Treating the Newly Diagnosed Glaucoma Patient

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Ben Gaddie's Financial Disclosures

- Consultant/Honoraria in last 12 months:
 - Allergan
 - Novartis
 - Aerie
 - Bausch and LombSun Pharma
 - Carl Zeiss Meditech



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rial		UX	Rangomization	ronow-up
OHTS1 (NEI)	1636 pts	OHT	Medical Tx vs observation	5 years
EMGT ² (NEI)	255 pts	OAG	Tx (ALT + betaxolol) vs observation	4-9 years
CNTGS ³ (GRF)	140 eyes	NTG	Medical Tx and/or surgery vs observation	7 years
CIGTS ⁴ (NEI)	607 pts	OAG	Medical Tx vs surgery	4 + years
AGIS ⁵ (NEI)	738 eyes	OAG	ALT vs surgery	8 years

	IOP	in Clinic	al ٦	Trials		
<u>s</u>	tudy	IOP Reducti	on	%Progre	ssion	
• (OHTS*	20%	9.5%	6/4.5%		
• 1	EMGT*	25%**	6	2%/45%		
• (CNTGS	30%	3	5%/12%		
• ,	AGIS	<18	n	o progress	sion	
• (CIGTS (m	eds) 38%	no p	rogressior	ı	
• (CIGTS (su	rg) 45%	n	o progress	sion	
*109	6 risk reduction	for every 1 mmHg la	owering			







Determining the Target IOP

- 1. Estimating the amount of glaucoma damage.
 This is based upon both structural functional assessment.
- 2. Estimating the damaging IOP
- One should make the best clinical assessment possible as to what the likely IOP was at which damage has already occurred. In some instances, multiple IOP measurements may help determine a baseline IOP and hence influence the initial determination of the target IOP

Determining the Target IOP

- 3. Estimate the patient's life expectancy.
 - In general, the longer the patient's life expectancy, the lower the target IOP will need to be. Actuarial tables can be helpful, keeping in mind that any give patient may live much longer or shorter than the mean. When in doubt, err on the side of estimating a longer life expectancy. Nevertheless, on average, 40 year olds and 90 year olds may be treated differently.

Determining the Target IOP

- 4. Consideration of the other risk factors for progression.
 Other proposed risk factors include severe damage in the other eye, family history of blindness from glaucoma, etc.
- 5. Guesstimate the Rate of Progression (RoP) of glaucoma damage, either disc and/or fileds, based upon the assessment of damage already occurred vs time

Target IOP Based Upon Initial Visual Field Loss and Highest IOP

	20 mm Hg	30 mm Hg	40 mm Hg
Mild	25%	30%	<u>40%</u>
Moderate	<u>35%</u>	<u>40%</u>	50%
Severe	45%	50%	60%

Target IOP	P Based Upon I and Hig	nitial Optic Nei ghest IOP	rve Damage
	20 mm Hg	30 mm Hg	40 mm Hg
Mild	25%	30%	<u>40%</u>
Moderate	<u>35%</u>	<u>40%</u>	50%
Severe	45%	50%	60%

Target Intraocular Pressure Based Upon Highest Untreated IOP and Severity of Damage				
	20mm Hg	30mm Hg	40mm Hg	
Mild	25%	35%	50%	
Moderate	35%	45%	60%	
Severe	50%	60%	75%	



















What Other Classes Can Be Used First Line

- Beta Blockers
- Alpha Agonists
- Combo agents
- Topical CAI's

SLT and the LIGHT Study

Introduction

• In most developed countries (including USA) the standard firstline treatment for OAG and OHT is IOP lowering eye drops

- Requires multiple office visits for monitoring and treatment adjustments or additions
- Long term use of single or multiple topical medications with many ocular and systemic side effects
 - Can be a large factor in compliance, adherence and future surgical effectiveness^{1,2}

Introduction

- SLT reduces IOP by increasing trabecular outflow with a single, painless outpatient procedure with good safety profile and limited recovery time
- Approved by the FDA in 2001
- IOP lowering effect comparable to medication without medication associated side effects
- While not permanent, it is repeatable
- Still not routinely offered as first line treatment

Selective Laser Trabeculoplasty versus eye drops for first-line treatment of ocular hypertension and glaucoma

- United Kingdom study set in 6 hospitals
 - Recruited patients from 2012-2014
 - Observer masked
 - Randomized
 - Treatment naïve patients/newly diagnosed OAG
 No previous IOP lowering drops, laser or surgery

LIGHT Study Design

- 718 patients entered the study (1235 eyes)
- Patients randomized on a 1:1 basis to either:
 - SLT (356 patients, 613 eyes)
 - Drops (362 patients, 622 eyes)

Entrance Criteria

- For OAG
 - MD not worse than -12dB in the better eye
- MD not worse than -15dB in the worse eye • Visual acuity of 6/36 or better in treated eyes
- NO previous intraocular surgery
- Except uncomplicated phacoemulsification at least 1 year prior to randomization
- into the trial
- Other exclusions: Contraindication to SLT
 - Unable to use eye drops
 - Symptomatic cataract
 - Active treatment for some other type of ocular condition

OAG Disease Definition for LIGHT Study

- · Used NICE thresholds for disease definitions and treatment initiation⁵
- Used real time web-based clinical decision support software
- ONH analysis by HRT
- HFA VF 24-2 + GPA
- IOP measurements
- Disease category and stage were defined at baseline using preset objective severity criteria from the Canadian Target IOP Workshop⁶

Topical Medication Algorithm

- Drug classes for 1st, 2nd, and 3d line treatment were determined by the NICE guidelines⁵
- First line-PGA's
- Second line- Beta Blockers
- Third line- TCAI or Alpha Agonist
- · Fixed combinations were allowed
- · MMT=Clinician judged max most intensive combination of medicines that could be tolerated

Results

- Overall 509 (95%) of 536 SLT treated eyes were at target IOP @ 3 years
- Target IOP achieved without medication in 419 (78.2%) of 536 eyes treated in SLT arm
 - 321 eyes (76.6%) required only one SLT session

Results

- 499 (93.1%) of the 526 eyes treated medically were at target IOP @ 3 years
 - 346 (64.6%) were using a single medication
- At 3 years:
 - 93.0% of visits were at target IOP for SLT group
 - 91.3% of visits were at target IOP for med group

Treatment Escalations and Progression of Disease **During Study**

- More treatment escalations occurred in the SLT group (348 eyes) than the Medication group (299 eyes) $% \left(\left(1-\frac{1}{2}\right) \right) =0$
- Progression
 - 36 eyes in the Medication group showed algorithm-confirmed progression
 3 eyes converted from OHT to OAG
 33 eyes with OAG progressed

 - 23 eyes in the SLT group
 2 eyes converted from OHT to OAG
 21 eyes with OAG progressed
- 11 eyes (1.8%) in the Medication group required incisional glaucoma surgery
- NO EYES IN SLT GROUP REQUIRED INCISIONAL SURGERY

Adverse Events

- SLT Group
 - 6 eyes had an IOP rise of 5mm Hg or more on day of treatment
 Only 1 eye required treatment
 - 122 eyes (34.4%) had transient discomfort, blurred vision or photophobia not requiring treatment
- Medication Group
 - 150 eyes had aesthetic side effects or allergic reactions

Cost of Therapy

- Eye drops were approximately double the cost effect of SLT
- Difficult to extrapolate to US market but general financial math should apply
- Eventual ophthalmic surgery (trab, tube, cataract etc) over the 3 years was significantly less in the SLT group compared to the Medication group

Cost and Cost Effectiveness

- SLT as first line resulted in a significant cost savings relative to surgery and medication
 - Approximately 451 dollars/pounds savings in provider related visit costs per patient
 - For every patient given SLT in lieu of drops, the cost savings are greater than the cost of SLT for 2 additional patients!
 - This is also equal to the cost of five additional office visits

Clinical effectiveness of SLT vs. Drops

- Rate of Disease Progression
 - In the Medication group 36 patients (5.8%) had disease progression
 - In the SLT group 23 patients (3.8%) had disease progression
 - 74% remained drop free at 3 years

Clinical effectiveness of SLT vs. Drops

• IOP Control

- SLT first approach provided better IOP control over 3 years with more visits at target IOP compared to drops
 - Less intense drop treatment than Medication group
 - NO glaucoma surgeries required compared to Medication group
- Could be due to adherence with SLT vs. Drops

Clinical effectiveness of SLT vs. Drops

IOP Control

- SLT provides better diurnal IOP stability⁶
 Could be due to continuous effect on TM versus episodic administration of medication
- Primary SLT afforded drop free control of IOP for 3 wars in 74.3% of nationtr
- years in 74.2% of patients
 This is much higher than in previous studies with less stringent success criteria
- Prior treatment and more severe disease likely reduce the
- effect of SLT in those patients⁷ • Likely the reason for such a robust response in treatment
- naïve patients in this study

Safety of SLT vs. Drops

- This study showed a greater safety profile of SLT than previously reported
 - No systemic side effects reported
 - Only 1 eye had an IOP spike
 - Compared to previously reported rates of 28.8%⁸
 - 2-week IOP checks did not change management for any patient and appears to be unnecessary

 Avoidance of this could save more \$ to the system
 - Avoidance of this could save more \$ to the system
 - Lower rate of cataract surgery in SLT arm which supports the existing evidence of drops increasing incidence of cataract and surgery⁹

Conclusions

- Selective laser trabeculoplasty provides superior IOP stability to drops, at a lower cost AND
 - 74% or % of patients are successfully controlled without drops for at least 3 years after a single treatment

Conclusions

- Selective laser trabeculoplasty as an initial treatment for glaucoma is associated with the following:
 - Lower cost
 - Good clinical outcomes
 - 2-week follow up not necessary
 - Lower symptom scores
 - Drop-freedom for most patients
- SLT should be offered as an alternative to IOP lowering drops as initial therapy on a more widespread basis

What Should You Expect After Starting Glaucoma Treatment?

- Doesn't matter if you use medication or laser, at a bare minimum we should expect a 25% reduction in IOP – 20% or less would be considered a "non-responder"
 - 40% or more would be considered a "super-responder"
- Clinical gold standard medically is the PGA class
- SLT laser has recently been shown to have advantages for initial therapy vs. eye drops
- The Monocular trial with glaucoma drops is not useful and you shouldn't waste your time

What Happens If We Don't Get to Target IOP With the Initial Therapy?

- If you started with a generic PGA, try a branded PGA before moving on
- If you started with drops, consider trying SLT laser next
- After that, trying another class altogether is a good next step – RhoKinase Inhibitors
 - Combos (Combigan, Cosopt, Simbrinza)

Bimatoprost Implant Overview

ARTEMIS











Important Safety Information

Contraindications

· Contraindications:

- Active or suspected ocular or periocular infections
- Corneal endothelial cell dystrophy (e.g. Fuch's Dystrophy)
- Prior corneal transplantation or endothelial cell transplants (e.g., Descemet's Stripping Automated Endothelial Keratoplasy [DSAEK])
- Absent or ruptured posterior lens capsule, due to the risk of implant migration into the posterior segment
- Hypersensitivity to bimatoprost or any other components of the product

Warnings and Precautions

• Warnings and Precautions:

- Corneal adverse reactions: The presence of bimatoprost implants has been associated with corneal adverse reactions and increased risk of corneal endothelial cell loss. Administration of bimatoprost implant should be limited to a single implant per eve without retreatment. Caution should be used when prescribing bimatoprost implant in patients with limited corneal advectory.
- eve without retreatment. Caution should be used when prescribing bimatoprost implant in patients with limited corneal endothelia cell reserve. Indocorneal angle: Bimatoprost implant should be used with caution in patients with narrow indocorneal angles (Shaffer grade < 3) or nanonical obstruction (e.g. scarring) that may prohibit setting in the inferior angle. Macular edema: Macular edema, including cycloid macular edema, has been reported during treatment with ophthalmic bimatoprost, Including bimatoprost implant. Bimatoprost implant should be used with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.

Please also see the Durysta full prescribing information.

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Warnings and Precautions

• Warnings and Precautions (Continued):

- Variantings array recallutions (Continuetar): Intraodus information: Prostagation analos, including bimatoprost implant, have been reported to cause intraocular inflammation. Bimatoprost implant should be used with caution in patients with active intraocular inflammation (e.g., uveitis) because the inflammation may be exacerbated. **Pigmentation:** Ophthalmic bimatoprost, including bimatoprost implant, has been reported to cause changes to pigmented tasses, such as increased pigmentation of the iris. Pigmentation of the iris is likely to be permanent. Pailents who receive treatment should be informed of the possibility of increased pigmentation. While treatment with bimatoprost mighanc can be confined in patients who develop noticeably increased iris pigmentation, these patients should be examined regularly. **Endophthalmits:** Intraocular surgical procedures and injections have been associted with henophthalmits. Progresseptit technique must always be used with administering bimatoprost implant, and patients should be monitored following the administration:

Please also see the Durysta full prescribing information.

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Adverse Reactions

- In controlled studies, the most common ocular adverse reaction reported by 27% of patients was conjunctival hyperemia.
- Other common adverse reactions reported in 5-10% of patients were foreign body sensation, eye pain, photophobia, conjunctival hemorrhage, dry eye, eye irritation, intraocular pressure increased, corneal endothelial cell loss, vision blurred, iritis, and headache.

Please also see the Durysta full prescribing information

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Bimatoprost Implant

Dosage and Administration

Dosage and Administration

- General Information:

 Bimatoprost implant is an ophthalmic drug delivery system for a single intracameral administration of a biodegradable implant. Bimatoprost implant should not be readministered to an eye that received a prior bimatoprost implant.
- Administration:
 - The intracameral injection procedure must be performed under magnification that allows clear visualization of the anterior chamber structures and should be carried out using standard aspetic conditions for intracameral procedures, with the patient's head in a stabilized position. The eyes should not be dilated prior to the procedure. Remove the foil pouch from the carton and examine for damage. Then, open the foil pouch over a sterile field and gently drop the applicator on a sterile tray. Once the foil pouch is opened, use promptly.

IOP = intraocular pressure nine C& Aleman IPSA Inc. March 2020



Administration (Continued)

- · Stabilize the eye as the needle is advanced through the cornea
- Enter the anterior chamber with the needle bevel visible through clear cornea. Enter parallel to the iris plane, adjacent to the limbus through the clear cornea in the superotemporal quadrant
- The needle should be inserted approximately two bevel lengths with the bevel completely within the anterior chamber; avoid positioning the needle bevel directly over the pupil. Ensure the needle is not bent before depressing the actuator button an

Depress the back half of the audible and/or palpable clic

Administration (Continued)

- Following the release of the implant, remove the needle via the same track in which it was inserted and tamponade the opening. The implant should not be left in the corneal injection track.
- Check for injection site leaks; make sure that it is self sealing and the anterior chamber is formed.
- After injection, **do not** recap the needle. Dispose of the used applicator in a sharps disposal container in accordance with local requirements.
- In a singly dispose total different according to at least one hour after the procedure so the implant can settle. Some degree of eye redness and discomfort is expected following administration. However, it is recommended to instruct patients that if the eye becomes progressively red, sensitive to light, painful, or develops a change in vision, they should immediately contact the physician.

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Summary

- · Bimatoprost implant is indicated for the reduction of intraocular pressure (IOP) in patients with open angle glaucoma (OAG) or ocular hypertension (OHT)
- Efficacy has been demonstrated in two Phase 3 studies with an IOP reduction of approximately 5 - 8 mmHg in patients with a mean baseline IOP of 24.5 mmHg
- The most common ocular adverse reaction observed in two randomized controlled clinical trials with bimatoprost implant in patients with OAG or OHT was conjunctival hyperemia, which was reported in 27% of patients

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Reassessing Target IOP After Starting Therapy

- · How do you know that the target you set is low enough to prevent further damage (VF or OCT)?
 - Imaging and Perimetry

 Has there been subsequent RNFL loss since starting treatment or development of new or first VF defects?

- How has the IOP fared against target?
 - Never meets target?
 - Sometimes meets target?
 - Always hits target?

Reassessing Target IOP After Starting Therapy

- If target IOP not reached or consistent, what is the next step: Consider replacing within class
 - i.e. Latanoprost for Bimatoprost or Latanoprostene bunod, etc
 - Consider adding a second bottle of IOP lowering medicine
 - Single agent adjunct (to a PGA for example):
 Beta blocker, TCAI, Alpha agonist, Netarsudil
 - Combination agent*

 - Combigan, Cosopt, Rocklatan, Simbrinza
 Laser Trabeculoplasty
- · Then reassess in same manner as before