

# **TRACK B – Clinical Research, Treatment and Care**

**4<sup>th</sup> IAS Conference on HIV Pathogenesis, Treatment and Prevention  
Sydney 2007**

**Rapporteurs**

**Sean Emery**

**Sarah Pett**

**Nick Paton**

**Helen Byakwaga**



# Conflicts of interest

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**Rapporteur**

**Research funding, grant support, travel assistance, consultancies, stock ownership/employment**

**Sean Emery**

**Abbott, Boehringer-Ingelheim, Bristol Myers Squibb, Chiron, Gilead Sciences, GlaxoSmithKline, Merck, Sharp and Dohme, Roche, Schering Plough, Tibotec, Virax, NIAID.**

**Sarah Pett**

**GlaxoSmithKline, Gilead Sciences, Merck Sharp and Dohme.**

**Nick Paton**

**None reported.**

**Helen Byakwaga**

**None reported.**



# Outline

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**New drugs and new ways of using the ones we have for better outcomes**

- **Resource limited settings**
- **New drugs/new data**
- **Toxicities**
- **Strategies**





# **Resource limited settings**

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## ***TB and HIV disease***

- **Has always been and continues to be a substantial clinical problem**
- **Impact is most pressing in late presenting HIV cases**

**Funding/policy/infrastructure (Getahun, TUSY 101)**

**PK interactions (Manosuthi et al, MOAB102; Chideya et al, MOAB104)**

**Diagnosis (Elliott et al, MOAB101)**

**Anti-TB/ART treatment protocols (Swaminathan, TUSY103)**

## ***ART failure***

**Clinical laboratory monitoring (Hossienipour et al, WEAB101;**

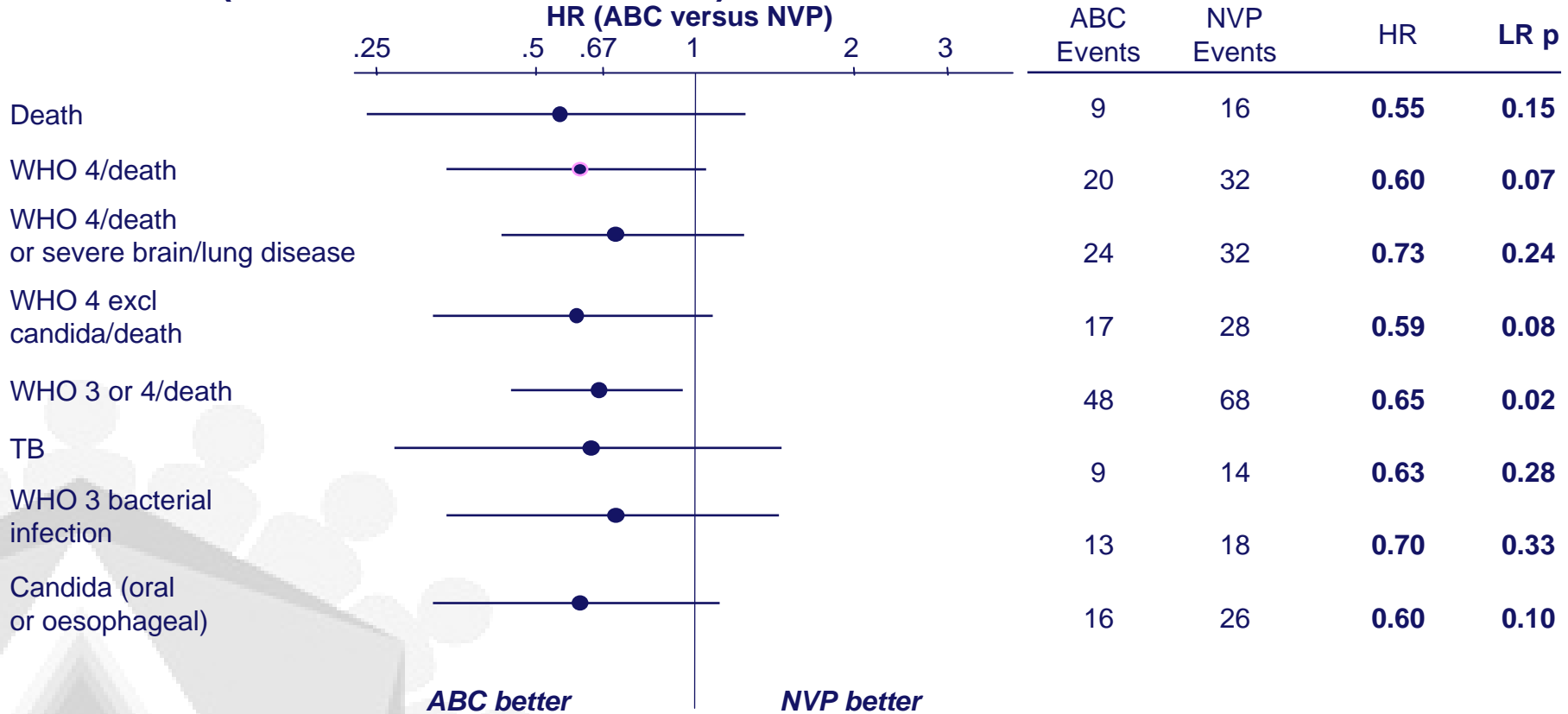
**Bananero et al, WEAB102; An et al, WEAB103)**

**Drug resistance - paediatric (Sohn, WEPL101; Vignoles et al, TUPEB054)**



# Resource limited setting

## DART (Munderi et al, WEAB1LB)



### Complex solutions for a complex problem

- Late use of ART
- Continued use of ART regimens that are unacceptable
- Inadequate monitoring of treatment responses



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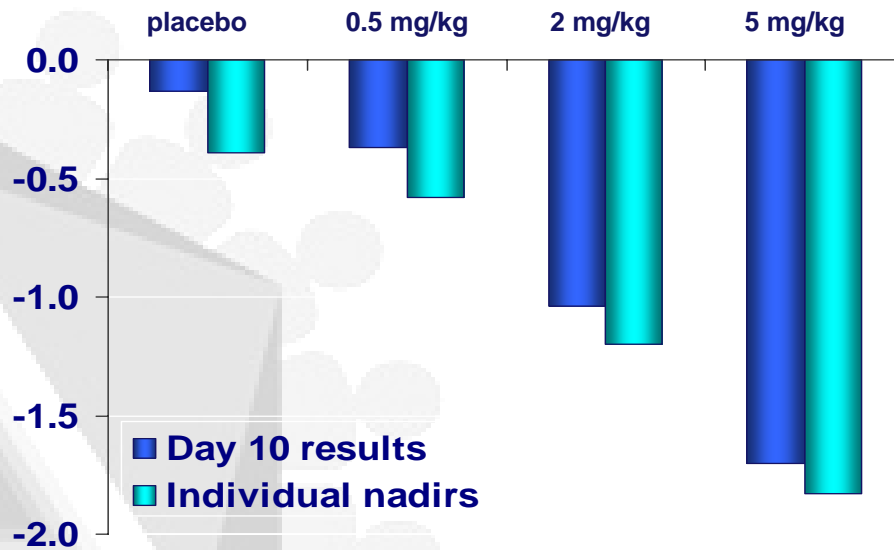


## New drugs/data

Promising data on early phase clinical evaluations (incl PK/PD) for a variety of new drugs from existing ART classes and against new virus targets (MOPDX01-06, WEPEB114LB, WESS202, WESS203).

**PRO140 – a CCR5 monoclonal antibody (Olsen et al, WESS201).**

Mean Log<sub>10</sub> Change in HIV-1 RNA

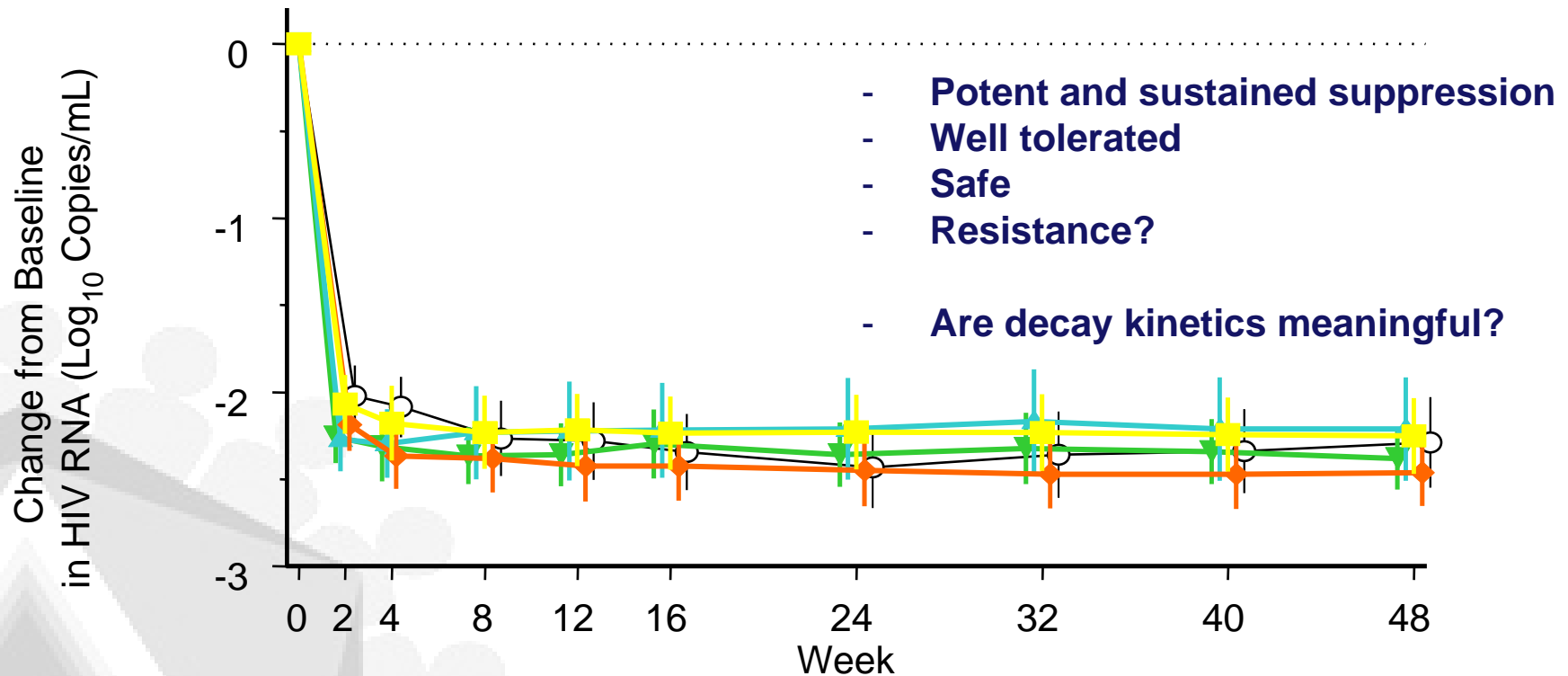


- Potentially active against CCR5 resistant HIV
- A role in combination with small molecule CCR5 inhibitors?



# New drugs/data

Integrase inhibitors – raltegravir (Markowitz et al, TUAB104;  
Murray et al, TUAB 103)



▼ Raltegravir 100 mg b.i.d. (n=39)

■ Raltegravir 400 mg b.i.d. (n=41)

○ Efavirenz 600 mg b.i.d. (n=38)

▲ Raltegravir 200 mg b.i.d. (n=40)

◆ Raltegravir 600 mg b.i.d. (n=40)



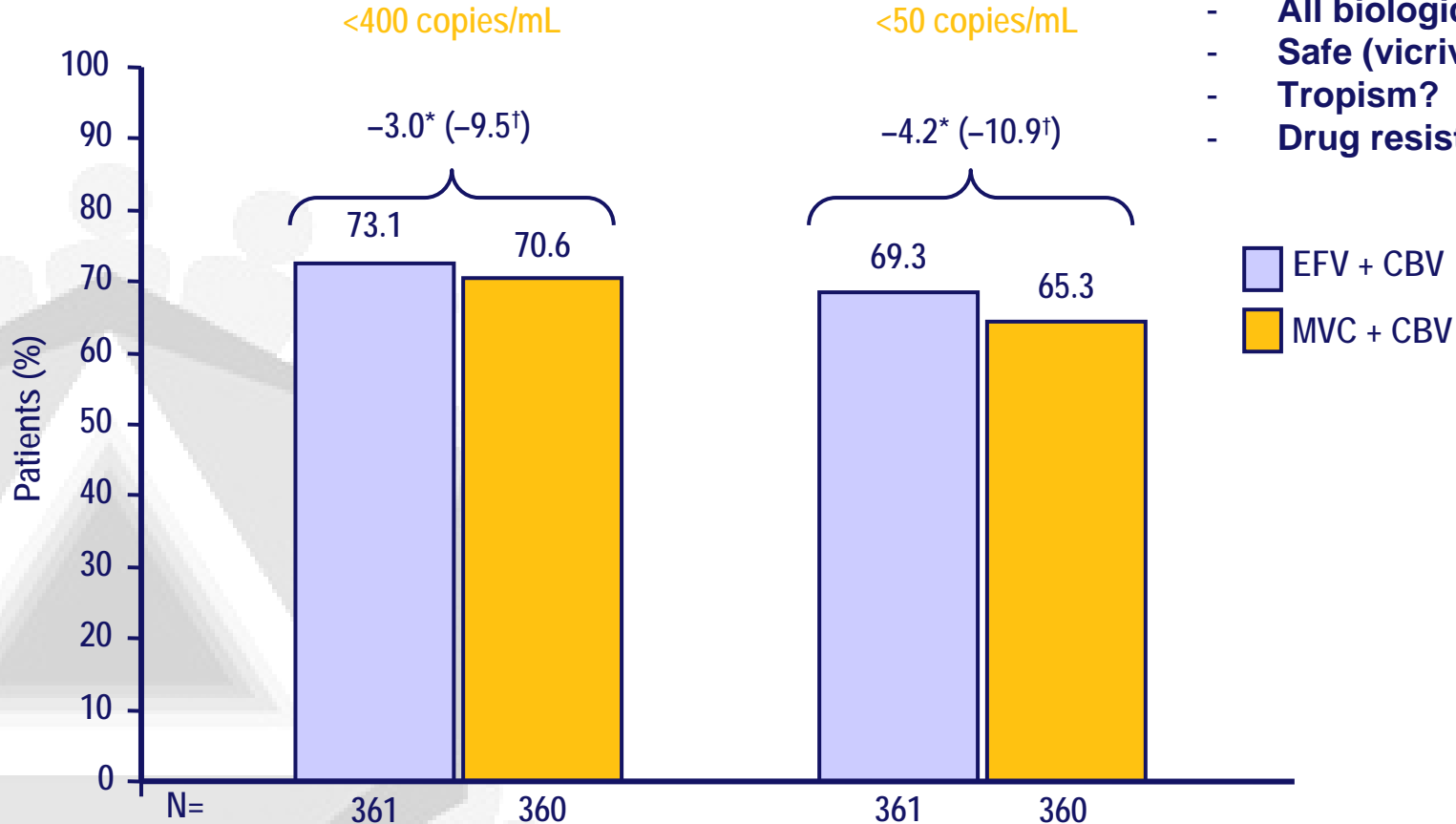
# New drugs/data

Small molecule CCR5 inhibitors – maraviroc, vicriviroc and INCB009471

(Gulick et al, TUAB102; Cohen et al, TUAB106; Saag et al, WESS104;

van der Ryst et al, WEPEB115LB; Gulick et al WEPEB116LB;

Moore, TUBS101; Richman, TUBS102)



- All biologically active
- Safe (vicriviroc – cancers?)
- Tropism?
- Drug resistance?

EFV + CBV  
MVC + CBV



## **New drugs/data**

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**Etravirine and r/darunavir (Mills et al, WESS204-1;  
Katlama et al, WESS204-2, Valdez-Madruga TUAB101; Lancet July 2007)**

- **Valuable new, safe NNRTI option in a salvage setting**
- **A credible option when considering r/PI in treatment-experienced patients**





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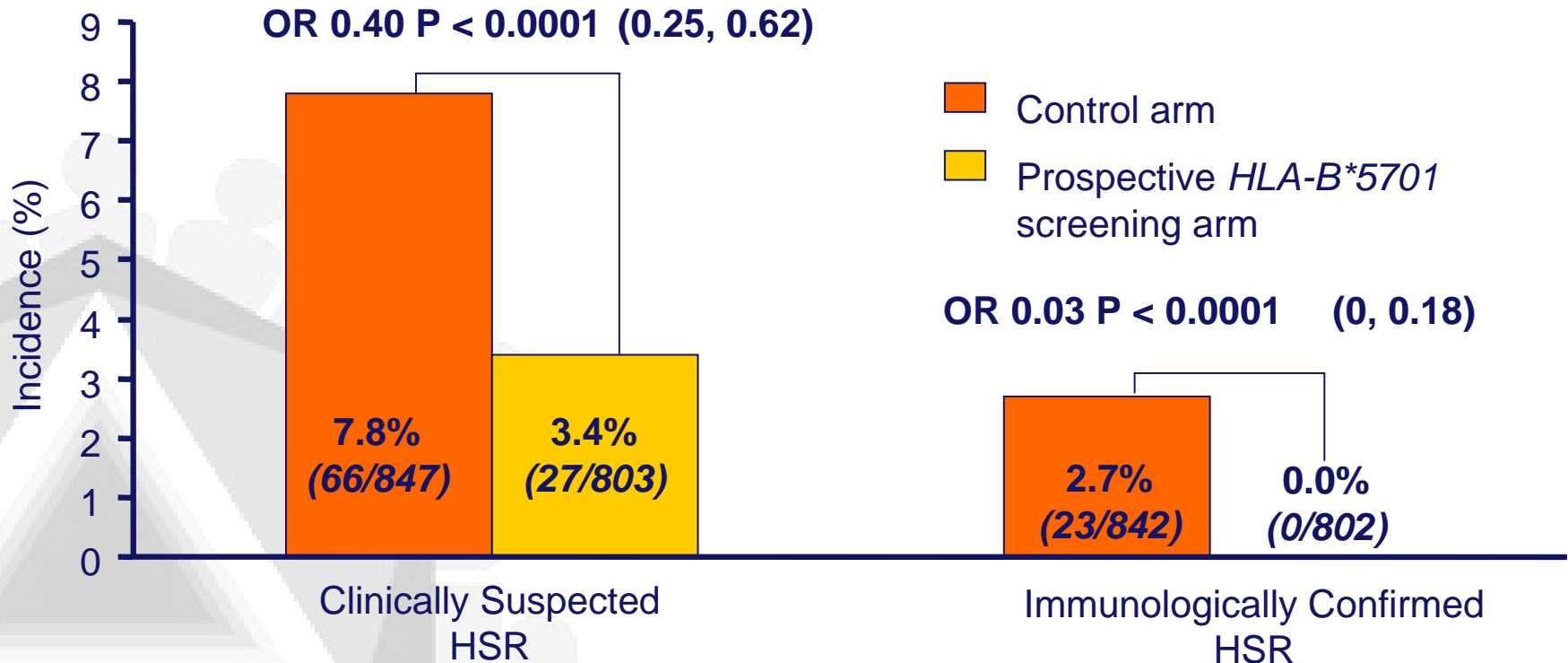




# Toxicities

## Abacavir hypersensitivity

- Mechanism elucidated (McCluskey et al, WEAB306)
- Rapid screening test validated (Kostenko et al, WEPEB113LB)
- Skin patch testing (Phillips et al, WEAB305)
- PREDICT study (Mallal et al, WESS101)

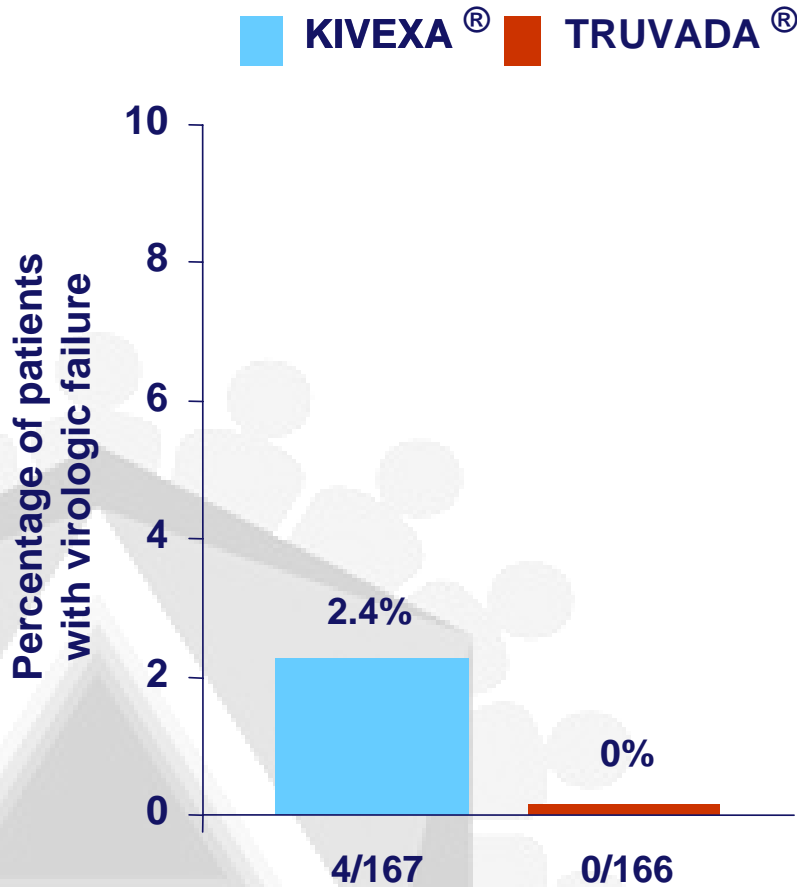


**WILL GLAXOSMITHKLINE NOW PROVIDE RESOURCES TO ALLOW TESTING?**

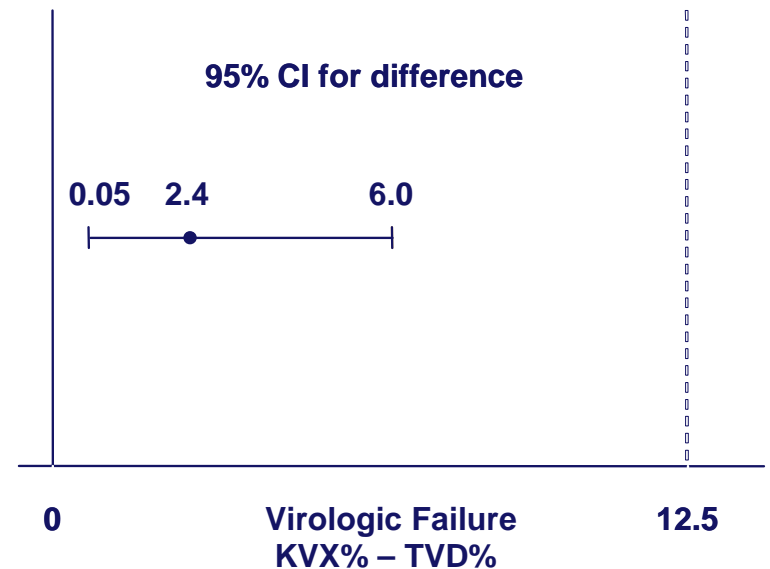


# Toxicities

## Switch studies – BICOMBO (Martinez et al, WESS102)



- Switch to either FDC is safe in treated patients with plasma HIV RNA <50 copies/mL
- TDF/FTC superior to ABC/3TC?
- CAUTION





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# Strategies

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**When to start treatment with antiretroviral therapy?**

**Paediatric HIV infection – CHER study (Violari et al, WESS103).**

**252 HIV+ve infants 6-12 weeks of age with CD4+%  $\geq$  25%.**

**Randomised to deferred ART (CD4+% <20%) or immediate ART for one or two years.**

**Deferred arm halted by DSMB recommendation after interim analysis revealed 75% reduction ( $p=0.0002$ ) in mortality for recipients of immediate ART versus deferred.**

**Immediate impact on treatment guidelines, practice, policy and research**



# Strategies

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## When to start treatment with antiretroviral therapy

- adult/adolescent HIV disease?

## Evidence to support the evaluation of early ART

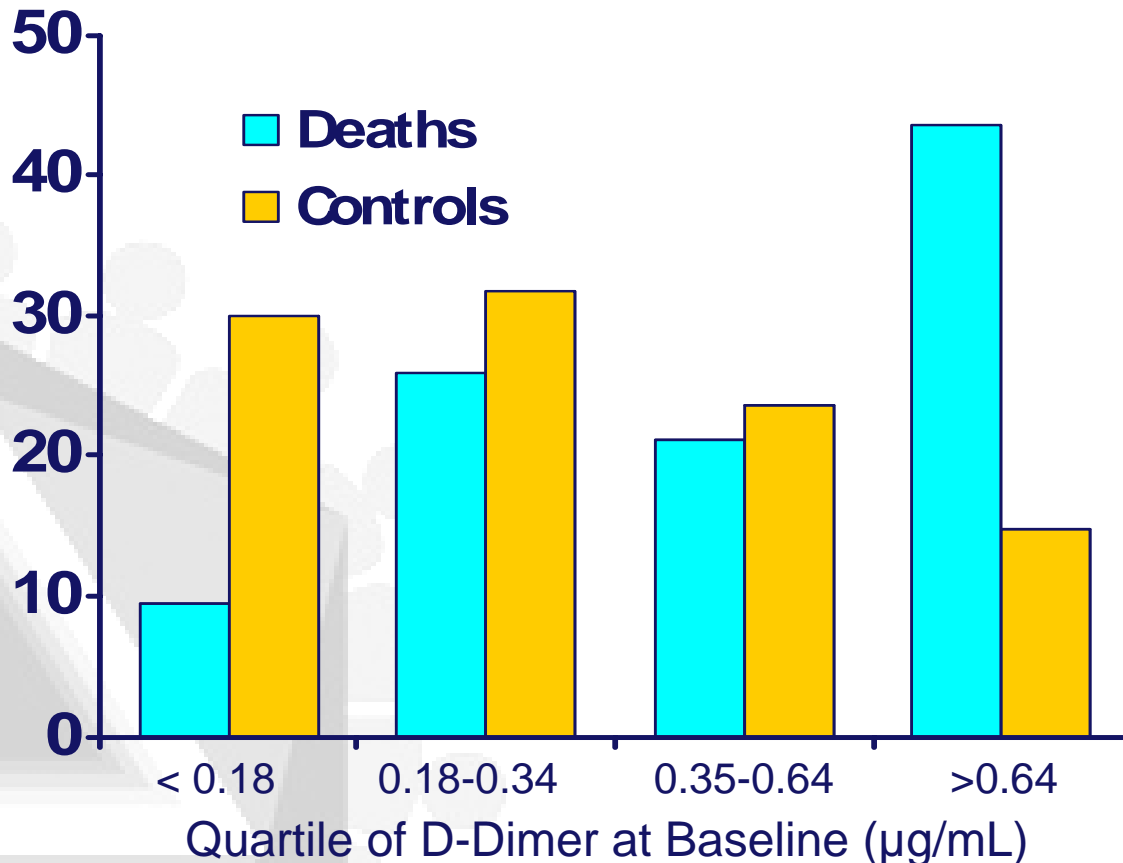
- Immunological (Lederman, MOPL102; Schacker, MOBS201; Levy MOSY201)
- Cohort data and biomarkers (Neaton, MOSY202; Pacheco et al, WEAB301, Torriani et al, WEAB302; Seaberg et al, WEPEB119LB)
- Clinical (Gazzard, MOPL103; Gordin, MOSY205; Emery et al, WEPEB030)
- Public health (Montaner, MOSY204)



# Strategies

## When to start treatment with antiretroviral therapy?

- d-dimer, a fibrin degradation product indicative of coagulopathy
- Increased in SMART patients at baseline (34% >ULN)
- Significant increases for DC patients after 1 month relative to VS



	D-Dimer (mean)
Deaths	1.07
Controls	0.37
Diff. (SE)	.70 (.17)
P-value	<0.0001
OR (4 <sup>th</sup> vs 1 <sup>st</sup> )	12.4



# Summary

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- **Welcome developments on all fronts**
- **Diverging research/outcomes based on the fate arising from place of birth**
- **No oncology?**
- **As always extraordinary passion/commitment/guile/devotion**
- **Maintain the rage – the enemy is the virus**

