Chelsea and Westminster Hospital NHS
NHS Foundation Trust

Safety of switching raltegravir 400mg twice daily to raltegravir 800mg once daily in virologically suppressed patients

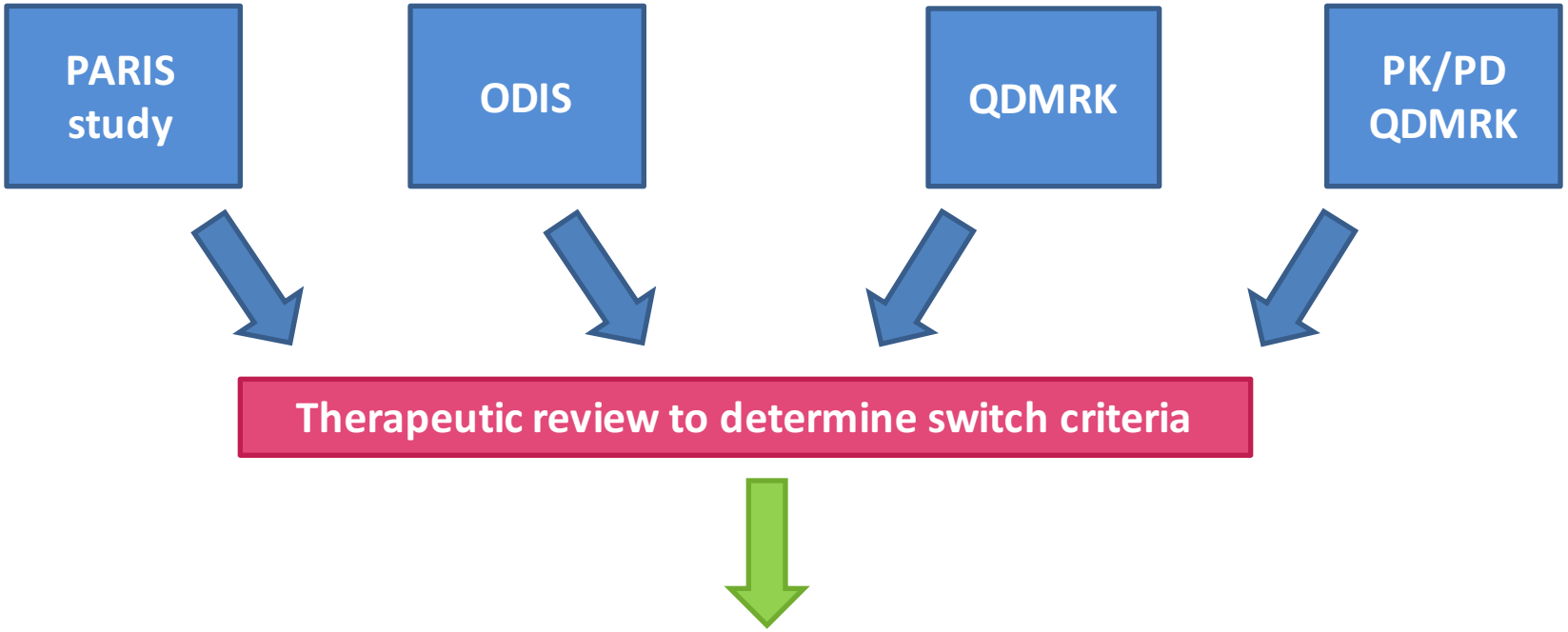
Amy Moore, Sonali Sonecha, Tristan Barber, Anton Pozniak, David Asboe, Marta Boffito

Chelsea and Westminster Hospitals NHS Foundation Trust

Background

- Raltegravir and efavirenz are first-line 3rd ARV agents in the London guidelines
- Twice-daily regimens may not be convenient for all patients
- Raltegravir is licensed at a dose of 400mg twice-daily, but its half-life and long binding to the HIV integration complex suggest it may be effective in a once-daily dose for select patients

Switch strategy



Undetectable viral load (<40 copies/mL) for > 6 months with 2 consecutive VL<40

Full virological history of no viral resistance/virological failure while on any ART

Eron J, Rockstroh J, Reynes J et al and the QDMRK investigators. Raltegravir once daily or twice daily in previously untreated patients with HIV-1: a randomised, active-controlled, phase 3 non-inferiority trial. Lancet Infect Dis 2011; **11**: 905-15

Vispo E, Barreiro P, Maida I et al. Simplification from protease inhibitors to once-or twice-daily raltegravir: The ODIS Trial. HIV Clin Trials 2010; **11**(4): 197-204

Caby F, Bonmarchand M, Soulie B et al. Efficacy of raltegravir once daily in switching strategies in HIV-1 infected patients with suppressed viraemia. 14th European AIDS Conference October 2013. Abstract

Rizk M, Hang Y, Luo W-L et al. Pharmacokinetics and Pharmacodynamics of once-daily versus twice-daily raltegravir in treatment naïve HIV-infected patients. Antimicrobial Agents and Chemotherapy 2012; **56**(6): 3101-3106

Molto J, Valle M, Back D et al. Plasma and intracellular (peripheral blood mononuclear cells) pharmacokinetics of once-daily raltegravir (800milligrams) in HIV-1 infected patients.

Switch strategy continued

- It was agreed in the HIV drugs sub group that;

All switches to be referred to the virtual HIV MDT clinic
Recommended that all patients are followed up for 1st VL within 3 months of switch

- It was agreed that pharmacy would;

Counsel all patients on unlicensed dosage
Provide all patients with a specially developed PIL
Take a full medication history for each patient to identify any DDIs
Counsel all patients to take with/after food
Document all of the above in the patients medical record using a specially designed counselling template

Aims

- Data was collected for all patients switched to RAL OD from October 2015 to January 2017 and analysed to observe;
  - The number of patients that maintained virological suppression
  - The number of patients who discontinued RAL OD for any reason

Results

Baseline characteristics			
Number of patients switched to RAL OD	271		
Mean CD4 (c/µL) prior to switch	603		
3rd ART agent prior to switch	RAL BD	NNRTI	Other
	200 (74%)	66 (24%)	5 (2%)
ART backbone prior to switch	TDF/FTC	ABC/3TC	Other
	205(75%)	61 (23%)	5 (2%)

1st VL Results

Number of pts with 1st VL result post-switch	192 (71%)
Median time to 1st VL post-switch (weeks)	12
Number of pts with 1st VL < 40	188 (98%)
Number of pts with 1st VL > 40	4 (2%)
Number of pts with 1st VL > 40 whose repeat VL < 40	3 (75%)

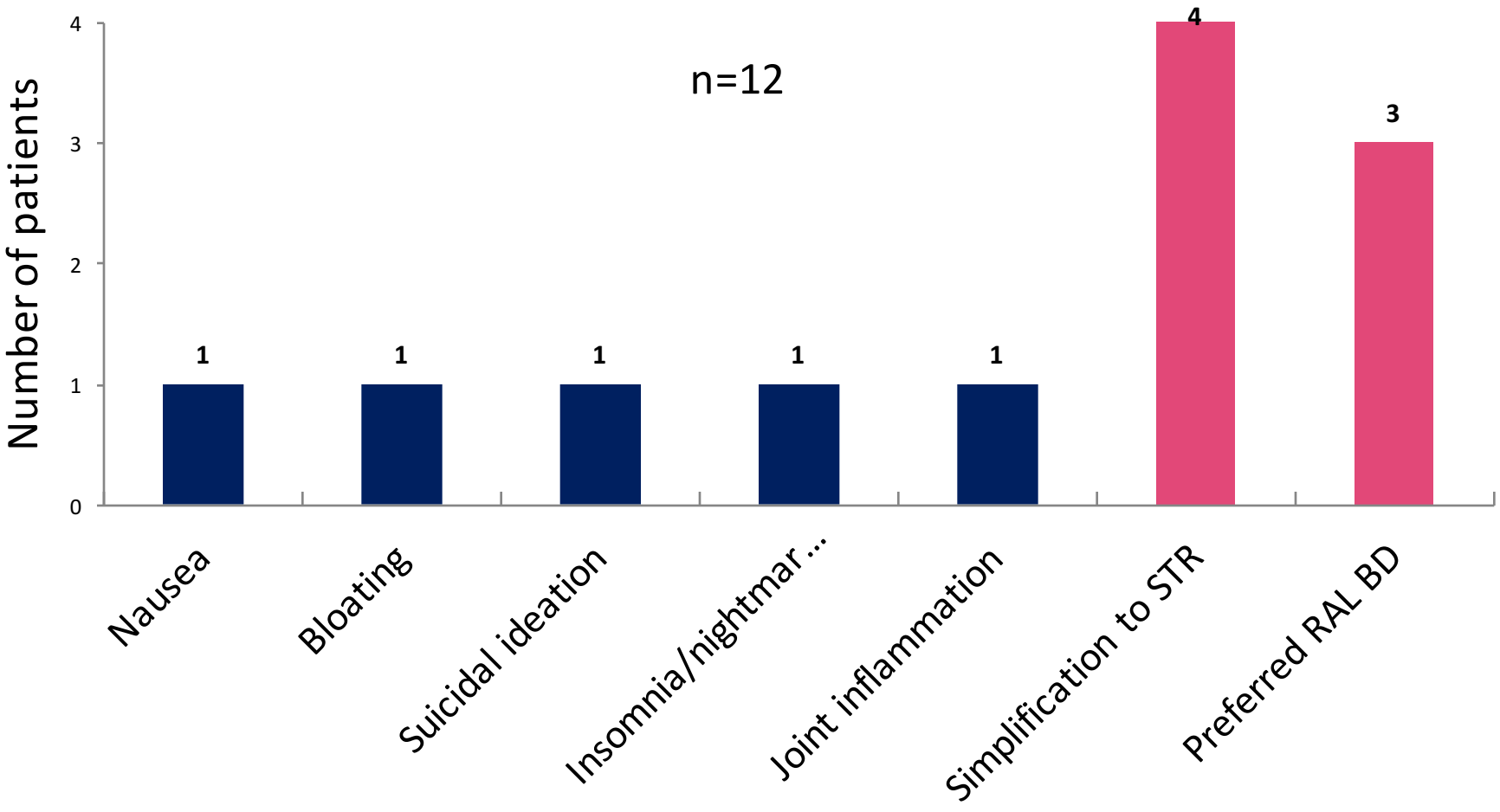
- Of the 4 patients with a 1st VL >40 the results were 43, 45, 59 and 68 respectively
- 3 of the 4 patients repeat VL was <40 with no change to the ARV regime
- 1 pts repeat VL (1st VL = 45) has yet to be repeated

2nd VL Results

Number of pts with 2nd VL post-switch	85 (43%)
Median time to 2nd VL post-switch (weeks)	28
Number of pts with 2nd VL < 40	81 (95%)
Number of pts with 2nd VL > 40	4 (5%)
Number of pts with 2nd VL > 40 whose repeat VL < 40	3 (75%)

- Of the 4 patients with a 2nd VL >40 the results were 41, 54, 65 and 153 respectively
- 3 of the 4 patients repeat VL was <40 with no change to the ARV regime
- 1 pts repeat VL (2nd VL = 41) has yet to be repeated

Switches from RAL OD for any reason including adverse events



Discussion

- Between October 2015 and January 2017, 271 patients who met the pre-determined switch criteria chose to switch to RAL OD
- 188/192 (98%) patients with a 1st VL post-switch have a VL<40
- 81/85 (95%) patients with a 2nd VL post-switch have a VL<40
- No patients have 2 consecutive VL>40 post-switch*
- Only 5/271 (1.8%) patients switched to an alternate regimen due to reported ADRs

*pending the 2 pts who are awaiting a repeat 1st/2nd VL respectively

Conclusions

In patients established on ART who desire a once-daily regimen and who meet the local guideline criteria, the use of raltegravir 800mg once-daily is safe in terms of maintaining an undetectable viral load as well as patient tolerability.

Acknowledgements

- All members of the Chelsea and Westminster HIV multidisciplinary team
- The HIV pharmacy team at Chelsea and Westminster for helping with data collection
- All our patients, without whom there could be no ‘good outcomes’ to ART
- BHIVA for inviting me to speak today