British HIV Association
BHIVA

Dr Sarah Fidler

Imperial College London

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COMPETING INTEREST OF FINANCIAL VALUE ≥ £1,000:	
Speaker Name	**Statement**
Dr Sarah Fidler	I have received research grants from MSD, ViiV and GSK as academic collaborations. I acted as a speaker for Gilead, MSD and ViiV at company sponsored events
Date	**October 2014**

Management of Acute HIV infection

The clinicians perspective

Sarah Fidler

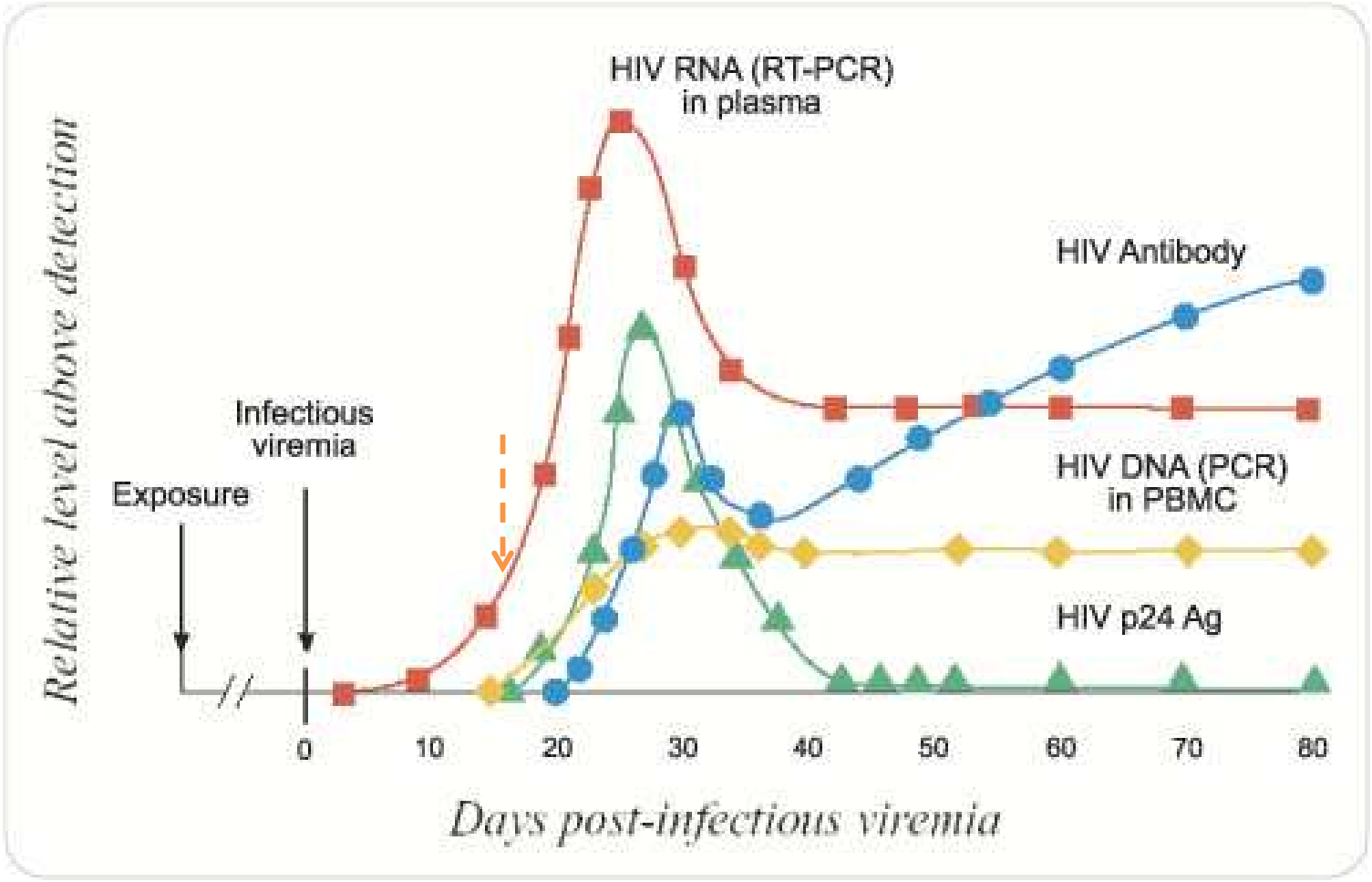
BHIVA Annual conference London

October 9th 2014

Case

- 35 year old man
- Asymptomatic MSM several CMP in preceding 2 months reported episodes of UPAI. No RMP
- STI screen negative for STS, CT GC, LGV
- HAV antibody positive, HBV antibody titre 260, HCV antibody & PCR negative
- HIV POCT NEGATIVE
- Venous blood *reactive* p24+ antibody negative

Days post-infection



Adapted from New York State Department of Health AIDS Institute. Available from http://www.hivguidelines.org/wp-content/uploads/2012/10/acute-hiv-infection-in-pregnancy-10-16-2012.pdf [accessed 26 Mar 2014].

Blood test results

- CD4 count 670
- CD4:8 ratio 0.3
- HIV Viral load 15 million copies
- HIV genotype WT B clade virus
- LFT: ALT 68,
- FBC normal
- Renal function normal
- UPC ratio normal
- HLA type B5701 negative

BHIVA Guidelines 2012 for Primary HIV infection

- “We recommend ART for patients presenting with primary infection and meeting any of the following criteria start ART:
- Neurological involvement (1D)
- Any AIDS defining illness (1A)
- Confirmed CD4 < 350 (1C)
- **Auditable measure**
- Proportion of patients presenting with primary HIV infection and either neurological involvement or an AIDS defining illness or confirmed CD4 count <350 cells/µL started on ART”

What would you discuss?

1. You don’t need immediate ART your CD4 count is > 350


9%

2. This is an important time to consider starting immediate ART to help protect your immune system and to prevent onward transmission


85%

3. There is no evidence that you need to start ART straight away, best to wait and you wont “need” ART for years


6%

Would you change your advice if the VL was 300 copies?

1. Yes

47%

2. No

53%

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

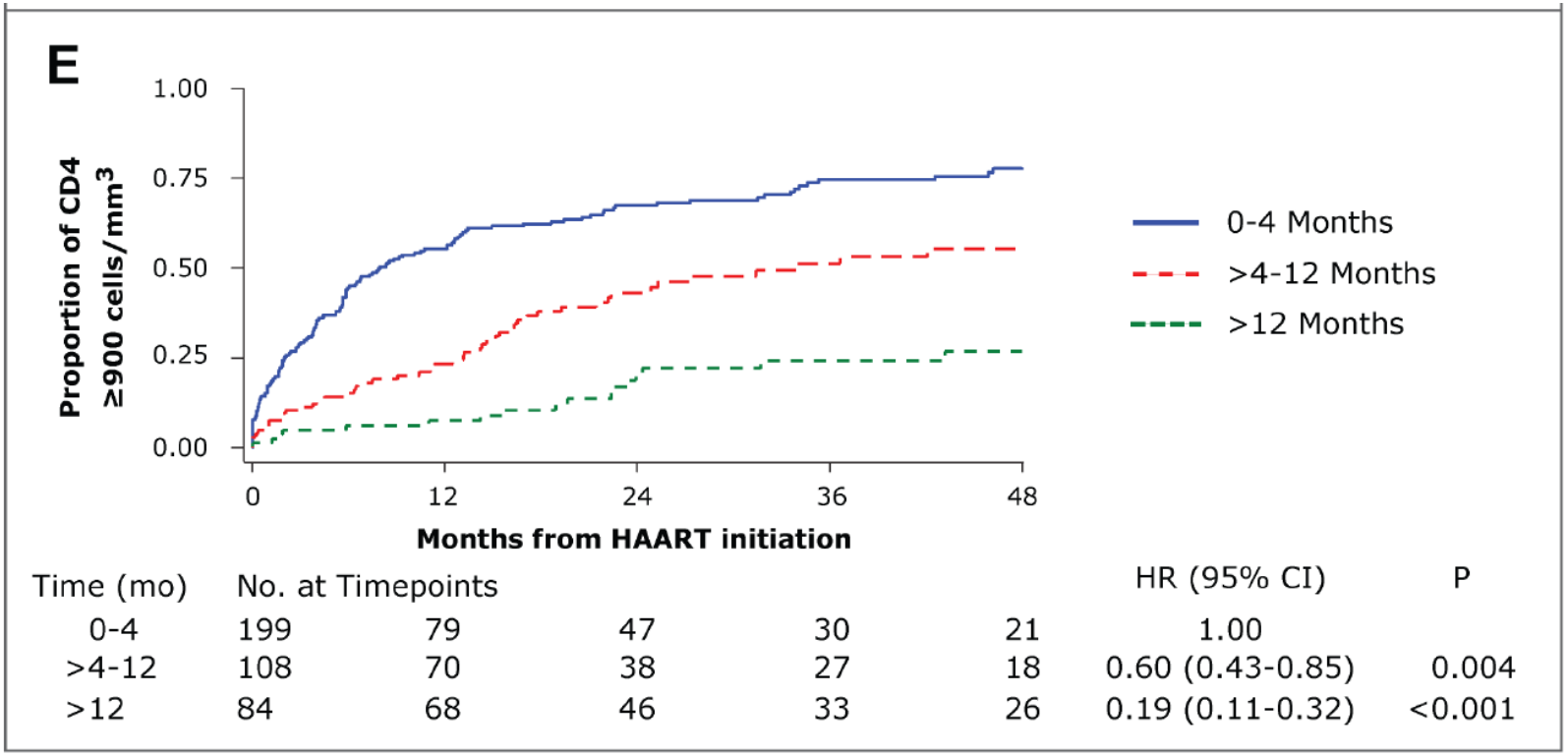
Enhanced CD4+ T-Cell Recovery with Earlier HIV-1 Antiretroviral Therapy

Tuan Le, M.D., Dr.P.H., Edwina J. Wright, M.D., Davey M. Smith, M.D., Weijing He, M.D., Gabriel Catano, M.D., Jason F. Okulicz, M.D., Jason A. Young, Ph.D., Robert A. Clark, M.D., Douglas D. Richman, M.D., Susan J. Little, M.D., and Sunil K. Ahuja, M.D.

Jan 18, 2013

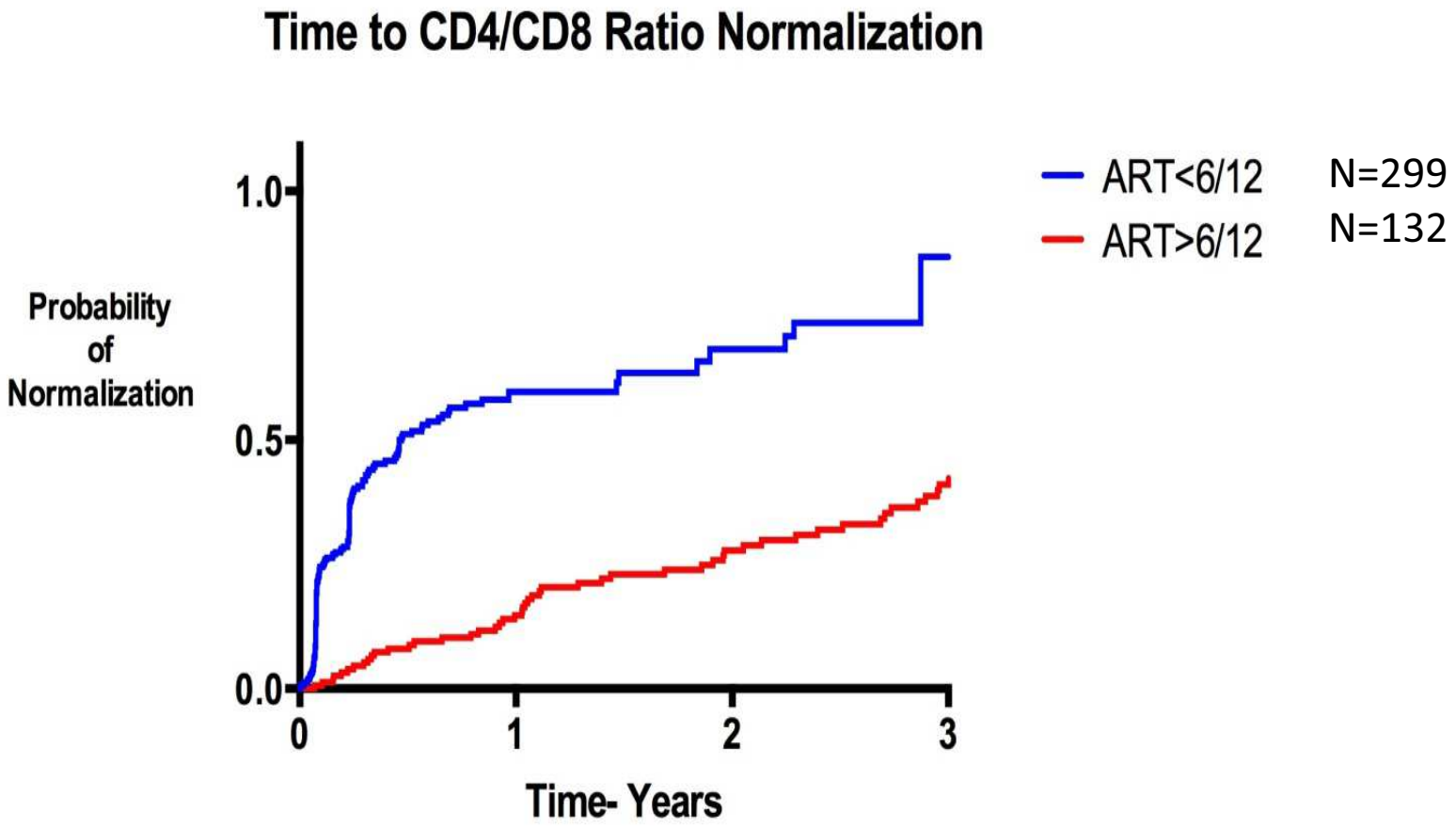
Imperial College London

Probability of attaining post-ART 900 CD4 cell count depends on time from EDI to ART initiation



Time (mo)	No. at Timepoints					HR (95% CI)	P
0-4	199	79	47	30	21	1.00	
>4-12	108	70	38	27	18	0.60 (0.43-0.85)	0.004
>12	84	68	46	33	26	0.19 (0.11-0.32)	<0.001

Time to CD4:8 ratio normalisation with ART started < or > 6 months from acute infection



Thornhill et al, Glasgow 2014

What about RCT evidence?

- In order to offer robust evidence RCT data with clear survival outcomes is needed
- There have been 3 RCT comparing immediate with deferred ART in PHI : Spartac, ACTG5217 and PRIMO-SMH
- All used transient ART schedules and end points were time to CD4 decline or initiation of lifelong ART.

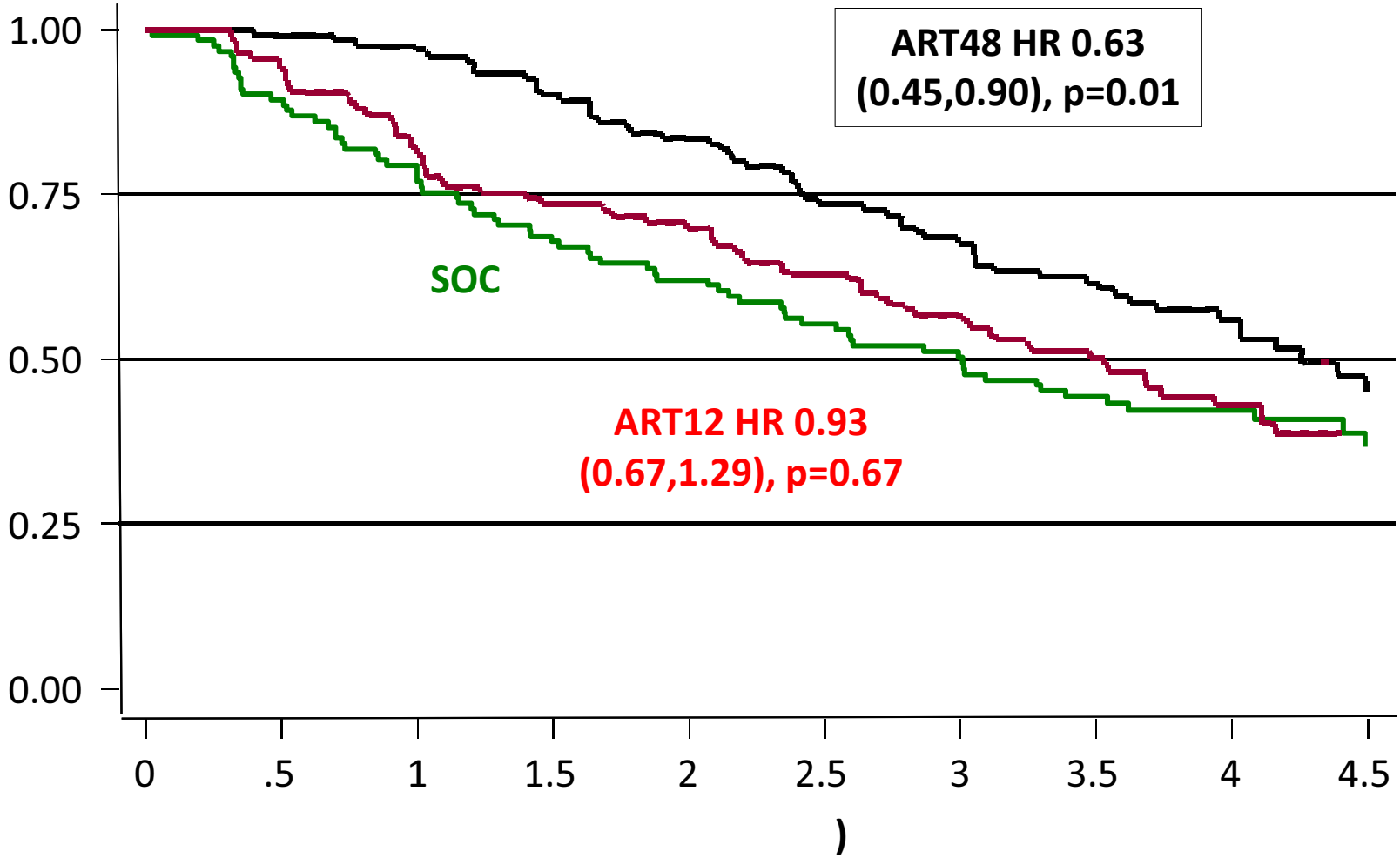
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 17, 2013 VOL. 368 NO. 3

Short-Course Antiretroviral Therapy in Primary HIV Infection

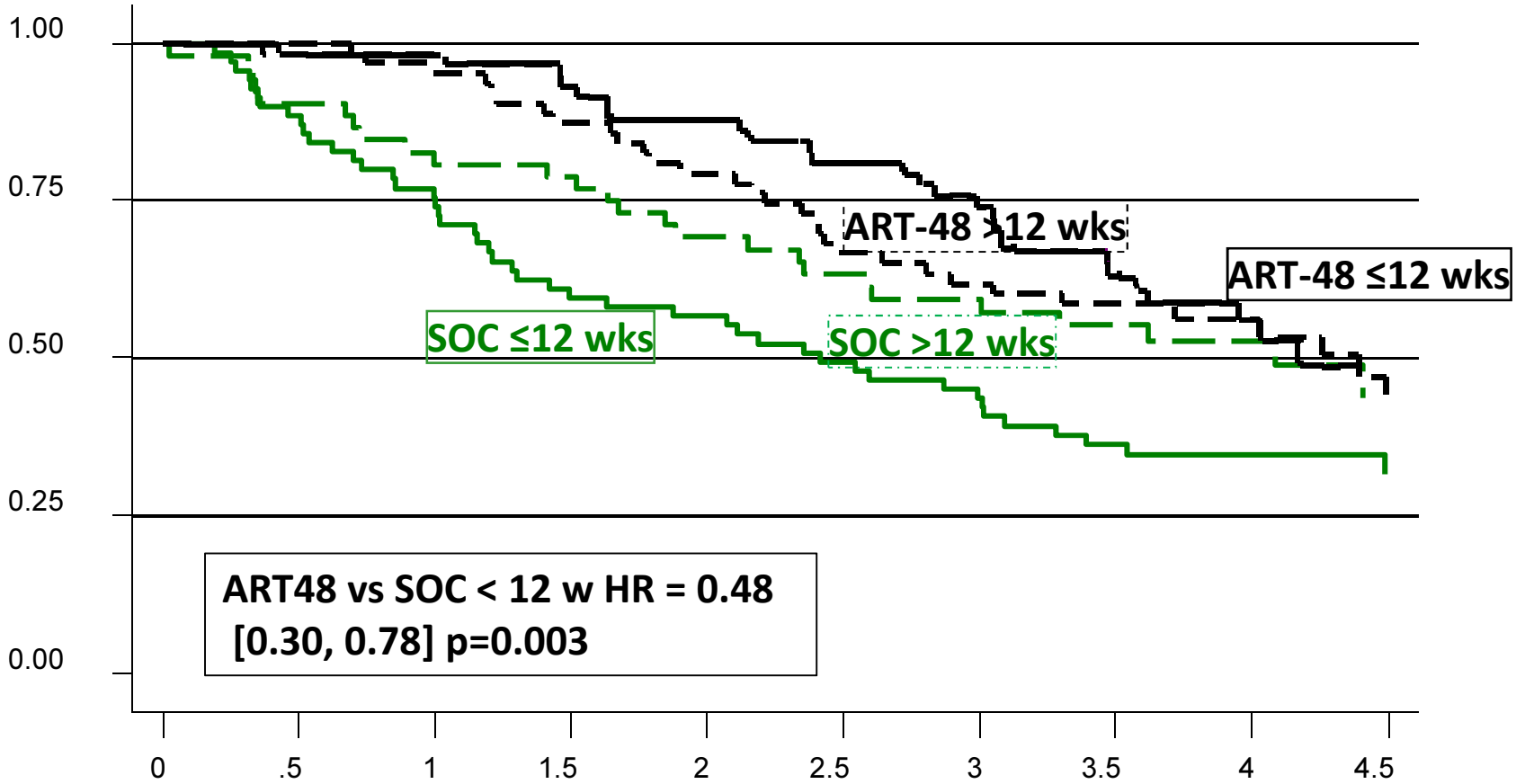
The SPARTAC Trial Investigators

Time to primary endpoint



SOC	123	109	93	82	75	66	59	46	30	18
ART-12	120	110	95	84	79	71	63	49	32	21
ART-48	123	121	117	109	100	88	80	63	41	19

Duration of infection and time to Primary Endpoint



Mr X decides he would like to start ART now
What ART regimen will you recommend?

1. Kivexa Efavirenz

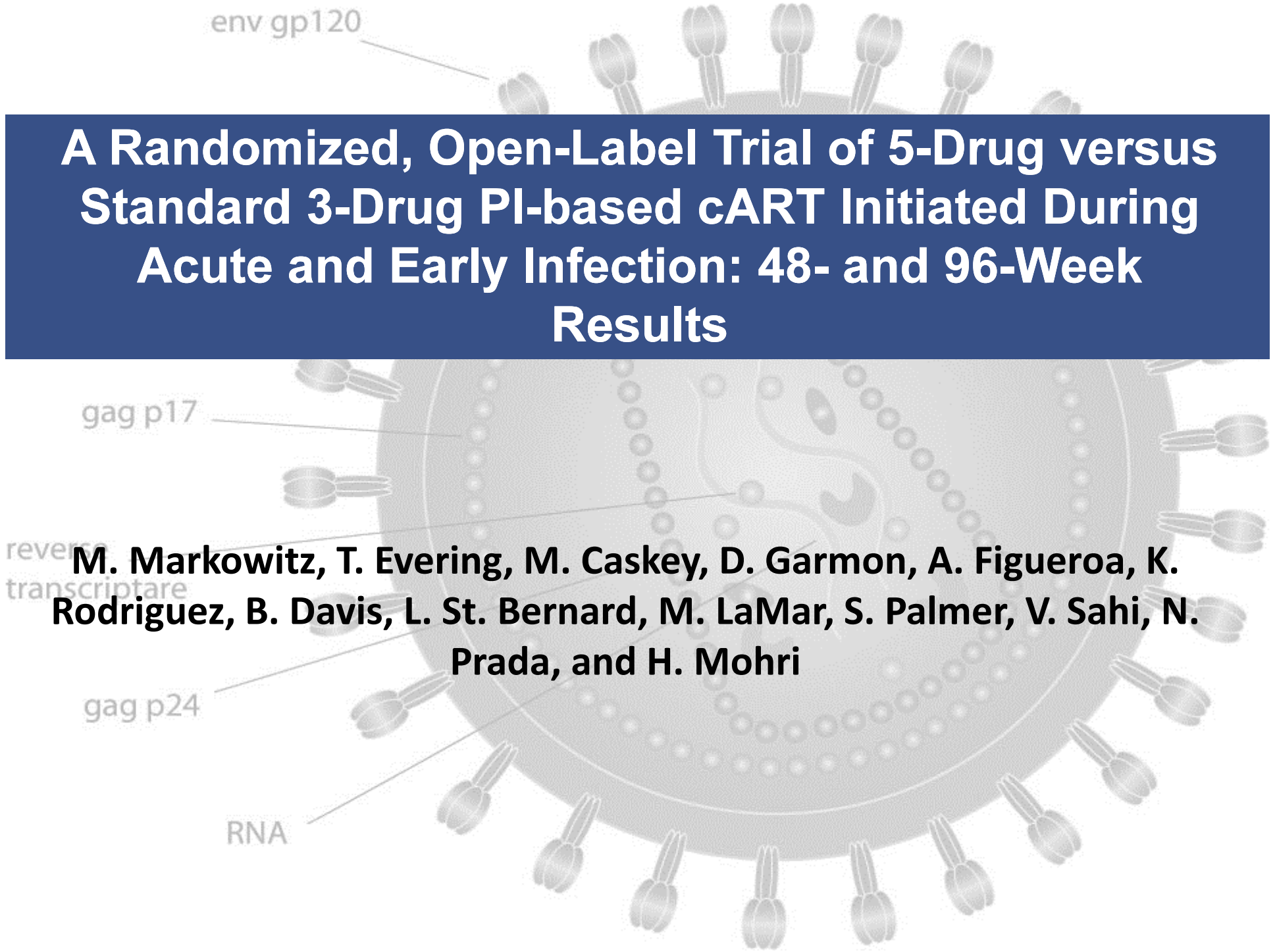
2. Kivexa Raltegravir

3. Truvada Raltegravir

4. Truvada Darunavir/Ritonavir

5. Truvada Darunavir/Ritonavir/Raltegravir

6. Truvada Dolutegravir



A Randomized, Open-Label Trial of 5-Drug versus Standard 3-Drug PI-based cART Initiated During Acute and Early Infection: 48- and 96-Week Results

M. Markowitz, T. Evering, M. Caskey, D. Garmon, A. Figueroa, K. Rodriguez, B. Davis, L. St. Bernard, M. LaMar, S. Palmer, V. Sahi, N. Prada, and H. Mohri

He has heard about the Visconti patients and he would be interested in HIV cure What would you tell him?

1. Visconti patients are very rare and shouldn't direct clinical decisions

10%

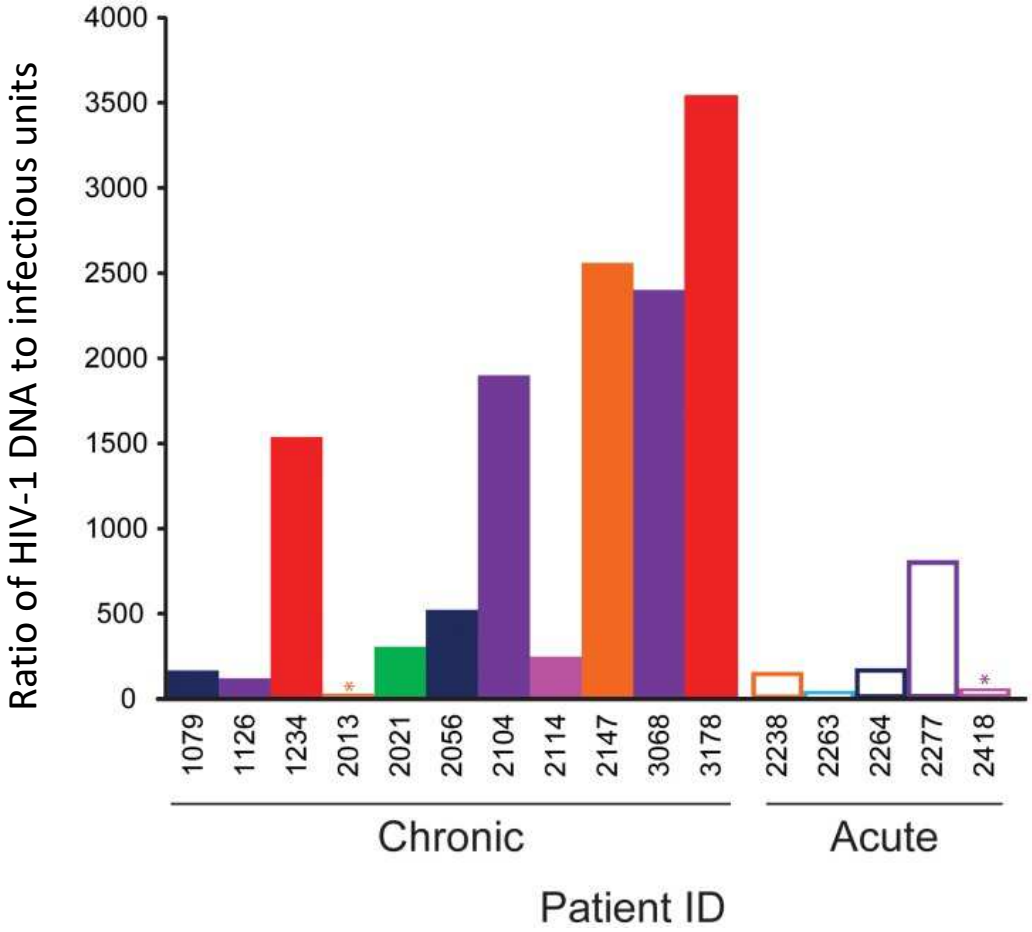
2. There is some evidence that ART in acute can reduce viral reservoirs and maybe very valuable for future cure interventions

84%

3. AIDS has no cure and there is only ONE patient in the world who has been cured so this should not direct ART choices

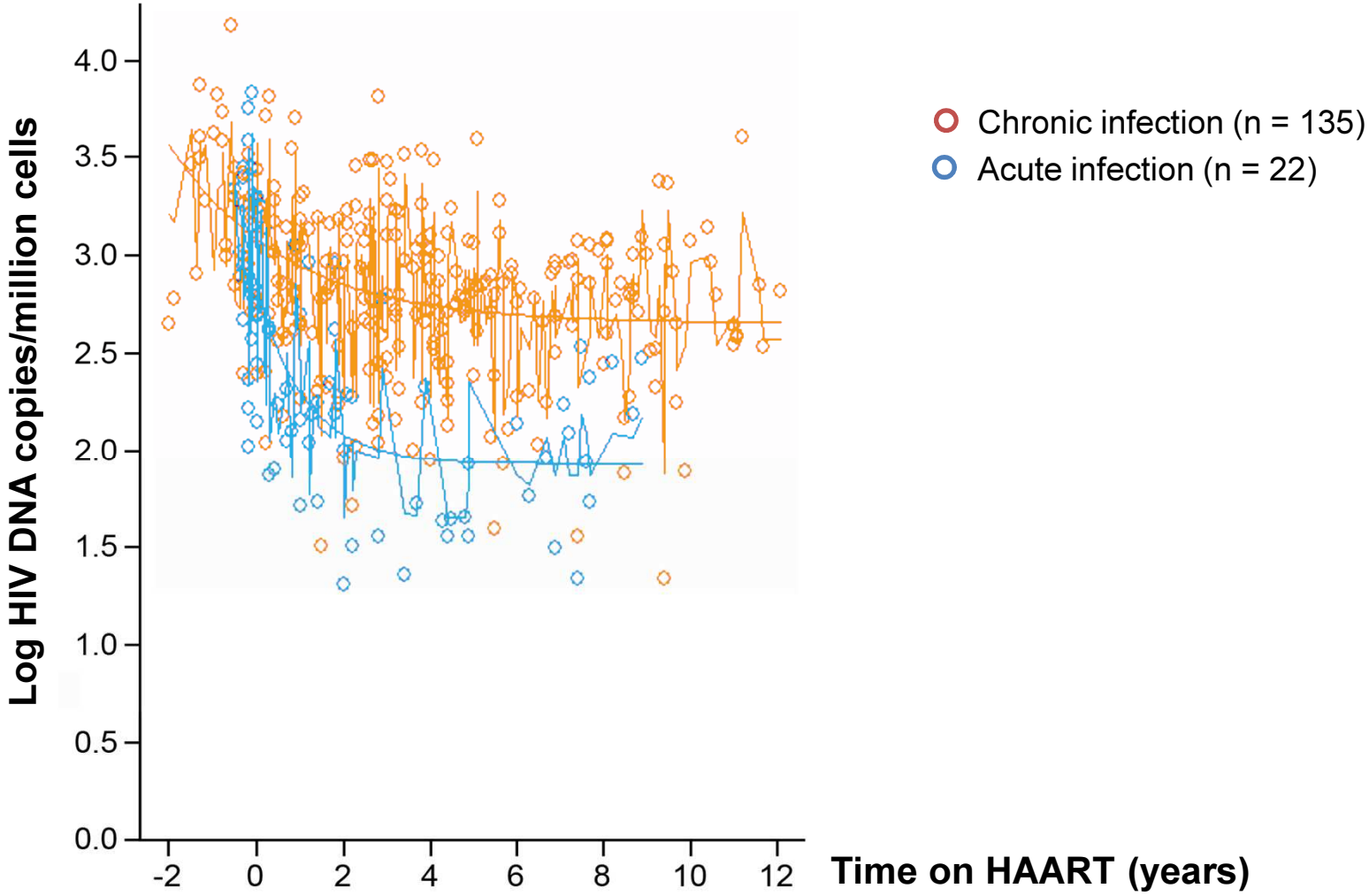
6%

Reservoir of HIV is less in acutely infected individuals



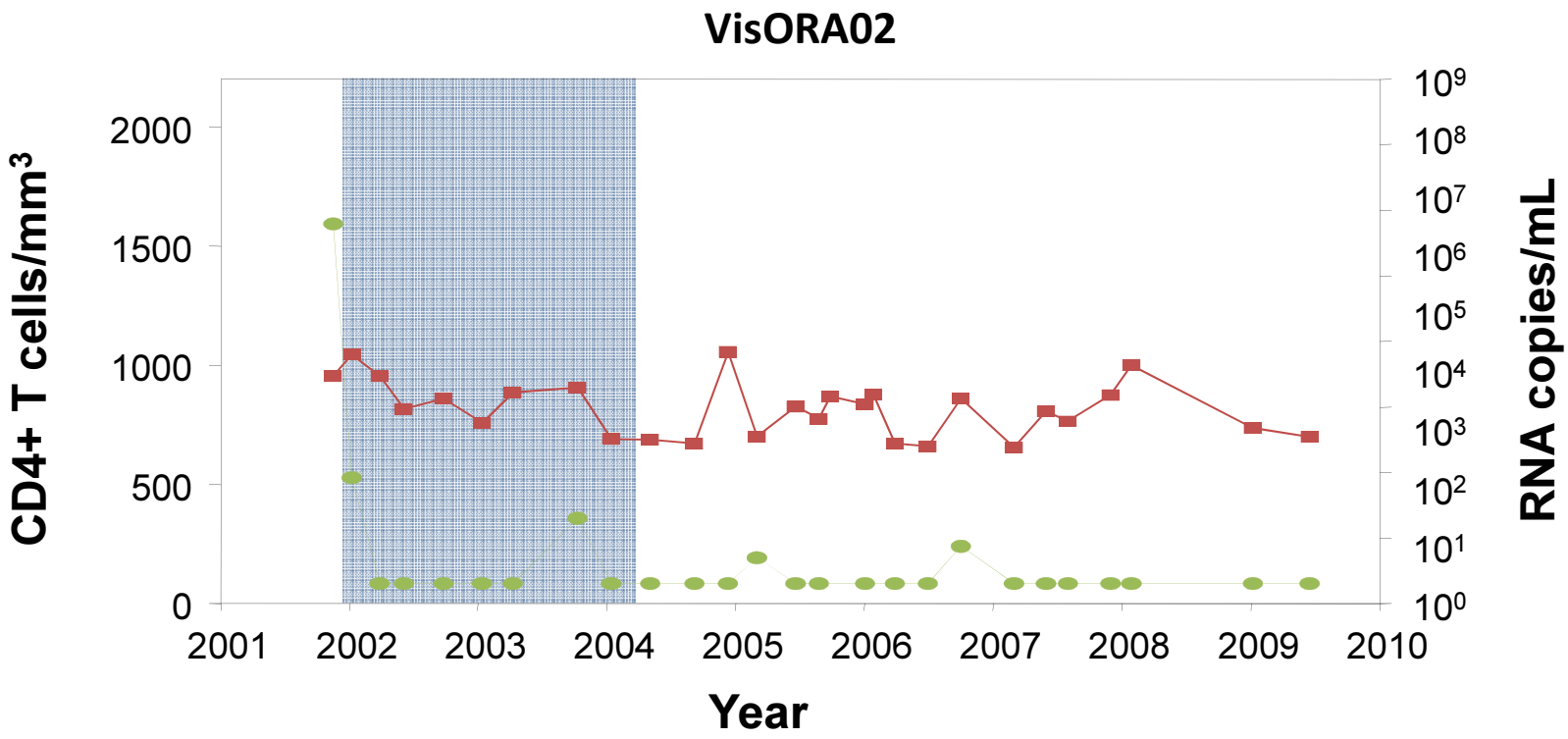
* Indicates maximum values in cases in which the HIV-1 DNA level was below the limit of detection (2 copies/ml).
Eriksson et al. PLoS Pathog 2013;9:e1003174.

Reservoir reduced with early treatment



Adapted from Hocqueloux L, et al. J Antimicrob Chemother 2013;68(5):1169-78.

VISCONTI
Functional cure: post-ART controllers



VISCONTI cohort; n = 12, treated in acute infection;
median times since treatment interruption at 72 months

Saez-Cirion et al. PLoS Pathog. 2013 Mar;9(3):e1003211

To treat or not to treat?

Yes

- Better chance of immune recovery
- Better chance of limitation of viral reservoir in preparation for cure interventions
- Reduce risk of onward transmission
- Reduce the years of on going immune activation

No now

- Patients have years of future ART why expose them any longer than needed to drug toxicities?
- Ambivalent to treatment and too many other psychological issues at time of PHI
- Increased risk of drug resistance developing if poorly adherent

THANKS

Participants of SPARTAC & HEATHER

- The SPARTAC trial Investigators

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- Sarah Fidler
- John Thornhill
- Jonathan Weber

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- John Frater
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- James Williams
- Matt Pace
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- Abdel Babiker
- Kholoud Porter

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- Tony Kelleher
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Upenn

Una O'Doherty

Patient Groups

Simon Collins
Damien Kelly

Clinical colleagues

Julie Fox
Sabine Kinloch
Gary Whitlock
Nneke Nwokolo
Martin Fisher

SPARTAC
Treating recent HIV infection

Imperial College London

The Peter Medawar Building for Pathogen Research

British HIV Association BHIVA

MRC Medical Research Council

OXFORDMARTIN SCHOOL

NHS National Institute for Health Research

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