

DUET-1: Week 48 results of a Phase III randomized double-blind trial to evaluate the efficacy and safety of etravirine (ETR; TMC125) versus placebo in 612 treatment-experienced HIV-1-infected patients

Richard Haubrich,¹ Pedro Cahn,² Beatriz Grinsztejn,³ Jacob Lalezari,⁴ José Valdez Madruga,⁵ Anthony Mills,⁶ Monika Peeters,⁷ Johan Vingerhoets,⁷ Kathy Iveson,⁸ Goedele De Smedt,⁷ on behalf of the DUET-1 study group

¹University of California San Diego, San Diego, CA, USA; ²Hospital Juan A. Fernández and Fundación Huesped, Buenos Aires, Argentina; ³Instituto de Pesquisa Clínica Evandro Chagas, Fiocruz, Brazil;

⁴Quest Clinical Research, San Francisco, CA, USA; ⁵Centro de Referência e Treinamento DST/AIDS, São Paulo, Brazil; ⁶Private Practice, Los Angeles, CA, USA; ⁷Tibotec BVBA, Mechelen, Belgium;

⁸Tibotec Inc, Yardley, PA, USA

Richard Haubrich, MD
Division of Infectious Diseases
University of California, San Diego
150 West Washington Street
Suite 100
San Diego, CA 92103
USA
Phone: +001 (619) 543 8080
rhaubrich@ucsd.edu

Abstract

Background

New, potent and tolerable antiretrovirals (ARVs) are needed, particularly for treatment-experienced, resistant HIV-1 patients.

Methods

DUET-1 is an ongoing 96-week randomized double-blind Phase III trial evaluating the efficacy and safety of ETR 200mg vs placebo, both given bid. All patients received a background regimen (BR) of darunavir with low-dose ritonavir (DRV/r), investigator-selected NRTI(s) and optional enfuvirtide (ENF). Patients had documented NNRTI resistance and ≥ 3 primary PI mutations. The primary efficacy endpoint for this Week 48 analysis was the percentage of patients with a confirmed viral load (VL) of < 50 copies/mL. Safety was also assessed throughout the study.

Results

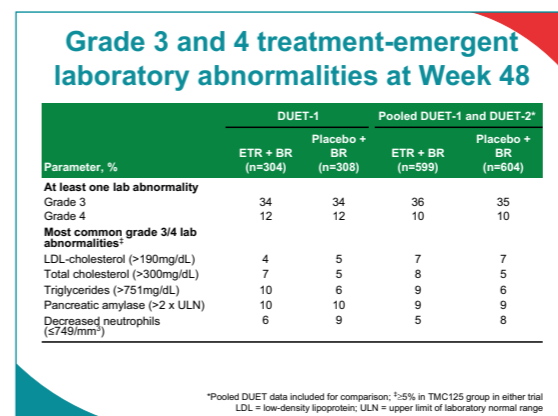
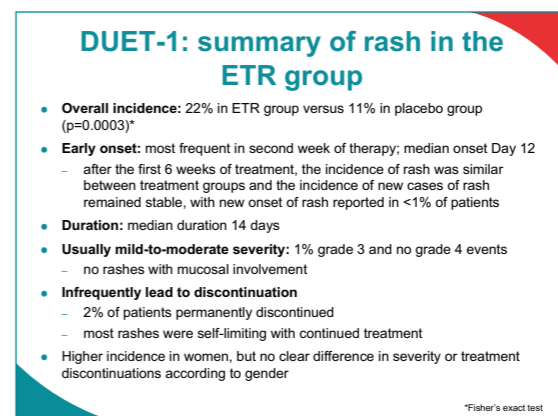
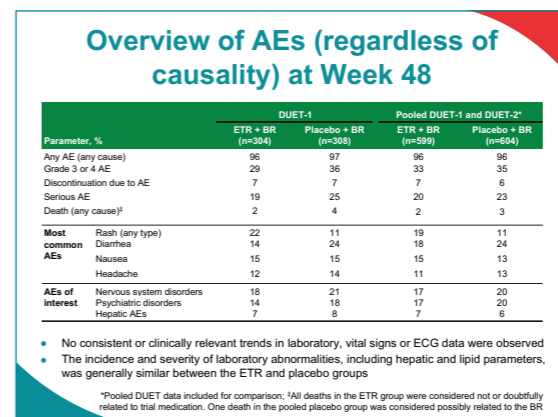
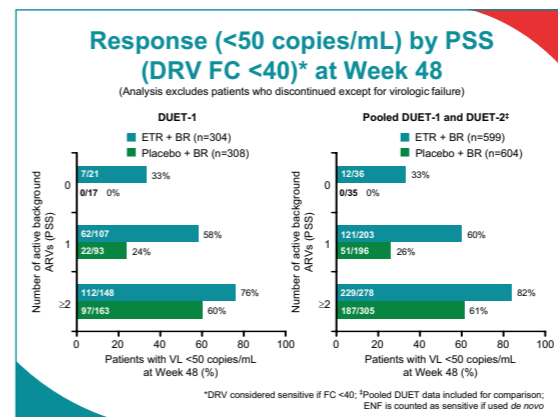
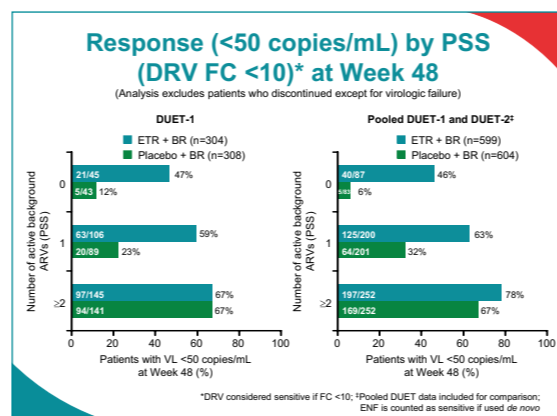
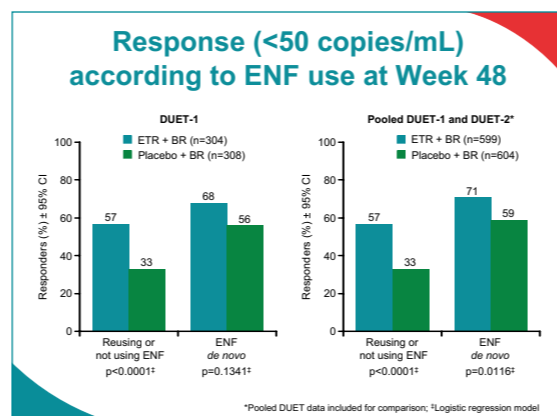
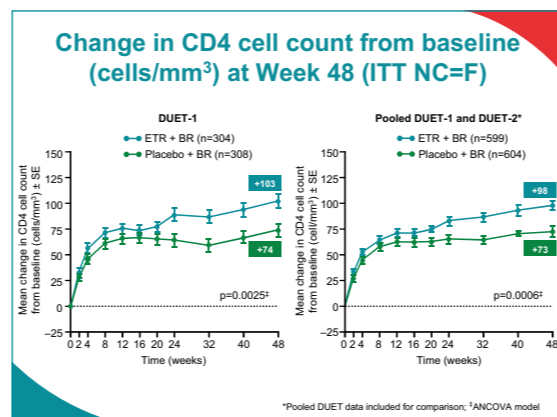
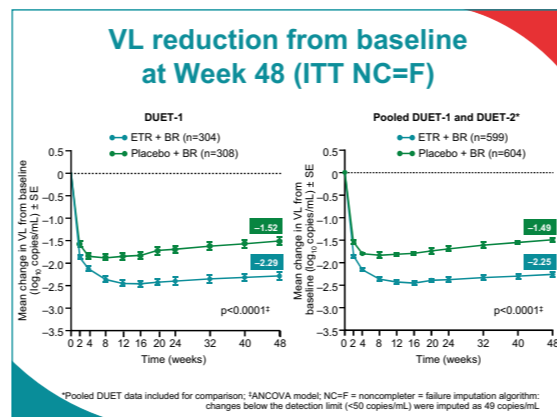
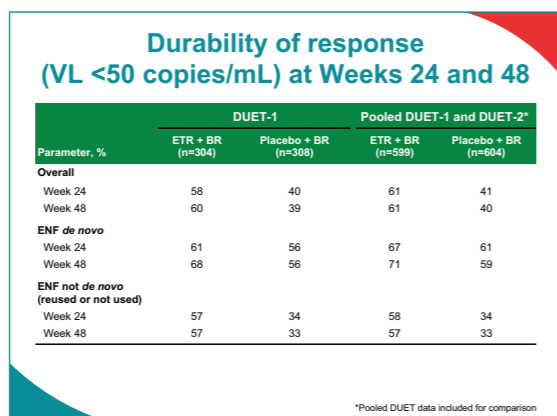
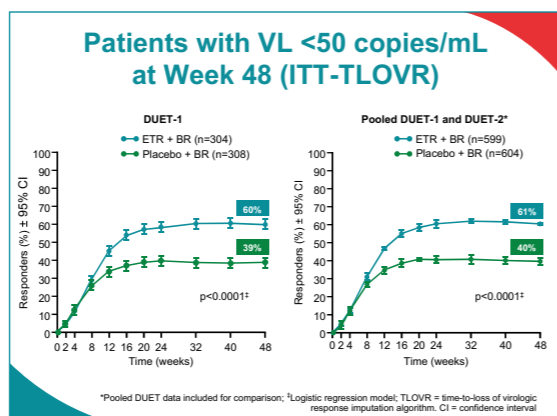
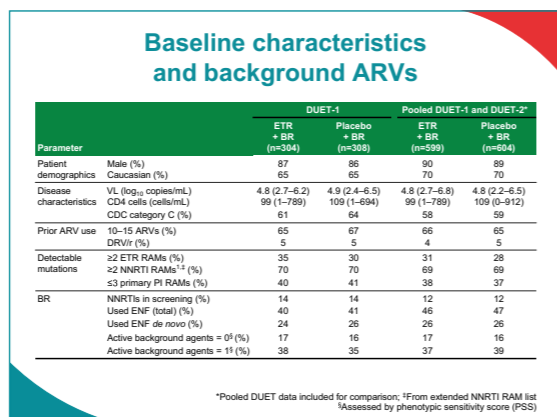
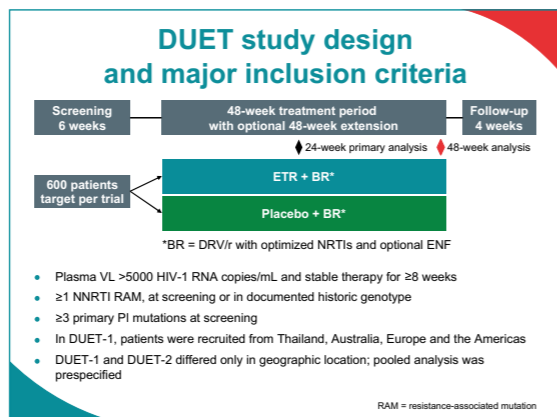
A total of 612 patients were included in the intent-to-treat (ITT) population (62% of patients were CDC Category C, the median number of NNRTI mutations was two, 25% of patients used ENF *de novo* [i.e. naïve]) with a median baseline VL of $4.9 \log_{10}$ copies/mL and a CD4 cell count of 106 cells/mm³.

	Week 24			Week 48		
	ETR + BR	Placebo + BR	Diff (95% CI)	ETR + BR	Placebo + BR	Diff (95% CI)
VL < 50 copies/mL, %	58	40	19 (11; 26) $p=0.0001^*$	60	39	21 (13; 29) $p<0.0001^*$
VL < 400 copies/mL, %	74	51	23 (16; 31) $p<0.0001^*$	71	47	24 (17; 32) $p<0.0001^*$
Mean (SE) change in CD4 cell count, cells/mm ³	89 (5.4)	65 (5.2)	32 [†] (48; 15) $p=0.0002^{**}$	103 (7.0)	74 (6.3)	32 [†] (52; 11) $p=0.0025^{**}$

SE = standard error; CI = confidence interval
*Logistic regression model; **ANCOVA model; [†]LS means difference

Of patients with a VL of < 50 copies/mL at Week 24, 94% maintained a VL of < 50 copies/mL at Week 48 with ETR + BR versus 89% with placebo + BR. In addition, at Week 48 the mean CD4 cell count was significantly increased in the ETR versus the placebo group.

As at Week 24, safety assessments at Week 48 showed that the incidences of any adverse event (AE) (96% ETR vs 97% placebo), serious AEs (19% vs 25%) and grade 3/4 AEs (29% vs 36%) with ETR were similar to placebo. Most AEs with ETR were mild-to-moderate in severity and infrequently led to discontinuation (7% vs 7%). Rash (any type) (22% vs 11%), diarrhea (14% vs 24%) and nausea (15% vs 15%) were the most common AEs. Nervous system (18% vs 21%) and psychiatric disorders (14% vs 18%) with ETR were comparable to placebo.



DUET-1: conclusions

- ETR + BR demonstrated superior virologic responses over placebo in treatment-experienced patients
 - 60% of patients in the ETR group achieved confirmed undetectable (< 50 copies/mL) VLs compared with 39% in the placebo group
 - in the ETR group 71% of patients achieved a VL < 400 copies/mL compared to 47% in the placebo group
- Virologic and immunologic responses with ETR were sustained
 - 94% of patients receiving ETR + BR achieving < 50 copies/mL at Week 24 maintained virologic suppression at Week 48
- The safety and tolerability of ETR was comparable to placebo, with the exception of rash
- ETR provides superior efficacy over placebo and extends and enhances the therapeutic options available for treatment-experienced HIV-infected patients

Reference

- Tambuyzer L, et al. 5th EHDRW 2007. Abstract 67.

Acknowledgments

We express our gratitude to the patients that participated in the study, as well as the study center staff, data safety and monitoring board, clinical event adjudication panel, Virco, Tibotec personnel and the following principal investigators

Argentina: HA Ariza, J Benetucci, LM Calanni, LI Cassetti, J Corral, DO David, A Krolewiecki, MH Losso, P Patterson, RA Teijeiro

Brazil: CA da Cunha, EG Kallas, EM Netto, JH Pilotto, M Schechter, J Suleiman, A Timerman

Chile: J Ballesteros, R Northland

Costa Rica: AA Alvielis Montoya, G Herrera Martinez, A Solano Chinchilla

France: M Dupon, C Katlama, JM Livrozet, P Morlat, G Pialoux, C Picketty, I Poizat-Martin

Mexico: J Andrade-Villanueva, G Reyes-Terán, J Sierra-Madero

Panama: A Canton, A Rodriguez, N Sosa

Puerto Rico: JO Morales Ramirez, JL Santana Bagur, R Soto-Malave

Thailand: T Anekthananon, P Mootsikapun, K Ruxrngtham

USA: M Albrecht, N Bellos, R Bolan, P Brachman, C Brinson, F Cruickshank, R Elion, WJ Fessel, T Hawkins, S Hodder, P Hutcherson, T Jefferson, H Katner, C Kinder, M Kozal, J Leider, D McDonough, K Mounzer, J Nadler, D Norris, W O'Brien, G Pierone, K Raben, B Rashbaum, M Rawlings, B Rodwick, P Ruane, J Sampson, S Schrader, A Scribner, M Senson, D Sweet, B Wade, D Wheeler, A Wilkin, T Willis, M Wohlfeller, K Workowski