- NNRTI

- PI/r

- Integrase inhibitor

- CCR5 inhibitor

- Intergrase inhibitor

TDF or recycling

NRTI

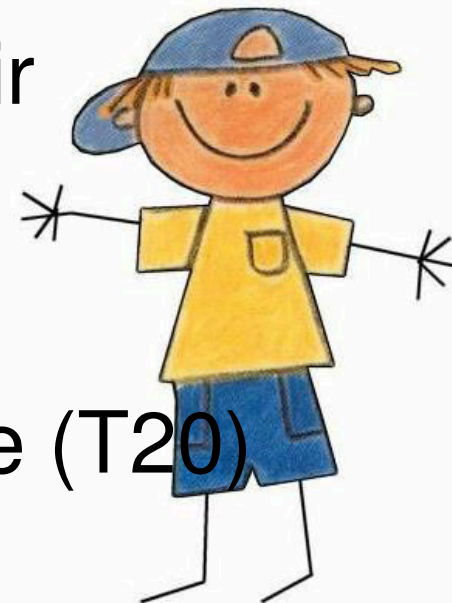
Etravirine

Darunavir/r

Raltegravir

Maraviroc

Enfuvirtide (T20)



Pt SS

- 9 yr old female
- Unknown PMTCT and breastfeeding history
- Started on ARVs at 3 yrs of age
 - D4T + 3TC + EFV
- Changed after 2 years due to Virological and clinical failure
 - AZT + DDI + LPV/r with boosted Ritonavir while on TB treatment



CD 4 count				Viral load	
		Children			
<i>Last 3 CD 4 counts results:</i>		CD4%		<i>Last 3 VL results:</i>	
Date: 21/5/2013	386		16%	Date: : 21/5/2013	243563
Date: 20/2/2013	455	Date:	16%	Date: 20/2/2013	429931
Date: 14/7/2011	112	Date:	6%	Date: 14/07/2011	5305687

- 24 kg
- Hb 10.9 g/dL
- ALT 8U/L
- Creat 24 umol/L



What is the next step?



Drug Resistance Interpretation: RT

NRTI Resistance Mutations: D67N, K70R, T215F, K219Q

NNRTI Resistance Mutations: V106M

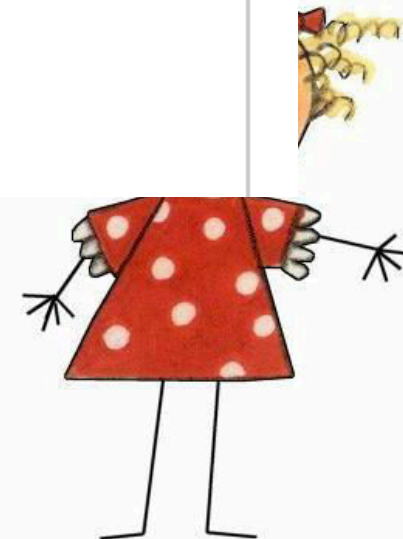
Other Mutations: None

Nucleoside RTI

lamivudine (3TC)	Susceptible
abacavir (ABC)	Intermediate resistance
zidovudine (AZT)	High-level resistance
stavudine (D4T)	High-level resistance
didanosine (DDI)	Intermediate resistance
emtricitabine (FTC)	Susceptible
tenofovir (TDF)	Intermediate resistance

Non-Nucleoside RTI

efavirenz (EFV)	High-level resistance
etravirine (ETR)	Susceptible
nevirapine (NVP)	High-level resistance
rilpivirine (RPV)	Susceptible



Drug Resistance Interpretation: PR

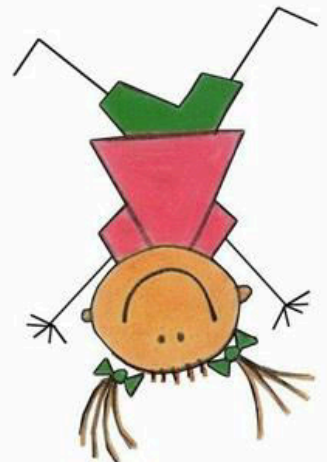
PI Major Resistance Mutations:	M46I, I54V, L76V, V82A, I84V
PI Minor Resistance Mutations:	L10V, Q58E
Other Mutations:	None

Protease Inhibitors

atazanavir/r (ATV/r)	High-level resistance
darunavir/r (DRV/r)	Intermediate resistance
fosamprenavir/r (FPV/r)	High-level resistance
indinavir/r (IDV/r)	High-level resistance
lopinavir/r (LPV/r)	High-level resistance
nelfinavir (NFV)	High-level resistance
saquinavir/r (SQV/r)	High-level resistance
tipranavir/r (TPV/r)	Intermediate resistance



What regimen options do we have?



- Options

- NRTI

TDF or susceptible
NRTI

- NNRTI

Etravirine

- PI/r

Darunavir/r

- Integrase inhibitor

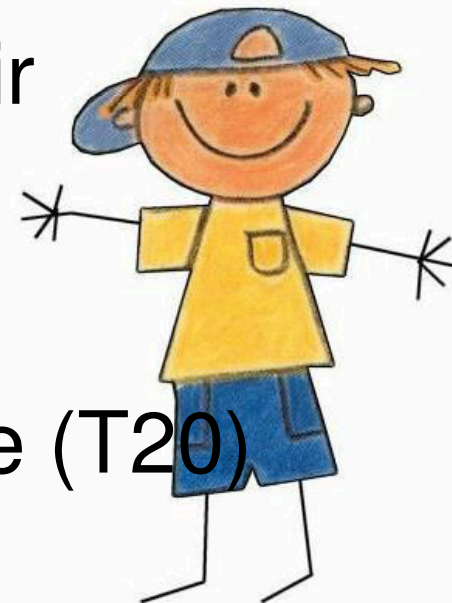
Raltegravir

- CCR5 inhibitor

Maraviroc

- Integrase inhibitor

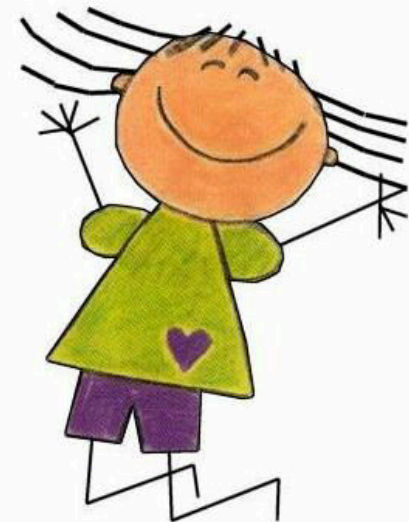
Enfuvirtide (T20)





Pt KN

- 2 yr 5 month old male
- Mom tested HIV positive in pregnancy
 - Para 1 Gravida 1
 - PIH and prem delivery at 32/40
 - Maternal AZT given – unsure of start and duration taken
 - Baby was given stat NVP
 - Neither mum nor Dad ART
 - Breastfed for 2 months



TB HISTORY

- Oct 2011- Diagnosed with disseminated TB and TB lymphadenitis
 - Tb culture positive on MGIT on blood and LN aspirate
 - Managed as per old TB guidelines with Intensive phase of RHZ only
 - Response was poor with no weight gain and multiple interim hospital admissions



TB history cont

- Admitted in March / April 2012 – with seizures
 - CT scan and MRI brain - Lt frontal ring enhancing lesion ? Tuberculoma
 - Changed in April 2012 to 4 drug TB meds (RHZ and ethionamide given as individual drugs at high dose)
 - Epilim for seizure control
 - Completed 8 months HD TB treatment – January 2013



ARVS

- Started in August 2011 (4 months old)
- Baseline CD4 235 (7,86%) VL unknown
 - ABC + 3TC + Kaletra
- Poor initial tolerance of all ARVS
 - persistent vomiting
 - Poor clinical response with no weight gain, multiple infections (HSV stomatitis, Klebsiella pneumonia, Ecoli UTI and sepsis)
 - Chronic diarrhoea

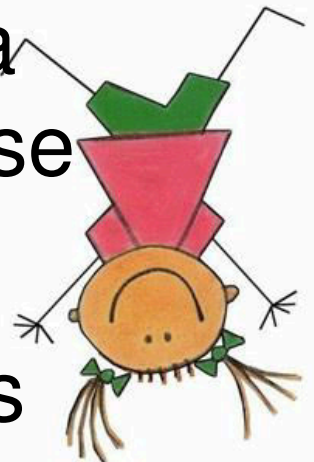


Date	CD4	VL	Regimen	Diagnosis
Aug 2011	235 (7.86%)		ABC + 3TC + Kaletra	Poor tolerance Poor clinical response
Oct 2011			ABC+3TC+ double dose Kaletra	Disseminated TB
Nov 2011	93 (7.1%)			
Dec 2011			ABC + 3TC + Kaletra + Ritonavir	
Feb 2012	228	> 10 million		
April 2012	241(13%)	7.8 million		Tuberculoma
Feb 2013	1132 (17%)	2.8 million		



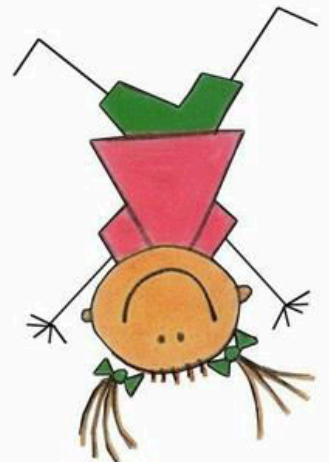
Summary

- 2 yr 4 month old
- PMTCT exposure to AZT and NVP
- On ART for 2yrs
- Disseminated TB – inadequately treated – Tuberculoma - total 15 months
- PI – Kaletra → dd Kaletra → Kaletra boosted with Ritonavir → normal dose
- Poor tolerance – now tolerating well
- Clinically failing – recurrent infections



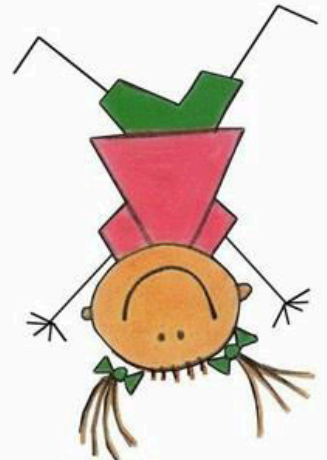
Concerns

- Never had a viral load under 2 million but has seen some CD4 response
- What are some possibilities ?



Concerns

- Never had a viral load under 2 million but has seen some CD4 response
- What are some possibilities ?
 - Complete ongoing non adherence
 - Viral resistance in view of
 - TB drug interaction
 - Poor initial ARV intolerance
 - Chronic gastroenteritis



Thank you



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