

Plasma Levels of Nevirapine following Interruption of ZDV/3TC/NVP in African Adults within the DART Trial

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on behalf of the **DART** Trial Team

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Background



DART Trial

- Development of **AntiRetroviral Therapy** in Africa

Objectives

- To compare different ART monitoring strategies
- To assess safety of structured treatment interruptions (STI)

STI in DART

LB Session: Thursday 17th August 06

Abstract No: THLB0207

Session Room 1

Rationale



NNRTIs have a longer elimination half life than NRTIs

Simultaneous interruption of all drugs exposes the patient to NNRTI monotherapy

Current recommendation: continuation of dual NRTI for 7 days

Few data on plasma clearance of NVP in patients on stable HAART in our population

Objectives



To measure rate of elimination of Nevirapine in patients undergoing structured treatment interruptions in DART

To inform the approach to STIs within DART and optimise patient safety

Methods (1)



- 21 patients undergoing STI
 - 52 weeks on NVP based HAART
 - Achieved **CD4 > 300**
 - No clinical events in preceding 3 months
- Plasma samples at 0, 1, 2, 3 & 4 weeks after stopping NVP
- 2 NRTIs (ZDV + 3TC or d4T + 3TC) continued for 7 days

Methods (2)



- Plasma levels of NVP analyzed by high performance liquid chromatography (HPLC)
- Lower Limit of Quantification (LLQ) = 100 ng/ml
- Lowest Limit of Detection , based on a chromatogram peak was ~20 ng/ml
- Therapeutic range: 3400-8000 ng/ml

Results



Total number of patients	21	16 female
		5 male
Excluded from analysis	2	1- no NVP levels at baseline
		1- barely detectable NVP levels
ART Regimen n=19	18	ZDV/3TC/NVP
	1	d4T/3TC/NVP

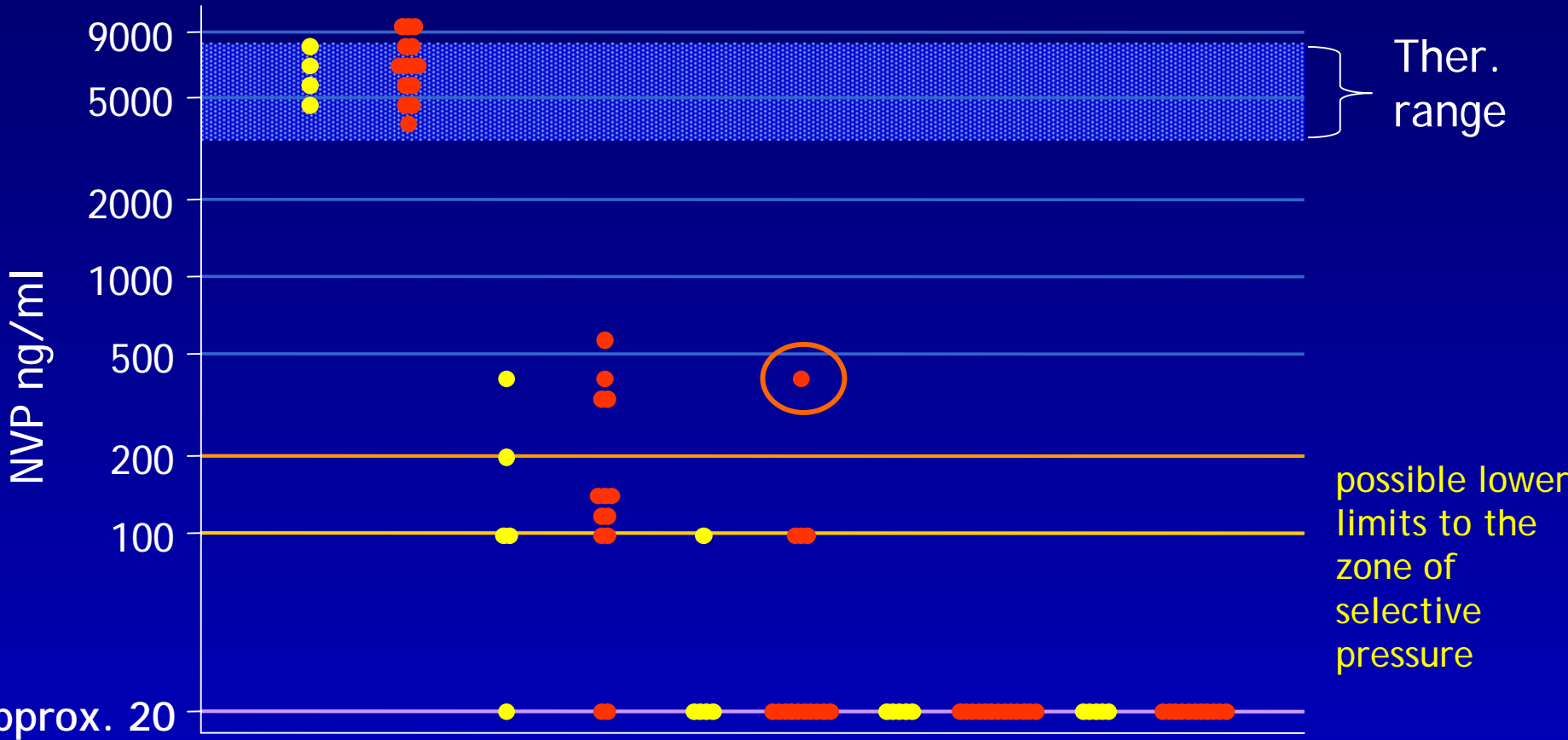
Baseline Characteristics (at the time of STI)



	MEDIAN	(RANGE)
Age	35	(23-61)
Body Weight (Kgs)	61	(52-77)
CD4 count (cells/mm ³)	341	(301-692)

Mean plasma NVP level **6479 ng/ml** (Range 3720 - 9500 ng/ml)

Levels of NVP over time

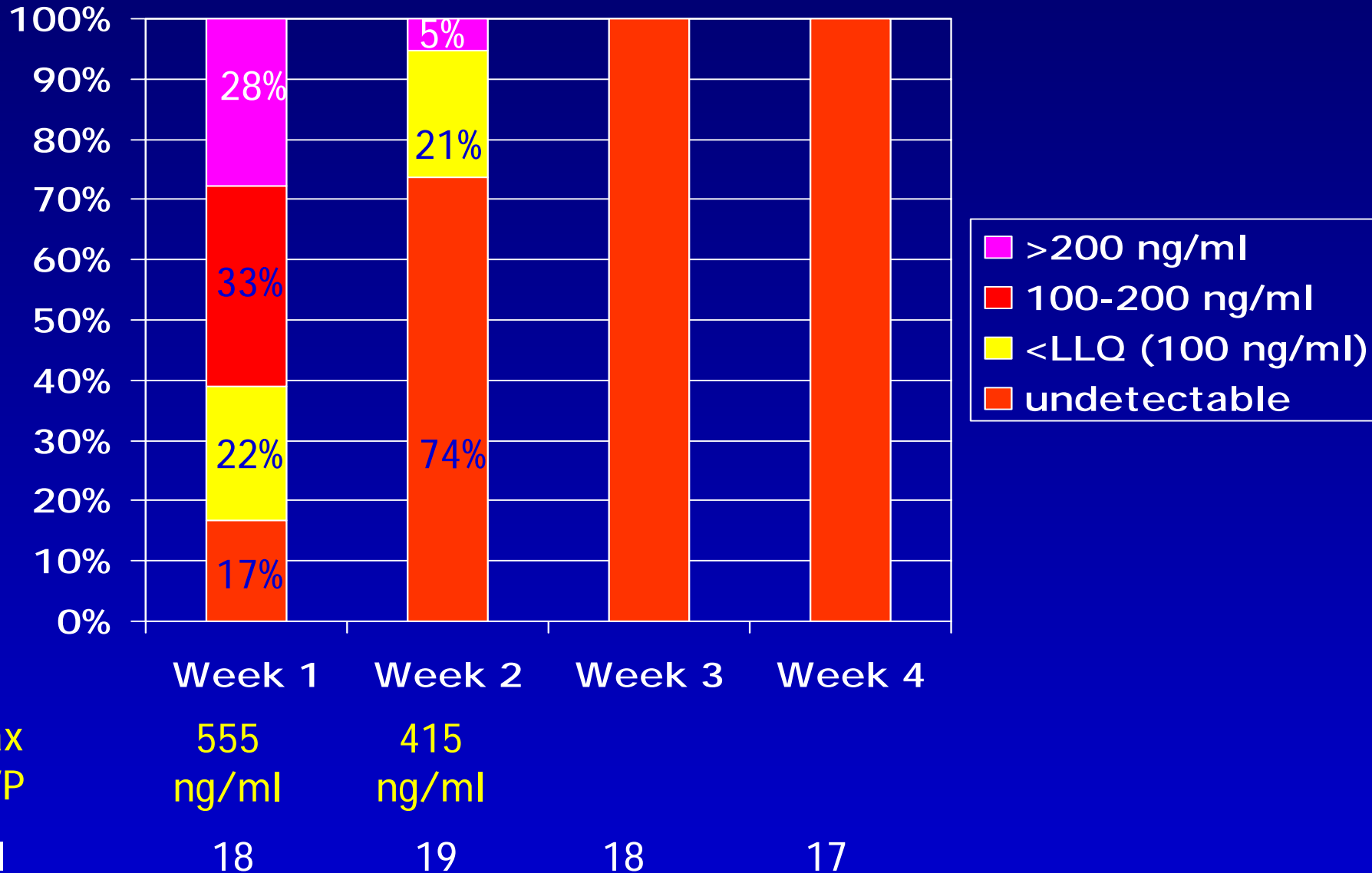


Sex	M	F	M	F	M	F	M	F	M	F
Weeks from stopping NVP	0	0	1	1	2	2	3	3	4	4

Patient with 415 ng/ml at week 2 had no sample at week 1 or 3

NVP levels over time

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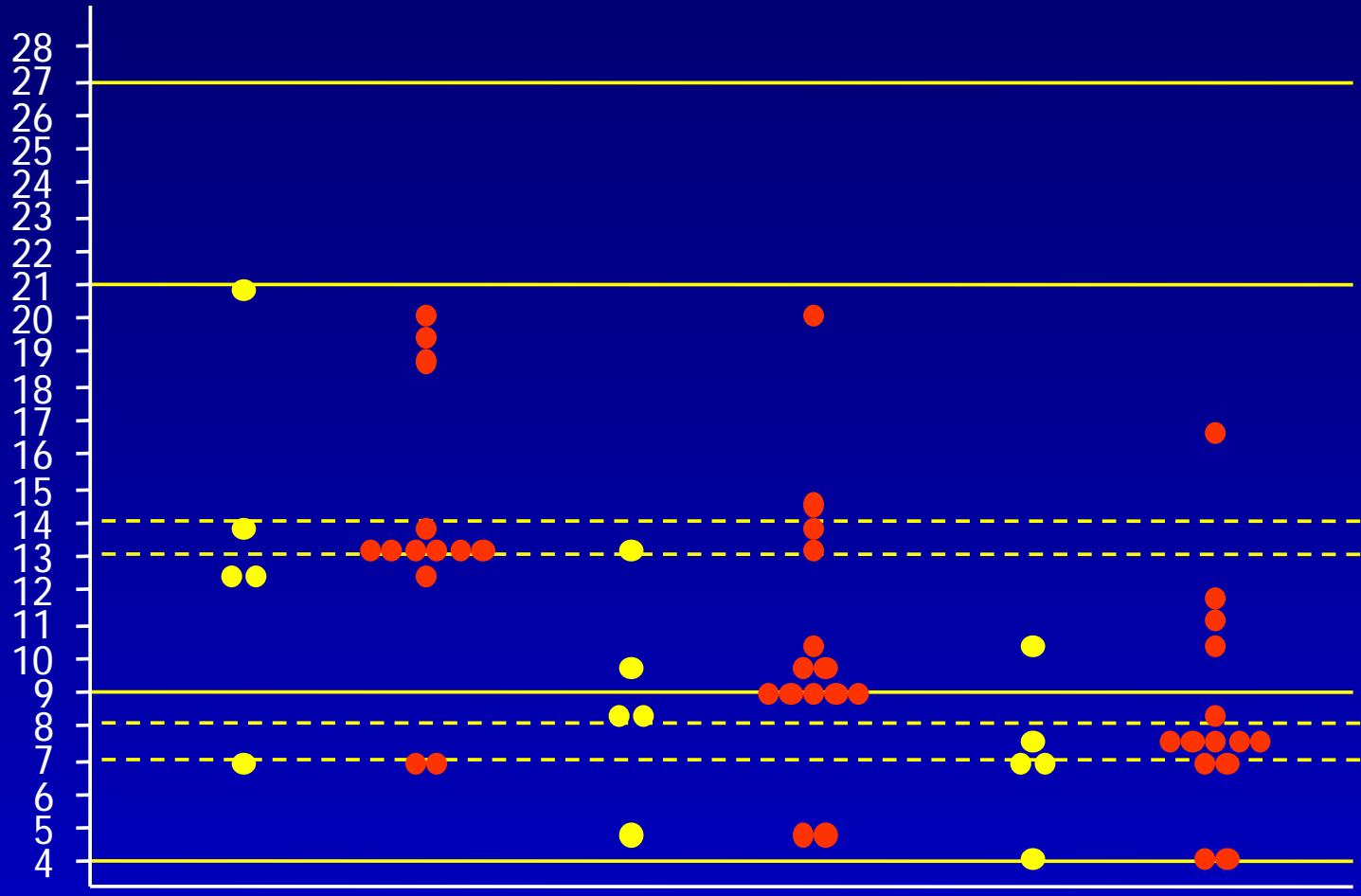


Estimated days to reach different plasma NVP thresholds



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Days to reach various NVP thresholds



Median days (IQR) 13.2 (12.3-18.4) 9.3 (8.7-13.0) 7.6 (7.0-10.1)

Conclusions

- 7 - 10 days after stopping NVP based HAART plasma levels of NVP were < 200 ng/ml in all but 1 patient
- 200 ng/ml level previously defined by Muro et al
- These data suggested the practice of continuing the dual - NRTI cover for 1 week is acceptable
- Elimination of NVP after STI, among patients on stable HAART is faster than previously reported following single dose NVP

Limitations



- Small number of patients sampled
- Long sample collection intervals

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