

# Does Early Treatment of Primary HIV-Infection Delay Treatment Indication?

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## Background

- Scientific data on optimal management of primary HIV-infection is non-conclusive.
- There is only poor evidence that early treatment of primary HIV infection can reduce the viral load (VL) set point and thereby delay disease progression.

## Methods

### Prime-DAG and Ac-DAG cohort studies

- Combined analysis of two prospective, observational, nationwide, multi-centric cohorts initiated by the DAGNAE (German Association of Physicians in Private Practice) in order to investigate treatment strategies and outcome in acute HIV-infection.
- Prime-DAG started in July 2001 with a focus on early treatment.
- Ac-DAG started in January 2003 with a focus on non-treatment of primary HIV-infection.

### Criteria for primary HIV-infection were

- a negative ELISA coupled with a detectable viral load
- or a documented western blot with less than 5 bands
- or a positive ELISA coupled with a negative HIV-test within the preceding six months

### Early treatment: Treatment start prior to or during seroconversion

- Combined endpoint:** CD4-decline to <350/ $\mu$ l and/or VL-increase to >100,000 copies/ml in treated and untreated seroconverters

## Results

- 200 patients (pts) from 35 private clinics and 7 hospital outpatient departments, 100 patients in Prime-DAG and 100 patients in Ac-DAG
- Median observation time: 21.4 months (range 0.1 – 43.5 months)
- Antiviral treatment**  
Pts without treatment N = 56  
Pts with treatment N = 144  
treatment stop\* N = 98/144  
\*discontinuation of HAART  $\geq$  3 months

## Baseline Characteristics

N=200 191 males, 9 females

Age mean 35 years, range 18 – 62 years

Transmission risk	N	%
homosexual contacts	167	(83 %)
heterosexual contacts	16	( 8 %)
other	17	( 9 %)

	pts without treatment (N=56)	pts with treatment (N=144)	p-value
<b>First recorded viral load [copies/ml]</b>			
Median	240,000	> 500,000	<0.001
Range	463 – 6 million	100 – 327 million	
<b>Absolute CD4 [<math>\mu</math>l]</b>			
Median	621	453	0.0017
Range	266 – 1543	120 -1342	
<b>Relative CD4 [%]</b>			
Median	29	24	0.053
Range	8 - 44	4 - 50	(n.s.)

## VL und CD4 in treated patients at preliminary treatment stop

98 of 144 patients discontinued antiretroviral therapy after a median treatment time of 9.0 months (range 1.2 – 28.7 months).

	Median	Range	Mean
Absolute CD4 cell counts [ $\mu$ l]	797	392 - 1701	825
Relative CD4 cell counts [%]	37	13 - 67	37
Viral load [copies/ml]	<50	<50 - 7,220	214

At treatment stop, 79/98 patients (81%) had an undetectable viral load, 14 patients (14%) a viral load below 400 copies/ml and 5 patients (5%) had a viral load below 10,000 copies/ml.

## Time to combined endpoint

Time to combined endpoint was evaluated for 154 patients (98 treatment discontinuers and 56 untreated patients).

37/98 of those discontinuing treatment (38%) reached the combined endpoint after a median treatment interruption of 14.3 months. In 20/56 untreated pts (36%), the combined endpoint was reached after a median observation time of 8.3 months after seroconversion. The time until reaching the combined endpoint was significantly different ( $p=0.016$ , Mann-Whitney U), the numbers of patients wasn't significant (Fisher's exact).

## Kaplan-Meier analysis

Figure 1 and 2 show the time until the combined endpoint was reached. Baseline was defined at seroconversion in untreated patients and at time point of discontinuation in treated patients. Patients who did not reach the combined endpoint and patients with a treatment (re-) start in case of CD4<350 or VL<100,000 were censored at the last observation time point. In the subgroup of patients with a baseline viral load > 50,000 copies/ml (Fig 2), the time until the combined endpoint was significantly shorter in treated patients compared with untreated patients.

Fig. 1: Kaplan-Meier analysis for all patients

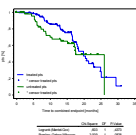
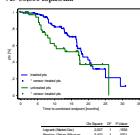


Fig. 2: Kaplan-Meier analysis for patients with a baseline VL>50,000 copies/ml.



## Summary

- 200 (191 male) cases of primary HIV-infection have been reported.
- In 144 patients, treatment was started immediately, 56 patients remained untreated.
- In untreated patients, the median first measured viral load was 240,000 cop/ml versus >500,000 cop/ml in treated patients ( $p<0.001$ ). The respective median absolute CD4 counts were 621/ $\mu$ l and 453/ $\mu$ l ( $p<0.01$ ).
- 98/144 treated patients stopped treatment after a median time of 9.0 months.
- 37/98 of those discontinuing treatment (38%) reached the combined endpoint after a median treatment interruption of 14.3 months. In 20/56 untreated patients (36%), the combined endpoint was reached after a median observation time of 8.3 months after seroconversion.
- For patients with a first measured VL of >50,000 cop/ml, the time until the combined endpoint was significantly shorter in treated patients compared with untreated patients (Breslow-Gehan,  $p=0.02$ ).

## Conclusion

Our cohort shows a trend that early treatment of primary HIV-infection delays the time until possible treatment indication (CD4 counts <350/ $\mu$ l and/or VL >100,000 copies/ml) in patients presenting a viral load VL >50,000 cop/ml during seroconversion.

## Participating centres – The Prime-DAG and Ac-DAG Study Group

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