P008

XIII CONGRESO NACIONAL GeSIDA Grupo de Estudio del SIDA - SEIMC

COMPARISON OF THE EFFICACY OF PREFERRED ANTIRETROVIRAL REGIMENS IN PATIENTS WITH CD4 CELL COUNTS <200 vs ≥200/µL OR VL >100.000 vs ≤100.000 Cop/mL. A SYSTEMATIC REVIEW WITH META-ANALYSIS. GeSIDA-11520 STUDY.

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OBJETIVE 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

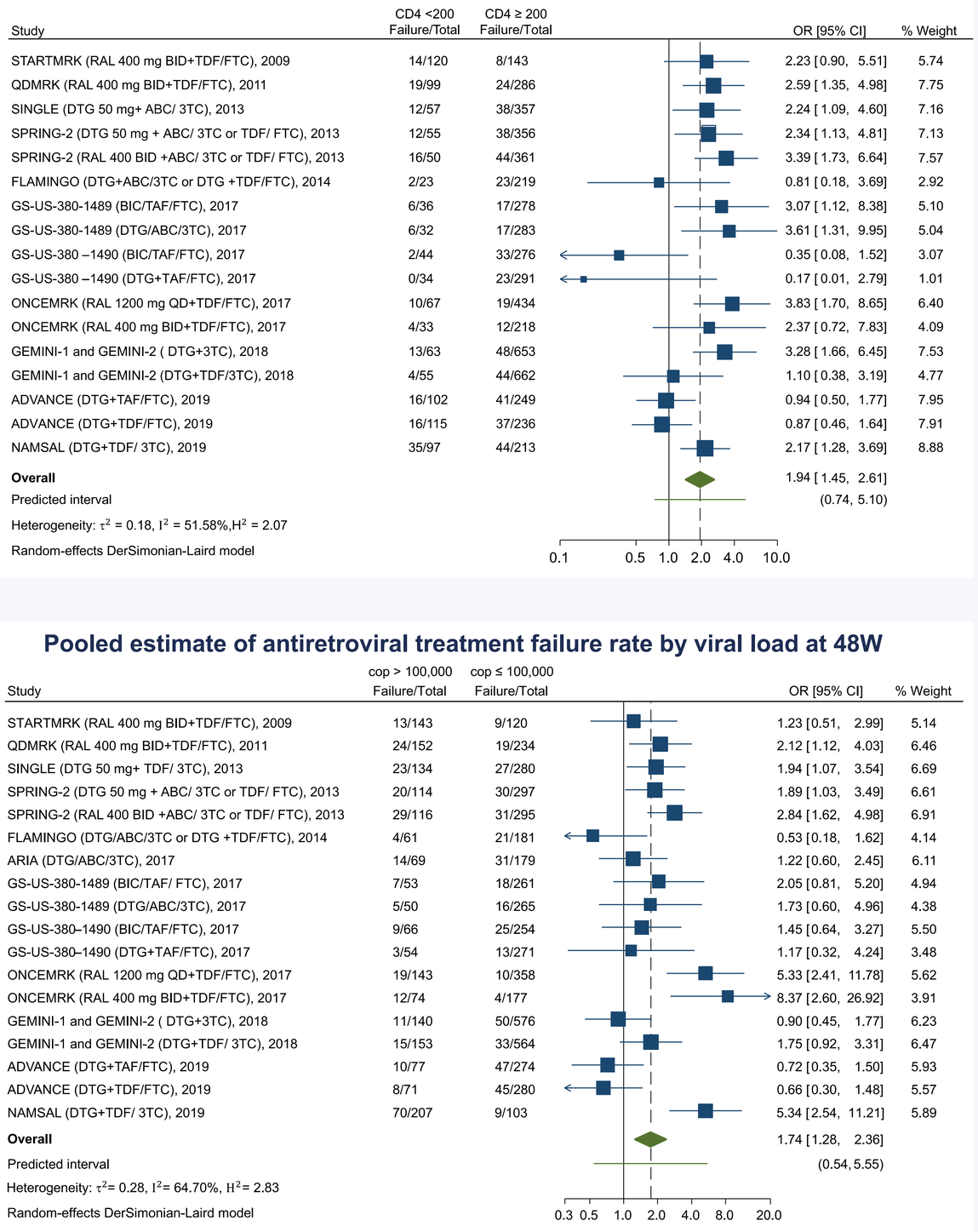
- We performed a **systematic literature review and meta-analysis** limited to articles published from JAN/2006 to SEP/2021 with no language restrictions, following the PRISMA statement to report our findings. The protocol of the study is available at https://osf.io/s7ahx. We selected **first-line ART 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 cell/µL) or **HIV-viral load** (<100.000 vs. ≥100.000 cop/mL) and information on treatment response in at least one of the two subgroups to be analysed.
- 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 metanalysis is **focus 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 cells/µL (or >100.000 cop/mL) to the odd of the same outcome in the subgroup of patients with CD4 ≥200 cells/µL (or ≤100.000 cop/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 Peter's test).

RESULTS

- We identified a total of **1223 articles** of which we finally selected 23, corresponding to **12 RCT: 17 ART arms (6597 participants) for CD4 cell and 18 ART arms (6845 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 1.94** (95% CI: 1.45-2.61; prediction interval 0.74-5.1) and **OR 1.74** (95%CI: 1.28-2.36; prediction interval 0.54-5.55) (Panel A), respectively. This effect was fairly homogeneous across all study arms, even in the subgroup with >500.000 cop/mL (Panel B).
- The **OR** for treatment failure remained **significantly higher at 96W**: **OR 1.46** and **OR 1.54** for CD4 cell <200 cell/mL and VL >100.000 cop/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.

Panel A

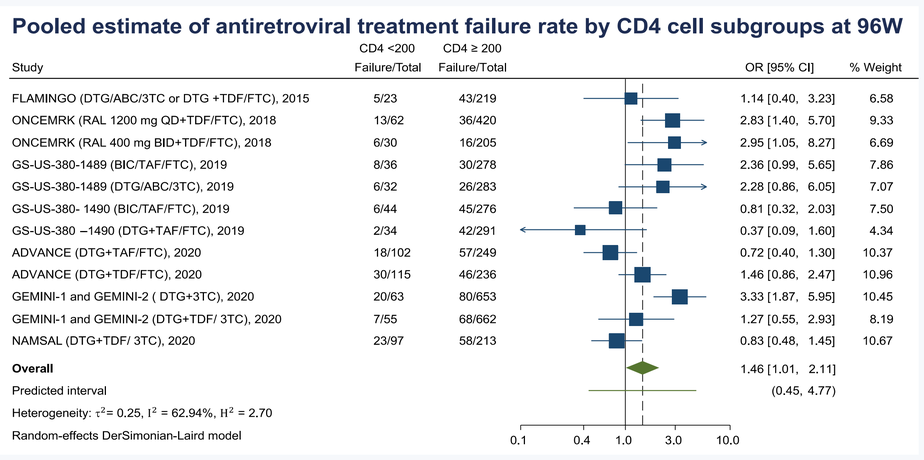
Pooled estimate of antiretroviral treatment failure rate by CD4 cell subgroups at 48 weeks



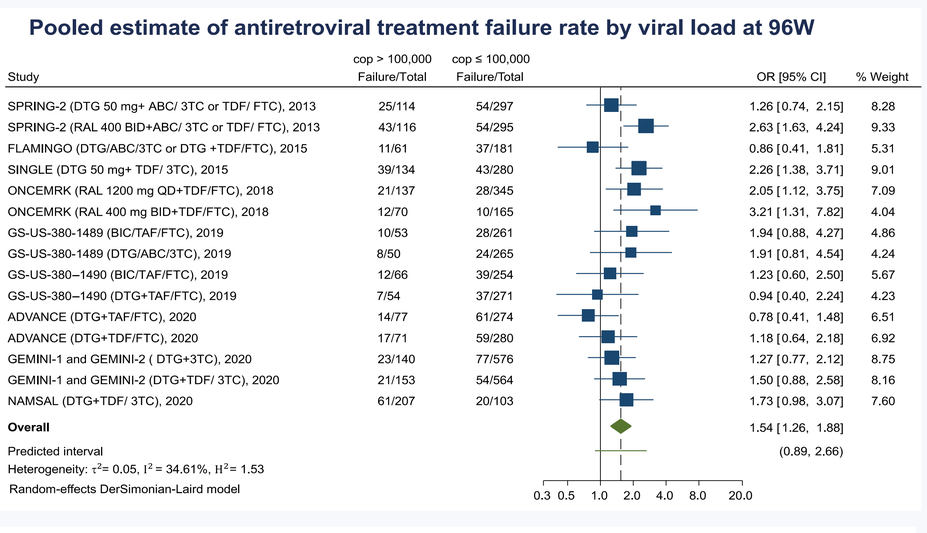
Pooled estimate of antiretroviral treatment failure rate by viral load at 48W

Panel B

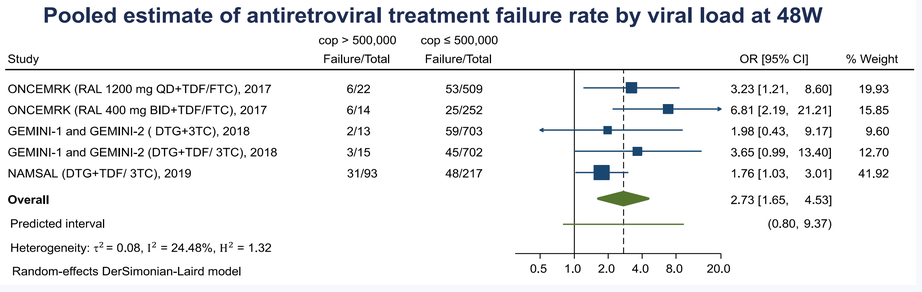
Pooled estimate of antiretroviral treatment failure rate by CD4 cell subgroups at 96W



Pooled estimate of antiretroviral treatment failure rate by viral load at 96W



Pooled estimate of antiretroviral treatment failure rate by viral load at 48W



We did not detect significant publication bias

CONCLUSIONS

- **Low CD4 cell counts and high VL are associated with poorer ART outcomes in treatment naïve 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.**