

PARTICIPATION IN CLINICAL TRIALS AT THE ROYAL FREE HOSPITAL: CHARACTERISTICS OF THOSE INCLUDED AND IMPACT ON TREATMENT OUTCOMES

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BACKGROUND

- Randomised controlled trials (RCT) are the gold standard for assessing the efficacy and safety of medical interventions, including antiretrovirals (ARV) for treatment of HIV infection.
- However, those included in RCTs may not be representative of the general HIV positive population and may have an improved response to ARV.
- We investigated the type of patients who start ARVs (using three or more ARVs in combination-HAART) as part of an RCT and the impact of participation in an RCT on response to HAART in a complete clinic population.

METHODS

- We included all ARV-naïve patients in the Royal Free cohort who started HAART from January 1996 onwards.
- Virologic response was defined as the occurrence of a viral load <400 copies/ml in the time period 12 to 48 weeks after starting HAART (two analyses were performed (i) missing=failure [M=F] and (ii) missing=excluded [M=E]).
- We chose this response measure as it is not sensitive to the number of viral load measurements available, assuming they are measured sufficiently frequently for at least one measurement to be available.
- We studied the factors associated with participation in an RCT using logistic regression models
- We studied the impact of participation in an RCT on both the virologic response to HAART and the tolerability of HAART regimens using logistic and Cox proportional hazards regression models respectively.
- All logistic and Cox proportional hazards regression models were adjusted for gender, ethnicity, risk group for HIV transmission, baseline viral load, baseline CD4 cell count, age, type of HAART regimen and year of starting HAART

RESULTS

- Of 828 patients who started HAART from 1996 onwards, 227 (27%) started HAART whilst participating in an RCT.
- Risk group, year of starting HAART and the type of HAART regimen received were associated with participation in an RCT (TABLE 1).
- Those in an RCT appeared to have an improved virological response to HAART compared to those starting HAART as part of routine care (FIGURE 1).

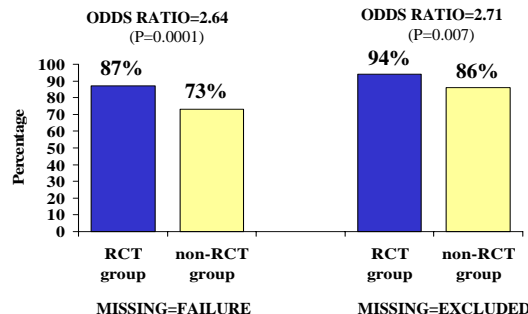
RESULTS (Continued)

TABLE 1- CHARACTERISTICS OF PATIENTS STARTING HAART AS PART OF AN RCT OR AS PART OF ROUTINE CLINICAL CARE

	Non-RCT group	RCT group	Odds ratio (95% CI)
N	601 (100%)	227 (100%)	
CD4 count	cells/mm ³ 181 (75, 303)	212 (94, 321)	NS
Viral load	log copies/ml 5.2 (4.7, 5.7)	5.2 (4.7, 5.6)	NS
Gender	Male 454 (76%)	180 (79%)	NS
Risk group	Homosexual 324 (54%) Heterosexual 231 (38%) Other 46 (8%)	144 (63%) 79 (35%) 4 (2%)	1.00 (reference) 0.79 (0.56, 1.11) 0.20 (0.07, 0.59)
Ethnicity	White 367 (61%) Black African 160 (27%) Other 74 (12%)	151 (67%) 57 (25%) 19 (8%)	NS
Age	years 36 (31, 41)	36 (31, 41)	NS
Year of starting HAART	1996+1997 98 (16%) 1998 92 (15%) 1999 92 (15%) 2000 74 (12%) 2001 85 (14%) 2002+2003 160 (27%)	36 (16%) 31 (14%) 32 (14%) 37 (16%) 48 (21%) 43 (19%)	1.37 (0.71, 2.64) 1.20 (0.63, 2.30) 1.00 (reference) 1.80 (0.98, 3.31) 1.48 (0.83, 2.65) 0.50 (0.28, 0.88)
Type of regimen	IPI+2NRTI 172 (29%) 2PI+2NRTI 94 (16%) INNRTI+2NRTI 282 (47%) ABA+2NRTI 53 (9%)	52 (23%) 66 (29%) 65 (29%) 44 (19%)	1.00 (reference) 0.83 (0.49, 1.43) 3.38 (1.83, 6.23) 3.95 (2.09, 7.45)

Entires are number (percentage) for categorical variables and median (interquartile range) for continuous variables. Odds ratios from multivariable logistic regression model. NS=not significant

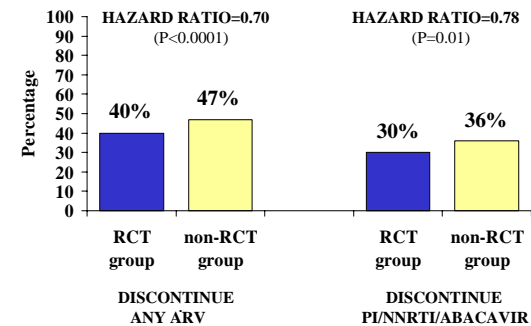
FIGURE 1- PERCENTAGE ACHIEVING A VIRAL LOAD <400 COPIES/ML 12-48 WEEKS AFTER STARTING HAART



RESULTS (Continued)

- The RCT group had a median (Interquartile range [IQR]) of 7 (5, 9) CD4 count measurements in the first 48 weeks of HAART. The non-RCT group had a median (IQR) of 6 (4, 8) CD4 count measurements in the first 48 weeks of HAART (p<0.0001).
- A lower percentage of individuals starting HAART whilst in an RCT discontinued an antiretroviral within the first 48 weeks of HAART compared to those starting HAART as part of routine care (FIGURE 2).

FIGURE 2- PERCENTAGE DISCONTINUING AN ANTIRETROVIRAL IN FIRST 48 WEEKS OF HAART



CONCLUSIONS

- RCTs remain the gold standard to compare drug regimens, as they are unbiased.
- However, absolute virological and discontinuation responses observed in trials may over-estimate what can be achieved in routine clinic practice.
- This may be due to unmeasured differences in the type of patients entering RCTs, in the clinical care received or in the HAART regimens used in RCTs.

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