

# 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 17<sup>th</sup> August 06

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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)

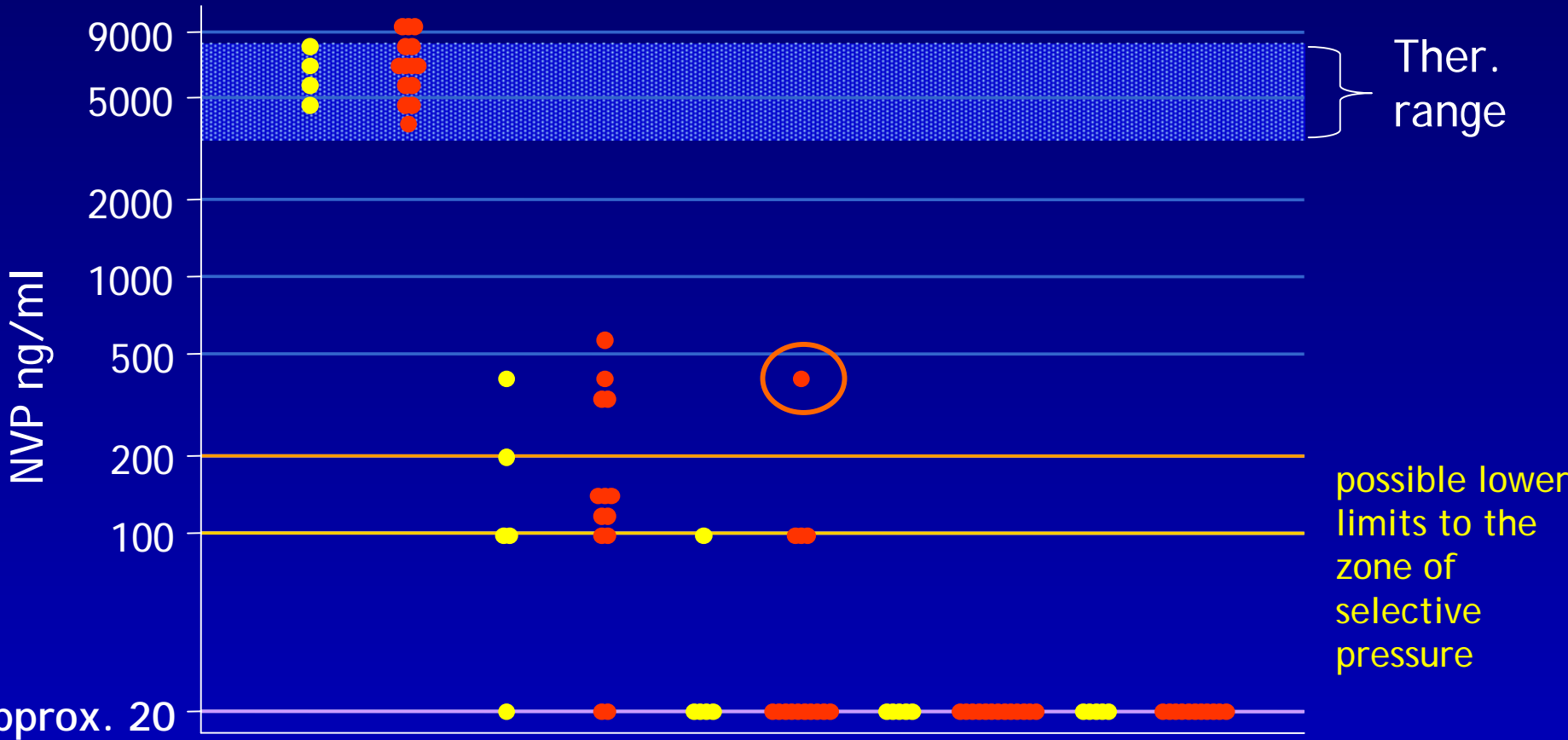


	MEDIAN	(RANGE)
Age	35	(23-61)
Body Weight (Kgs)	61	(52-77)
CD4 count (cells/mm <sup>3</sup> )	341	(301-692)

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



# Levels of NVP over time

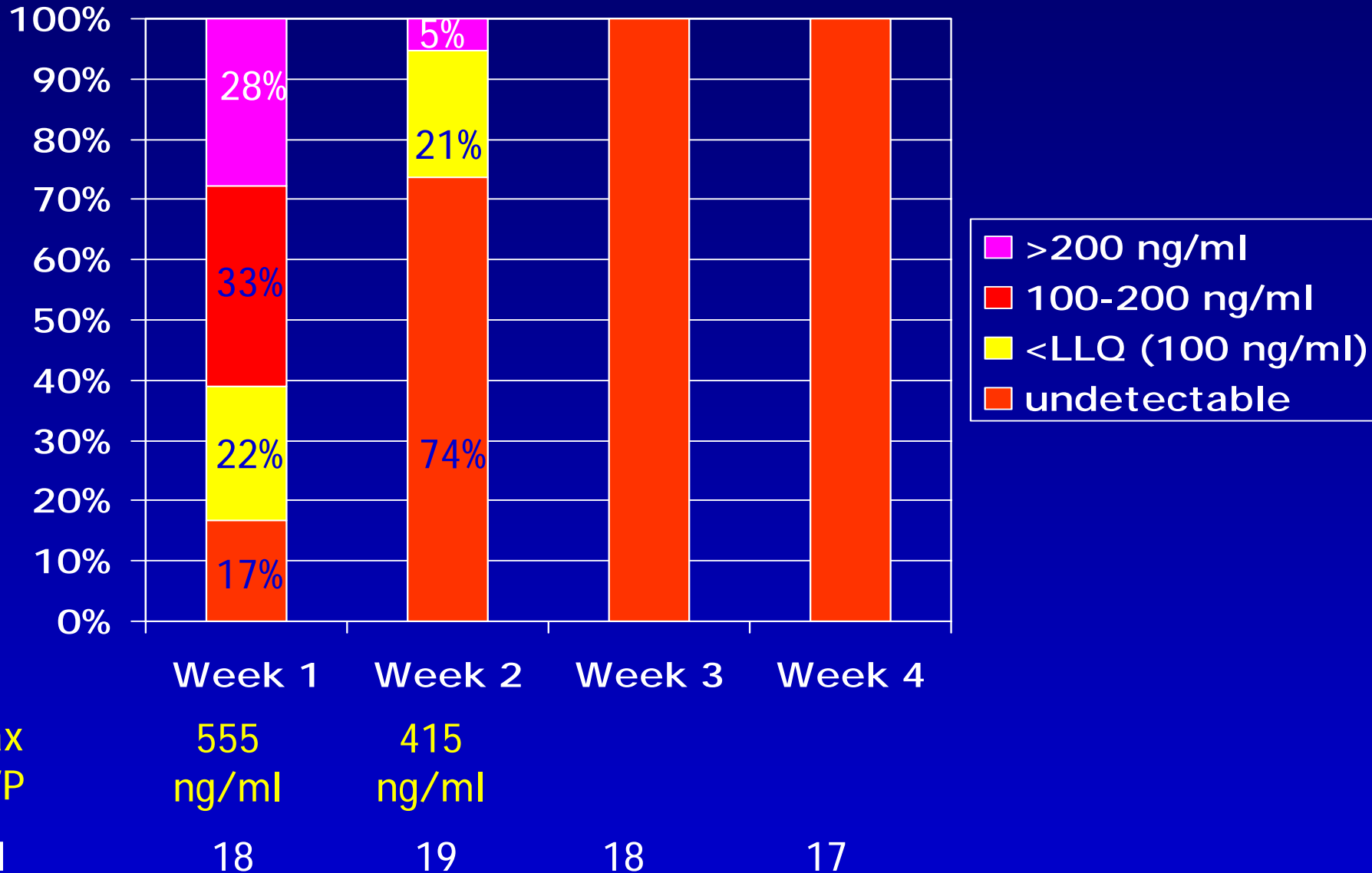


Sex	M	F	M	F	M	F	M	F	M	F
Weeks from stopping NVP	0	0	1	1	2	2	3	3	4	4

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

# NVP levels over time

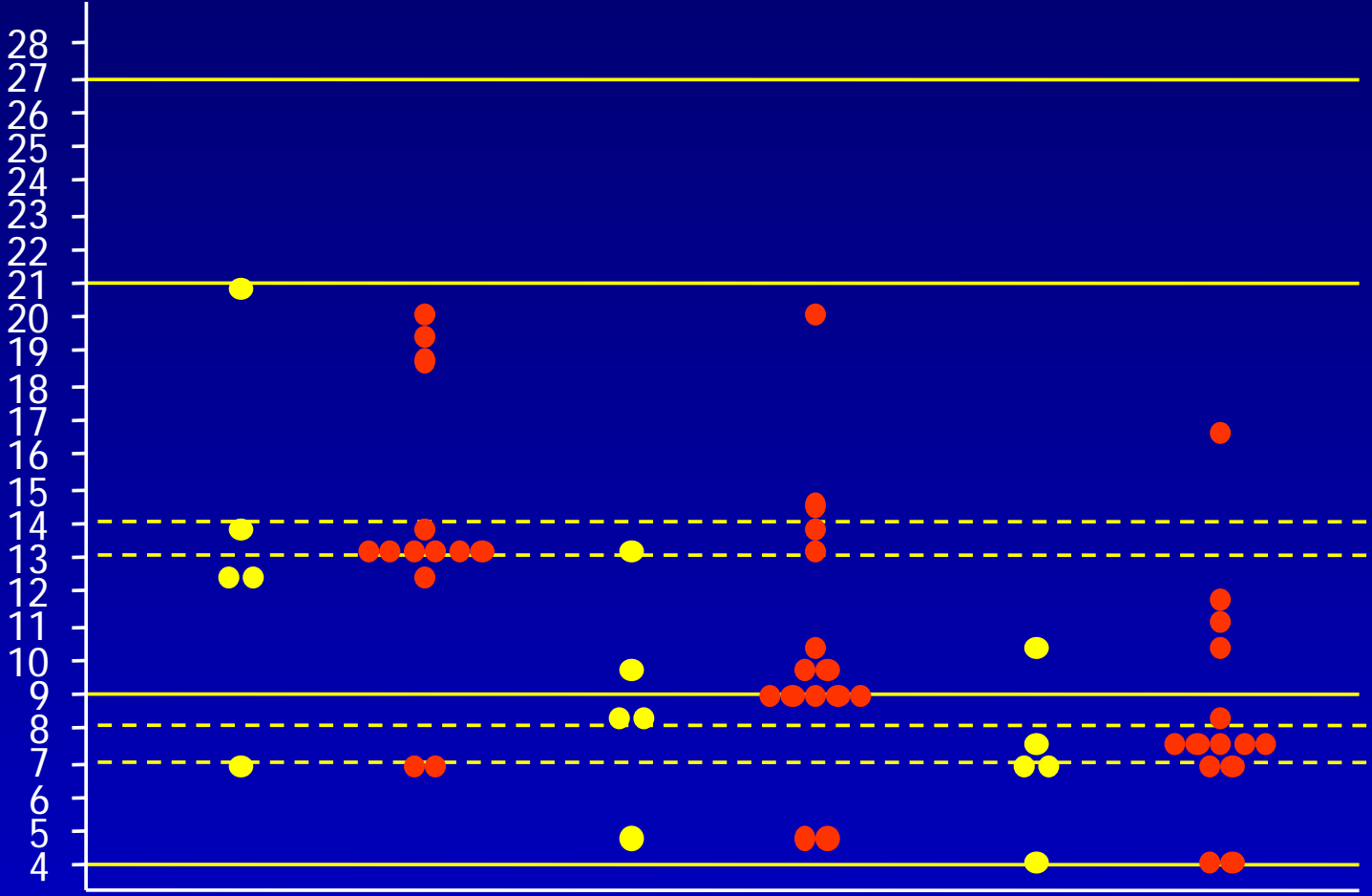
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# Estimated days to reach different plasma NVP thresholds



Days to reach various NVP thresholds



Sex	NVP (ng/ml)	Median days (IQR)
M	~20	13.2 (12.3-18.4)
F	~20	13.2 (12.3-18.4)
M	100	9.3 (8.7-13.0)
F	100	9.3 (8.7-13.0)
M	200	7.6 (7.0-10.1)
F	200	7.6 (7.0-10.1)

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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