Patient-Reported Outcomes in the PROTECT Clinical Trial Comparing Sparsentan With Irbesartan for Immunoglobulin A Nephropathy

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RESULTS

- Demographics and baseline characteristics for the full analysis set of 404 patients in PROTECT have been reported previously and were similar between the 2 treatment arms.[1]
- Baseline KDQOL-36 scores were similar for SPAR and IRB except for Burden of Kidney Disease scores, which were somewhat higher for IRB (**Table 1**).

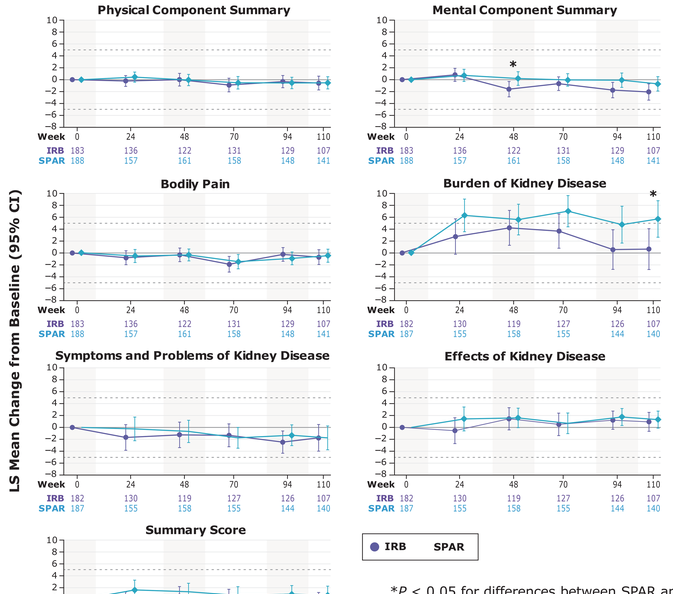
Table 1. Baseline KDQOL-36 Subscale Scores by Treatment Arm

Subscale	SPAR (n=188) mean (SD)	IRB (n=183) mean (SD)
Physical Component Summary	51.1 (8.08)	51.7 (7.02)
Mental Component Summary	50.4 (8.30)	51.4 (8.63)
Bodily Pain	52.5 (8.06)	53.8 (6.67)
Burden of Kidney Disease*	70.1 (25.25)	76.9 (22.80)
Symptoms and Problems of Kidney Disease*	88.8 (11.22)	89.2 (11.02)
Effects of Kidney Disease*	88.4 (13.12)	89.0 (12.96)
Summary score*	85.4 (11.74)	87.0 (11.49)

*SPAR, sparsentan; IRB, irbesartan; SD, standard deviation. *N=187 and 182 for SPAR and IRB, respectively.*

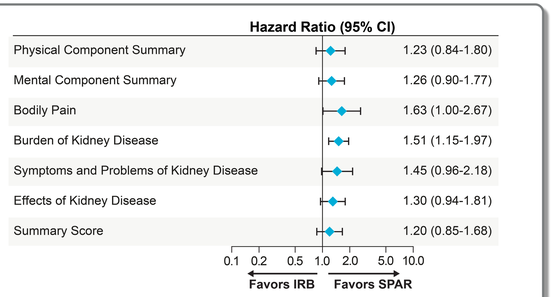
- Compared with IRB, SPAR exhibited consistent improvement in Burden of Kidney Disease scores at all follow-up visits (week 110 difference [SPAR-IRB], 5.1; P=0.0316) and directional improvement in other scores at each timepoint (**Figure 1**).
- Hazard ratios for time to first improvement in Burden of Kidney Disease favored SPAR with other hazard ratios numerically favored SPAR (**Figure 2**).
- Hazard ratios for time to first confirmed improvement in Burden of Kidney Disease, KDQOL-36 Summary score, and Mental Component Summary score favored SPAR with other hazard ratios also numerically favored SPAR (**Figure 3**).

Figure 1. LS Mean Changes From Baseline in PRO Scores By Treatment and Visit



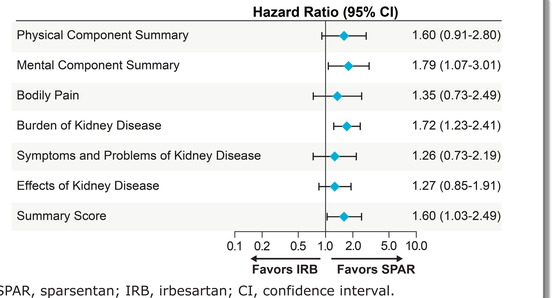
*$P < 0.05$ for differences between SPAR and IRB. Note: Vertical bars indicate 95% CIs. Dotted lines indicate meaningful changes thresholds. A higher score indicates better HRQOL/functioning. SPAR, sparsentan; IRB, irbesartan; CI, confidence interval.

Figure 2. Hazard Ratios for Time to First Improvement in KDQOL-36 Scores



SPAR, sparsentan; IRB, irbesartan; CI, confidence interval.

Figure 3. Hazard Ratios for Time to First Confirmed Improvement in KDQOL-36 Scores



SPAR, sparsentan; IRB, irbesartan; CI, confidence interval.

CONCLUSIONS

These results suggest that patients with IgAN receiving sparsentan had less burden of kidney disease over time and a general trend toward improved HRQOL compared with those receiving maximally dosed irbesartan.

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BACKGROUND

- PROTECT (NCT03762850) demonstrated that sparsentan (SPAR) was superior to maximally dosed irbesartan (IRB) in reducing proteinuria and preserving kidney function.[1]
- Patient-reported outcomes (PROs) provide an assessment of whether SPAR's demonstrated clinical efficacy in PROTECT translates to improvements in patients' health-related quality of life (HRQOL), an important goal in the treatment of glomerular diseases.[2]

OBJECTIVE

- To evaluate the effect of SPAR compared with IRB on PROs in patients with IgAN enrolled in PROTECT during the double-blind period.

METHODS

Data:

- Kidney Disease Quality of Life-36 (KDQOL-36) administered at baseline and weeks 24, 48, 70, 94, and 110 of the double-blind period for patients in the full analysis set.

PRO Scores:

- KDQOL-36 Kidney-target subscale and Summary[3] scores (range 0 to 100, with higher scores representing better quality of life);[4] Physical Component Summary, Mental Component Summary, and Bodily Pain scales from the SF-12 (normalized to mean of 50 and standard deviation of 10 based on the 1998 general US population).

Analysis:

- Changes from baseline analyzed using least-squares (LS) means from mixed models for repeated measures as applied for the longitudinal analyses of primary efficacy endpoints in the PROTECT trial.[1]
- Time-to-event (in weeks) analyses using Cox proportional hazards models with randomization stratification factors and a score change of 5 considered clinically meaningful[5-7] reporting hazard ratios (HRs) and 95% confidence interval; First improvement was defined as the earliest beneficial change in score relative to baseline reaching or exceeding the threshold during the treatment period, Confirmed improvement was defined as reaching or exceeding the threshold which was then maintained at the next visit with a nonmissing PRO score.

LIMITATIONS

- PROTECT was not powered to evaluate treatment differences in PROs. All analyses presented here are considered exploratory.
- The KDQOL-36 may not be sensitive enough to detect all the differences associated with the between-treatment-arm differences in clinical parameters observed in the PROTECT study.
- Time-to-event analyses rely on definition of a meaningful change threshold that is clinically relevant.[8,9] Although a change of 3 to 5 points in KDQOL-36 scale scores is generally considered clinically meaningful change[5-7] thresholds of meaningful change have not been standardized for patients with IgAN.

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