COMPARISON OF THE EFFICACY OF PREFERRED ANTIRETROVIRAL REGIMENS IN PATIENTS WITH CD4 CELL COUNTS <200 or ≥200/μL OR VL >100,000 or ≤100,000 Cop/mL. A SYSTEMATIC REVIEW WITH META-ANALYSIS. GeSiDA-1152 STUDY.

Jose A. Pérez-Molina1, Clara Crespo Andújar2, Javier Zamora1, Borja M. Fernández-Feliú2, Andrea Gaetano-Gil3, Juan Carlos López Bernolda de Quirós4, Sergio Serrano-Villar2, Santiago Moreno1, Juan Berenguer1
1Infectious Diseases Department, Hospital Universitario Ramón y Cajal (HRUC) and CIBERHIV, Madrid, Spain. 2Clinical Biostatistics Unit, Hospital Universitario Ramón y Cajal (HRUC) and CIBERESP, Madrid, Spain. 3Institute of Metabolism and Systems Research. University of Birmingham, UK. 4HIV Unit, Hospital Universitario Gregorio Marañón, Madrid, Spain

OBJECTIVE To assess the impact of low CD4 cell counts or high HIV-RNA viral load on the efficacy of currently preferred ART regimens for HIV-1-infected naïve adults.

MATERIALS AND METHODS

- We performed a systematic literature review and meta-analysis limited to articles published from JAN/2006 to SEP/2021 with no language restrictions, following the PRISMA statement to report our findings. The protocol of the study is available at https://ufafud.hgf.
- We selected first-line ART recommended in the leading guidelines (US DHHS, IAS-USA, EACS and GeSiDA) for the year 2021. We included randomized, controlled, clinical trials of naïve adult patients with a follow-up of at least 48 weeks which provided subgroup analysis by CD4 cell count (<200 vs. ≥200/μL) or HIV-viral load (>100,000 vs. ≤100,000 copies/mL) and information on treatment response in at least one of the two subgroups to be analyzed.
- We analyzed the primary outcome of efficacy for every arm of included studies (by CD4 cell count and VL subgroups), as the proportion of participants with an undetectable VL at 48 weeks by intent-to-treat analysis, as defined in each trial (time to virologic failure or snapshot algorithms). We also analyzed as secondary outcomes: the proportion of participants with undetectable VL at 96 weeks and the proportion of participants with undetectable VL at 48 weeks by baseline VL >500,000 copies/mL vs. ≤500,000 copies/mL.
- This meta-analysis is focused on whether there was an increased risk of failure in particular subgroups. To test that hypothesis, for each study arm, we calculated the ratio of the odd of treatment failure at 48/96 weeks of the subgroup of patients with CD4 <200/μL (or >100,000 copies/mL) to the odd of the same outcome in the subgroup of patients with CD4 ≥200/μL (or ≤100,000 copies/mL). Across studies ORs were pooled using a random effects model.
- We explored different sources of heterogeneity by fitting meta-regression models and subgroup analysis to explore the following characteristics: year of publication, type of integrase inhibitor or NRTI included in ART. The likelihood of publication bias was evaluated through funnel plots and statistical tests for ‘small study effects’ (Egger’s test and Pater’s test).

RESULTS

- We identified a total of 1,233 articles of which we finally selected 23, corresponding to 12 RCT: 17 ART arms (659 participants) for CD4 cell and 18 ART arms (884 participants) for VL subgroups, respectively.
- Patients with <200 CD4 cell or VL >100,000 copies showed an increased odds of treatment failure at 48W: OR 1.84 (95 CI: 1.45-2.31; p-value: 0.07) and OR 1.74 (95%CI: 1.26-2.41; p-value: 0.045) (Panel A), respectively. This effect was fairly homogeneous across all study arms, even with the subgroup <500,000 copies/mL (Panel B).
- The OR for treatment failure remained significantly higher at 96W OR 1.54 for CD4 cell <200/μL and VL >100,000 copies/mL, subgroups, respectively (Panel B).
- We did not identify significant heterogeneity at 48W regarding INSTI, NRTI backbone, quality of subgroup analysis, or studies’ year of publication. Significant heterogeneity was detected at 96W for the NRTI backbone in the CD4 cell subgroup and for the INSTI in the VL subgroup.

CONCLUSIONS

- Low CD4 cell counts and high VL are associated with poorer ART outcomes in treatment naive patients. At 48W, this effect does not seem related to the individual drugs comprising the ART regimen though more information is needed given the high uncertainty of the estimations.
- As these factors are not modifiable in treatment-naive patients, comparative RCTs should determine the best ART in patients with severe immunosuppression or high VL.