Meta-analysis of efficacy for DTG versus PI/r as second-line treatment in 4 randomised trials, 2662 participants

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Manya Mirchandani[1], Ambar Qavi[1], Bryony Simmons[2], Andrew Hill[3]

1.Imperial College London, Faculty of Medicine, London, UK
2.London School of Economics and Political Science, LSE Health, London, UK
3.University of Liverpool, Department of Pharmacology and Therapeutics, Liverpool, UK

BACKGROUND

- For second-line treatment, WHO recommends either dolutegravir (DTG) or boosted protease inhibitors (PI/r) with optimised nucleoside reverse transcriptase inhibitors (NRTIs)
- Disadvantages of PIs include drug interactions, multi-pill dosing, adverse events and higher costs
- However, the genetic barrier to resistance is high for PIs
- This analysis compares the efficacy of DTG and PI/r as second line regimens for HIV

METHODS

- Data on HIV RNA was included from 4 randomised trials: VISEND (n=783), DAWNING (n=624), NADIA (n=464) and 2SD (n=791)
- They recruited NNRTI experienced patients given second line treatment with either DTG or a PI/r.
- Data on HIV RNA suppression <50 and <1000 copies/mL from each study was extracted
- The meta-analysis was conducted using RevMan Software
- The risk differences (RD) for HIV RNA suppression were calculated using the Cochrane Mantel-Haenszel test (Random-effects model)
- The sensitivity analyses included only 2 of the 4 studies
- The non-inferiority margin was -10%

RESULTS

- The VISEND trial (Zambia), DAWNING (International) and NADIA (sub-Saharan Africa) recruited patients with HIV RNA >1000 copies/mL at baseline
- 2SD (Kenya) recruited patients stable on PIs with undetectable HIV RNA.
- At week 48, for patients viraemic at baseline, there was a significant difference between the DTG and PI/r arms in the number of patients with RNA <50 (RD = +10%, 95% CI. +2%,+17%, p=0.01) (Fig. 1)
- However, for patients already suppressed by PI/r at baseline, there was no significant difference between the DTG and PI/r arms (RD -1%, 95% CI. -5%,+3%, p=0.47) (Fig. 1)
- DTG was non-inferior to PI/r between the arms in the number of patients with RNA <1000 at week 48 (RD = +5%, 95% CI. -7%,+16%, p=0.43) (Fig. 2)
- At week 96, DTG was non-inferior to PI/r in the number of patients with RNA <50 (RD +11%, 95% CI. +1%,+21%, p=0.04) and RNA <1000 (RD = +10%, 95% CI. -6%,+26%, p=0.22) (Fig. 3 & Fig. 4)

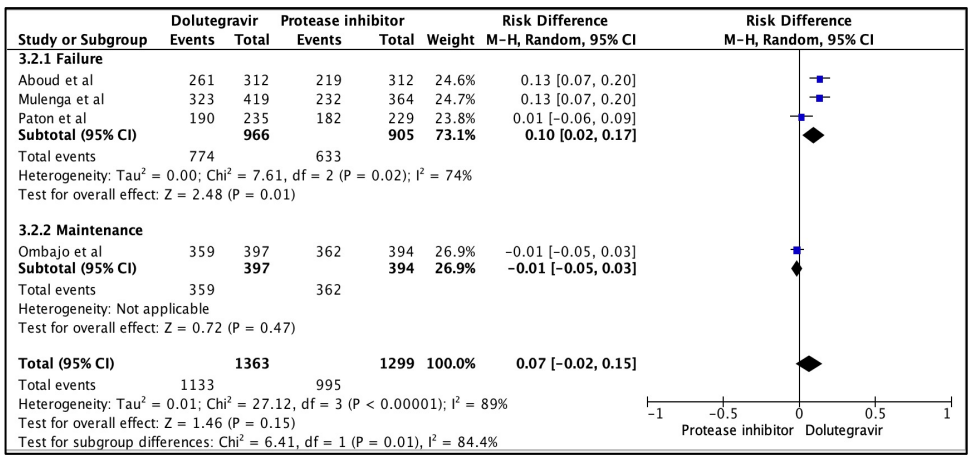

Figure 1: Forest plot for primary analysis of HIV RNA <50 at week 48

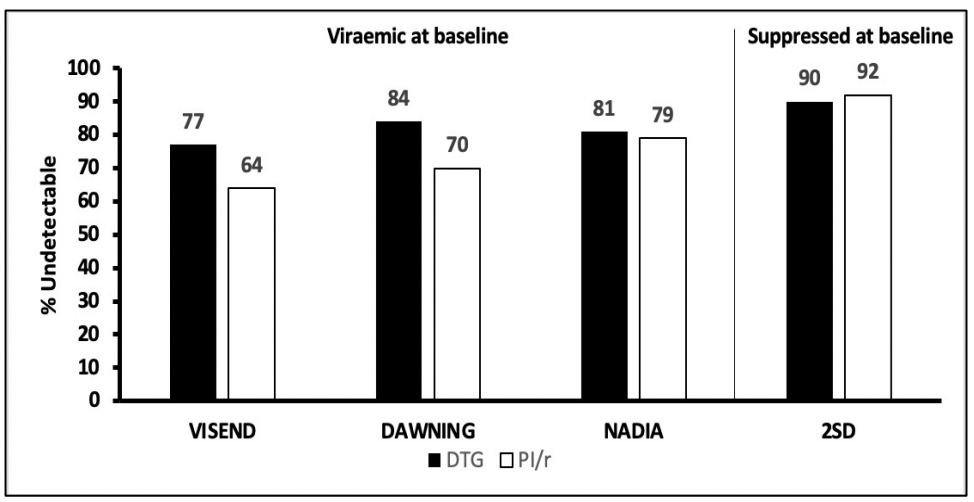

Figure 5: Results from the primary analysis based on each study

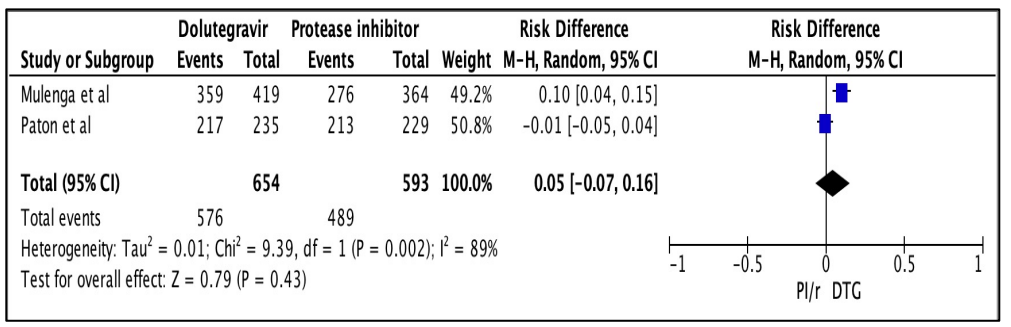

Figure 2: Forest plot for sensitivity analysis of HIV RNA <1000 at week 48

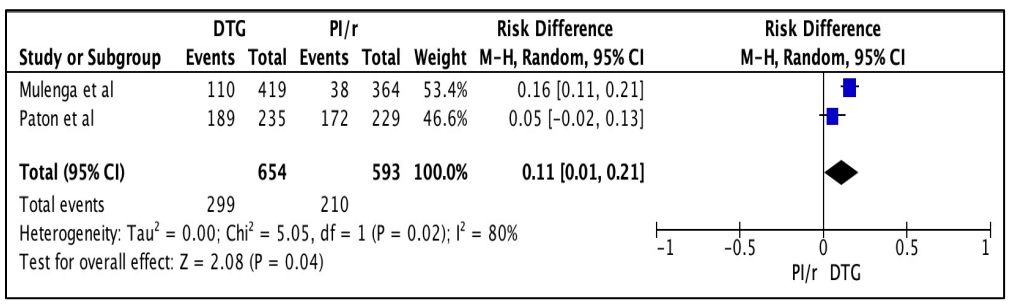

Figure 3: Forest plot for sensitivity analysis of HIV RNA <50 at week 96

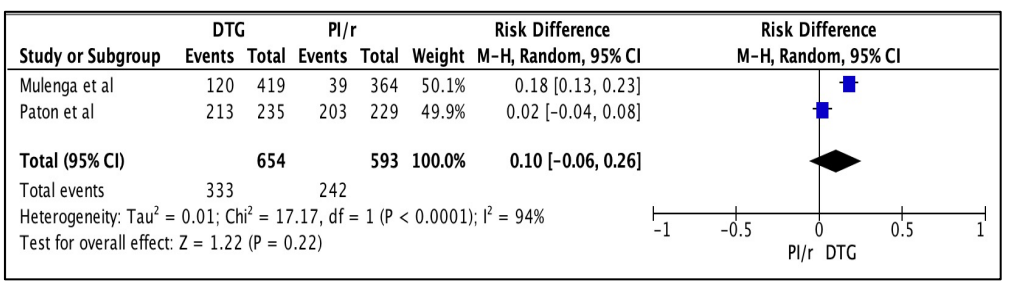

Figure 4: Forest plot for sensitivity analysis of HIV RNA <1000 at week 96

DISCUSSION AND CONCLUSION

- In this meta-analysis of HIV RNA suppression <50 copies/mL at week 48, there were 2662 participants evaluated in 4 randomised trials of second-line treatment. These trials enrolled patients taking NNRTI based treatment
- DTG showed a superior rate of HIV RNA suppression compared to PI/r based treatment in the primary analysis at week 48.
- In the sensitivity analyses, DTG was non-inferior to PI/r