

Report for BHIVA/Janssen Scholarship

Chloe Orkin

I attended IAS thanks to the generous scholarship award.

The key data from the conference for my practice were:

START, GS US 0109, GS US 112, MIDAS, LASA, WAVES (which unfortunately was only presented as a poster), MODERN and also the data on starting treatment immediately after testing. START was presented without much ability for discussion as organisational heads gave position statements after the data had been presented. I think this was a shame.

There was an interesting plenary on the Tuesday on looking after IVDU patients in Vancouver and offering them rooms to self-inject under supervision. This offered safer injection and ability for resuscitation in the event of overdose. Injecting did not increase after setting up these services.

I presented the Going Viral study during the Wednesday session. From 13–20 October 2014, nine UK-wide emergency departments (ED) where diagnosed HIV prevalence was >0.2% took part in an opt-out screening programme for HIV, HCV and HBV. Uptake was defined as ED attendees who accepted BBV testing as part of routine bloods. HIV Ab, HBV surface Ag & HCV Ab were tested locally. Patients who tested BBV positive were recalled. Results: 7,807 ED patients had venepuncture, 2,118 (27%) of whom had BBV testing. Testing uptake range was 9.5–60.5% between EDs. 71 BBV tests were positive (3.4%) with 32 (45.1%) new diagnoses. There were 39 HCV infections (15 new), 17 HIV infections (6 new), and 15 HBV infections (11 new). 25–54 year olds had the highest prevalence: HCV 2.46%, HIV 1.36% and HBV 1.09%. Assuming cost per test as £7 for each virus, the cost per new case detected is £988 for HCV, £1,351 for HBV and £2,478 for HIV.

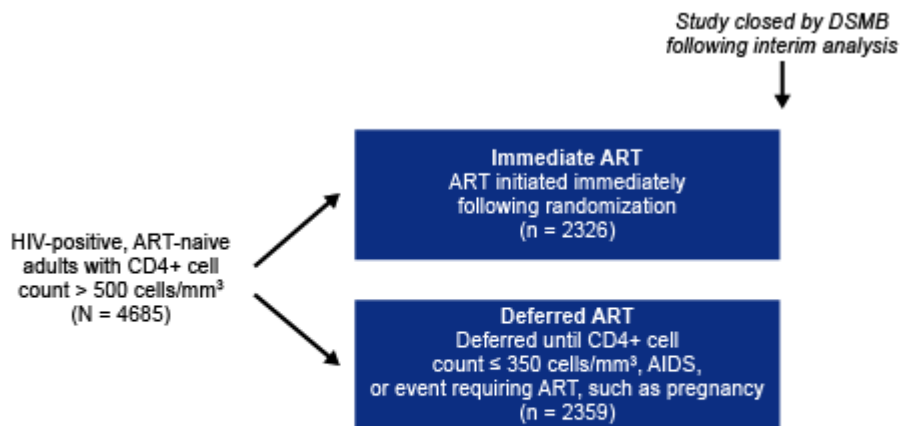
Here follow two summaries on two key studies.

START study:

START: ART Initiation at CD4+ Cell Counts > 500 cells/mm³ Significantly Reduces Serious AIDS and Non-AIDS Morbidity and Mortality (Jens Lundgren)

- Current study was a randomised comparison of the impact of immediate vs deferred ART on disease progression in HIV-positive, treatment-naïve, asymptomatic patients with CD4+ cell counts > 500 cells/mm³ [1]
- Patients randomised to deferred arm initiated ART at CD4+ cell count ≤ 350 cells/mm³ or at development of AIDS-related event or other event indicative of need for ART

Schematic of study design



DSMB, data and safety monitoring board.

Any ART recommended in US Department of Health and Human Services ART guidelines allowed.

Eligibility

- Main inclusion criteria:
 - HIV-infected adults
 - No previous ART
 - Two CD4+ cell count values > 500 cells/mm³ at least 2 weeks apart within 60 days before enrolment
- Exclusion criteria:
 - Pregnant or breast-feeding at screening

Baseline characteristics

- Study conducted within 215 sites in 35 countries
 - 54% of participants from low- or middle-income countries
- Distribution of baseline CD4+ cell counts across two arms (median: 651; interquartile range [IQR]: 584–765)
 - 500–599 cells/mm³: 32%
 - 600–699 cells/mm³: 31%
 - 700–799 cells/mm³: 17%
 - 800–899 cells/mm³: 9%
 - ≥ 900 cells/mm³: 11%
- Distribution of HIV-1 RNA levels across two arms (median: 12,759; IQR: 3,019–43,391)
 - 0–200 copies/mL: 5%
 - 201–3,000 copies/mL: 20%
 - 3,001–30,000 copies/mL: 43%
 - 30,001–100,000 copies/mL: 22%
 - > 100,000 copies/mL: 10%
- Study arms well matched at baseline

Main findings

- Patients who began ART immediately significantly less likely to experience any serious AIDS-related event, any serious non-AIDS-related event, or death from any cause than those who deferred ART
 - 42 patients in immediate ART arm reached composite primary endpoint vs 96 patients in deferred ART arm
 - HR for composite primary endpoint: 0.43 (95% CI: 0.30–0.62; $p<0.001$) with no significant variation during follow-up
 - HR for serious AIDS-related event: 0.28 (95% CI: 0.15–0.50; $p<0.001$)
 - HR for serious non-AIDS-related event: 0.61 (95% CI: 0.38–0.97; $p=0.04$)
 - HR for all-cause death: 0.58 (95% CI: 0.28–1.17; $p=0.13$)
- Most common primary endpoint components were CVD (29% immediate vs 15% deferred arm), non-AIDS-defining cancer (21% immediate vs 19% deferred arm), tuberculosis (14% immediate vs 20% deferred arm)
 - Most tuberculosis occurred in patients in Africa
 - Most CVD and cancer occurred in patients in Australia, Europe, Israel, United States
 - 10% of primary endpoints in immediate arm occurred before ART initiation vs 71% in deferred arm

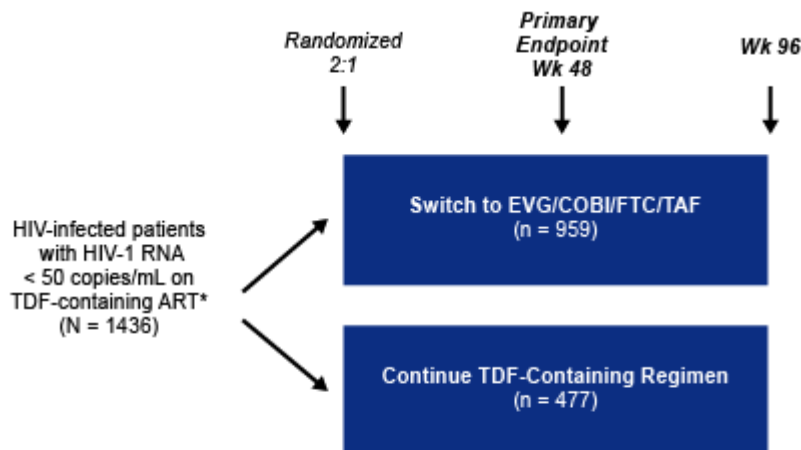
Other outcomes

- ART started by 98% of patients in immediate vs 48% in deferred arm
 - Median CD4+ cell count at ART initiation in deferred arm: 408 cells/mm³
- ART received for 94% of total follow-up time in immediate vs 28% in deferred arm
 - Most patients received tenofovir disoproxil fumarate (89% both arms), emtricitabine (89% immediate vs 88% deferred arm), efavirenz (73% immediate vs 51% deferred arm)
- Similar proportions of patients across arms had HIV-1 RNA suppression 12 months after ART initiation (98% immediate vs 97% deferred arm)
- During follow-up, median CD4+ cell count was 194 cells/mm³ higher in immediate vs deferred arm
- 61% of deaths due to causes other than AIDS
- Frequency of grade 4 events or unplanned hospitalisations due to causes other than AIDS did not differ between arms
 - Bacterial infections more common in deferred arm ($p=0.002$)

Oral presentations of interest on ARV therapy:

GS-US-292-0109 study: international, randomized, active-controlled, open-label phase III study (Tony Mills)

Schematic of study design



*Baseline therapy comprised EVG/COBI/FTC/TDF (n = 459), EFV/FTC/TDF (n = 376), or boosted ATV + FTC/TDF (n = 601). ATV boosted by either ritonavir or COBI. All ART given at standard doses.

Baseline characteristics

- Treatment arms well matched at baseline

Characteristic	Switch to EVG/COBI/FTC/TAF (n = 959)	Continue TDF- containing ART (n = 477)
Median age, years	41	40
Male, %	89	89
Race, %		
• White	68	66
• Black	18	21
• Hispanic/Latino	26	17
Median CD4+ cell count, cells/mm ³	675	662
CD4+ cell count <200 cells/mm ³ , %	0.5	0.8
Median eGFR,* mL/min	106	108

Characteristic	Switch to EVG/COBI/FTC/TAF (n = 959)	Continue TDF- containing ART (n = 477)
Dipstick proteinuria, %		
• Grade 1	8.5	9.2
• Grade 2	0.4	0.6

*Calculated using Cockcroft-Gault method.

Summary of key conclusions

- In patients with virologic suppression on tenofovir DF (TDF)-containing antiretroviral therapy (ART), switching to elvitegravir (EVG)/cobicistat (COBI)/emtricitabine (FTC)/tenofovir alafenamide (TAF) is associated with significantly higher rate of maintained virologic suppression at week 48 vs remaining on baseline therapy
 - HIV-1 RNA <50 copies/mL in 97% vs 93%, respectively ($p < 0.001$)
 - Benefit observed in patients on efavirenz (EFV)/FTC/TDF or boosted atazanavir (ATV) + FTC/TDF at baseline, but not in patients on EVG/COBI/FTC/TDF at baseline
- Overall frequency of adverse events (AEs) similar between arms
 - Discontinuation due to AEs more common in patients remaining on baseline TDF-containing therapy
 - Switch to EVG/COBI/FTC/TAF associated with significant increases in bone mineral density (BMD) at spine and hip, significant decreases in proportion of patients with diagnosis of osteopenia or osteoporosis by T-score, and significant improvements in markers of renal function at week 48 vs remaining on TDF-containing ART