ADVERSE EVENT DATA FROM STUDIES OF INITIAL ANTIRETROVIRAL THERAPY ARE UNDER-REPORTED AND THEIR REPORTING IS BIASED

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Background: We evaluated adverse event (AE) reporting completeness and potential reporting bias from studies of initial antiretroviral therapy (ART; since 1994) for major clinical adverse outcome (death, AIDS, serious non-AIDS, serious adverse events [SAEs]) and for the most commonly reported AEs (nausea, diarrhoea, headache, rash, fatigue).

Methods: AE data through July 2017 were abstracted from 181 studies (354 groups, 77,999 subjects). Reporting rates were compared using Fisher's exact test. Reporting bias was evaluated by comparing ART discontinuation rates between groups that did or did not report incident AEs (t-tests).

Results : Only death (73%) and SAEs (56%) were reported in more than 50% of studies at Week 48. Reporting rates did not increase in more recent studies; reporting of AIDS and serious non-AIDS events declined over time. Variables significantly and consistently associated with a greater likelihood of reporting data for all AE outcomes related to: study design (randomised design, use of placebo, phase 2-3 study, industry sponsorship); recruitment in America/Europe/Australia; eligibility restrictions (HIV viral load, raised liver enzymes); integrase inhibitor therapy; and subject characteristics (younger age, white race, no prior AIDS, higher CD4 count, lower viral load), but not ART backbone/dosing/pill burden, group size or year of study commencement. Groups not reporting Week-48 AE data were significantly more likely to cease ART at Week 48 than groups that did report these data e.g. groups not reporting nausea had greater ART discontinuation at Week 48 (25.1% vs. 17.7%, p=0.004) and greater ART discontinuation at Week 48 for AEs (8.6% vs. 5.5%, p=0.002).

Conclusions: Major AE outcomes and specific AEs with initial ART are under-reported, particularly from phase-4, academic-sponsored, cohort studies. Reported AE data appear biased towards groups with healthier participants that experience fewer serious adverse events and lower rates of ART discontinuation.

Disclosure of Interest: NIL