Received: 18 December 2024 | Accepted: 23 April 2025

DOI: 10.1111/aos.17513

Acta Ophthalmologica

ORIGINAL ARTICLE

A fast protocol for photodynamic therapy in exudative choroidal circumscribed hemangioma: Early laser irradiance after end of verteporfin infusion

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Abstract

Purpose: The aim of the study is to compare the risk of first-line photodynamic therapy (PDT) failure according to the PDT protocol performed in patients with exudative choroidal circumscribed hemangioma (CCH).

Methods: We retrospectively included patients from 11 European centres in France, Italy and Denmark. Two groups were established: patients treated with Standard Protocol PDT (SP-PDT) and patients treated with a 'Fast' Protocol PDT (FP-PDT), characterised by laser irradiation without delay after the end of the verteporfin infusion (8 min after start of infusion). We analysed groups on the risk of exudative CCH recurrence requiring a second line of treatment, defining the first-line PDT failure.

Results: A total of 111 patients were included in the study: 76 treated with the SP-PDT and 35 with the FP-PDT. First-line PDT failure was observed for 45 patients (59%) in the SP-PDT group and 9 patients (26%) in the FP-PDT group, with a median follow-up of 3.5 [1.7–6.7] years and 2.3 [0.8–3.9] years, respectively. Final best-corrected visual acuity (BCVA) improvement did not differ between groups ($p=0.49$). A multivariate survival analysis including initial CCH thickness and initial BCVA was performed over a two-year follow-up period: FP-PDT as first-line treatment was significantly associated with a lower risk of PDT failure [HR = 0.27, 95%CI (0.11–0.65)].

Conclusion: FP-PDT shows encouraging results in the treatment of CCHs, as it is associated with a lower risk of PDT failure. It may therefore represent an interesting avenue for optimised PDT parameters, although these results need to be confirmed by randomised trials.

KEYWORDS
choroidal diseases, choroidal tumour, circumscribed choroidal hemangioma, laser protocol, onco-ophthalmology, photodynamic therapy, retina, verteporfin

1 | INTRODUCTION

Choroidal circumscribed hemangioma (CCH) is a hamartoma of the choroid characterised by an abnormal distribution of vessels within the choroid, with a pseudo-tumour appearance. CCH is a benign tumour and is not associated with any pathological growth and/or invasion of adjacent tissues as this can be the case in malignant choroidal tumours (metastasis, lymphoma, melanoma). CCH may remain asymptomatic but is often

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diagnosed when complications occur, such as subretinal or intra-retinal fluid related to retinal pigment epithelium (RPE) dysfunction. In the medium term, it impairs photoreceptor function and can lead to permanent loss of vision (Witschel & Font, 1976).

Currently, two therapeutic options are used to treat the disease, verteporfin photodynamic therapy (PDT) and proton beam therapy (PBT). PDT has proven its effectiveness in long-term resorbing exudation and improving best-corrected visual acuity (BCVA) (Blasi et al., 2010; Boixadera et al., 2009; Dalvin et al., 2019; Elizalde et al., 2012; Jurklies et al., 2003; Papastefanou et al., 2018; Singh et al., 2004). Nevertheless, there is a non-negligible risk of exudative recurrence. Indeed, nearly half the patients treated with PDT required multiple sessions, and repeated PDT increases the risk of RPE damage and poor visual recovery (Jurklies et al., 2003; Mathis et al., 2021). PBT has shown its effectiveness in complete exudative resolution and improvement in BCVA with almost no exudative recurrence (Frau et al., 2004; Levy-Gabriel et al., 2009; Mahdjoubi et al., 2019; Zografos et al., 1998), but it remains an expensive treatment with limited access.

The standard verteporfin PDT protocol (SP-PDT) used consists of: verteporfin infusion (6 mg/m^2) over 10 min, then irradiation of the lesion 5 min after the end of infusion, with a fluence of 50 J/cm^2 (spot size adapted to the lesion, up to a maximum diameter of 7.5 mm) delivered over a period of 83 s. This protocol was designed and optimised for the treatment of neovascularisation in age-related macular degeneration (AMD) (TAP Study, 1999). However, CCH vascular dynamics differ radically from AMD choroidal neovascularisation. Taking into consideration the fast vascular filling of CCH during indocyanine green angiography (ICGA), we hypothesized that a 'Fast' Protocol (FP-PDT) with no delay between the end of verteporfin infusion and irradiation could reduce the risk of CCH exudative recurrence after one PDT session. The aim of our study is to compare patients treated with FP-PDT with those being treated with SP-PDT and to identify eventual predictive factors for exudative recurrence.

2 | METHODS

This is a retrospective study carried out in 11 European centres in France, Italy and Denmark from 2002 to 2022. Data collection was performed retrospectively using medical records by the contact onco-ophthalmologist of each centre. The Ethics Committee of the French Society of Ophthalmology approved the study (IRB00008855; Société Française d'Ophtalmologie IRB#1).

Inclusion criteria were a diagnosis of CCH treated with PDT. CCH diagnosis was made using multimodal imaging (retinography, optical coherence tomography (OCT), A-scan and B-scan ultrasonography and ICGA). CCH exudation was defined as the presence of intra-retinal fluid (IRF) or subretinal fluid (SRF) identified by spectral domain optical coherence tomography (SD-OCT). Patients who had any treatment before PDT, no CCH exudation, no information on PDT parameters or no follow-up after PDT were excluded from the analyses.

Patients features collected were gender, age, side of affected eye, date of diagnosis, initial BCVA (logMAR, equivalent Snellen), date of first-line PDT, date of second-line treatment if any, last date of follow-up and final BCVA (logMAR, equivalent Snellen). CCH thickness and diameter were measured using ultrasonography. CCH localisation was defined as macular (if the tumour was located in a 3-mm circle around the fovea), out of the macula (if out the 3-mm circle) or juxtapupillary (if the tumour was located at less than 1 mm from the optic nerve).

PDT parameters had to be specified, such as the verteporfin dose (6 mg/m^2), time of infusion (8 or 10 min), waiting time before irradiation (no delay or at least 5 min), fluence (50 J/cm^2 with 600 mW/cm^3 light dose for 83 s).

From these data, two groups were established:

- 'Fast Protocol' group (FP-PDT) was defined as a verteporfin (dose = 6 mg/m^2) infusion during an 8-minute period, followed by immediate laser irradiation, of which the fluence was 50 J/cm^2 over 83 s.
- 'Standard Protocol' group (SP-PDT) was defined as a verteporfin (dose = 6 mg/m^2) infusion during a 10-minute period, then-after at least 5 minutes-irradiation was performed, of which the fluence was 50 J/cm^2 over 83 s.

Main outcome measure analysed was the rate of first-line PDT failure. PDT failure was defined as macular exudative recurrence (IRF or SRF) requiring a second-line treatment. Time to PDT failure was measured between the date of first-line treatment and the date of second-line treatment.

For the main objective, a statistical descriptive analysis was performed comparing patients features and PDT failure according to their PDT groups (FP-PDT or SP-PDT) and including a Kaplan–Meier curve. Then, to assess the association between PDT group and risk of failure, a survival analysis was performed using Cox models. Hazard ratio (HR) and 95% confidence interval (95% CI) were calculated. Initial CCH thickness, initial BCVA and IRF before treatment were considered as potential risk factors for first-line PDT failure and were included in adjusted models. Proportional hazard assumption was tested. As most PDT failures were noticed within the first 2 years of follow-up, both Kaplan–Meier curves and Cox models were censored two years after first-line PDT. Patients followed for less than 2 years were censored at their end of follow-up. A secondary descriptive analysis was performed comparing first-line PDT failure according to initial BCVA (≤0.3 logMAR equivalent to ≥20/40 Snellen or >0.3 logMAR equivalent to <20/40 Snellen). A sensitive analysis was also made over a five-year period.

3 | RESULTS

A total of 131 patients in 11 centres were reviewed and 111 patients with a diagnosis of CCH treated with PDT were included. Twenty patients were excluded from the analysis: 14 patients had no exudative criteria, 2 patients had

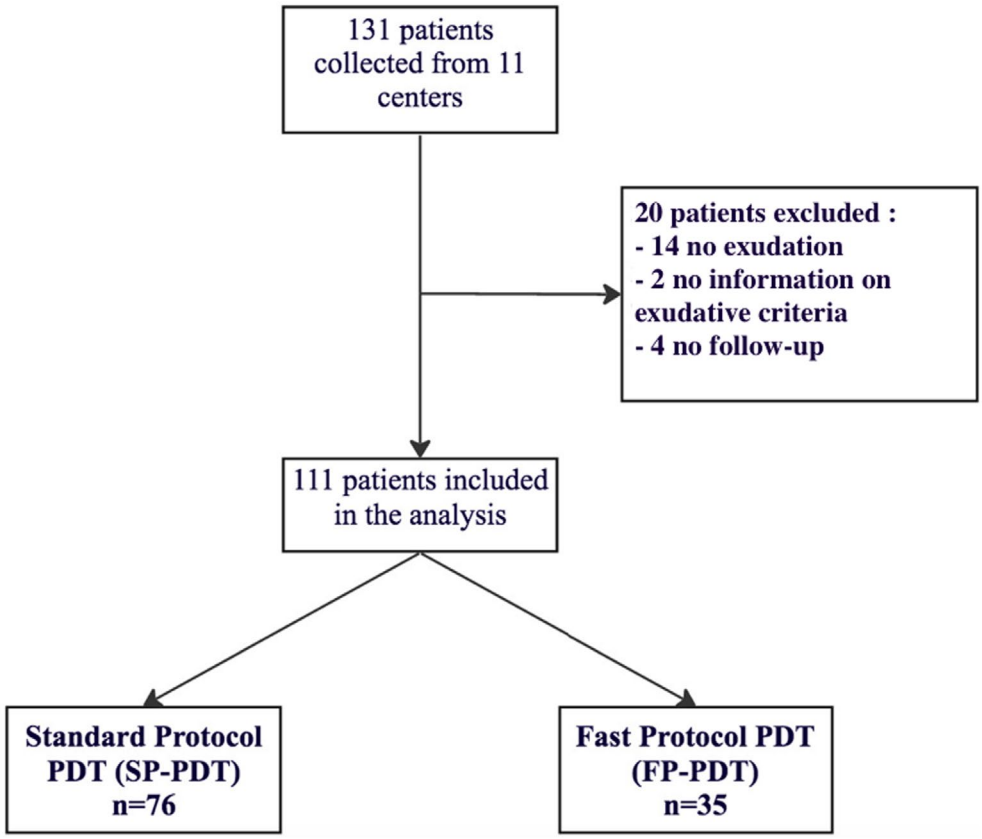

FIGURE 1 Flow chart.

no information on exudative criteria, and 4 patients had no follow-up after PDT (Figure 1). Included patients did not differ significantly from excluded patients on age, sex, initial BCVA, initial CCH thickness, PDT protocol used and rate of first-line PDT failure (see Tables S1 and S2).

Mean (SD) age of patients included was 54.6 (13.3) years, and patients were predominantly men (64.0%). A total of 108 (97.3%) patients had SRF, 37 (33.9%) patients had IRF before treatment and 34 (30.6%) patients had both. The median [IQR] initial BCVA was 0.3 logMAR [0.2–0.5] (20/40 equivalent Snellen) and the median [IQR] initial CCH thickness was 2.8 mm [2.1–3.0]. CCH localisation was macular for 64 patients (58.7%), juxtapapillary for 29 patients (26.6%) and out of macula for 16 patients (14.7%). Median [IQR] follow-up was 2.8 [1.2–5.6] years. During the follow-up, 54 patients (48.7%) had macular exudative recurrence (IRF or SRF) requiring a second-line treatment, defined as first-line PDT failure. Median [IQR] time to PDT failure was 0.7 [0.4–1.7] year (Table 1).

3.1 | First-line PDT failure according to PDT protocol

As first-line treatment, 76 patients underwent SP-PDT and 35 patients underwent FP-PDT. The SP-PDT group and the FP-PDT group did not differ significantly on patient initial features. First-line PDT failure was significantly lower in the FP-PDT group ($p=0.001$), with a median [IQR] time to failure of 1.7 [1.0–4.5] years, compared with 0.6 [0.3–1.5] year in the SP-PDT ($p=0.06$). Median [IQR] follow-up was significantly longer in SP-PDT in comparison to FP-PDT (3.5 [1.7–6.7] vs. 2.3 [0.8–3.9], $p<0.001$). Final VA improvement was not different between groups ($p=0.49$) (Table 2).

3.2 | First-line PDT failure comparing SP-PDT and FP-PDT through a 2-year survival analysis

Kaplan–Meier survival curves showed a trend towards more frequent first-line PDT failure in the SP-PDT group (Figure 2). The survival analysis comparing the two PDT protocols found that FP-PDT as a first-line protocol was statistically associated with a lower risk of PDT failure [HR = 0.30 (CI95% 0.13–0.70)]. Adjusted model 1 was performed considering initial BCVA and initial CCH thickness as potential confounders. Greater initial CCH thickness was significantly associated with a higher risk of PDT failure [HR 1.98 (1.04–3.76)]. However, a poor initial BCVA was a protective factor against PDT failure [HR 0.39 (CI95% 0.16–0.95)]. Adjusted model 2 added IRF before CCH treatment as another potential confounder. Both adjusted models confirm the statistical association between FP-PDT and a lower rate of PDT failure through the two-year period: adjusted model 1 [HR 0.27 (CI95% 0.11–0.65)] and adjusted model 2 [HR 0.28 (CI95% 0.12–0.68)] (Table 3).

3.3 | Description of patient characteristics according to initial visual acuity

Initial BCVA >0.3 logMAR (<20/40 equivalent Snellen) was statistically associated with a higher initial CCH thickness ($p=0.02$). First-line PDT failure was not

TABLE 1 Description of patients included.

	md	*N* = 111
Gender	0	
Male/Female		71/40
Age, years	0	
Mean (SD)		54.6 (13.3)
Median (IQR)		54.9 (46.2–63.5)
Min-Max		27.7–92.1
Eye side	0	
Left eye/Right eye		59/52
Tumour location	2	
Macular		64 (58.7%)
Out of macula		16 (14.7%)
Juxtapapillary		29 (26.6%)
Exudation before treatment		
Intraretinal fluid	2	37 (33.9%)
Subretinal fluid	0	108 (97.3%)
Initial BCVA, logMAR, Snellen	2	
Mean (SD)		0.4 (0.4), 20/50
Median (IQR)		0.3 (0.2–0.5), 20/40
Min-Max		0–1.7, 20/20–20/1000
Initial CCH thickness, mm	5	
Mean (SD)		2.7 (0.8)
Median (IQR)		2.8 (2.1–3.0)
<3 mm/≥3 mm		60/46
Follow-up time, years	0	
Mean (SD)		3.7 (3.1)
Median (IQR)		2.8 (1.2–5.6)
First-line PDT failure	0	54/111 patients = 48.7%
Time to PDT failure, years	1	
Mean (SD)		1.4 (1.5)
Median (IQR)		0.7 (0.4–1.7)

Note: Number (percentage); Mean [standard deviation (SD)]; Median [interquartile (IQR)].
Abbreviation: md, Missing Data.

different between groups ($p = 0.80$). However, we observed a trend to earlier PDT failure in the initial BCVA ≤0.3 logMAR group (≥20/40 eq. Snellen) than in the BCVA >0.3 logMAR group (<20/40 eq. Snellen) without statistical difference ($p = 0.30$) (Table 4). This earlier relapse occurrence in the BCVA group is well shown on the 2-year survival curves (Figure 3).

4 | DISCUSSION

Several studies have shown that PDT is effective in treating CCH, but the rate of exudative recurrence after a single session is not negligible (Di Nicola et al., 2020; Mathis et al., 2021). Our results show that patients treated with an early laser irradiance PDT (8 min after the start of infusion) have significantly fewer exudative relapses than patients treated with standard PDT over a median follow-up of more than 2 years. These results suggest that modifying the PDT protocol could improve the treatment of CCH, assuming that verteporfin reaches pathological choroidal vessels more rapidly than other conditions such as AMD neovascularisation (Figures 4 and 5).

Up to now, no consensus has been reached on the parametric management of PDT for CCH treatment. Sobol et al. (2020) observed that fellow eyes of patients with CCH demonstrate thicker subfoveal central thickness when compared with age- and gender-matched control eyes, associated with an irregular choroidal architecture without segmented vascular layers. These findings strengthen the hypothesis that the standard PDT protocol, designed for AMD neovascularization with a thin choroid, could be not suitable for choroidal vascular architecture in CCH patients. Secondly, CCH hyperfluorescence in ICGA occurs between 30 s and 3 min after injection with a centripetal filling of the tumour (Arevalo et al., 2000; Shields et al., 1995). These insights suggest that verteporfin impregnates the therapeutic target much earlier than the new vessels in AMD. Therefore, removing the post-infusion waiting time represents an attractive option.

Many authors have proposed alternative PDT protocols to optimise its efficacy on CCH: 'Bolus' PDT, designed by Schmidt- Erfurth et al. (2002), consists of a 1 or 2-minute verteporfin infusion, followed by irradiation 5 min later. At first, results were promising, but Guagnini et al. (2006) and then Pilotto et al. (2011) reported cases of subretinal fibrosis and reactive RPE hyperplasia after bolus PDT. More recently, Stehouwer et al. (2020) outlined an unexpected significant relapse rate over a mean follow-up of 6 years (6 out of 17 patients). Another 'double-fluence' PDT protocol was proposed, consisting of a standard infusion and waiting time but using a double time of irradiation over 166 s (Fluence 100 J/cm^2), instead of 83 s (Blasi et al., 2010; Papastefanou et al., 2018; Pellegrini et al., 2022; Porrini et al., 2003; Su et al., 2014). In particular, Blasi et al. (2010) decided to double the duration of irradiation after observing a partial response to the standard protocol in 3 patients, and 22 patients treated with double-fluence showed no exudative recurrence. However, this prospective study used symptom onset within 3 months as inclusion criteria. These results are therefore not applicable to all routine patients, especially those with poor PDT outcomes. Recently, a retrospective study from Pellegrini et al. (2022) reported interesting results on 23 patients treated with double-fluence PDT. The mean BCVA increased from 20/45 to 20/28 in 12 months. Only two patients had persistence of tumour-associated IRF up to 12 months. No cases of side effects or need for retreatment were reported during the follow-up (average time of 25 months). Moreover, Papastefanou et al. (2018) compared the standard protocol with the double-fluence protocol on post-treatment BCVA. Median decimal BCVA was reduced by 0.05 in the standard protocol group (5 patients) and improved by 0.33 in the double-fluence PDT group (11 patients), though this difference failed to reach statistical significance.

To the best of our knowledge, no study has statistically demonstrated the superiority of one PDT protocol over another for the treatment of CCH. Considering the rarity of this condition, establishing a multicentre

TABLE 2 Description of patient characteristics according to PDT protocol.

	md	SP-PDT $N=76$		md	FP-PDT $N=35$		*p*-value
Sex	0			0			0.56
Male		50	(65.8)		21	(60.0)	
Female		26	(34.2)		14	(40.0)	
Age, years	0			0			0.40
Mean (SD)		53.8	(13.7)		56.1	(12.4)	
Median (IQR)		53.3 (45.5–62.1)			46.5 (48.6–65.3)		
Min; Max		27.7; 92.1			30.6; 85.1		
Eye side	0			0			0.87
Left eye		40	(52.6)		19	(54.3)	
Right eye		36	(47.4)		16	(45.7)	
IRF before treatment	2	29	(39.2)	0	8	(22.9)	0.09
SRF before treatment	0	73	(96.1)	0	35	(100.0)	0.55
Initial BCVA, logMAR – Snellen	1			1			0.09
Mean (SD)		0.5 (0.4) 20/63			0.3 (0.4) 20/40		
Median (IQR)		0.3 (0.2–0.7) 20/40			0.3 (0.1–0.5) 20/40		
Min-Max		0–1.7 20/20–20/1000			0–1.7 20/20–20/1000		
Initial CCH thickness, mm	5			0			0.61
Mean (SD)		2.7	(0.8)		2.7	(0.6)	
Median (IQR)		2.8 (2.0; 3.0)			2.8 (2.2; 3.1)		
Min; Max		0.8; 6.0			1.5; 3.8		
Initial CCH thickness	5			0			0.62
<3 mm		39	(54.9)		21	(60.0)	
≥3 mm		32	(45.1)		14	(40.0)	
Final VA improvement, LogMAR	1			2			0.49
Mean (SD)		−0.1	(0.5)		−0.05	(0.3)	
Median (IQR)		−0.2 (−0.3; 0.0)			−0.1 (−0.2; 0.0)		
Min; Max		−1.0; 1.6			−0.6; 1.2		
First-line PDT failure	0	45	(59.2)	0	9	(25.7)	0.001
Time to PDT failure, years	1			0			0.06
Mean (SD)		1.1	(1.2)		2.6	(2.0)	
Median (IQR)		0.6 (0.3–1.5)			1.7 (1.0–4.5)		
Min; Max		0.1; 5.2			0.7; 5.9		
Follow-up time, years	0			0			<0.001
Mean (SD)		4.4	(3.4)		2.3	(1.9)	
Median (IQR)		3.5 (1.7–6.7)			2.3 (0.8–3.9)		
Min; Max		0.1; 13.5			0.05; 6.3		

Note: Number (percentage); Mean [standard deviation (SD)]; Median [interquartile (IQR)].
Abbreviation: md, Missing Data.

registry would represent the most effective way to reach conclusions. That is why we gathered patient data from 11 specialised European centres from France, Italy and Denmark. Herein, the occurrence of an exudative recurrence requiring a second-line treatment was defined as the variable of interest in order to compare the effectiveness of different protocols. This variable is an intermediate criterion, as it does not consider visual prognosis, but it remains an objective and practical criterion in the therapeutic approach to CCH. In addition, the large size of the present cohort allowed us to take into consideration potential confounders for PDT failure, as we previously found that an initial CCH thickness of at least 3 mm was a significative predictive factor for first-line PDT failure (Mathis et al., 2021). This result could be explained by the fact that PDT is unable to penetrate deeply into tumour tissue. We further suspected poor initial BCVA and baseline IRF to be predictive factors for first-line PDT failure as well. Di Nicola et al. (2020) indeed reviewed 79 cases of CCH treated with PDT comparing different baseline variables on the final visual prognosis and showed that good final visual acuity was associated with initial visual acuity of 20/40 or better, and the lack of IRF or retinoschisis. Likewise, Gündüz et al. (2021) compared clinical records of 60 CCH on visual prognosis and observed that lower initial visual acuity, presence

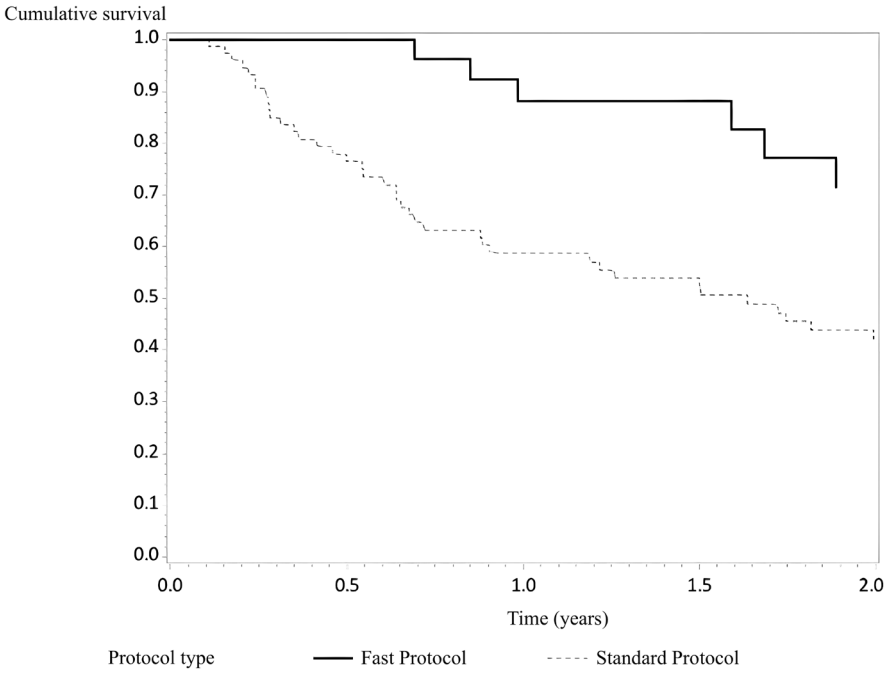

FIGURE 2 Kaplan–Meier survival curves comparing PDT protocols on first-line PDT failure with end of follow-up at 2 years.

TABLE 3 Association between first-line PDT failure and PDT protocol, survival models end of 2-year follow-up.

	Hazard ratio	CI 95%
Raw model (*N* = 110, PDT failure = 45)		
PDT protocol		
SP-PDT	1.	–
FP-PDT	0.30	(0.13–0.70)
Adjusted model 1 (*N* = 103, PDT failure = 41)		
PDT protocol		
SP-PDT	1	–
FP-PDT	0.27	(0.11–0.65)
Initial BCVA (logMAR)	0.39	(0.16–0.95)
Initial CCH thickness		
<3 mm	1	
≥3 mm	1.98	(1.04–3.76)
Adjusted model 2 (*N* = 101, PDT failure = 39)		
PDT protocol		
SP-PDT	1	–
FP-PDT	0.28	(0.12–0.68)
Initial BCVA (logMAR)	0.36	(0.14–0.91)
Initial CCH thickness		
<3 mm	1	
≥3 mm	2.09	(1.08–4.04)
IRF before CCH treatment		
No	1	–
Yes	1.23	(0.63–2.38)

of retinoschisis, and longer symptom duration were risk factors for worse visual outcomes. All these results are furthermore consistent with those of Shields et al. (2001) on prognostic factors before the PDT era: patients treated within 6 months of symptoms had better final visual acuity than those treated after 6 months of symptoms. These findings suggest that chronic exudation could result in cystoid macular edema associated with poor visual acuity and may lead to durable alteration of the RPE pump. That is why we included initial BCVA and baseline IRF in multivariate analysis as potential confounders for PDT failure. Interestingly, we observed that good initial BCVA was a predictive factor for first-line PDT failure and that failure tends to occur earlier in the group with good initial BCVA. This result may be due to closer monitoring of this group of patients, who are themselves more sensitive to any alteration in their vision. One alternative hypothesis could be that the factor triggering exudation is recent and still operating in the pathological process. In our cohort, baseline IRF was not found to be a confounder for first-line PDT failure, possibly due to the lack of distinction between acute cystoid macular edema and chronic retinoschisis.

Finally, our adjusted model for first-line PDT failure, including baseline CCH thickness and initial BCVA, strengthened our results about the effectiveness of the Fast protocol. The FP-PDT treatment further remained significantly associated with a lower risk of failure than SP-PDT over a two-year follow-up period. Likewise, similar results were observed when we added baseline IRF to the adjusted model, and furthermore, sensitivity analysis over a five-year period supported our conclusions (see Tables S1 and S2).

Our study still has several limitations. Firstly, data collection was carried out retrospectively. Most centres maintain a local register of all patients with a diagnosis of CCH. But some patients may not have been included in the registers, especially as this is not a single multicentre register. The retrospective nature of the data collection prevented us from gathering information from

TABLE 4 Description of patient characteristics according to initial visual acuity.

	Initial BCVA ≤0.3 logMAR ≥20/40 Snellen *N* = 61		Initial BCVA >0.3 logMAR <20/40 Snellen *N* = 48		*p*-value
Sex					0.38
Male	37	(60.7)	33	(68.8)	
Female	24	(39.3)	15	(31.3)	
Age, years					
Mean (SD)	52.1	(11.0)	57.3	(15.6)	
Median (IQR)	51.6 (45.6; 58.4)		56.1 (47.4; 67.2)		
Min-Max	30.1; 82.1		27.7; 92.1		
IRF before treatment	17	(28.3)	19	(40.4)	0.19
Initial CCH thickness, mm					0.02
Mean (SD)	2.5	(0.7)	2.9	(0.8)	
Median (IQR)	2.5	(2.0–3.0)	3.0	(2.5–3.2)	
PDT Protocol					0.41
SP-PDT	40	(65.6)	35	(72.9)	
FP-PDT	21	(34.4)	13	(27.1)	
First-line PDT failure	29	(47.5)	24	(50.0)	0.80
Time to PDT failure, years					0.30
Mean (SD)	1.2	(1.5)	1.6	(1.4)	
Median (IQR)	0.7 (0.4; 1.2)		1.4 (0.5; 1.9)		
Min-Max	0.1; 5.9		0.2; 5.0		
Follow-up time, years					
Mean (SD)	3.2	(2.6)	4.4	(3.6)	0.06
Median (IQR)	2.5 (1,1; 4.5)		3.2 (1.4; 6.3)		
Min-Max	0.1; 12.0		0.05; 13.5		

Note: Number (percentage); Mean [standard deviation (SD)]; Median [interquartile (IQR)].

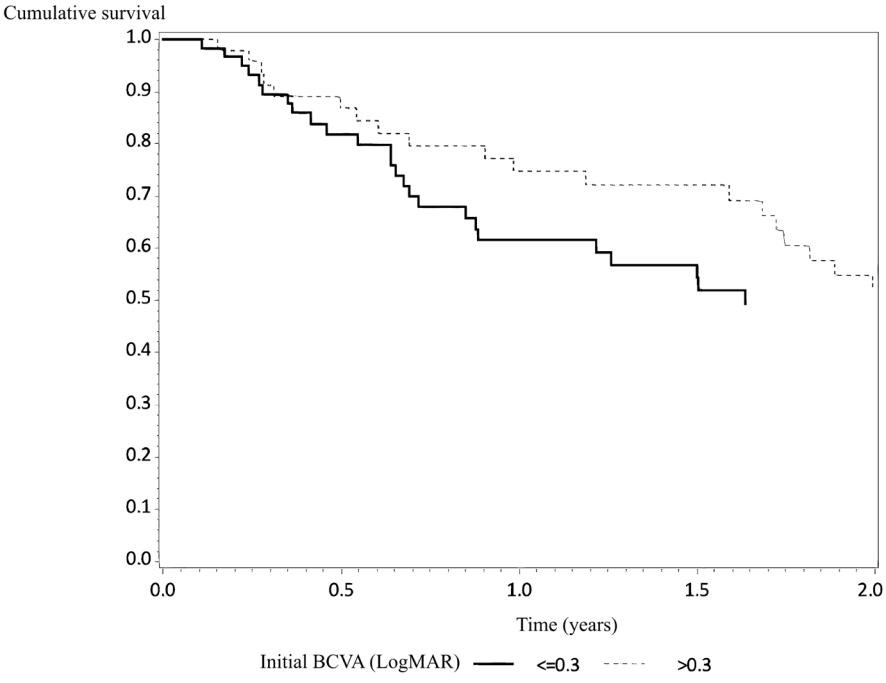

FIGURE 3 First-line PDT failure survival curves according to initial BCVA with end of follow-up at 2 years.

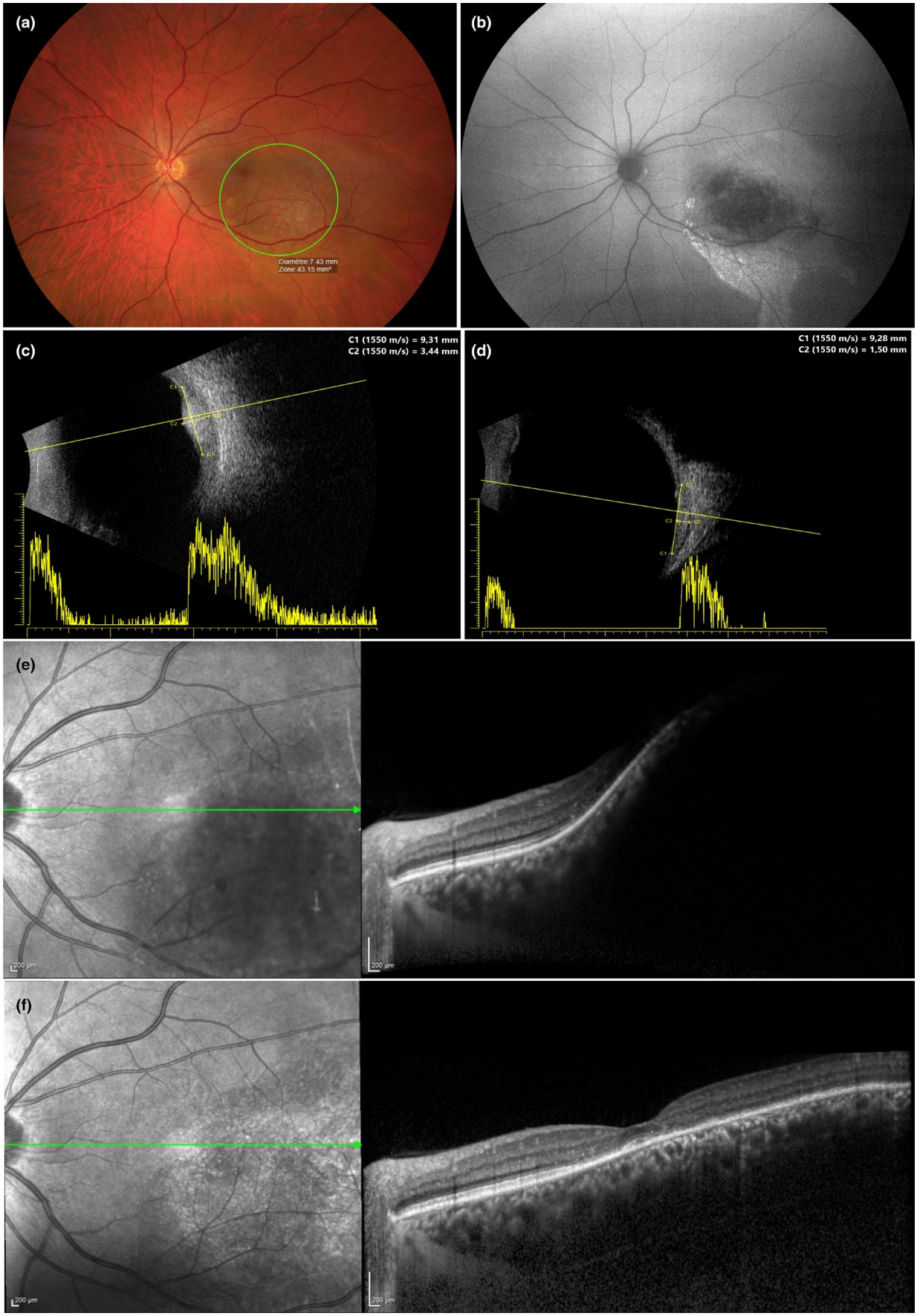

FIGURE 4 Circumscribed choroidal hemangioma treated by a single session of Fast Protocol PDT. (a) Baseline colour fundus photography showing a 7.4 mm PDT spot performed over an orange-red macular lesion. (b) Baseline autofluorescence photography showing hypo-autofluorescence of the lesion and a lower hyper-autofluorescence corresponding to a recent exudation. (c) Baseline B-scan echography showing an iso-hyperreflective lesion. (d) B-scan echography 6 months after FP-PDT showing the reduction of tumour thickness. (e) Baseline infrared imaging and optical coherence tomography showing a large choroidal lesion with macular tilt. (f) Infrared imaging and optical coherence tomography 6 months after FP-PDT showing the reduction of tumour thickness with no subretinal fluid observed.

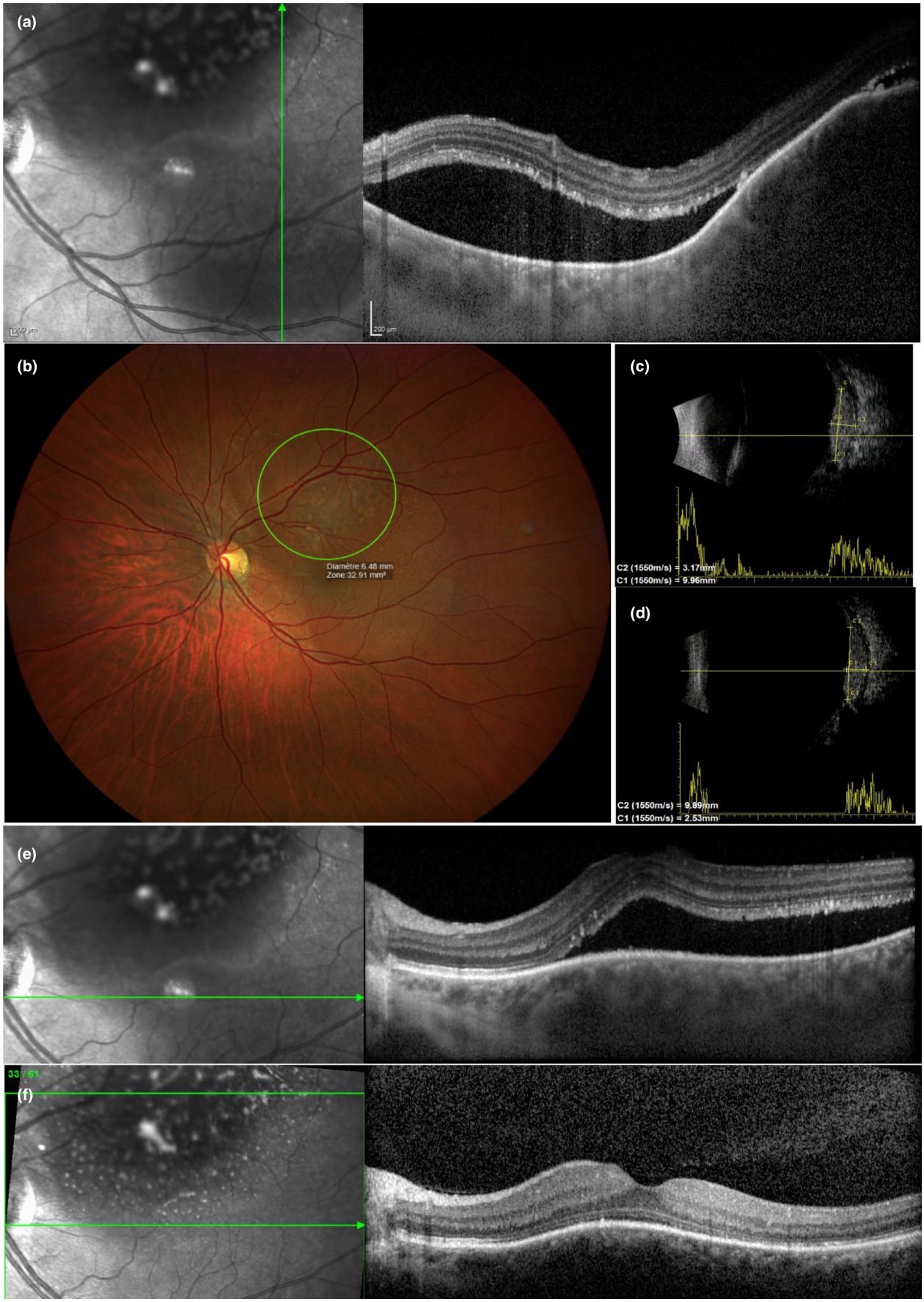

FIGURE 5 Another circumscribed choroidal hemangioma treated by a single session of Fast Protocol PDT. Baseline BCVA was 20/63 (Snellen) and 24 months post treatment BCVA was 20/25 (Snellen). (a) Baseline infrared imaging and optical coherence tomography showing a choroidal tumour with a large exudation. (b) Baseline colour fundus photography showing a 6.5 mm single-spot FP-PDT performed over the choroidal tumour. (c) Baseline B-scan echography measuring the CCH thickness at 3.2 mm. (d) B-scan echography 12 months after FP-PDT showing the reduction of CCH thickness to 2.5 mm. (e) Baseline infrared imaging and optical coherence tomography showing the central subretinal exudation. (f) Infrared imaging and optical coherence tomography 6 months after FP-PDT showing the resorption of the macular exudation.

part of patients, such as the onset of symptoms prior to treatment. Similarly, PDT parameters were not collected prospectively, and therefore the waiting time after injection for the standard protocol group may have varied, although national guidelines recommend a waiting period of 5–10 min. Secondly, the spot size was not documented in some patient files, which prevented any analysis of its potential effect on CCH. Furthermore, patients treated with FP-PDT were from specific centres (Bordeaux, Lyon and Nice, France) from 2012 to 2023, whereas patients treated with SP-PDT were from all centres from 2002 to 2023. Therefore, there may have been differences in practices, particularly in the frequency and duration of the follow-up. This may be a selection bias for group comparability. The use of a survival analysis enabled us to limit this bias as much as possible, considering different follow-up lengths and risk factors.

In conclusion, the 'Fast' PDT protocol with immediate irradiation after verteporfin infusion is an interesting possibility for treating exudative CCH as it could prevent exudative recurrence. Given that multiple PDT sessions are associated with a poor long-term visual outcome, the FP protocol could represent an encouraging pathway for more optimised PDT parameters for CCH than the standard 'AMD-fitted' protocol. However, further prospective multicentre studies are required to confirm our results and further compare the long-term visual outcome of FP-PDT with other alternative protocols, such as the double-fluence protocol.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Dubar, P., Mathis, T., Hucteau, E., Thariat, J., Nhari, M., Maschi, C. et al. (2025) A fast protocol for photodynamic therapy in exudative choroidal circumscribed hemangioma: Early laser irradiance after end of verteporfin infusion. *Acta Ophthalmologica*, 00, 1–11. Available from: https://doi.org/10.1111/aos.17513