Community feedback: START study

Simon Collins
HIV i-Base
www.i-Base.info

Strategic Timing of Antiretroviral Treatment

A Multicenter Study of the International Network for Strategic Initiatives in Global HIV Research (INSIGHT)

Type of evidence

- Observational databases

Can report associations but not prove that one thing is the cause of another.

Can never fully account for “confounding” – where something that is either known or not known might explain the results.

- Randomised controlled trials

The randomisation equally distributes known and unknown factors linked to the outcome.

START design (2009)

HIV positive people, ART-naïve with CD4+ count > 500

Early ART

Initiate ART immediately following randomization (N=2,000)

Deferred ART

Defer ART until the CD4+ count declines to < 350 or AIDS (N=2,000)

Follow until 370 endpoints reached

START timeline

Dec 2009 – First US patients enrol (pilot)

April 2010 – Broader enrollment

2009-2015 – 10 Annual DSMB safety reports

https://insight.ccbr.umn.edu/start/index.php

May 2013 – Events reduced from 370 to 213
plus 600 more pts aged > 45 yo.

April 2014 – Fully enrolled

Dec 2016 – Expected close date

May 2015 – Study stopped – after 127 events

START key results

- ART was safe at high CD4 counts. Many people (20%) had CD4 >800.
- Early ART reduced serious AIDS-related illnesses, even at high CD4 counts.
- Little impact on heart, liver, kidney disease and non-AIDS cancers.
- Similar results in both low- and high-income countries.
- Dataset and sub studies will follow.

Combined endpoints

START had three ways of defining serious AIDS and non-AIDS events.

1. The combined endpoint of AIDS, serious non-AIDS or death.
2. The combined endpoint of AIDS or death.
3. The combined endpoint of serious non-AIDS events or non-AIDS related deaths.

Primary endpoints.1

Table 1a. Number of primary endpoints in each arm (15 May 2015)

	Number of events	
	Early arm (A)	Later arm (B)
Category 1:AIDS, serious non-AIDS, or death (primary).	41	86
Category 2:AIDS or AIDS death.	14	46
Category 3:Serious non-AIDS or non-AIDS death.	28	41

* PY = patient years, ** NS = not statistically significant

Primary endpoints.2

Table 1b. Relative rates of primary endpoints in each arm (15 May 2015)

	Rate per 100 PY		Hazard Ratio
	Early arm (A)	Late arm (B)	Arm A/B (95% CI)
Category 1:AIDS, serious non-AIDS, or death (primary).	0.60	1.25	0.47 (0.32 to 0.68)
Category 2:AIDS or AIDS death.	0.20	0.66	0.30 (0.17 to 0.55)
Category 3:Serious non-AIDS or non-AIDS death.	0.41	0.59	0.67 (0.42 to 1.09) NS **

* PY = patient years, ** NS = not statistically significant

Who was in START

- 1685 people in 35 countries at 211 sites
- Median age 36 (IQR: 29 to 41), range 18 to 81.
- ~ 25 % women and ~ 50% gay men
- 33% of participants in Europe, 25% in South America or Mexico, 21% in Africa, 11% in the US, 8% in Asia and 2% in Australia.
- Med CD4: 651 (IQR: 584-765; range 503 to 2296).
- Med VL: 12,000 c/mL (IQR: 3,000 to 40,000), 8% <400 copies/mL.

Medical at baseline

- ~ 30 were current smokers
- ~50% had half had at least one cardiovascular risk based on the Framingham calculator
- ~ 20% hypertension or HT treatment treatment
- 8% either had high blood lipids treatment.
- 3% had diabetes or related.
- 2.9% HBV and 3.7% HCV.
- 3% alcohol or substance use issues
- 6% had a psychiatric diagnosis (including depression, bipolar and other conditions).

Sub studies

- Neurological function
- Bone health
- COPD (chronic obstructive pulmonary disease).
- Genomics – single sample
- Arterial elasticity
- Liver fibrosis

Also:

- Monitoring (sites)
- Informed consent (short vs long)

Implications

- CD4 threshold is no longer criterion for ART.
- How to interpret absolute risk when resources are limited.
- Linking treatment and TasP
- Already included in draft BHIVA guidelines
- Potential in WHO guidelines
- Your conclusions?

BHIVA guidelines

- Comments back by Friday 17 July

http://www.bhiva.org/treatment-guidelines-consultation.aspx

- When to start: irrespective of CD4
- What to start – changes for efavirenz, Atripla, rilpivirine, Eviplera, lopinavir, fosamprenavir, nevirapine etc. 3TC vs FTC.
- Primary HIV infection
- When to change
- Special populations

Thanks