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Efficacy, Safety and Tolerability of Etravirine With and Without Darunavir and/or Raltegravir in Treatment-Experienced Patients: Preliminary Analysis of TMC125-C214 Early Access Program (EAP) in the US

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Data in the poster body have been updated since the abstract was originally submitted

Introduction

- Etravirine (ETR, INTELENCE™ [TMC125]) is an FDA-approved next-generation non-nucleoside reverse transcriptase inhibitor (NNRTI) active against NNRTI-resistant HIV-1[1]
- TMC125-C214 was a phase III, non-randomized, open-label trial within and outside of the US providing early access of ETR to HIV-1 infected patients who had failed multiple antiretroviral (ARV) regimens
- The TMC125-C214 trial allowed the use of other new and investigational agents where appropriate PK data were available
- The purpose of this preliminary analysis is to report 12- and 24-week efficacy and safety of ETR with or without co-administration of darunavir/ritonavir (DRV/r) and/or raltegravir (RAL) among patients enrolled in the TMC125-C214 early access program (EAP) in the US
- Rationale for sub-analysis:
  - Within the ETR EAP, DRV/r (600/100mg bid) and/or RAL (400mg bid) were frequently used in the background regimen
  - Limited clinical data are available on use of ETR in combination with RAL
  - A sub-analysis provides the opportunity to obtain some data on the efficacy and safety of ETR in combination with RAL and/or DRV/r

Methods

- The primary objective of TMC125-C214 was to provide early access to ETR for treatment-experienced HIV-1 infected patients; secondary objectives were to assess ETR safety, tolerability and efficacy
- Key inclusion criteria:
  - Limited treatment options due to virologic failure or intolerance to multiple ARV regimens, including efavirenz and nevirapine
  - 3-class experience (N[t]RTIs, PIs, NNRTIs) or 2-class experience (N[t]RTIs, PIs) with primary NNRTI resistance
  - Previous receipt of two different PI-based regimens
  - Inadequate viral suppression on current regimen
- Treatment regimen
  - All patients received ETR 200mg bid plus an investigator-selected background regimen (BR)
  - Allowed background medications are summarized in **Table 1**
    - RAL and maraviroc became available through expanded access in January and July of 2007, respectively, and were allowed based on available pharmacokinetic interaction data
  - Background ARVs could be changed at any time at investigator's discretion

Table 1. Allowed ARVs

ARV Class	Allowed	Disallowed
PIs	DRV/r, LPV/r, ATV/r, FPV/r IDV/r, and SQV/r	TPV/r, all other PIs unboosted PIs
NRTIs	All approved NRTIs	All investigational NRTIs
NNRTIs	None	All approved and investigational NNRTIs
Fusion Inhibitors	ENF	None
Investigational Agents	RAL, MVC	Other investigational agents

LPV, lopinavir; ATV, atazanavir; FPV, fosamprenavir; IDV, indinavir; SQV, saquinavir; TPV, tipranavir; ENF, enfuvirtide; RAL, raltegravir; MVC, maraviroc

- Assessments
  - Follow-up visits were recommended at Weeks 4 and 12, and every 12 weeks thereafter
  - Lab assessments of viral load (VL) and CD4 count were performed locally and reported electronically
  - Only serious adverse events (AEs) and AEs leading to discontinuation were collected
- Sub-analysis
  - Inclusion criteria:
    - Participation in ETR EAP in the United States
    - New use of ETR (roll-overs from other ETR studies not included)
    - HIV-1 RNA data available for Week 12 and/or Week 24 visits as of June 26, 2008
  - Methods:
    - Virologic response was defined as HIV-1 RNA <75 copies/mL due to frequent use of assays with <75 copies/mL as the lower limit of detection
    - Descriptive statistics are provided based on observed cases
    - Analysis does not control for baseline activity of ETR, DRV/r, RAL, or background ARVs
    - Treatment groups were defined based on the regimen received on Day 7

Results

- Among 2212 patients analyzed from the US EAP, 1675 met the inclusion criteria for this sub-analysis **(Table 2)**:
  - Approximately 10% were female, 23% were black, and 16% were Hispanic

Table 2. Baseline demographics and disease characteristics[a] (N=1675)

	ETR + DRV/r + RAL + BR n=689	ETR + DRV/r + BR (no RAL) n=432	ETR + RAL + BR (no DRV/r) n=356	ETR + BR (no DRV/r or RAL) n=198	All patients N=1675
Sex					
Male, n (%)	636 (92.3)	395 (91.4)	311 (87.4)	175 (88.4)	1636 (89.6)
Age, mean (SD), years	47.2 (8.67)	47.9 (7.83)	47.4 (8.16)	48.1 (8.36)	47.5 (8.31)
Race/ethnicity, n (%)					
Caucasian	419 (61.2)	230 (53.2)	207 (58.5)	127 (64.1)	983 (58.9)
Black	154 (22.5)	104 (24.1)	96 (27.1)	31 (15.7)	385 (23.1)
Hispanic	98 (14.3)	82 (19.0)	43 (12.2)	37 (18.7)	260 (15.6)
Other	14 (2.1)	16 (3.7)	8 (2.3)	3 (1.5)	41 (2.5)
HIV-1 RNA, mean (SD), $\log_{10}$ copies/mL	4.4 (1.02)	4.1 (1.19)	4.5 (0.98)	4.0 (1.31)	4.3 (1.11)
CD4 count, median (IQR), cells/mm^3	115 (32, 250)	184 (58, 319)	143 (40, 283)	217 (110, 362)	152 (48, 287)

[a]Patients with available data; IQR, interquartile range (25%–75%)

- Enfuvirtide (ENF) was used in the background regimen by 15% of patients overall **(Table 3)**

Table 3. Background ARVs other than N(t)RTIs and ritonavir used in ≥10% of patients within each group

ARV, n (%)	ETR + DRV/r + RAL + BR n=689	ETR + DRV/r + BR (no RAL) n=432	ETR + RAL + BR (no DRV/r) n=356	ETR + BR (no DRV/r or RAL) n=198
ENF	70 (10)	87 (20)	64 (18)	32 (16)
LPV/r	—	—	37 (10)	40 (20)
FPV	—	—	—	29 (15)
ATV	—	—	—	27 (14)

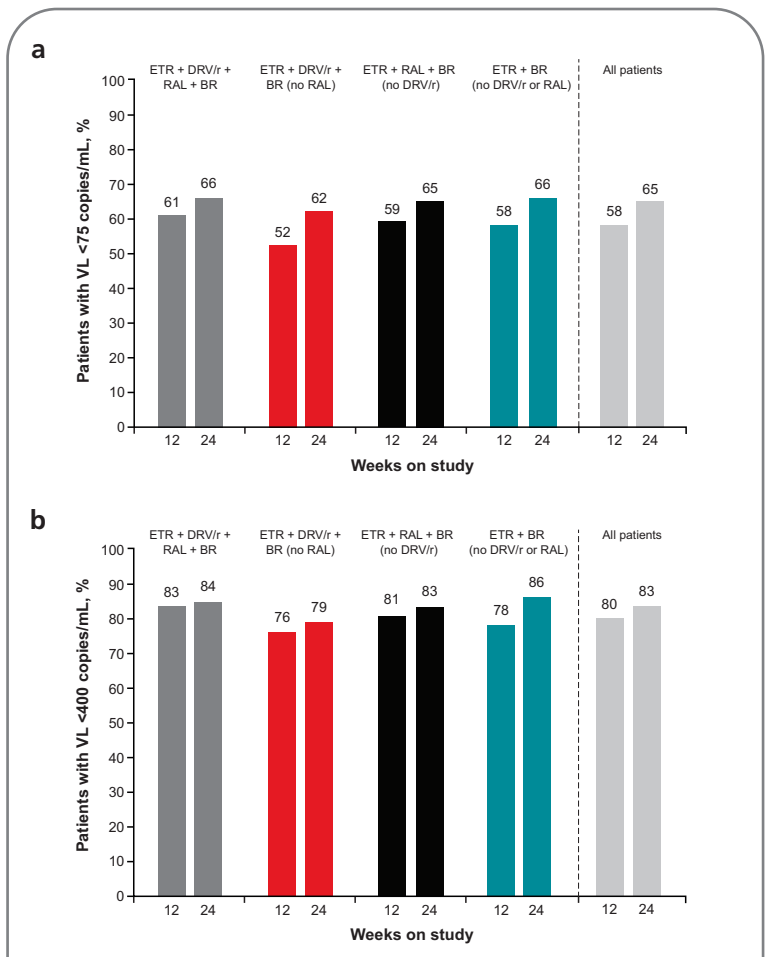
ENF, enfuvirtide; LPV, lopinavir, FPV, fosamprenavir; ATV, atazanavir

- At Week 24, the observed virologic response (VL <75 copies/mL) overall exceeded 60%. Results were generally similar across all subgroups **(Table 4 and Figures 1a and 1b)**

Table 4. Virologic and immunologic response[a]

	ETR + DRV/r + RAL + BR n=689		ETR + DRV/r + BR (no RAL) n=432		ETR + RAL + BR (no DRV/r) n=356		ETR + BR (no DRV/r or RAL) n=198		All patients N=1675	
	Week 12 n=665	Week 24 n=486	Week 12 n=419	Week 24 n=338	Week 12 n=345	Week 24 n=234	Week 12 n=191	Week 24 n=140	Week 12 N=1620	Week 24 N=1198
Virologic response (observed), n (%)										
VL <75 copies/mL	406 (61)	320 (66)	217 (52)	209 (62)	204 (59)	152 (65)	110 (58)	92 (66)	937 (58)	773 (65)
VL <400 copies/mL	550 (83)	408 (84)	317 (76)	268 (79)	281 (81)	194 (83)	149 (78)	121 (86)	1297 (80)	991 (83)
VL reduction from baseline, mean (SD), $\log_{10}$ copies/mL	–2.2 (1.12)	–2.3 (1.14)	–1.7 (1.26)	–1.9 (1.28)	–2.2 (1.16)	–2.3 (1.18)	–1.7 (1.35)	–1.8 (1.43)	–2.0 (1.22)	–2.1 (1.24)
Increase in CD4 count from baseline, median (IQR),cells/mm^3	65 (20, 128)	91 (39, 154)	50 (–2, 122)	82 (18, 148)	70 (20, 143)	98 (31, 175)	57 (2, 119)	88 (17, 188)	62 (12, 129)	88 (30, 158)

[a]Patients with available data; IQR, interquartile range (25%–75%)



Figures 1a and 1b. Observed virologic response: patients with VL (a) <75 copies/mL and (b) <400 copies/mL at Week 12 and Week 24

- Overall, the median change in CD4 count from baseline was 88 cells/mm^3 at Week 24
  - Immunologic response rates were generally similar across sub-groups **(Table 4 and Figure 2)**

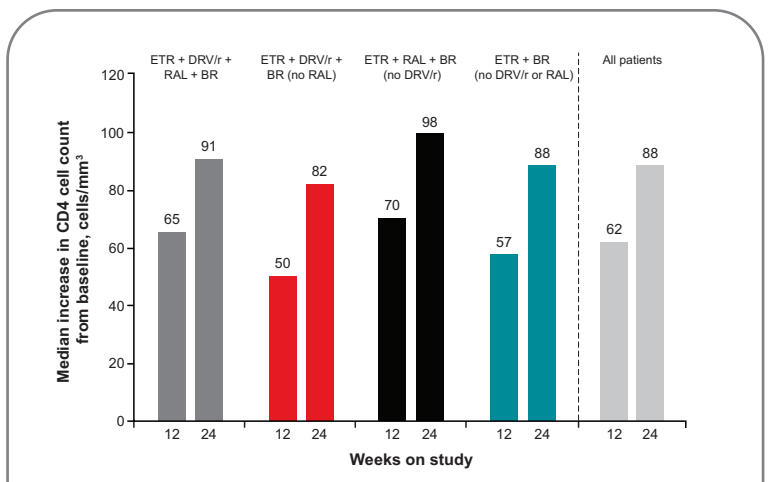


Figure 2. Observed immunologic response: median increase in CD4 cell count from baseline, cells/mm^3

- Rates of serious AEs and AEs leading to discontinuation are summarized in **Table 5**

Table 5. Serious AEs and AEs leading to discontinuation[a]

	ETR + DRV/r + RAL + BR n=689	ETR + DRV/r + BR (no RAL) n=432	ETR + RAL + BR (no DRV/r) n=356	ETR + BR (no DRV/r or RAL) n=198	All patients N=1675
Serious AEs, n (%)					
Overall	96 (13.9)	46 (10.7)	35 (9.8)	18 (9.1)	195 (11.6)
Possibly related to therapy	18 (2.6)	4 (0.9)	3 (0.8)	2 (1.0)	27 (1.6)
Discontinuations due to AEs, n (%)	12 (1.7)	7 (1.6)	4 (1.1)	8 (4.0)	31 (1.9)

[a]Patients with available data

Conclusions

- The US EAP provided early access of etravirine to a racially diverse US-based patient population
- In these univariate analyses, the observed response rates in the US EAP at Week 24 (VL <75 copies/mL) exceeded 60% and were generally similar across subgroups of investigator-selected regimens
- Results suggest that etravirine and appropriate selection of the background regimen was an effective treatment approach in this treatment-experienced patient population
- Reported rates of SAEs and discontinuations due to AEs were low and similar across subgroups

Reference

1. INTELENCE™ (etravirine), US Prescribing Information, Tibotec, Inc.

Acknowledgments

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If you have any additional questions or would like a copy of this poster, call +1-877-REACH-TT (+1-877-732-2488)