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Switch to 3TC+Darunavir/ritonavir (DRV/r) dual therapy Subgroup analysis of DUAL clinical trial (GESIDA-8014-RIS-EST45)

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DUAL-GESIDA-8014-RIS-EST45 Study Group

INTRODUCTION

Dual therapy with a boosted protease inhibitor and Lamivudine can have advantages in terms of toxicity and costs

OLE[1], SALT[2] and ATLAS-M[3] have demonstrated that dual therapy (DT) with Lamivudine (3TC) and Lopinavir/r or Atazanavir/r is non inferior to triple therapy (TT) with 2 nucleos(t)ides and Lopinavir/r or Atazanavir/r for maintenance of virological suppression

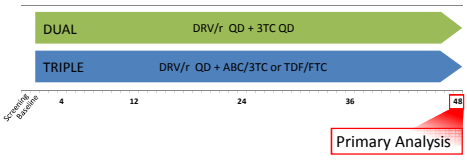
Boosted Darunavir is currently the preferred protease inhibitor in most international guidelines of HIV therapy. Switching to lamivudine and Darunavi/r (DRV/r) has been tested in a clinical trial (DUAL Study[4]), showing that switch to 3TC+DRV/r is non-inferior to maintenance of triple therapy with 2 nucleos(t)ides and DRV/r, in patients with suppressed viral load.

Here we present a subgroup analysis of the DUAL study results.

1.- The Lancet Infectious Diseases 2015. 15:785–792.
2.- Journal of Antimicrobial Chemotherapy 2017. 72:246-253.
3.- Journal of Antimicrob Chemotherapy 2017. 72:1163-1171.
4. HIV Drug Therapy / Glasgow 2016. 23-26 October 2016, Glasgow, UK #O331

DUAL STUDY DESIGN

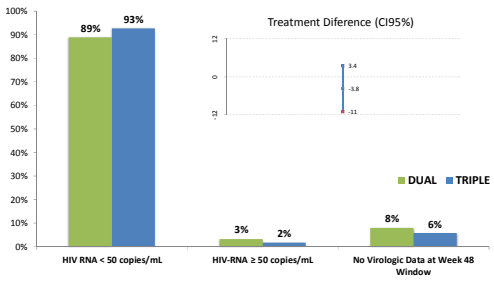
- VL < 50 c/mL > 6 months
- No resistance to DRV/r o 3TC
- On treatment with DRV/r + ABC/3TC or TDF/FTC ≥ 2 months
- HBsAg negative
- Randomized 1:1. Stratified by baseline nucleos(t)ides



PRIMARY ENDPOINT

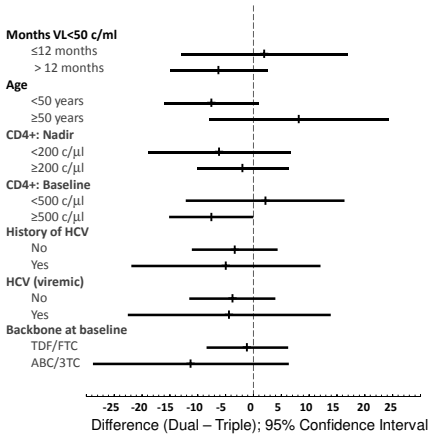
Proportion of patients with suppressed viral load (HIV-RNA < 50 copies/mL) after 48 weeks of follow-up according to the FDA snapshot algorithm in the ITT exposed population.

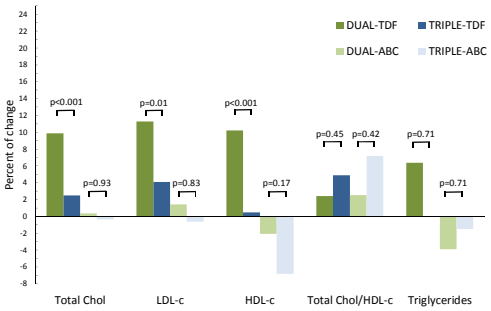
PRIMARY ENDPOINT: Snapshot, ITT-e population

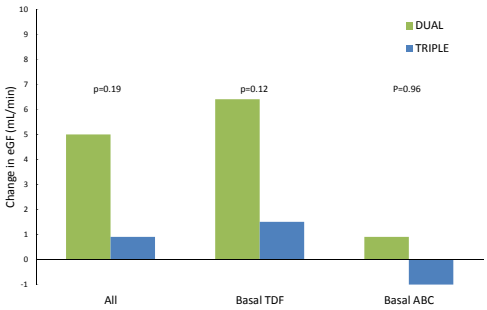


SUBGROUP ANALYSIS

	TOTAL	DUAL		TRIPLE		Difference of Proportions (95%CI)	Interaction p-value
		Virological Success					
	N = 249	N = 126		N = 123			
Months VL<50 c/ml							
<=12	61	37/40	93%	19/21	90%	2.0 (-13.0;17.0)	0.367
>12	186	73/84	87%	95/102	93%	-6.2 (-15.0;2.5)	
Unknown	2						
Age							
<50 ys	190	77/89	87%	95/101	94%	-7.5 (-16.0;0.9)	0.078
>=50 ys	59	35737	95%	19/22	86%	8.2 (-7.9;24.3)	
CD4: Nadir							
<200 cell/mm3	101	39/46	85%	50/55	91%	-6.1 (-19.0;6.7)	0.757
>=200 cell/mm3	145	71/77	92%	64/68	94%	-1.9 (-10.1;6.3)	
Unknown	3						
CD4: Baseline							
<500 cell/mm3	92	40/46	87%	39/46	85%	2.2 (-12.1;16.4)	0.107
>=500 cell/mm3	156	71/79	90%	75/77	97%	-7.5 (-15.1;0.0)	
Unknown	1						
History of HCV							
No	189	85/94	90%	89/95	94%	-3.3 (-11.0;4.4)	0.985
Yes	60	27/32	84%	25/28	89%	-4.9 (-21.9;12.1)	
HCV (viremic)							
No	214	95/107	89%	99/107	93%	-3.7 (-11.5;4.0)	0.929
Yes	35	27/32	89%	15/16	94%	-4.3 (-22.5;13.9)	
Backbone at baseline							
Tenofovir/emtricitabine	186	86/93	92%	87/93	94%	-1.1 (-8.4;6.3)	0.444
Abacavir/lamivudine	63	26/33	79%	27/30	90%	-11.2 (-28.8;6.4)	







RESULTS

There were no significant differences in efficacy when different subgroups were analyzed:

- time with viral load < 50 c/ml: > or < 12 months;
- Age: > or < 50 ys;
- CD4+ nadir: > or < 200;
- Baseline CD4+: > or < 500;
- HCV seropositivity;
- HCV replication; and
- Baseline nucleosides: (TDF/FTC or ABC/3TC).

In the whole population, switching to DT was not associated with significant changes in e-GFR and TC/HDL ratio relative to maintaining TT.

At baseline, patients treated with TDF/FTC had significantly:

- lower total-cholesterol (tC): 178 vs 202 mg/dl,
- lower LDL-cholesterol: 109 vs 122 mg/dl,
- lower triglycerides (Tg): 127 vs 146 mg/dl,

but similar tC/HDL ratio: 4 vs. 4.

In those patients switching from TDF/FTC, there was a non-significant trend towards higher increases in tC, LDL and Tg, without changes in Tc/HDL ratio.

Changes in the estimated glomerular filtrate, or the proportion of patients with proteinuria, or pathologic uric acid or phosphate excretion between arms were not different when patients with TDF/FTC or ABC/3TC at baseline were compared.

CONCLUSIONS

Switching to 3TC+DRV/r dual therapy in patients with suppressed viral load for more than 6 months maintains similar efficacy to triple therapy irrespective of the length of undetectability, age, nadir or baseline CD4+ count, HCV coinfection or baseline nucleosides.

No differences were seen in changes of lipids or renal function between patients switching from TDF/FTC or ABC/3TC.

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Patients

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