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ARTEMIS: Week 48 safety and efficacy of darunavir/r by gender, age and race

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Introduction

- The protease inhibitor darunavir (DRV; TMC114) with low-dose ritonavir (DRV/r) at a dose of 600/100mg bid has been approved in the USA¹ and Europe² for the treatment of HIV-1 infection in treatment-experienced adult patients. Based on the 24-week dose-finding results from the POWER 1 and 2 (TMC114-C213 and C202) studies,^{3,4} once-daily DRV/r 800/100mg was selected as the dose for evaluation in treatment-naïve, HIV-1-infected patients.
- Once-daily DRV/r 800/100mg is being examined in ARTEMIS (TMC114-C211; **AntiRetroviral Therapy with TMC114 Examined In Naïve Subjects**), an ongoing, open-label, Phase III study comparing the efficacy and safety of DRV/r versus lopinavir with low-dose ritonavir (LPV/r) in treatment-naïve, HIV-1-infected adult patients across 26 countries.
- In ARTEMIS, the primary 48-week analysis showed that 84% of patients in the DRV/r arm achieved HIV-1 RNA <50 copies/mL at Week 48 vs 78% of patients in the LPV/r arm (time-to-loss of virologic response [TLOVR], p value for noninferiority, p<0.001).⁵ Furthermore, patients in the DRV/r arm compared with those in the LPV/r arm had a lower incidence of grade 2–4 gastrointestinal adverse events (AEs) at least possibly related to treatment (7% vs 14%, p<0.01) and grade 2–4 triglyceride elevations (3% vs 11%).
- The aim of the present analysis was to determine the influence of gender, age and race on the safety and efficacy at Week 48 of patients receiving DRV/r 800/100mg qd in the ARTEMIS trial.

Methods

Patients and study design

- In ARTEMIS, treatment-naïve, HIV-1-infected adult patients with HIV-1 RNA >5000 copies/mL were randomized to receive DRV/r 800/100mg qd or LPV/r 800/200mg total daily dose.
- All patients received a fixed background regimen of tenofovir disoproxil fumarate (TDF) 300mg qd and emtricitabine (FTC) 200mg qd.

Assessments and endpoints

- Safety and efficacy assessments were performed at screening, baseline, Week 2 and every 4 weeks until Week 16, at Week 24 and every 12 weeks thereafter.
- The intent-to-treat (ITT) population was used for the analysis.
- Virologic response (defined as viral load <50 copies/mL) at Week 48 was determined using the TLOVR algorithm.
- The incidence of AEs and laboratory abnormalities were evaluated. For laboratory abnormalities the cut-off was at least two abnormalities in any subgroup.
- All available safety data and Week 48 efficacy data were analyzed according to gender (male or female), baseline age (≤30, 31–45 or >45 years) and race (Oriental/Asian, Black, Caucasian/White or Hispanic).
- Written informed consent was obtained from all patients. Study protocols were reviewed and approved by the appropriate institutional ethics committees and health authorities, and were conducted in accordance with the Declaration of Helsinki.

Results

Baseline disease characteristics according to subgroup

- The trial included a diverse group of patients broadly representative of the general clinical population with HIV-1 infection: 30% were women; 60% were non-Caucasian; mean age was 34 years (range: 18–70).
- Baseline disease characteristics were generally similar between the subgroups (Table 1).
- Overall, the mean viral load was 4.86 (standard deviation [SD]: 0.64) log₁₀ copies/mL and the median CD4 cell count was 228 (range: 4–750) cells/mm³ at baseline for patients randomized to DRV/r treatment.

Table 1. Baseline disease characteristics according to gender, age and race of patients receiving DRV/r 800/100mg qd (n=343).

Subgroup	n (%)	Mean known duration of HIV infection (years [SE])	Mean log ₁₀ viral load (copies/mL [SE])	Median CD4 cell count (cells/mm ³ [range])
Gender				
Male	239 (70)	2.50 (0.26)	4.94 (0.04)	226 (4–742)
Female	104 (30)	2.33 (0.26)	4.69 (0.07)	240 (13–750)
Age, years (range)				
≤30	115 (34)	2.10 (0.22)	4.75 (0.06)	268 (9–750)
31–45	175 (51)	2.44 (0.27)	4.95 (0.05)	218 (4–748)
>45	53 (15)	3.24 (0.76)	4.82 (0.08)	227 (11–686)
Race*				
Oriental/Asian	44 (13)	1.82 (0.34)	4.91 (0.09)	196 (13–552)
Black	80 (23)	2.92 (0.54)	4.81 (0.07)	225 (5–748)
Caucasian/White	137 (40)	2.86 (0.31)	4.97 (0.06)	228 (4–750)
Hispanic	77 (22)	1.67 (0.32)	4.71 (0.07)	246 (13–624)
Other	4 (1)	1.27 (0.89)	4.59 (0.24)	153 (49–353)

*Race for one patient was not reported; SE = standard error

Efficacy

- Virologic response at Week 48 (percentage of patients with viral load <50 copies/mL) was similar across the analyzed subgroups and consistent with that of the overall population (84%) (Figures 1a–c). The highest response rate (100%) was observed in Oriental/Asian patients; although the number of patients in this group was small (n=44).

Safety

- The most frequently reported AEs regardless of severity or causality (≥10% incidence in any subgroup) in the DRV/r arm by gender, age and race subgroups are shown in Figures 2a–c.

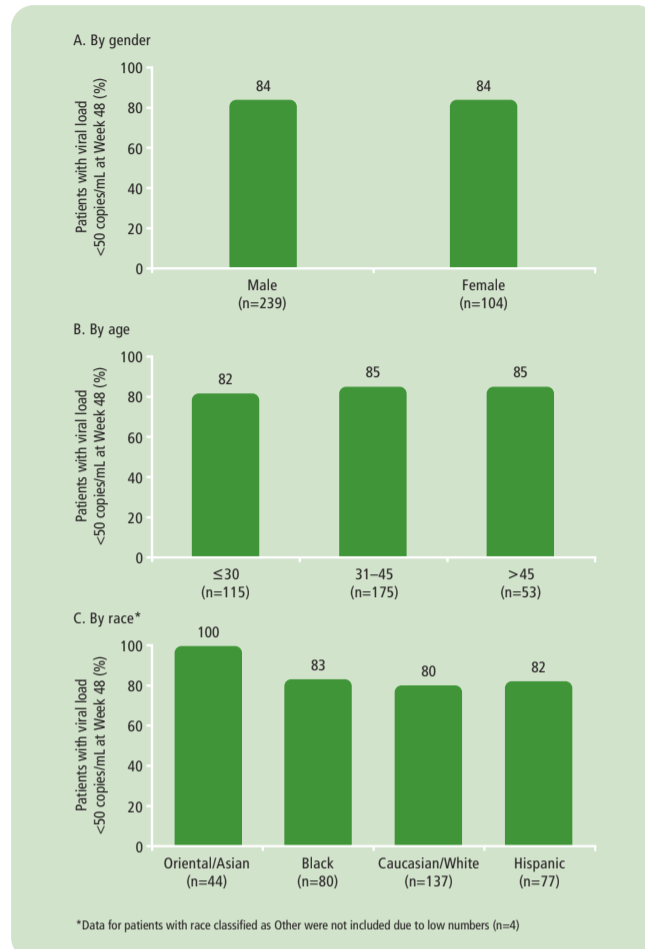


Figure 1. Virologic response (percentage of patients with viral load <50 copies/mL) at Week 48 (ITT-TLOVR) according to gender, age and race of patients receiving DRV/r 800/100mg qd.

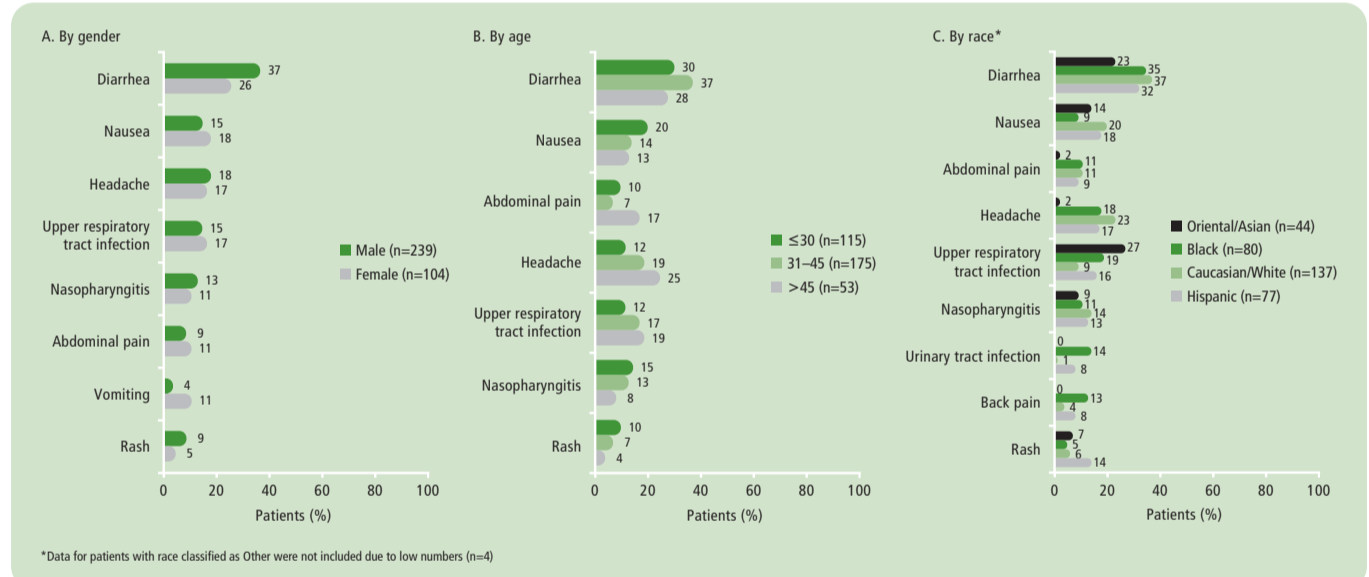


Figure 2. Overview of the most frequently reported AEs regardless of severity or causality (≥10% incidence in any subgroup) according to gender, age and race of patients receiving DRV/r 800/100mg qd.

Table 2. Incidence of grade 3–4 treatment-emergent laboratory abnormalities observed in ≥1 patient in any subgroup through Week 48 according to gender, age and race of patients receiving DRV/r 800/100mg qd.

Laboratory parameter, n (%)	Worst grade*	Gender		Age (years)			Race*			
		Male (n=239)	Female (n=104)	≤30 (n=115)	31–45 (n=175)	>45 (n=53)	Oriental/Asian (n=44)	Black (n=80)	Caucasian/White (n=137)	Hispanic (n=77)
Amylase (increased)	3	9 (4)	0	1 (1)	3 (2)	5 (9)	0	1 (1)	5 (4)	3 (4)
ALT (increased)	3	8 (3)	2 (2)	7 (6)	2 (1)	1 (2)	1 (2)	2 (3)	5 (4)	2 (3)
AST (increased)	3	8 (3)	2 (2)	5 (4)	3 (2)	2 (4)	0	1 (1)	6 (4)	3 (4)
LDL (increased)	3	4 (2)	1 (1)	1 (1)	1 (1)	3 (6)	1 (2)	2 (3)	1 (1)	1 (1)
Total cholesterol (increased)	3	3 (1)	1 (1)	1 (1)	0	3 (6)	0	2 (3)	1 (1)	1 (1)
Triglycerides (increased)	3	4 (2)	0	2 (2)	2 (1)	0	1 (2)	0	3 (2)	0
Hyperglycemia	3	1 (0)	0	0	1 (1)	0	0	0	1 (1)	0
Hypophosphatemia	3	1 (0)	2 (2)	0	3 (2)	0	0	1 (1)	1 (1)	1 (1)
Neutrophils (decreased)	3	2 (1)	2 (2)	2 (2)	1 (1)	1 (2)	0	1 (1)	3 (2)	0
	4	4 (2)	3 (3)	1 (1)	6 (3)	0	0	6 (8)	1 (1)	0
	4	0	1	0	1 (1)	0	0	1 (1)	0	0

*Data for patients with race classified as Other were not included due to low numbers (n=4); *Based on the Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events 2004, which does not have a grade 4 classification for total cholesterol and LDL. ALT = alanine aminotransferase; AST = aspartate aminotransferase

Conclusions

- ARTEMIS enrolled a broad and diverse population of treatment-naïve patients.
- No clinically meaningful differences were observed in the tolerability of DRV/r 800/100mg qd in treatment-naïve patients at Week 48, irrespective of gender, age or race.
- The majority of AEs and laboratory abnormalities observed in all subgroups were of mild-to-moderate severity. These incidences were similar to those reported for the overall population and were infrequently associated with treatment discontinuation.
- The efficacy of DRV/r through Week 48 was similar across the subgroups, and was comparable to the overall population.
- DRV/r 800/100mg qd is an effective, well-tolerated once-daily treatment option for treatment-naïve patients regardless of gender, age or race.

References

- Tibotec Inc. PREZISTA™ (darunavir) Prescribing Information. Revised February 2008 [accessed 16 May 2008]. Available from: <http://www.prezista.com>.
- PREZISTA™ (darunavir) Summary of Product Characteristics. February 2007 [accessed 10 March 2008]. Available from: <http://www.emea.europa.eu/humandocs/PDFs/EPAR/prezista/H-707-PI-en.pdf>.
- Katlama C, et al. AIDS 2007;21:395–402.
- Haubrich R, et al. AIDS 2007;21:F11–F18.
- Ortiz R, et al. AIDS 2008;22:1389–97.

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