SYSTEMATIC REVIEW OF NEVIRAPINE VERSUS EFAVIRENZ CONTAINING THREE DRUG REGIMENS FOR INITIAL TREATMENT OF HIV INFECTION

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ABSTRACT

Background: Comparative trials have shown that 3-drug combination regimens containing a non-nucleoside reverse transcriptase inhibitor (NNRTI) are equivalent to or better than those containing a protease inhibitor. In this systematic review we compared the efficacy of a 3-drug initial regimen containing the NNRTI efavirenz (EFV).with one containing nevirapine (NVP) in antiretroviral-naïve patients.

Methods: We compared studies that included a 3-drug regimen comparing two nucleoside reverse transcriptase inhibitors (NRTI) plus EFV with 2 NRTIs plus NVP in separate arms. Our primary end-point was the proportion of antiretroviral-naïve participants who achieved virologic suppression. We searched AIDSDRUGS, AIDSLINE, AIDSTRIALS, specialized Cochrane Collaboration registries, EMBASE, MEDLINE and MetaRegister of Controlled Trials for the years 1996-2001 and searched conference abstracts through March 2003. We compared efficacy using random-effects meta-analysis and computed Peto odds ratios with 95% confidence intervals.

Results: We identified six completed studies with 3,205 antiretroviral-naïve participants, including two randomized controlled trials (RCT) and four cohort studies in which results were separately reported for antiretroviral-naïve subjects. EFV-containing regimens were equivalent to NVP-containing regimens at 24 and 48-52 weeks (OR=1.20, 95% CI=0.85, 1.69). The results from the RCTs (OR=1.17, 95% CI =0.90, 1.53) were similar to those from the cohort studies (OR=1.15, 95% CI=0.67, 1.97).

Conclusions: We conclude that the short-term efficacy of EFV-containing and NVP-containing regimens for treatment of antiretroviral-naïve patients is equivalent. Deciding which NNRTI to use for initial therapy should be based on differences in longer-term efficacy, adherence, toxicity, cost and availability.

BACKGROUND

Advantages of NNRTIs

Adherence	PI-sparing
•Dosing	•Efficacy NNRTIs = PIs
•Diet	•Metabolic effects
•Tolerability	•PI salvage therapy

METHODS

Meta-Analysis

- Initial therapy
- Primary endpoint = viral suppression, a surrogate marker for clinical progression

Arm #1	Arm #2
2NRTIs + EFV	2NRTIs + NVP

METHODS (cont'd)

Literature search:
(1996-2002)
- MEDLINE
- EMBASE
- AIDSDRUGS
- AIDSLINE
- AIDSTRIALS
- MetaRegister of Controlled Trials
- Cochrane Library

Statistical methods:
- Dichotomous odd ratios (Peto) with 95% confidence intervals
- Random-effects meta-analysis

RESULTS: Studies Identified

6 Studies Identified:
4 published
+
2 meeting abstracts
→ 2 RCTs + 4 Cohort

3,205 ARV-naïve study participants

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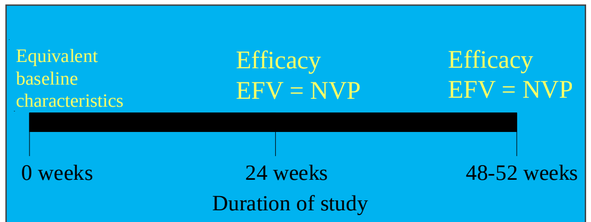
RESULTS: Study Arm Comparison



Viral suppression with EFV compared to NVP
- RCTs: OR=1.17, 95%CI = 0.90,1.53
- Cohort studies: OR=1.15, 95%CI = 0.67,1.97

CONCLUSIONS

Recently available results from the 2NN study found equivalent efficacy of EFV and NVP
(Results of the 2NN Study. F van Leth et al. Presented at the 10th Conference on Retroviruses and Opportunistic Infections, Feb. 10-14, 2003, Boston. Abstract 176.)

1st direct comparison in large RCT	Study sites include resource poor countries	But… NVP reduces TC/HDL and is associated with more liver lab AEs

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CONCLUSIONS (cont'd)

We conclude that the short-term efficacy of EFV-containing regimens and NVP-containing regimens for treatment of antiretroviral-naïve patients is equivalent.

Which NNRTI do you choose, EFV or NVP???

- Longer-term efficacy → Future RCT
- Adherence → Future studies
- Toxicity → NVP more liver, EFV more CNS
- Availability/Cost → Local considerations

SUMMARY

EFV	NVP
• CNS toxicity	• LFT monitoring
• No lipid-lowering	• Rarely severe rash (Stevens-Johnson)
• Contraindicated in pregnancy	• Resistance to PMTCT