Treatment update

Bronagh McBrien

June 2016

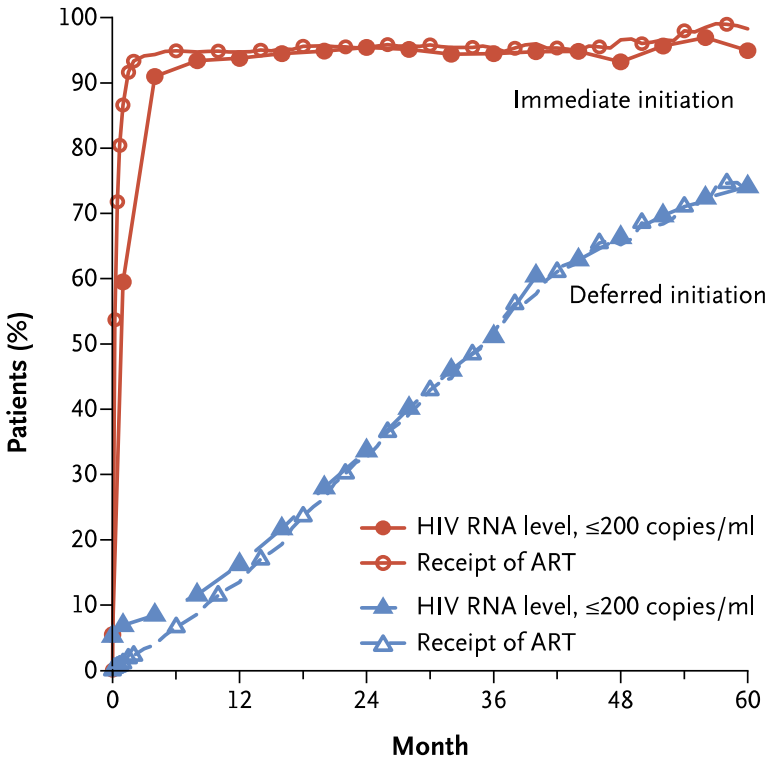
Speaker Name	Statement
Bronagh McBrien	Received educational funding and support from Gilead, Merck, Boehringer Ingelheim, Janssen-Cilag
Date :	**27 June 2016**

Brief

- BHIVA guidelines
  - When to start
  - What to start
  - Added extras
- Novel strategies
- New kids on the block

START

ART Use and HIV RNA Level



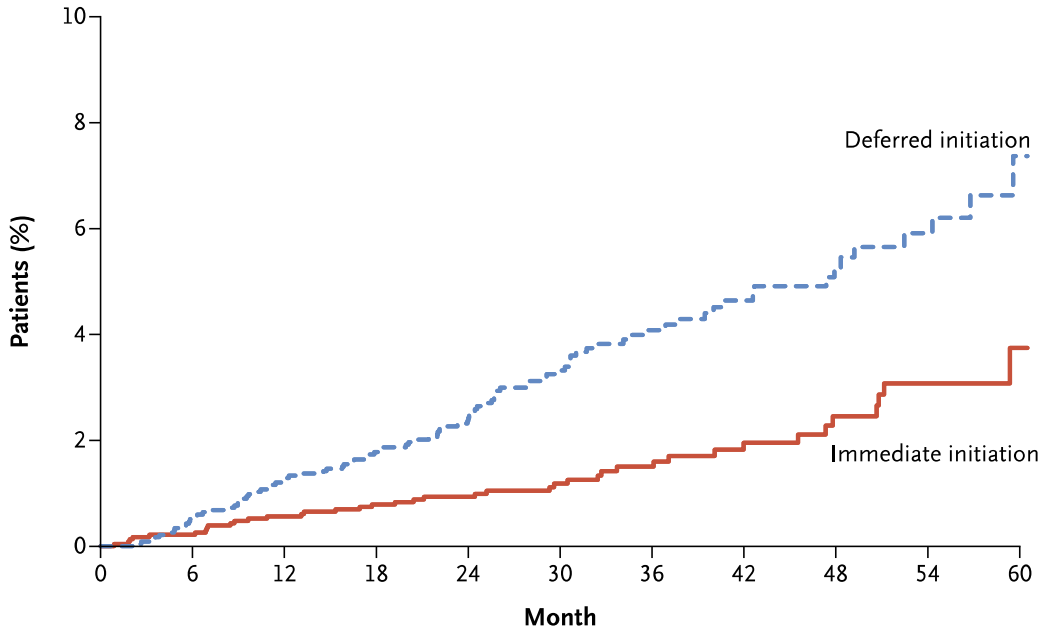
No. of Patients						
Immediate initiation	2326	2287	1809	1040	551	115
Deferred initiation	2359	2303	1837	1055	546	109

The INSIGHT START Study Group NEJM 2015

Central Manchester University Hospitals NHS
NHS Foundation Trust

START

Time to First Primary Event



No. at Risk											
Immediate initiation	2326	2302	2279	2163	1801	1437	1031	757	541	336	110
Deferred initiation	2359	2326	2281	2135	1803	1417	1021	729	520	334	103
Estimated Percentage											
Immediate initiation		0.2	0.6	0.8	0.9	1.2	1.5	2.0	2.5	3.1	3.7
Deferred initiation		0.5	1.2	1.8	2.4	3.3	4.1	4.6	5.3	5.9	7.4

The INSIGHT START Study Group NEJM 2015; 373

BHIVA Recommendations

2013

People with chronic infection start ART if the CD4 cell count is 350 cells/mL

Or with the following conditions:

- AIDS
- HIV-related co-morbidity
- HBV
- HCV if the CD4 count is ≤500
- nADM requiring immunosuppressive radiotherapy or chemotherapy
- Or to reduce the risk of transmission of HIV to others

2015

- People with HIV start ARV

What to start

	Preferred	Alternative
NRTI backbone	Tenofovir and Emtricitabine	Abacavir and Lamivudine
Third agent	Atazanavir/r	Efavirenz
	Darunavir/r	
	Dolutegravir	
	Elvitegravir/c	
	Raltegravir	
	Rilpivirine	

Case study

- GM 33 year old MSM
- Occupation - builder
- Feb 2016 diagnosed HIV positive
- PMHx Nil
- CD4 731cells/mm^3 ; VL 53,000 WT
- HLA B*5701 negative
- Trouble accepting diagnosis
- Not currently sexually active

Treatment options

A Truvada® Darunavir Ritonavir

B Triumeq®

C Kivexa® Efavirenz

D Something else

E Defer treatment

Commissioning

- NHS England recognises the impact of the START trial on BHIVA recommendations
- Assess cost effectiveness alongside clinical efficacy
- Local engagement
- Implement regional drug frameworks to guide drug usage

Case study

- GM in a new relationship with a HIV negative partner
- Would like to start TasP
- What would you recommend?

Treatment options

A Truvada® Darunavir Ritonavir

B Triumeq®

C Kivexa® Efavirenz

D Something else

E Defer treatment

Useful resources

- Special populations
  - Women
  - Adolescents
  - Bone disease
  - Later life

- Appendix 4: Food requirements for antiretrovirals

- Appendix 5: Dose adjustments of ARV's for renal impairment

Novel Strategies

- Nuc-sparing
- Monotherapy

Novel Strategies

Benefits

- Reduced toxicity
- Patient tolerability
- Cost effectiveness
- Increased NRTI resistance with PrEP use???

Novel Strategies

Boosted **Darunavir** and **Raltegravir**

in treatment naïve patients with CD4 count >200cells/µL

and a viral load <100,000copies/ml

where there is a need to avoid Abacavir and Tenofovir

Monotherapy

- PI monotherapy suboptimal for initial treatment
- Reasonable efficacy as switch
  - Better virological outcomes correlate with longer period of prior viral suppression

New(er) Agents

- Dolutegravir
- Evotaz
- Rezolsta
- Tenofovir Alafenamide

Dolutegravir

- Licensed Jan 2014
- Integrase inhibitor
- High genetic barrier to resistance
- Reduced side effects and improved tolerability compared with some alternatives
- May 2015 SmPC update Undesirable effects
  - Depression common side effect (1-10%)

Dolutegravir in the real word: is it all plain SAILING?

J Shaw, B McBrien, A Hatley, C Wood, S Jewsbury, C Ward
The Hathersage Integrated Contraception, Sexual Health and HIV Service,
Central Manchester University Hospitals NHS Foundation Trust, UK
Contact email: jonathan.shaw2@cmft.nhs.uk

- 178 patients initiated on DTG until Oct 2015
- 26 (~15%) patients discontinued DTG:
  - 15 (8%) due to side effects,
- Side effects were reported by 23% patients
  - gastrointestinal (33.9%)
  - CNS disturbance (32.1%).
- Two virological failures occurred in patients taking Triumeq, both failing with Raltegravir associated mutations (T97AT, E157Q)

Dolutegravir

- Post marketing experience Royal Victoria Hospital
- 68 patients on Dolutegravir
- Side effects reported in 32% of patients
- 16% reported CNS effects
- 9% discontinued due to intolerable side effects

Todd, Rafferty, Dinsmore et al. HIV Medicine, 16 Suppl 2 P8

New PI agents

- Evotaz (Atazanavir / Cobicistat)
- Rezolsta (Darunavir /Cobicistat)
- PK booster
- Review interactions when switching patients
- Increase serum creatinine

Tenofovir Alafenamide

- New prodrug of Tenofovir

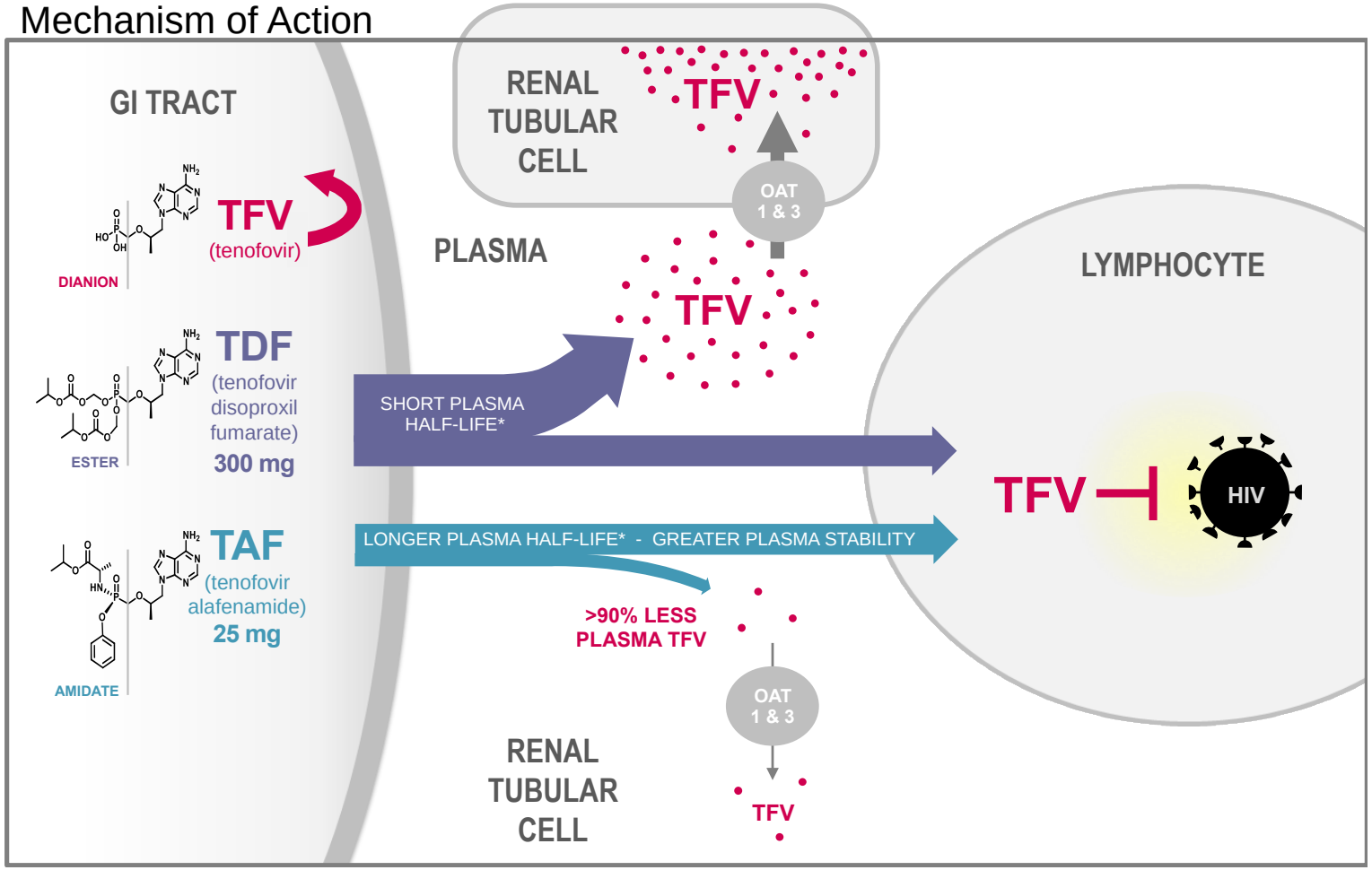
- Three licensed fixed dose combinations

  Genvoya

  Descovy

  Odefsey

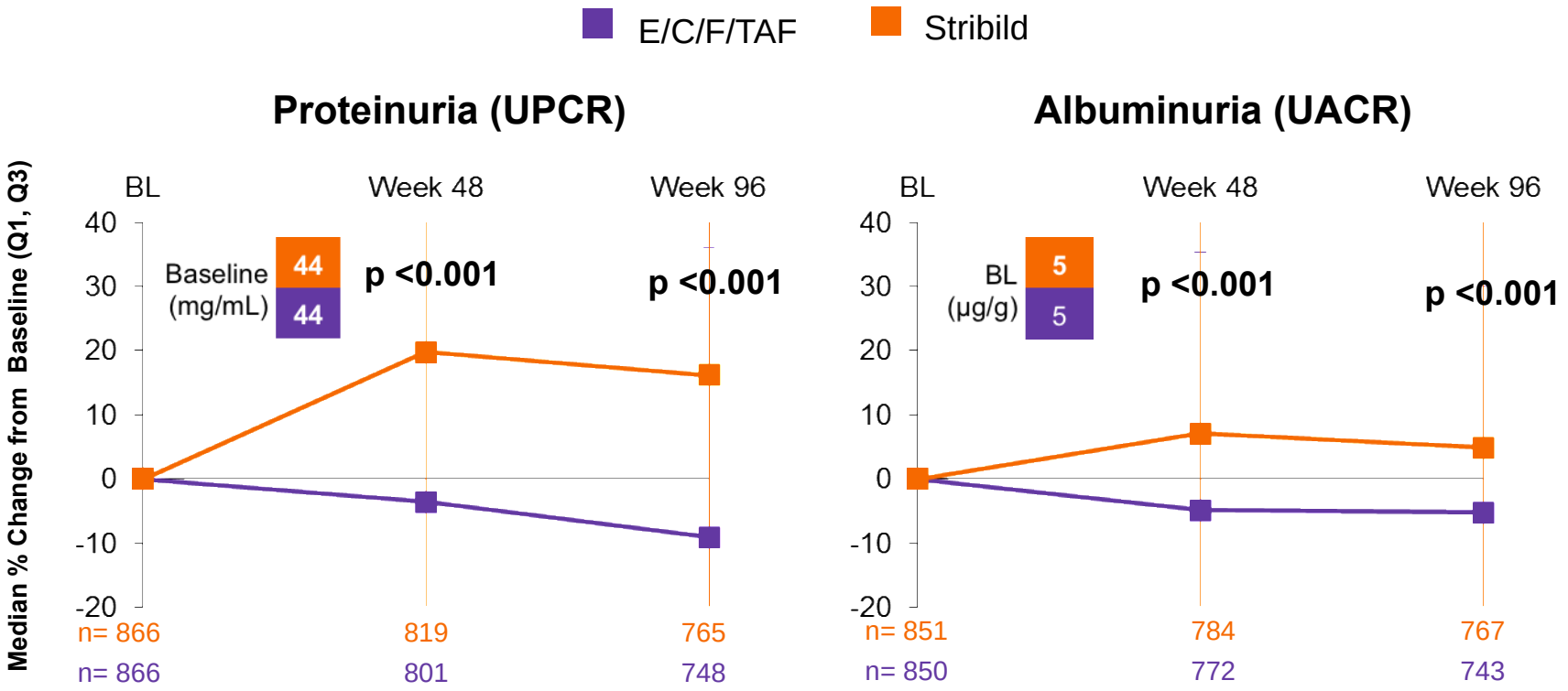
Mechanism of action



Lee W et al. *Antimicr Agents Chemo* 2005; Birkus G et al. *Antimicr Agents Chemo* 2007; Babusis D, et al. *Mol Pharm* 2013; Ruane P, et al. *J Acquir Immune Defic Syndr* 2013; Sax P, et al. *JAIDS* 2014; Sax P, et al. *Lancet* 2015.

Changes in Quantitative Proteinuria

Studies 104 and 111: ART-Naïve Adults, Week 96 Combined Analysis



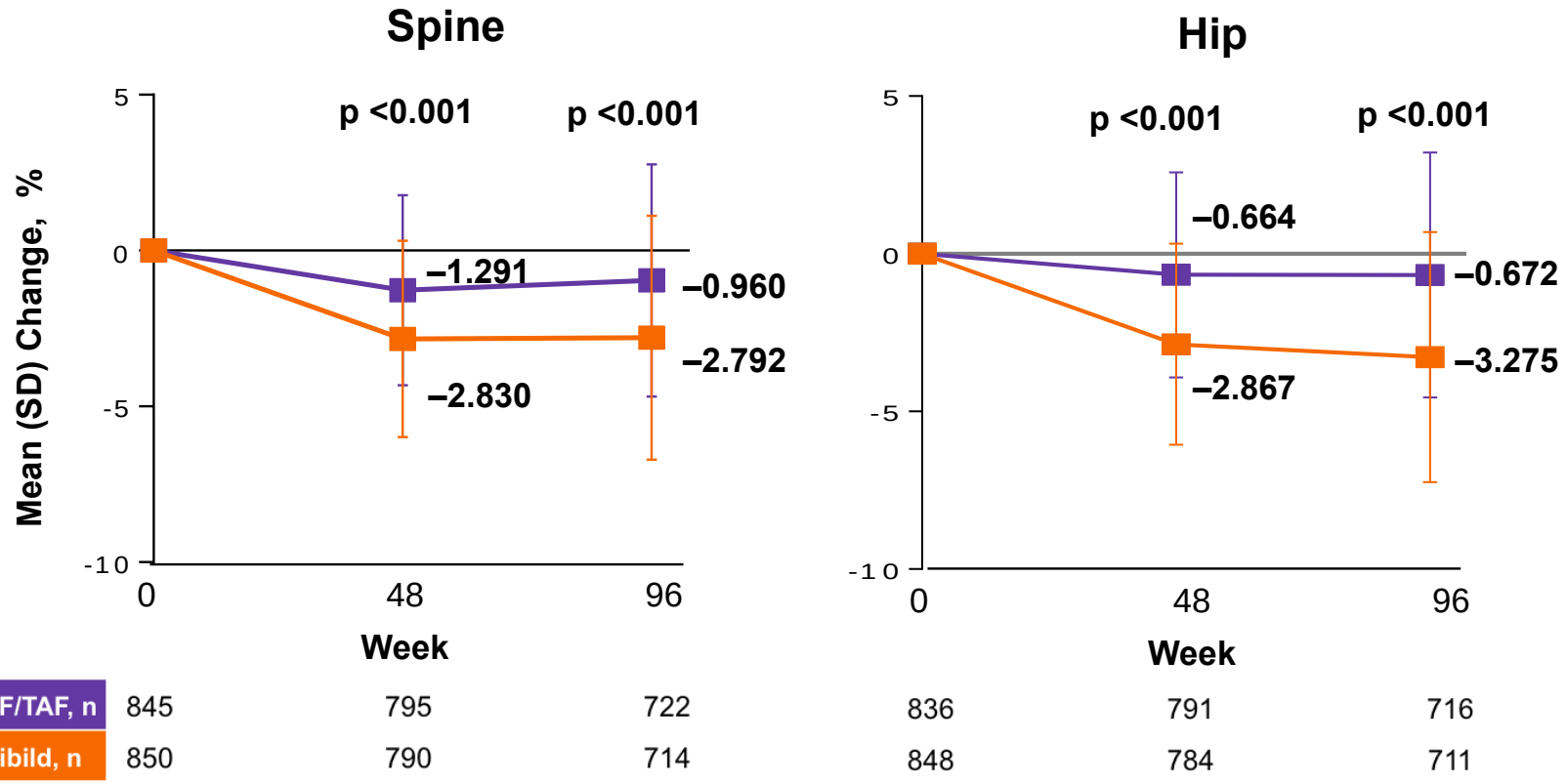
Median change in $eGFR_{CG}$ at Week 96 for TAF vs TDF: -2.0 mg/dL vs -7.5 mg/dL (p <0.001)

Decreases in proteinuria and albuminuria on E/C/F/TAF maintained through week 96

Wohl D, et al. EACS 2015. Barcelona, Spain. Best Poster #LBBPD1/1

Changes in Spine and Hip BMD

Studies 104 and 111: ART-Naïve Adults, Week 96 Combined Analysis



Less spine and hip BMD loss on E/C/F/TAF maintained through week 96 with no further BMD loss after week 48

Wohl D, et al. EACS 2015. Barcelona, Spain. Best Poster #LBBPD1/1

Summary

- Ongoing research into new treatment
- Increase testing
- Keeping patients engaged with care
- Access to treatment for everyone