Nijmegen Institute for Infection, Inflammation & Immunity

Nevirapine dose escalation or immediate full dose when switching from efavirenz to nevirapine in HIV-infected patients in the ATHENA Cohort Study.

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1. BACKGROUND

- When switching from efavirenz (EFV) to nevirapine (NVP) it is unclear whether NVP should be dose escalated or not because of EFV-related enzyme induction.
- Dose escalation of NVP after EFV treatment may be associated with temporary subtherapeutic NVP plasma levels.
- Immediate full dose of NVP may lead to an increased risk of toxicity (e.g. skin rash or hepatotoxicity).

2. OBJECTIVE

- To evaluate the safety and efficacy of dose escalation vs. full dose of NVP in HIV-infected patients switching from EFV to NVP using data from the observational ATHENA cohort.

3. METHODS

- A retrospective analysis was conducted with data from the ATHENA cohort study to compare dose escalation to full dose NVP after treatment switch from EFV.
- We selected HIV-infected patients (≥18 years) from five Dutch hospitals with a treatment switch from EFV to NVP immediate release between 2001 and 2011.
- Patients were required to have used at least 2 weeks of EFV treatment prior to switching, with a maximum of 1 week between the last dose of EFV and the first dose of NVP.
- Dose escalation was defined as 200 mg lead-in daily dose for 1-2 weeks followed by 400 mg/day in two divided doses or once daily.
- Immediate full dose was defined as 400 mg/day in two divided doses or once daily.
- Safety and efficacy outcomes were toxicity-related discontinuation of NVP ≤ 12 weeks after start of NVP treatment and an undetectable viral load at week 24.

4. RESULTS

- Of the 201 included HIV-infected patients the majority of patients (n=159, 79%) switched directly to full dose NVP (Table 1).

Table1: Baseline characteristics of patients with treatment switch to NVP

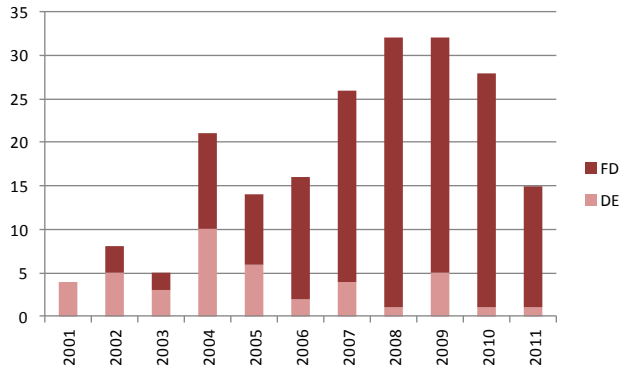
Dosing strategy NVP	Dose escalation		Full dose		p
Total; n=201 (%)	42	(20.9)	159	(79.1)	
Age, median years (IQR)	42	(36-50)	42	(35-49)	0.511
Gender					
Male (%)	29	(69.0)	130	(81.8)	0.071
Female (%)	13	(31.0)	29	(18.2)	
Region of origin					
Western Europe (%)	29	(69.0)	101	(63.5)	0.543
Sub-Saharan Africa (%)	9	(21.4)	32	(20.1)	
Other (%)	4	(9.5)	26	(16.4)	
Undetectable HIV load (%)	28	(66.7)	101	(63.5)	0.741
Nadir CD4 cell count/mm^3, median (IQR)	177	(69-276)	193	(89-260)	0.971
CD4 cell count/mm^3, median (IQR)	505	(315-748)	500	(345-690)	0.963
CD4 cell count/mm^3					
Low; ≤250 female ≤400 male (%)	12	(28.6)	52	(32.7)	0.609
High; >250 female >400 male (%)	30	(71.4)	107	(67.3)	
Duration of EFV treatment, median weeks (IQR)	23	(6-71)	49	(15-101)	0.012
EFV stopped due to toxicity (%)	22	(52.4)	96	(60.4)	0.349

Data are no.(%) of patients, unless otherwise indicated; IQR = interquartile range.

4. RESULTS (continued)

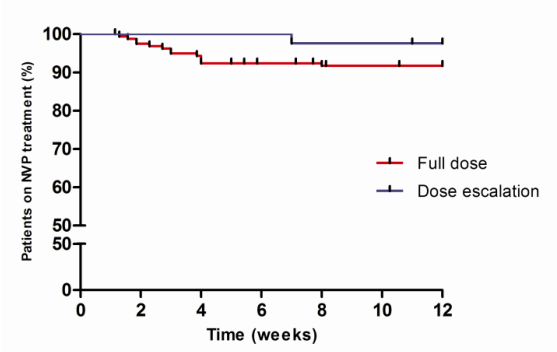
- In the period 2001-2011 there was an increase in switching from EFV to immediate full dose NVP over time (Figure 1).

Figure 1: Number of patients switching from EFV to dose escalation (DE) NVP or immediate full dose (FD) NVP and year of treatment switch.



- In the first 12 weeks after initiating NVP, 13 patients (8.2%) with full dose NVP (n=159) stopped NVP due to toxicity compared to 1 patient (2.4%) in the dose escalation group (n=42). Figure 2 shows the Kaplan-Meier curves for both groups (p=0.18).
- The incidence of toxicity-related NVP discontinuation in our cohort is similar to or below the range of incidences reported in literature.

Figure 2 Kaplan-Meier curves for toxicity-related discontinuation of NVP ≤12 weeks of treatment switch.



- In a Cox proportional hazards model adjusted for CD4 cell count at baseline, the hazard ratio for toxicity-related NVP discontinuation within 12 weeks after starting NVP was 4.19 for patients starting with immediate full dose (95% CI 0.53-32.9; p=0.17).
- No significant association was found between the starting dose of NVP and virological outcome (adjusted odds ratio 0.97, 95% CI 0.34-2.73; p=0.95).
- The limitation of our study is the relatively small number of included patients and toxicity-related NVP discontinuations, especially in the dose escalation group. The impact of other known risk factors for the safety and efficacy of NVP treatment could therefore not be fully assessed.

5. CONCLUSION

- In our Dutch cohort, immediate full dose NVP after switching from EFV is more frequently used than dose escalation, especially in recent years.
- No significant difference was found in toxicity-related discontinuations or virological failures between immediate full dose or dose escalation of NVP after treatment switch from EFV.
- No preference can be given for either dosing strategy.

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