Patient Characteristics Affecting Incidence of Vision-Threatening Events (VTC) and Center-Involved Diabetic Macular Edema (CI-DME) in Moderately Severe to Severe Nonproliferative Diabetic Retinopathy (NPDR)

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Disclosures

- Dr Marcus has acted as a consultant for Regeneron Pharmaceuticals, Inc., Genentech/Roche, and has received research funding from Allergan, Alcon, Aerpio, Kalvista, Ionis, Mylan, Samsung, Novartis, Opthea, Chenghdu, Clearside, Astellas, Allegro, Alimera, Ophthotech, Outlook, Gemini, Genentech, ThromboGenics, Tyrogenex, Topcon, Gyroscope, Stealth Spiam, Aerie, Apellis, Roche, Novartis, OHR, Xplore, Regenxbio and Regeneron Pharmaceuticals, Inc.
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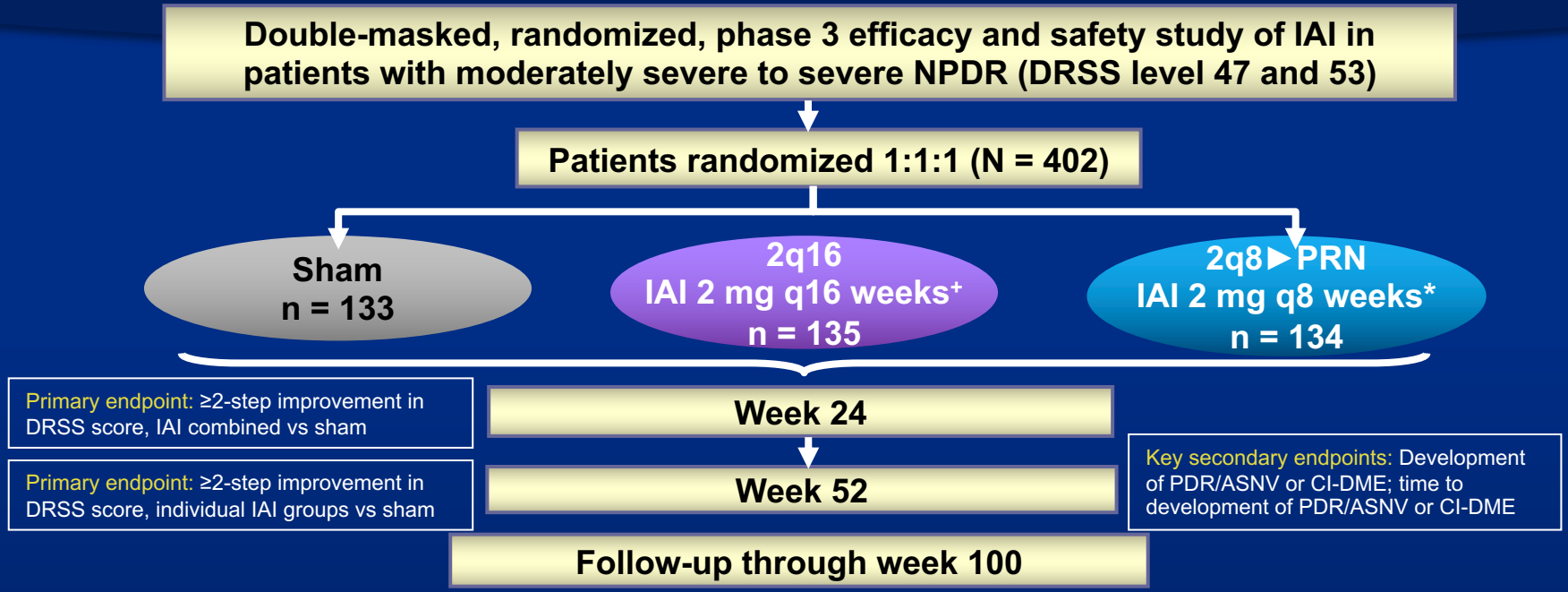
- Medical writing support was provided by Prime, Knutsford, UK, according to Good Publication Practice guidelines, and was funded by Regeneron Pharmaceuticals, Inc.

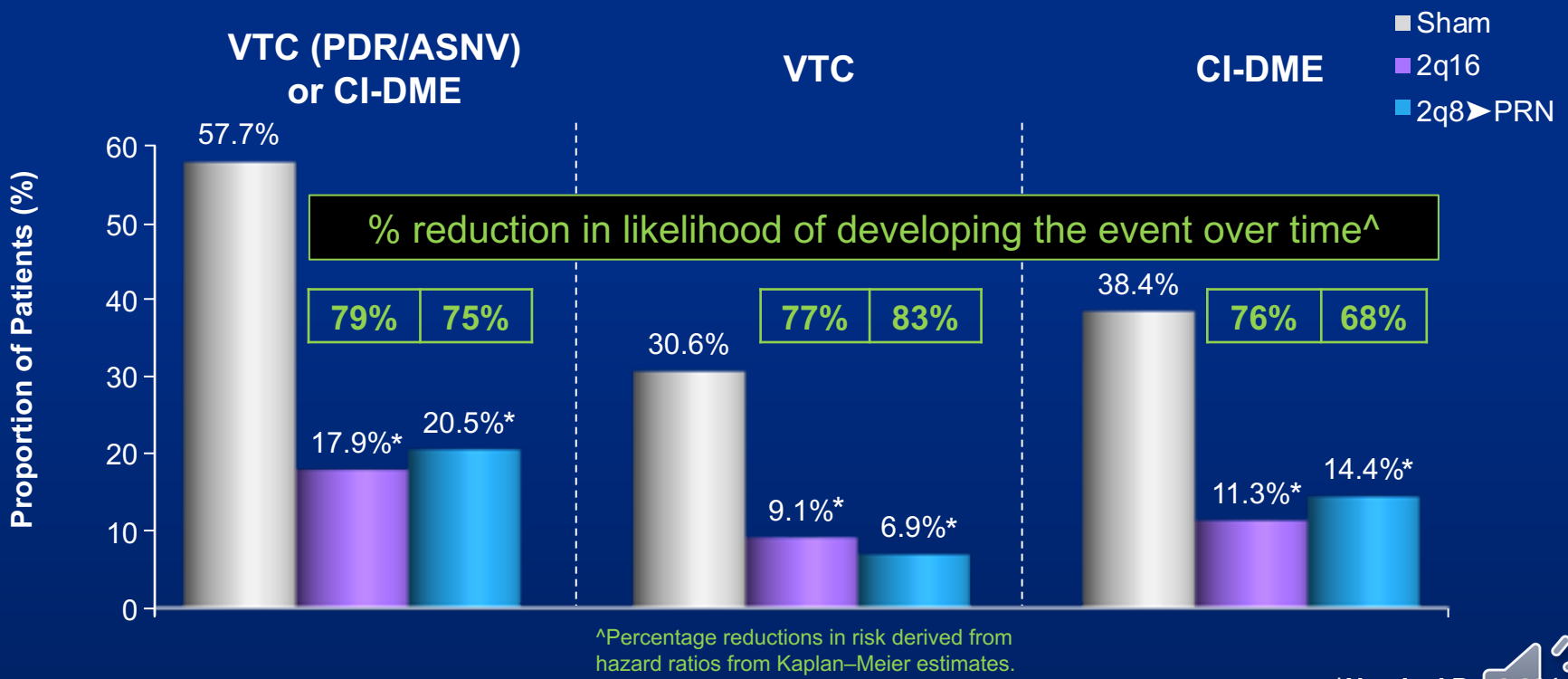
PANORAMA Study Design



- At week 100, a significantly higher proportion of eyes receiving 2q16 and 2q8 had a ≥2-step improvement in DRSS score vs sham (62.2% and 50.0% vs 12.8%; $P < 0.0001$ for both)
- Rates of VTC (9.1% and 6.9% vs 30.6%) and CI-DME (11.3% and 14.4% vs 38.4%) were significantly lower with IAI 2q16 and 2q8 compared with sham through week 100

+After 3 initial monthly doses and 1 q8 interval; *After 5 initial monthly doses, flexible treatment schedule after week 52.
ASNV, anterior segment neovascularization; CI-DME, center-involved diabetic macular edema; DRSS, Diabetic Retinopathy Severity Score; IAI, intravitreal aflibercept injection; NPDR, nonproliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy; PRN, pro re nata; VTC, vision-threatening complication defined as PDR/ASNV.

Proportion of Patients Developing a VTC or CI-DME through Week 100: Kaplan–Meier Analysis



^Percentage reductions in risk derived from hazard ratios from Kaplan–Meier estimates.

*Nominal P < 0.001 vs. sham

Full analysis set; Sham n = 133, 2q16 n = 135, 2q8 n = 134.

Objective and Post Hoc Analysis

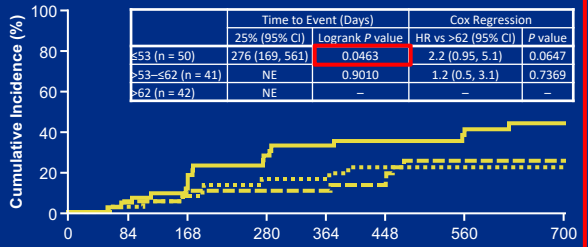
- **Objective**
  - To evaluate the development of VTC or CI-DME through week 100 by baseline patient characteristics* in patients treated with sham, mimicking the natural history of the disease
- **Methods**
  - Only patients treated with sham (n = 133) were included
  - Differences in subgroup effect across baseline patient characteristics were evaluated by Mantel-Haenszel weighting scheme adjusted by baseline DRSS stratification variable
  - Between-subgroup comparisons were evaluated by 2-sided Cochran-Mantel-Haenszel test adjusted by baseline DRSS stratification variable
  - Time to an event was evaluated by Kaplan–Meier and Cox regression methods; Logrank test was used to test the difference between two Kaplan–Meier curves
  - Observed cases were used. For any patient who received rescue treatment, data were censored from the time rescue treatment was given

Time to development of VTC (PDR/ASNV) through Week 100

By Age Tertiles

≤53 years
>53–≤62 years
>62 years

	Time to Event (Days)		Cox Regression	
	25% (95% CI)	Logrank *P* value	HR vs >62 (95% CI)	*P* value
≤53 (n = 50)	276 (169, 561)	0.0463	2.2 (0.95, 5.1)	0.0647
>53–≤62 (n = 41)	NE	0.9010	1.2 (0.5, 3.1)	0.7369
>62 (n = 42)	NE	–	–	–

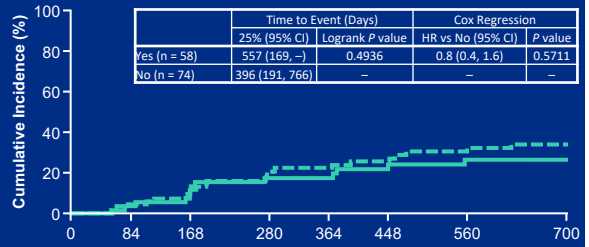


Age:								
≤53 years	0	2	5	12	14	15	16	18
>53–≤62 years	0	2	4	4	4	5	9	9
>62 years	0	1	3	6	6	8	8	8

By Ethnicity

Hispanic or Latino: Yes
Hispanic or Latino: No

	Time to Event (Days)		Cox Regression	
	25% (95% CI)	Logrank *P* value	HR vs No (95% CI)	*P* value
Yes (n = 58)	557 (169, –)	0.4936	0.8 (0.4, 1.6)	0.5711
No (n = 74)	396 (191, 766)	–	–	–

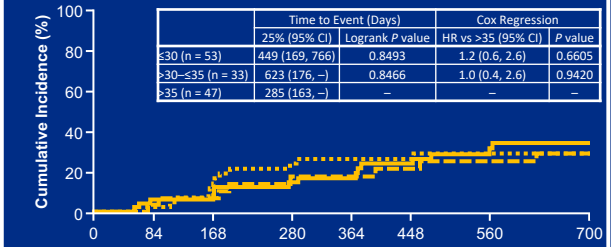


Hispanic or Latino:								
Yes	0	2	6	9	9	11	13	13
No	0	3	6	13	15	17	20	22

By BMI Subgroups

≤30
>30–≤35
>35

	Time to Event (Days)		Cox Regression	
	25% (95% CI)	Logrank *P* value	HR vs >35 (95% CI)	*P* value
≤30 (n = 53)	449 (169, 766)	0.8493	1.2 (0.6, 2.6)	0.6605
>30–≤35 (n = 33)	623 (176, –)	0.8466	1.0 (0.4, 2.6)	0.9420
>35 (n = 47)	285 (163, –)	–	–	–

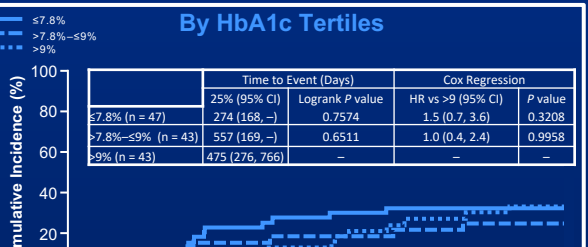


BMI:								
≤30	0	3	4	7	8	11	14	15
>30–≤35	0	1	2	5	5	6	7	8
>35	0	1	6	10	11	11	12	12

By HbA1c Tertiles

≤7.8%
>7.8%–≤9%
>9%

	Time to Event (Days)		Cox Regression	
	25% (95% CI)	Logrank *P* value	HR vs >9 (95% CI)	*P* value
≤7.8% (n = 47)	274 (168, –)	0.7574	1.5 (0.7, 3.6)	0.3208
>7.8%–≤9% (n = 43)	557 (169, –)	0.6511	1.0 (0.4, 2.4)	0.9958
>9% (n = 43)	475 (276, 766)	–	–	–

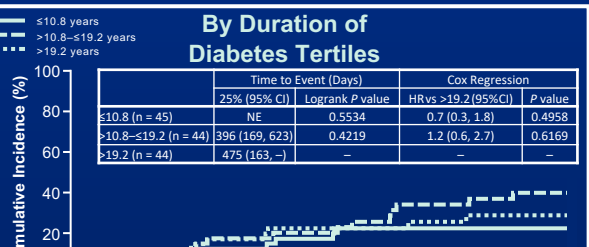


HbA1c:								
≤7.8%	0	2	6	11	12	13	14	14
>7.8%–≤9%	0	2	3	6	7	7	9	9
>9%	0	1	3	5	5	8	10	12

By Duration of Diabetes Tertiles

≤10.8 years
>10.8–≤19.2 years
>19.2 years

	Time to Event (Days)		Cox Regression	
	25% (95% CI)	Logrank *P* value	HR vs >19.2 (95%CI)	*P* value
≤10.8 (n = 45)	NE	0.5534	0.7 (0.3, 1.8)	0.4958
>10.8–≤19.2 (n = 44)	396 (169, 623)	0.4219	1.2 (0.6, 2.7)	0.6169
>19.2 (n = 44)	475 (163, –)	–	–	–

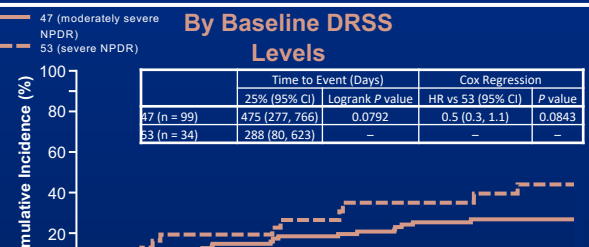


Duration of Diabetes:								
≤10.8	0	2	4	6	7	9	9	9
>10.8–≤19.2	0	2	3	7	8	10	13	15
>19.2	0	1	5	9	9	9	11	11

By Baseline DRSS Levels

47 (moderately severe NPDR)
53 (severe NPDR)

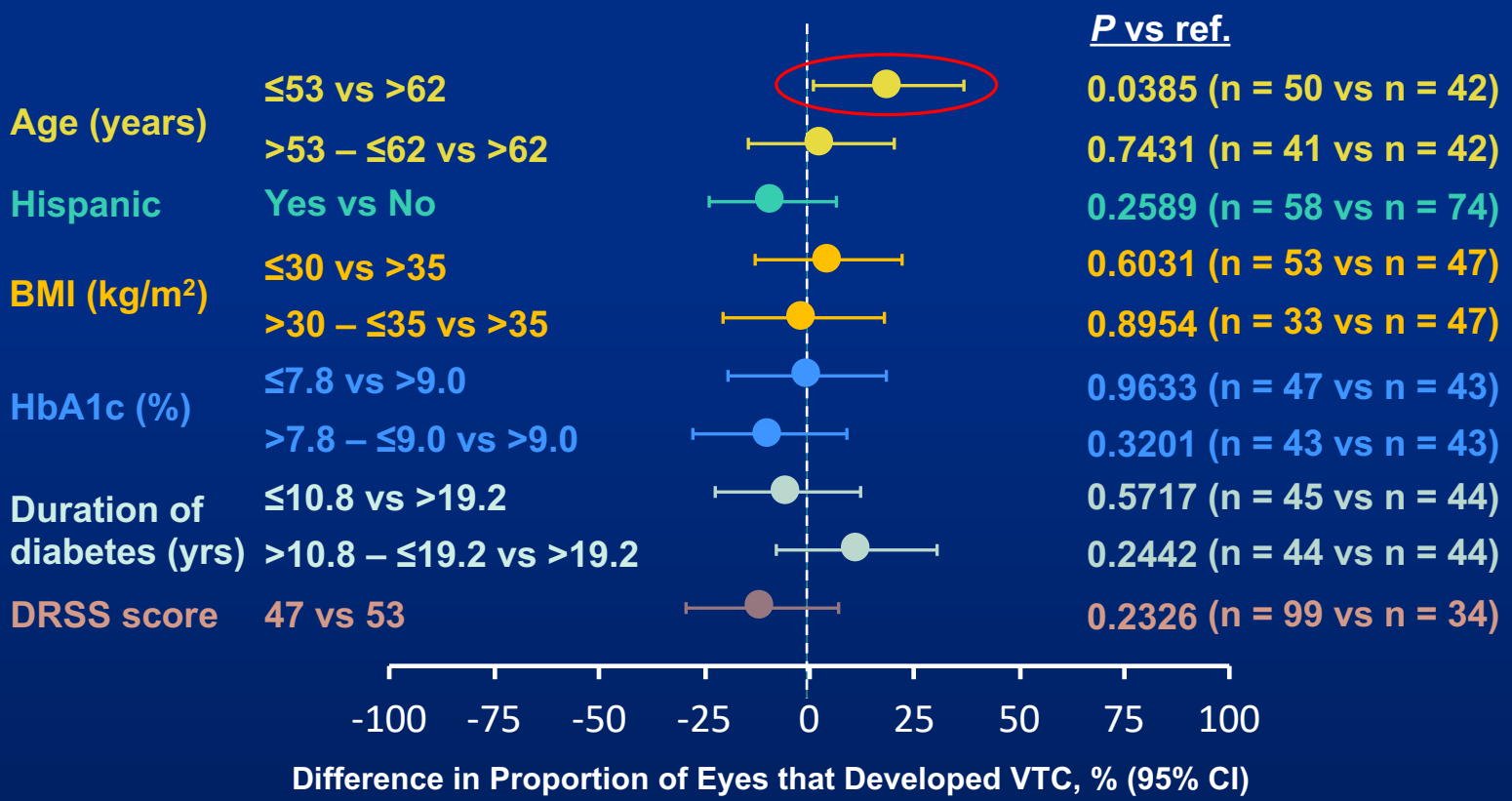
	Time to Event (Days)		Cox Regression	
	25% (95% CI)	Logrank *P* value	HR vs 53 (95% CI)	*P* value
47 (n = 99)	475 (277, 766)	0.0792	0.5 (0.3, 1.1)	0.0843
53 (n = 34)	288 (80, 623)	–	–	–



DRSS score level:								
47	0	2	6	15	16	18	23	23
53	0	3	6	7	8	10	10	12

Race and diabetes type were not included because of overwhelmingly imbalance number of patients in subgroups (race: 80% White; Diabetes type: 93% type 2 diabetes).
BMI, body mass index; CI, confidence interval; HbA1c, glycated hemoglobin; HR, hazard ratio; NE, not evaluable. VTC defined as PDR/ASNV.

Difference* in Proportion of Eyes That Developed VTC (PDR/ASNV) Through Week 100 Among Subgroups of Baseline Characteristics



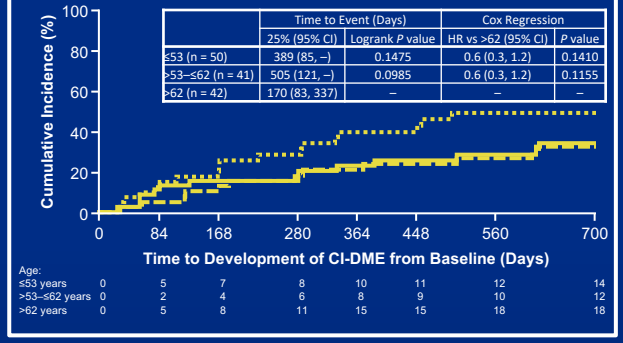
*Differences in proportions represent the first subgroup minus the second subgroup. VTC defined as PDR/ASNV.

Time to development of CI-DME through Week 100

By Age Tertiles

≤53 years
>53–≤62 years
>62 years

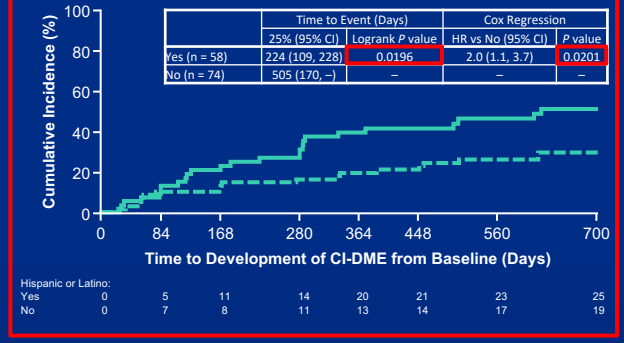
	Time to Event (Days)		Cox Regression	
	25% (95% CI)	Logrank *P* value	HR vs >62 (95% CI)	*P* value
≤53 (n = 50)	389 (85, –)	0.1475	0.6 (0.3, 1.2)	0.1410
>53–≤62 (n = 41)	505 (121, –)	0.0985	0.6 (0.3, 1.2)	0.1155
>62 (n = 42)	170 (83, 337)	–	–	–



By Ethnicity

Hispanic or Latino: Yes
Hispanic or Latino: No

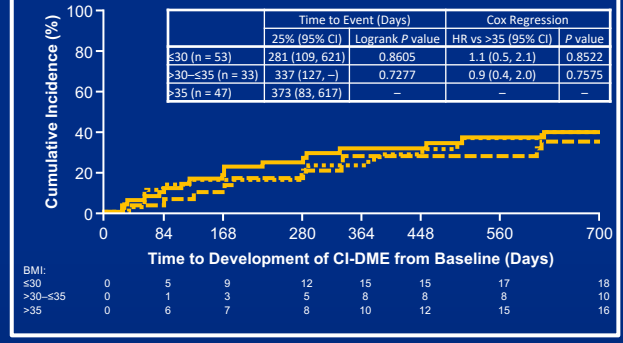
	Time to Event (Days)		Cox Regression	
	25% (95% CI)	Logrank *P* value	HR vs No (95% CI)	*P* value
Yes (n = 58)	224 (109, 228)	0.0196	2.0 (1.1, 3.7)	0.0201
No (n = 74)	505 (170, –)	–	–	–



By BMI Subgroups

≤30
>30–≤35
>35

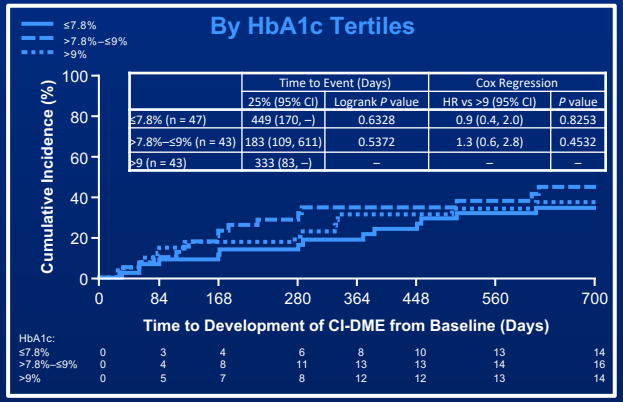
	Time to Event (Days)		Cox Regression	
	25% (95% CI)	Logrank *P* value	HR vs >35 (95% CI)	*P* value
≤30 (n = 53)	281 (109, 621)	0.8605	1.1 (0.5, 2.1)	0.8522
>30–≤35 (n = 33)	337 (127, –)	0.7277	0.9 (0.4, 2.0)	0.7575
>35 (n = 47)	373 (83, 617)	–	–	–



By HbA1c Tertiles

≤7.8%
>7.8%–≤9%
>9%

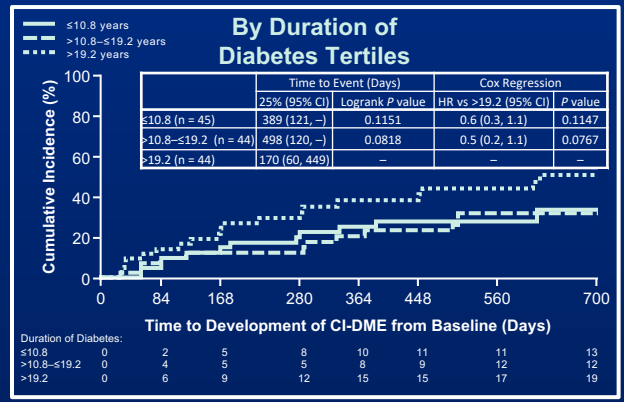
	Time to Event (Days)		Cox Regression	
	25% (95% CI)	Logrank *P* value	HR vs >9 (95% CI)	*P* value
≤7.8% (n = 47)	449 (170, –)	0.6328	0.9 (0.4, 2.0)	0.8253
>7.8%–≤9% (n = 43)	183 (109, 611)	0.5372	1.3 (0.6, 2.8)	0.4532
>9 (n = 43)	333 (83, –)	–	–	–



By Duration of Diabetes Tertiles

≤10.8 years
>10.8–≤19.2 years
>19.2 years

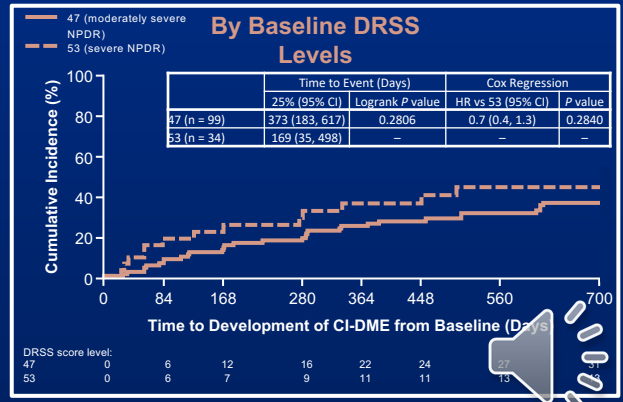
	Time to Event (Days)		Cox Regression	
	25% (95% CI)	Logrank *P* value	HR vs >19.2 (95% CI)	*P* value
≤10.8 (n = 45)	389 (121, –)	0.1151	0.6 (0.3, 1.1)	0.1147
>10.8–≤19.2 (n = 44)	498 (120, –)	0.0818	0.5 (0.2, 1.1)	0.0767
>19.2 (n = 44)	170 (60, 449)	–	–	–



By Baseline DRSS Levels

47 (moderately severe NPDR)
53 (severe NPDR)

	Time to Event (Days)		Cox Regression	
	25% (95% CI)	Logrank *P* value	HR vs 53 (95% CI)	*P* value
47 (n = 99)	373 (183, 617)	0.2806	0.7 (0.4, 1.3)	0.2840
53 (n = 34)	169 (35, 498)	–	–	–



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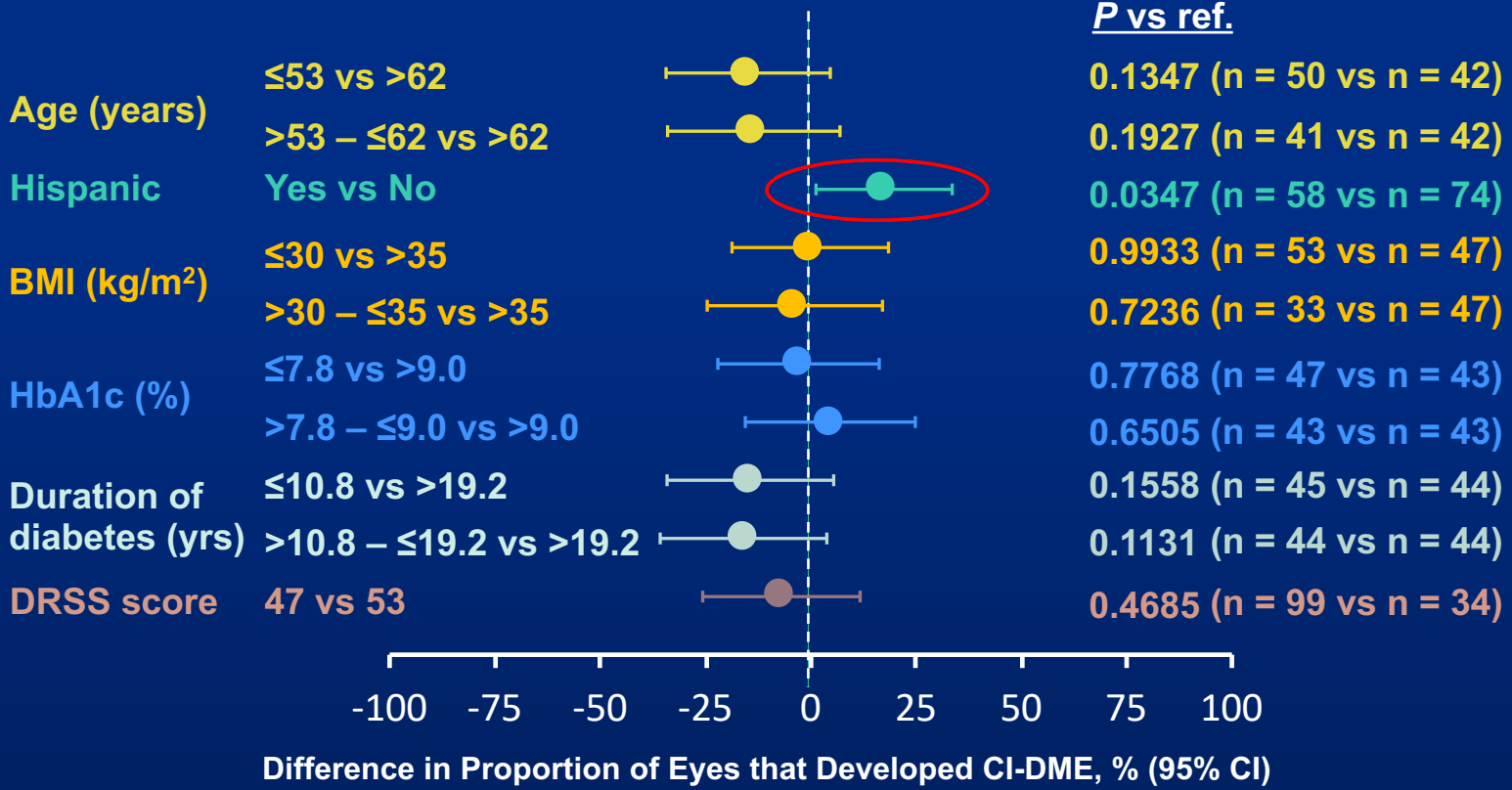
Difference* in Proportion of Eyes That Developed CI-DME Through Week 100 Among Subgroups of Baseline Characteristics



*Differences in proportions represent the first subgroup minus the second subgroup.

Conclusions

- Younger age showed an association with a higher risk of VTC events
- Hispanic ethnicity was associated with a higher risk of CI-DME events
  - Older age and longer duration of diabetes trended towards association with a higher risk of CI-DME events
- These data provide an insight into the natural history of diabetic retinopathy and may help identify patients at risk for VTC and CI-DME events
- These findings should be interpreted with caution due to small sample sizes and the post hoc nature of this analysis
- Further studies are warranted to evaluate risk factors associated with the incidence of VTC and CI-DME events