Photodynamic therapy is beneficial for long-standing Central Serous Chorioretinopathy but the chronic damage may impair visual outcomes

Gabriel Katz ( gabrielkatz.dr@gmail.com )
Sheba Medical Center at Tel Hashomer: Sheba Medical Center  https://orcid.org/0000-0002-7597-6281

Efrat Gur
Sheba Medical Center The Goldschleger Eye Institute

Joseph Moisseiev
Sheba Medical Center at Tel Hashomer

Ari Leshno
Sheba Medical Center The Goldschleger Eye Institute

Research Article

Keywords: Central serous chorioretinopathy, photodynamic therapy, longstanding, verteporfin

Posted Date: February 11th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1276411/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License
Abstract

Purpose: Central serous chorioretinopathy (CSCR) patients are often referred to Photodynamic Therapy (PDT) with very long-term disease because of concerns about the potential negative effects of PDT on the retina and on the visual acuity. The purpose of this study was to analyze the results of PDT in CSCR eyes with long standing disease.

Methods: The medical records of the patients that underwent PDT for CSCR between 2009 and 2019 were reviewed. Cases were divided into two groups based on the duration of disease before PDT treatment: early treatment (3 to 6 months), delayed treatment (longer than 6 months). The treatment was defined as successful when the subfoveal fluid was absorbed during follow up.

Results: The PDT treatment was successful in 76% and 77% of eyes in the early and delayed treatment groups respectively. Both groups showed significant improvement in central retina measurements at the 3-months follow up which persisted to the last follow-up visit. The visual acuity (VA) at baseline was significantly worse in the delayed treatment group (0.5±0.26 vs 0.3±0.24, P=0.042) and improved in both groups but remained low in the delayed treatment group during the study.

Conclusion: PDT is not associated with loss of vision in eyes with chronic CSCR, and can be safely used in eyes with relatively good VA. We suggest that if CSCR is not spontaneously improving over 3 months the patient should be offered PDT, to prevent VA loss from the long-term presence of subretinal fluid in the macula.

Introduction

Photodynamic therapy (PDT) with intravenous verteporfin has been the gold standard treatment of central serous chorioretinopathy (CSCR) for over a decade. The reported anatomic success rates vary between 80 to 90% [1–5] either using half of the verteporfin dose or half of the laser fluence [6–12]. Half fluence, reducing the energy from 50 J/cm² to 25 J/cm², was achieved by either reducing the time of the PDT from 83 seconds to 42 seconds (half time) or by reducing the irradiance from 600 mW/cm² to 300 mW/cm² (half irradiance). The prognostic factors for anatomic or functional success were also studied. Poor prognosis was associated with older age and lower baseline visual acuity [13], diffuse leakage on FA and absence of intense hyperfluorescence on ICGA [14–17].

Other treatment options were also suggested in numerous studies. The latest Cochrane review published looked at 25 studies including 1098 patients summarized that PDT or micropulse laser treatment appear the most promising treatment options for CSCR [18]. In a randomized controlled study published later, micropulse laser was found inferior to PDT [19]. Another more recent review study [20] concluded that the available evidence suggests that half-dose (or half-fluence) photodynamic therapy should be the treatment of choice in chronic CSC. Eplerenone, a drug that was considered for a while as an alternative to PDT was recently shown to be ineffective in a randomized controlled study [21].
CSCR is typically a self-limited disease that does not require treatment in the acute phase. Recurrence rates in the absence of intervention are reported to range from 15 to 50%, depending on study type and length of follow up. Approximately third to half of the patients have a second recurrence, often within a year of the first episode, while 10% have three or more recurrences when followed for up to 15 years [22]. In most studies the definition of a "chronic" disease that requires treatment is persistent subfoveal fluid (SRF) over 3 months [4, 5, 8, 10]. Other studies define chronic disease as persistent SRF over 6 months [1, 2, 7, 9, 23]. There is no consensus in the literature concerning the best timing of PDT in eyes with CSCR, and whether it should be used early or delayed. Patients are often referred to our clinic with very long term CSCR because of concerns about the potential negative effects of PDT on the retina and on the visual acuity. Some of these patients present with significant retinal atrophy and poor visual acuity. PDT may probably be beneficial even in such long-standing cases, with a positive anatomic result but the visual acuity will remain poor [24]. The purpose of this study was to analyze the results of PDT in CSCR eyes with long standing subretinal fluid treated at our retina service, and compare the anatomic and functional outcomes between patients with early vs delayed treatment.

**Methods**

**Study design**

Charts of patients with CSCR that received PDT at the Goldschleger Eye Institute, the Sheba Medical Center, Israel, between 2009 and 2019 were retrospectively reviewed. Only patients that were PDT naïve were included in this study. Approval for data collection and analysis was obtained from the ethics committee of the hospital, and all patients provided informed consent for the PDT procedure. The methodology of the study was designed in accordance with the tenets of the Declaration of Helsinki.

**Subjects**

Patients aged 18 years or older diagnosed with CSCR (based on fluorescein and/or indocyanine green angiography which were performed prior to treatment) were included in the study if they had documented persistent subfoveal fluid for at least 3 months prior to the PDT with a follow-up of at least 3 months post-treatment at our retina service with ocular coherence tomography (OCT) scans. We excluded cases who underwent prior retinal laser treatments or those treated by subthreshold laser. Cases in which follow-up duration was less than 3 months, diagnosis was questionable, or OCT scan were missing/poor quality were excluded.

**PDT protocol**

All patients were treated with half verteporfin dose or with half fluence PDT (half time or half irradiance). For each case we collected the details of PDT protocol, number and size of PDT applications per session and the number of PDT sessions for each eye.

**Diagnostic evaluation and follow-up examinations**
The medical records of the study subjects were reviewed and the following data were retrieved: demographics (age, gender), ocular history, disease duration, use of corticosteroids, and prior treatments for CSCR (e.g. spironolactone, acetylsalicylic acid, intravitreal anti-VEGF injections). Data at the baseline examination and at the 1- and 3-months follow-up visits were recorded as well as details of the final follow-up visit. The data retrieved from the ocular examination at each visit included: visual acuity (VA) (Snellen charts), mydriatic slit-lamp examination by a retina specialist, and spectral domain OCT findings (Spectralis, Heidelberg Engineering, Germany, or Zirrus Carl Zeiss Meditec Inc, Dublin, CA). The OCT scans were reviewed by one of the authors (GK) and the presence of subretinal fluid (SRF), subretinal hyper reflective material (SHRM), irregular retinal pigment epithelium (RPE) and pigment epithelium detachment (PED) was documented for each scan. We also measured manually the central thickness (CRT) of the fovea and the height of the central subretinal fluid in each scan when available. We expected to find significantly thin retina as compatible with the chronic damage. The treatment was defined as successful when the subfoveal fluid was absorbed during follow up.

Statistical analysis

The statistical software SPSS version 25.0 (SPSS, Inc., Chicago, IL, USA) was used for data analysis. Statistical significance was set at P < 0.05. According to the different approaches in the literature, cases were divided into two groups based on the duration of disease before PDT treatment: early treatment (3 to 6 months), delayed treatment (longer than 6 months). If a subject suffered from bilateral disease and both eyes qualified based on the inclusion and exclusion criteria one eye was randomly selected for the analysis.

Due to the relatively small sample size of each independent group non-parametric tests were used. Mann-Whitney and Pearsons’ Chi square tests were applied for comparison of continuous and categorical variables respectively between groups at each specific time point. The Wilcoxon signed rank test and McNemar test were applied for comparison of continuous and categorical variables respectively between baseline and follow-up visits within each group. Repeated measures analysis was applied to determine differences in trends over time in terms of BCVA and CRT. Spearmans’ correlation coefficient and multivariant analysis were applied to detect possible prognostic factors for BCVA at the last follow-up visit.

Results

One hundred and two patients were coded as receiving PDT for CSCR between 2009 and 2019. Fifty-three cases (55 patients) were excluded for the following reasons: unclear diagnosis and/or suspected choroidal neovascularization (10 patients), insufficient data or follow up shorter than 3 months (38 patients), not central PDT (3 patients), previously treated (4 patients).

Forty-seven eyes (47 patients) were included in the final analysis, 21 eyes in the early treatment group and 26 eyes in the delayed treatment group. The baseline characteristics of the two groups are detailed in table 1.
There was a significantly higher percentage of women in the long duration group (4.8% vs 38.5%, P=0.007) but the mean age was similar. The BCVA at baseline was significantly worse in the delayed treatment group (0.500±0.26 vs 0.331±0.24, P=0.042). The delayed treatment group had longer follow-up duration post PDT treatment (Table 1), but the difference between the two groups was not statistically significant (P=0.195).

Prior to PDT treatment, CRT was higher among subjects in the early treatment group as compared to those in delayed treatment group, almost reaching statistical significance (P=0.052). No other significant differences were observed in baseline OCT scans or PDT treatment parameters. Most treatments in both groups were performed using half fluence (66%). There was also no difference between the groups in terms of recurrent treatments (1.5 vs 1.2). Prior oral treatments or intravitreal injections had no significant effect on the PDT treatment outcomes.

**Treatment success**

The PDT treatment was successful (i.e. absorption of SRF – P<0.001) in 76% and 77% of eyes in the early and delayed treatment groups respectively. A statistically significant resolution of SHRM and RPE irregularities was also observed in the delayed treatment group (P<0.001). Both groups showed significant improvement in CRT measurements at the 3-months follow up which persisted to the last follow-up visit (Fig. 1). Both CRT and max retinal thickness decreased significantly after the PDT treatment (P<0.001) and the gap between the two groups narrowed (figure 1a and 1b respectively).

In the subgroup of 29 patients (9 early and 20 delayed) with available manual measurements, the retina was significantly thinner in the delayed treatment group (193.3±49.2 microns vs 132.3±61.4, P=0.014, figure 2a) yet there was non-statistically significant difference in SRF height (144.4±85.0 vs 132.2±77.2, P=0.570, figure 2b). Manual CRT measurements also had a significantly negative correlation with BCVA at baseline and at the 3-months and last follow-up visit (Spearman's rho -0.498, P=0.006; -0.691, P<0.001; -0.533, P=0.003 respectively).

**Visual acuity**

Overall, BCVA improved significantly by nearly 1 line at last follow-up (from 0.42±0.26 to 0.36±0.33 LogMAR, P=0.017). BCVA improved in both groups (figure 3). In sub-analysis of only successful cases, BCVA improved from 0.44±0.28 to 0.36±0.36 (P=0.013), however the improvement was statistically significant only in the delayed treatment group (from 0.52±0.28 to 0.43±0.42, P=0.046) and the early treatment group had a non-significant change (from 0.34±0.26 to 0.26±0.24, P=0.126).

Compared to the early treatment group, the rate of improvement in BCVA was higher in the delayed treatment group at the 3-months follow-up visit (15/26, 57.7% vs. 5/21, 23.8%; P=0.014) but the difference did not reach statistical significance at the last follow-up visit analysis (15/27, 57.7% vs. 8/21, 38.1%; P=0.181). Figure 4 depicts the rate of clinically significant improvement/deterioration in BCVA (i.e. equivalent to 3 ETDRS lines) at the 3-months (a) and at the last follow-up (b) visits. Most of the subjects
in both groups did not show a clinically significant change in BCVA and the rates of improvement were quite similar.

Overall, the BCVA at each visit had a significant negative correlation with CRT and max retinal thickness at the 3-month follow-up visit (Spearman’s rho -0.359, P=0.014 and -0.401, P=0.021 respectively) but not at the last follow-up visit (-0.177, P=0.235; -0.246, P=0.155).

**Discussion**

Complete resolution of the SRF was achieved in about 77% of eyes in both the early and delayed treatment groups. Evidently, PDT is effective in reducing the subretinal leakage and promoting the absorption of the SRF even in eyes with long term persistent subretinal fluid. The retrospective nature of this study may introduce some biases. A significant proportion of patients were lost to follow up after their one month follow up or even earlier. Many patients were referred to us for the PDT procedure itself because it is not available in most medical centers in Israel and continued follow up at their primary physician after the procedure. This may explain the relatively low success rate of SRF absorption in both groups. Some patients that did not need further treatment were probably not referred again to our center.

A significant proportion of patients improved by more than 3 ETDRS lines in both groups. In the early treatment group, the VA improved from 20/42 to 20/38 (logMAR 0.33 to 0.28), while in the delayed treatment group it improved from 20/63 to 20/47 (logMAR 0.5 to 0.38). The delayed group improved relatively more, but the difference was not statistically significant. The delayed group entered the study with significantly lower VA, and despite resolution of the SRF in most eyes the final VA was worse than the VA of the early group. The explanation is probably provided by the subgroup analysis of eyes where we could manually measure the height of the SRF and the thickness of the central macula. Manual CRT measurements had a significantly negative correlation with BCVA.

It should be noted that we did not detect any case of immediate vision loss after treatment and at the last follow-up visit only a minor reduction in BCVA was observed in less than 5% of cases overall. As this reduction develop only long after the PDT treatment it seems to result from the longstanding disease and its natural course rather than the treatment itself.

The pre-PDT height of the SRF was similar in both groups, but the central retinal thickness was significantly reduced in the delayed treatment eyes (370 vs 311 microns), reflecting a more severe loss of retinal tissue. While PDT induces resolution of SRF whether it is used early or late in CSCR, the final VA is determined by the extent of irreversible damage to the macula and is directly associated with the duration of the disease and the baseline visual acuity.

These findings are compatible with the reported prognostic factors in previous studies on PDT treatment for CSCR [13]. Scholz et al. recently published a review of 12 studies regarding subthreshold laser in chronic CSCR [25]. The results were slightly lower than ours: overall, 79.6% of 191 patients showed
reduction of CMT and 63.6% a complete resolution of SRF. In the PDT arm complete fluid resolution was observed in 46% of cases, significantly lower than our series.

Another important finding was that in general the VA either improved or remained stable in most treated eyes. None of the treated patients suffered medium vision loss (>3 ETDRS lines) at the 3 months follow up. Due to the chronic nature of CSCR, around 4% of patients experienced medium vision loss at the end of follow up in both groups. This finding indicates that PDT is not associated with loss of vision in eyes with chronic CSCR, and can be safely used in eyes with relatively good VA. We suggest that if CSCR is not spontaneously improving over 3 months the patient should be offered PDT, to prevent VA loss from the long-term presence of SRF in the macular area.

Declarations

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial conflict of interest in the subject matter or materials discussed in this manuscript. No funding was received for conducting this study.

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Efrat Gur, Gabriel Katz and Ari Leshno. The first draft of the manuscript was written by Gabriel Katz and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript

Ethics approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Bioethics Committee of Sheba Medical Center (No. 623-19-SMC).

Consent to participate

This was a retrospective study on electronic data. There was no intervention within the study and therefore informed consent was not required.

References

1. Silva RM, Ruiz-Moreno JM, Gomez-Ulla F, Montero JA, Gregório T, Cachulo ML, Pires IA, Cunha-Vaz JG, Murta JN (2013) Photodynamic therapy for chronic central serous chorioretinopathy: a 4-year follow-up study. Retina 33(2):309–315. doi: 10.1097/IAE.0b013e3182670fbe

2. Smretschnig E, Ansari-Shahrezaei S, Hagen S, Glittenberg C, Krebs I, Binder S (2013) Half-fluence photodynamic therapy in chronic central serous chorioretinopathy. Retina 33(2):316–323. doi: 10.1097/IAE.0b013e318280769c
3. Erikitola OC, Crosby-Nwaobi R, Lotery AJ, Sivaprasad S (2014) Photodynamic therapy for central serous chorioretinopathy. Eye (Lond) 28(8):944–957. doi: 10.1038/eye.2014.134

4. Fujita K, Imamura Y, Shinoda K, Matsumoto CS, Mizutani Y (2015) One-year outcomes with half-dose verteporfin photodynamic therapy for chronic central serous chorioretinopathy. Ophthalmology 122(3):555–561. doi: 10.1016/j.ophtha.2014.09.034

5. Sheptulin V, Purtskhvanidze K, Roider J (2018) Half-time photodynamic therapy in treatment of chronic central serous chorioretinopathy. Graefes Arch Clin Exp Ophthalmol 256(11):2027–2034. doi: 10.1007/s00417-018-4086-6

6. Hashizume K, Mizota A, Yuzawa M, Lim JI, Glassman AR, Aiello LP, Chakravarthy U, Flaxel CJ, Spaide RF, Macula Society CSC Collaborative Study Group, Research and Education Committee and Website Committee (2014) Collaborative retrospective macula society study of photodynamic therapy for chronic central serous chorioretinopathy. Ophthalmology 121(5):1073–1078. doi: 10.1016/j.ophtha.2013.11.040

7. Nicoló M, Eandi CM, Alovisi C, Grignolo FM, Traverso CE, Musetti D, Cardillo Piccolino F (2014) Half-fluence versus half-dose photodynamic therapy in chronic central serous chorioretinopathy. Am J Ophthalmol 157(5):1033–1037. doi: 10.1016/j.ajo.2014.01.022

8. Alkin Z, Perente I, Ozkaya A, Alp D, Agca A, Aygit ED, Korkmaz S, Yazici AT, Demirok A (2014) Comparison of efficacy between low-fluence and half-dose verteporfin photodynamic therapy for chronic central serous chorioretinopathy. Clin Ophthalmol 5:8:685–690. doi: 10.2147/OPTH.S58617

9. Kim YK, Ryoo NK, Woo SJ, Park KH (2015) Comparison of visual and anatomical outcomes of half-fluence and half-dose photodynamic therapy in eyes with chronic central serous chorioretinopathy. Graefes Arch Clin Exp Ophthalmol 253(12):2063–2073. doi: 10.1007/s00417-014-2926-6

10. Shiode Y, Morizane Y, Kimura S, Hosokawa M, Kawata T, Doi S, Hosogi M, Fujiwara A, Shiraga F (2015) Comparison of halving the irradiation time or the verteporfin dose for chronic central serous chorioretinopathy. Retina 35(12):2498–2504. doi: 10.1097/IAE.0000000000000621

11. Liu HY, Yang CH, Yang CM, Ho TC, Lin CP, Hsieh YT (2016) Half-dose Versus Half-time Photodynamic Therapy for Central Serous Chorioretinopathy. Am J Ophthalmol 167:57–64. doi: 10.1016/j.ajo.2016.04.001

12. Cheng CK, Chang CK, Peng CH (2017) Comparison of Photodynamic Therapy using Half Dose of Verteporfin or Half-fluence of Laser Light for the Treatment of Chronic Central Serous Chorioretinopathy. Retina 37(2):325–333. doi: 10.1097/IAE.0000000000001138

13. Haga F, Maruko R, Sato C, Kataoka K, Ito Y, Terasaki H (2017) Long-term prognostic factors of chronic central serous chorioretinopathy after half-dose photodynamic therapy: A 3-year follow-up study. PLoS ONE 12(7):e0181479. doi: 10.1371/journal.pone.0181479.24;

14. Matušková V, Vysloužilová D, Uher M (2018) Half-Fluence Photodynamic Therapy for Chronic Central Serous Chorioretinopathy: Predisposing Factors for Visual Acuity Outcomes. Semin Ophthalmol 33(5):690–699. doi: 10.1080/08820538.2017
15. Chung CY, Chan YY, Li KKW (2018) Angiographic and Tomographic Prognostic Factors of Chronic Central Serous Chorioretinopathy Treated with Half-Dose Photodynamic Therapy. Ophthalmologica 240(1):37–44. doi: 10.1159/000484100

16. van Rijssen TJ, van Dijk EHC, Dijkman G, Boon CJF (2018) Clinical characteristics of chronic central serous chorioretinopathy patients with insufficient response to reduced-settings photodynamic therapy. Graefes Arch Clin Exp Ophthalmol 256(8):1395–1402. doi: 10.1007/s00417-018-4003-z. Epub 2018 May 7

17. Asano KS, Asaoka R, Asano S, Azuma K, Inoue T, Obata R (2020) Elongated Photoreceptor Outer Segment Length and Prognosis of Chronic Central Serous Chorioretinopathy. Retina 40(4):750–757. doi: 10.1097/IAE.0000000000002445

18. Salehi M, Wenick AS, Law HA, Evans JR, Gehlbach P (2015) Interventions for central serous chorioretinopathy: a network meta-analysis. Cochrane Database Syst Rev Dec 22(12):CD011841. doi: 10.1002/14651858.CD011841.pub2

19. van Dijk EHC, Fauser S, Breukink MB, Blanco-Garavito R, Groenewoud JMM, Keunen JEE, Peters PJH, Dijkman G, Souied EH, MacLaren RE et al (2018) Half-Dose Photodynamic Therapy versus High-Density Subthreshold Micropulse Laser Treatment in Patients with Chronic Central Serous Chorioretinopathy: The PLACE Trial. Ophthalmology Oct 125(10):1547–1555. doi: 10.1016/j.ophtha.2018.04.021

20. van Rijssen TJ, van Dijk EHC, Yzer S, Ohno-Matsui K, Keunen JEE, Schlingemann RO, Sivaprasad S, Querques G, Downes SM, Fauser S et al (2019) Central serous chorioretinopathy: Towards an evidence-based treatment guideline. Prog Retin Eye Res 73:100770. doi: 10.1016/j.preteyeres.2019.07.003

21. Lotery A, Sivaprasad S, O'Connell A, Harris RA, Culliford L, Ellis L, Cree A, Madhusudhan S, Behar-Cohen F, Chakravarthy U, on behalf of the VICI trial investigators et al (2020) Eplerenone for chronic central serous chorioretinopathy in patients with active, previously untreated disease for more than 4 months (VICI): a randomised, double-blind, placebo-controlled trial. Lancet 25(10220):294–303. doi: 10.1016/S0140-6736(19)32981-2

22. Liew G, Quin G, Gillies M, Fraser-Bell S (2013) Central Serous Chorioretinopathy: A Review of Epidemiology and Pathophysiology. Clin Exp Ophthalmol 41(2):201–214. doi: 10.1111/j.1442-9071.2012.02848.x

23. Mrejen S, Balaratnasingam C, Kaden TR et al (2019) Long-term Visual Outcomes and Causes of Vision Loss in Chronic Central Serous Chorioretinopathy. Ophthalmology 126(4):576–588. doi: 10.1016/j.ophtha.2018.12.048

24. Reibaldi M, Boscia F, Avitable T, Russo A, Cannemi V, Uva MG, Reibaldi A (2009) Low-fluence photodynamic therapy in longstanding chronic central serous chorioretinopathy with foveal and gravitational atrophy. Eur J Ophthalmol 19(1):154–158

25. Scholz P, Altay L, Fauser S (2017) A review of subthreshold micropulse laser for treatment of macular disorders. Adv Ther 34:1528–1555
### Table 1. Baseline Characteristics

|                                | Early Treatment N=21 | Delayed Treatment N=26 | P-value |
|--------------------------------|-----------------------|-------------------------|---------|
| Age, years (mean±SD)           | 52.6±8.8              | 54.2±12.7               | 0.357   |
| Female (n, %)                  | 1/21, 4.8%            | 10/26, 38.5%            | 0.007   |
| **Side**                       |                       |                         |         |
| RE                             | 10/21, 47.6%          | 11/26, 42.3%            | 0.716   |
| LE                             | 11/21, 52.4%          | 15/26, 57.7%            |         |
| Disease duration, months (mean±SD) | 4.3±1.3              | 25.4±21.0               | <0.001  |
| Hx of steroid use              | 1/21, 4.8%            | 4/26, 15.4%             | 0.240   |
| Avastin IVI                    | 3/21, 14.3%           | 6/26, 23.1%             | 0.446   |
| Oral Rx (Acetylsalicylic acid) | 0/21, 0%              | 1/26, 3.8%              | 0.364   |
| BCVA, LogMAR (mean±SD)         | 0.331±0.24            | 0.500±0.26              | 0.042   |
| CRT, μm (mean±SD)              | 370.4±98.7            | 311.2±68.1              | 0.052   |
| Max retinal thickness μm (mean±SD)* | 419.1±104.6          | 351.2±53.8              | 0.071   |
| SHRM                           | 14/21, 66.7%          | 21/26, 80.8%            | 0.270   |
| Irregular RPE                  | 9/21, 42.9%           | 18/26, 69.2%            | 0.069   |
| PED                            | 2/21, 9.5%            | 2/26, 7.7%              | 0.823   |
| **PDT protocol**               |                       |                         |         |
| Half dose                      | 6/21, 28.6%           | 4/26, 15.4%             |         |
| Half time                      | 0/21, 0%              | 1/26, 3.8%              |         |
| Half fluence                   | 14/21, 66.7%          | 17/26, 65.4             |         |
| Unspecified                    | 1/21, 4.8%            | 4/26, 15.4%             |         |
| No. of spots (mean±SD)         | 1.5±0.8               | 1.2±0.5                 | 0.238   |
| Maximal spot size μm (mean±SD) | 3022±1491             | 3284±1051               | 0.513   |
| **Follow-up duration, months (mean±SD)** | 16.7±16.4          | 27.3±26.5               | 0.195   |
Figure 1

Change in central (a) and maximal (b) retinal thickness post PDT treatment
Figure 2

Change in manual central thickness. (a) overall thickness (b) SRF
Figure 3

Changes in Best-Corrected Visual Acuity (BCVA) post PDT treatment
Figure 4

Prevalence of clinically significant change in BCVA at 3-months (a) and last-visit follow-up (b) post PDT treatment