Description of d4T toxicities among 3 OI/ART clinics patients on ARV in Cambodia

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Introduction

- Scale up of access to HAART has become a reality in Cambodia, by the year 2005, over 12,000 patients PLHA had started HAART.
- The overall majority of these patients have started on a standard 1st line regimen: 3TC-d4T-NVP.
- Through this, we are increasing worried about d4T related toxicities.
- Lactic acidosis, neuropathy and lipodystrophy are well known and prominent forms of toxicity.
- The referral hospitals of Siem Reap, Sotnikum and Takeo has been started AIDS care since 03/02 in Cambodia, ART since 10/02.
- We attempted to analyse the extent of stavudine toxicity in these cohorts.

Objectives

To analyse the occurrence of stavudine (d4T) related toxicity in a large cohort of patients on HAART.

Methods

- Close analysis of all patients that changed regimen because of d4T toxicity among adult patients in Siem Reap, Sotnikum and Takeo CoCs in the course of the year 2005 (as recorded in Fuchia 1.5) (earlier data were less reliable).
- Analysis of the files of all patients that died after the start of HAART since the start of the 3 cohorts to estimate the number of deaths due to (suspect) lactic acidosis.

Results:

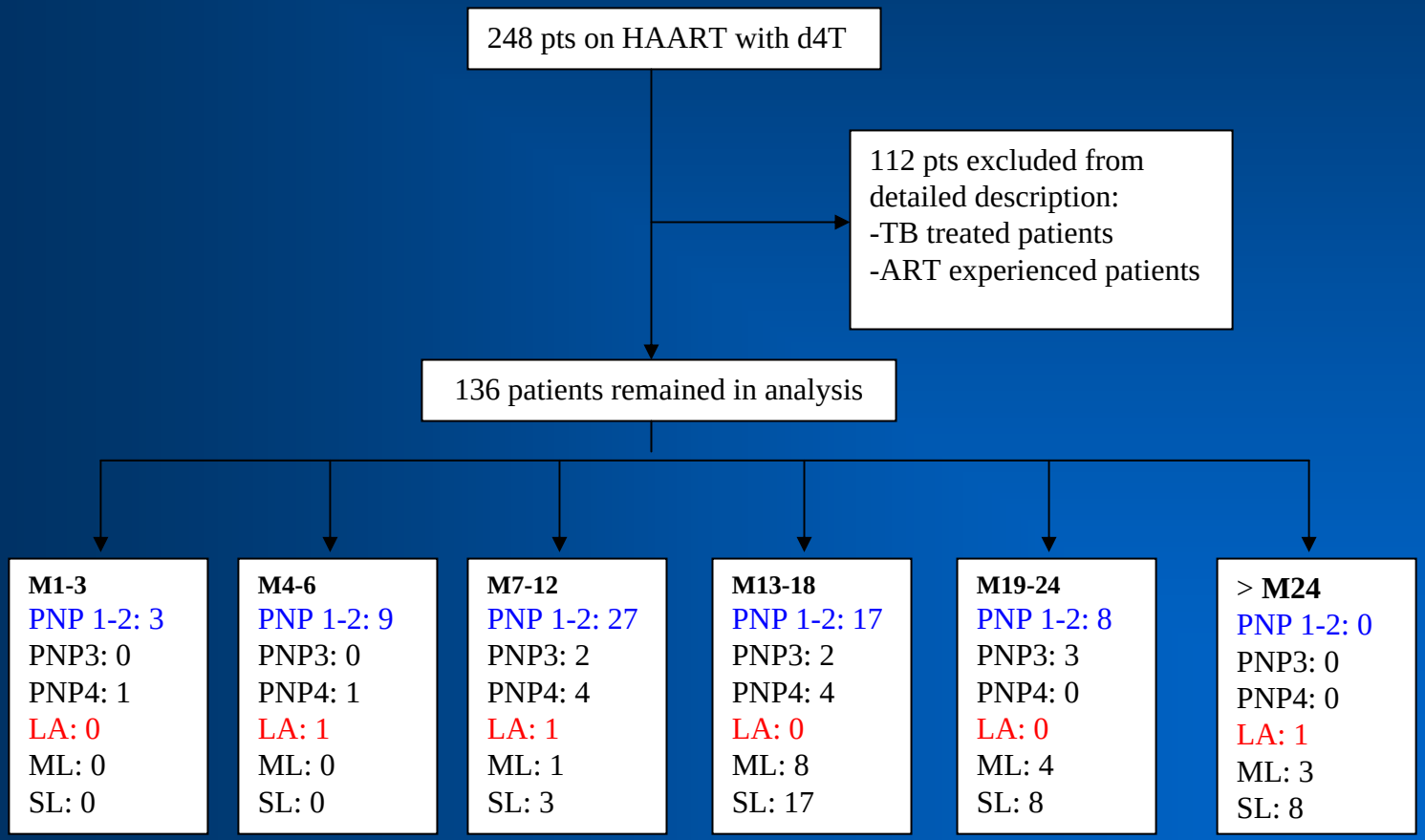
1) Switches because of d4T toxicity in 2005.

- Active cohort ART 2005:

  - on 01/01/05: 1425 patients on HAART.

  - on 31/12/05: 2538 patients on HAART in our projects (+ 200, transferred out).
- 248 patients of switching d4T for toxicity between 16/01/05 and 4/01/06
- We decided to exclude 112 patients of the descriptive analysis : 95 (38%) because simultaneous TB treatment and 17 (7%) because of ART experience before the start of follow up.
- 136 patients were further analysed.

Results: description of toxicity (1)



Results: description of toxicity (2)

	M 1-3	M 4-6	M 7-12	M 13-18	M 19-24	> M 24		
Peripheral neuropathy 1-2	3	9	27	17	8	0	64	47%
Peripheral neuropathy 3	0	0	2	2	3	0	7	5%
Peripheral neuropathy 4	1	1	4	4		0	10	7%
Lactic acidosis	0	1	1	0	0	1	3	2%
Mild lipodystrophy	0	0	1	8	4	3	16	11%
Severe lipodystrophy	0	0	3	17	8	8	36	26%
	4	11	38	48	12	12	136	

Patient characteristics

- Median baseline CD4: 19 cells (versus: 54 cells, all patients)
- Time on ART at switch: from 1 to 32 months, median: 14 months
- M/F: 52/84 or 0.6

Results:

2) Deaths of suspect lactic acidosis.

Clinical image of lactic acidosis

- Rapid development, high mortality.
- Rather “rare” (3.9-14.5/1000 patient years)
- Symptoms: nausea, vomiting, abdominal distension and pain, tachypnea
- Biological parameters: high lactate, high anion gap and acidosis (all tests that are difficult to obtain in Cambodian hospitals).
- Physiopathology: mitochondrial toxicity
- Risk factors: women, higher bodyweight, very good adherence, between 6 and 24 months on HAART with NRTI (in the first place d4T or DDI).

Results:

2) Deaths of suspect lactic acidosis.

- Total number of deaths of patients that had started HAART between October 2002 and December 2005: 237.
- 16 (6.8%) patients had died with a biological or clinical image of lactic acidosis (7 in Siem Reap, 6 in Takeo and 3 in Sotnikum)

We suspect that this number is an underestimation, probably some LFU have died at home because of LA and some of the other deaths are due to LA as well.

=> 16/3000 pts-years HAART died of NRTI induced lactic acidosis.

Conclusion

- Our data should be analysed more into depth because toxicity to stavudine appears clearly an important problem.
- Lactic acidosis appears proves difficult to diagnose timely to avoid death of the patients.
- To avoid these deaths, 2 options seem most obvious:
  - Switch all patients to a less toxic NRTI (zidovudine) after around 6 months of treatment.
  - Start patients straight on on a less toxic first line like a Tenofovir containing regimen.
- More research should be implemented to evaluate the value of these alternatives in Cambodia.