SUCCESS AND FAILURE OF INITIAL ANTIRETROVIRAL THERAPY (ART) IN ADULTS: AN UPDATED SYSTEMATIC REVIEW INCLUDING 77,999 SUBJECTS FROM 1994 TO 2017

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Background:
We updated a prior (1994 to 2012) systematic review of adult initial ART efficacy through Week 144.

Methods:
Studies (1/2013-7/2017) were drawn from PubMed, ClinicalTrials.gov, Cochrane Library, and HIV conferences; study design, eligibility, subject and ART data were abstracted. Summary measures are expressed as group size-weighted means. Mixed-effect, meta-regression was used to identify sources of efficacy heterogeneity.

Results:
We analysed 354 groups (181 studies, 77,999 subjects [37,875 new]): baseline age 36.9 years, 74.7% men, 61.0% white, CD4 262 cells/mm^3, HIV viral load 4.8 logs. Subjects took 4.8 pills (including placebo) in 1.6 doses/day. Principal backbones were tenofovir (TDF/TAF)/emtricitabine (44.2%), thymidine-based (27.7%), and abacavir-lamivudine (9.7%). Principal anchors were non-nucleoside analogue (49.7%), boosted protease inhibitor (28.1%) and integrase inhibitor (INSTI; 11.5%). Data were highly heterogeneous (I^2=96.1%). Mean ITT efficacy (RNA<50 cp/mL) was 71.3%, 63.5% (145 groups) and 61.8% (48 groups) at Weeks 48, 96, and 144, respectively. Week-48 efficacy increased substantially over time (p-trend<0.0001; **Figure 1**). For post-2010 studies, Week 48, 96 and 144 efficacy was 83.8%, 79.9% and 77.1%, respectively. Independent predictors of greater efficacy at Week 48 were pre-ART genotyping (vs. none: adjusted difference 4.3% [1.4,7.2], p=0.0003); higher baseline CD4 counts (per 100 CD4-cell increment: 2.2% [1.0,3.4], p=0.0003); once-daily ART (vs. 2 doses/day: 3.4% [0.9,5.9]; p=0.008); INSTI-based ART (vs. other anchors: p<0.001); and ART including TDF/TAF-FTC (vs. other nucleosides, p=0.02). Cessation at Weeks 48, 96 and 144 was 20.5%, 26.9% and 29.4%, respectively. Cessation by Week 144 overall and for adverse events (8.9%) declined substantially over time, but cessation for virological failure (5.2%) did not.

Conclusions:
Initial ART continues to improve, but >20% of post-2010 subjects failed over 3 years. All guidelines should list INSTI-based initial ART as preferred. Strategies are needed to improve access to pre-ART genotyping and to increase early initiation of once-daily ART.

Figure 1 Efficacy at Week 48 by year of study commencement