

Efavirenz versus Boosted Atazanavir or Zidovudine and Abacavir in Antiretroviral Treatment–Naive, HIV-Infected Subjects: Week 48 Data from the Altair Study

BACKGROUND:

- Current guidelines for HIV treatment recommend 2 nucleo(t)side reverse transcriptase inhibitors (NtRTIs) with either a non-nucleoside reverse transcriptase inhibitor (NNRTI), a boosted protease inhibitor (PI), or an integrase inhibitor.
- Drug interactions and conditions such as pregnancy, opiate replacement, and tuberculosis treatment make current regimens difficult.
- Previous trials have shown triple NtRTI therapy to be less efficacious than conventional treatment due to lower levels of antiretroviral potency and drug resistance.
- A study comparing quadruple NtRTI therapy showed promising results, but it was not powered appropriately.

OBJECTIVES:

- To determine the efficacy and safety of three strategic regimens of initial antiretroviral therapy containing a fixed dose formulation of tenofovir and emtricitabine, with either efavirenz or ritonavir boosted atazanavir or zidovudine plus abacavir.

METHODS:

- **Design:** Randomized, open-label, parallel trial; data presented is from 48 weeks, but will extend to 96 weeks.
- **Inclusion Criteria:**
 - Otherwise healthy antiretroviral treatment-naïve adults with HIV
 - CD4+ cell counts >50 cells/mL
 - Plasma HIV-1 RNA >2000 copies/mL
 - Creatinine clearance of ≥70 mL/min
 - No evidence of HIV resistance
- **Exclusion Criteria:**
 - HLA-B*5701–positive
 - Pregnant and/or breastfeeding
 - Used prohibited substances
 - Had serious infection or illness requiring intervention
 - Known renal insufficiency, obstructive liver disease, intractable diarrhea, cardiomyopathy, or substantial cardiovascular disease
- **Primary Outcome Measure:** Virological efficacy, as measured by the time-weighted mean change from baseline plasma HIV-RNA
- **Secondary Outcome Measure:** Virologic, immunologic and safety end points:
 - Proportion of patients w/ <200 copies/mL, virologic rebound, Increase in CD4 count, number of serious adverse events and the number of patients experiencing them, immune reconstitution inflammatory syndrome (IRIS) occurrence and mean time to occurrence, and other health outcomes
- 322 patients completed the study
 - Arm I – 114 received:
 - Tuvada (tenofovir 300mg qd + emtricitabine 200mg qd) once daily
 - Efavirenz 600mg qd once daily
 - Arm II – 105 received:
 - Tuvada (tenofovir 300mg qd + emtricitabine 200mg qd) once daily
 - ritonavir/atazanavir 100mg/300mg qd once daily (taken with food)
 - Arm III – 103 received:
 - Tuvada (tenofovir 300mg qd + emtricitabine 200mg qd) once daily

- Zidovudine 250mg/300mg qd (taken in two equal doses approximately 12 hours apart)
- Abacavir 600mg qd

RESULTS:

- The intention-to-treat population comprised 322 patients (Arm I, $n=114$; Arm II, $n=105$; and Arm III, $n=103$).
- Noninferiority for the primary end point was established.
- The proportions of patients in each of Arm I (95%) and Arm II (96%) with <200 copies/mL were not statistically significantly different ($p=0.75$), but Arm III (82%) was significantly lower ($p=0.005$)
- Serious AEs were more common in Arm III ($n=30$) than in Arms I or II ($n=15$) ($p=0.062$)
- The authors concluded that quadruple NtRTI therapy is noninferior in terms of virological efficacy but inferior in terms of secondary endpoints. It should not be used first-line in patients with other treatment options.

STRENGTHS:

- Randomized, parallel groups
- Used both Intent-to-treat and per protocol statistical analyses
- Inclusion/exclusion criteria were appropriate and representative
- Active control was gold standard HAART treatment
- Data handling methods were very clear

LIMITATIONS:

- Open label
- How/from where patients recruited was not clear
- Race/ethnicity breakdown in the study was not representative of race/ethnicity breakdown in the diagnosed general population
- Secondary outcomes not clearly listed in the methods, and some are not reported completely in the text
- Power not reported, and Type II error was a concern for several outcome measures
- Adherence was only measured for two one-week periods and was self-reported
- Inherent differences in dosing regimens (qd vs. bid) which could have affected adherence
- Disproportionate number of dropouts from one treatment arm due to adverse effects of medication
- Other medications taken/diet/other variables were not reported

CONCLUSION:

- Due to efficacy and safety concerns, quadruple NtRTI therapy should not be used first-line in patients with other treatment options.
- Quadruple NtRTI therapy could be a possible treatment options in individuals with contraindications to other conventional regimens or in individuals with multiple drug resistances.
- Further studies looking at quadruple NtRTI therapy against other salvage regimens could be useful.

REFERENCE:

Puls RL, Srasuebku P, Petoumenos K, Boesecke C, Duncombe C, Belloso WH, Molina JM, Li L, Avihingsanon A, Gazzard B, Cooper DA, Emery S; Altair Study Group. Efavirenz versus boosted atazanavir or zidovudine and abacavir in antiretroviral treatment-naive, HIV-infected subjects: week 48 data from the Altair study. Clin Infect Dis. 2010 Oct 1;51(7):855-64.

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09-28-2010