18th Annual Conference of the British HIV Association (BHIVA)



Dr Nick Paton

MRC Clinical Trials Unit, London

18-20 April 2012, The International Convention Centre, Birmingham

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COMPETING INTEREST OF FINANCIAL VALUE ≥ £1,000:				
Speaker Name	Statement			
Dr Nick Paton:	No conflict of interest			
Date	April 2012			

18-20 April 2012, The International Convention Centre, Birmingham

Update on MRC adult HIV treatment trials

Nick Paton MD FRCP MRC Clinical Trials Unit BHIVA conference, April 2012

Summary

- MRC CTU strategy
- Current trials
- Future directions

MRC CTU trials - characteristics

- Large trials
 - Multi-centre
 - Often multinational
 - Require the expertise of an experienced coordinating centre
 - Occasionally smaller trials if likely to lead to definitive strategic trial
- Address important strategic questions applicable to large patient populations
- Designed to impact treatment guidelines

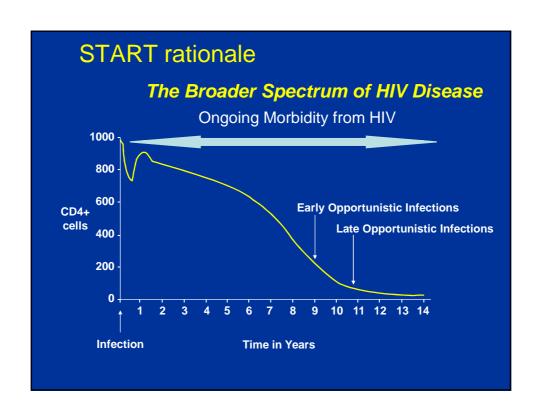
MRC CTU trials - characteristics

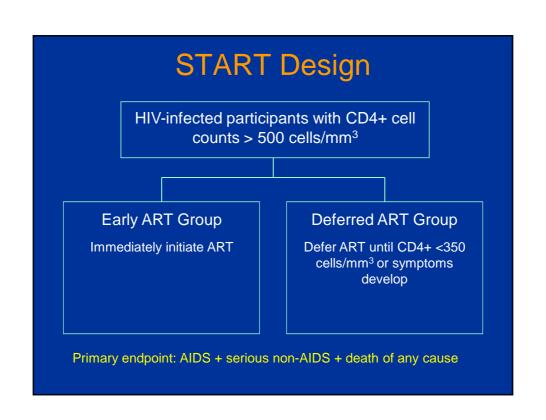
- "Take a long time" [..usually not short-term VL endpoints]
- Address scientific questions in sub-studies
- *Methodological innovation
- ** Relevance to global health [MRC strategy + funding opportunities]

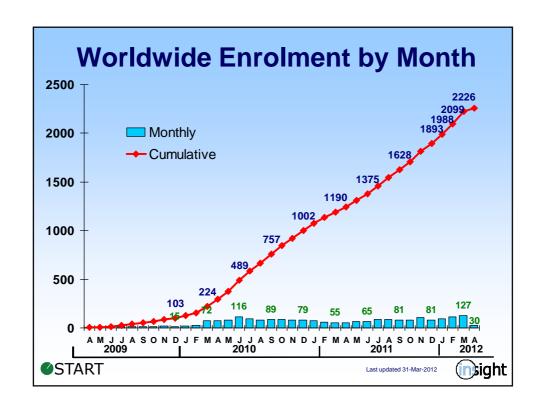
Adult HIV treatment trials: 2010-15

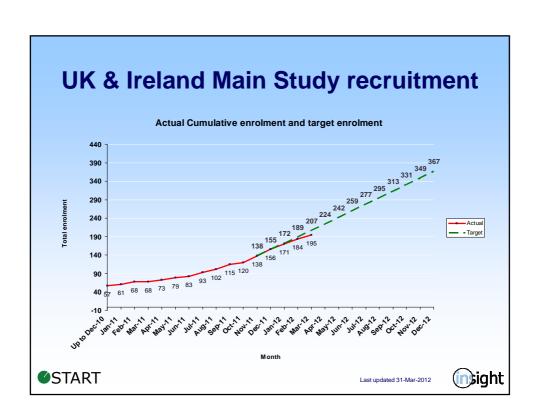
- · Optimising treatment in early chronic HIV disease
 - Early antiretroviral therapy
 - Immune based / anti-inflammatory therapy
- Optimising first-line therapy
 - Protease inhibitor monotherapy
 - Raltegravir-based dual therapy
 - Strategies to decrease early mortality in late presenters
- Optimising second-line therapy
 - Raltegravir-based dual therapy / PI monotherapy
- Trials in co-infections
 - Tuberculosis, Hepatitis B, Hepatitis C

1. Optimising treatment in early chronic disease

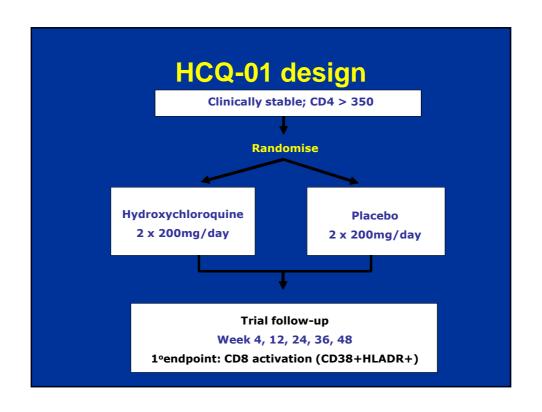








Worldwide Substudy Enrolment						
	Goal	N	% of goal			
Genomics	As many as possible	1551				
Neurology	600	595	99			
Inf. Consent.	2000	2034	102			
Art. Elasticity	300	222	74			
Pulmonary	1000	424	42			
BMD	400	97	24			
LFP	990	19	0			
START						



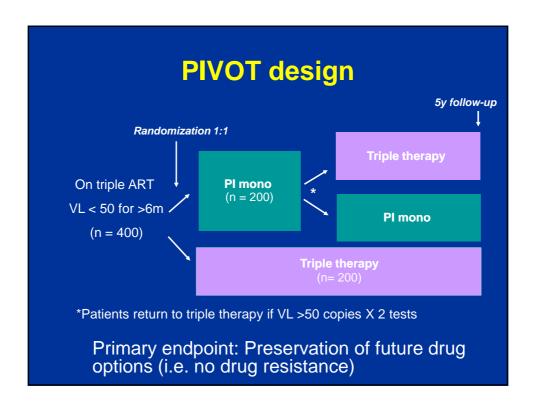
2. Optimising first-line therapy

- PI monotherapy PIVOT
- Raltegravir-based dual therapy NEAT001
- Strategies to decrease early mortality in late presenters-REALITY



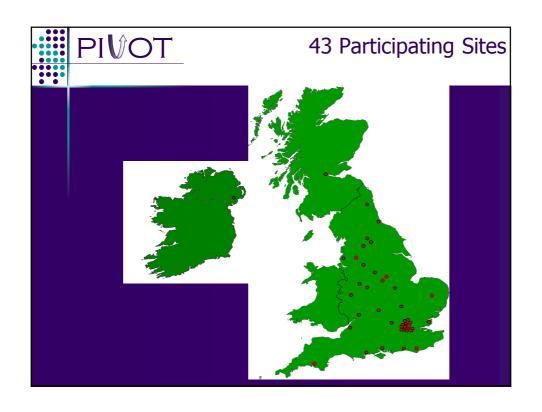
Protease Inhibitor monotherapy Versus Ongoing Triple-therapy in the long term management of HIV infection

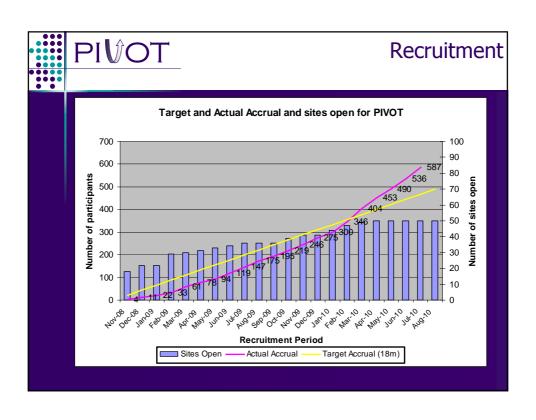
Funded by HTA (NIHR), sponsored by MRC



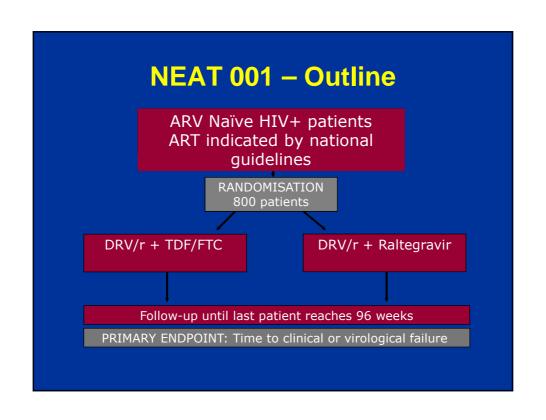
Secondary endpoints

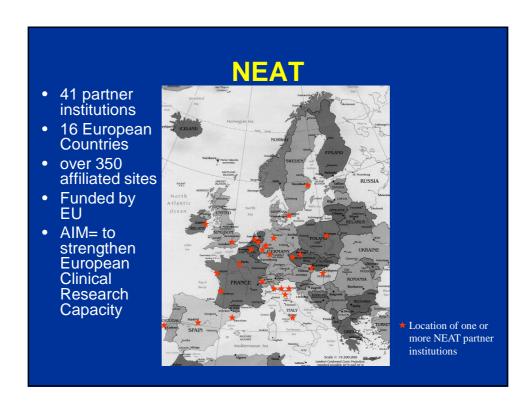
- Serious drug or disease-related complications
- Adverse events
- Viral load rebound
- CD4 count change
- Quality of life change
- Neurocognitive function change
- Health care costs





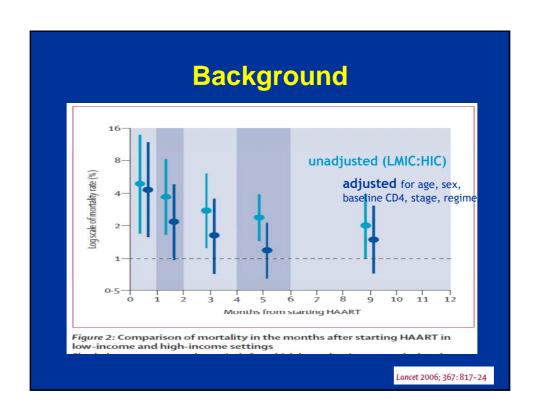
PIVOT	- -	Follow -up
Withdrawa	als: 4 (<1%)	
• Visits not	attended	
• 0	86%	
• 1	9%	
• 2	3%	
• >=3	2%	
	h 2012: no safety concerns follow up to end 2013	





REALITY

Reduction of EArly mortaLITY in HIV-infected adults and children starting antiretroviral therapy

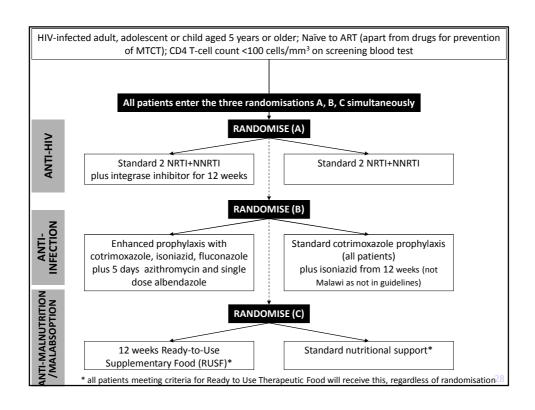


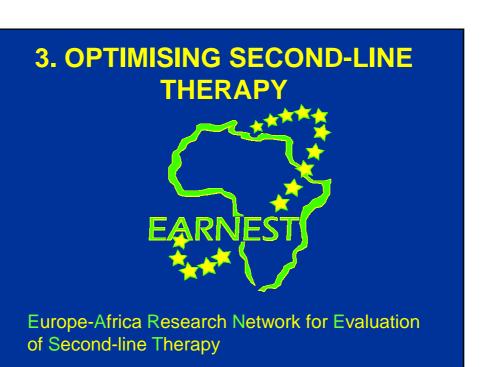
Interventions to reduce early mortality after starting HAART More potent ART Preventing early infections Antibiotics TB prophylaxis: INH Antifungal prophylaxis De-worming at starting ART Extra Nutrition

Study Design

- 2x2x2 open-label factorial design
- 1800 adults and children
- Kenya, Malawi, Uganda, Zimbabwe
- 48 weeks follow up
- · Primary endpoint: mortality

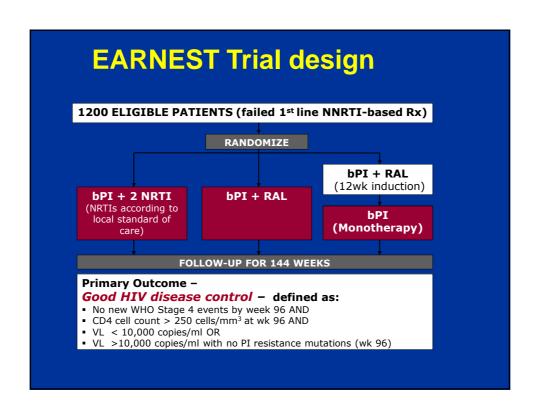
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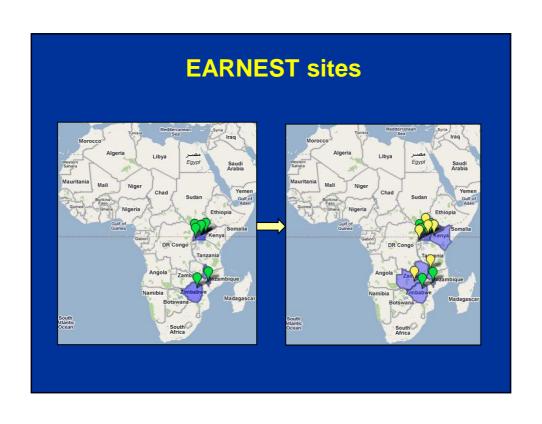


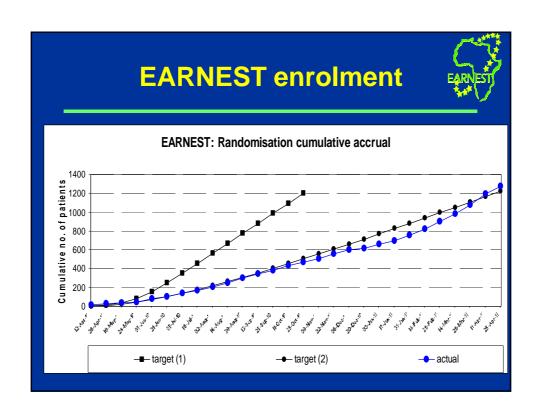


EARNEST Rationale

- In African rollout settings, failure on 2NRTI + NNRTI often a/w extensive resistance
- 2nd line SOC = Pl/r + 2NRTIbut contribution of 2NRTIs uncertain
- No evidence from RCTs for 2nd line
- AIM: to determine optimal 2nd line treatment in a setting relevant to the public health rollout-approach to HIV Rx

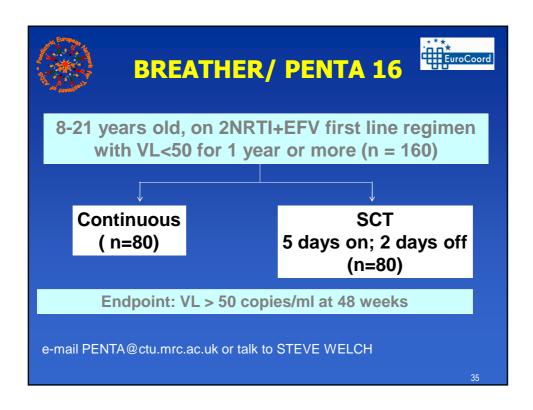






4. TRIALS IN CO-INFECTIONS

- Tuberculosis
 - Rifaquine
 - ReMoxTB
 - STREAM
- Hepatitis B
- Hepatitis C



Summary of future directions

- For adult HIV treatment
 - Comprehensive portfolio of active studies
 - Few big strategic treatment questions left
 - Future funding mainly directed to global health
 - Focus will shift to co-infections and to resource-limited settings
- Prevention.....