Photodynamic Therapy for AMD and Non-AMD Patients: Two-Year Results in Thais

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Objective: *To determine the long-term effect of photodynamic therapy (PDT) with verteporfin for age-related macular degeneration (AMD) and non-AMD in Thailand and to compare with the Treatment of Age-Related Macular Degeneration with Photodynamic Therapy (TAP) and Verteporfin in Photodynamic Therapy (VIP) study.*

Material and Method: *The data of patients who received PDT between July 2003 and December 2004 and had completed two-year follow-up were prospectively reviewed. Treated eyes were classified into two main groups, the AMD (group 1) and non-AMD (group 2) groups. The AMD group was further divided into three subgroups, group1A, AMD with subfoveal choroidal neovascularization (CNV) and TAP/VIP compatible if they followed the recommendation guidelines characteristics, group 1B, AMD with subfoveal CNV and TAP/VIP incompatible, and group 1C, AMD with non-subfoveal CNV. The main outcomes were visual acuity change, number of treatments and the comparison with the first year results.*

Results: *Of 56 eyes, 46 eyes (82.14%) had completed 24-month follow-up. Thirty-four eyes had CNV-related AMD and 12 eyes were non-AMD. At the 24-month follow-up, mean visual acuity change in group 1A, 1B, 1C were increased 0.25 (p = 0.13), 0.05 (p = 0.52), and 0.28 (p = 0.003), respectively. The total number of treatments in the first and second year was 1.8 and 0.1 in group 1A, 2.3 and 0.1 in group 1B, 1.5 and 0.25 in group 1C.*

Conclusion: *PDT was effective in Thai patients for the two-year follow-up even if they were not compatible with TAP/VIP criteria. The treatment demonstrated stabilization or less visual loss in long-term results.*

Keywords: *Photodynamic therapy, Age-related macular degeneration, Thai patient*

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Photodynamic therapy (PDT) with verteporfin has been found to be an effective treatment for subfoveal choroidal neovascularization (CNV)[1-8]. It has been observed to have better visual results in Asian patients than Caucasians[9,10]. The present study, after previously 12 months report[11], reviewed the 24 months visual outcomes of PDT with verteporfin in Thai patients with CNV due to age-related macular degeneration (AMD) & non-AMD.

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Material and Method

Fifty-six patients were prospectively included and followed up for 24 months, underwent PDT for various etiologies between July 2003 and December 2004 at Retina unit, Prince of Songkla University, Thailand. Demographic data, diagnosis, best corrected visual acuity (BCVA) using ETDRS charts were collected at baseline. Baseline color photographs and fluorescein angiography (FA) were reviewed by four retina specialists (MR, SV, PH & DP) as described in the first-year study[11]. The lesion composition was classified according to the treatment of age-related macular degeneration with photodynamic therapy (TAP) and verteporfin in photodynamic therapy (VIP)

study criteria and if at least three of the reviewers were in consensus.

Patients were assessed every three months and visual acuity (VA), color photograph, and FA were scheduled at each visit. PDT with verteporfin was recommended if any fluorescein leakage was detected. Any adverse event was recorded.

The patients were divided into two groups: group 1) CNV-related AMD group and group 2) non-AMD group. For group 1, all eyes were classified into three subgroups.

Group 1A) Subfoveal CNV compatible with TAP/VIP[8] *i.e* lesion characteristics following the standard TAP/VIP studies: 1). The greatest linear dimension (GLD) $\leq$ 5400 μm 2) For predominantly classic or minimally classic subfoveal CNV, the BCVA should be 20/40 to 20/200 3). For occult with no classic subfoveal CNV, the BCVA should be approximately 20/100 or better. Group 1B) Subfoveal CNV incompatible with TAP/VIP *i.e* lesion characteristics does not follow standard TAP/VIP studies. Group 1C) Non-subfoveal CNV *i.e* juxtafoveal or extrafoveal CNV.

The primary outcome was the change in BCVA from baseline until 24 months follow-up period. Paired t-test was used to test for significance. A p-value of less than 0.05 was considered statistically significant.

Results

Out of fifty-six patients, four patients lost follow-up and one refused to continue the treatment. After 1 year, 51 eyes (91%) completed 1-year follow-up and at the end of the study (2 years), 46 eyes of 46 patients (82.14%) completed 2-year follow-up.

From the completed follow-up 46 patients, the diagnosis of CNV-related AMD was made in 34 eyes (74%), idiopathic CNV in six eyes (13%), myopic CNV in two eyes (4%), central serous chorioretinopathy in two eyes (4%), choroidal hemangioma and adult vitelliform dystrophy in one eye each (2%).

Of 34 eyes with CNV-related AMD, nine eyes (26.5%) were subfoveal CNV with TAP/VIP compatible (group1A), 18 eyes (52.9%) were subfoveal CNV with TAP/VIP incompatible (group 1B), and seven eyes (20.6%) were non-subfoveal CNV (group 1C).

In group 1A (9 eyes), two eyes were classified as predominantly classic CNV, four as minimally classic CNV, and three as occult with no classic CNV (Table 1, 2). After 2 year, in group 1A, eight out of nine eyes (88.9%) lost less than 15 letters, six eyes (66.7%) gained more than 0 letters, and four eyes (44.4%) gained $\geq$ 15 letters. The mean BCVA at 24-month visit (0.39 logMAR) was slightly improved compared to the mean baseline BCVA (20/87 or 0.64 logMAR) (increased 0.25 logMAR, p = 0.13). The average total number of treatments in this group after the first and second year was 1.8 and 0.1, respectively (Table 1).

In group 1B (18 eyes, Table 1, 2), five eyes (27.8%) were classified as predominantly classic CNV, three eyes (16.7%) were minimally classic CNV, and 10 eyes (55.5%) were occult with no classic CNV. All of them completed the 24-month follow-up. With the average GLD of 4799 μm, eight eyes (44.4%) had GLD beyond 5400 μm and half of them had baseline BCVA worse than 20/200. For the eyes with GLD less than 5400 μm, two eyes (11.1%) had baseline BCVA better than 20/40 and eight eyes (44.4%) had baseline BCVA that was not compatible with TAP/VIP criteria. At the

Table 1. Demographic data and treatment results of the AMD eyes

Study group (eyes)	Average age (years)	Mean GLD (μm)	Mean baseline BCVA (LogMAR)	Mean 24-month BCVA (LogMAR)	p-value	Average total number of treatments in year 1, 2
Group 1A (9 eyes)	67	2797	0.64	0.39	0.130	1.8, 0.1
Group 1B (18 eyes)	67	4799	0.99	0.94	0.520	2.3, 0.1
Group 1C (7 eyes)	62	3069	0.69	0.41	0.003	1.5, 0.25

BCVA = best corrected visual acuity, LogMAR = logarithm of minimal angle of resolution, GLD = greatest linear dimension, m = month

Group 1A; subfoveal choroidal neovascularization with TAP/VIP compatible criteria

Group 1B; subfoveal choroidal neovascularization with TAP/VIP incompatible criteria

Group 1C; non-subfoveal choroidal neovascularization

24-month follow-up, 15 out of 18 eyes (83.3%) lost less than 15 letters, seven eyes (38.9%) gained more than 0 letters, and five eyes (27.8%) gained ≥ 15 letters (Table 2). The mean BCVA at 24-month visit (0.94 logMAR) was slightly improved compared with baseline (20/195 or 0.99 logMAR) (increased 0.05 logMAR, p = 0.52). The average total number of treatments in this group in the first and second year was 2.3 and 0.1, respectively (Table 1).

Table 2. Summary of visual acuity changes in the AMD eyes

Parameter	Group 1A (n = 9)	Group 1B (n = 18)	Group 1C (n = 7)
Mean VA change (logMAR)	+0.25	+0.05	+0.28
VA loss < 15 letters	8 (88.9%)	15 (83.3%)	7 (100%)
VA gain > 0 letter	6 (66.7%)	7 (38.9%)	6 (85.7%)
VA gain ≥ 15 letters	4 (44.4%)	5 (27.8%)	4 (57.1%)
VA 20/200 or worse			
Baseline	2	11	2
24-month	1	10	1
VA 20/40 or better			
Baseline	2	3	0
24-month	2	1	3

VA = visual acuity, LogMAR = logarithm of minimal angle of resolution
Group 1A; subfoveal choroidal neovascularization with TAP/VIP compatible criteria
Group 1B; subfoveal choroidal neovascularization with TAP/VIP incompatible criteria
Group 1C; non-subfoveal choroidal neovascularization

In group 1C (7 eyes), all eyes were graded incompatible based on non-subfoveal CNV. At the 24-month follow-up, six eyes gained more than 0 letter and four eyes (57.1%) gained ≥ 15 letters. The mean BCVA at 24-month visit (0.41 logMAR) significantly improved compared to baseline (20/98 or 0.69 logMAR) (increased 0.28, p = 0.003). The average total number of treatments in this group in the first and second year was 1.5 and 0.25, respectively (Table 1). The progression of the VA in each subgroup is summarized in Fig. 1.

Those patients who received PDT from causes other than CNV-related AMD were classified in group 2 and summarized in Table 3.

Two eyes (4%) experienced acute severe visual acuity loss[11,12]. They showed this symptom at the following day after PDT. Both eyes had exudative retinal detachment on fundus examination, which completely disappeared after one week. This complication occurred only during the first year of the present study. Four patients (8%) had minimal to severe back pain during infusion of verteporfin, as previous reported in the one-year study.

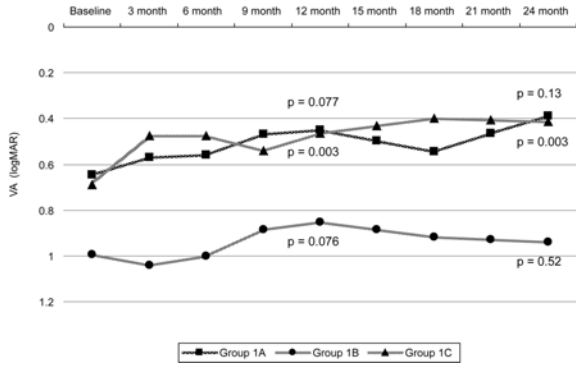
Discussion

From a previous report of the one-year results[11], all groups showed comparable benefit from PDT with the standard studies[1-10]. Although the mean visual changes in all groups were decreased with time,

Table 3. Demographic data and treatment results of the non-AMD eyes

No.	Age (years)	Diagnosis	GLD (μm)	Baseline BCVA	24-month BCVA	No. of treatments at year 1, 2
1	46	Idiopathic CNV	3000	20/125	20/25	3, 0
2	34	Idiopathic CNV	1625	20/40	20/63	3, 1
3	45	Idiopathic CNV	3031	20/80+2	20/40	2, 0
4	45	Idiopathic CNV	3142	20/200	20/32	1, 0
5	45	Idiopathic CNV	2240	20/25	20/40-2	2, 2
6	31	Idiopathic CNV	1479	20/25	20/20-2	2, 0
7	16	CNV in PM	1100	20/200-2	20/25	1, 0
8	60	CNV in PM	3865	20/200-1	20/160	1, 0
9	56	Choroidal hemangioma	5500	Counting fingers	10/200	2, 0
10	62	Adult vitelliform dystrophy	5583	20/100+2	20/50	1, 0
11	44	CSC	2885	20/25+2	20/20	1, 0
12	46	CSC	4010	20/50-2	20/50-1	1, 0

GLD = greatest linear dimension, μm = micron, BCVA = best corrected visual acuity, m = month, F = female, M = male, CNV = choroidal neovascularization, PM = pathologic myopia, CSC = central serous chorioretinopathy



VA = visual acuity, LogMAR = logarithm of minimal angle of resolution
Group 1A; subfoveal choroidal neovascularization with TAP/VIP compatible criteria
Group 1B; subfoveal choroidal neovascularization with TAP/VIP incompatible criteria
Group 1C; non-subfoveal choroidal neovascularization

Fig. 1 Mean visual acuity score over time of AMD eyes in each group

the percentage of patients with BCVA lost less than 3 lines (15 letters) were still high. At 12-month results, 91.7% of eyes in group 1A (compatible with TAP/VIP guidelines) showed BCVA loss less than 3 lines, and after 24-month follow-up, the percentage decreased to 88.9%. Even after taking out the possibility of idiopathic polypoidal choroidal vasculopathy (IPCV) from this group (25%)[13], the 24-month results might decrease from 88.9% to approximately 66.7%. The results still demonstrated comparable benefit with the second year results from TAP/VIP studies that showed 59% and 45%, respectively[2,6]. Moreover, the mean number of treatments in group 1A was decreased from 1.8 in the first year to only 0.1 in the second year. This finding confirmed the previous explanation[11] that most of the patients came to be treated at the late conditions. Although the authors used the strict retreatment criteria (any fluorescein leakage), only a few patients in the present study still needed the treatment in the second year. Furthermore, the authors did not perform any adjuvant intravitreal injection such as triamcinolone or anti-vascular endothelial growth factor (VEGF) in this group of patients, so no other treatment regimens affected the retreatment rates and visual results in the present study.

In group 1B with TAP/VIP incompatible criteria, 83.3% lost less than 3 lines in the second year. Although the baseline characteristics suggested poorer prognosis and could not be compared with the standard studies, the results in this group still showed much better than expectation. In contrast, group 1C with extra- or juxtafoveal CNV, the 24-month demonstrated significant visual improvement ($p = 0.003$), the same as in the first year[11]. The authors did not notice progression of CNV into subfoveal area in the second year in this group (1C) so the visual acuity still showed excellent results for the total 2-year follow-up.

Overall, all cases of AMD patients in the present study gave successful results with monotherapy by PDT. The authors believed that they were a lot of IPCV hidden in all study groups and resulted in good visual outcomes overall. Many studies demonstrated a high success rate from IPCV treated with monotherapy PDT[14-16]. However, combination therapy such as PDT and anti-VEGF might give a higher rate of success in AMD or AMD-like patients in Asians.

In the non-AMD group (group 2), many patients showed excellent visual results in the 2-year follow-up although the sample size was small and limited. Two patients of central serous chorioretinopathy demonstrated good visual results and no recurrence with only one session of PDT. In the idiopathic CNV group, only two cases needed additional PDT treatments in the second year but the visual results were still stable for 24 months.

For 24-month follow-up, the treatment with PDT was well tolerated as in the first year. The infusion related-back pain or severe visual loss in the second year was not noticed. This is because the retreatment rate in the second year was low and most of the patients might tolerate better with the additional treatments.

In conclusion, PDT still showed benefit in stabilization of vision in Thais in the 2-year follow-up. Few patients need additional treatments in the second year. Further studies are warranted to assess the results of combination therapy of PDT and anti-VEGF injection for AMD or AMD-like (IPCV) in Thai patients.

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การรักษาผู้ป่วย AMD และ non-AMD ด้วย photodynamic therapy: ผลการรักษา 2 ปีในคนไทย

แมนสิงห์ รัตนสุคนธ์, ปฐมา ภูรยานนทชัย, พิชัย จิรรัตนโสภา

วัตถุประสงค์: *เพื่อประเมินประสิทธิผลในระยะยาวของการรักษาผู้ป่วยโรคจุดภาพชัดเสื่อม (age-related macular degeneration - AMD) และผู้ป่วยที่ไม่เป็นโรคจุดภาพชัดเสื่อม (non-AMD) ด้วยวิธี photodynamic therapy (PDT) ในคนไทย เปรียบเทียบผลการรักษากับการศึกษา the treatment of age-related macular degeneration with photodynamic therapy (TAP) และ verteporfin in photodynamic therapy (VIP) study*

วัสดุและวิธีการ: *เก็บรวบรวมข้อมูลผู้ป่วยแบบไปข้างหน้า จากผู้ป่วยที่ได้รับการรักษาด้วย PDT ตั้งแต่กรกฎาคม พ.ศ. 2546 ถึง ธันวาคม พ.ศ. 2547 และสามารถติดตามผลการรักษาได้ครบ 2 ปี การประเมินแบ่งเป็นสองกลุ่ม กลุ่มแรกเป็นผู้ป่วยโรคจุดภาพชัดเสื่อมสามกลุ่มย่อย คือ กลุ่ม 1A เป็นผู้ป่วยโรคจุดภาพชัดเสื่อมที่มี choroidal neovascularization (CNV) ชนิด subfovea และมีลักษณะตรวจพบตรงตามข้อบ่งชี้ในการรักษาด้วย PDT จากการศึกษา TAP/VIP กลุ่ม 1B เป็นผู้ป่วยโรคจุดภาพชัดเสื่อมที่มี CNV ชนิด subfovea แต่มีลักษณะตรวจไม่พบตาม TAP/VIP กลุ่ม 1C ผู้ป่วยโรคจุดภาพชัดเสื่อมที่มี CNV แบบ non-subfovea ส่วนกลุ่ม 2 เป็นผู้ป่วยที่ไม่เป็นโรคจุดภาพชัดเสื่อม การวัดผลที่ได้รับประกอบด้วยการเปลี่ยนแปลงระดับการมองเห็น จำนวนครั้งของการรักษา และเปรียบเทียบกับผลการรักษาในระยะ 1 ปี*

ผลการศึกษา: *มีผู้ป่วยทั้งหมด 46 คน (82.14%) ที่ติดตามผลการรักษาครบ 2 ปี โดยจากทั้งหมดมีตา 34 ข้างเป็นโรคจุดภาพชัดเสื่อมและ 12 รายไม่เป็นโรคจุดภาพชัดเสื่อม การตรวจหลังการรักษา 24 เดือน พบว่าระดับการมองเห็นของผู้ป่วยในกลุ่ม 1A, 1B, 1C เพิ่มขึ้น 0.25 ($p = 0.13$), 0.05 ($p = 0.52$) และ 0.28 ($p = 0.003$) ตามลำดับ ส่วนจำนวนครั้ง ของการรักษาในปีที่ 1และ 2 เท่ากับ 1.8 และ 0.1 ในกลุ่ม 1A, 2.3 และ 0.1 ในกลุ่ม 1B, 1.5 และ 0.25 ในกลุ่ม 1C*

สรุป: *การรักษาผู้ป่วยโรคจุดภาพชัดเสื่อมด้วยวิธี PDT ได้ประโยชน์ในผู้ป่วยคนไทย ให้ผลการรักษาที่น่าพึงพอใจในระยะเวลา 2 ปี แม้ว่ามีลักษณะตรวจพบไม่ตรงกับเกณฑ์การรักษาจากการศึกษา TAP/VIP การรักษาสามารถยับยั้งการสูญเสียการมองเห็นได้ในระยะยาว*