RESULTS (CONTINUED)

Ophthalmic Findings

No rAAV2YF-GKR1-RPGRCo-related ophthalmic findings were observed at Weeks 4 and 12. All findings (Table 2) were considered procedure-related or background findings. Lesions were detected in all eyes receiving subretinal injection for all Groups at Week 4 and Week 12.

All dosed eyes showed the effect of transcorneal administration procedure. The location of cataract origin in the dosed eyes corresponded with the location of the corneal lesion, consistent with this being an effect of the subretinal injection. Across the treatment Groups, some eyes showed pigment mottling in the fundus in addition to some retinal hemorrhage or vessel attenuation. These phenomena were also considered a consequence of the surgery.

Immunohistochemistry

Immunolabeling of RGR protein, mainly in the inner segment of photoreceptors and the adjacent connecting cilia region, was observed in a dose-dependent manner in all vector-treated eyes examined (Figure 1).

ERG

Statistical analysis of ERG was performed for the response to scotopic (0.025, 0.25 and 2.5 cd/m²) and photopic light intensity (1.25, 5, 10 and 25 cd/m²).

No statistically significant differences were detected at any flash intensities in the scotopic series nor the photopic series, therefore this decision was considered not to be related to dosing with of rAAV2YF-GKR1-RPGRCo.

Comparison between groups is presented in Figure 2, using a representative intensity of scotopic and photopic respectively.

RESULTS (CONTINUED)

Histopathology

No rAAV2YF-GKR1-RPGRCo-related histopathology findings were observed at Weeks 4 and 12. All findings were considered to be procedure related.

Retinal findings in the injected eye include the presence of pigmented cells in the subretinal space and within the subretinal space of photoreceptors. The photoreceptor cells and/or outer nuclear layer in addition, some cells showed slight to moderate photoreceptor degeneration.

The findings were present across all groups, including Vehicle controls, and the findings lacked a dose response; as such, these were considered injection procedure related and not related to rAAV2YF-GKR1-RPGRCo.

CONCLUSIONS

Subretinal injection of AAV2YF-GKR1-RPGRCo in XLRP-deficient Rd9 mice induced predominant RPGR expression in the retina and was well tolerated with no vector-related effects at either 4 x 10⁹ or 4 x 10¹⁰ vg/eye.

The no observed adverse effect level (NOAEL) for this study was considered to be 4 x 10⁹ vg/eye.

REFERENCES