Session 209

Poster H-2296

Toxicity Is Not Related to CD4+ Cell Counts in 221 Patients Switching to Nevirapine (NVP) Due to Simplification or Substitution Strategies (Toscana Study).

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ABSTRACT

Background: In ARV-naïve patients, NVP liver toxicity is related to high CD4+ cells. It is not clear whether this also happens in simplification or substitution strategies.
Methods: Retrospective analysis of 221 patients treated with NVP due to simplification (n=141) or substitution for toxicity (n=43) or bad tolerability (n=37). Liver toxicity defined as increase in 5 times the upper normal level of AST or ALT. CD4+ cell counts defined as high if greater than 250/µL in women and 400/µL in men. Summary statistics for describing variables, relative risk for prevalence, and logistic regression model for liver toxicity associated factors were performed with SAS 9.1.3.
Results: 221 patients were included (164 men, 57 women), with a follow-up of 1134.83 patient-years. Median previous time on viral suppression was 15 months (IQR 4-34), median exposure time to NVP was 36 months (IQR 12-66), median baseline CD4+ cell count was 464/µL (IQR 298-710), with 167 (75.6%) and 54 patients (24.4%) initiating NVP with high (H) and low (L) CD4 + cell counts, respectively. HCV and HBV co-infection were present in 45.7% and 4.5% of patients. Liver toxicity was detected in 18 patients (8.14%), with a prevalence of 6.59% in H and 12.96% in L, and a relative risk of 0.508 (95% CI: 0.207, 1.245) for H. Incidence rate was 1.58/100 patient-years (2.63 in L vs 1.26 in H). The only factor significantly associated to liver toxicity was hepatitis C co-infection (OR: 3.53; 95% CI: 1.19, 10.39). Overall, there were more cases of liver toxicity after 6 months of therapy (61%).
Conclusions: In our cohort, incidence of liver toxicity was low and not related to high CD4+ cell counts. The only factor related to liver toxicity was hepatitis C co-infection. Liver toxicity presented mainly after six months of therapy, was mild to moderate in intensity and always reversible upon suspension of NVP.

BACKGROUND

In ARV-naïve patients, NVP liver toxicity is more frequent with higher CD4+ cell counts (>250/µL in women and >400/µL in men). It is important to clarify if it also happens when NVP is initiated as part of a simplification or substitution strategy.

OBJECTIVES

• To analyse the influence of CD4+ cell counts in the emergence of liver toxicity in patients initiating NVP in the context of a simplification or substitution strategy.

• To determine the factors associated to the development of liver toxicity in those patients.

METHODS

• Design: Retrospective analysis of 221 patients treated with NVP due to simplification (n=141), or substitution for toxicity (n=43) or bad tolerability (n=37).

• Setting: Outpatient clinics for patients with HIV infection/AIDS in 6 different urban hospitals in Galicia (Spain).

• Main outcome measures: Liver toxicity was defined as increase in 5 times the upper normal level of AST or ALT. CD4+ cell counts defined as high if greater than 250/µL in women and 400/µL in men.

• Statistical analysis: Summary statistics for describing variables, relative risk for prevalence, and logistic regression model for liver toxicity associated factors were performed with SAS 9.1.3.

RESULTS

Baseline Characteristics (n=221 patients)

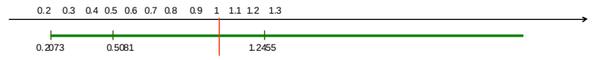
GENDER:	
- Male	164 (74%)
- Female	57 (26%)
AGE (median, range)	42 (31-54)
RISK FACTORS FOR HIV INFECTION:	
- IVDU	53 (47%)
- Unsafe sex	59 (53%)
CD4 Count, cells/ mm^3	
- High (women >250/µL, men >400 µL)	167 (75.6%)
- Low (women <250/µL, men <400 µL)	54 (24.4%)
HIV RNA < 1.7 log	166 (75.1%)
Time on previous virologic suppression	
- Median	15 months
- Mean	22 months
- IQR (25-75)	4-34 month
Reason for initiating NVP:	
- Simplification	141 (63.8%)
- Toxicity	43 (19.5%)
- Bad tolerability	37 (16.7%)
HCV infection:	
- Anti-HCV antibodies	101 (45.7%)
- Detectable HCV RNA	69 (31.2%)
HBV infection:	
- HBsAg (+)	10 (4.5%)

Liver toxicity and CD4+ cell counts

	Liver toxicity					
	No		Yes		All	
	#	%	#	%	#	%
Baseline CD4+						
High	156	93.41	11	6.59	167	100.00
Low	47	87.04	7	12.96	54	100.00
All	203	91.86	18	8.14	221	100.00

BaselineCD4+	Lower limit	Ratio	Upper limit
High	0.03717	0.06587	0.11409
Low	0.06424	0.12963	0.24422
All	0.05214	0.08145	0.12506
Difference	-0.18189	-0.06376	0.01749

Relative risk			
	Value	95% Confidence limits	
Low CD4+ Cohort	1.0733	0.9610	1.1987
High CD4+ Cohort	0.5081	0.2073	1.2455



Relative risk of having high CD4+ cells count for liver toxicity when switching to NVP

	Episodes of liver toxicity	Lower limit	Incidence (100 pat-year)	Upper limit
High CD4+	11	0.632	1.265	2.265
Low CD4+	7	1.058	2.632	5.424
All	18	0.940	1.586	2.507

Moment of liver toxicity appearance

		#	%
High CD4+	**Before 3 months of NVP**	2	18.18
	3 to 6 months of NVP	3	27.27
	After 6 months of NVP	6	54.55
Low CD4+	**Before 3 months of NVP**	1	14.29
	3 to 6 months of NVP	1	14.29
	After 6 months of NVP	5	71.43

NVP therapy durability and reasons of NVP discontinuation

Reason for NVP discontinuation	#	Mean	Median	Minimum	Maximum	IQR 25	IQR 75
Withdrawal	24	25.60	22.00	0.50	69.00	12.00	39.00
Failure	164	46.79	45.50	4.00	132.00	18.50	70.50
Toxicity	29	13.74	6.00	0.25	78.00	1.00	13.00

Factors associated to liver toxicity

Factor	Odds ratio	95% Confidence interval		P (Chi Square)
HCV co-infection	3.530	1.198	10.399	0.0221
Rash	3.833	0.919	15.978	0.0651

CONCLUSIONS

• In our cohort, incidence of liver toxicity was low and not related to high CD4+ cell counts.

• The only factor related to liver toxicity was hepatitis C co-infection.

• Liver toxicity presented mainly after six months of therapy, was mild to moderate in intensity and always reversible upon suspension of NVP.