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Subthreshold Laser Treatment for Reticular Pseudodrusen and Geographic Atrophy Secondary to AMD

ID: PASCAL-GA

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Study protocol

After obtaining informed consent and after the screening visit, at the Baseline (Day 0) the following evaluations were performed:

- Ophthalmic history, including prior medication use;
- Best Corrected ETDRS Visual Acuity (BCVA) at 4 meters prior to dilatation;
- Slit lamp examination;
- Fundus examination (by indirect ophthalmoscopy);
- Intraocular pressure (IOP);
- Spectral Domain Optical Coherence Tomography (SD-OCT);
- Fundus autofluorescence (FAF) in the area later treated with laser;
- Microperimetry in a customized area later treated with laser;
- An extramacular area of 1.27 mm^2 (½ of a disk area, disk area= 2.54 mm2) was treated with subthreshold laser;
- Record concomitant medications;
- Post treatment assessment.

Follow-up visits were performed at week 4 +/- 7 days and at week 12 +/- 7 days). During the follow-up examinations, the following evaluations were performed:

- BVCA;
- Slit lamp examination;
- Fundus examination (by indirect ophthalmoscopy);
- IOP;
- SD-OCT;
- FAF in the area later treated with laser;
- Microperimetry in a customized area previously treated with laser;
- Record concomitant medications.

Investigational products and treatment

All the treatments were performed by an expert senior author (GQ). The treatment was performed using the Pascal Synthesis 577 system (Topcon Corporation, Tokyo, Japan). The Pascal Synthesis 577 system was delivered by Topcon with an operating manual. During the study, Topcon personnel was available as needed to support the investigators. In addition, investigators underwent training on Pascal Synthesis 577 system operation prior to study initiation.

During the treatment, the investigator identified the threshold layer outside the vascular arcades. In detail, the threshold level output power was set to obtain barely visible burn at approximately 200mW to 250mW using the titration mode. After that, the investigator identified an area inside the vascular arcades affected by RPD. The irradiation was conducted on this area after switching over to Endpoint Management (30% of the power of the barely visible burn) with a pattern of 5 for 3 spots (area of 1.27 mm^2).

Multimodal imaging analysis

Enrolled patients underwent a multimodal imaging examination by means of confocal scanning laser ophthalmoscope (cSLO) integrated with SD-OCT (SPECTRALIS HRA+OCT, Heidelberg Engineering, Inc., USA). SD-OCT were used to analyze the outer retinal morphology in the treated area, including evaluation of the stages of RPD at the baseline and during the follow-up, and the thickness of the outer nuclear layer (ONL) at the baseline and during the follow-up.

Microperimetry was used to assess changes of retinal sensibility in the customized treated area. After training, all subjects underwent to scotopic microperimetry

examinations of the central retina in the study eye using the Nidek MP-1S (Nidek Technologies, Padova, Italy). The eyes will be fully covered with an opaque eye patch, followed by a waiting period of 30 minutes in a dark room (< 0.1 lux). Test stimuli were placed around the fovea (Goldmann size V, 200 msec, 4-2 strategy, background luminance 0.0032 cd/m2, grid centered on the anatomical position of the fovea). As fixation target, a ring with a 3° radius and 1 pixel thickness was presented. Due to the testing under scotopic conditions, the fixation ring was not necessarily centered on the fovea. The following parameters were recorded in each timepoint: overall retinal sensitivity (MS) of the macular area and the MS of the treated area, fixation percentage calculated within the central 2° and 4°.

Statistical Analysis

All statistical analyses were performed using SPSS Statistics Version 20 (IBM, Armonk, New York, USA). Categorical variables were expressed as count and percentage, whereas quantitative variables were expressed as mean±standard deviation. The Gaussian distribution of continuous variables was verified with the Kolmogorov-Smirnov test. Comparisons of BCVA, CMT, retinal and choroidal thickness in the treated area, ONL thickness, IOP, overall retinal sensitivity (MS) of the macular area and of the treated area between different timepoints (baseline, 4-week follow-up and 12-week follow-up) were performed using Analysis of Variance (ANOVA) for paired samples with Bonferroni post-hoc analysis. In all analyses, p values <0.05 were considered statistically significant.