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Efficacy and safety by baseline HIV-RNA and CD4 count in treatment-naive patients treated With atazanavir/r and lopinavir/r in the CASTLE study

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Purpose of the study

In the CASTLE study, lower response rates were observed in patients with baseline HIV-RNA ≥100,000 copies/mL in both arms and were associated with lower baseline CD4 cell count for LPV/r but not ATV/r.

Methods

Randomized, open-label, prospective study comparing once-daily ATV/r with twice-daily LPV/r, both with fixed-dose TDF/FTC in 883 treatment-naive patients. Treatment outcomes of HIV-RNA <50 c/mL at week 48 using confirmed virologic response (CVR) and grade 2–4 treatment-related AEs through week 48 are presented by pre-specified baseline HIV-RNA and CD4 cell count strata.

Summary of results

The proportion of responders (CVR HIV-RNA <50 c/mL, ITT) at week 48 by baseline HIV RNA strata (<100,000, 100,000–<500,000, and ≥500,000) were 83%, 76%, and 64% for ATV/r and 80%, 74%, and 61% for LPV/r (Table 1).

In patients with both baseline CD4 <100 and HIV-RNA ≥100,000, 60/83 (72%) on ATV/r and 40/64 (63%) on LPV/r achieved HIV RNA <50 c/mL (CVR, ITT). Incidence of grades 2–4 treatment-related AEs through week 48 by baseline HIV-RNA strata (<100,000, 100,000–<500,000, and ≥500,000) were 29%, 26%, and 15% for ATV/r; and 31%, 27%, and 30% for LPV/r. (Table 2.)

Table 1: CVR Treatment Outcomes of HIV RNA <50 c/mL at Week 48 by Baseline CD4 Cell Count, n (%).

	ATV/r				LPV/r			
As-Randomized	<50	50–<100	100–<200	≥200	<50	50–<100	100–<200	≥200
ITT	n = 58	n = 45	n = 106	n = 222	n = 48	n = 29	n = 134	n = 228
Responder	45 (78)	34 (76)	80 (75)	178 (80)	30 (63)	20 (69)	104 (78)	182 (80)
Virologic failure*	7 (12)	7 (16)	17 (16)	26 (12)	6 (13)	7 (24)	13 (10)	24 (11)
Discontinued	6 (10)	4 (9)	9 (8)	16 (7)	12 (25)	2 (7)	16 (12)	20 (9)
On-treatment, n/N (%)	45/52 (87)	34/40 (85)	80/95 (84)	178/202 (88)	30/35 (86)	20/25 (80)	104/114 (91)	182/201 (91)

*Includes never suppressed and on study through week 48, discontinued due to insufficient viral load response through week 48, and rebound without resuppression.

Table 2: Grade 2–4 Treatment-Related AEs through Week 48 by Baseline CD4 Cell Count (cells/mm3), n (%).

	ATV/r				LPV/r			
As-treated	<50	50–<100	100–<200	≥200	<50	50–<100	100–<200	≥200
	n = 59	n = 45	n = 106	n = 222	n = 47	n = 29	n = 133	n = 224
Any	12 (20)	9 (20)	22 (21)	71 (32)	19 (40)	7 (24)	35 (26)	65 (29)
Jaundice	1 (2)	0	2 (2)	12 (5)	0	0	0	0
Diarrhea	0	1 (2)	3 (3)	6 (3)	8 (17)	3 (10)	12 (9)	26 (12)
Nausea	2 (3)	0	6 (6)	9 (4)	5 (11)	2 (7)	9 (7)	16 (7)

Conclusion

Lower response rates at higher baseline HIV-RNA were seen for both ATV/r and LPV/r. The trend for lower response rates at lower baseline CD4 cell counts for LPV/r observed in the ITT analysis did not appear to be present in the on-treatment analysis. ATV/r and LPV/r had consistent adverse event (AE) profiles within each arm by baseline HIV-RNA. More AEs, most commonly diarrhea and nausea, were observed with LPV/r at low baseline CD4 cell counts.