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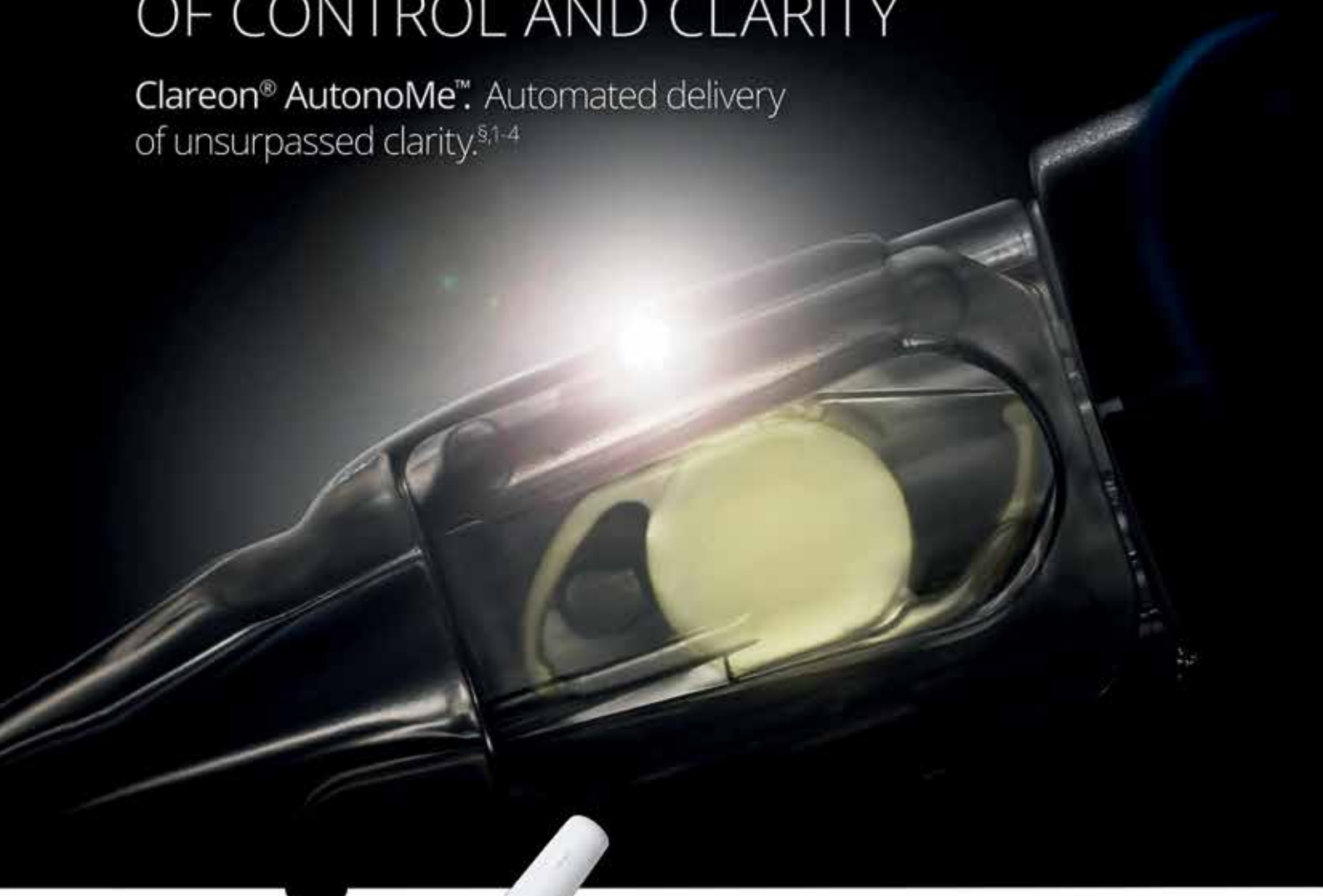

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HONG KONG JOURNAL OF OPHTHALMOLOGY

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香 港 眼 科 醫 學 院

THE HONG KONG JOURNAL OF OPHTHALMOLOGY
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To encourage submissions to the *Hong Kong Journal of Ophthalmology* (HKJO) by trainees and fellows of the College of Ophthalmologists of Hong Kong (COHK).

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Two awards will be given out every year. Each awardee will be given a $1000 cash prize (HK dollars), which is supported generously by the Timothy KC Liu Fund.

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- Applicants must be a paid-up member or fellow of COHK at the time of submission.
- Trainees refer to those who have not been conferred the title 'FCOphthHK' at the time of submission.
- Only the first author of the article will be eligible for the prize. If the first author is not eligible for the award, i.e. not a member of fellow of COHK, then the order of consideration of awardee will be from the second author onwards to the last author.
- Original articles (including, but not limited to, prospective or retrospective clinical studies, observational studies, epidemiological studies, basic science studies, meta-analysis, etc) published in the HKJO during the year will automatically enter the selection process.
- Case reports (with case number <3), review articles and letters to the editor will not be eligible for this award.
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- Originality
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The awards will be given out at the following year's conferment ceremony.

EDITORIAL

A new beginning for the *Hong Kong Journal of Ophthalmology*, the official journal of the College of Ophthalmologists of Hong Kong

As the new Editor-in-Chief of the *Hong Kong Journal of Ophthalmology* (HKJO), it is my great pleasure and honor to have the opportunity to work with the distinguished Editorial Board and to continue to provide the College and our Fellows with a first-class publication. Owing to the invaluable achievements of my predecessors and colleagues, articles of HKJO are already easily accessible and retrievable through Google Scholar. One of the missions of the Editorial Board is to advance the scientific standard and reputation of our Journal. We would like to promote our Journal to regional and international scholars, and having the Journal included a citation index is an important step on the path to our future success. We have been working hard to prepare our Journal to be included in PubMed Central, subject to vigorous evaluation standards.[1] The following actions have been undertaken: (1) current National Library of Medicine policies for PubMed Central inclusion have been reviewed; (2) current standards and best practices for scholarly journals have been discussed with the publisher (HKAM Press; https://www.hkampress.org/) and areas for improvement have been identified; (3) the Journal's online submission platform has been updated to the latest version, to ensure future seamless integration to PubMed Central and compliance with the latest publication standards; and (4) an improved plagiarism detection service (iThenticate; http://www.ithenticate.com/) has been subscribed to. Actions in progress include (1) updating the author guidelines and submission processes to meet the latest standards of the International Committee of Medical Journal Editors,[2] (2) applying for inclusion of HKJO in the Directory of Open Access Journals (DOAJ; https://doaj.org/) as a quality test, and (3) planning to collect at least 25 new articles for submission to PubMed Central for quality assessment. A crucial pre-requisite for inclusion in PubMed Central is the regular publication of quality peer-reviewed articles. We would like to take this opportunity to solicit your kind support to help HKJO getting indexed.

In this issue, we have two informative original articles. Lau et al[3] share with us on the safety and efficacy of atropine treatment in a private hospital in Hong Kong for slowing myopia progression in children in a 5-year review. Wong et al[4] reviewed cases of retinoblastoma in a tertiary referral public hospital in Hong Kong from 2008-2019, highlighting the incidence, clinical features, and outcomes of this importance disease. Multiple-choice questions related to the above two articles have been designed to provide CME credits for Fellows of the Hong Kong Academy of Medicine. It is the first time that Fellows can complete the CME questions online at https://www.icmecpd.hk/ for immediate credit of the points. We strongly encourage our Fellows to use the above electronic method, as the old hard copy method will not be provided in future issues.

I warmly thank all of our valued readers, College Fellows, and the Editorial Board, and especially our Associate Editor, Dr Alvin Au Ka Hong, for all of the precious contributions to HKJO in the past and coming years.

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4. *Wong E, Chan A, Lam C, Lau W, Yam J, Yu C. Retinoblastoma in Hong Kong from 2008 to 2019: looking back and moving forward. Hong Kong J Ophthalmol 2020;24:6-10.* Crossref

ORIGINAL ARTICLE

Retinoblastoma in Hong Kong from 2008 to 2019: looking back and moving forward

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Abstract

Purpose: To report the incidence, clinical features, and treatment outcomes of retinoblastoma at a tertiary referral center in Hong Kong.

Methods: Medical records of all patients with retinoblastoma presenting to Hong Kong Eye Hospital from 2008 to 2019 were reviewed.

Results: 75 eyes in 55 patients were treated for retinoblastoma during the 10-year study period. The mean age at presentation was 19.8±16.4 months. The mean duration of symptoms before diagnosis was 1.1±2.1 months. The most common presenting sign was leukocoria and/or strabismus (n=33, 60.1%). 65% of patients presented with advanced disease of groups D and E. The tumor was unilateral (n=35, 63.6%), bilateral (n=18, 32.7%), or trilateral (n=2, 3.6%). The enucleation rate was 0% in groups A to C, 70% in group D, and 93.3% in group E. With the introduction of intra-arterial chemotherapy since 2016, the globe salvage rate has increased from 29.4% to 33.3% in group D eyes and from 4.5% to 12.5% in group E eyes. The overall globe salvage rate was 40.0%, and the overall 5-year survival rate was 100%.

Conclusions: The prognosis of retinoblastoma is good in cases with early detection and appropriate treatment. Unfortunately, most patients presented with relatively advanced disease, which lowers the overall globe salvage rate. There is a need for enhanced public awareness and education for healthcare professionals to facilitate early detection and improve ocular outcomes for children with retinoblastoma.

Key words: Eye enucleation; Hong Kong; Incidence; Retinoblastoma; Treatment outcome

Introduction

Retinoblastoma is the most common intraocular malignancy of childhood[1] and constitutes 3% of all pediatric cancers,[2], with the incidence ranging from 1 in 15000 to 20000 live births.[3,4] The most common presenting signs and symptoms are leukocoria and strabismus, followed by glaucoma, decreased visual acuity, orbital cellulitis, and others.[5] Retinoblastoma is often diagnosed in relatively later stages,[5] as early detection requires vigilant screening and public awareness.

Once detected, treatment for retinoblastoma is multimodal and dictated by the stage of the disease, laterality, presence of extraocular extension, and visual prognosis. Management of retinoblastoma has evolved over the past four decades. In the 1970s, enucleation was important for ensuring survival. Enucleation remains relevant for advanced retinoblastoma, particularly in Asia and Africa. In the 1980s, external beam radiotherapy was widely used, but risks of radiation-related secondary malignancies have led to its reduced use. In the 1990s to 2000s, systemic intravenous chemotherapy was

used, typically with combinations of vincristine, etoposide, and carboplatin.[6] Currently, systemic chemotherapy remains popular for intraocular retinoblastoma control as well as prevention of systemic metastasis. In general, earlier presentation is associated with improved prognosis in terms of patient survival and globe salvage rates. With advancements in globe salvage techniques and new treatments, the prospect of preserving the eye even in advanced disease has steadily improved. In the recent decade, intra-arterial chemotherapy (IAC) and other forms of locally delivered chemotherapy and combination therapies have been explored.

To the best of our knowledge, there has been one study describing clinical features and treatment outcomes of retinoblastoma in Hong Kong in 2008.[7] The present study was conducted to report updated epidemiological data, advances in treatment, and management outcomes for retinoblastoma from 2008 to 2019.

Patients and methods

In Hong Kong, most patients with retinoblastoma are managed in the Kowloon Central Cluster by a multidisciplinary team of pediatricians, ophthalmologists, pediatric oncologists, radiologists, pathologists, social workers, and volunteers from non-governmental organizations. We retrospectively reviewed records of all patients with retinoblastoma treated at Hong Kong Eye Hospital from January 2008 to January 2019. Data were retrieved from the Hospital Authority clinical management system and included sex, age at diagnosis, presenting symptoms or signs, laterality, presenting stage, family history, treatment modality, recurrence rate, survival rate, and results of genetic testing.

Each of the eyes was classified according to the International Classification of Retinoblastoma (ICRB) [**Table 1**]. If such classification was not available, RetCam (Natus Medical, Pleasanton [CA], USA) photography on first presentation was used for tumor grading according to the documented tumor size and features. The diagnosis of retinoblastoma was confirmed by dilated fundus examination, ultrasonography, and magnetic resonance imaging, which aids the identification of poor prognostic features such as pineal gland involvement, extra-scleral extension, and optic nerve spread.[8] We included only those patients who were followed up for at least 1 year after diagnosis was made.

Table 1. International Classification of Retinoblastoma

Group A	Retinoblastoma ≤3 mm (in basal dimension or thickness)
Group B	Retinoblastoma >3 mm (in basal dimension or thickness) or • Macular location (≤3 mm to foveola) • Juxtapupillary location (≤1.5 mm to disc) • Additional subretinal fluid (≤3 mm from margin)
Group C	Retinoblastoma with: • Subretinal seeds ≤3 mm from tumor • Vitreous seeds ≤3 mm from tumor • Both subretinal and vitreous seeds ≤3 mm from tumor
Group D	Retinoblastoma with: • Subretinal seeds >3 mm from tumor • Vitreous seeds >3 mm from tumor • Both subretinal and vitreous seeds >3 mm from retinoblastoma
Group E	Extensive retinoblastoma occupying >50% globe or with: • Neovascular glaucoma • Opaque media from hemorrhage in the anterior chamber, vitreous, or subretinal space • Invasion of postlaminar optic nerve, choroid (>2 mm), sclera, orbit, anterior chamber

Treatment modalities included chemotherapy (systemic, intra-arterial, and intravitreal mode of delivery), focal therapy with laser or cryotherapy, and enucleation. Radiotherapy was avoided owing to the lifetime risk of secondary malignancies, and the option of plaque radiotherapy was not provided. In our center, IAC has been introduced since 2016 and is currently offered to patients for salvage treatment in bilateral disease and selected patients with ICRB groups C or D localized unilateral retinoblastoma. Intravitreal chemotherapy is offered occasionally as a combination therapy for recurrent vitreous seeding following incomplete control with other methods. Systemic chemotherapy is often given as a chemoreduction regimen in bilateral retinoblastoma, as combination therapy for resistant or recurrent unilateral cases, or as a bridging therapy in neonates who are too young for IAC or surgery. Agents used were a combination of carboplatin, etoposide, and vincristine, given every 21 to 28 days for up to 4 to 6 cycles.[9] After a few cycles of chemotherapy, focal therapy (laser therapy or cryotherapy) is applied when there is a significant reduction in tumor size with improved laser uptake.

Results

75 eyes in 35 boys and 20 girls of Chinese ethnicity were treated for retinoblastoma at our hospital during 2008-2019. The incidence of retinoblastoma in Hong Kong during the study period was estimated to be 1 per 14309 live births, based on 787000 live births during the study period.[10]

The mean age at presentation was 19.8±16.4 months (23.2±17.3 months for unilateral cases and 13.1±13.1 months for bilateral cases). The mean duration of symptoms before diagnosis was 1.1±2.1 months. Upon presentation to an ophthalmologist, retinoblastoma was suspected after clinical examination, and there was no misdiagnosis.

The most common presenting sign was leukocoria (n=25, 45.5%), followed by decreased visual acuity (n=6, 10.9%), strabismus (n=4, 7.3%), and combined leukocoria and strabismus (n=4, 7.3%). In two (3.6%) patients, the diagnosis was picked up during screening for positive family history.

The tumor was unilateral (n=35, 63.6%), bilateral (n=18, 32.7%), or trilateral (n=2, 3.6%). The ICRB group at presentation was A in 8 eyes (10.7%), B in 8 eyes (10.7%), C in 4 eyes (5.3%), D in 20 eyes (26.7%), E in 30 eyes (40.0%), and not available in the remaining 5 eyes (6.7%). More

patients presented in the later groups (D and E) than in the earlier groups (A to C), and this trend had not changed over the study period.

Five (9.1%) patients had a positive family history for retinoblastoma, but four of them had no available data regarding this. The remaining 46 (83.6%) patients were not observed to have the disease in the family prior to the index case. Genetic testing was performed in 38 (69.1%) patients: 22 (57.9%) had non-germline mutation and 16 (42.1%) had germline mutation.

42 (56.0%) eyes underwent primary enucleation. In three (9.1%) eyes, chemoreduction with focal therapy was attempted but failed and eventually required enucleation. The rate of enucleation was proportionally related to the presenting stage (0% in groups A to C, 70% in group D, and 93.3% in group E) [**Table 2**].

32 (58.2%) patients were given systemic chemotherapy, and two (3.6%) received radiotherapy (external beam radiotherapy or plaque radiotherapy) in overseas centers. Intravitreal melphalan was administered in two patients with resistant vitreous seeding despite systemic chemotherapy, IAC, and focal laser. IAC was used in seven patients as salvage therapy when first-line systemic chemotherapy or local therapy could not control the disease.

Four patients developed complications from IAC. One patient developed transient cellulitis and lid swelling, which resolved spontaneously 3 weeks after IAC. One patient developed ischemic optic neuropathy after three cycles of IAC and required a course of pulsed methylprednisolone followed by prolonged oral steroid and intravitreal anti-VEGF injection to control the disc swelling. Two patients developed ischemic retinopathy and neovascular glaucoma with vitreous hemorrhage after three and six cycles, respectively, of IAC in an overseas center; the involved eye was eventually enucleated due to high-risk features. With the introduction of IAC in Hong Kong since 2016, the globe salvage rate has improved from 29.4% to 33.3% in group D eyes and from 4.5% to 12.5% in group E eyes (**Table 2**).

Table 2. Enucleation rate and globe salvage rates before and after introduction of intra-arterial chemotherapy in 2016

Presenting stage*	No. (%) of eyes		
	Enucleation rate	Globe salvage rate before 2016	Globe salvage rate after 2016
Group A (n=8)	0 (0)	6/6 (100)	2/2 (100)
Group B (n=8)	0 (0)	7/7 (100)	1/1 (100)
Group C (n=4)	0 (0)	3/3 (100)	1/1 (100)
Group D (n=20)	14 (70)	5/17 (29.4)	1/3 (33.3)
Group E (n=30)	28 (93.3)	1/22 (4.5)	1/8 (12.5)

** Staging in 5 eyes was not documented*

Six patients received post-enucleation chemotherapy for high-risk features, including tumor invasion posterior to lamina cribosa of the optic nerve, ≥3 mm of choroidal invasion, and any degree of optic nerve and uveal invasion on pathological examination after enucleation.[11,12] These patients had group E eyes on presentation, but there were no features suspicious of choroidal invasion or optic nerve invasion detected on preoperative magnetic resonance imaging. The overall globe salvage rate was 40.0%, and the 5-year survival rate was 100% including the two patients with trilateral retinoblastoma.

Discussion

Consistent with the literature,[13-17] in the present study, the most common presenting symptoms were leukocoria and/or strabismus (60.1%), and the mean age at presentation was younger in bilateral cases than unilateral cases (13.1±13.1 months vs 23.2±17.3 months). Compared with studies in other Asian centers,[18-21,26-29] in the present study, the mean duration of symptoms before diagnosis was 1.1±2.1 months, and the diagnosis of retinoblastoma was suspected upon presentation to an ophthalmologist, with no misdiagnosis. This is likely due to the centralized management model in a quaternary referral center with relatively high awareness among ophthalmological staff. In addition, most patients had advanced retinoblastoma (groups D and E) at presentation and there was no improvement in early detection over the years. As early-stage disease carries a much higher globe salvage rate and better survival prognosis, there is a need for more public education and healthcare professional awareness to enable early detection of disease.

In the present study, the 5-year overall survival rate of retinoblastoma was 100%, which is consistent with the 95% reported in Europe,[22,23] and the >96% in the United States,[24] and is higher than the 35% to 86% in most parts of Asia.[25-29] Traditionally, trilateral retinoblastoma (intraocular retinoblastoma combined with a histologically similar brain tumor – most commonly in the pineal gland) is associated with poor prognosis.[30] However, facilitated by early detection and the use of high-dose chemotherapeutic agents with stem cell rescue and radiotherapy, the 5-year survival of patients with pineal and non-pineal trilateral retinoblastoma has increased substantially from 6% to 44% from 1995 onwards.[31] In the present study, the two patients with trilateral retinoblastoma exhibited rapid tumor control and regression with high-dose chemotherapy with vincristine, carboplatin, etoposide, and cyclophosphamide (according to the COG ARET0321 protocol) for six cycles along with autologous stem cell transplant.[32] In one patient the more severe eye was enucleated, and in the other patient total regression of tumors in both eyes occurred after chemotherapy alone without the need for enucleation. Both patients have remained in remission for 2 years and 9 years, respectively.

Over the last decade, advances in the globe salvage therapies have improved disease control and minimized late effects of systemic chemotherapy. In addition, IAC and intravitreal chemotherapy have improved treatment outcomes for

advanced retinoblastoma. Shields and Shields[6] reported that primary therapy with IAC was better than systemic chemotherapy alone and was successful in 100% of group C eyes, 100% of group D eyes, and 33% of group E eyes. IAC was effective in inducing 92% of solid tumor regression and controlling 80% to 95% of subretinal seeds.[6] Since the introduction of IAC in our center in 2016, the globe salvage rate for unilateral and bilateral retinoblastoma has increased from 29.4% to 33.3% in group D eyes and 4.5% to 12.5% in group E eyes. Besides IAC, intravitreal chemotherapy is available as a second-line therapy in patients with resistant vitreous seeding. Suzuki et al[33] achieved a globe salvage rate of nearly 51% in the largest series of intravitreal melphalan at 8 micrograms for eyes with vitreous seeding. However, they reported one case of metastasis (0.4%) and suggested that intravitreal chemotherapy should be combined with triple freeze-thaw cryotherapy upon needle withdrawal at the injection site. We used intravitreal melphalan to control resistant vitreous seeding in two patients who remained recurrence-free at 2 and 4 years of follow-up, respectively. Our rate of globe salvage for groups A, B, and C eyes is comparable to that of most developed countries, with the exception of group D eyes.[34-37] The primary goal of retinoblastoma treatment is to preserve life, and hence enucleation remains a favored option as opposed to globe salvage therapy among parents. In Hong Kong, IAC is a relatively new treatment modality and is limited by manpower and logistical requirements, and hence it has only been used as a salvage therapy or secondary treatment in resistant or recurrent cases. More funding is needed to widen the use of IAC.

Nonetheless, IAC must be used with caution. Our series reported ischemic retinopathy and optic neuropathy after >3 cycles of IAC for globe salvage therapy. Despite having a lower rate of systemic side effects of chemotherapy such as neutropenia and fever, IAC has increased local effects ranging from eyelid edema to lower limb ischemia, arterial dissection, and retroperitoneal bleeding. There is also the risk of missing or downgrading high-risk characteristics such as choroidal or optic nerve invasion, which can only be revealed by pathological examination after enucleation. Long-term data on risk for systemic metastases are lacking, although a multicenter retrospective survey reported the risk of metastatic death to be <1% with IAC.[38]

Genetic testing was performed in 69% of our patients, which is lower than that reported in European or North American centers.[39,40] This is partially explained by the relatively high cost of genetic testing, which is offered on a self-financed basis with a limited number of families fulfilling financial criteria for subsidies from non-governmental organizations such as the Children's Cancer Fund. With the establishment of the Hong Kong Children's Hospital, we hope that there is wider availability of genetic testing and counseling to families, fast track imaging and IAC services, and increased use of local chemotherapy and other globe salvage techniques, as well as more frequent multidisciplinary interactions with pediatricians, clinical psychologists, and social workers; and more collaboration with non-governmental organizations such as Children's Cancer Fund to promote awareness among parents, general practitioners, and pediatricians for earlier referral and identification of retinoblastoma symptoms. Early detection and treatment are keys to better outcomes. Our team has launched a series of public education campaigns targeted to the general public, primary healthcare doctors, and pediatricians to educate and raise public awareness on the importance of early detection and referral of cases of retinoblastoma.

There are limitations to this study. Hong Kong Eye Hospital is a tertiary referral center for retinoblastoma in Hong Kong, but patients who attended private ophthalmic centers and were managed elsewhere or overseas were not included in the database, and therefore their disease outcomes were not known.

Conclusion

The prognosis of retinoblastoma is good in cases with early detection and appropriate treatment. Increased availability of local chemotherapy delivery such as IAC has improved the overall globe salvage rate, especially in groups C or D advanced disease. Unfortunately, most patients still presented with relatively advanced disease, which lowers the overall globe salvage rate. There is a need for enhanced public awareness and education for healthcare professionals to facilitate early detection and improve ocular outcomes for children with retinoblastoma.

Author contributions

Concept or design: all authors
Acquisition of data: EW, AC, WL
Analysis or interpretation of data: EW, AC
Drafting of the article: EW, AC
Critical revision for important intellectual content: all authors

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

As Editors of the Journal, WL and JY were not involved in the peer review process for this article. All other authors have no conflicts of interest to disclose.

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Ethics approval

This study was approved by the Kowloon Central / Kowloon East Cluster Research Ethics Committee (reference: KC/KE-20-0035/ER-3).

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ORIGINAL ARTICLE

Safety and efficacy of atropine treatment for slowing myopia progression in children: a 5-year review

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Abstract

Aim: To report the efficacy and safety of atropine treatment (0.01% and 0.125%) in slowing myopia progression in children.

Methods: This is a retrospective non-interventional case series. All patients aged <18 years who received topical atropine for myopia control from 2011 to 2016 in the Hong Kong Sanatorium & Hospital were included for analysis. Myopia progression, atropine treatment, and other factors affecting treatment outcomes were analyzed. We also reported any adverse effects associated with atropine use.

Results: A total of 346 patients were recruited, with mean a follow-up period of 2.26±0.82 years. The patients had a mean reduction of myopia progression of 68.4% after atropine treatment (p<0.001). The mean myopia progression rate (in spherical equivalent) was -0.38±0.36 D/year, and the mean axial length elongation rate was 0.23±0.19 mm/year. More reduction of myopia progression was associated with baseline myopia progression of <-1 D/year (p<0.001) and initial atropine dosage of 0.125% (p<0.001). Reduction of myopia progression was associated with starting age (p=0.041) and baseline myopia progression (p=0.004). Patients aged <6 years who received atropine treatment (n=17) showed reduction of myopia progression by 71.1%. Only mild adverse effects such as photophobia were reported.

Conclusion: Topical atropine is an efficacious and safe treatment for slowing myopia progression.

Key words: Atropine; Axial length, eye; Myopia; Refractive errors

Background

Myopia is the most common refractive error and a major public health problem worldwide.[1-4] A study conducted in Hong Kong showed 36.71% of children aged 5 to 16 years (n=7560) had myopia.[3] In a prospective cohort study in Singapore,[2] the 3-year cumulative incidence rates of myopia were 47.7%, 38.4%, and 32.4% for children aged 7, 8, and 9 years, respectively, and Chinese had the highest 3-year cumulative incidence rate of myopia, compared with Malays and Indians.

Various methods are effective in slowing myopia progression, including pharmacological treatments (atropine and pirenzepine), optical interventions (peripheral defocus modifying contact lenses, progressive addition spectacle lenses), and orthokeratology. A meta-analysis in 2016 reported that topical use of atropine is the most effective.[4]

Atropine is a nonspecific muscarinic antagonist. Two randomized control trials have shown that topical application of atropine significantly reduces myopia progression, in terms of spherical equivalent (SE) progression and axial length (AL) elongation.[1,5] A daily dose of 1% atropine reduced myopia progression to -0.28 D over 2 years, compared with -1.20 D in the placebo group (p<0.001).[5] Atropine in 0.5%, 0.1%, and 0.01% concentrations reduced myopia progression to -0.30 D, -0.38 D, and -0.49 D, respectively.[1] Nevertheless, the exact mechanism of how atropine inhibits myopia progression remains unclear.[1,4]

In clinical practice, dosage of atropine may be titrated according to the clinical response. A step-down approach (rather than immediate discontinuation) may be used to reduce the effect of rebound of myopia progression after discontinuation of the medication. However, there were different opinions regarding the dose-dependent effect of

atropine treatment. Yam et al[6] showed the dose-dependent effect in low-dose atropine treatment, whereas Gong et al[7] showed that only adverse effects, rather than efficacy, of atropine, are dose-dependent.

In the present study, we aim to evaluate the efficacy and safety of topical atropine (with or without dosage titration) in myopia control in a large cohort of pediatric patients.

Methods

This study is a retrospective non-interventional case series. Patients aged <18 years who received topical atropine of any concentration for myopia control from 2011 to 2016 in the Hong Kong Sanatorium & Hospital, Hong Kong and were followed up for ≥1 year were included for analysis. Data were extracted from the electronic system of the hospital. Approval was obtained from the institutional review board (Reference number: RC-2018-28), and the study was conducted in accordance with the principles of Declaration of Helsinki.

The following data were collected: demographics (sex, age, date of birth), ophthalmic history, past health, parent with history of high myopia (defined as myopia of ≥-6 D), baseline ophthalmic data (visual acuity, cycloplegic refraction, AL (measured by IOL Master, Carl Zeiss), atropine regimen (frequency and concentration), subsequent titration of treatment regimen, adverse effects, and ophthalmic parameters (AL and SE) of first 3 years and most recent follow-up.

SE progression and AL elongation after treatment were calculated as the difference in measurements between the beginning and end of treatment divided by the treatment period (in years). Baseline SE progression was defined as the mean change in SE by cycloplegic refraction over 1 or 2 years before atropine treatment.

Statistical analysis was performed using SPSS (Windows version 22.0; IBM Corp., Armonk [NY], United States). Only one eye from each patient was selected at random for analysis. Normality of data distribution was assessed with Kolmogorov-Smirnov statistic. Changes in SE and AL were analyzed with paired *t* test. Factors that may affect reduction of myopia progression was determined with Student's *t* test or Mann-Whitney *U* test according to normality of data distribution. Correlations between reduction of myopia progression and various factors were analyzed with Pearson correlation and analysis of covariance. Level of significance was defined as $p<0.05$.

Results

A total of 346 eyes from 346 children (161 male and 185 female) were included for analysis (**Table 1**). Of them, 254 children were initially prescribed a daily dose (n=244) or twice daily dose (n=10) of 0.01% atropine eye drops (Aseptic Innovative Medicine, Taiwan), 90 children were initially prescribed a daily dose (n=88) or 2 doses per week (n=2) of 0.125% atropine eye drops, and the remaining two children were initially prescribed 0.02% and 0.5% atropine (after dilution of 0.125% and 1% atropine with lubricant eye drops, respectively). The mean baseline SE was -3.72±2.5 D and AL was 24.73±1.13 mm. The mean follow-up period was 2.26±0.82 years.

The mean SE at the latest follow-up visit was -4.54±2.51 D, and the mean SE progression reduced to -0.38±0.36 D/year during atropine treatment from -1.20±0.70 D/year at baseline (68.4%; $p<0.001$). The AL elongation during atropine treatment was 0.23±0.19 mm/year. The distribution of the rate of SE progression changed after atropine treatment, with most

Table 1. Demographic data and baseline parameters of patients receiving atropine for myopia control (n=346)

Baseline parameter	Value*
Sex	
Male	161 (46.5)
Female	185 (53.5)
Laterality†	
Right eye	184 (53.2)
Left eye	162 (46.8)
Parent with high myopia	119 (34.4)
Age of starting atropine, y	8.64±2.19
Visual acuity, logMAR	0±0.07
Axial length, mm	24.73±1.13
Spherical equivalent, D	-3.72±2.5
Baseline spherical equivalent progression, D/y	-1.2±0.7
Follow-up, y	2.26±0.82
Ophthalmic health	
Intermittent exotropia	10 (2.9)
Amblyopia	2 (0.6)
Retinal break	2 (0.6)
Ptosis + superior oblique palsy	1 (0.3)
Cataract	1 (0.3)
Epiblepharon	1 (0.3)

* *Data are presented as mean±standard deviation or No. (%) of patients*
† *Only one eye from each patient was selected at random for analysis*

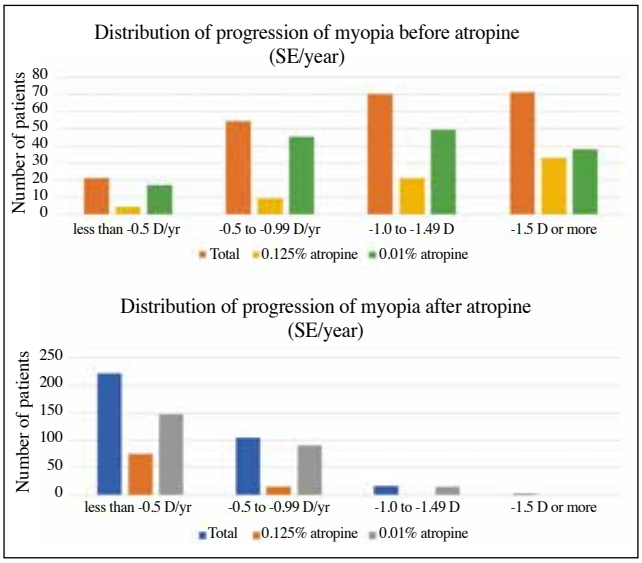

Figure. Patient distribution of myopia progression (in spherical equivalent [SE]/year) before and after atropine treatment

children had less than -0.5 D/year SE progression (**Figure**).

Subgroup analysis was performed to identify factors that affected reduction of SE progression with atropine (ie, difference between SE progression before and after atropine treatment). More reduction of SE progression after atropine was associated with the starting age of ≤8 years, the baseline SE progression of <-1 D/year, and initial atropine dosage of 0.125% (**Table 2**). Further analysis with analysis of covariance showed that only the baseline SE progression of <-1 D/year (p<0.001) and initial atropine dosage of 0.125% (p<0.001) remained significant after controlling for other independent variables.

Regarding AL elongation and SE progression during atropine treatment, those with starting age of >8 years (n=160) had slower SE progression (-0.34 D/year vs -0.41 D/year, p=0.031) and AL elongation (0.18 mm/year vs 0.25 mm/year, p=0.038) than did those with starting age of ≤8 years (n=186). Children who initially received 0.125% atropine (n=90) had slower SE progression (-0.25 D/year vs -0.42 D/year, p<0.001) and slower AL elongation (0.19 mm/year vs 0.26 mm/year, p=0.031), compared with children who initially received 0.01% atropine (n=254). Children with baseline high myopia (n=43) had slower SE progression (-0.18 D/year vs -0.33 D/year, p=0.046) but not slower AL elongation (p=0.117), compared with children without baseline high myopia (n=303). Further analysis with analysis of covariance showed that starting age (p=0.012) and initial dosage of atropine (p<0.001) remained significant factors for SE progression. No significant differences were identified in other parameters including sex, children with high myopia parents, or children with baseline SE progression more than -1 D/year. Reduction of SE progression was correlated with the starting age (r= –0.227, p=0.041) and baseline SE (r= –0.319, p=0.004).

Table 2. Factors that affect reduction of myopia progression (in spherical equivalent [SE]/year) after atropine treatment

Factor	No. (%) of patients (n=346)	Mean±SD reduction of myopia progression, SE/year	p Value
Age, y			0.031
≤8	186 (53.8)	0.98±0.78	
>8	160 (46.2)	0.71±0.63	
Sex			0.850
Male	161 (46.5)	0.85±0.72	
Female	185 (53.5)	0.87±0.73	
Baseline high myopia			0.550
Yes	43 (12.4)	0.95±0.64	
No	303 (87.6)	0.82±0.80	
Baseline myopia progression (n=216)			<0.001
>-1 D/y	101 (29.2)	1.37±0.59	
≤-1 D/y	115 (33.2)	0.42±0.50	
Parent with high myopia (n=175)			0.720
Yes	119 (34.4)	0.99±0.81	
No	56 (16.2)	0.94±0.61	
Atropine preparation at start (n=344)			<0.001
0.125%	90 (26.0)	1.23±0.66	
0.01%	254 (73.4)	0.8±0.67	

Of 346 patients, 186 had change in frequency or concentration of atropine during the study period, and dosage of atropine were titrated according to the rate of myopia progression or adverse effects experienced by patients. 95 of the 186 patients required up-titration of atropine (36 had increase in concentration, 50 had increased frequency, and 9 had both), and their mean SE progression reduced from -1.01 D/year during initial regimen of atropine to -0.5 D/year after up-titration of atropine (p<0.001). 61 of 186 patients had atropine down-titrated (6 had decrease in concentration, 49 had decreased frequency, and 6 had both), their mean SE progression was -0.16 D/year before down-titration and -0.22 D/year after down-titration (p=0.09). The remaining 30 patients received both up- and down- titration during the study period.

Adverse effects were reported in 14 (4.05%) patients; 10 of them were using 0.125% atropine daily. Photophobia was the most commonly reported adverse effects (n=8) despite usage of photochromatic spectacles. Other adverse effects included dizziness, eye irritation, allergic conjunctivitis, and blurred near vision.

Discussion

The findings of the present study are consistent with those of the ATOM2 study[1] that myopia progression can be controlled by atropine (both 0.01% and 0.125% preparation). However, the 0.01% group in the ATOM2 study showed better control of myopia progression (-0.49 D progression over 2 years) than did the same group in the present study (-0.38 D/year). The difference could be accounted partially by the difference in treatment regimen and the age of patients. In the ATOM2 study, all patients received daily dose of 0.01% atropine in the treatment arm and the patients recruited were aged 6 to 12 years, whereas in our study, we included patients aged 4 to 16 years and some received 0.01% atropine with lower frequency (eg. 2 to 3 times a week) when there was no significant myopia progression. Moreover, AL elongation results of the two studies are similar (0.41 mm over 2 years in ATOM2 study and 0.23 mm/year in our study). However, in ATOM1 study[5] and ATOM2 study[1] the effect of 0.01% atropine on AL elongation was negligible (0.38 mm in ATOM1study and 0.41 mm over 2 years in ATOM2 study).

In the present study, patients with higher baseline myopia progression (<-1 D/year) benefitted more from atropine treatment in terms of reduction in SE progression (1.37 D/year, reduction of 76.5% from baseline) than patients with baseline myopia progression of >-1 D/year (0.42 D/year, reduction of 55.8% from baseline). Mouse and Syrian hamster models showed that there was upregulation of muscarinic receptors in the myopic sclera.[8,9] This may indicate that eyes with higher myopia progression are more sensitive to atropine, a muscarinic

receptor antagonist; however, this is yet to be elucidated.

Previous observational studies in Hong Kong[2] and Singapore[10] showed that younger children have higher myopia progression than do older children. This was also reflected in the present study that patients aged >8 years experienced slower AL elongation and SE progression after atropine treatment than did patients aged ≤8 years. Owing to the high prevalence of myopia in Hong Kong students and public awareness of the complications related to pathological myopia, parents may prefer earlier treatment for their children, especially those parents who also have high myopia. In our cohort, 17 children received atropine treatment when aged <6 years and their baseline SE was -0.875 D to -9.5 D and mean myopia progression before treatment was -2 D/year. Ten (58.8%) of them had a family history of high myopia. After atropine treatment, the myopia progression was significantly reduced by 71.1% (p=0.007) and no adverse events were reported. Moreover, earlier starting age of atropine treatment was correlated with greater reduction in myopia progression (r= –0.227, p=0.041). This suggests that earlier commencing atropine treatment for myopia control may be recommended in selected patients.

There were modifications in atropine concentration and frequency in some patients during the treatment period, based on patient response to the treatment regimen and the individual ophthalmologist's judgment on the control of myopia progression. Although there was no standard on the timing or magnitude of atropine titration, the principle adopted was to use the minimum atropine dose that still controls myopia progression at a reasonable level.

Our study has a relatively homogenous study population (>90% were Chinese) and a reasonable sample size; however, it is limited by its non-randomized and retrospective nature. Only data on baseline SE progression instead of baseline AL elongation were available for the analysis because AL was not measured routinely in patients who were not receiving atropine treatment. Furthermore, patients were managed by different ophthalmologists in the team, so the choice of atropine regime may not be standardized. Nevertheless, the study reflects the practical use of atropine treatment with titrations according to the patient's clinical response.

Conclusion

Atropine treatment slows myopia progression by 68.4% in pediatric patients. Early treatment is considered safe for selected children aged <6 years with a high rate of myopia progression. With regular monitoring of patient's clinical response, titration of atropine could be applied to optimize its effects on myopia control while minimizing adverse effects.

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Author contributions

Concept or design: CSLL, DSPF.
Acquisition of data: CSLL.
Analysis or interpretation of data: CSLL, DSPF.
Drafting of the article: all authors
Critical revision for important intellectual content: all authors.

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

As an Advisor of the Journal, DF was not involved in the peer review process for this article. All authors have no conflicts of interest to disclose.

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Ethics approval

Ethics approval was obtained from the institutional review board (Reference number: RC-2018-28), and the study was conducted in accordance with the principles of Declaration of Helsinki.

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CASE REPORT

Frontalis suspension surgery for blepharospasm with apraxia of eyelid opening: a case report

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Abstract

An 86-year-old man presented with benign essential blepharospasm with apraxia of eyelid opening unresponsive to botulinum toxin type A treatment. He was successfully treated with bilateral frontalis suspension with upper blepharoplasty. Postoperatively, he was able to open his eyes without difficulty and resume his daily activities.

Introduction

Benign essential blepharospasm (BEB) is characterized by repeated, involuntary, and intermittent forceful closure of eyelids without any ocular irritation. BEB can usually be controlled by repeat injections of botulinum toxin type A. Among patients with BEB, 7% have associated apraxia of eyelid opening (AEO). Rarely, some patients have pure AEO and were unresponsive to botulinum toxin therapy.[1,2] Surgical treatments such as blepharoplasty, limited myectomy, aponeurosis repair, and frontalis suspension operation can be considered.[3] We report on a patient who had refractory BEB with AEO and dermatochalasis and was successfully treated with frontalis suspension and blepharoplasty.

Case presentation

In September 2015, an 86-year-old man presented with a 3-year history of difficulty in opening his eyes with involuntary eyelids closure. His eyes were closed for most of the time and could only be opened mechanically by fingers. His daily activities were greatly affected. The patient had undergone bilateral cataract surgeries. He had medically controlled glaucoma, hypertension (with Norvasc), dementia (with Exelon), iron deficiency anemia (with iron supplements) and hearing impairment (with hearing aids).

On examination, his eyes were forcefully closed with bilateral dermatochalasis (**Figure a**). His cornea, tear film, and eyelid margins were unremarkable. His intraocular pressure was within normal limits, and fundi were unremarkable. The patient was not able to follow instructions for examinations owing to dementia and eyelid spasm. Therefore, the levator function and marginal reflex distance could not be properly measured. He was initially diagnosed with BEB and was treated with repeat injections of botulinum toxin type A (17.5 units per eye per session). The botulinum toxin was injected at seven points into the orbital parts and palpebral parts (preseptal / pretarsal regions) of orbicularis oculi (four points in the upper eyelid laterally and medially, two points in the lower eyelid laterally and medially, and one at the lateral canthus). However, 3 months later, the patient still could not open his eyes. AEO was suspected, and he was referred to the oculoplastic clinic for surgical management. Frontalis suspension and upper eyelid blepharoplasty were discussed. Surgeries were performed at the left side first and then the right side. About 12 mm of skin was excised on both sides. A silicone rod was sutured directly to the tarsal plate with 6-O dermalon, and it was retrieved onto the forehead using Fascia Wright needle. Skin wounds were closed with 6-O vicryl and silk.

Postoperatively, the ptosis and dermatochalasis were corrected without any complications (**Figure b**). The patient

Figure. (a) A patient presented with bilateral benign essential blepharospasm, dermatochalasis, and apraxia of eyelid opening. (b) The patient could open his eyes after bilateral frontalis suspension with blepharoplasty.

had no lagophthalmos nor dry eyes symptoms. He was able to rapidly open his eyes and resume normal daily activities. Two more botulinum toxin treatments were given to improve blepharospasm. He was satisfied with the improvement and declined further botulinum toxin treatment.

Discussion

Frontalis suspension is a minimally invasive surgical option for blepharospasm and AEO (the latter is known to unresponsive to botulinum toxin treatment).[2-7] The traction of the frontalis muscles is directed to the upper eyelids by non-elastic materials (eg, silicone rod, Gore-Tex thread).[5] Frontalis suspension has good long-term effects and is well-accepted by patients.[5,7] Most patients receive continued botulinum therapy to alleviate the orbicularis oculi contraction.[5] Frontalis suspension with concomitant upper blepharoplasty achieves good cosmetic and functional results in patients with dermatochalasis.[4]

Other surgical techniques have been suggested as treatment for BEB. Selective peripheral facial nerve avulsion showed high recurrence rate and risk of facial nerve palsy.[8] Orbicularis muscle resection (orbicularis stripping) was more effective. It involves resecting muscles for eyelid closure (the orbicularis, procerus, and corrugator muscle), but recurrence may occur owing to incomplete removal of all orbicularis oculi.[8-10]

Botulinum toxin therapy is most commonly used for blepharospasm. Five type A formulations and one type B formulation are commercially available.[11] Various botulinum toxin type A show similar safety and efficacy, but they are not interchangeable. Botulinum toxin type B is approved by US Food and Drug Administration for cervical dystonia only.

In addition, FL-41 tinted lenses were helpful for BEB. They are rose-tinted lens that can improve light sensitivity and blepharospasm, and also reduce the mean blink rate.[12] Nevertheless, there is little information regarding the use of FL-41 tinted lenses for AEO.

In conclusion, frontalis suspension can be a treatment option for patients with BEB with AEO, especially in those who failed botulinum toxin therapy. In the presence of coexisting dermatochalasis, frontalis suspension can be combined with blepharoplasty with direct fixation of silicone rod onto the tarsal plate.

Author contributions

Concept or design: HKLY.
Acquisition of data: HKLY.
Analysis or interpretation of data: JCKC.
Drafting of the article: JCKC.
Critical revision for important intellectual content: HKLY.

The authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

As an Editor of the Journal, HKLY was not involved in the peer review process for this article. All authors have no conflicts of interest to disclose.

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Ethics approval

The patient was treated in accordance with the Declaration of Helsinki. Informed consent was obtained from the patient for the operations and the publication of clinical photos.

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CASE REPORT

Long-term outcomes of free internal limiting membrane transplant for unclosed macular holes after extensive internal limiting membrane peeling and silicone oil tamponade: a report of two cases

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Abstract

We report the long-term outcome of two cases of free internal limiting membrane (ILM) transplant for unclosed macular holes after extensive internal limiting membrane peeling and silicone oil tamponade. Free ILM graft was harvested and then successfully tucked against the inner edges of the macular hole in two eyes. All macular holes closed. In one case, the ILM filled the macular hole 100% in all meridians and remained closed 7 years after surgery. In another case, the ILM filled the gap of the macular hole 100% in the horizontal meridian and approximately 70% in the vertical meridian and re-opened 5 weeks after surgery. Filling the entire macular hole area with the ILM graft may improve long-term anatomical outcomes.

Introduction

The first randomized controlled study of internal limiting membrane (ILM) peeling on macular hole surgery was published in 2005.[1] Subsequently vitrectomy with ILM peeling has been shown to significantly improve the anatomical and visual outcomes of idiopathic full-thickness stage 2, 3, and 4 macular holes.[1,2] In order to avoid the demanding face-down posturing after idiopathic macular hole surgery, intraoperative broad ILM peeling up to the temporal vascular arcades has been reported.[3] The combination of these techniques gives the patient the best chance of macular hole closure with postoperative comfort. However, not all macular holes close after this approach, especially those that are large and chronic.[4-8] The inverted ILM flap technique for large primary macular holes has been reported with encouraging results.[4] However, this technique is unsuitable for eyes with unclosed macular holes after previous surgery with extensive ILM peeling and silicone oil tamponade. We herein describe the long-term outcomes of two patients who underwent a novel free ILM transplant technique for treating unclosed macular holes after previous surgery with extensive ILM peeling and silicone oil tamponade.

Case presentation

Case 1

On 22 February 2011, a 52-year-old Chinese man presented with loss of right eye vision after an impact from a soccer ball 1 week before. His past health was unremarkable, except for having undergone bilateral laser-assisted in situ keratomileusis (LASIK) in 2011 and left conductive keratoplasty for presbyopic correction in 2008. On examination, unaided distant visual acuity was hand movement for the right eye and 20/25+2 for the left eye. The right eye was found to have traumatic hyphaemia, cataract, and vitreous hemorrhage without fundal view. Intraocular pressure was 5 mmHg for the right eye and 24 mmHg for the left eye. Ultrasonography of the right eye had been performed 1 day before at a different hospital, and cataract and vitreous surgery had been advised. Left eye examination results were unremarkable.

On 24 February 2011, phacoemulsification, intraocular lens implant, and vitrectomy of the right eye were performed. Intraoperatively, the temporal half of the retina was found detached with superior retinal dialysis associated with multiple retinal holes, as well as a macular hole and holes temporal and inferotemporal to the macula. The macular epiretinal membrane and extensive macular ILM were removed from arcade to arcade with staining by Membrane Peel (Dutch Ophthalmic, USA). The retina was then fully reattached with heavy liquid, retinal endophotocoagulation, and silicone oil tamponade.

On 9 April 2011, unaided distant visual acuity of the right eye was 20/300. The retina was fully reattached, but a macular hole remained open. We discussed with the patient about the inverted ILM flap technique and the free ILM transplant technique (which had not been reported in the world). After consultation, the patient agreed to another vitreous surgery with free ILM transplant.

On 26 April 2011, repeat vitrectomy with oil removal was performed. The ILM outside the inferior vascular arcade was stained with Membrane Blue (Dutch Ophthalmic, USA), and a piece of the ILM similar in size to the macular hole was harvested and then tucked against the inner edges of the macular hole. The ILM filled the gap of the macular hole 100% in the horizontal meridian and approximately 70% in the vertical meridian. Silicone oil was re-instituted.

On 3 May 2011, unaided distant visual acuity of the right eye was 20/300+. Optical coherent tomography (OCT) at 5 weeks showed that the retina was fully reattached, and the macular hole was completely closed (flat/close), except for a suspicious gap (flat/open) in the 300° meridian scan (**Figure 1**).

On 2 June 2011, unaided distant visual acuity of the right eye remained 20/300+. The retina was fully reattached, but the macular hole re-opened. Further macular hole surgery was declined. His eye condition remained stable at the most recent follow-up in 2019.

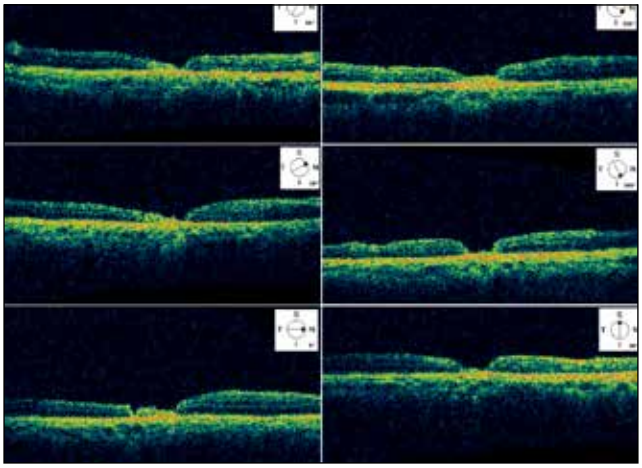

Figure 1. Patient 1: optical coherent tomography scans of the right eye at 5 weeks after free internal limiting membrane transplant showing the fully reattached retina and the completely closed (flat/close) macular hole, except for a suspicious gap (flat/open) in the 300° meridian scan.

Case 2

On 11 July 2011, a 41-year-old Chinese man presented with a history of poor right eye vision with a macular hole since age 7 years. His past health was unremarkable, except for having undergone right inferior laser barrier during adolescence. On examination, aided distant visual acuity was 20/150 (-2 D) for the right eye and 20/20 (-2.75 D/-0.75×180) for the left eye. Ocular examination using OCT was unremarkable, except for the presence of a right chronic stage 4 macular hole with a large rim of subretinal fluid and inferior peripheral retinal laser marks (**Figure 2a**). Management options (observation, vitrectomy with gas or oil tamponade, and sequential or combined cataract and vitreous surgery) for the right chronic macular hole was discussed, with very guarded prognosis.

On 2 September 2011, phacoemulsification, intraocular lens implant, vitrectomy, extensive macular ILM peeling, and silicone oil tamponade of the right eye was performed. Postoperatively, right eye vision was stable, and the macular hole was smaller with almost complete resolution of subretinal fluid but did not fully close (**Figure 2b**). We discussed with the patient about the inverted ILM flap technique and the free ILM transplant technique (which had not been reported in the world). After consultation, the patient agreed to another vitreous surgery with free ILM transplant.

On 20 January 2012, vitrectomy of the right eye with oil removal was performed. The ILM outside the inferior vascular arcade was stained with Membrane Blue (Dutch Ophthalmic, USA) and two pieces of ILM larger than the macular hole were harvested and tucked against the inner edges of the macular hole. The first ILM did not fill the macular hole 100% in all meridians. A second piece of ILM was added to fill the macular hole 100% in all meridians. A two-stage air/fluid exchange was performed, followed by air / 12% perfluoropropane gas exchange. Through the gas

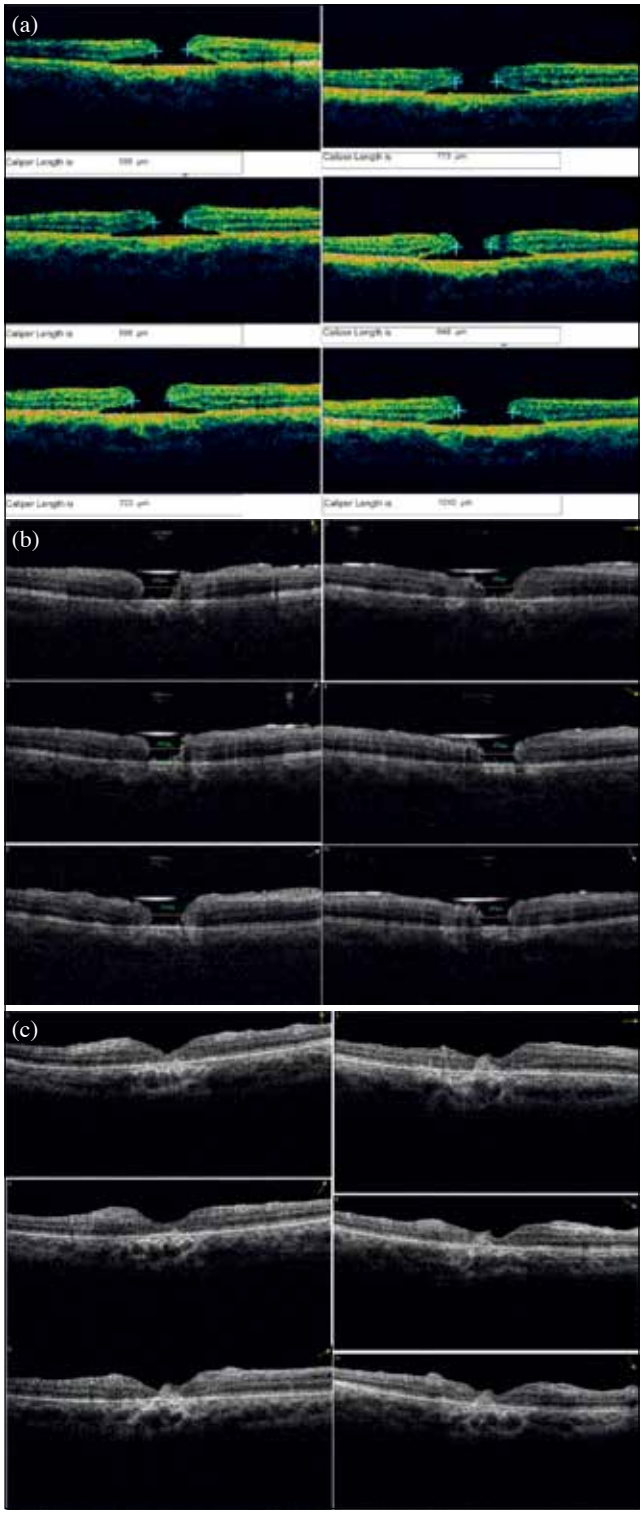

Figure 2. Patient 2: optical coherent tomography scans of the right eye (a) before the first macular hole surgery showing the presence of a chronic stage 4 macular hole with a large rim of subretinal fluid; (b) before free internal limiting membrane transplant showing the smaller macular hole with almost complete resolution of subretinal fluid but did not fully close; (c) after free internal limiting membrane transplant showing the remained closed macular hole at 26 months.

bubble, the macular hole was seen stained blue by the stained ILMs. For the first 2 weeks postoperatively, the patient was advised to adopt a reading posture when awake and lying lateral when sleep.

On 20 February 2012, his unaided visual acuity of the right eye was 20/200-, with a closed macular hole. On 15 April 2014, aided distant visual acuity of the right eye was 20/150+. The patient considered that right eye vision was subjectively improved. At 26 months after surgery, OCT showed that the macular hole remained closed (**Figure 2c**). He subsequently developed glaucoma in the right eye that was finally controlled by trabeculectomy surgery with mitomycin C. His visual acuity and eye condition remained stable at the most recent follow-up in 2018.

Discussion

To the best of our knowledge, these are the first two patients worldwide to undergo free ILM transplant for treating unclosed macular holes after previous surgery with extensive ILM peeling and silicone oil tamponade. We herein report the long-term outcomes of this novel treatment. Morizane et al[5] reported a similar technique in five eyes with failed primary macular hole surgery, with four holes closed. Their first case was performed 15 months after our first case and they did not report whether these macular holes received extensive ILM peeling and/or silicone oil tamponade in previous surgery. Intraoperatively, they used an ILM graft of similar size to that of the macular hole. Additionally, they used a viscoelastic device to help keeping the graft in place. We advocate to use one or more layers of ILM graft larger than the size of the macular hole for several reasons. Firstly, the ILM graft is elastic and curls over itself, decreasing the overall size. Secondly, a larger graft is easier to tuck against the edge of the macular hole, which then has a greater chance of staying in place without the need of injecting a viscoelastic device. Such a procedure might open up the macular hole further and dislodge the graft inadvertently or distort the surgical view of the macula. However, some surgeons use a viscoelastic device to lift the edges of the macular hole, especially in flat or open holes, to facilitate tucking in of the graft material. Thirdly, a larger graft provides a larger number of Muller cells, as well as a larger scaffold for Muller cells to proliferate. These are essential for macular hole closure.[4] Morizane et al asked the patients to stay face down for 3 days after surgery; however, we believe that this is unnecessary as long as extensive ILM is peeled and the ILM graft fills the entire macular hole.[3] In addition, they did not report any long-term change of the implanted ILM; they only showed OCT scans from 14 days and 3 months after surgery.[5] In summary, the novel free ILM transplant technique is a viable option to treat unclosed macular holes after previous surgery of extensive internal limiting membrane peeling and silicone oil tamponade. Other sources of graft material, include contralateral ILM graft, autologous neurosensory retinal transplantation, and lens capsular flap transplantation.[6-8] Further studies are needed to determine the best graft sizes for different graft materials.

Author contributions

Concept or design: AKHK.
Acquisition of data: AKHK.
Analysis or interpretation of data: AKHK.
Drafting of the article: AKHK.
Critical revision for important intellectual content: AKHK.

The author had full access to the data, contributed to the study, approved the final version for publication, and takes responsibility for its accuracy and integrity.

Conflicts of interest

As an editor of the Journal, Dr Alvin KH Kwok was not involved in the peer review process for this article.

Declaration

Presented in part at (1) Conjoint Grand Round held by Departments of Ophthalmology, Hong Kong Sanatorium and Hospital, Hong Kong East Cluster, Queen Mary Hospital and University of Hong Kong, and United Christian Hospital, December 2011; and (2) Meeting, Department of Ophthalmology, Yokohama City University Medical Centre, Yokohama, Japan, 7 March 2018.

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Ethics approval

This study was approved by the Hong Kong Sanatorium & Hospital Research Ethics Committee (Reference No.: 201821). The patients provided written informed consent for treatments and procedures.

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Report on the 33rd Asia-Pacific Academy of Ophthalmology Congress, Hong Kong, 8-11 February 2018

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Introduction

The 33rd Asia-Pacific Academy of Ophthalmology (APAO) 2018 Congress in conjunction with the 29th Hong Kong Ophthalmological Symposium took place at the Hong Kong Convention and Exhibition Centre from 8 to 11 February 2018. It was attended by 5206 delegates from 63 countries.

Scientific Program

Under the chairmanship of Prof Dennis Lam, the scientific program committee (http://2018.apaophth.org/program-committee/), with its 117 members from across the world, put together the invited scientific program. The invited scientific program comprised 177 sessions, covered 17 subspecialty areas, and was presented by 602 distinguished clinicians and scientists from around the world. In addition to the established clinical ophthalmology subspecialties, the program also encompassed areas such as ophthalmic education, translational research and visual sciences, which are important for the future development of ophthalmology (**Figure 1**).

In the submitted program, out of 1500 submissions, 274 abstracts were presented in Free Paper sessions, while 381 abstracts were presented as scientific posters. A total of 22 submitted instruction courses were also presented. Additionally, there were a total of 389 e-poster and 62 video abstract presentations. The presented abstracts covered 16 different subspecialties and represented 28 different countries across the globe. For the first time in an APAO Congress, awards were presented to the best submitted free papers (26 oral presentation awards chosen by the Abstract Review Committee), as well as the most popular posters, e-posters, and videos (5 in each category, selected based on delegate voting).

In addition, the APAO 2018 Congress was the first APAO Congress to feature 'wet lab' surgical teaching sessions (**Figure 2**). With 21 sponsored courses covering a wide range of topics, including intravitreal injection, SMILE, phacoemulsification, DMEK, DSAEK and more, the popular sessions provided delegates with interactive hands-on experience and were fully booked even before the Congress began.

Social Program

The Opening Ceremony was held on 8 February 2018 with Prof Sophia Chan, Hong Kong Secretary for Food and Health, as the Guest of Honor. After opening speeches from Prof Chan and other distinguished guests, the APAO named awards and lectures were presented (**Figure 3**).

The APAO 2018 Presidential Dinner was held on racing night at the Hong Kong Jockey Club on February 7, 2018, where members of the scientific program committee and other guests enjoyed horse racing and tried their luck at the betting counters.

Figure 1. Academy of Asia-Pacific Professors of Ophthalmology Academic Development Mentorship Scheme & Asia-Pacific Vitreo-retina Society Leadership Development Program: Meeting the Masters and Keynote Lecture, 9 February 2018.

Figure 2. Participants at one of the many Wet Laboratory Instruction Courses.

Figure 3. Opening Ceremony, 8 February 2018. From left: Dr Carmen Chan, Prof Jimmy Lai, Dr Gullapalli Nag Rao, Prof Charles McGhee, Prof Sophia Chan (Guest of Honour), Prof Clement Tham, Dr Hugh Taylor, Dr Jeffrey Pong, and Prof Dennis Lam.

The 3rd APAO Charity Run took place on the morning of 10 February 2018, starting from the Hong Kong Observation Wheel. More than 180 participants raised nearly US$13 000, which was divided equally between the new APAO Satellite Congress educational program and Blind Sports Hong Kong. A complete list of winners in the different race categories is available online (http://2018.apaophth.org/charity-run-result/). On the same evening, the APAO 2018 Gala Dinner, held at the Hong Kong Convention and Exhibition Centre, offered delegates a taste of old Hong Kong, including traditional Chinese medicine, fresh *gai daan zai* and more. The APAO awards (Distinguished Service, Prevention of Blindness, Senior Achievement, Achievement), best scientific paper awards and Yasuo Tano Travel grants were presented during the Gala Dinner. The full list of award recipients can be found in the APAO 2018 program book (http://2018.apaophth.org/publications/)

The APAO 2018 social program also included the first APAO Women in Ophthalmology lunch, Young Ophthalmologists' night and the Leadership Development Program Alumni Reception.

Conclusion

APAO 2018 no doubt achieved the objectives of providing an

excellent platform for professional and scientific exchanges in the field of ophthalmology, as well as raising the standard of eye care through world-class educational programs. We look forward to the future APAO Congresses. The full details of the APAO 2018 Congress, including a PDF copy of the complete program book can be found on http://2018.apaophth.org/.

Author contributions

Concept or design: CCYT
Acquisition of data: All
Analysis or interpretation of data: All
Drafting of the article: All
Critical revision for important intellectual content: All

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of Interest

Clement Tham was the Congress President of the Asia-Pacific Academy of Ophthalmology (APAO) Congress 2018 Hong Kong, and the Secretary-General & CEO of APAO. Carmen Chan was the Chair of the APAO 2018 Organizing Committee.

Acknowledgment

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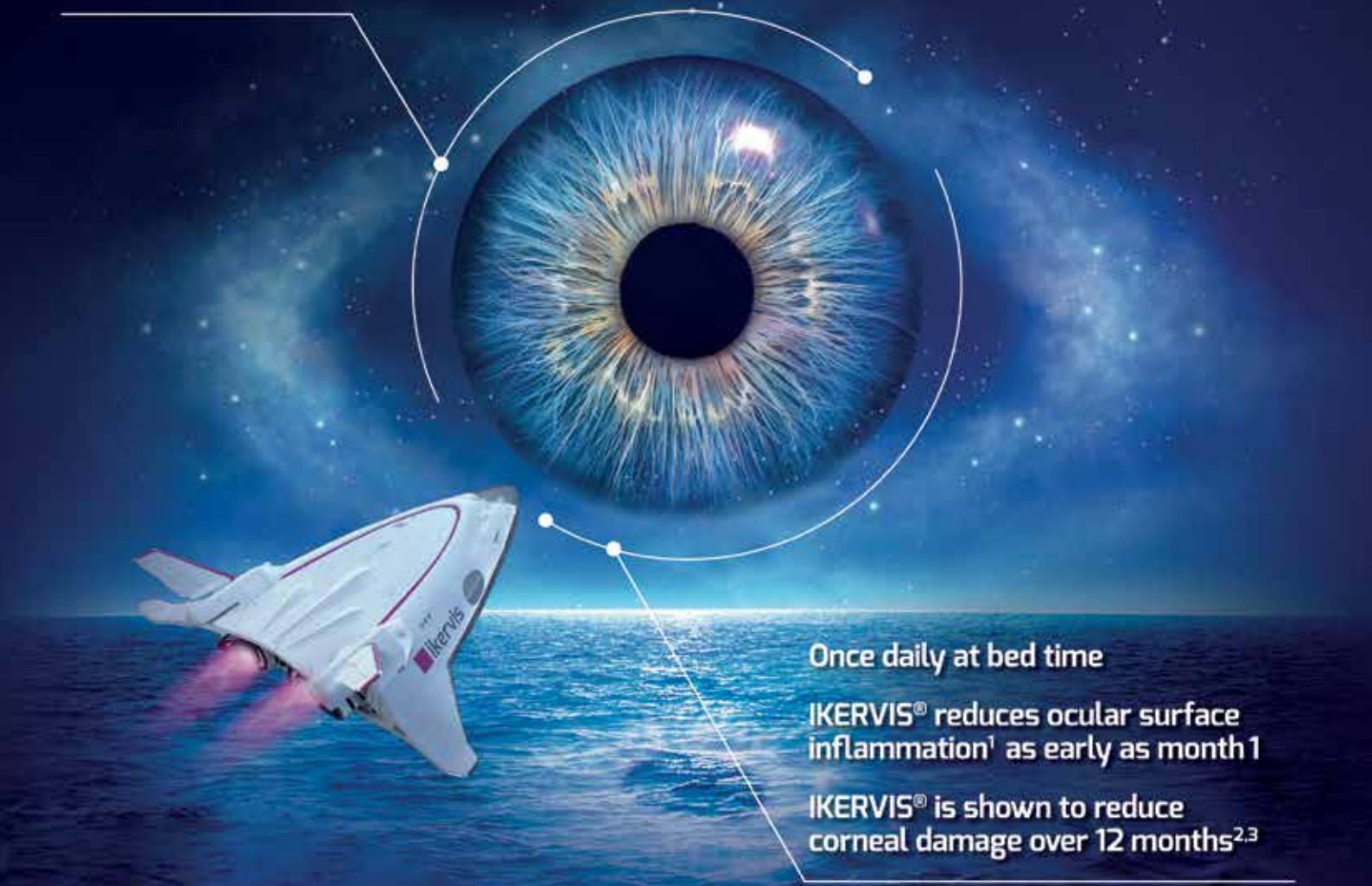

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IKERVIS® 1 mg/mL eye drops, emulsion (ciclosporin) ABBREVIATED PESCRIBING INFORMATION. One mL of emulsion contains 1 mg of ciclosporin. IKERVIS® is supplied in 0.3 mL single-dose, low-density polyethylene (LDPE) containers presented in a sealed laminate aluminium pouch. One pouch contains five single-dose containers. Pack size: 30 single-dose containers. One mL of emulsion contains 0.05 mg of cetalkonium chloride. **Indication:** Treatment of severe keratitis in adult patients with dry eye disease, which has not improved despite treatment with tear substitutes. **Posology:** IKERVIS® treatment must be initiated by an ophthalmologist or a healthcare professional qualified in ophthalmology. The recommended dose is one drop of IKERVIS®, once daily, to be applied to the affected eye(s) at bedtime. Response to treatment should be reassessed at least every 6 months. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. Active or suspected ocular or peri-ocular infection. **Warnings /Precautions:** IKERVIS® has not been studied in patients with a history of ocular herpes and should therefore be used with caution in such patients. Contact lenses: Patients wearing contact lenses have not been studied. Careful monitoring of patients with severe keratitis is recommended. Contact lenses should be removed before installation of the eye drops at bedtime and may be reinserted at wake-up time. Concomitant therapy: There is limited experience with IKERVIS® in the treatment of patients with glaucoma. Caution should be exercised when treating these patients concomitantly with IKERVIS®, especially with beta-blockers which are known to decrease tear secretion. Effects on the immune system: Medicinal products, which affect the immune system, including ciclosporin, may affect host defences against infections and malignancies. Co-administration of IKERVIS® with eye drops containing corticosteroids could potentiate the effects of IKERVIS® on the immune system. IKERVIS® contains cetalkonium chloride which may cause eye irritation. **Interaction with other medicinal products and other forms of interaction:** No interaction studies have been performed with IKERVIS®. **Pregnancy:** IKERVIS® is not recommended during pregnancy unless the potential benefit to the mother outweighs the potential risk to the foetus. **Effects on ability to the drive and use machines:** IKERVIS® has moderate influence on the ability to drive and use machines. **Undesirable effects:** In four clinical studies including 532 patients who received IKERVIS® and 398 who received IKERVIS® vehicle (control), IKERVIS® was administered at least once a day in both eyes, for up to one year. The most common adverse reaction were eye pain (19%), eye irritation (17.8%), lacrimation (6.2%), ocular hyperaemia (5.5%) and eyelid erythema (1.9%), which were usually transitory and occurred during instillation. The majority of adverse reactions reported in clinical studies with the use of IKERVIS® were ocular and mild to moderate in severity. **Special precautions for storage:** Do not freeze. After opening of the aluminium pouches, the single-dose containers should be kept in the pouches in order to protect form light and avoid evaporation. Any opened individual single-dose container with any remaining emulsion should be discarded immediately after use. **Last text revision:** Dec 2017

HK-KIR-0002/2018_06

Reference: 1. Leonardi A et al. Cornea. 2013;32(3):345-354. 2. Baudouin C et al. Eur J Ophthalmol. 2017; 27(6): 678 – 685. 3. Pisella PJ et al. Clin Ophthalmol. 2018;12:289-299.

Please consult the full prescribing information prior to administration. For adverse events reporting, please email Santen Pharmaceutical (Hong Kong) Ltd. at hk_product_safety@santen.com

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A Clear Vision For Life®

Santen Pharmaceutical (Hong Kong) Ltd.
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For Healthcare Professionals Only

LUCENTIS®:

THE ANTI-VEGF IN A PRE-FILLED SYRINGE (PFS)

Significant Time- & Step-Saving in Daily Practice[1,2]

PREPARATION TIME*

×2.9 longer than PFS[2] ($p < 0.001$)

3 LESS steps†,2

PREPARATION STEPS

3 steps in total

LUCENTIS® PFS

6 steps in total

aflibercept vial

- Treat more patients per session[2]
- Treat the same number of patients in a shorter time[2]
- Spend more time in discussion with patients[2]

LUCENTIS® is indicated for[3]:

· nAMD · DME · BRVO · CRVO · CNV

* Mean total syringe preparation time. Based on the results of a non-interventional, real-world study[2] conducted in Canada, which the syringe preparation time of LUCENTIS® PFS (n = 84), LUCENTIS® vial (n = 84) and aflibercept vial (n = 52) at 4 centres (3 centres for aflibercept vial) was compared.

† With LUCENTIS® PFS, it is no longer required to "attach filter needle", "disinfect vial lid" and "draw drug from vial using filter needle"[2].

BRVO = branch retinal vein occlusion. CNV = choroidal neovascularisation. CRVO = central retinal vein occlusion. DME = diabetic macular oedema. nAMD = neovascular age-related macular degeneration. PFS = prefilled syringe. VEGF = vascular endothelial growth factor.

References: 1. Subhi Y, Kjer B, Munch IC. Dan Med J. 2016;63:A5214. 2. Giunta M, Lalonde L, Cordahi G, et al. 7th COPHy World Congress; 2016 Mar 31-Apr 2; Warsaw (Poland). Poster 28 (Group A). 3. LUCENTIS® (ranibizumab) solution for injection in pre-filled syringe prescribing information. Hong Kong; 2017 Jul.

LUCENTIS®

Note: Before prescribing, consult full prescribing information.

Presentation: Vial: Ranibizumab. Each vial contains 2.3 mg of ranibizumab in 0.23 mL solution. Pre-filled syringe: Ranibizumab. Each pre-filled syringe contains 1.65 mg of ranibizumab in 0.165 mL solution. The extractable volume of one pre-filled syringe is 0.1 ml. This provides a usable amount to deliver a single dose of 0.05 ml containing 0.5 mg ranibizumab. **Indications:** •Treatment of neovascular (wet) age-related macular degeneration (AMD). •Treatment of visual impairment due to diabetic macular oedema (DME). • Treatment of visual impairment due to macular oedema secondary to retinal vein occlusion (branch RVO or central RVO). • Treatment of visual impairment due to choroidal neovascularisation (CNV). **Dosage and administration**: • The recommended dose is 0.5 mg (0.05 mL) given as a single intravitreal injection. The interval between two doses injected into the same eye should be at least four weeks. • Treatment is initiated with one injection per month until maximum visual acuity is achieved and/or there are no signs of disease activity. •Thereafter, monitoring and treatment intervals should be determined by the physician and should be based on disease activity as assessed by visual acuity and/or anatomic parameters. • Monitoring for disease activity may include clinical examination, functional testing or imaging techniques (e.g. optical coherence tomography or fluorescein angiography). In patients with wet AMD, DME and RVO, initially, three or more consecutive, monthly injections may be needed. The treatment of visual impairment due to CNV should be determined individually per patient based on disease activity. Some patients may only need one injection during the first 12 months; others may need more frequent treatment, including a monthly injection. For CNV secondary to pathologic myopia (PM), many patients may only need one or two injections during the first year. • **treat-and-extend regimen** :While applying the treat-and-extend regimen, the treatment interval should be extended by no more than two weeks at a time for wet AMD and extended by up to one month at a time for DME. For RVO, treatment intervals may also be gradually extended, however there are insufficient data to conclude on the length of these intervals. If disease activity recurs, the treatment interval should be shortened accordingly. •**Lucentis and laser photocoagulation in DME or in branch RVO**: Lucentis has been used concomitantly with laser photocoagulation in clinical studies. When given on the same day, Lucentis should be administered at least 30 minutes after laser photocoagulation. Lucentis can be administered in patients who have received previous laser photocoagulation. •Lucentis must be administered by a qualified ophthalmologist using aseptic techniques. Broad-spectrum topical microbicide and anesthetic should be administered prior to the injection. •Not recommended in children and adolescents. **Contraindications**: Hypersensitivity to ranibizumab or to any of the excipients, patients with active or suspected ocular or periocular infections, patients with active intraocular inflammation. **Warnings and precautions**: •Intravitreal injections have been associated with endophthalmitis, intraocular inflammation, rhegmatogenous retinal detachment, retinal tear and iatrogenic traumatic cataract. Therefore proper aseptic injection techniques must be used. Patients should be monitored during the week following the injection to permit early treatment if an infection occurs. •Transient increases in intraocular pressure (IOP) have been seen within 60 minutes of injection of Lucentis. Sustained IOP increases have also been reported. Intraocular pressure and the perfusion of the optic nerve head must be monitored and managed appropriately. Patients should be informed of the symptoms of these potential adverse reactions and instructed to inform their physician if they develop signs such as eye pain or increased discomfort, worsening eye redness, blurred or decreased vision, an increased number of small particles in their vision, or increased sensitivity to light.•There is a potential risk of arterial thromboembolic events following intravitreal use of VEGF inhibitors. A low incidence rate of arterial thromboembolic events was observed in the Lucentis clinical trials in patients with AMD, DME, RVO and CNV and there were no major differences between the groups treated with ranibizumab compared to control. Patients with known risk factors for stroke, including history of prior stroke or transient ischemic attack should be carefully evaluated by their physicians as to whether Lucentis treatment is appropriate and the benefit outweighs the potential risk. •Available data do not suggest an increased risk of systemic adverse events with bilateral treatment. •As with all therapeutic proteins, there is a potential for immunogenicity with Lucentis. •Lucentis has not been studied in patients with active systemic infections or in patients with concurrent eye conditions such as retinal detachment or macular hole. •There are insufficient data to conclude on the effect of Lucentis in patients with RVO presenting irreversible ischaemic visual function loss.•Should not be used during pregnancy unless the expected benefit outweighs the potential risk to the fetus. For women who wish to become pregnant and have been treated with ranibizumab, it is recommended to wait at least 3 months after the last dose of ranibizumab before conceiving a child; use of effective contraception is recommended for women of child-bearing potential; breast-feeding is not recommended. •Following treatment patients may develop transient visual disturbances that may interfere with their ability to drive or use machines. Patients should not drive or use machines as long as these symptoms persist. •Risk factors associated with the development of a retinal pigment epithelial tear after anti-VEGF therapy for wet AMD and potentially also other forms of CNV, include a large and/or high pigment epithelial retinal detachment. When initiating Lucentis therapy, caution should be used in patients with these risk factors for retinal pigment epithelial tears. **Interactions**: No formal interaction studies have been performed. **Adverse drug reactions**: • **Very common (≥10%)**:, vitritis, vitreous detachment, retinal hemorrhage, visual disturbance, eye pain, vitreous floaters, conjunctival hemorrhage, eye irritation, foreign body sensation in eyes, lacrimation increased, blepharitis, dry eye, ocular hyperemia, eye pruritus, intraocular pressure increased, nasopharyngitis, headache, arthralgia. • **Common (1 to 10%)**: hypersensitivity, retinal degeneration, retinal disorder, retinal detachment, retinal tear, detachment of the retinal pigment epithelium, retinal pigment epithelium tear, visual acuity reduced, vitreous hemorrhage, vitreous disorder, uveitis, iritis, iridocyclitis, cataract, cataract subcapsular, posterior capsule opacification, punctuate keratitis, corneal abrasion, anterior chamber flare, vision blurred, injection site hemorrhage, eye hemorrhage, conjunctivitis, conjunctivitis allergic, eye discharge, photopsia, photophobia, ocular discomfort, eyelid edema, eyelid pain, conjunctival hyperemia, urinary tract infection*, anemia, anxiety, cough, nausea, allergic reactions (rash, pruritus, urticaria, erythema). • **Uncommon (0.1 to 1%)** : blindness, endophthalmitis, hypopyon, hyphema, keratopathy, iris adhesions, corneal deposits, corneal edema, corneal striae, injection site pain, injection site irritation, abnormal sensation in eye, eyelid irritation. • **Serious adverse events** related to intravitreal injections include endophthalmitis, blindness, rhegmatogenous retinal detachment, retinal tear and iatrogenic traumatic cataract. **observed only in the DME population* A meta-analysis of pooled safety data from completed, randomized, double masked global studies showed a higher incidence rate of non-serious, non-ocular wound infection/inflammation in DME patients treated with ranibizumab 0.5 mg (1.85/100 patient years) compared to control (0.27/100 patient years). The relationship to ranibizumab remains unknown. **Packs**: 1 vial or 1 pre-filled syringe per pack. Not all packs are marketed. **Legal classification:** P1S1S3.

NOVARTIS

Novartis Phamaceuticals (HK) Limited

7/F, Citi Tower, One Bay East, 83 Hoi Bun Road, Kwun Tong, Kowloon, Hong Kong Tel: (852) 2882 5222 Fax: (852) 2577 0274

HK1909730357

LUCENTIS® RANIBIZUMAB

DESIGNED TO SAVE SIGHT

Simbrinza Important note: Before prescribing, consult full prescribing information. **Presentation:** Eye drops, suspension: One mL of eye drop suspension contains 10 mg brinzolamide, 2 mg brimonidine tartrate (equivalent to 1.3 mg brimonidine). **Indications:** Decrease of elevated intraocular pressure (IOP) in adult patients with open-angle glaucoma or ocular hypertension for whom monotherapy provides insufficient IOP reduction. **Dosage and administration:** ♦**Adults:** One drop in the affected eye(s) 2 times daily. ♦**Paediatric patients (below 18 years):** Must not be used in neonates and infants younger than 2 years old. Not recommended in children or adolescents aged 2 to 17 years. ♦**Method of administration:** For ocular use. ♦If more than one topical ophthalmic medicinal product is used, the medicines must be administered at least 5 minutes apart. **Contraindications:** ♦Hypersensitivity to the active substances or to any of the excipients or to sulphonamides. ♦Patients receiving monoamine oxidase (MAO) inhibitor therapy. ♦Severe renal impairment. ♦Hyperchloraemic acidosis. ♦Neonates and infants younger than 2 years old. ♦Patients on antidepressants which affect noradrenergic transmission (e.g. tricyclic antidepressants and mianserin) **Warnings and precautions:** ♦In case of allergic reactions due to brimonidine tartrate, treatment should be discontinued. ♦Risk of delayed ocular hypersensitivity reactions associated with an increase in IOP. ♦If signs of serious reactions or hypersensitivity occur, discontinue the use of the product. ♦Careful monitoring of patients with compromised corneas, such as patients with diabetes mellitus or corneal dystrophies, is recommended. ♦Caution in patients with risk of renal impairment because of the possible risk of metabolic acidosis. ♦Caution in patients with hepatic impairment ♦Caution in patients with depression, cerebral or coronary insufficiency, Raynaud's phenomenon, orthostatic hypotension or thromboangiitis obliterans. ♦Benzalkonium chloride may cause eye irritation and is known to discolor soft contact lenses. ♦Contact lenses must be removed before administration and wait at least 15 minutes before reinsertion. ♦Temporary blurred vision or other visual disturbances may affect the ability to drive or use machines, patient must wait until the vision clears before driving or using machines. **Paediatric population:** Simbrinza is not recommended in children or adolescents aged 2 to 17 years because of the potential for CNS-related side effects. **Pregnancy, lactation, females and males of reproductive potential:** ♦**Pregnancy:** ♦No or limited amount of data in pregnant women. ♦ **Lactation:** It is unknown whether following topical administration the drug is excreted in human milk. Brimonidine administered orally was excreted in breast milk. **Adverse drug reactions:** ♦**Common (≥ 1/100 to <1/10):** somnolence, dysgeusia, eye allergy, keratitis, eye pain, ocular discomfort, blurred vision, ocular hyperaemia, dry mouth ♦**Uncommon (≥1/1,000 to <1/100):** insomnia, headache, corneal erosion, blepharitis, corneal deposits (keratic precipitates), conjunctival disorder (papillae), photophobia, eyelid oedema, conjunctival oedema, dry eye, eye discharge, lacrimation increased, erythema of eyelid, abnormal sensation in eye, asthenopia, vertigo, hypotension, dry throat, nasal congestion, nasal dryness, postnasal drip, dyspepsia, abdominal discomfort, paraesthesia oral, dermatitis contact, medication residue **Overdose:** Due to the brinzolamide component of Simbrinza, electrolyte imbalance, development of an acidotic state, and possible nervous system effects may occur. Oral overdoses of other alpha-2-agonists have been reported to cause symptoms such as hypotension, asthenia, vomiting, lethargy, sedation, bradycardia, arrhythmias, miosis, apnoea, hypotonia, hypothermia, respiratory depression and seizure. **Paediatric population overdose:** Serious adverse effects related to the brimonidine component following inadvertant ingestion of Simbrinza include CNS depression, typically temporary coma or low level of consciousness, lethargy, somnolence, hypotonia, bradycardia, hypothermia, pallor, respiratory depression and apnoea. **Interactions:** The drug is known to interact with Monoamine oxidase inhibitors, oral carbonic anhydrase inhibitors, antihypertensive and/or cardiac glycosides, tricyclic antidepressants, medicinal products which can affect the metabolism and uptake of circulating amines (e.g. chlorpromazine, methylphenidate, reserpine), CNS depressants (e.g. alcohol, barbiturates, opiates, sedatives or anaesthetics), agonists or antagonists of the adrenergic receptor (e.g. isoprenaline, prazosin). Concomitant use with oral carbonic anhydrase inhibitors is not recommended. **Packs:** 5 ml **Legal classification:** P1S1S3 **Reference:** EMA CPP Sep 2016 V2

References:
1. SIMBRINZA® Suspension Summary of Product Characteristics.

*1 mL of suspension contains 10 mg of brinzolamide and 2 mg of brimonidine tartrate

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Get rid of the frustration of dry eyes

- 0.24% hyaluronic acid
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- Compatible with contact lenses

*PFMD= Preservative Free Multi-Dose

Reference: Product Insert of Artelac® Splash MDO

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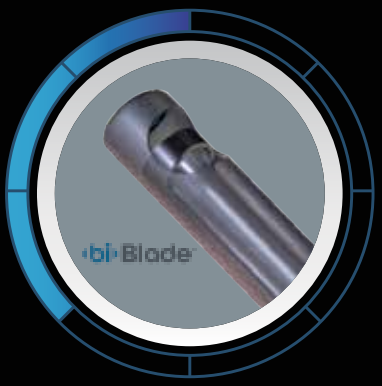
Stellaris Elite™ has the built-in capability to optimize value for multi-use enviroments now and as future practice needs arise.



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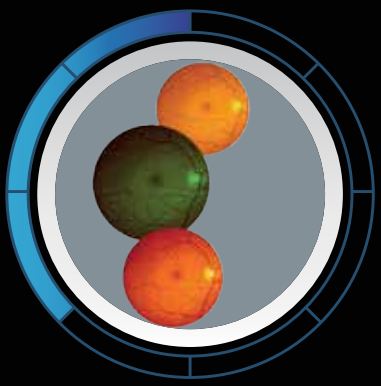
Stellaris Elite™ adapts to a wide range of procedural needs from 20Ga to 27Ga, from 7500cpm up to 15000cpm.



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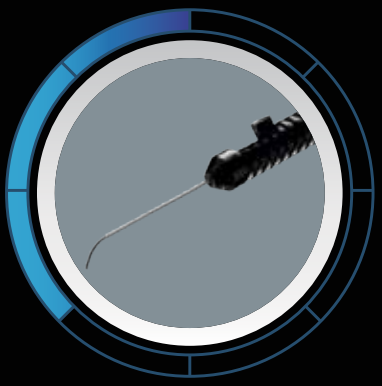

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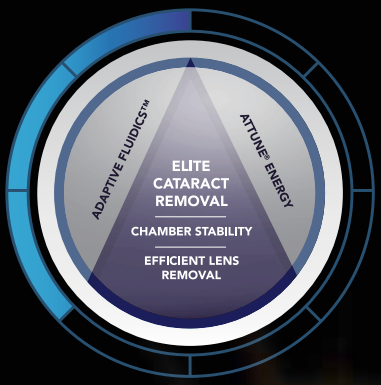

ELITE CATARACT REMOVAL

Reference: Stellaris Elite™ IFU

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Clinically Proven Treatment To Reduce the Risk of Advanced Age-Related Macular Degeneration[1-3]

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- ß-carotene free, suitable for smokers/non-smokers[4]

Enquiry: (852) 2213-3877

Reference: 1) Press Release for the Media: Questions and Answers about AREDS2, National Eye Institute, 2013 2) The Age-Related Eye Disease Study 2 (AREDS2) Research Group. Lutein + Zeaxanthin and Omega-3 Fatty Acids for Age-Related Macular Degeneration: the Age-Related Eye Disease Study 2 (AREDS2) Randomized Clinical Trial. JAMA. 2013, 15;309(19): 2005-15 3) Chew EY. Nutrition, Genes, and Age-Related Macular Degeneration: What Have We Learned from the Trials? Ophthalmologica. May 6, 2017 4) Product Insert of Ocuvite® AREDS 2 5) Hobbs RP. Bernstein PS; Nutrient Supplementation for Age-related Macular Degeneration, Cataract, and Dry Eye. J Opthalmic Vis Res. 2014, 9(4): 487-93 6) Aronow ME, Chew EY; Age-related Eye Disease Study 2: perspectives, recommendations, and unanswered questions. Curr Opin Ophthalmol. 2014, 25(3): 186-9

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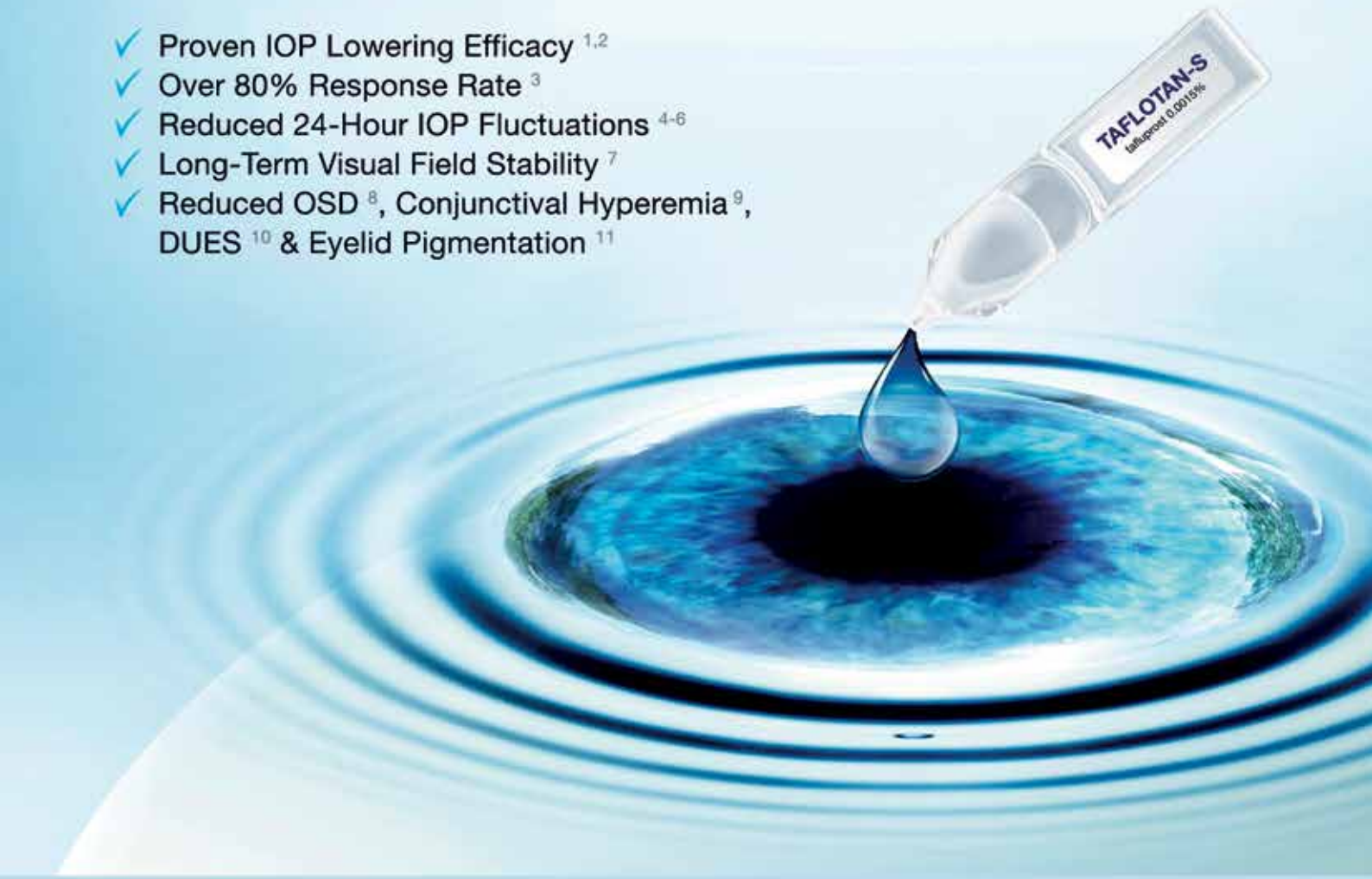
- ✓ Over 80% Response Rate [3]
- ✓ Reduced 24-Hour IOP Fluctuations [4-6]
- ✓ Long-Term Visual Field Stability [7]
- ✓ Reduced OSD [8], Conjunctival Hyperemia [9], DUES [10] & Eyelid Pigmentation [11]



Taflotan®-S
ophthalmic solution
Tafluprost 0.0015%w/v

Tapcom®-S
ophthalmic solution
Tafluprost 0.0015% / Timolol 0.5%

Active ingredients: Tafluprost 0.0015%.
Indications: Glaucoma and ocular hypertension.
Dosage: Instill 1 drop in the affected eye(s) once daily. Do not use more than once daily because more frequent administration may lessen the IOP lowering effect.
Pack size: 0.3mL; 30 plastic bottles (10 bottles per aluminium foil pouch x 3 pouches).
Contraindications: Patients with a history of hypersensitivity to any of the ingredients of this product.
Precautions: This product should be administered with care to the following patients: (1) Patients with aphakia or pseudophakia (other drugs in this category have been reported to induce macular oedema including cystoid macular oedema, and the associated visual acuity reduced.) (2) Patients with bronchial asthma or a history of bronchial asthma [this product may aggravate or induce asthmatic attack.] (3) Patients with endophthalmitis (iritis, uveitis) [other drugs in this category have been reported to cause elevation of intraocular pressure.] (4) Pregnant, parturient and lactating women [see details in PI].
Adverse Reactions: Following safety data were based on the clinical study results of tafluprost ophthalmic solution 0.0015% containing benzalkonium chloride. Upon approval Adverse drug reactions (including abnormal change in laboratory test values) were reported in 326 of 483 patients (67.5%). The major adverse drug reactions were conjunctival injection in 151 patients (31.3%), abnormality in eyelashes in 93 patients (19.3%), itching in 85 patients (17.6%), eye irritation in 65 patients (13.5%), iris pigmentation in 29 patients (6.1%), etc. Post-marketing surveillance in Japan [Upon issuance of the 5th Periodic Safety Report] Adverse drug reactions were reported in 396 of 3,260 patients (12.1%). The major adverse drug reactions were blepharal pigmentation in 93 patients (2.9%), conjunctival injection in 74 patients (2.3%), corneal epithelium disorder including corneal erosion in 58 patients (1.8%), hypertrichosis of eyelids in 40 patients (1.2%), abnormality in eyelashes in 39 patients (1.2%), etc.
Storage Conditions: Store in a refrigerator (2-8°C) under protection from light.
Instruction for Handling: After opening the aluminium foil pouch, store in a refrigerator (2-8°C under protection from light and use within 6 months. If the product is stored below 25°C after opening under protection from light, it should be used within one month. Use the product in the pouch which has been opened first.

Active ingredients: 15micrograms/mL x 3 mg/mL eye drops, solution in single-dose container.
Indications: Reduction of intraocular pressure (IOP) in adult patients with open angle glaucoma or ocular hypertension who are insufficiently responsive to topical monotherapy with beta-blockers or prostaglandin analogues and require a combination therapy, and who would benefit from preservative free eye drops.
Dosage: Recommended therapy is one eye drop in the conjunctival sac of the affected eye(s) once daily. If one dose is missed, treatment should continue with the next dose as planned. The dose should not exceed one drop in the affected eye(s) daily. Tapcom-S is a preservative free sterile solution packaged in a single-dose container. For single use only, one container is sufficient to treat both eyes. Any unused solution should be discarded immediately after use.
Contraindications: Hypersensitivity to the active substances or to any of the excipients listed in section 'list of excipients'. Reactive airway disease including bronchial asthma, or a history of bronchial asthma, severe chronic obstructive pulmonary disease. Sinus bradycardia, sick sinus syndrome, including sino-atrial block, second or third degree atrioventricular block not controlled with pace-maker. Overt cardiac failure, cardiogenic shock.
Precautions: Systemic effects. Like other topically applied ophthalmic agents, tafluprost and timolol are absorbed systemically. Due to the beta-adrenergic component timolol, the same types of cardiovascular, pulmonary and other adverse reactions as seen with systemic beta-adrenergic blocking agents may occur. Incidence of systemic adverse reactions after topical ophthalmic administration is lower than for systemic administration. To reduce the systemic absorption, see section 'method and administration' in the original product insert.
Adverse Reactions: In clinical studies, over 484 patients have been treated with Tapcom-S. The most frequently reported treatment-related adverse event was conjunctival/scular hyperaemia, it occurred in approximately 7% of the patients participating in the clinical studies in Europe, was mild or moderate in most cases, and was associated with discontinuation of treatment in 1.2% of patients. The adverse reactions reported in the clinical studies using Tapcom-S were limited to those earlier reported for either of the single active substances tafluprost or timolol. No new adverse reactions specific for Tapcom-S were observed in the clinical studies. The majority of adverse reactions reported were ocular, mild or moderate in severity and none were serious. Like other topically applied ophthalmic agents, tafluprost and timolol are absorbed systemically. This may cause similar undesirable effects as seen with systemic beta-blocking agents. Incidence of systemic adverse reactions after topical ophthalmic administration is lower than for systemic administration. Listed adverse reactions include reactions seen within the class of ophthalmic beta-blockers. The following adverse reactions have been reported with Tapcom-S during clinical trials (within each frequency grouping, adverse reactions are presented in order of decreasing frequency). The frequency of possible adverse reactions listed below is defined using the following convention: Very common: ≥1/10; common: ≥1/100 to <1/10; uncommon: ≥1/1,000 to <1/100; rare: ≥1/10,000 to <1/1,000; very rare: <1/10,000; not known: frequency cannot be estimated from the available data.
Storage Conditions: Store in a refrigerator (2°C - 8°C). After opening the foil pouch: (1) Keep the single-dose containers in the original foil pouch in order to protect from light (2) Do not store above 25°C (3) Discard an opened single-dose container with any remaining solution immediately after use.

Before Prescribing, please consult the full prescribing information

References: 1. Kuwayama Y et al. Adv Ther 2017;34:1411-25. 2. Hommer A et al. Curr Med Res Opin 2010;26(8):1905-13. 3. Kuwayama Y et al. Atarashii Ganka 2008;25:1595-1602. 4. Cho SY et al. Jpn J Ophthalmol 2016;60(1):27-34. 5. Konstas A-G et al Adv Ther 2017;34:221-35. 6. Konstas A-G et al. Br J Ophthalmol 2013;97:1510-15. 7. Shibata M et al. Jpn J Clin Ophthalmol 2015;69(5):741-47. 8. Uusitalo H et al. Clin Ophthalmol 2016;10:445-54. 9. Sumi T et al. Cornea 2013;32(Suppl):S52-9. 10. Inoue K et al. J Glaucoma 2013;22(8):626-31 11. Inoue K et al. Eye 2012;26:1465-72.

For Healthcare Professionals Only

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HK-TTS-001/2019-12

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LUBRICANT EYE DROPS

Soothe the Compromised Cornea in Dual Actions

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- Reduce Inflammation[2]

HYALURONIC ACID

- 6000X Water Retention[3]
- Enhance Wound Healing[4]

Preservative-free [1]


Contact lens safe [1]

10mL multi-dose bottle

In-use shelf life: 3 months [1]


Manufactured in Germany [1]

Reference: 1. Hydrelo PI August 2018 SA 0080.01. 2. Internal Data, Ectoin® Scientific Information . Bitop. Santen. 3. Lilian C. Becker et al. Final Report of the Safety Assessment of Hyaluronic Acid, Potassium Hyaluronate, and Sodium Hyaluronate. Internal Journal of Toxicology Volume 28, Number 45, July/ August 2009 5-67. 4. Nakamura M, Nakano T, Mitsu H et al. Hyaluronan Stimulates Epithelial Wound Healing in the Rabbit Cornea. Folia Ophthalmologica Japonica 1995 45 1256-1260.
Composition: HYDRELO DUAL ACTION LUBRICANT EYE DROPS contains 0.5% Ectoin and 0.2% Hyaluronic Acid. Indications: HYDRELO DUAL ACTION LUBRICANT EYE DROPS is intended to treat and prevent symptoms of dry and irritated eyes. HYDRELO DUAL ACTION LUBRICANT EYE DROPS reduces further dehydration by stabilizing the lipid layer of the tear film. Additionally, HYDRELO DUAL ACTION LUBRICANT EYE DROPS protects ocular cells from hyperosmolarity and aids cell regeneration. HYDRELO DUAL ACTION LUBRICANT EYE DROPS is suitable for wearers of contact lenses. HYDRELO DUAL ACTION LUBRICANT EYE DROPS is free of preservatives. Storage Conditions: HYDRELO DUAL ACTION LUBRICANT EYE DROPS should be stored between 2°C-25°C. Dosage: Always use HYDRELO DUAL ACTION LUBRICANT EYE DROPS according to these instructions for use. Consult your healthcare provider or pharmacist before use if you are not sure. If not otherwise prescribed by your healthcare provider, please apply 1-2 drops per eye, several times a day. Children 10 years of age and younger and patients unable to use HYDRELO DUAL ACTION LUBRICANT EYE DROPS on their own should be assisted during the application of HYDRELO DUAL ACTION LUBRICANT EYE DROPS. Warnings and Precautions: If recommended by your doctor/healthcare professional, HYDRELO DUAL ACTION LUBRICANT EYE DROPS may be used after eye/ocular surgery and trauma. HYDRELO DUAL ACTION LUBRICANT EYE DROPS should not be used in the case of hypersensitivity to Ectoin or any of the other ingredients of the eye drops. If allergic reactions occur, the use of HYDRELO DUAL ACTION LUBRICANT EYE DROPS must be discontinued immediately. To ensure safe hygiene, each eye drops bottle should only be used by one person. Do not use for more than 3 months after opening. Content of HYDRELO DUAL ACTION LUBRICANT EYE DROPS and other information: 10 mL solution

Full prescribing information is available upon request.

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