

Topic	Comparison of first line antiretroviral therapy with regimens including Nevirapine, efavirenz, or both drugs, plus stavudine and lamivudine: a randomized open – label trial, the 2 NN Study
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Audience	Medical School staff and students, staff and students of Makerere University Institute of Public Health, staff of Non governmental Organizations
Main Points Background	The 2NN Study was a randomized comparison of non- nucleoside reverse-transcriptase inhibitors (NNRTI) NVP and efavirenz
Methods	<ul style="list-style-type: none"> ▪ Study participants were recruited during regular visits to HIV/AIDS treatment centers ▪ Eligible patients were ART naïve, chronically infected with HIV-1 RNA of more than 5000 copies per mL ▪ There were no inclusion criteria for the number of CD4 – positive T lymphocytes or disease stage. This was because of pregnancy or lactation ▪ The study was approved by the ethics review bodies in the participating countries and all the patients gave written informed consent <p>Design and interventions;</p> <ul style="list-style-type: none"> ▪ All patients received stavudine 40 mg twice daily (30 mg twice daily if weight was less 60 kg) and lamivudine 150 mg once daily ▪ They also received NVP 400mg once daily, NVP 200mg twice daily, efavirenz 600mg once daily or a combination of NVP 400 mg once daily and efavirenz 800 mg once daily ▪ The higher dose of efavirenz when it is used in combination is recommended because efavirenz concentrations are lowered when the drug is used in normal dosing in the presence of NVP ▪ A treatment allocation sequences was generated by use of the minimization variables CD4- positive T- cells. Treatment allocation was stratified by baseline plasma HIV-1 RNA concentration ▪ The study started with 3 comparison of groups, an estimated sample size of 450 and treatment allocation ratio of 1:1:1 for NVP once daily, efavirenz and NVP plus efavirenz ▪ The group assigned NVP twice daily, was assigned 5 months later because another study had found that the efficacy of NVP was related to the minimum concentration and raised the issue of once –daily NVP resulted in a highly enough minimum concentration. ▪ The focus of the trial shifted to comparisons of NVP twice

	<p>daily Vs effivirens and of NVP once daily Vs twice</p> <ul style="list-style-type: none"> ▪ By protocol, patients were not allowed to change any component of their allocated treatment for more than 5% of the follow up time. The only exception was change of stavudine for reasons of toxicity, provided that the 2 NRTI drugs were used at all times ▪ Women who had become pregnant while taking effivirens were switched to NVP and could remain in the study, but they were judged to have had a change of allocated treatment
Results	<ul style="list-style-type: none"> ▪ Treatment failure occurred in 43.6 % of 200 patients assigned NVP once daily, 43.7% of the 387 assigned NVP twice daily, 37.8% of 400 assigned effivirens and 53.1 of the 209 assigned NVP plus effivirens ▪ The difference between NVP twice daily and effivirens was 5.9% ▪ There was no significant differences among the study groups in the proportions with HIV-1 RNA concentrations below 50 copies per mL at week 48 weeks or the increase in CD4-positive cells ▪ NVP plus effivirens was associated with the highest frequency of clinical adverse events and NVP once daily with significantly more hepatobiliary laboratory toxicities than the effivirens.
Conclusion	<ul style="list-style-type: none"> ▪ The Antiretroviral therapy with NVP or effivirens showed similar efficacy, so triple-drug regimens either NNRTI are valid for first line treatment ▪ There are however, differences in safety profiles. Combination of NNP and effivirens did not improve efficacy but caused more adverse effects