



# Twelve-month efficacy and safety of glaucoma filtration device for surgery in patients with normal-tension glaucoma

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## Abstract

**Purpose** To assess the efficacy and safety of filtration surgery using the EX-PRESS glaucoma filtration device in patients with normal-tension glaucoma (NTG).

**Study design** Prospective, single-arm, multicenter interventional case series.

**Methods** Eyes with NTG underwent EX-PRESS implantation with or without cataract surgery. The efficacy and safety were assessed at 1 day; 1 and 2 weeks; and 1, 3, 6, and 12 months after surgery. The main outcome measure was reduction in intraocular pressure (IOP) from baseline at 3, 6, and 12 months after surgery. Safety assessments included adverse event incidence, postoperative inflammation, and corneal endothelial cell density.

**Results** Thirty-two Japanese patients (37 eyes) with NTG were enrolled. The mean IOP decreased from  $14.8 \pm 2.3$  mmHg at baseline to  $10.0 \pm 3.1$  mmHg at 12 months after surgery (mean reduction  $4.9 \pm 4.2$  mmHg [31.1%];  $P < .0001$ ). IOP-lowering medication use decreased from a mean of 3.3 medications per eye before surgery to 0.1 medications per eye at 12 months after surgery. IOP reductions  $> 20\%$  were achieved by 61.5% of the eyes at 12 months. Adverse events were typical for filtration procedures, and none was deemed device-related. Postoperative inflammation was mild and self-limiting. The mean corneal endothelial cell density had decreased by 3.3% at 12 months after surgery.

**Conclusion** The EX-PRESS glaucoma filtration device is safe and effective for filtration surgery in patients with NTG, providing mean IOP reduction consistent with recommendations based on the Collaborative NTG Study.

**Keywords** Corneal endothelial cell density · Filtration surgery · Glaucoma filtration device · Intraocular pressure · Normal-tension glaucoma

## Introduction

Normal-tension glaucoma (NTG) is defined as primary open-angle glaucoma (POAG) with intraocular pressure (IOP) within the statistically normal range of 10–21 mmHg. Despite normal baseline IOP, IOP reduction has been demonstrated to slow the progression of NTG. Following promising results of a small trial [1], the landmark Collaborative Normal-Tension Glaucoma Study (CNTGS) showed that IOP was reduced approximately 30% from untreated baseline, significantly reducing the risk of future disease progression [2, 3]. Because baseline IOP in eyes with NTG is relatively low, many eyes with NTG require surgical interventions to achieve meaningful IOP reductions. In the CNTGS, patients with progressing and/or fixation-threatening NTG were randomized to observation or treatment. Treatment consisted of a stepped regimen of medications

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first, followed by laser treatment and surgery, advanced as needed to achieve a minimum 30% reduction goal. In that study, 33 of the 61 eyes randomized to treatment (54%) required surgery to achieve the 30% reduction in IOP [4].

Despite the observation that half or more of eyes with NTG may require surgery to achieve adequate IOP control, little is known about the efficacy and safety profiles of the various glaucoma procedures for eyes with NTG. Historically, trabeculectomy and tube-shunt procedures have been the mainstay of glaucoma surgery. Both are effective in eyes with high-pressure POAG, and the efficacy and safety profiles of these procedures have been well characterized [5, 6]. Notably, these procedures carry a risk of hypotony, which is critically important when operating on eyes with NTG, as the therapeutic target is lower than in POAG. This may potentially increase the risk of hypotony and its attendant complications (including hypotony maculopathy and cataract) in these eyes [7]. This risk is increased further with the use of antimetabolites such as mitomycin C to augment trabeculectomy [7].

Unmet needs for safer glaucoma procedures have led to the introduction of less-invasive surgical interventions [8]. Among these is implantation of the EX-PRESS glaucoma filtration device (Alcon Laboratories) [9], a small mini-shunt designed for *ab externo* transscleral implantation into the anterior chamber under the conjunctiva. This device facilitates the flow of aqueous humor from the anterior chamber to the subconjunctival space. The advantages of the EX-PRESS device include its relative ease of implantation, the standardization of the size of the outflow tract, and the lack of need to incise the uveal tissue (trabecular meshwork or iris). Scarring of the filtering bleb due to inflammation and occlusion of the outflow tract due to bleeding may be reduced because iridectomy is unnecessary. Early issues with erosion and postimplantation migration of the device were reported [10], leading to a modified approach in which the device was implanted under a scleral flap [11]. In a retrospective comparison with trabeculectomy in eyes with POAG, the EX-PRESS device under a scleral flap provided comparable IOP-lowering efficacy with a lower incidence of hypotony and choroidal effusions [12], likely due to standardization of the sclerostomy size and improved regulation of the aqueous flow. Subsequently, a prospective randomized trial comparing the EX-PRESS device with trabeculectomy in eyes with POAG found better IOP-lowering efficacy and a lower rate of surgical interventions for complications in the EX-PRESS group throughout 5 years of follow-up [13].

The outcomes of EX-PRESS device implantation in eyes with NTG have been less robustly characterized. One study comparing the outcomes of EX-PRESS device implantation in eyes with NTG with those in eyes with high-pressure POAG found that the IOP reductions and overall surgical success rates were poorer in eyes with NTG than in those

with POAG, although the safety profiles of the 2 groups were comparable [14].

Given the relative paucity of outcomes data for the EX-PRESS device in eyes with NTG, we conducted a prospective case series of EX-PRESS device implantation to better characterize the efficacy and safety profile of this device for eyes with NTG.

## Patients and methods

This prospective, single-arm, multicenter interventional case series included patients who underwent filtration surgery using the EX-PRESS device between February 2014 and September 2015. The study protocol was reviewed and approved by the institutional review board of each participating institution, in accordance with the Declaration of Helsinki and the Ethical Guidelines for Clinical Studies [15], and was registered with ClinicalTrials.gov (study number NCT02246777). All the patients provided written informed consent before enrollment.

Patients were eligible to participate in the study if they had been diagnosed with uncontrolled NTG requiring filtration surgery, were candidates for filtration surgery using the EX-PRESS device, were aged 20 years or older, and were able to provide consent. Patients were ineligible to participate if they had any form of glaucoma other than NTG, any corneal pathology that would preclude accurate applanation tonometry (including prior or planned penetration keratoplasty), any significant ocular surface disease, any history of incisional glaucoma surgery, or any contraindications to EX-PRESS device implantation (e.g., allergy to the materials constituting the device).

After confirming patient eligibility, baseline assessments included determination of best-corrected visual acuity (BCVA) and refraction, measurement of IOP by Goldmann applanation tonometry (a mean of 3 measurements constituted the baseline IOP), anterior and posterior segment examinations, anterior chamber cell and flare assessments, and corneal endothelial cell counts. Anterior chamber cells were graded by slit-lamp examination on a 0–4 scale, in which 0 indicated no cells, 1 indicated 1–5 cells, 2 indicated 6–15 cells, 3 indicated 16–30 cells, and 4 indicated more than 30 cells visible per high-power field. Flare was graded as none, mild, moderate, or severe. Corneal endothelial cell counts were assessed using noncontact specular microscopy.

EX-PRESS device implantation was performed as described by the manufacturer. Briefly, a fornix-based peritomy was fashioned to expose the perilimbal sclera. A limbus-based scleral flap was fashioned in the same manner as for trabeculectomy. The size of the scleral flap was 2.0–3.0 mm by 2.0–3.0 mm. MMC was used at a concentration of 0.05% for 90 s. A 25-gauge needle was used to create

a sclerostomy track, through which the EX-PRESS device (model P50PL) was implanted using the inserter provided by the manufacturer. Once aqueous flow was visualized through the lumen, the scleral flap was sutured into position and the peritomy sutured closed. In eyes undergoing combined EX-PRESS device implantation and phacoemulsification cataract surgery, the cataract procedure was performed before the implantation. Postoperatively, topical steroids and antibiotics were prescribed. The patients were examined 1 day; 1 and 2 weeks; and 1, 3, 6, and 12 months after the filtration surgery.

The primary objective of this study was to characterize the efficacy and safety of EX-PRESS device implantation in eyes with NTG. The efficacy data included the mean IOP, mean IOP reduction from baseline, percent IOP reduction from baseline, and proportion of patients achieving a minimum 20% IOP reduction from baseline at 3, 6, and 12 months. The number of IOP-lowering medications used at each visit was also recorded. Additionally, Kaplan–Meier survival analysis was performed, with failure defined as either IOP  $\geq 12$  mmHg or  $< 20\%$  IOP reduction from baseline at two consecutive observation points. The safety data included the incidence of adverse events observed during the postoperative follow-up, as well as changes from baseline in refractive status, cell and flare assessment, and corneal endothelial cell counts. The means are reported with standard deviations. The longitudinal changes in the continuous variables were assessed using a mixed-regression model for repeated measures. As no specific hypothesis testing was planned, probability values were calculated only for descriptive purposes and not adjusted for multiplicity. The sample size was chosen to specify the precision of the estimate of IOP reduction. A sample size of 40 eyes was determined to produce a 2-sided 95% confidence interval around the mean IOP reduction with a distance from the mean to the limits equal to 0.32 times the standard deviation of the mean IOP reduction. The statistical analyses were performed by Alcon Japan and by the Contract Research Organization (Oculus Co, Ltd) using SAS version 9.3 (SAS) and Microsoft Excel software.

## Results

A total of 37 eyes of 32 patients were enrolled and underwent filtration surgery; these eyes comprised the safety population. Both eyes of 5 patients underwent filtration surgery; these both eyes were included in the safety analysis, but only the eye with the higher baseline IOP (or the right eye if equal) was included in the efficacy analysis. Three patients (3 eyes) were enrolled inappropriately, having had prior incisional glaucoma surgery; these eyes were included in the safety analysis but excluded from the efficacy analysis.

Thus, the safety analysis included all 37 eyes of 32 patients, while the efficacy analysis included 29 eyes of 29 patients. Three patients (3 eyes) did not complete the study, two due to adverse events (1 eye with epiretinal membrane and macular edema and 1 eye with blebitis) and one that was lost to follow-up; these three eyes were included in both the safety and the efficacy analyses without imputation of missing data.

The demographic characteristics of the patients in the full data set (37 eyes of 32 patients) are shown in Table 1. The patients were predominantly female (56.8%), with a mean age at the time of surgery of  $61.2 \pm 10.8$  years, and all were ethnically Japanese. Of the 37 eyes, 22 (59.5%) underwent EX-PRESS device implantation as a stand-alone procedure, and 15 (40.5%) underwent combined EX-PRESS device implantation and cataract extraction.

The mean IOP, IOP change from baseline, and percent IOP change from baseline at each time point in the efficacy data set (29 eyes of 29 patients) are shown in Table 2 and Fig. 1. The mean IOP at baseline was  $14.8 \pm 2.3$  mmHg and was significantly reduced from baseline ( $P < .0001$ ) at all postoperative time points. Following the immediate postoperative period, the IOP stabilized at 1 month, and from month 1 through month 12, the mean IOP ranged from 9.4 to 10.0 mmHg; the mean IOP reductions, from 4.9 to 5.4 mmHg; and the percent IOP reductions, from 21.1 to 35.4%. At month 12, the mean IOP was  $10.0 \pm 3.1$  mmHg, which was a reduction of 4.9 mmHg (31.1%) from baseline ( $P < .0001$ ). The proportions of patients with a minimum 20% IOP reduction from baseline at 3, 6, and 12 months were 72.4%, 82.1%, and 61.5%, respectively.

These IOP reductions were accomplished while nearly eliminating the need for IOP-lowering medications. At baseline, all 34 eyes in the efficacy analysis set were on topical IOP-lowering therapy, with a mean of  $3.3 \pm 1.0$  medications per eye. Between day 1 and month 6 postoperatively, no eyes required IOP-lowering medication, and at month 12,

**Table 1** Baseline demographic and clinical characteristics of the full data set (37 eyes of 32 patients)

Parameter	Value
Sex, female, n (%)	18 (56.3)
Age, mean $\pm$ SD, years	$61.2 \pm 10.8$
Ethnicity, Japanese, n (%)	32 (100)
Surgery type	
EX-PRESS for phakic eye, n (%)	10 (27.0)
EX-PRESS for pseudophakia, n (%)	12 (32.4)
Combined EX-PRESS and cataract surgery, n (%)	15 (40.5)
Visual field, MD, mean $\pm$ SD	$-19.27 \pm 8.15$
PSD, mean $\pm$ SD	$10.66 \pm 3.38$
Manifest refraction (spherical equivalent), D, mean $\pm$ SD	$-5.44 \pm 5.13$

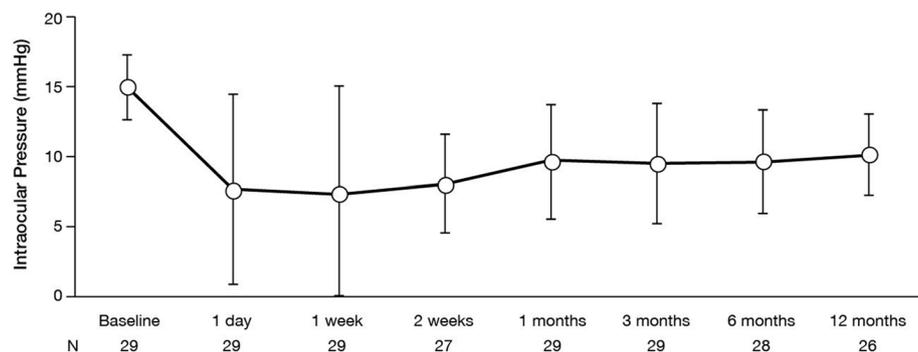
**Table 2** Mean intraocular pressure (IOP) and IOP-lowering medication parameters at each study time point in the efficacy population (n=29 eyes)

	Baseline	1 day	1 week	2 weeks	1 month	3 months	6 months	12 months
<b>IOP, mmHg</b>								
Mean (SD)	14.8 (2.3)	7.6 (6.8)	7.3 (7.8)	8.1 (3.7)	9.6 (4.1)	9.4 (4.3)	9.5 (3.8)	10.0 (3.1)
<b>IOP change from baseline, mmHg</b>								
Mean (SD)	–	–7.2 (7.6)	–7.5 (6.7)	–6.7 (4.3)	–5.2 (4.7)	–5.4 (4.6)	–5.4 (4.8)	–4.9 (4.2)
95% CI*	–	–9.2, –5.2	–9.6, –5.5	–8.8, –4.6	–7.2, –3.2	–7.4, –3.4	–7.2, –3.2	–6.6, –2.4
<i>P</i> value from baseline*	–	< .0001	< .0001	< .0001	< .0001	< .0001	< .0001	< .0001
<b>Percent IOP change from baseline (%)</b>								
Mean (SD)	–	–46.2 (52)	–53.5 (41)	–44.2 (27)	–34.1 (29)	–35.4 (30)	–33.7 (34)	–31.1 (24)
95% CI*	–	–59.2, –33.3	–66.4, –40.5	–57.3, –30.7	–47.0, –21.1	–48.3, –22.4	–45.9, –19.6	–42.0, –14.9
<i>P</i> value from baseline*	–	< .0001	< .0001	< .0001	< .0001	< .0001	< .0001	< .0001
Proportion with > 20% IOP reduction from baseline, %	–	72.4	82.8	77.8	65.5	72.4	82.1	61.5
Mean number of glaucoma medications, n (SD)	3.3 (1.0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0.1 (0.4)

*IOP* intraocular pressure

\*The *P* values and 95% CIs were determined by *t* tests using a mixed model for repeated measures, a statistical model that accounts for within-subject correlations between study visits

**Fig. 1** Mean intraocular pressure (IOP) over time in the efficacy population. Error bars indicate standard deviations



only one eye required topical medical therapy (mean 0.1 medications per eye).

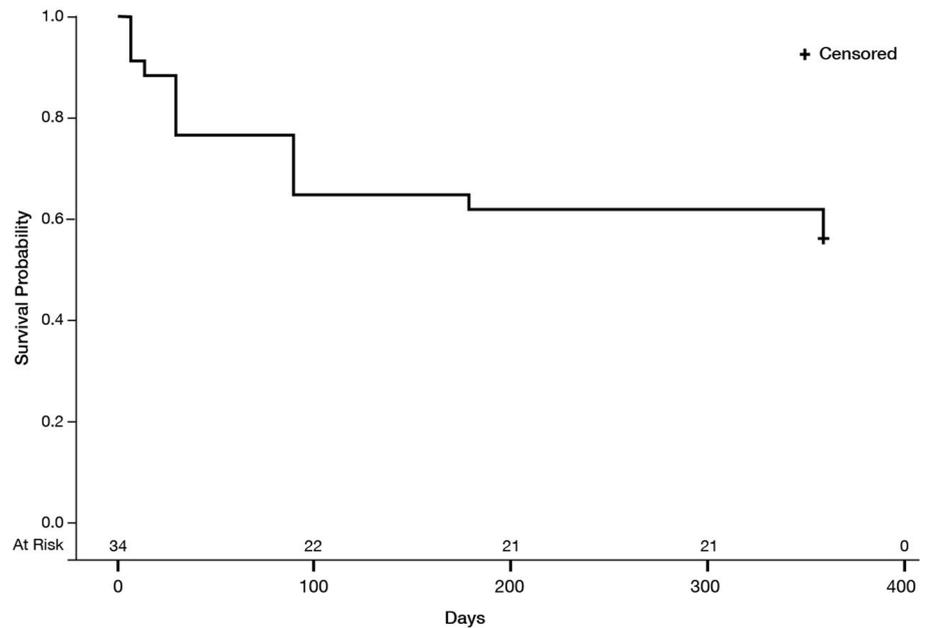
The survival analysis defined clinically relevant treatment failure as  $IOP \geq 12$  mmHg or a < 20% reduction from baseline at two consecutive study visits. According to this analysis, the cumulative survival rate 12 months after surgery was 55.9% (Fig. 2).

The surgical procedure was well tolerated in all the eyes, with none experiencing intraoperative complications (Table 3). Mild anterior chamber inflammation was noted postoperatively, with 30 eyes (81.1%) having cells in the anterior chamber on day 1 (22 with grade 1, 8 with grade 2—all of which resolved by month 1) and 21 eyes (56.8%) having flare in the anterior chamber on day 1 (all mild and all resolved by week 1). During follow-up, contact between

the EX-PRESS device tip and the anterior surface of the iris was observed in 11 eyes at various time points; however, no adverse events attributable to this contact were noted.

Needling was performed for 1 eye (3%) at 2 weeks, 4 eyes (12%) at 1 month, 4 eyes (12%) at 3 months, and 1 eye (3%) at 6 months after the surgery. Laser suture-lysis was performed for 6 eyes (18%) at 1 day, 10 eyes (29%) at 1 week, 7 eyes (22%) at 2 weeks, and 5 eyes (15%) at 1 month after surgery. Postoperative ocular adverse events in the full data set of 37 eyes included choroidal detachment in 5 eyes (13.5%), hyphema in 4 eyes (10.8%), corneal epithelial defect in 2 eyes (5.4%), and epiretinal membrane, macular edema, blebitis, optic disc hemorrhage, and hypotony maculopathy in 1 eye each (2.7%; Table 4). Most adverse events were self-limiting and resolved spontaneously. One

**Fig. 2** Kaplan–Meier survival analysis of postoperative maintenance of IOP in the efficacy population. Failure was defined as IOP  $\geq$  12 mmHg or IOP reduction  $<$  20% from baseline



**Table 3** Shape of filtering blebs based on slit-lamp examination

		12 months after surgery	
		n	(%)
Width	> 1 quadrant	14	(41.2)
	Greater than the scleral flap	20	(58.8)
	Less than the scleral flap	0	0
Depth	Greater than the scleral flap	34	(100)
	Less than the scleral flap	0	0
Length	$\geq$ 2 times the corneal thickness	34	(100)
	$<$ 2 times the corneal thickness	0	0
Border	Diffuse	27	(79.4)
	Partially localized	7	(20.6)
	Fully localized	0	0
Avascular area	None	28	(82.4)
	$<$ 50%	5	(14.7)
	$\geq$ 50%	1	(2.9)
Wall thickness	Invisible scleral suture/incision line	9	(26.5)
	Barely observed	16	(47.1)
	Clearly observed	9	(26.5)
Leakage	No leakage	34	(100)
	Oozing within 10 s	0	0
	A clear leakage point present	0	0

eye experienced blebitis 5 months postoperatively, which was resolved with topical and oral antibiotics without any impact on vision. Similarly, 1 eye experienced hypotony maculopathy 5 months after surgery; this adverse event resolved over several months, also without affecting vision.

**Table 4** Incidence of adverse events and contact with the cornea/iris and device in the safety population (N = 37 eyes)

Adverse event and contact with the cornea/iris	Frequency, n (%)
Choroidal detachment	5 (13.5)
HypHEMA	4 (10.8)
Corneal epithelial defect	2 (5.4)
Epiretinal membrane	1 (2.7)
Macular edema	1 (2.7)
Blebitis	1 (2.7)
Optic disc hemorrhage	1 (2.7)
Hypotony maculopathy	1 (2.7)
Contact with the cornea and device <sup>a</sup>	0
Contact with the iris and device <sup>a</sup>	5 (14.7)

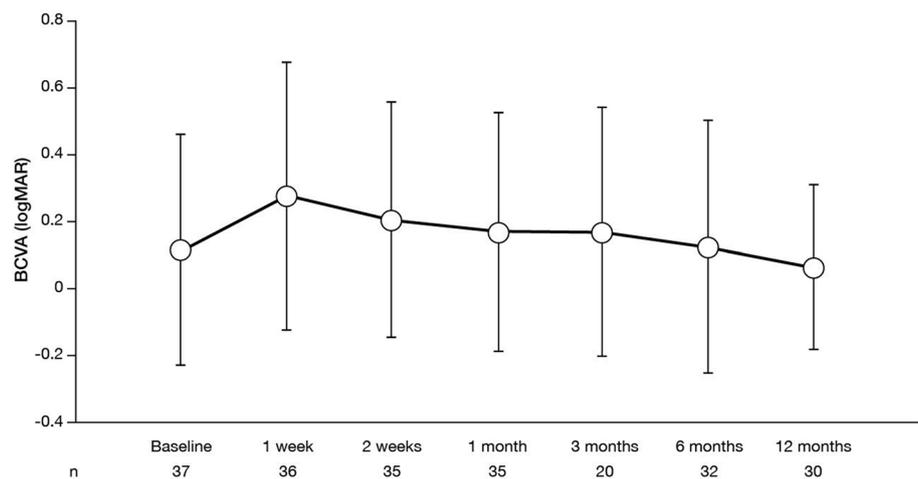
<sup>a</sup>Observed at 12 months

None of these events was considered related to the device. No eyes with a flat anterior chamber were observed. No non-ocular or unanticipated adverse events occurred, nor were there any device failures during the study period.

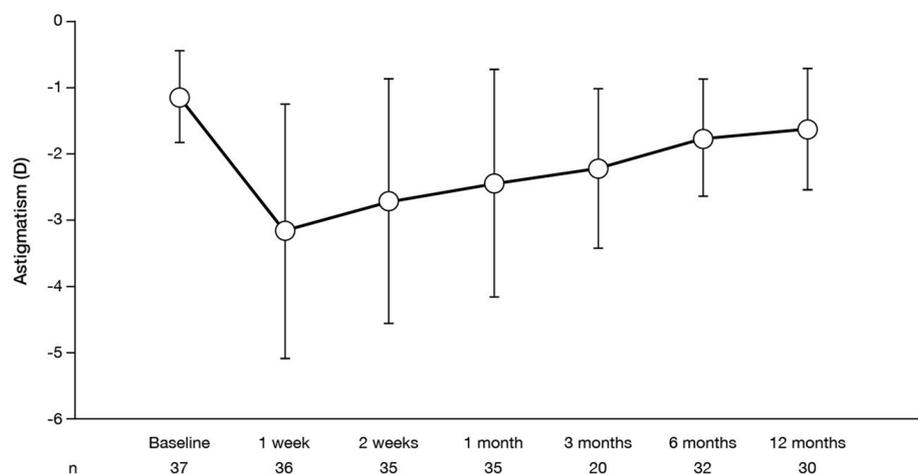
The mean BCVA over the study period remained unchanged, being  $0.115 \pm 0.346$  logMAR at baseline and  $0.062 \pm 0.250$  logMAR at month 12 ( $P = .6196$ ; Fig. 3). The mean astigmatism was also unaffected by the procedure, being  $-1.136 \pm 0.693$  D at baseline and  $-1.635 \pm 0.923$  D at month 12 ( $P = .0922$ ; Fig. 4).

The mean corneal endothelial cell density decreased from  $2658.9 \pm 287.7$  cells/mm<sup>2</sup> at baseline to  $2546.8 \pm 246.1$  cells/mm<sup>2</sup> 12 months after surgery. Although the difference, 95 cells/mm<sup>2</sup>, was significant ( $P = .0095$ ), it represented only a 3.3% reduction in endothelial cell density.

**Fig. 3** Mean best-corrected visual acuity (logMAR) over time in the safety population. Error bars indicate standard deviations



**Fig. 4** Mean astigmatism over time in the safety population. Error bars indicate standard deviations



## Discussion

This prospective interventional case series demonstrated that implantation of the EX-PRESS glaucoma filtration device in eyes with normal-tension glaucoma safely achieves a mean 31% IOP reduction at 12 months, consistent with the 30% target reduction in IOP reported by the landmark Collaborative Normal Tension Glaucoma Study (CNTGS) [2, 3], while virtually eliminating the need for daily topical IOP-lowering medical therapy.

Most patients with NTG will require surgical intervention to achieve the CNTGS-recommended 30% IOP reduction [4]. Surgical therapy poses well-described safety concerns, with the risk of cataract being particularly high in eyes with NTG. In the CNTGS, the rate of cataract formation (38%) was nearly three times higher in the treatment group than in the control group, and was higher still in treated eyes that underwent surgery (16 of 33, or 48.5%) [3, 4]. Also, because the range of target IOP in NTG is narrow and approaches the limit of hypotony, the risk of

hypotony-related complications is higher in these eyes than in those with high-pressure POAG [7].

Relatively little is known about surgical intervention for IOP control in eyes with NTG. Studies of trabeculectomy in eyes with NTG have revealed mean IOP reductions in the range of 34–43% [6–20]. Less is known about the EX-PRESS device in eyes with NTG. A recent study of 63 eyes that underwent EX-PRESS device implantation included 15 eyes with NTG, which were analyzed separately [14]. The mean IOP of these 15 eyes was reduced from  $13.3 \pm 1.0$  mmHg at baseline to  $10.3 \pm 2.9$  mmHg at 12 months, a 22% reduction. Moreover, nine of these patients (60%) showed a  $\geq 20\%$  reduction in IOP while having an IOP  $\geq 5$  mmHg but  $\leq 15$  mmHg at 12 months. The need for medical therapy was also greatly reduced, from a mean of 3.3 medications preoperatively to 0.3 medications at 12 months. In comparison, our study found a mean 31% reduction in IOP with a similarly low rate of medication use at 12 months postoperatively.

Our study also showed that EX-PRESS device implantation had an acceptable safety profile in eyes with NTG.

No device failures or device-related adverse events were observed. Most observed adverse events were self-limiting and not vision-threatening in nature. We observed a 3.3% reduction in corneal endothelial cell density at 12-months, similar to the 12-month results of EX-PRESS device implantation in eyes with high-tension POAG (5.6%) [21] and of trabeculectomy in eyes with various forms of glaucoma (3.2%) [22]. A comparison of the changes in endothelial cell density at 3 months after trabeculectomy, EX-PRESS device implantation, and Ahmed valve implantation showed that only the eyes that had undergone EX-PRESS surgery maintained statistically stable endothelial cell counts, whereas reductions of 4.2% and 3.5% were seen in the trabeculectomy and Ahmed groups, respectively [23].

This study had several limitations. The single-arm design precluded comparison of our results with other procedures or with eyes affected by glaucomas other than NTG. Also, the planned sample size of 45 eyes (40 needed for analysis plus an additional 10% to account for attrition) was not met, owing to the small number of patients in our practice who met the eligibility criteria. This had no effect on power, as no hypotheses were tested, but did slightly reduce the precision of the estimates of IOP reduction. The second limitation was the analysis cohort. Three types of surgery were performed according to the condition of the crystalline lens. It is thought that the results of surgery should be evaluated using three cohorts, but such evaluation was difficult because the number of cases was small. Therefore, in future studies, the number of cases should be increased.

In conclusion, filtration surgery using the EX-PRESS glaucoma filtration device safely provided significant IOP reductions consistent with the CNTGS-based guidelines recommending a 30% reduction in IOP from baseline. Future studies should include evaluation of the long-term efficacy and safety of filtration surgery using the EX-PRESS device and comparison of those with the evaluations of other surgical procedures in eyes with NTG.

**Conflicts of interest** M. Aihara, Research fee (Alcon), Support for Study design/Manuscript preparation/ Statistical analysis (Alcon), Financial support (Alcon Pharma, AMO, CREWT medical systems, Glaukos, Kowa Pharmaceutical, Nitten, Novartis, Ono, Otsuka, Pfizer, Santen, Senju, TOMEY, Wakamoto), Consultant fee (Alcon Pharma, CREWT medical systems, Glaukos, HOYA, InnFocus, Iridex, Kowa, Ono, Otsuka, Pfizer, Santen, Senju, Wakamoto), Lecture fee (Alcon Pharma, AMO Japan, Canon, Carl Zeiss Meditec, CREWT medical systems, Glaukos, HOYA, InnFocus, Iridex, Ivantis, Kowa Pharmaceutical, NIDEK, Nitten, Novartis, Ono, Otsuka, Pfizer, Santen, Senju, TOMEY, Alcon), Travel fee (Alcon Pharma, AMO Japan, Canon, Carl Zeiss Meditec, CREWT medical systems, Glaukos, HOYA, InnFocus, Iridex, Ivantis, Kowa Pharmaceutical, NIDEK, Nitten, Novartis, Ono, Otsuka, Pfizer, Santen, Senju, TOMEY) Grant (Alcon); Y. Kuwayama, Research fee (Alcon), Lecture fee (Alcon Pharma, Glaukos Japan, Kowa, Otsuka, Pfizer, Santen, Senju), Consultant fee (Kowa, Otsuka, Pfizer, Santen, Senju, Aerie Pharmaceuticals, Wakamoto); K. Miyata,

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