

Table 1. Eye-specific baseline characteristics of laser peripheral iridotomy-treated eyes and control eyes

Characteristic	Laser peripheral	
	iridotomy (N=480)	Control (N=480)
Axial length (mm)	22.7 (1.0)	22.7 (0.9)
Anterior chamber depth (mm)	2.7 (0.4)	2.7 (0.4)
Lens thickness (mm)	4.3 (0.9)	4.3 (0.9)
Spherical equivalent	2.1 (1.9)	2.2 (1.8)
Cup:disc ratio	0.4 (0.1)	0.4 (0.1)
LOCS grade		
NC	2.3 (0.7)	2.3 (0.7)
NO	2.3 (0.7)	2.3 (0.7)
C	1.4 (1.2)	1.4 (1.2)
P	0.1 (0.5)	0.2 (0.5)
Pre-dilation IOP (mmHg)	14.2 (2.3)	14.3 (2.4)
Post-dilation IOP (mmHg)	14.8 (2.7)	14.9 (2.8)
Total angle width on Gonioscopy	2.5 (2.0)	2.4 (2.0)
Number of closed quadrants		
2	1 (0.2%)	1 (0.2%)
3	20 (4.2%)	29 (6.0%)
4	459 (95.6%)	450 (93.8%)
Limbal anterior chamber depth grade		
0%	47 (9.8%)	45 (9.4%)
5%	189 (39.4%)	186 (38.8%)
15%	182 (37.9%)	182 (37.9%)
25%	53 (11.0%)	56 (11.7%)
40%	9 (1.9%)	11 (2.3%)
Central Corneal thickness (microns)	543.6 (34.2)	545.9 (34.2)
Corneal Curvature (Keratometry, mm)	7.7 (0.2)	7.6 (0.2)
Cell density (per mm ²)	2566.3 (408.6)	2549.9 (421.6)
Mean deviation (dB)	-2.3 (3.0)	-2.3 (3.3)
Pattern standard deviation (dB)	2.5 (1.7)	2.6 (1.8)
Distance corrected VA (LogMAR)	0.2 (0.2)	0.2 (0.2)
Near corrected VA (LogMAR)	0.2 (0.2)	0.2 (0.2)

All values are mean (SD) unless state otherwise.

*Mean total angle width was the mean of modified Shaffer grading of all four quadrants (range from 0 to 16, larger number indicates wider angle). \$ A closed quadrant is defined as modified Shaffer grade of 0,1 or 2 for angle width.

Table 1a. Overall Demographics and Baseline Characteristics

Characteristic	Mean (SD) or n (%)
Age (year)	62.8 (6.9)
Gender	
Female	364 (75.8%)
Male	116 (24.2%)
Ethnicity	
Chinese	445 (92.7%)
Indian	13 (2.7%)
Malay	16 (3.3%)
Others	6 (1.3%)
Height (cm)	157.6 (7.8)
Weight (kg)	58.8 (12.1)
Body Mass Index	23.6 (4.2)
Diabetes mellitus	70 (14.6%)
Hypertension	229 (47.7%)
Ischaemic heart disease	30 (6.3%)

Table 2. Summary of primary outcome and its components at 60 months

	Laser peripheral iridotomy (N=480)	Control (N=480)	Hazard ratio (95% CI)	p- value
Development of PAC and/or PACG				
Raw data, n (%)	24 (5.0)	45 (9.4)		
% estimated with survival analysis (95% CI)	5.50 (4.01, 7.53)	10.21 (8.03, 12.99)	0.52 (0.35, 0.78)	0.002
Incidence rate (per 1000 eye-years)	11.65	21.84		
Time of reaching primary endpoint				
Year 1	7	12		
Year 2	5	12		
Year 3	3	10		
Year 4	3	5		
Year 5	6	6		
Peripheral anterior synechiae				
Raw data, n (%)	6 (1.3)	23 (4.9)		
% estimated with survival analysis (95% CI)	1.36 (0.63, 2.94)	5.17 (3.62, 7.39)	0.26 (0.12, 0.55)	<0.001
Incidence rate (per 1000 eye-years)	2.91	11.16		
Time of progression to PAS				
Year 1	1	7		
Year 2	3	8		
Year 3	0	6		
Year 4	1	0		
Year 5	1	2		
IOP elevation to > 21 mm Hg				
Raw data, n (%)	16 (3.4)	18 (3.8)		
% estimated with survival analysis (95% CI)	3.73 (2.46, 5.64)	4.18 (2.88, 6.08)	0.89 (0.54, 1.46)	0.639
Incidence rate (per 1000 eye-years)	7.77	8.74		
Time of IOP elevation to > 21 mm Hg				
Year 1	5	3		
Year 2	2	4		
Year 3	3	4		
Year 4	3	4		
Year 5	3	3		
Acute angle closure				
Raw data, n (%)	1 (0.2)	2 (0.4)		
% estimated with survival analysis (95% CI)	0.22 (0.04, 1.30)	0.45 (0.11, 1.79)	0.50 (0.05, 5.53)	0.572
Incidence rate (per 1000 eye-years)	0.49	0.97		
Time of acute angle closure				
Year 1	1	0		
Year 3	0	2		

	Laser peripheral iridotomy (N=480)	Control (N=480)	Hazard ratio (95% CI)	p- value
PACG (GON + visual field loss compatible with glaucoma)				
Raw data, n (%)	3 (0.6)	7 (1.5)		
% estimated with survival analysis (95% CI)	0.73 (0.24, 2.27)	1.70 (0.80, 3.62)	0.43 (0.11, 1.66)	0.219
Incidence rate (per 1000 eye-years)	1.46	3.40		
Time of PACG				
Year 1	0	2		
Year 2	1	2		
Year 4	0	1		
Year 5	2	2		

All values are number of events unless stated otherwise. P-values were obtained from Chis-square test of hazard ratio in Cox regression model.

Table 3. Cross-tabulation of primary outcome at 60 months

		Laser peripheral iridotomy		
		No endpoint	Endpoint	Total
Control	No endpoint	424 (88.3)	11 (2.3)	435 (90.6)
	Endpoint	32 (6.7)	13 (2.7)	45 (9.4)
	Total	456 (95.0)	24 (5.0)	480 (100.0)

Values are number and proportion of patients.

P-value = 0.001 from McNemar's test, difference in proportion of subjects achieving the primary outcome = -4.4% (95% CI: -7.2% to -1.7%).

Table 4. Cox regression analysis of primary outcome (development of Primary angle closure and/or Primary angle closure glaucoma) and its association with demographics and baseline ocular factors at 60 months

	Eyes that did not reach endpoint (N = 891)	Eyes that reached endpoint (N = 69)	Unadjusted Analysis		Adjusted Analysis*	
			HR (95% CI)	p-value	HR (95% CI)	p-value
Laser peripheral iridotomy (vs. control)	456 (51.2)	24 (34.8)	0.52 (0.35, 0.78)	0.002	0.55 (0.37, 0.83)	0.004
Age (per 1 year older)	62.63 (6.89)	65.59 (5.67)	1.07 (1.04, 1.10)	< 0.0001	1.06 (1.03, 1.10)	< 0.001
Female (vs. male)	682 (76.5)	46 (66.7)	0.61 (0.34, 1.08)	0.087	0.72 (0.41, 1.25)	0.244
DM (vs. non-DM)	124 (13.9)	16 (23.2)	1.88 (0.98, 3.63)	0.059	1.42 (0.70, 2.89)	0.336
Baseline Post dilatation IOP (per 1 mm Hg increase)	14.65 (2.62)	17.53 (3.41)	1.38 (1.26, 1.52)	< 0.0001	1.35 (1.22, 1.50)	< 0.0001
Total angle width (per 1 score higher)	2.48 (1.98)	2.04 (1.79)	0.88 (0.76, 1.02)	0.096	1.01 (0.88, 1.16)	0.876
Limbal ACD grade (per 1% increase)	11.22 (8.33)	12.46 (9.95)	1.01 (0.98, 1.05)	0.367	Not included	
Anterior Chamber depth (per 1 mm deeper)	2.70 (0.39)	2.64 (0.31)	0.58 (0.28, 1.20)	0.140	1.01 (0.54, 1.90)	0.979
Lens thickness (per 1 mm thicker)	4.25 (0.90)	4.45 (0.81)	1.30 (0.97, 1.73)	0.081	1.09 (0.78, 1.51)	0.624
Central Corneal thickness (per 1 micron increase)	400.39 (72.00)	415.12 (92.93)	1.00 (1.00, 1.01)	0.234	Not included	
Cup-disc ratio (per 0.1 unit increase)	0.44 (0.13)	0.46 (0.12)	1.16 (0.94, 1.43)	0.177	1.14 (0.91, 1.42)	0.255

DM: Diabetes mellitus; HR: hazard ratio; *Analysis performed after adjusting for age, gender, diabetic status, baseline intraocular pressure, total angle width on gonioscopy, ACD, lens thickness and cup-disc ratio

Covariates with a p-value > 0.200 are excluded from the final model of adjusted analysis.

Table 5. Comparison of Ocular parameters at each visit

	Laser peripheral iridotomy (N=480)	Control (N=480)	Mean difference (95% CI)	p-value
Best corrected distance VA (logMAR)				
Baseline (n=182)	0.10 (0.11)	0.09 (0.10)	0.00 (-0.01,0.01)	0.592
Week 1 (n=476)	0.08 (0.10)	0.08 (0.10)	0.00 (-0.01,0.01)	0.784
Year 1 (n=462)	0.13 (0.12)	0.12 (0.11)	0.01 (-0.00,0.02)	0.188
Year 2 (n=433)	0.14 (0.13)	0.13 (0.12)	0.00 (-0.01,0.02)	0.531
Year 3 (n=408)	0.11 (0.14)	0.12 (0.14)	-0.00 (-0.01,0.01)	0.777
Year 4 (n=109)	0.22 (0.16)	0.19 (0.15)	0.02 (-0.01,0.05)	0.171
Year 5 (n=373)	0.14 (0.16)	0.13 (0.13)	0.02 (0.00,0.03)	0.010
Best corrected near VA (logMAR)				
Baseline (n=182)	0.09 (0.09)	0.08 (0.09)	0.01 (-0.00,0.02)	0.169
Week 1 (n=474)	0.06 (0.08)	0.07 (0.08)	-0.00 (-0.01,0.01)	0.790
Year 1 (n=460)	0.15 (0.15)	0.15 (0.16)	0.01 (-0.00,0.02)	0.225
Year 2 (n=433)	0.15 (0.17)	0.15 (0.18)	-0.00 (-0.01,0.01)	0.943
Year 3 (n=407)	0.07 (0.11)	0.06 (0.10)	0.00 (-0.01,0.01)	0.772
Year 4 (n=109)	0.11 (0.11)	0.10 (0.13)	0.01 (-0.01,0.04)	0.358
Year 5 (n=373)	0.08 (0.13)	0.07 (0.09)	0.01 (-0.00,0.02)	0.124
Pre dilatation IOP (mmHg)				
Baseline (n=480)	14.20 (2.34)	14.27 (2.43)	-0.07 (-0.19,0.04)	0.193
Week 1 (n=476)	13.69 (2.72)	13.62 (2.48)	0.07 (-0.09,0.24)	0.374
Year 1 (n=462)	13.93 (2.55)	14.11 (2.53)	-0.18 (-0.31,-0.05)	0.006
Year 2 (n=433)	14.27 (2.76)	14.29 (2.62)	-0.02 (-0.17,0.12)	0.765
Year 3 (n=413)	14.31 (3.21)	14.28 (2.84)	0.03 (-0.15,0.21)	0.732
Year 4 (n=392)	14.74 (2.97)	14.71 (2.85)	0.04 (-0.13,0.20)	0.652
Year 5 (n=380)	14.86 (3.07)	14.86 (2.99)	0.00 (-0.19,0.19)	0.993
Post dilatation IOP (mmHg)				
Baseline (n=480)	14.84 (2.74)	14.88 (2.83)	-0.05 (-0.17,0.08)	0.469
Year 1 (n=451)	14.72 (2.68)	15.04 (2.71)	-0.32 (-0.45,-0.20)	< 0.0001
Year 2 (n=422)	14.99 (2.93)	14.91 (2.71)	0.08 (-0.07,0.23)	0.286
Year 3 (n=407)	14.72 (3.03)	14.65 (3.00)	0.07 (-0.09,0.22)	0.388
Year 4 (n=389)	15.35 (3.32)	15.26 (3.09)	0.09 (-0.10,0.28)	0.349
Year 5 (n=378)	14.88 (3.26)	14.81 (3.16)	0.07 (-0.14,0.28)	0.520
Total angle width on Gonioscopy				
Baseline (n=480)	2.46 (1.98)	2.43 (1.96)	0.03 (-0.07,0.12)	0.590

	Laser peripheral			
	iridotomy	Control	Mean difference	
	(N=480)	(N=480)	(95% CI)	p-value
Week 1 (n=461)	7.01 (2.99)	2.53 (2.11)	4.49 (4.22,4.76)	< 0.0001
Year 1 (n=462)	7.24 (2.98)	2.53 (2.15)	4.72 (4.45,4.99)	< 0.0001
Year 2 (n=433)	7.59 (3.07)	2.70 (2.32)	4.89 (4.61,5.18)	< 0.0001
Year 3 (n=412)	7.90 (3.01)	3.35 (2.57)	4.55 (4.27,4.83)	< 0.0001
Year 4 (n=391)	8.10 (3.12)	3.81 (2.93)	4.29 (3.97,4.62)	< 0.0001
Year 5 (n=380)	8.31 (3.40)	4.35 (3.38)	3.96 (3.62,4.30)	< 0.0001
Limbal ACD grade (%)				
Baseline (n=480)	11.17 (8.34)	11.46 (8.57)	-0.29 (-0.75,0.16)	0.207
Week 1 (n=476)	40.02 (22.20)	12.74 (9.39)	27.28 (25.44,29.12)	< 0.0001
Year 1 (n=462)	37.06 (20.03)	12.90 (9.94)	24.16 (22.54,25.77)	< 0.0001
Year 2 (n=433)	35.69 (20.79)	13.53 (11.24)	22.16 (20.54,23.78)	< 0.0001
Year 3 (n=412)	37.52 (22.41)	15.47 (14.26)	22.05 (20.29,23.81)	< 0.0001
Year 4 (n=391)	38.66 (21.67)	17.93 (14.62)	20.73 (18.90,22.56)	< 0.0001
Year 5 (n=380)	39.03 (20.72)	21.26 (17.95)	17.76 (15.80,19.72)	< 0.0001

VA: visual acuity; IOP: intraocular pressure; ACD – Anterior Chamber Width

Table 6. Adverse events and specular microscopy results at 60 months

	Laser peripheral iridotomy (N = 477)	Control (N = 477)	Difference (95% CI)	p-value
Eye specific AE, n(%)				
Any eye specific AE	105 (22.01)	69 (14.47)	7.55 (4.48, 10.70)	< 0.0001
Eye pain	20 (4.19)	10 (2.10)	2.10 (0.52, 3.98)	0.013
Dry eye	2 (0.42)	1 (0.21)	0.21 (-0.81, 1.32)	1.000
Redness	5 (1.05)	4 (0.84)	0.21 (-1.16, 1.63)	1.000
Ocular discomfort	14 (2.94)	11 (2.31)	0.63 (-0.54, 1.96)	0.375
IOP spike after LPI (≥ 30 mm Hg at 1 week)	0 (0.00)	0 (0.00)	0.00 (-0.79, 0.79)	NA
Other eye-specific AEs	85 (17.82)	54 (11.32)	6.50 (3.68, 9.46)	< 0.0001
Specular microscopy at 60 months, mean (SD)				
Cell density (per mm ²)	2557 (437)	2588 (409)	-28 (-56,1)	0.059
Change from baseline	2.1 (389.1)	47.4 (371.3)	-44.1 (-77.7,-10.5)	0.010
Mean cell area (u m ²)	413 (192)	399 (82)	14 (-1,30)	0.064
Change from baseline	12.2 (176.4)	-6.2 (68.5)	18.3 (2.1,34.4)	0.027
Standard deviation	153 (77)	145 (46)	7 (-0,14)	0.055
Change from baseline	-15.6 (125.7)	-31.0 (98.7)	15.3 (1.2,29.3)	0.033
Coefficient of variation	36.7 (7.9)	36.5 (7.9)	0.2 (-0.8,1.2)	0.665
Change from baseline	-3.1 (13.1)	-5.6 (17.2)	2.4 (0.7,4.2)	0.006
Hexagonality (%)	56.9 (7.8)	57.5 (7.8)	-0.6 (-1.5,0.4)	0.269
Change from baseline	2.4 (10.9)	3.2 (11.1)	-0.8 (-2.3,0.6)	0.261
Number of cells analyzed	3.06 (0.92)	2.97 (0.86)	0.09 (0.05,0.12)	< 0.0001
Change from baseline	-62.24 (10.91)	-61.43 (12.14)	-0.73 (-1.72,0.26)	0.146

LPI: Laser peripheral iridotomy; values are number and proportion of subjects for eye specific AE.