



A Structured Treatment Interruption (STI)  
strategy of 12 week cycles on and off ART  
is clinically inferior to continuous therapy  
in patients with low CD4 counts  
before ART:  
a randomisation within the DART trial

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on behalf of the **DART** Trial Team



# Background



- Intermittent therapy has the potential
  - to reduce long-term toxicity
  - to reduce ART costs
  - to improve adherence
- whilst maintaining clinical well-being
- One randomised trial in Africa has reported inferiority of a CD4-guided treatment interruption strategy (TRIVACAN)
- The feasibility of CD4-guided strategies may be limited by high CD4 variability



# DART trial design: main randomisation



3316 previously untreated HIV-infected patients  
stage WHO 2, 3 or 4 and  $CD4 < 200$  cells/mm<sup>3</sup>

randomise to  
initiate triple  
drug ART plus

Clinical and  
Laboratory Monitoring  
(12 weekly biochemistry,  
FBC & CD4; no virology)

Clinical Monitoring  
Only  
(biochemistry and/or FBC  
if clinically indicated)

- Planned follow-up 4-5 years
- **Primary endpoints**
  - efficacy: new WHO 4 event or death
  - toxicity: Serious Adverse Events



# STI trial design within DART



- A second randomisation in a subset of patients
  - same primary endpoints
- Patients with  $CD4 \geq 300$  cells/mm<sup>3</sup> after 48 or 72 weeks on ART were randomised to
  - STI (12 week cycles on/off treatment), or
  - continuous ART (CT)
- 813 eligible patients randomised between July 2004 and March 2006
- Following 2nd DSMC review in March 2006 based on data to mid-Jan 2006, the STI/CT randomisation was terminated on 15 March 2006, and all patients moved to continuous therapy



# Characteristics at STI/CT randomisation



		CT	STI
Total patients		405	408
Weeks after starting ART	52	60%	61%
	76	40%	39%
Women		74%	73%
Age (years)	median (range)	37 (19-63)	37 (21-67)
CD4 count (cells/mm <sup>3</sup> )	median (range)	358 (300-819)	357 (300-1054)
CD4 nadir (cells/mm <sup>3</sup> )	median (range)	128 (2-199)	136 (1-199)
ART: 2NRTIs plus	TDF	68%	66%
	ABC	12%	9%
	NVP *	20%	25%

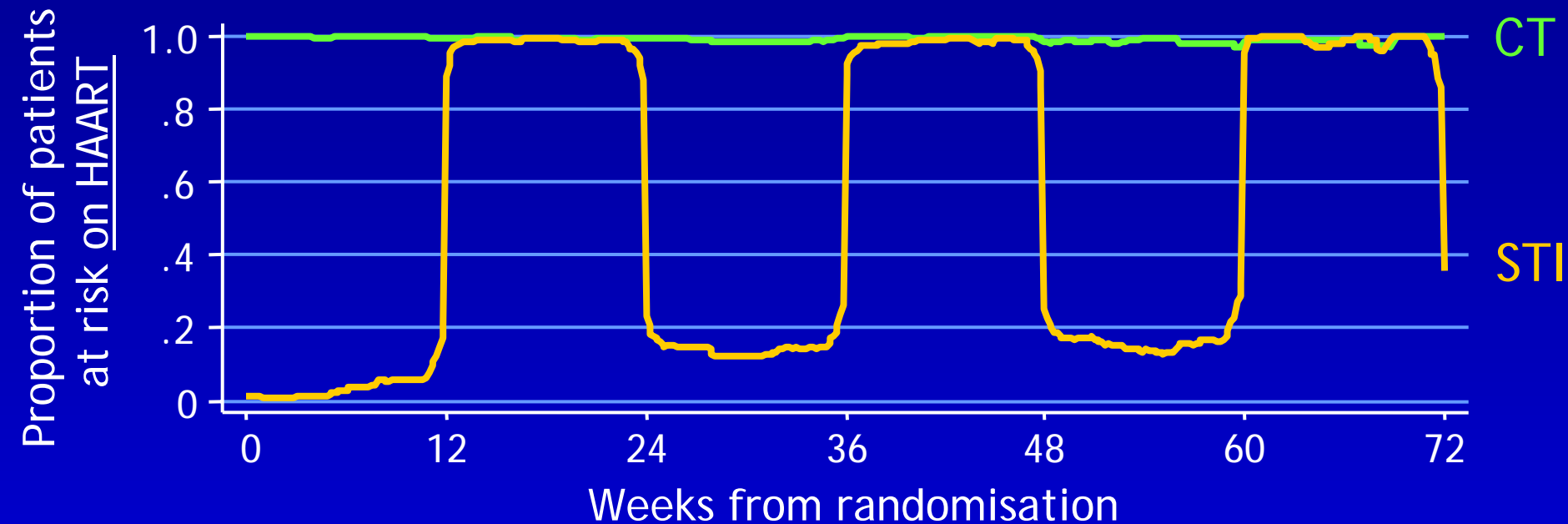
\* all used a 7 day stagger stop



# Follow-up & ART received

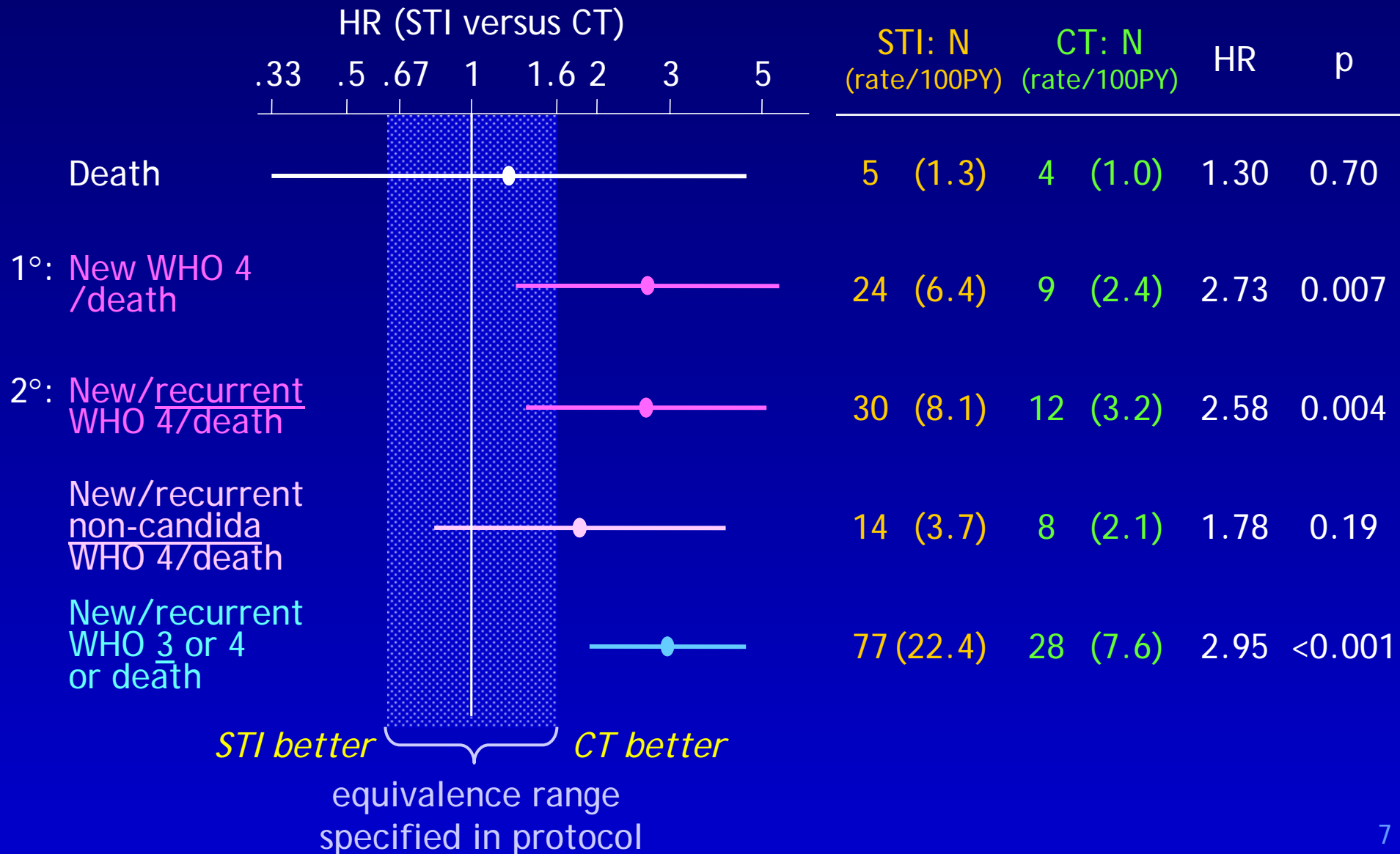


- Median follow-up to 15 March 2006 51 weeks (IQR 37-64, range 0-85 weeks)
  - 99% of 386 PY in CT on triple drug ART
  - 50% of 388 PY in STI on triple drug ART
- 304/408 patients started 2 more STI cycles: max 4 cycles



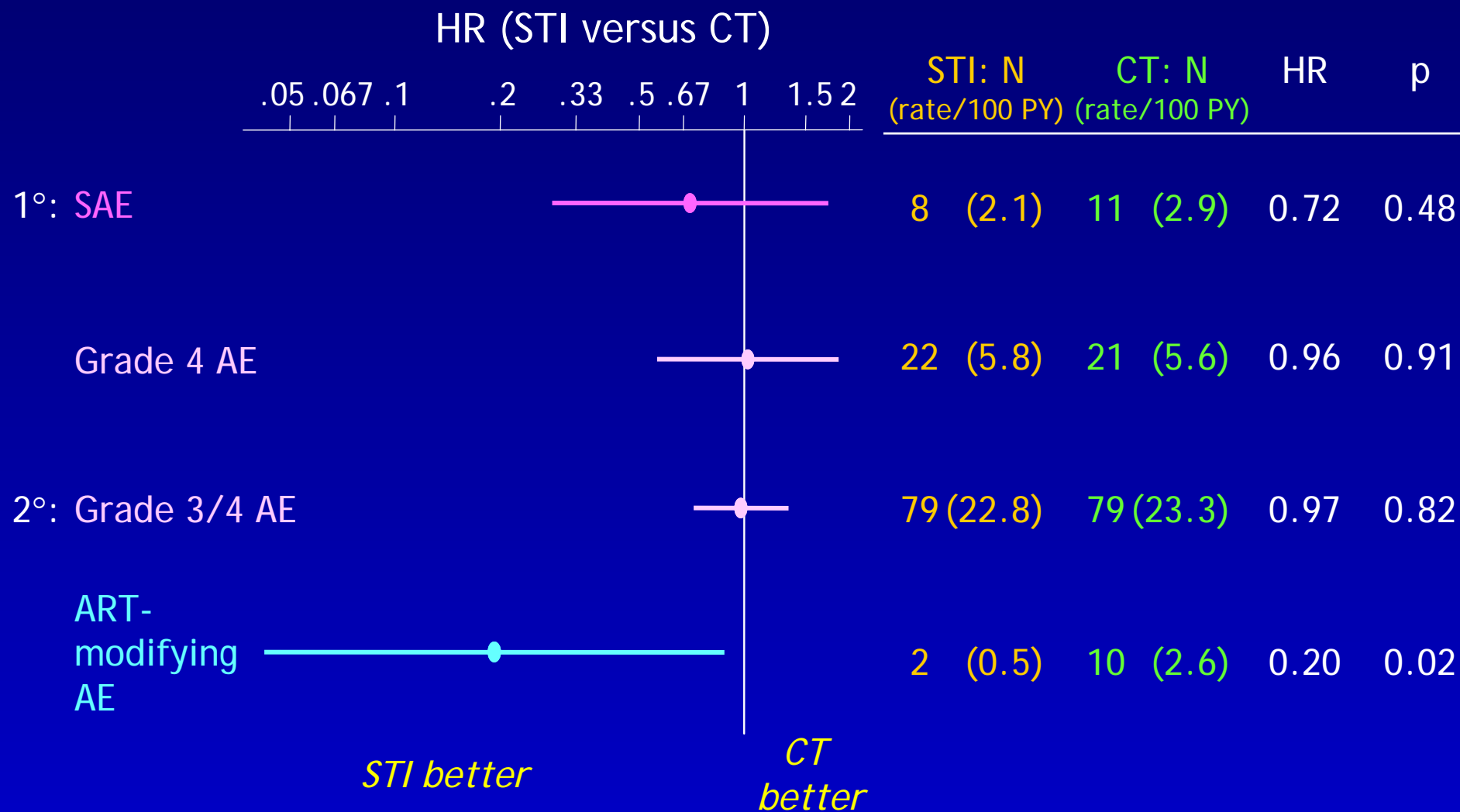


# Summary of clinical outcome





# Summary of reported AEs

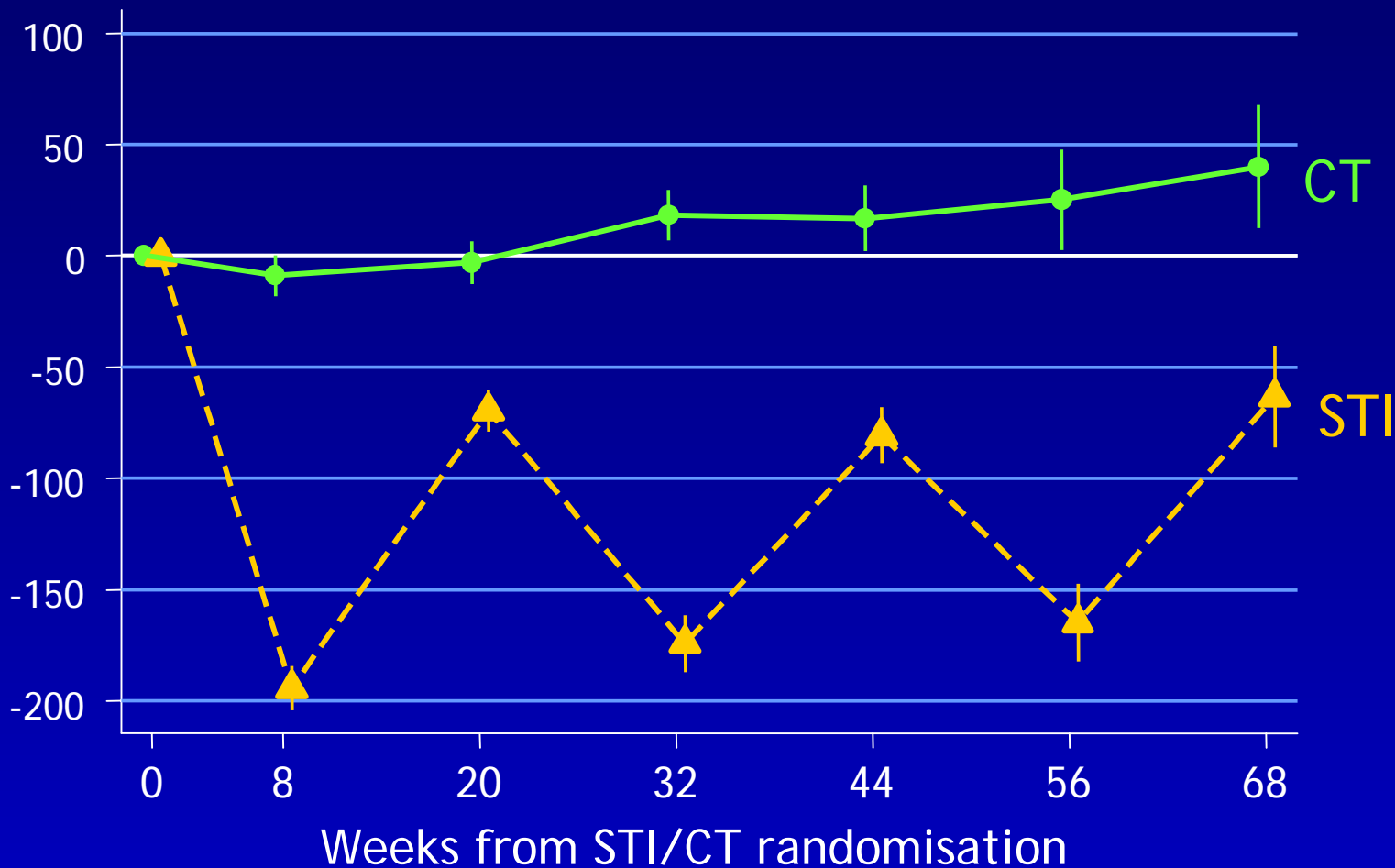




# Change in CD4 count (ITT, secondary endpoint)



Mean change following  
randomisation to STI/CT  
(pointwise 95% CI)



Numbers at risk

CT	405	395	380	328	257	151	74
STI	408	393	373	319	248	149	79



# Conclusions



- Over median follow-up of 51 weeks, the majority of STI patients were able to take ART intermittently without developing WHO 4 events
- However, the STI strategy in DART was associated with a 2.6 fold increased rate of clinical WHO stage 4 events, and cannot therefore be recommended
  - no evidence of difference in mortality between STI and CT
- DART continues to follow-up patients to its primary goal of comparing different monitoring strategies



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# First new WHO 4 event



	New		Additional recurrences	
	STI	CT	STI	CT
Oesoph candida	13	3	4	1
Ex pulm TB	4	1	0	0
Cryptococcosis	1	0	0	1
Herpes simplex	1	0	1	1
PCP	0	1	0	0
HIV wasting	0	0	1	0