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Antiretroviral treatment use and HIV RNA suppression rates for 941 European patients in the etravirine early access programme

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Abstract

The next-generation NNRTI etravirine (ETR; TMC125) has shown strong and durable efficacy in the DUET trials in combination with a background regimen (BR) of darunavir with low-dose ritonavir (DRV/r), NRTIs and optional enfuvirtide (ENF). The early access programme included a wider range of BR.

The TMC125-C214 trial (ETR early access programme) included patients with triple-class experience (NRTI, protease inhibitor [PI], NNRTI) and who were unable to use currently approved NNRTIs owing to either intolerance or drug resistance. Patients were recruited from 10 countries in Europe. Patients received ETR 200mg bid with a range of background antiretrovirals (ARVs).

By 2 May 2008, there were 941 European patients with data available: 21% were female, 87% were Caucasian, with a mean age of 46 years. The baseline mean CD4 cell count was 299 cells/uL (range 0–1,647) with baseline mean HIV RNA 4,677 copies/mL (range 40–3,263,277). Overall, 69.8% used DRV/r. 70.6% patients used NRTIs in the BR. Of the 664 patients using NRTIs, the most common were tenofovir (70%), lamivudine or emtricitabine (91%), zidovudine (20%) and abacavir (18%). Other ARVs used included raltegravir (54%) and maraviroc (15%). The percentage of patients with HIV RNA <50 copies/mL was 51% at Week 4, 70% at Week 12 and 74% at Week 24 (observed data analysis). CD4 cell counts rose by mean 79 cells/uL at Week 12 and by 101 cells/uL at Week 24. There were 131 serious adverse events (SAEs) recorded, of which 118 (89%) were judged to be not related to ETR or doubtful causality. There were 13 SAEs judged to be at least possibly related to ETR. Of these, there were five (0.6%) cases of rash (ETR permanently stopped for four of the cases), one elevation of alanine aminotransferase (ALT) levels (0.1%) (ETR dose not changed) and one case of cholestatic acute hepatitis (0.1%) (ETR dose not changed).

The use of ETR in the early access programme included a wide range of ARVs in the BR, with a high percentage of patients showing HIV RNA suppression below 50 copies/mL by Weeks 12–24.

Introduction

- The next-generation NNRTI ETR has shown strong and durable efficacy in the DUET trials in combination with a BR of DRV/r, NRTIs and optional ENF
- The early access programme included a wider range of BRs
- This updated analysis contains data to 2 September 2008

Methods

- The TMC125-C214 trial (ETR early access programme) included patients with triple-class experience (NRTI, PI, NNRTI) and who were unable to use currently approved NNRTIs owing to either intolerance or drug resistance
- Within this global early access programme, patients were recruited from 10 countries in Europe. Patients received ETR 200mg bid with a range of background ARVs

Baseline characteristics

Parameter	European patients (N=941)
Age, years (mean, range)	46 (18–81)
Gender, n (%)	
Male	741 (79)
Female	200 (21)
Race, n (%)	
Caucasian	821 (87)
Black	80 (8.5)
Hispanic	24 (2.6)
Oriental/Asian	8 (0.9)
Other	8 (0.9)
CD4 cell count, cells/uL (mean, 95% CI)	299 (284–313)
HIV RNA	3.67 (3.59–4.03)

CI = confidence interval

Countries included

Country, n (%)	European patients (N=941)
Spain	250 (26.6)
Germany	225 (23.9)
Italy	185 (19.7)
The Netherlands	92 (9.8)
Belgium	85 (9.0)
Denmark	37 (3.9)
Greece	37 (3.9)
Sweden	19 (2.0)
Russia	7 (0.7)
Luxembourg	4 (0.4)

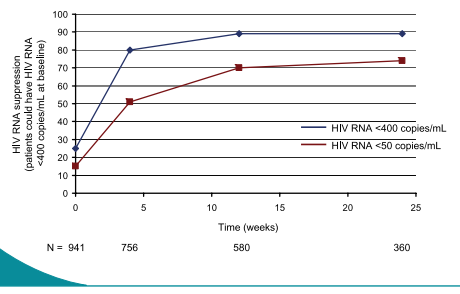
NRTIs used with ETR

NRTI, n (%)	Number of patients (N=941)
Any NRTI	664 (70.6)
Tenofovir	463 (49.2)
Lamivudine	302 (32.1)
Emtricitabine	299 (31.8)
Zidovudine	135 (14.3)
Abacavir	120 (12.8)
Didanosine	40 (4.3)
Stavudine	19 (2.0)

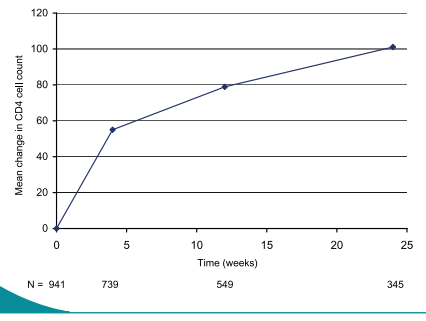
Use of new ARVs

ARV, n (%)	European patients (N=941)
Total use of	
DRV/r	657 (69.8)
Raltegravir	508 (54.0)
Maraviroc	142 (15.1)
ENF	143 (15.2)
Of which new use of	
DRV/r	531 (56.4)
Raltegravir	425 (45.2)
Maraviroc	121 (12.9)
ENF	93 (9.9)

European ETR early access programme (N=941) % HIV RNA <400 copies/mL (and <50 copies/mL) observed data



European ETR early access programme (N=941) change in CD4 cell count versus time observed data



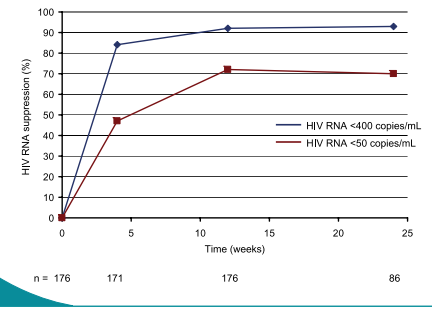
Safety summary

- There were 131 SAEs recorded, of which 118 (89%) were judged to be not related to ETR or doubtful causality. There were 13 SAEs judged to be at least possibly related to ETR
- Of these 13, there were five cases of rash (ETR permanently stopped for four of the cases), one elevation of ALT levels (ETR dose not changed), one cholestatic acute hepatitis (ETR dose not changed), one coronary heart disease, one seizure, four others (*Staphylococcus aureus* bacteraemia, pancreatic lesions, hip pain and haemarthrosis of knee)

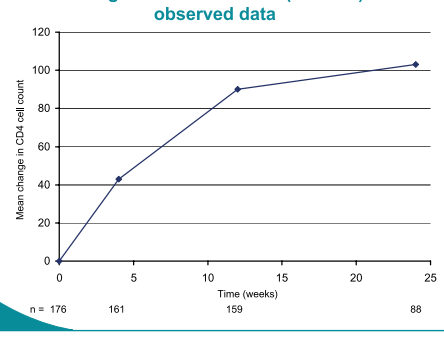
Subset taking ETR + DRV/r + raltegravir

- In a pre-planned sub-study, 176 patients started this combination *de novo* in the early access programme in Europe with HIV RNA >400 copies/mL at baseline. 40% of these patients used no NRTIs with ETR + raltegravir + DRV/r
- 86/176 patients had HIV RNA data at Week 24 – efficacy results shown for overall group and subset with full data available
- Mean age 46 years, 82% male, 87% Caucasian
- Baseline HIV RNA = 4.3 $\log_{10}$ copies/mL (range 2.36–6.17 $\log_{10}$ copies/mL)
- Baseline CD4 cell count = 249 cells/uL (range 1–910 cells/uL)

Patients taking ETR + DRV/r + raltegravir (n=176) % HIV RNA <400 copies/mL and <50 copies/mL observed data



Patients taking ETR + DRV/r + raltegravir (n=176) change in CD4 cell count (cells/uL) observed data



Conclusions

- ETR has been used with a wide range of ARVs in the early access programme in Europe
- In the overall cohort (N=941), the per cent of patients with HIV RNA <50 copies/mL increased from 15% at baseline to 74% at Week 24 (observed data)
- In a pre-planned substudy, the cohort of 176 patients who took ETR, DRV/r and raltegravir showed strong efficacy – 93% had HIV RNA levels below 400 copies/mL by Week 24, with 70% showing HIV RNA <50 copies/mL at this time
- It is difficult to reliably evaluate efficacy by use of different ARVs in the early access cohort, since baseline drug resistance data is not available and there is minimal data collection in this very diverse patient population

Acknowledgements

We express our gratitude to the patients that participated in the studies, as well as the study centre staff, the Tibotec personnel (particularly Hilde Vanaken, Yvonne van Delft and Tunde Gyarmati), the principal investigators and the country coordinators (shown below).

Aguirrebengoa, Aleman, Antinori, Arasteh, Baldelli, Barrufet, Bassaris, Berenguer, Bernardino, Boecher, Bogner, Brinkman, Brockmeyer, Bronsveld, Caramello, Carganico, Carls, Carocci, Carosi, Casado, Castano, Cauda, Chiodo, Chiodo, Chirianni, Chrysos, Clotet, Clumeck, Colebunders, Dalmau, Di Perri, Dokuzoguz, Domingo, Epple, Esposito, Esser, Estrada, Faetkenheuer, Fenske, Filice, Flamholc, Florence, Flores, Galindo, Gargalianos, Gatell, Geijo Martinez, Gerstoft, Ghinelli, Giamarellou, Gisolf, Gisslen, Goffard, Gonzalez-Lahoz, Gutierrez Rodero, Harrer, Hemmer, Hernandez Quero, Hildebrand, Hoffmann, Jaeger, Jensen, Karlsson, Katsambas, Kauffmann, Klinker, Knecht, Knechten, Koeppe, Koopmans, Kordossis, Kozyrev, Kroon, Kuhlmann, Lacor, Laursen, Lazanas, Lazzarin, Legrand, Lopez Aldeguer, Lopez Cortes, Lozano, Lutz, Mathiesen, Mauss, Mazzotta, Meraviglia, Mezzaroma, Miguelez, Minoli, Miralles Alvarez, Moll, Moutschen, Mulder, Muniain, Mutz, Narciso, Nikolaidis, Orani, Ortega, Oteo, Pasquau, Pedersen, Pedrol, Penco, Perez Guzman, Ploumidis, Podzamczer, Poggio, Pokrovsky, Portilla, Portu, Prieto, Prins, Pronin, Pulido, Quirino, Reichelt, Ribera, Richter, Rijnders, Rizzardini, Rockstroh, Rubio, Rump, Santamaria, Santos, Santos, Schleehauf, Schlote, Schnaitmann, Schuchmann, Schuermann, Schuster, Segura, Skoutelis, Sola, Sprenger, Staszewski, Stoehr, Stoll, Suter, Telenti, Theisen, Titone, Toti, Tozzi, Unal, Usadel, Van Der Geest, Van Kasteren, Van Lunzen, Van Wijngaerden, Vandecasteele, Vandercam, Vera, Vigano, Viscoli, Vogelaers, Volkert, Yakovlev, Zakharova

Supported by Tibotec

Presented at the 9th International Congress on Drug Therapy in HIV Infection, Glasgow, UK, 9–13 November 2008.

This poster is available on-line at www.tibotec.com