Abstract #94

Comparison between abacavir, efavirenz and nevirapine combined with zidovudine-lamivudine in antiretroviral naive patients

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Introduction

Compared to efavirenz containing regimens, AZT-3TC-ABC has been reported to be less effective in naive patients with a plasma viral load at baseline ≥100,000 copies/ml (ACTG 5095 study). The present study evaluates virological, immunological and toxicity related outcome in patients from the Dutch ATHENA national observational cohort who initiated HAART with AZT-3TC-ABC in comparison to nevirapine or efavirenz containing regimens.

Methods

- 1099 patients were selected who started HAART between 2000 and 2004 with an AZT-3TC NRTi backbone and either abacavir (ABC), nevirapine (NVP) or efavirenz (EFV) as additions.

- Cause specific hazards were modelled using Cox proportional hazard models. The following endpoints were used:

1. Time to virological success (two consecutive HIV-RNA measurement <50 copies/ml).
2. Time to virological failure(2 consecutive HIV-RNA measurements >50 copies/ml) in those who suppressed HIV-RNA to <50 copies/ml within 9 months after starting HAART.
3. Time to increase of ≥100 CD4 cells/mm^3 from baseline.
4. Toxicity driven change of the regimen.

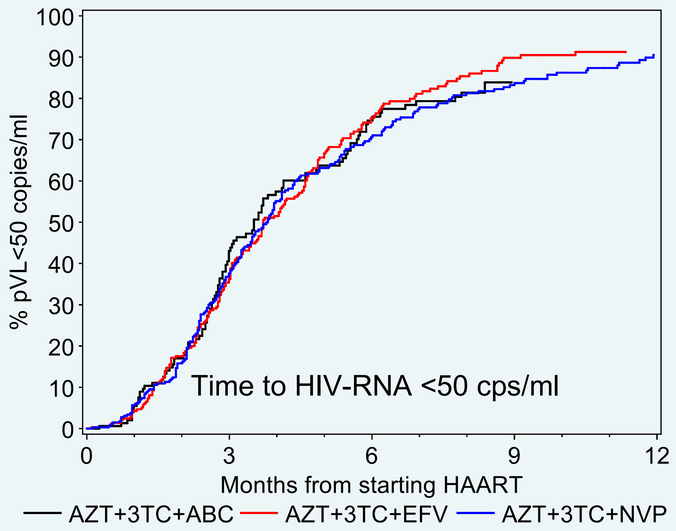
- To study whether there were different rates in regimen change between patients starting ABC, NVP or EFV, time to change of the regimen before reaching the endpoint, was included as a competing event in the model. Parametric survival models, taking care of the interval censored nature of the immunological and virological endpoints led to similar conclusions.

Results

Characteristics of 1099 patients at the start of HAART	ABC	EFV	NVP
Total	202	400	497
Male gender (%)	75	78	71
Transmission risk group (%)			
Homosexual	44	45	48
Heterosexual	32	42	42
IDU	8	2	2
Born in the Netherlands (%)	55	48	47
HIV-RNA at T_0			
<100,000 cps/ml (%)	72	48	58
≥100,000	18	40	34
Missing	10	12	8
CD4 count (cells/mm^3) at T_0	240 (160-376)	173 (70-263)	230 (138-315)
CDC-C event before T_0 (%)	15	33	16

Continuous variables reported as median (IQR); T_0: start of HAART

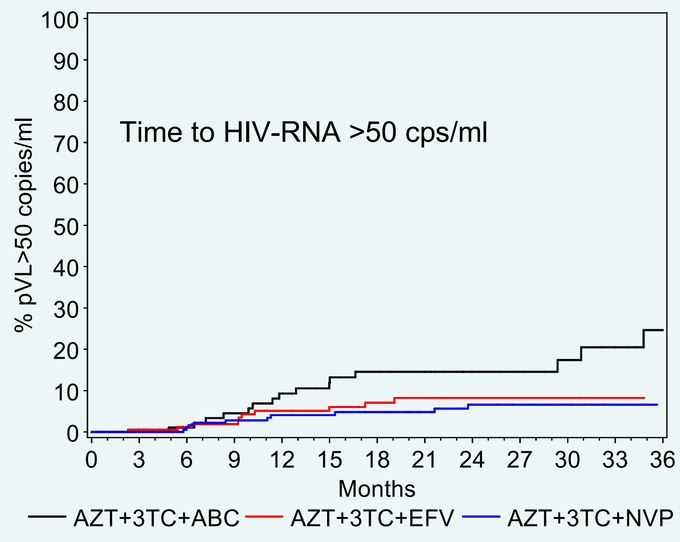
Baseline RNA		Adjusted HR (95% CI) vs EFV
Overall	ABC	0.80 (0.62-1.05)
	NVP	0.87 (0.71-1.07)
<100.000	ABC	0.84 (0.62-1.15)
	NVP	0.87 (0.67-1.14)
≥100.000	ABC	0.67 (0.38-1.20)
	NVP	0.86 (0.61-1.21)



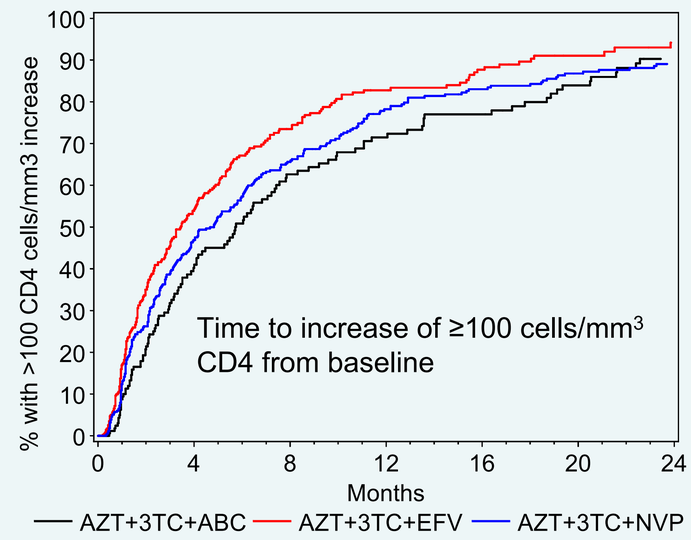
Lower pre-HAART HIV-RNA was associated with a shorter time to suppression of HIV-RNA <50 copies/ml. There were no significant differences between regimens in time to stop for any reason.

Baseline RNA		Adjusted HR (95% CI) vs EFV
Overall	ABC	2.29 (0.99-5.27)
	NVP	0.84 (0.35-2.02)

HR ABC vs NVP 2.71 (1.20-6.12). Younger age was associated with a shorter time to rebound of HIV-RNA >50 copies/ml. Patients starting on efavirenz had a significantly shorter time to change in the regimen than patients starting with ABC. There were not enough patients to allow for a stratified analysis.

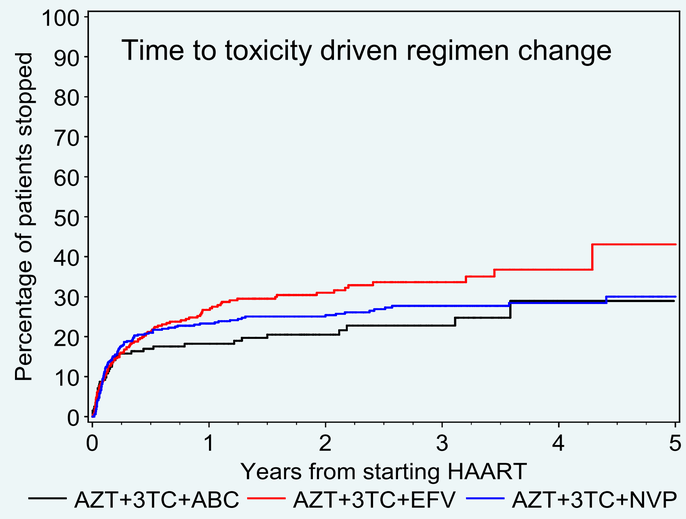


Baseline RNA		Adjusted HR (95% CI) vs EFV
Overall	ABC	0.80 (0.64-1.01)
	NVP	0.84 (0.70-1.00)
<100.000	ABC	0.96 (0.72-1.28)
	NVP	0.83 (0.65-1.06)
≥100.000	ABC	0.48 (0.29-0.79)
	NVP	0.83 (0.63-1.08)



Higher HIV-RNA at the start of HAART was associated with a shorter time to increase of ≥100 CD4 cells/mm^3 from baseline. Patients starting HAART with EFV had a longer time to change in the regimen.

Baseline RNA		Adjusted HR (95% CI) vs EFV
Overall	ABC	0.68 (0.46-0.99)
	NVP	0.81 (0.62-1.06)
<100.000	ABC	0.68 (0.43-1.08)
	NVP	0.93 (0.66-1.32)
≥100.000	ABC	0.70 (0.31-1.57)
	NVP	0.61 (0.38-0.97)



Older age and female gender were associated with a shorter time a toxicity driven change in the regimen. There were no differences between regimens in time to stop because of other reasons.

Conclusion

- There were no significant differences in time to virological success between the three regimens
- There as an increased risk of rebound to HIV-RNA >50 copies/ml in patients starting with AZT-3TC-ABC
- Patients starting HAART with EFV had a shorter time to toxicity driven change in the regimen compared to ABC.