Incidence of New Diabetic Macular Edema in Fellow Eyes of Patients in the VISTA and VIVID studies

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Disclosures

- Dr Dhoot is a consultant for Regeneron Pharmaceuticals, Inc., Genentech, Allergan, Alimera, Santen, Allegro, and Notal Vision
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Background

VIVID and VISTA are randomized, multicenter, double-masked trials in patients with clinically significant DME with central involvement and ETDRS BCVA 20/40 to 20/320
Randomized and treated: N = 404 (VIVID) & N = 461 (VISTA)

Patients randomized 1:1:1

IAI 2 mg q4 wks

IAI 2 mg q8 wks*

Laser photocoagulation

Primary endpoint: mean change in BCVA

Primary endpoint: week 52

Key secondary endpoints: mean change in OCT % with ≥2-step DRSS improvement

Continued treatment through year 3

*After 5 initial monthly doses

- IAI given q4 weeks or q8 weeks (following 5 monthly doses) significantly improved visual and anatomic outcomes over laser at week 52. These improvements were sustained through week 100 with both IAI regimens
- In an integrated safety analysis, the most frequent serious ocular adverse event at week 100 was cataract (2.4%, 1.0%, and 0.3% for 2q4, 2q8, and control)

BCVA, best corrected visual acuity; DME, diabetic macular edema; DRSS, Diabetic Retinopathy Severity Scale; ETDRS, Early Treatment Diabetic Retinopathy Study; IAI, intravitreal aflibercept injection; OCT, optical coherence tomography.

Objectives

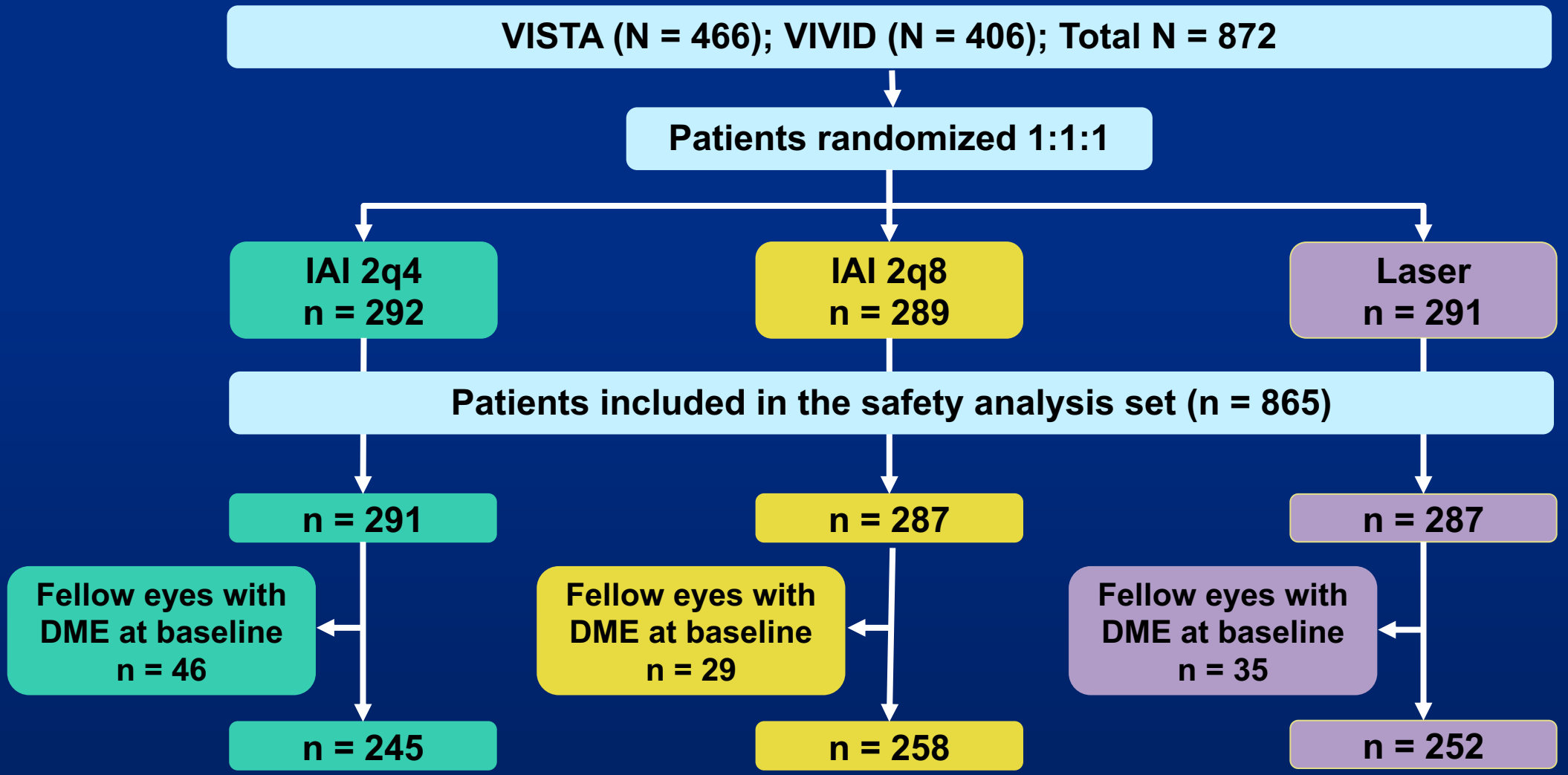
- To characterize occurrence of DME in fellow eye of patients treated for DME in study eye in the VISTA and VIVID studies through year 2
- Following parameters were evaluated:
  - Incidence of DME in fellow eye
  - Time to development of DME in fellow eye
  - Baseline factors predicting DME occurrence in fellow eye
  - Cumulative rates of DME occurrence in fellow eye by various baseline risk factors

Methods

- Inclusion criteria
  - No DME in fellow eye at baseline (from 6 weeks before baseline through 4 weeks after first study eye treatment)
- Presence of DME in fellow eye was evaluated based on related AEs and reported medications (anti-VEGF agents) or procedures (laser) for treatment of DME
- Safety analysis set, observed case
- Statistical analyses included t-test, Kaplan–Meier, Cox proportional hazards model
- Post hoc analysis, *P* value < 0.05 was considered nominally significant

AEs, adverse events; VEGF, vascular endothelial growth factor.

Patient Disposition



2q4, 2 mg every 4 weeks; 2q8, 2 mg every 8 weeks.

Baseline Characteristics

	Laser (n = 252)	IAI 2q4 (n = 245)	IAI 2q8 (n = 258)	Total (n = 755)
Age, mean (SE), years	62.9 (0.5)	62.8 (0.6)	63.6 (0.5)	63.1 (0.3)
Male, n (%)	145 (57.5)	141 (57.6)	151 (58.5)	437 (57.9)
Ethnicity				
Hispanic or Latino	19 (7.5)	30 (12.2)	28 (10.9)	77 (10.2)
Not Hispanic or Latino, n (%)	230 (91.3)	215 (87.8)	230 (89.2)	675 (89.4)
Mean duration of diabetes, years (SE)[a]	16.6 (0.64)	16.0 (0.62)	16.1 (0.64)	16.2 (0.36)
Hemoglobin A1c, Mean (SE), %[b]	7.7 (0.1)	7.9 (0.1)	7.8 (0.1)	7.8 (0.1)
>8%, n (%)	83 (32.9)	95 (38.8)	91 (35.3)	269 (35.6)
Mean study eye BCVA, letters[a] (SE)	60.4 (0.7)	60.0 (0.7)	59.5 (0.7)	59.9 (0.4)
Study eye DRSS score, n (%)				
≤35	11 (4.4)	15 (6.1)	14 (5.4)	40 (5.3)
43	87 (34.5)	71 (29.0)	75 (29.1)	233 (30.9)
47	42 (16.7)	35 (14.3)	50 (19.4)	127 (16.8)
53	68 (27.0)	75 (30.6)	76 (29.5)	219 (29.0)
≥61	11 (4.4)	11 (4.5)	12 (4.7)	34 (4.5)
Missing	33 (13.1)	38 (15.5)	31 (12.0)	102 (13.5)

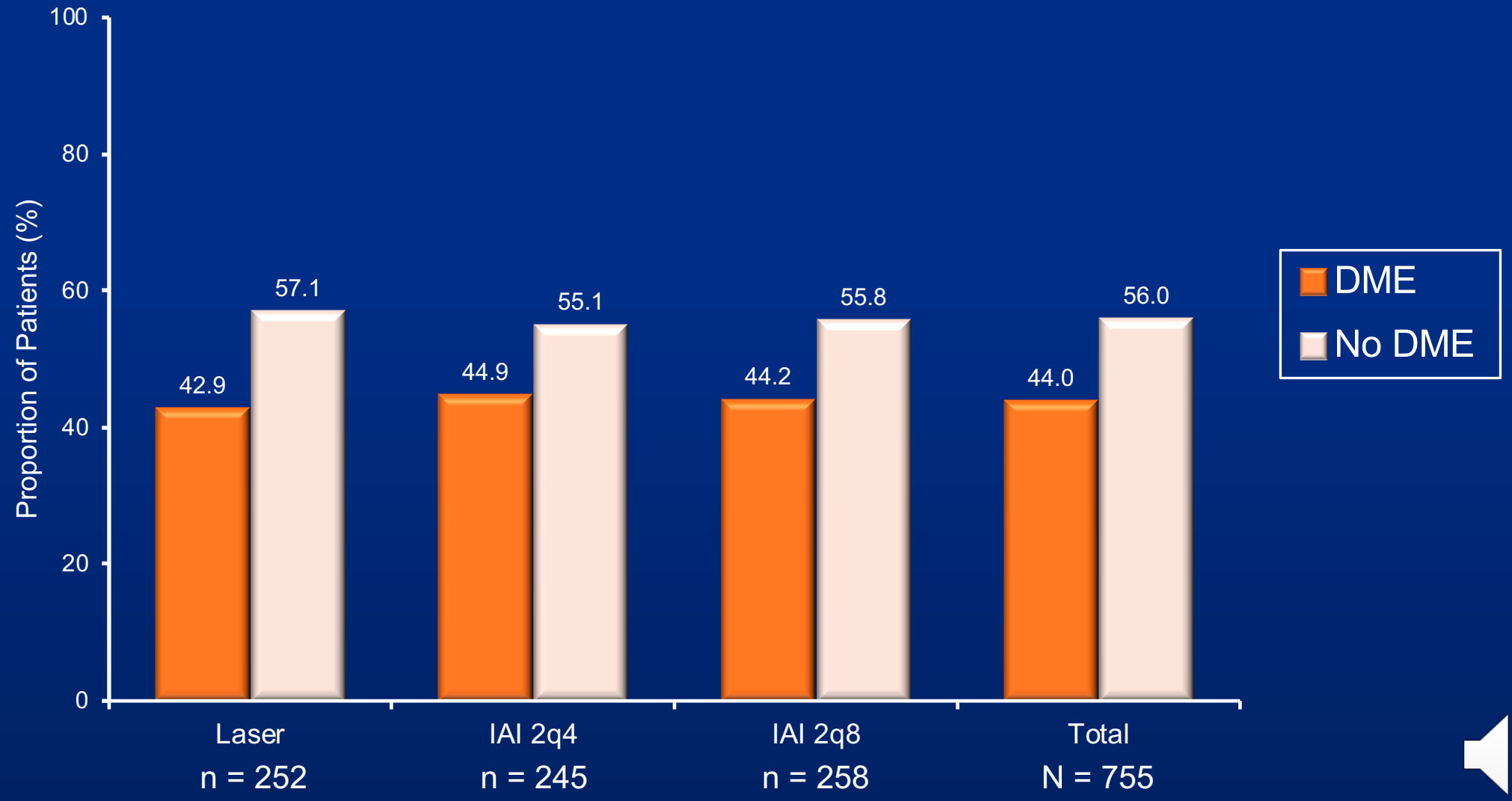
Data for patients without DME in fellow eye at baseline. [a]Laser (n = 251), IAI 2q4 (n = 244), IAI 2q8 (n = 257), Total (N = 752); [b]Laser (n = 250), IAI 2q4 (n = 241), IAI 2q8 (n = 258), Total (N = 749).
SE, standard error.

Medical History

	Laser (n = 252)	IAI 2q4 (n = 245)	IAI 2q8 (n = 258)	Total (n = 755)
Hyperlipidemia, n (%)	54 (21.4)	53 (21.6)	46 (17.8)	153 (20.3)
Dyslipidemia, n (%)	10 (4.0)	8 (3.3)	9 (3.5)	27 (3.6)
Depression, n (%)	36 (14.3)	23 (9.4)	37 (14.3)	96 (12.7)
Anxiety, n (%)	22 (8.7)	10 (4.1)	14 (5.4)	46 (6.1)
Any antidepressants, n (%)	43 (17.1)	41 (16.7)	30 (11.6)	114 (15.1)
Hypertension, n (%)	196 (77.8)	189 (77.1)	211 (81.8)	596 (78.9)
Insulin use, n (%)	173 (68.7)	168 (68.6)	161 (62.4)	502 (66.5)
Smoking history, n (%)				
Never	133 (52.8)	142 (58.0)	151 (58.5)	426 (56.4)
Former	95 (37.7)	71 (29.0)	91 (35.3)	257 (34.0)
Current	24 (9.5)	32 (13.1)	16 (6.2)	72 (9.5)

Data for patients without DME in fellow eye at baseline.

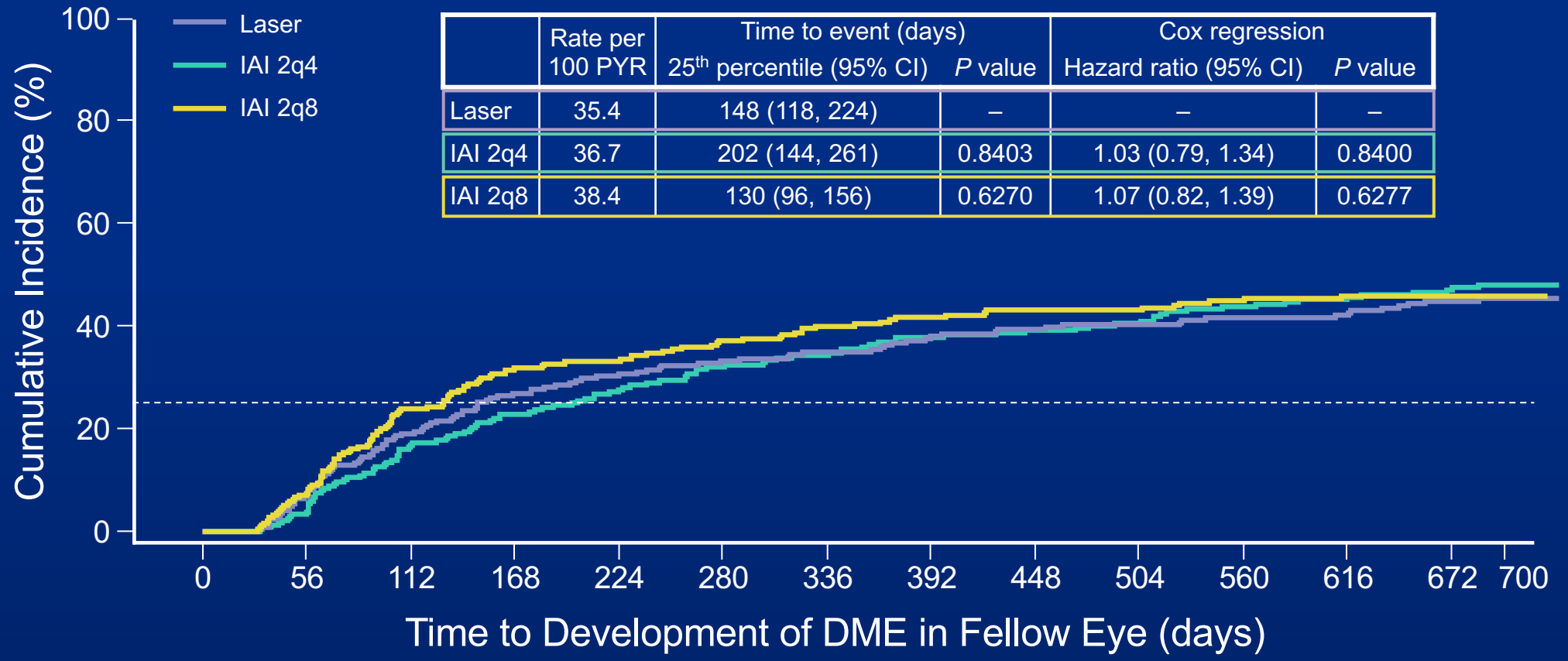
Proportion of Fellow Eyes That Developed DME Through Week 100



*IAI per protocol when available.

Cumulative Incidence of DME in Fellow Eye

	Rate per 100 PYR	Time to event (days) 25th percentile (95% CI)	*P* value	Cox regression Hazard ratio (95% CI)	*P* value
Laser	35.4	148 (118, 224)	–	–	–
IAI 2q4	36.7	202 (144, 261)	0.8403	1.03 (0.79, 1.34)	0.8400
IAI 2q8	38.4	130 (96, 156)	0.6270	1.07 (0.82, 1.39)	0.6277



Laser (n = 252)	0	17	47	66	75	81	85	92	95	97	100	101	107	108
IAI 2q4 (n = 245)	0	9	40	54	65	75	80	88	91	94	101	105	108	110
IAI 2q8 (n = 258)	0	19	61	81	84	94	101	105	108	108	112	114	114	114

CI, confidence interval; PYR, person-years at risk.

Time to Development of DME in Fellow Eye Through Week 100

	Laser	IAI 2q4	IAI 2q8	IAI 2q4+2q8	Total
Patients developed DME	108	110	114	224	332
Mean time to DME development, days (SE)	201 (17)	236 (17)	161 (13)	198 (11)	199 (9)
Min, max (days)	30, 687	31, 687	30, 613	30, 687	30, 687
Mean difference vs laser, days (95% CI)	–	35.0 (–13.1, 83.2)	–40.6 (–82.6, 1.4)	–3.5 (–42.4, 35.5)	–
P value	–	0.1530	0.0581	0.8613	–

Difference, CI and *P* value were calculated using t-test.

Baseline Factors Predicting Development of DME in Fellow Eyes

Univariate Analysis of Baseline Characteristics

Baseline Variables Included in Cox Regression Model

Demographics & Characteristics	Disease Characteristics	Comorbidities	Concomitant Medications
Age	Diabetes duration	Hypertension	Antidepressants
Gender	BCVA in study eye	Anxiety	Insulin
Ethnicity	DRSS score in study eye	Depression	
BMI	CST in study eye	Dyslipidemia	
Smoking history		Hyperlipidemia	

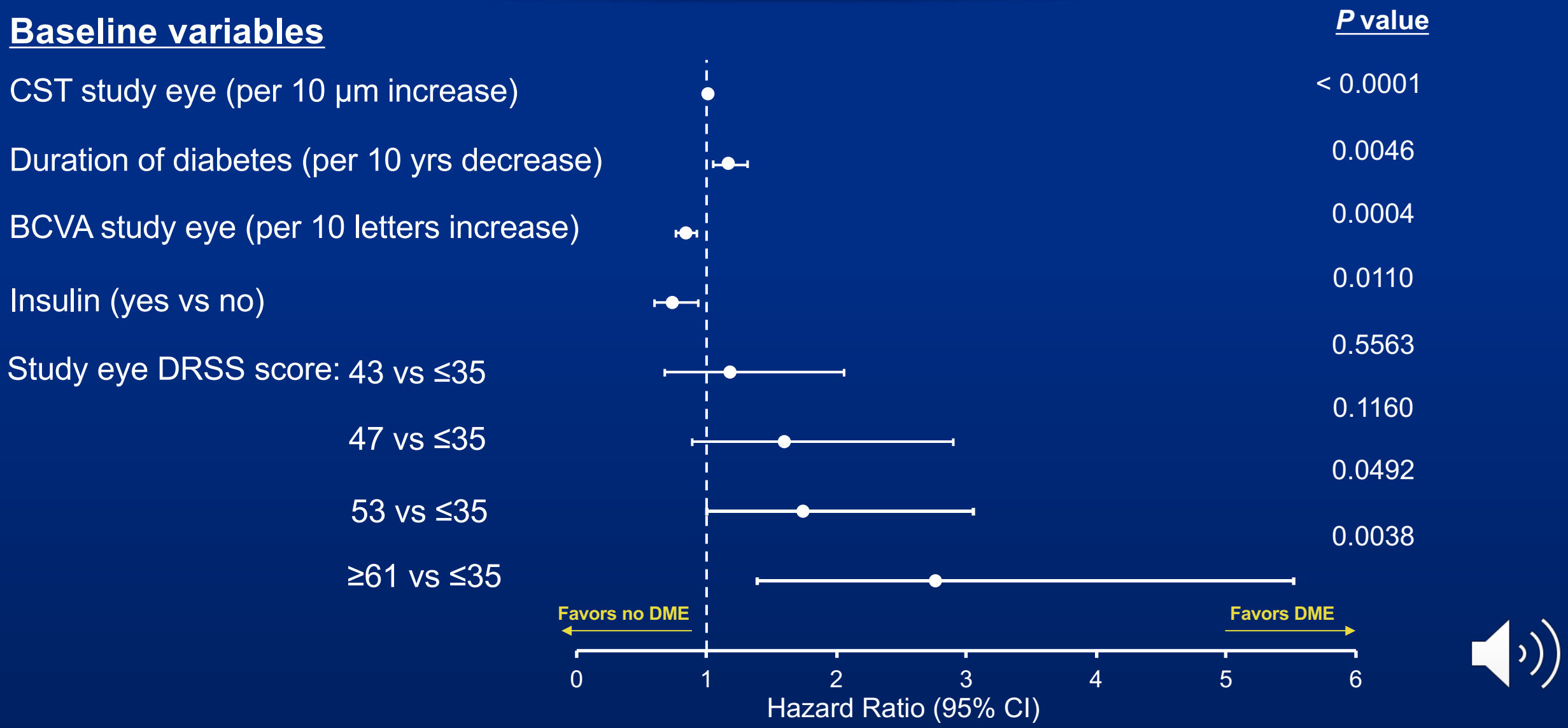
BMI, body mass index; CST, central subfield thickness.

Univariate Analysis of Baseline Characteristics

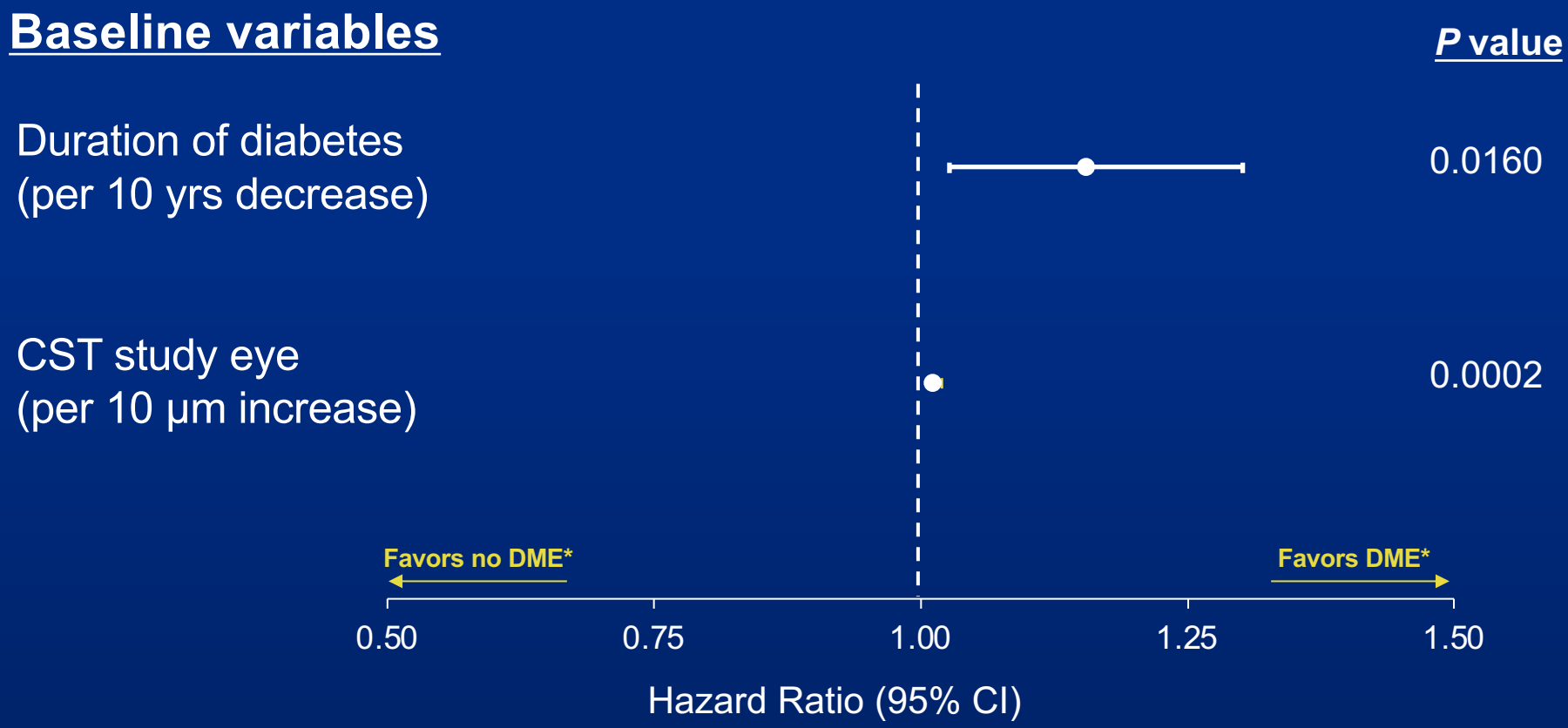
Baseline Variables Identified as Risk Factors in Cox Regression Model

Demographics & Characteristics	Disease Characteristics	Comorbidities	Concomitant medications
Age	Diabetes duration	Hypertension	Antidepressants
Gender	BCVA in study eye	Anxiety	Insulin
Ethnicity	DRSS score in study eye	Depression	
BMI	CST in study eye	Dyslipidemia	
Smoking history		Hyperlipidemia	

Univariate Analysis: Hazard Ratio of DME Development in Fellow Eyes



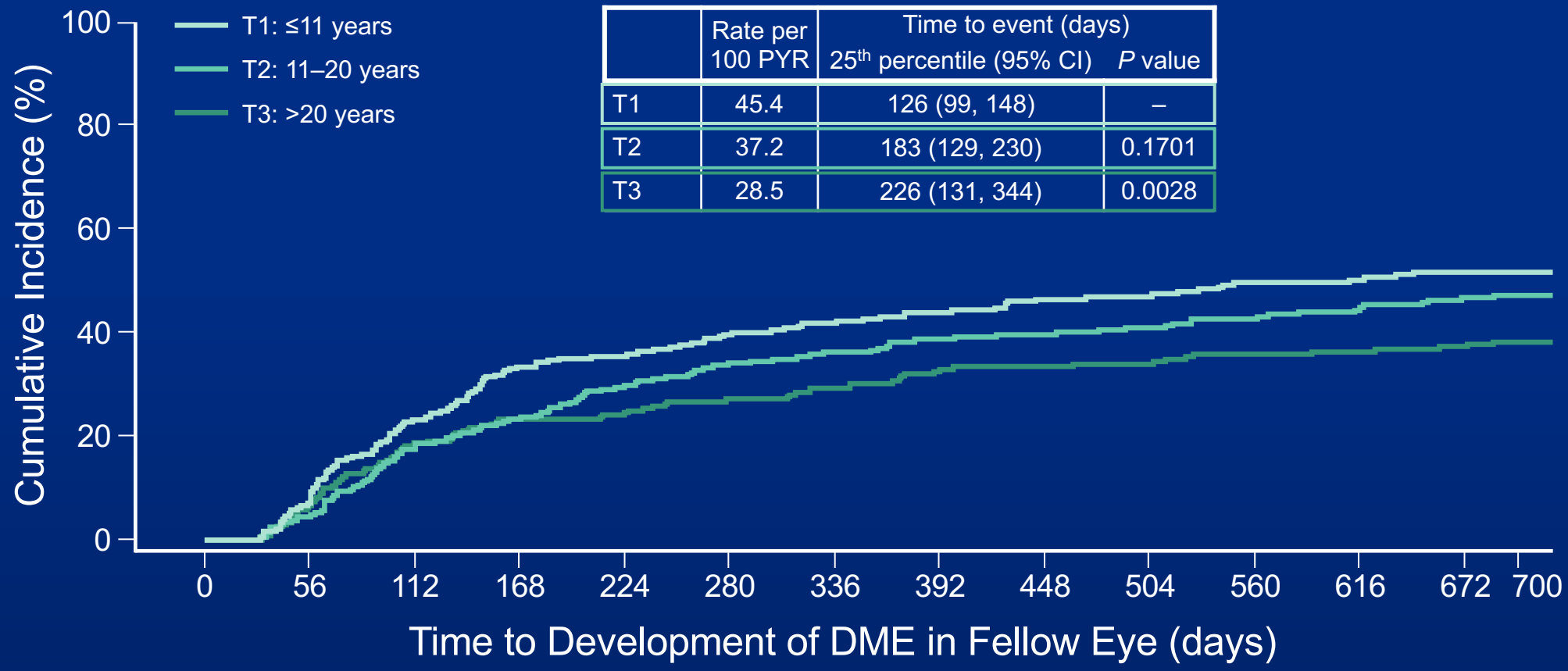
Multivariate Analysis: Hazard Ratio of DME Development in Fellow Eyes



Hazard ratio was estimated using Cox regression model and stepwise selection with baseline CST study eye, baseline duration of diabetes diagnosis, baseline study eye BCVA, baseline insulin use, and baseline DRSS score category as the covariates.

Model was decided by stepwise selection.

Cumulative Incidence of DME Development in Fellow Eye By Baseline Duration of Diabetes

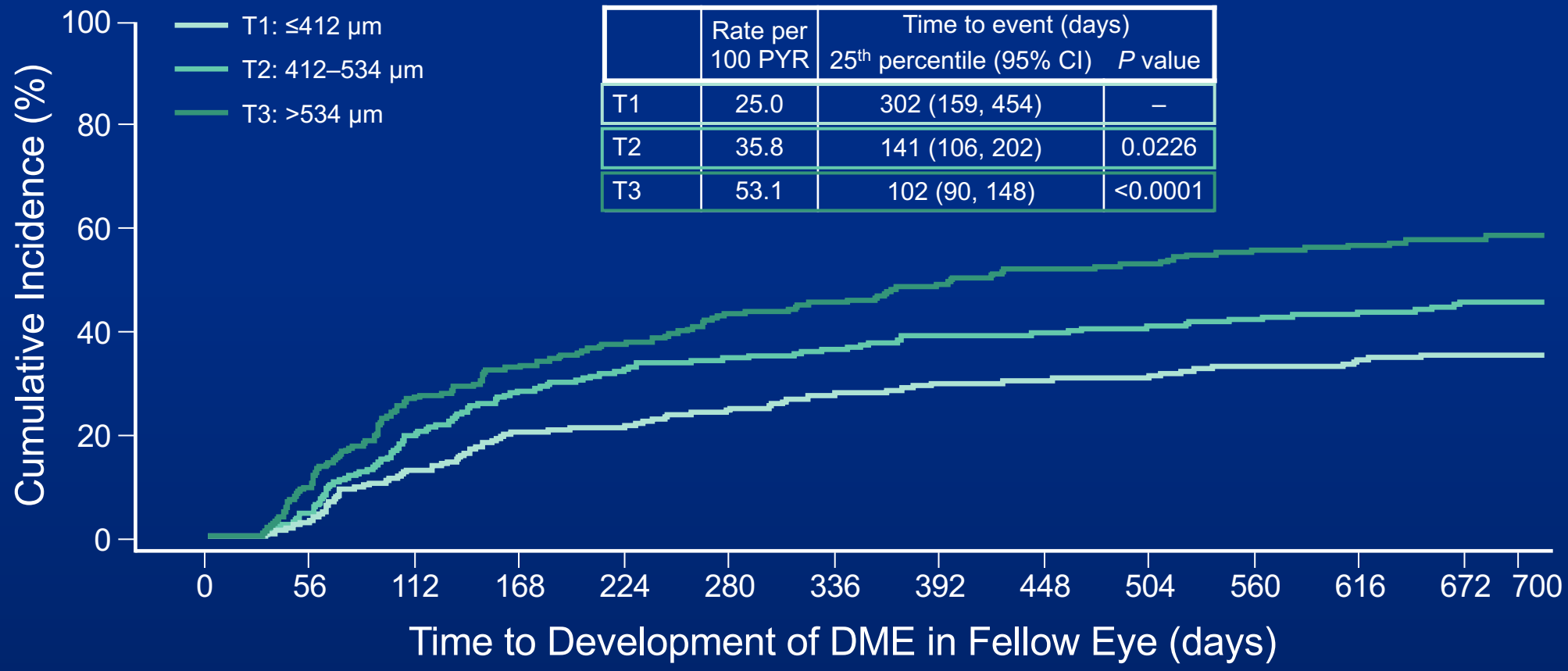


	Rate per 100 PYR	Time to event (days) 25th percentile (95% CI)	*P* value
T1	45.4	126 (99, 148)	–
T2	37.2	183 (129, 230)	0.1701
T3	28.5	226 (131, 344)	0.0028

T1: (n = 262)	0	18	60	86	91	101	106	111	117	118	124	125	128	128
T2: (n = 249)	0	11	43	58	73	83	88	94	96	99	103	108	112	113
T3: (n = 241)	0	16	45	56	59	65	70	78	79	80	84	85	87	89

Data for all groups combined. T, tertile.

Cumulative Incidence of DME Development in Fellow Eye By Baseline CST in Study Eye

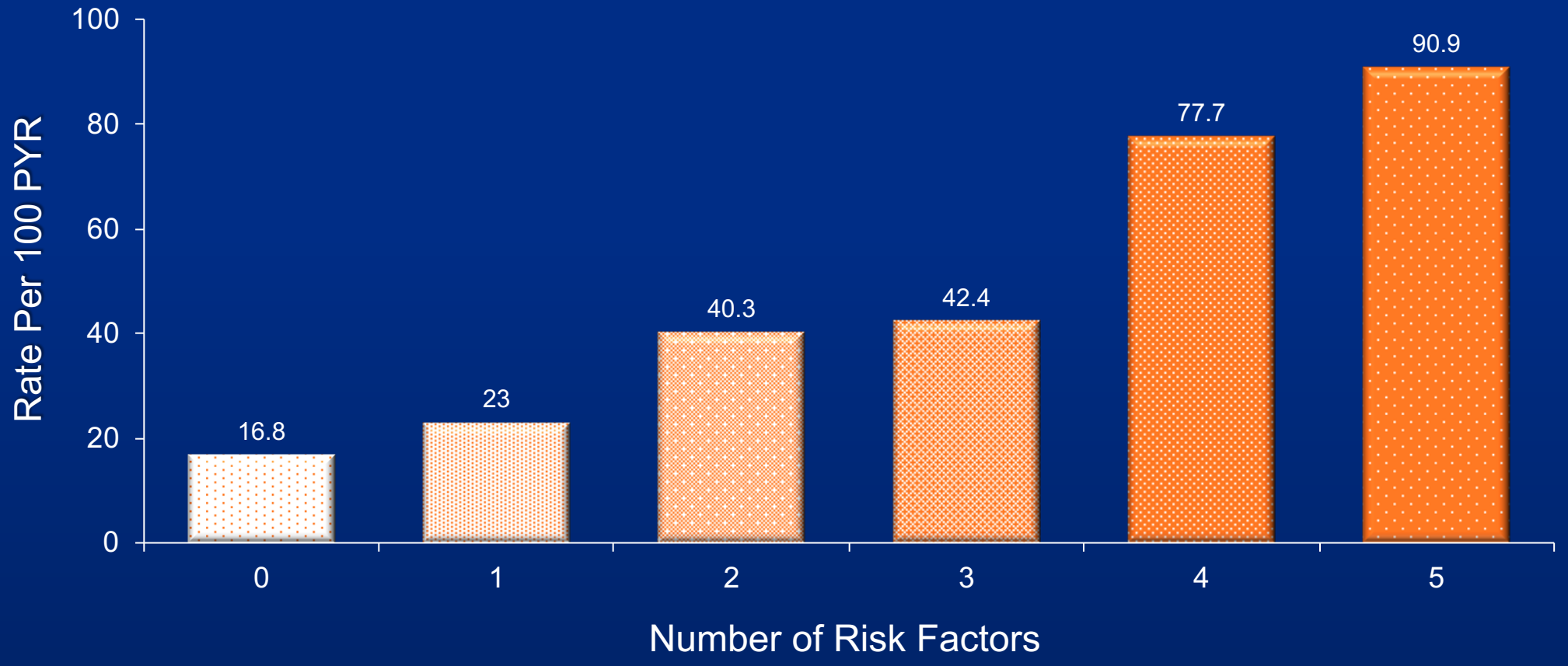


	Rate per 100 PYR	Time to event (days) 25th percentile (95% CI)	*P* value
T1	25.0	302 (159, 454)	–
T2	35.8	141 (106, 202)	0.0226
T3	53.1	102 (90, 148)	<0.0001

T1: (n = 252)	0	8	32	50	53	60	67	72	73	74	79	81	84	84
T2: (n = 252)	0	11	49	69	79	84	88	94	95	97	101	103	107	108
T3: (n = 251)	0	26	67	82	92	106	111	119	126	128	133	136	138	140

Data for all groups combined.

Rates of Fellow Eye DME by Number of Initially Identified Baseline Risk Factors

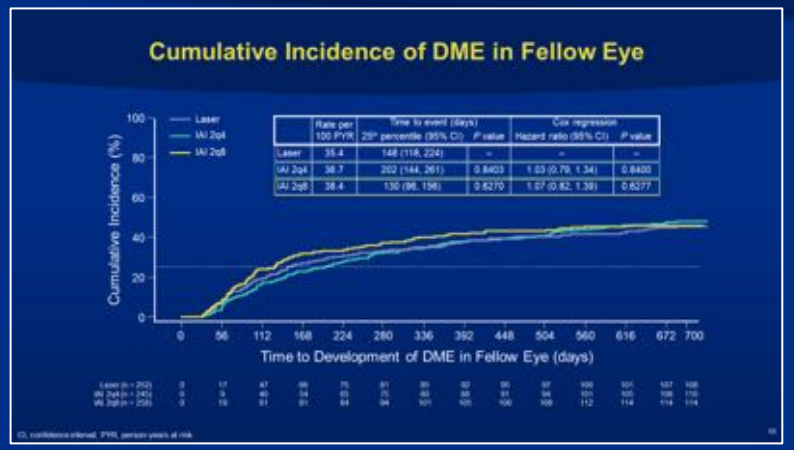


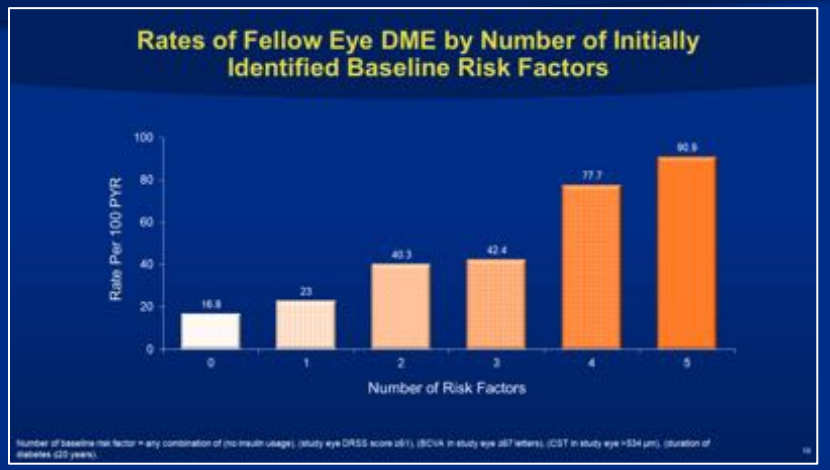
Number of baseline risk factor = any combination of (no insulin usage), (study eye DRSS score ≥61), (BCVA in study eye ≤67 letters), (CST in study eye >534 µm), (duration of diabetes ≤20 years).

Limitations

- Post hoc analysis
- DME identified based on AEs and concomitant medications and procedures
- BCVA data was not available for analysis
- No CST data collected for fellow eye

Conclusions





- Almost half of patients with DME in one eye developed DME in fellow eye over 2 years of follow-up
  - Time to development of DME in fellow eye was approximately 6 months
- Shorter duration of diabetes and thicker baseline CST in the study eye were identified as key risk factors for DME development in fellow eye
- Rate of DME development in fellow eye increased with the increasing numbers of risk factors
- These findings suggest that patients with DME in one eye should be closely monitored for DME development in fellow eye