

Verteporfin photodynamic therapy for subfoveal choroidal neovascularization in pathologic myopia: A 12-month retrospective review

C. COSTAGLIOLA¹, C. CAMPA², C. INCORVAIA², F. PARMEGGIANI², M. MENZIONE³, M. DELLA CORTE³, M. RINALDI³, M. ROMANO³, F. SEMERARO⁴

¹Dipartimento di Scienze per la Salute, Università degli Studi del Molise, Campobasso

²Dipartimento di Discipline medico-chirurgiche della comunicazione e del comportamento Sezione Clinica Oculistica, Università degli Studi di Ferrara, Ferrara

³Clinica Oculistica, Il Università degli Studi di Napoli, Napoli

⁴Clinica Oculistica, Università degli Studi di Brescia, Brescia - Italy

PURPOSE. To evaluate the visual outcome of patients with subfoveal choroidal neovascularization (CNV) secondary to pathologic myopia treated with verteporfin photodynamic therapy (PDT-V) and to verify the predictive role of visual and angiographic parameters.

METHODS. This is a retrospective, interventional, consecutive case series study of subjects with subfoveal CNV secondary to pathologic myopia. All patients received PDT-V according to VIP guidelines. A complete ophthalmologic evaluation was performed on all patients and included best-corrected visual acuity (BCVA), fundus examination, and fluorescein angiography (FA, IMAGENet System, Topcon Corp., Japan). CNV size (mm²) was directly measured on the early phase of the angiogram using the software included with the IMAGENet package. All checks were scheduled at 3-month intervals for a period of 1 year. A review of medical and angiographic records was performed and assessed throughout a 12-month follow-up period.

RESULTS. A total of 62 patients (62 eyes) were examined. Best-corrected visual acuity (BCVA) moderately decreased without reaching a statistically noticeable level throughout the follow-up; reduction in lesion size reached a significant level at the second checkup. A significant correlation between higher baseline BCVA and better final visual outcome was detected.

CONCLUSIONS. Standardized PDT-V minimizes central vision deterioration in patients with CNV secondary to pathologic myopia. Better BCVA at presentation represents a good predictive sign. (*Eur J Ophthalmol* 2008; 18: 955-9)

KEY WORDS. Choroidal neovascularization, Myopia, Photodynamic therapy

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INTRODUCTION

Pathologic myopia (PM) is a condition characterized by the progressive elongation of the eyeball (axial length of the globe more than 26 mm) and highly negative spherical equivalents (typically -6.0 D or more). Choroidal neovascularization (CNV) represents its most important complication, occurring in a percentage ranging from 5% to 10% of cases (1, 2), with a positive correlation between risk and

degree of myopia (3). The underlying cause of CNV in PM involves degeneration of Bruch membrane, followed by ingrowths of new vessels. Different modalities of treatment, including direct laser photocoagulation and submacular surgery, have been proposed in the management of subfoveal CNV secondary to PM, but the outcomes have not been encouraging (4, 5). However, large-scale, randomized, controlled, double-masked clinical trials have demonstrated that photodynamic therapy with verteporfin

(PDT-V) is able to stabilize and, sometime, even to improve the visual acuity of patients with myopic CNV (6, 7). Despite the recent diffusion of intravitreal anti-VEGF compounds in the treatment of neovascular eye diseases, only a few small studies evaluating the role of this approach to myopic CNV have been carried out (8-10). Herein, we report our 12-month experience with 62 patients with subfoveal PM-related CNV and treated with PDT-V.

METHODS

A retrospective investigation was carried out jointly at the Retina Services of the University of Ferrara, Naples, and Brescia on subjects treated with PDT-V for subfoveal CNV secondary to pathologic myopia from January 2004 to June 2006, who completed 12 months of follow-up.

Inclusion criteria for treatment followed the protocol of the Verteporfin in Photodynamic Therapy (VIP) Study (6). Briefly, PDT-V was administered to patients with 1) CNV under the geometric center of the foveal avascular zone secondary to PM; 2) an area of CNV comprising at least 50% of the area of the total neovascular lesion; 3) a maximum linear dimension no greater than 5400 μm ; 4) a best-corrected visual acuity letter score of at least 50 (Snellen equivalent, approximately 20/100 or better). Exclusion criteria were 1) any significant ocular disease and/or alteration other than PM compromising or potentially affecting retinal integrity; 2) intraocular surgery performed within the previous 2 months; 3) Nd:YAG laser capsulotomy within the previous month. Each patient gave written informed consent to the treatment after a detailed description of the procedure to be used.

A complete ophthalmologic evaluation was performed on all patients and included best-corrected visual acuity (BCVA, standard ETDRS charts at 4 meters) converted to the logarithm of the minimum angle of resolution (logMAR) scale for statistical analyses; fundus examination (no-contact 90-D lens); and fluorescein angiography (FA, IMAGEnet System, Topcon Corp., Japan). CNV size (mm^2) was directly measured on the early phase of the angiogram using the software included with the IMAGEnet package.

Each course of standardized PDT-V followed the VIP guidelines and was performed within 7 days from the diagnosis or the follow-up angiography. All checks were scheduled at 3-month intervals for a period of 1 year. A complete ophthalmologic evaluation, including FA, was

repeated at each check-up. Additional courses of treatment were performed if FA leakage from CNV occurred and, independently, when the ophthalmologists deemed it necessary. The angiographies were reviewed by two masked examiners (C.I. and M.M.), who retrospectively evaluated the angiograms both separately and concurrently: any lack of consensus between the two retinal specialists was considered an exclusion criterion.

The PDT-V efficacy variables were represented by the progression of CNV size beyond the area of the entire lesion, identified at baseline, and modification of the BCVA from baseline. One-way, repeated measures analysis of variance (ANOVA-RM) was used to assess the trend of these clinical parameters within follow-up times, taking into account the patient's age as a covariate. The correlations among the demographic/clinical variables (i.e. patient age, PDT-V number, baseline BCVA, and baseline CNV size) and therapeutic efficacy of the PDT-V protocol were evaluated, considering both the mean final BCVA (multiple linear regression model) and the mean difference between final and baseline BCVA (analysis of variance/covariance [ANCOVA]). For all the abovementioned tests a p value < 0.05 was considered statistically significant. Data analyses were carried out using SPSS V8 (SPSS Inc., Chicago, IL, USA) and STATGRAPH 4.0 (Statistical Graphics Corp., Princeton, NJ, USA). The statistical analyses investigator was masked in order to protect the integrity of results obtained.

RESULTS

A total of 62 eyes of 62 patients, selected upon examination of patient records, were included in this retrospective analysis. The average number of PDT-V treatments administered before the 12-month examination (including PDT-V application at baseline and subsequent treatments performed at the 3-, 6-, and 9-month evaluations) was 3 (± 0.77). The demographic characteristics, pre-PDT-V ophthalmologic data, and PDT-V-application attributes of the study population are summarized in Table I.

Mean BCVA decreased moderately over the follow-up period from 0.72 to 0.78 logMAR (Fig. 1). A reduction of mean CNV size occurred, reaching a statistically significant level by the 3rd month of follow-up (Fig. 2). A significant correlation between greater baseline BCVA level and better final central vision was observed in all patients (Tab. II). Moreover, ANCOVA analysis indicated that at a

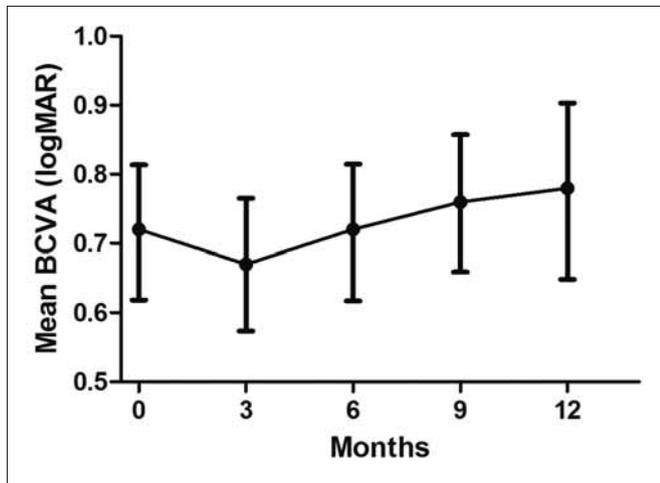


Fig. 1 - Mean best-corrected visual acuity (logMAR) and 95% CI at baseline and at each checkup after verteporfin photodynamic therapy protocol in patients with myopic choroidal neovascularization.

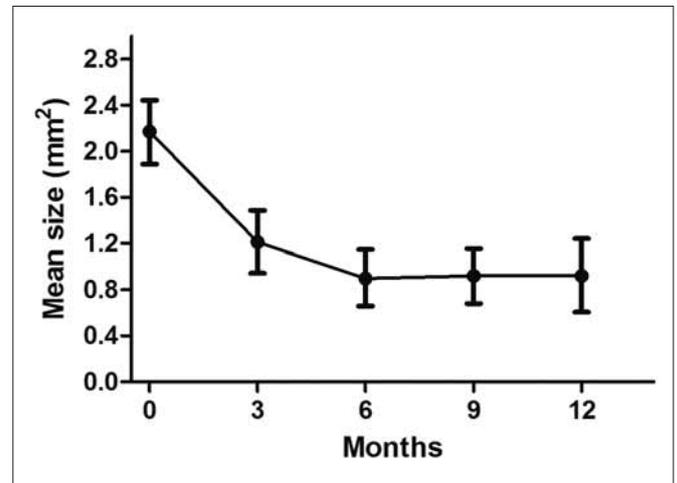


Fig. 2 - Mean choroidal neovascularization size (mm²) and 95% CI at baseline and at each checkup after verteporfin photodynamic therapy protocol in patients with myopic choroidal neovascularization.

higher baseline BCVA was associated a significantly better visual final outcome ($p < 0.001$). A smaller baseline CNV size did not favorably influence the final BCVA mean value. The patient's age was not statistically correlated with the 12-month BCVA level. Mean PDT-V number did not in-

duce any significant effect on the final BCVA in the population studied (Tab. II).

No adverse events judged clinically relevant by the investigators were detected over the entire follow-up period.

TABLE I - DEMOGRAPHIC CHARACTERISTICS, PRE-PDT-V OPHTHALMOLOGIC DATA, AND PDT-V APPLICATION ATTRIBUTES OF THE STUDY POPULATION

Data	N = 62
Females/males	48/14
Mean age ± SD (range), y	53.53±13.84 (28-82)
Mean BCVA ± SD (range), logMAR	0.72±0.38 (0.1-1.3)
Mean CNV area ± SD (range), mm ²	2.17±1.10 (0.40-4.50)
Mean PDT-V ± SD (range), n	3±0.77 (1-4)

PDT-V = Photodynamic therapy with verteporfin; SD = Standard deviation; BCVA = Best-corrected visual acuity; MAR = Minimum angle of resolution

DISCUSSION

The clinical outcomes after standardized PDT-V procedure, documented during a 12-month follow-up period of VIP protocol application in Caucasian subjects with myopia-related subfoveal CNV, were the following: 1) diminution of the deterioration in central vision and 2) significant reduction in neovascular lesion size. A higher baseline BCVA was associated with a better final central vision, whereas a smaller baseline CNV size did not positively influence the visual outcome.

In our series, the functional result at 12 months' follow-up was not as good as that reported in the VIP trial: 75.3% of

TABLE II - MULTI-REGRESSION RESULTS IN THE STUDY POPULATION, CONSIDERING THE DEMOGRAPHIC/CLINICAL DATA AS VARIABLES AND THE MEAN FINAL BCVA AS CONSTANT

Variables	m	R2	p
Myopic CNV (n = 62): mean final BCVA ± SD = 0.78 ± 0.50 logMAR			
Patient age	-0.00256	0.49	NS
Baseline BCVA	0.69830	28.61	<0.001
Baseline CNV size	0.05643	1.53	NS
Number of PDT-V	-0.05830	0.80	NS

BCVA= Best-corrected visual acuity; CNV = Choroidal neovascularization; SD = Standard deviation; MAR = Minimum angle of resolution; NS = Not significant; PDT-V = Photodynamic therapy with verteporfin

the patients lost fewer than 15 letters of visual acuity (in comparison to 86% of the verteporfin-treated patients in the VIP trial) (6).

Untreated neovascular lesions lead to severe visual loss (six or more lines of visual acuity) in approximately 34% of patients during the first year following diagnosis (6) and our findings confirm that PDT-V can efficiently reduce the risk of critical central low vision in subjects with myopic CNV. After 1 year, we recorded a mean decrease in BCVA of 0.06 logMAR: this datum is comparable to that obtained by other authors who performed the same standardized PDT-V protocol in patients with analogous forms of CNV. Pece and coworkers (11) detected a BCVA reduction of 0.08 logMAR, Axer-Siegel and coworkers (12) of 0.06 logMAR, and Montero and Ruiz-Moreno (13) of 0.04. On the other hand, Lam and coworkers (14), in a prospective, consecutive, interventional study involving 30 Chinese patients, described a mean BCVA improvement of 0.04 logMAR and Hayashi and coworkers (15), studying 42 Japanese subjects with myopic CNV, showed a mean improvement of 0.02 logMAR after 1 year of PDT therapy. Ethnic differences could explain, at least in part, this discrepancy (15).

In the course of our study the mean number of PDT-V applications per patient was rather inferior to that observed during VIP trials. At the 12th month our patients had received an average of 3 treatments, compared to 3.4 for VIP patients (6). There are no specific reasons able to justify this difference. As in other studies (11, 16) we also observed that CNV size at baseline did not represent a significant predictor of the effectiveness of verteporfin therapy in terms of visual improvement. Nevertheless, our data documented that a higher baseline BCVA at the time of first PDT-V was a favorable predictive factor, significantly related to a greater central vision level at the end of the follow-up period. These findings were not observed during VIP trial (6) but resemble those reported by Ergun and coworkers, who have found a similar positive prognostic correlation (17). They also reported that younger patients had a better treatment outcome, in accordance with other investigators (11-14): our retrospective findings did not confirm this datum as we were unable to find any correlation between patient age and visual outcome.

In conclusion, the results of our clinical consecutive case series should be carefully assessed alongside those of randomized, double-masked trials regarding PDT-V efficacy in myopic CNV (6, 7). The current study provides further evidence that verteporfin therapy for CNV in patho-

logic myopia counteracts the severe visual loss to which untreated patients are unavoidably predisposed. A greater baseline BCVA seems to be a favorable prognostic element in all forms of CNV, whereas neither a smaller initial CNV size nor the patient's age seems influence the final outcome. Further independent clinical trials are required to establish whether the positive therapeutic effects, retrospectively documented in this investigation, are confirmed over a more prolonged follow-up period.

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Reprint requests to:
Ciro Costagliola, MD
Dipartimento di Scienze per la Salute
Università degli Studi del Molise
Via F. De Sanctis
86100 Campobasso, Italy
ciro.costagliola @unimol.it

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