Nevirapine use in a large multi-ethnic South London HIV cohort

Roberta Brum[1], Emily Mabonga[1], Ronak Rajani[2],Chris Taylor[1], Emily Cheserem[1]

[1]Department of Sexual Health and HIV, King's College Hospital London UK,

[2]Guy's and St Thomas' Hospital, London ,UK

Introduction

- British HIV Association (BHIVA) guidelines[1] suggest that nevirapine (NVP) may be used as a third agent in the treatment of treatment-naive HIV-1 infection where the CD4 count is <250 cells/μL in women and <400 cells/μL in men. Additionally, antiretroviral therapy may require changing because of side effects or for other reasons. A switch to NVP may be considered in patients due to tolerability issues.
- Despite this recommendation, NVP is not used widely, owing to concerns relating to reported severe drug hypersensitivity beyond these thresholds.
- The aim of the current study was to describe our experience in using NVP within the BHIVA guidelines.

Methods

- A retrospective analysis of patients commenced on NVP at the Caldecot Centre King's College Hospital between January 2011 and December 2012 was performed.
- Full demographic data was collected along with the indication for NVP usage, CD4 count, drug tolerability, virological outcome and adverse drug reactions during the study period.
- All data was collected and analyzed with SPSS for MAC.

Table 1: Rash - severity grading[2]

Grade 1	Localised skin eruption
Grade 2	Diffuse skin eruption up to 50% of the body surface area (BSA)
Grade 3	Generalized skin eruption involving >50% BSA, or rash with bullae, vesicles, mucous membrane, ulceration, target lesions, purpura, or with epidermal detachment

Table 2: Drug induced liver injury - severity grading, with values expressed as multiples of the upper limit of the normal range (ULN)[3]

Feature	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
ALT	<1.25	1.25-2.5	2.5-5.0	>5.0-10	>10
AST	<1.25	1.25-2.5	2.5-5.0	>5.0-10	>10
ALP	<1.25	1.25-2.5	2.5-5.0	>5.0-10	>10
GGT	<1.25	1.25-2.5	2.5-5.0	>5.0-10	>10
Bilirubin	Normal	>1.0-1.5	>1.5-2.5	>2.5-5	>5

Results

- 97 patients were identified, with a median age of 38 years (range 18-68), of whom 49% were male, 65% were of black ethnicity and 71% were heterosexual.
- Of these, 64 (66%) patients were ARV naive whilst 33 patients (34%) were switched to NVP. For naive individuals the median CD4 count at NVP initiation for women was 115(2-366) cells/μL and for men 222(1-404) cells/μL (p<0.001). For patients switched to NVP the median CD4 count was 363(90-1198) cells/μL.
- The main indications for initiation of NVP in naive patients were clinician choice (42%) and psychiatric illness (11%) whilst switching to NVP was mainly due to CNS side effects of Efavirenz (66%) and pregnancy planning (15%). Other side effects which led to a switch to NVP were effects of protease inhibitors which were gastrointestinal (10%) and metabolic (3%).
- The main nucleoside backbone prescribed with NVP was Truvada (50/97).
- Tuberculosis was present in 5 patients whilst just one was co-infected with hepatitis. PCP was the commonest opportunistic infection amongst this cohort and HIV encephalitis was the main reason to start NVP for three patients.
- During follow-up NVP was stopped in 16 patients [11(17%) naive vs. 5 (15%) switchers (p=0.78)] after a median of 30 (range 15-420) days. A total of 8 patients developed a rash [grade ≥ 2 rash: 4(6%) naive vs. 2(6%) switchers, p=0.97]. Hepatotoxicity developed in 14 patients [10(15%) naive vs. 4(12%) switchers, p=0.79].

Table 3: Reasons for discontinuation of NVP

Related to NVP hypersensitivity	
Rash	6
Rash and hepatotoxicity	2
Hepatotoxicity	4
Unrelated to NVP hypersensitivity	
Compliance	3
Virological failure	1
Drug-drug interactions	1
Total	**16**

Fig 1: Rates of hepatotoxicity - naïve patients (n=64)

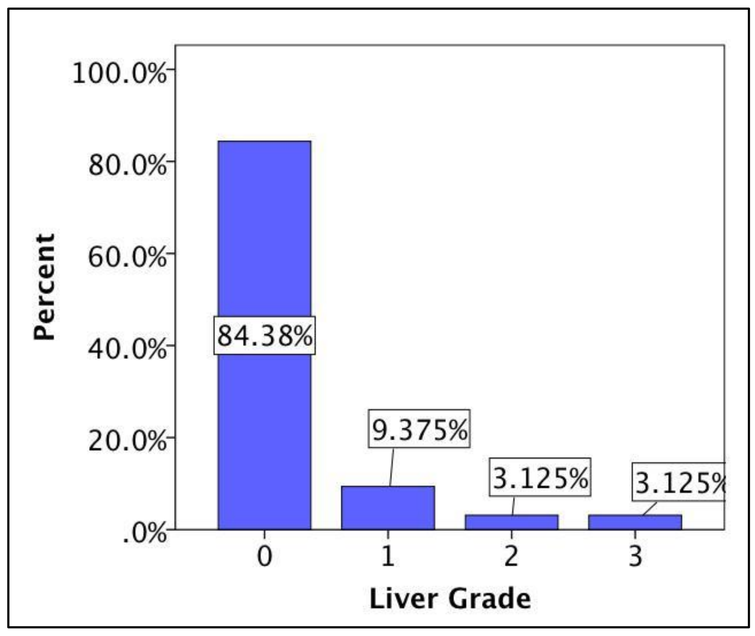


Fig 2: Rates of rash- naïve patients (n=64)

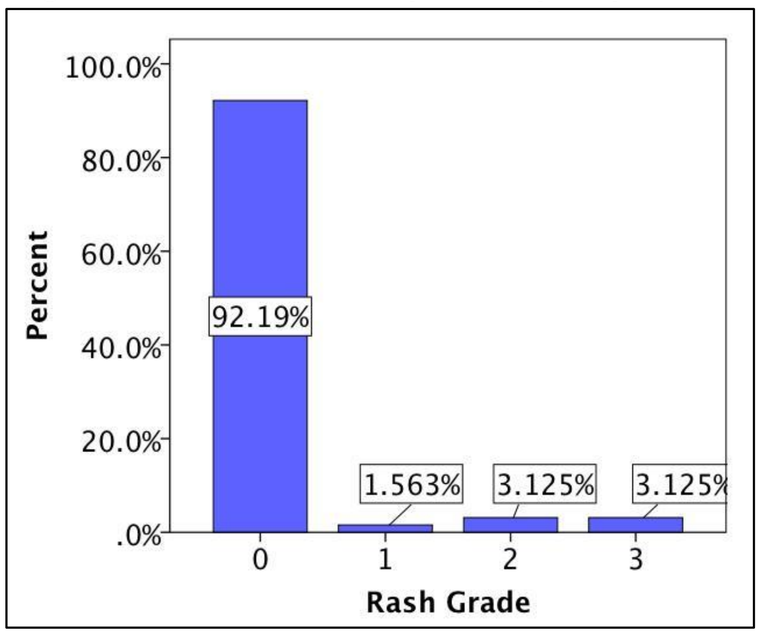


Fig 3: Rates of hepatotoxicity – switch patients (n=33)

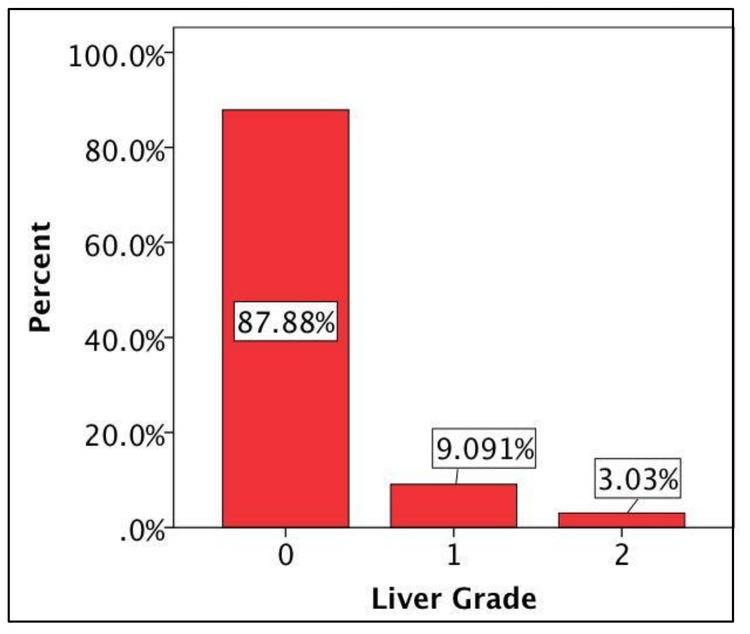
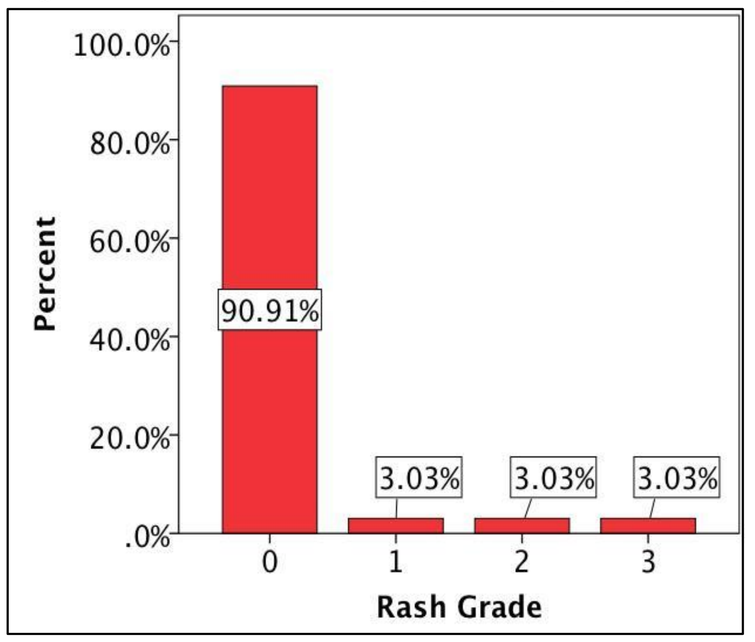


Fig 4: Rates of rash- switch patients (n=33)



Conclusions

The use of NVP as a third agent for the treatment of HIV-1 is equally well tolerated in naive patients and patients switched to NVP. In 12% of individuals adverse drug reactions (rash and hepatotoxicity) were responsible for NVP cessation. There was only one serious adverse reaction requiring hospital admission, this occurred in a male switch patient day 12 of NVP initiation CD4 836 cells/μL. In all patients symptoms resolution occurred following the cessation of NVP. Our findings confirm that NVP can be used safely in both naive and patients switching treatment for HIV.

References

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