Supplementary File S5: Statistical analysis details

Hypotheses of primary objective for noninferiority and superiority were tested using a sequentially rejective multiple testing procedure that protects the multiple one-sided alpha level of 0.025. In order to protect the multiple one-sided alpha level of 0.025, a sequentially rejective testing procedure was established.

Hypotheses related to noninferiority were:

•Null hypotheses: H_{01}: μIII - μI >4 letters and H_{02}: μIII - μII >4 letters

•Alternative hypotheses: H_{11}: μIII - μI ≤4 letters and H_{12}: μIII - μI ≤4 letters,

where μI, μII and μIII were defined as the primary efficacy variable mean of the average change from baseline to Month 1 through Month 12 in BCVA obtained from all treatment groups (0.5 mg ranibizumab T&E+laser, 0.5 mg ranibizumab T&E alone and 0.5 mg ranibizumab PRN).

Hypotheses related to superiority were:

•Null hypotheses: H_{03}: μIII - μI ≥0 letters and H_{04}: μIII - μII ≥0 letters

•Alternative hypotheses: H_{13}: μIII - μI < 0 letters and H_{14}: μIII - μII <0 letters

The noninferiority margin of 4 letters was used during testing (indicated by the U.S. Food and Drug Administration in regulatory discussions of Visudyne studies in 2008). The primary analysis was carried out after patients had completed the Month 12 visit using the full analysis set (FAS) which consisted of all randomised patients who received at least one application of the study treatment (ranibizumab or laser), and had at least one postbaseline assessment for BCVA in the study eye. The mean value imputation/last observation carried forward (MV/LOCF) approach was employed to compensate for the missing data. Following the intent-to-treat principle, patients were analysed according to the treatment assigned at randomisation. All analyses for the secondary efficacy variables were carried out on untransformed data. For analyses based on proportions, corresponding 95% confidence intervals (CIs) for each treatment group were calculated using exact methods, and the 95% CI of the difference in proportions between treatment groups was computed based on the normal approximation. For continuous variables, descriptive statistics by scheduled visit were provided for absolute values and changes from baseline. Variables expressed as proportion of patients were also presented by scheduled visit with number and percentage of patients. The statistical analysis was performed by Parexel personnel according to the statistical analysis plan.