PE8/20
DUAL THERAPY WITH LOPINAVIR/R AND RALTEGRAVIR (LPV/R+RAL) IN TREATMENT-EXPERIENCED HIV-INFECTED PATIENTS: DATA FROM THE GERMAN MULTICENTER PROTEKT COHORT

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BACKGROUND

PROTEKT is a non-interventional cohort study including HIV-1-infected patients receiving LPV/r plus an antiretroviral agent other than nucleoside/nucleotide reverse transcriptase inhibitor (NRTI), i.e. an integrase inhibitor (INI). There were no restrictions concerning additional antiretroviral drugs. Choice of antiretroviral therapy (ART) was part of routine clinical care and independent from the conduct of PROTEKT. Ethics approval was obtained prior to the study.

METHODS

Study design

Non-interventional, observational cohort study with prospective data collection in routine clinical practice. Data were collected at baseline, weeks 4 and 12, and 3-monthly thereafter until week 144. 48 week analyses was performed for a subgroup of the PROTEKT cohort, namely pre-treated patients switched to dual therapy with LPV/r+RAL.

Primary outcome measures

- Virologic outcome measures were:
  Percentage of patients with HIV-RNA < 50, 50 – 200, and > 200 c/mL using snapshot analysis at week 48 (ITT, failure = discontinuation for any reason, missing data excluded) and as-treated (AT) analysis.
- Immunologic outcome was assessed by the change in absolute CD4 cell count (cells/uL; median and interquartile range [IQR]).
- Safety was evaluated based on incident adverse events (AEs) of WHO grade 1 – 4 and discontinuations attributed to AEs.

RESULTS

Study population

209 treatment-experienced patients who were switched to LPV/r+RAL were included in this sub-analysis of PROTEKT.
At baseline, HIV-RNA levels were < 50 c/ml in 48 % of patients. Baseline characteristics stratified by HIV-RNA and pre-treatment are shown in Table 1.

Table 1: Baseline (BL) Characteristics

	Group 1a	Group 1b	Group 2a	Group 2a
	HIV-RNA < 50 c/mL at BL PI- and INI-naïve	HIV-RNA < 50 c/mL at BL PI- and/or INI-experienced	HIV-RNA ≥ 50 c/mL at BL PI- and INI-naïve	HIV-RNA ≥ 50 c/mL at BL PI- and/or INI-
		PI-exp.: 98.6 % INI-exp.: 13.9 %		PI-exp.: 98.4 % INI-exp.: 11.3 %
Total, n	29	72	46	62
Median age, years (IQR)	41 (36 – 49)	47 (40 – 54)	42 (36 – 47)	46 (40 – 53)
Female	7 (24 %)	9 (13 %)	6 (13 %)	17 (27 %)
Time since HIV diagnosis, years (IQR)	10.3 (6.5 – 11.6)	12.4 (8.3 – 15.1)	11.9 (6.5 – 16.1)	10.0 (6.0 – 14.0)
Median BL HIV-RNA, log c/mL (IQR)	< 1.7	< 1.7	4.2 (3.4 – 4.5)	4.1 (2.6 – 4.8)
Median BL CD4, cells/µL (IQR)	461 (307 – 634)	597 (404 – 820)	357 (253 – 494)	294 (162 – 535)

IQR = interquartile range

Previous ART and documented reasons for switch to LPV/r+RAL

Previous ART and documented reasons for switch to LPV/r+RAL (> 5 %) are shown in Table 2.

Table 2

	Group 1a		Group 1b		Group 2a		Group 2a	
	HIV-RNA < 50 c/mL at BL PI- & INI-naïve		HIV-RNA < 50 c/mL at BL PI- and/or INI-experienced		HIV-RNA ≥ 50 c/mL at BL PI- & INI-naïve		HIV-RNA ≥ 50 c/mL at BL PI- and/or INI-experienced	
Previous ART	NRTI only	41.4 %	NRTI only	4.2 %	NRTI only	39.1 %	NRTI only	1.6 %
	NRTI+PI	0.0 %	NRTI+PI	63.9 %	NRTI+PI	0.0 %	NRTI+PI	53.2 %
	NRTI+NNRTI	44.8 %	NRTI+NNRTI	1.4 %	NRTI+NNRTI	58.7 %	NRTI+NNRTI	6.5 %
	PI(s) only	0.0 %	PI(s) only	12.5 %	PI(s) only	0.0 %	PI(s) only	16.1 %
	Other	13.8 %	Other	18.0 %	Other	2.2 %	Other	22.6 %
Documented reasons for switch to LPV/r+RAL (> 5 %)	Side effects	41.4 %	Side effects	54.2 %	Treatment failure/ drug resistance	67.4 %	Treatment failure/ drug resistance	50.0 %
	Patient wish	10.4 %	Patient wish	8.3 %	Patient wish	8.7 %	Therapy break	12.9 %
	Treatment failure/ drug resistance	6.9 %	Treatment failure/ drug resistance	6.9 %	Noncompliance	6.5 %	Patient wish	9.7 %
			Simplification	6.9 %	Therapy break	6.5 %	Side effects	9.7 %

Virologic response

The virologic response rates in the four groups are shown in Figure 1 (ITT analysis) and Figure 2 (AT analysis).

Confirmed HIV-RNA > 200 c/mL after 48 weeks or HIV-RNA > 200 c/mL at week 48 plus subsequent discontinuation was 0 % in group 1a, 2 % in group 1b, 3 % in group 2a and 13 % in group 2b.

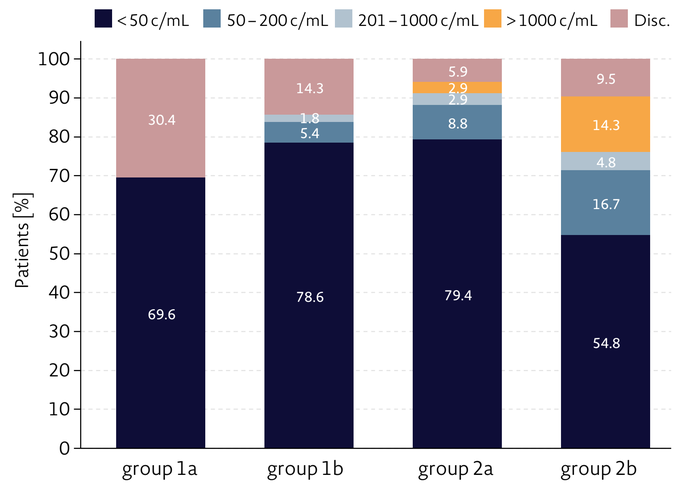

Fig. 1: Virologic response at week 48; ITT
snapshot analysis; failure = discontinuation for any reason, missing data excluded

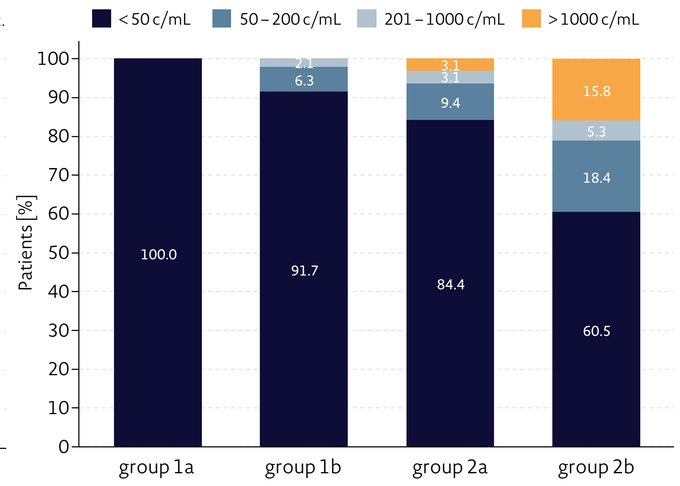

Fig. 2: Virologic response at week 48; AT
snapshot analysis, discontinuations unrelated to efficacy were excluded

Immunologic response

Table 3: Median absolute CD4 cell count and change in CD4 cell count at week 48

	Group 1a	Group 1b	Group 2a	Group 2a
Median CD4/µL, week 48 (IQR)	436 (260 – 581)	578 (422 – 843)	507 (411 – 615)	480 (316 – 704)
Median change in CD4/µL, week 48 (IQR)	+32 (-27 – 105); P = n.s.	+32 (-125 – 198); P = n.s.	+121 (26 – 261); P = 0.0011	+111 (4 – 201); P = 0.0002

Safety

By week 48, 21 patients (10 %) discontinued LPV/r and/or RAL; 9 discontinuations were attributed to AEs, none to virologic failure. In 14 discontinuers (67 %) HIV-RNA was < 50 c/mL at discontinuation. In 41 % of patients at least one AE was documented including seven grade 3 (abdominal pain, fever, fatigue, 2x diarrhea, 2x elevated triglycerides) and two grade 4 events (diarrhea, hyperglycemia).

Table 4: Most commonly reported adverse events AEs (grad 1 – 4)

Per patient (%)	Group 1a	Group 1b	Group 2a	Group 2a
Diarrhea	4 (13.8 %)	13 (18.1 %)	11 (23.9 %)	19 (30.6 %)
Abdominal pain	0 (0 %)	3 (4.2 %)	2 (4.3 %)	4 (6.5 %)
Vomiting	0 (0 %)	0 (0 %)	1 (2.2 %)	3 (4.8 %)
Fatigue	0 (0 %)	2 (2.8 %)	1 (2.2 %)	1 (1.6 %)
Hypercholesterolemia	0 (0 %)	8 (11.1 %)	11 (23.9 %)	10 (16.1 %)
Hypertriglyceridemia	1 (3.4 %)	9 (12.5 %)	10 (21.7 %)	6 (9.7 %)

CONCLUSION

In the PROTEKT cohort, the nucleoside-sparing regimen LPV/r+RAL is used in a heterogeneous group of pre-treated HIV-infected patients. Switching was mainly driven by virologic failure (57 %) or – in patients on suppressive cART – adverse events (50 %). LPV/r+RAL showed good virologic effectiveness in patients on suppressive cART and in PI- and INI-naïve patients on failing ART (70 – 79 % with HIV-RNA levels < 50 c/mL at week 48) with no unexpected safety findings.

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Disclosures

AbbVie participated in the interpretation of data, review, and approval of the content.
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J.H. is an Abbvie employee and may hold stock or options.

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