

A Multicenter Observational Study on the Efficacy and Metabolic Safety of Dolutegravir plus either TDF/FTC or ABC/3TC as a Simplification Strategy in HIV-1 Positive, Antiretroviral-experienced Patients

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Glasgow, 22 nd October 2016

HIV FORA: INTEGRATING SCIENCE AND CLINICAL PRACTICE

**EUROPEAN HIV CLINICAL FORUM:
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GLASGOW, UNITED KINGDOM • 22 OCTOBER 2016



Study design and methods

- Retrospective, observational, multicenter (ODOACRE study group) clinical study aiming to assess differences in treatment discontinuation, virological failures and metabolic changes among pts switching to TDF/FTC or ABC/3TC plus DTG
- **Inclusion criteria**
 - ✓ HIV-infected pts, with HIV-RNA < 50 cp/mL at baseline (BL);
 - ✓ Starting DTG combined with either TDF/FTC or ABC/3TC
- **Exclusion criteria**
 - ✓ Previous use of dolutegravir

Patients characteristics at BL

Variables	TDF/FTC arm n=66	ABC/3TC arm n=107	<i>p</i>
Age*	51 (45-56)	51 (46-57)	0.793
Male sex	51 (77.3)	73 (68.2)	0.199
Caucasians	62 (93.9)	100 (93.5)	0.335
Risk factors for HIV:			
Heterosexual	22 (33.3)	50 (46.7)	0.040
MSM	13 (19.7)	29 (27.1)	
IDU	22 (33.3)	22 (20.6)	
Other	9 (13.6)	6 (5.6)	
Time since HIV diagnosis (years)*	15 (9-23)	13 (5-23)	0.439
Time on ARV therapy (years)*	12 (5-19)	10 (3-18)	0.376
Previous use of INIs	25 (37.9)	28 (26.2)	0.105
CDC stage C	22 (33.3)	35 (32.7)	0.933
Zenith HIV-RNA (log ₁₀ cp/mL)*	4.98 (4.70-5.50)	5.08 (4.65-5.50)	0.812
Nadir CD4 count (cells/mmc)*	179 (27-286)	171 (62-288)	0.505

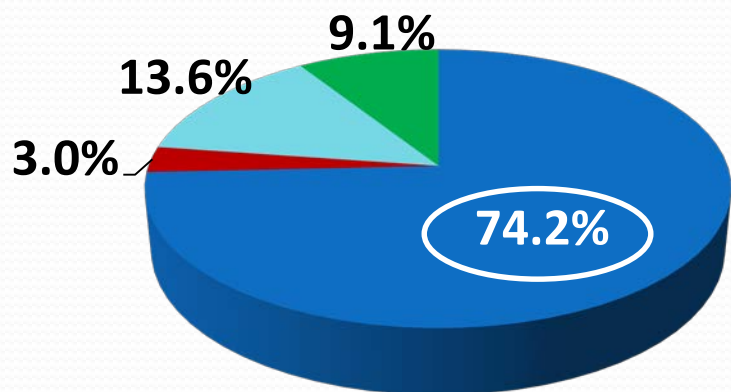
Patients characteristics at BL (2)

Variables	TDF/FTC arm	ABC/3TC arm	<i>p</i>
Years of viral suppression before switch*	5 (1-8)	5 (2-9)	0.395
Previous virological failures	36 (54.5)	38 (35.5)	0.014
Previous resistance mutation to 3TC	8/33 (24.2)	11/45 (24.4)	0.984
Previous resistance mutation to ABC	12/33 (36.4)	17/45 (37.8)	0.898
Previous resistance mutation to TDF	9/33 (27.3)	9/45 (20.0)	0.451
Resistance to NRTIs-backbone	7/33 (21.2)	8/45 (17.8)	0.704
Anti-HCV positive	15 (22.7)	28 (26.2)	0.611
HBsAg positive	11 (16.7)	1 (0.9)	<0.001
CD4+ count at BL (cells/mm ³) *	568 (430-763)	563 (412-850)	0.854
Reasons for starting dolutegravir:			
Toxicity	15 (22.8)	31 (28.9)	0.473
Simplification	21 (31.8)	24 (22.4)	
Drug-interactions	16 (24.2)	38 (35.5)	
Other	14 (21.2)	14 (13.1)	

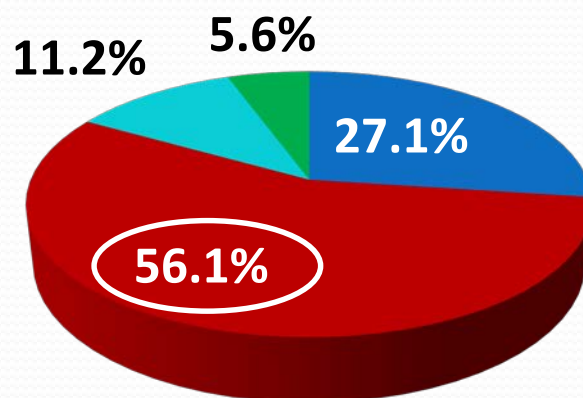
Values within brackets are expressed in percentage, except for *(interquartile range)

Therapies before switch to DTG

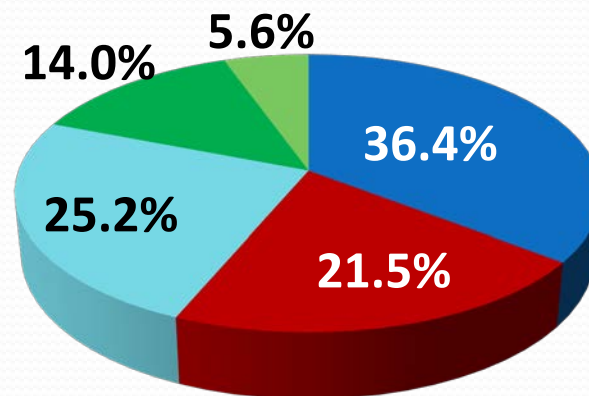
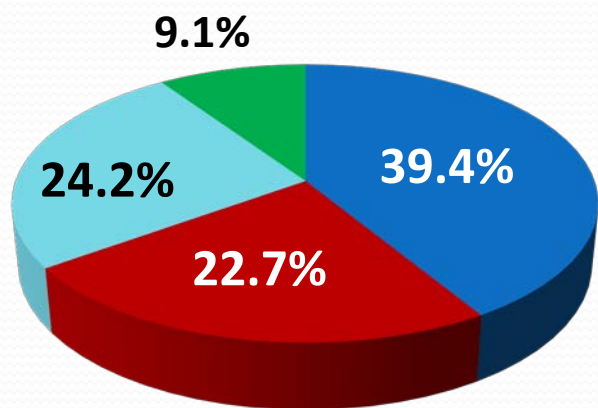
TDF/FTC



ABC/3TC



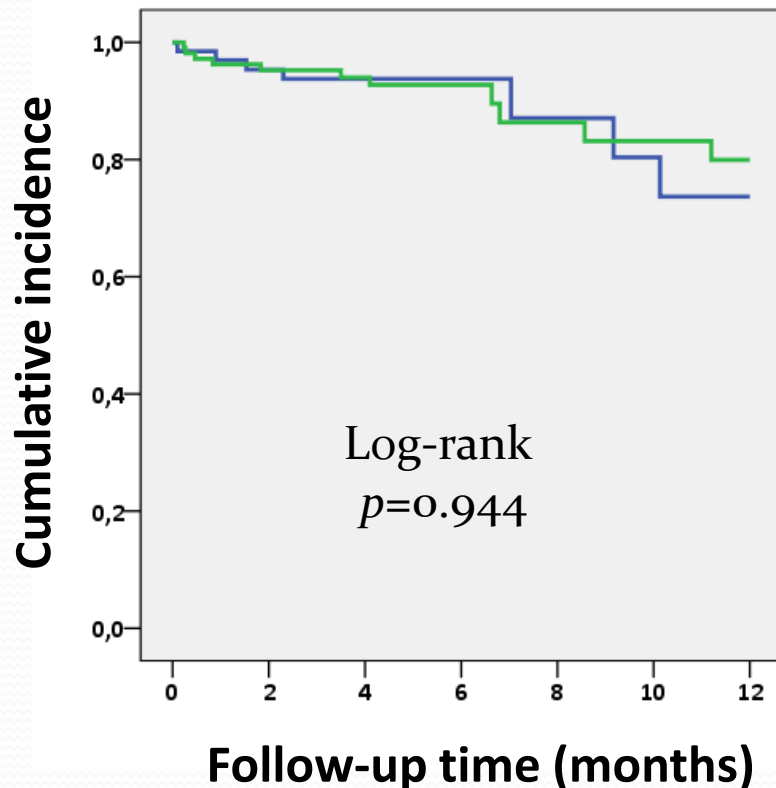
- TDF/FTC
- ABC/3TC
- Mono/Dual
- Other



- PI-based cART
- NNRTI-based cART
- INI-based cART
- Mono/Dual
- Other

Treatment discontinuation and virological failures

Treatment discontinuation



Estimated probability of remaining on DTG at week 48:

TDF/FTC: 76.3% (95% CI 56.5-96.1)

ABC/3TC: 83.2% (95% CI 71.9-94.5)

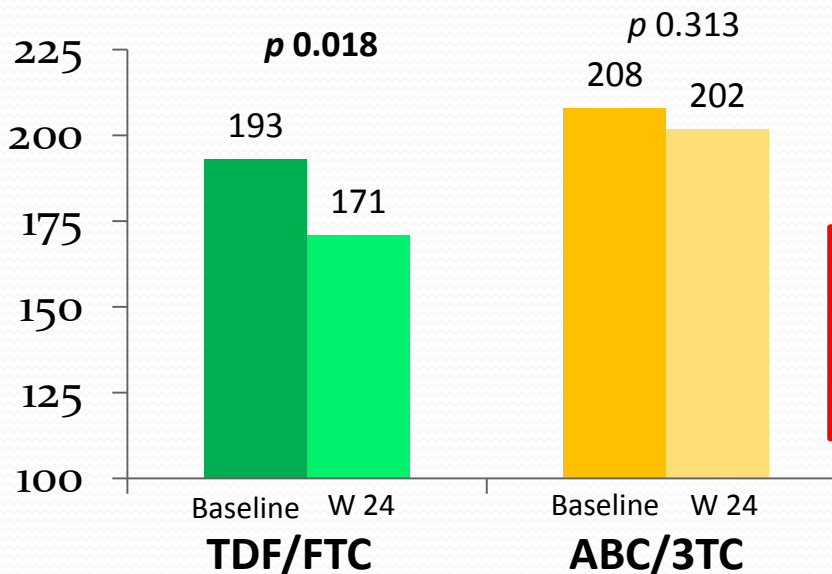
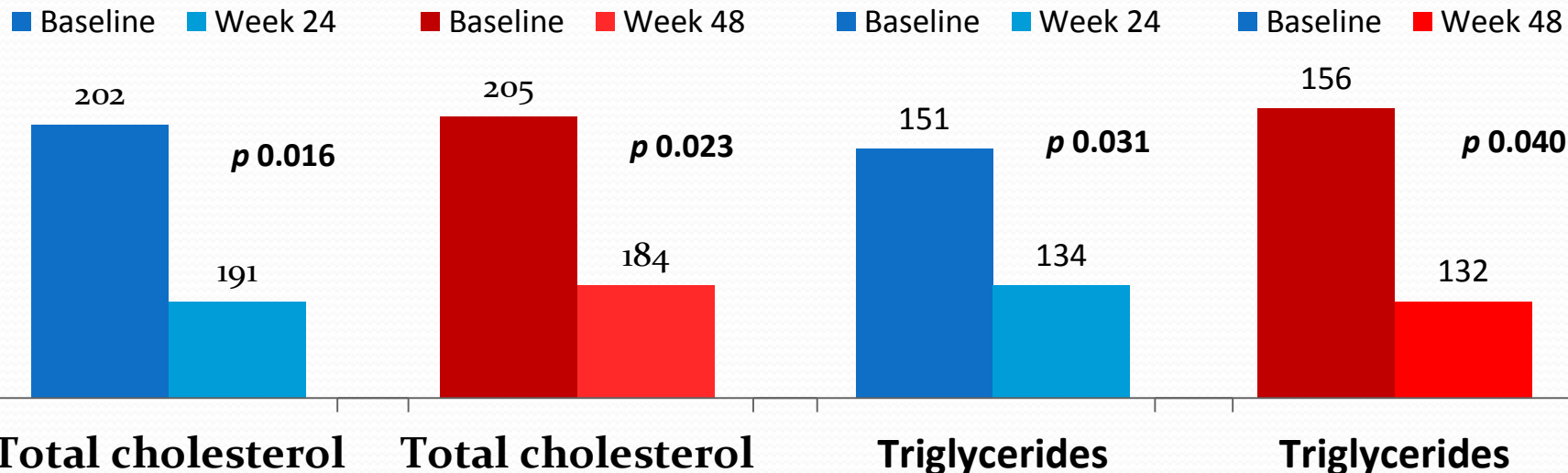
No virological failures during 1090 patient-months FU.

Reasons for treatment discontinuation

Adverse event	TDF/FTC arm	ABC/3TC arm
Hypersensitivity reaction	1	1
Gastro-intestinal	0	1
Liver	3	0
Kidney	0	1
Neurological*	1	5
Drug interactions	0	1
Unspecified	1	1

*Neurological toxicities included: headache (1 case in the TDF/FTC arm and 2 in the ABC/3TC arm), sleepiness (1), suicidal ideation (1), unspecified (1)

Metabolic improvement

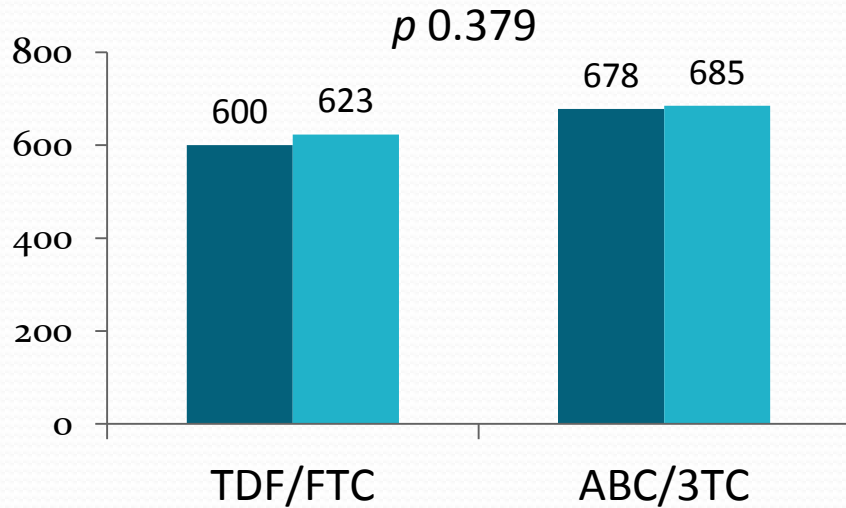


Predictors of change in total cholesterol at W24

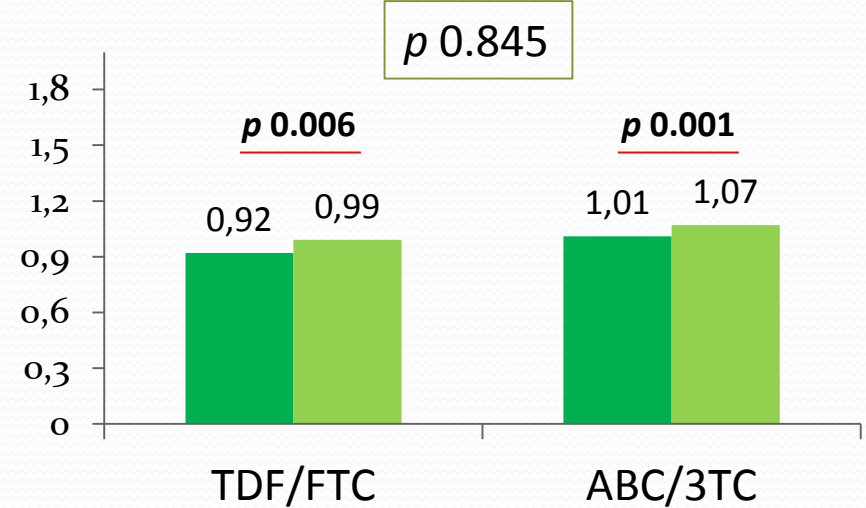
Variables	OR (95% CI)	p
Baseline TC	-0.25 (-0.41;-0.08)	0.005
TDF/FTC (vs ABC/3TC)	-28.81 (-48.20;-9.41)	0.004
TDF in previous regimen	23.92 (4.67;43.16)	0.016
HBsAg-positive	-26.10 (-61.60; 9.41)	0.147

Immunological, renal and liver functions

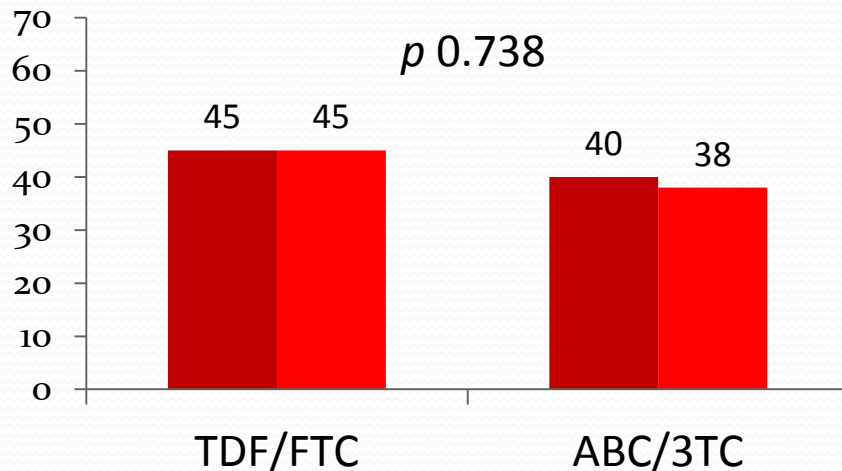
CD₄ count (cells/ μ L)



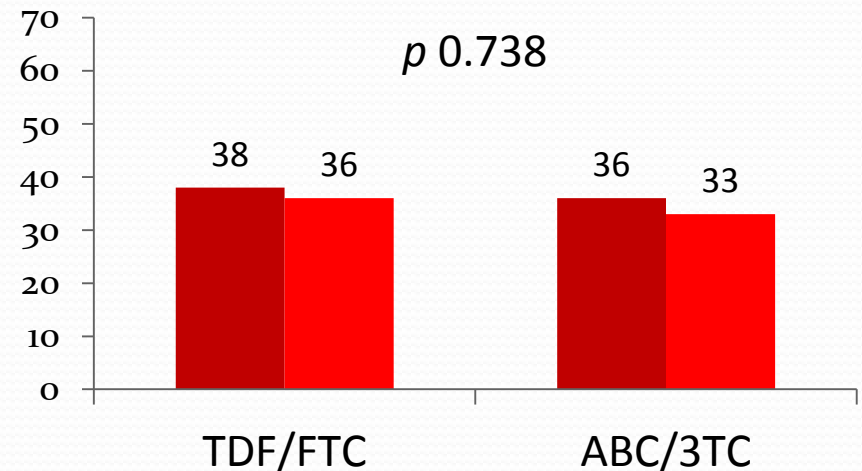
Creatinine (mg/dL)



ALT (UI/L)



AST (UI/L)



Conclusions

- **Sustained virological control** over 24 and 48 weeks, even in the setting of previously detected resistance mutation to NRTIs;
- Discontinuation mainly for altered liver enzymes and neurological toxicity (mild-moderate grade), unpredictable by baseline characteristics of study population;
- **Safe metabolic profile**, especially in TDF/FTC group;
- Increased mean creatinine levels in both group, without alteration of glomerular filtration rate;
- Immunological and liver functions usually unchanged.

Acknowledgements

Doc. Simona Di Giambenedetto and Andrea De Luca, and the ODOACRE Study Group:

- ✓ Doc. Amedeo Capetti and Vittoria Cossu (Luigi Sacco University Hospital);
- ✓ Doc. Gaetana Sterrantino and Filippo Lagi (Careggi Hospital)
- ✓ Doc. Stefano Rusconi (DIBIC Luigi Sacco)
- ✓ Doc. Alessandra Latini and Manuela Colafigli (IFO S. Gallicano Institute)
- ✓ Doc. Andrea Giacometti (Università Politecnica delle Marche)
- ✓ Doc. Giordano Madeddu (University of Sassari)