ANRS 146 OPTIMAL PHASE III TRIAL: MARAVIROC PLUS CART IN ADVANCED HIV-1+ PATIENTS

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General Abstract

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Background:

Late HIV diagnosis is associated with an excess risk of AIDS-Defining-Events (ADE) and mortality that is associated with excessive immune activation. Clinical trials with maraviroc (MVC) have showed that its use may impact immune activation and improve CD4 T cell recovery. We hypothesized that the addition of MVC to cART in naïve patients with low CD4 cell counts will accelerate the kinetics of immune restoration and decrease the risk of disease progression and death.

Methods:

ANRS 146 OPTIMAL trial (NCT01348308) was an European, multicenter, randomized, double-blind, phase III trial, in France, Spain and Italy in ART-naïve HIV1 infected adults with CD4+ count <200/μL or an ADE. Participants were randomized (1:1) to receive cART plus placebo or MVC for 72 weeks. The primary composite end point was any new ADE, serious non–AIDS-defining event, IRIS, or death from any cause. The primary endpoint and its components were compared using Kaplan–Meier estimates and Cox proportional-hazards models. In a post-hoc analysis, a Poisson regression model was used to analyze occurrence of all events and the study period (0-24 versus 24-72 weeks) treatment effect interaction.

Results:

Between October 2011 and November 2014, 416 participants were randomized, 409 did not withdraw before week 0. At study entry, the median HIV viral load was 5.39 log10 copies/mL, the median CD4+ count 80 cells/μL and 42% of participants had an ADE. Up to 72w, no difference was seen in the CD4 cell increase (+258.3±8.9 vs +254.2±9.2/μL) (p=0.746). 74 events occurred in 53 participants: 42 events in 27 participants in the placebo group and 32 events in 26 participants in the MVC group. The incidence of the first event was 11.2 events per 100 person-years in the placebo group versus 11.1 events per 100

person-years in the MVC group with a hazard ratio of 0.97 (95% confidence interval [CI], 0.57-1.67). The Poisson regression analysis showed that the incidence rate ratio (IRR) of the two groups differed significantly between periods 0-24 and 24-72 weeks with respective IRR of 0.61 (95% CI: 0.33-1.08) and 2.90 (95% CI: 0.86-12.49) (p =0.016).

Conclusion:

The results of this large randomized trial showed that adding MVC to cART does not impact the occurrence of serious disease or death in advanced HIV1+ patients. However, post hoc analysis showed a trend for a beneficial effect of the addition of MVC in the first 24 weeks that disappeared thereafter. Mechanisms associated with this dual effect are currently under investigation.

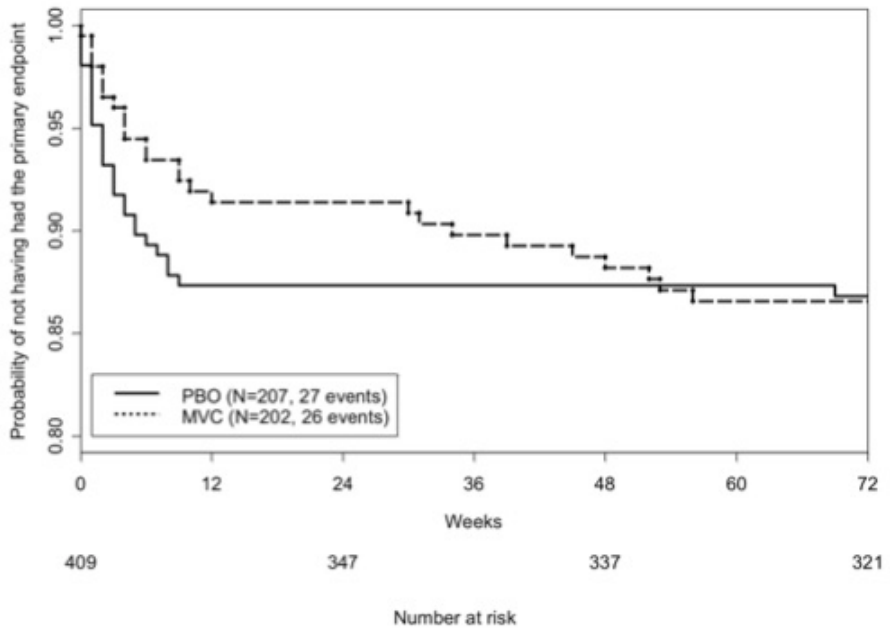
Clinical:

(H) Antiretroviral Therapy: Pre-Clinical and Randomized Trials

Keywords:

Antiretroviral therapy intensification
Late presentation
Randomized double-blind placebo-controlled trial

Figure: Kaplan–Meier estimates of the cumulative percentages of patients not having had the composite primary end point (Time to first primary endpoint)



(https://ww2.aievolution.com/cro1701/files/content/abstracts/abs_2212/OptimalFigure.jpg)

Additional Information about the Submission

Prior Presentation or Publication: In general, CROI does not accept work that has been previously published or publically presented (especially if at conference of more than 400 attendees). Consideration may be given to a submission if

meaningful newer data or different analyses are included. Have your study data or abstract information been published, submitted for publication where publication is anticipated on or before December 31, 2016, or presented at any other major national or international scientific or medical conferences (ie, generally 400 or more attendees)?

No