REINFORCE: A Prospective Multicenter Study of Dexamethasone Intravitreal Implant (DEX) in Diabetic Macular Edema (DME)

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DISCLOSURES

REINFORCE Study

- Allergan was the study sponsor
- **Michael A. Singer** is a speaker and/or consultant for Allergan, Genentech, and Regeneron, and has received research funding from Allegro, Ampio, Neurotech, Ophthotech, Pfizer, and Santen
- **Pravin U. Dugel** is a consultant for Abbott/AMO, Acucela, Aerpio, Alcon, Alimera, Allergan, Annidis, ArcticAx, Avalanche, Clearside, Digisight, DOSE Medical, Genentech, Lutronic, Lux BioScience, Novartis, OD-OS, Omeros, Ophthotech, Opthea, Optovue, ORA, Regeneron, Roche, Pentavision, Stealth, Thrombogenics, and TopCon, and is a minor stockholder of Aerpio, Alimera, Annidis, Neurotech, Ophthotech, and TrueVision
- **Howard F. Fine** is a consultant for and/or has received research funding from Allergan, Auris, Genentech, and Regeneron, and has a patent with Auris Surgical Robotics
- **Antonio Capone Jr.** is a consultant for and/or has received research funding from Acucela, Allergan, Novartis, Spark, and Synergetics, has a patent with Retinal Solutions, and owns stock in FocusROP and Retinal Solutions
- **John Maltman** is an employee of Allergan

INTRODUCTION

- Dexamethasone intravitreal implant (DEX) has shown efficacy in patients with diabetic macular edema (DME) in controlled trials
- Data on real-world outcomes in DME patients receiving DEX as monotherapy or adjunctive therapy are limited

Study Objective

- To assess the effectiveness, safety, and real-world use of DEX in clinical practice in patients with DME

Study Design / Methods

- Prospective, multicenter, observational registry study
- Study did not provide, nor require by protocol, any treatment beyond the initial DEX treatment required for registry inclusion
- Ocular history, treatment, and outcomes data were collected at the patient's first DEX injection and each subsequent visit up to 1 year
- Assessments and schedule of follow-up visits at the discretion of the physician
- Amount of data collected depended upon the number of follow-up visits
- Snellen visual acuity was converted to approximate ETDRS letters for analysis using the method of Gregori et al[1]

Primary Endpoints

- Mean maximum BCVA change (best improvement) from baseline following each DEX injection
- Percentage of patients with ≥15-letter improvement in BCVA
- Average improvement in BCVA (area-under-the-curve [AUC] approach)

ETDRS = Early Treatment Diabetic Retinopathy Study.

[1]Gregori NZ, et al. Retina 2010;30:1046–1050.

Baseline Patient Demographics and Study Eye Characteristics

Parameter	Patient Population (N=177)	Study Eyes (N=180)[a,b]
Mean age (range), years	67.0 (38–90)	
Male, %	52.5	
White, %	84.2	
BCVA *(n = 172)* Mean (range), approx. ETDRS letters Mean (range), Snellen equivalent		 54.4 (0–85) ~20/80 (CF–~20/20)
Mean CRT (range), µm *(n = 140)*		424.6 (179–920)
Mean IOP (range), mm Hg		15.2 (8–27)
Phakic, %		29.4
Pseudophakic, %		60.6

[a] Three patients had both eyes included in the study.
[b] Means calculated using observed values and percentages calculated based on total number of study eyes; some study eyes had missing data.

BCVA=best corrected visual acuity; CR=counting fingers; CRT=central retinal thickness; ETDRS=Early Treatment Diabetic Retinopathy Study; IOP=intraocular pressure.

Baseline Diabetes Characteristics and Previous Treatment

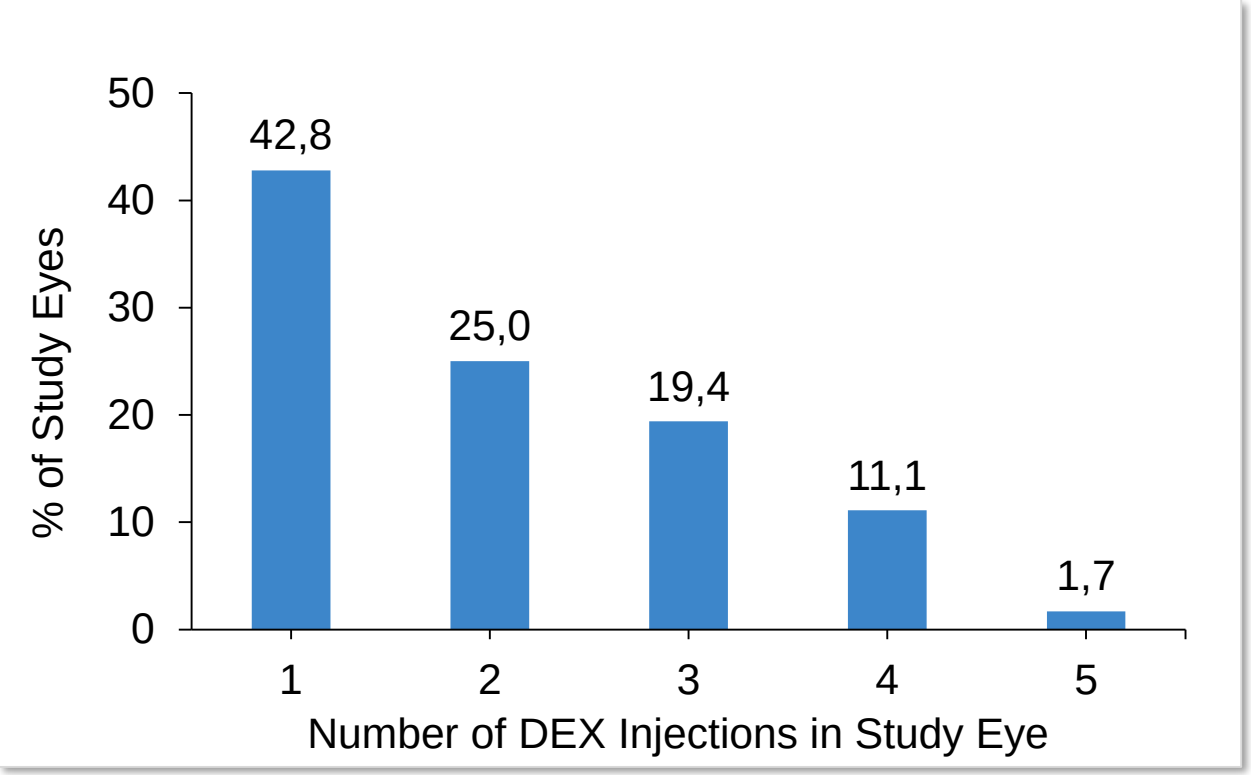
Characteristic, n (%)	Patient Population (N=177)[a]
Diabetes duration >15 years	92 (52.0)
Type 2 diabetes	121 (68.4)
HbA1c ≤8%	30 (16.9)
HbA1c >8%	6 (3.4)
Missing HbA1c data	141 (79.7)
Nonischemic DME perfusion status	113 (63.8)
Ischemic DME perfusion status	8 (4.5)
Nonapplicable or missing DME perfusion status	56 (31.6)
DME duration ≥1 year	118 (65.6)[b]
Previous DME treatment	166 (93.8)
Previous laser	63 (35.6)

[a] Percentages calculated on the patient level for all parameters except DME duration; some patients had missing data.
[b] Number of study eyes with DME duration ≥1 year; percentage calculated based on total number of study eyes.

DME = diabetic macular edema; HbA1c = glycated hemoglobin.

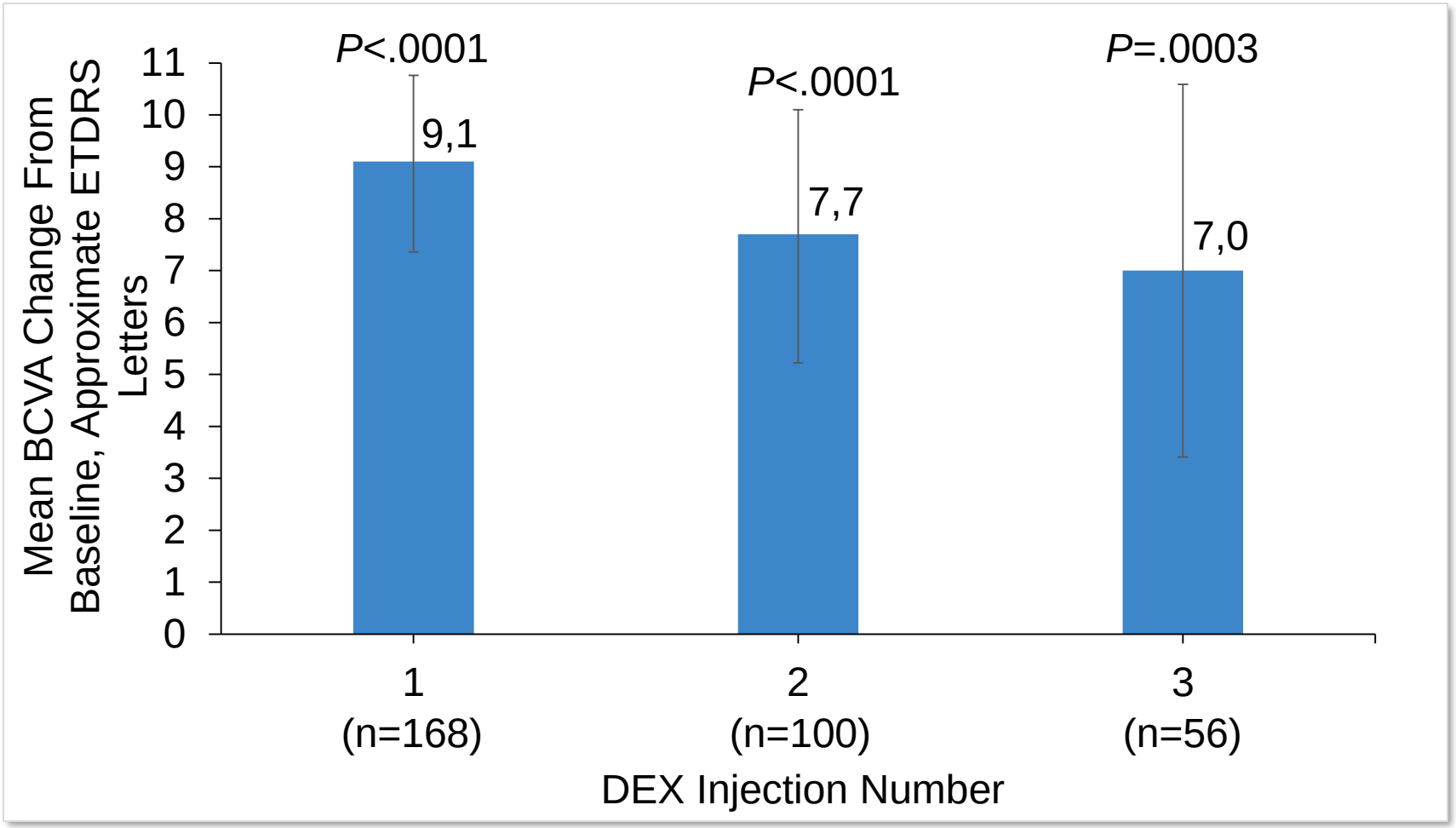
DEX USAGE

Frequency Distribution of Number of DEX Injections Administered During Year 1



- Mean DEX injection frequency was 2.0 (± 1.1, SD) injections in Year 1
- Mean time between DEX injections was 152.7 (± 64.5, SD) days
- DEX was used as monotherapy in 99 (55.0%) study eyes
- 81 study eyes (45%) received 1 or more other intravitreal injections during the study
  - Most common: aflibercept, ranibizumab, or bevacizumab

Mean Peak Improvement in BCVA From Baseline After Each DEX Injection



Error bars indicate 95% CI

Subgroup Analyses

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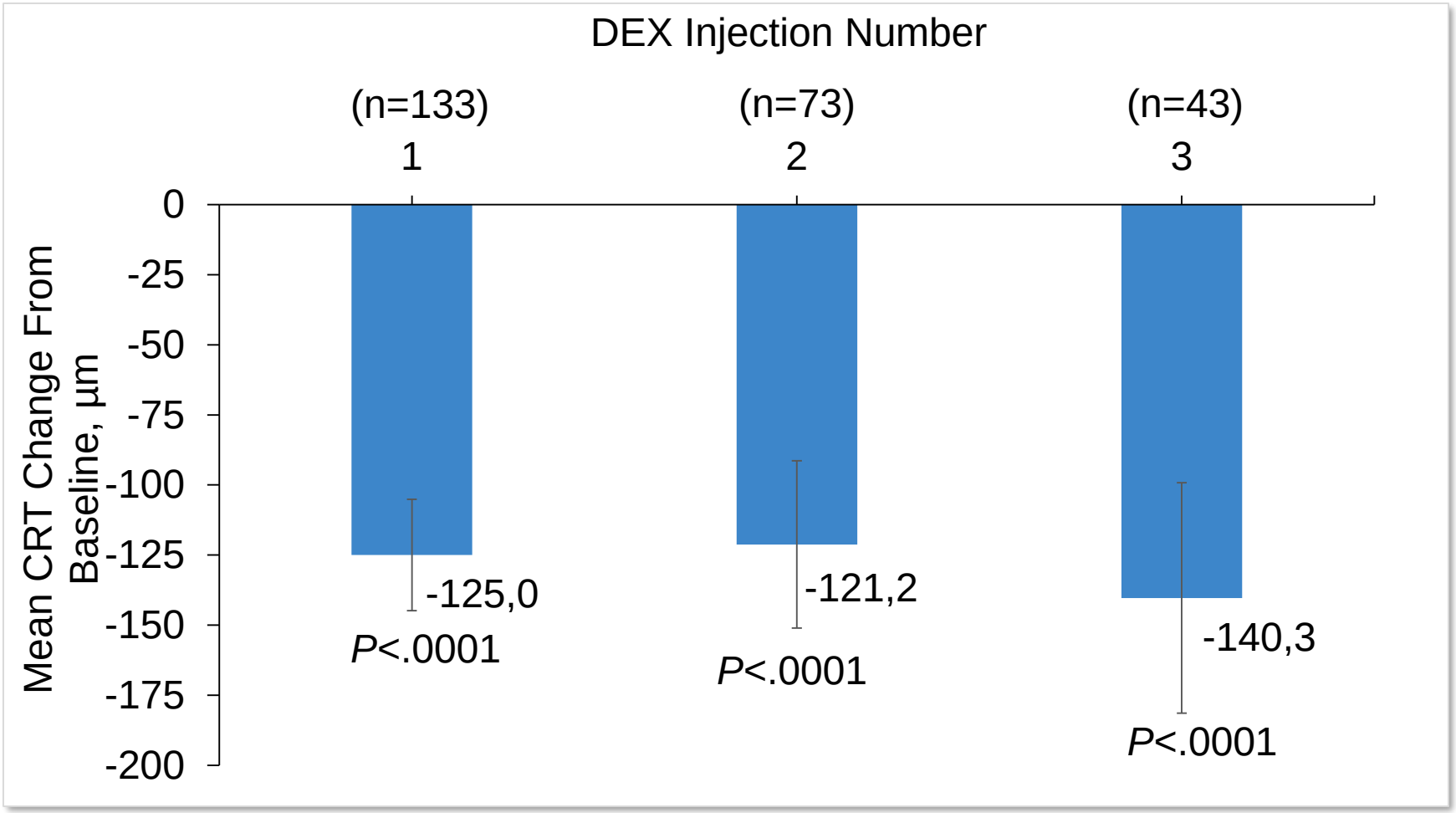
Mean ± SD Peak Improvement in BCVA From Baseline After Each DEX Injection, Approximate ETDRS Letters

Subgroup	Injection 1	Injection 2	Injection 3
Baseline lens status			
Phakic	8.6 ± 11.5 (n=52)	8.5 ± 14.8 (n=29)	5.2 ± 17.8 (n=13)
Pseudophakic	9.4 ± 11.6 (n=100)	7.4 ± 11.1 (n=60)	7.6 ± 12.4 (n=37)
Intravitreal treatment during study			
DEX only	9.4 ± 11.7 (n=92)	7.3 ± 12.7 (n=51)	7.9 ± 14.0 (n=31)
DEX and other treatment	8.6 ± 10.5 (n=76)	8.0 ± 12.0 (n=49)	5.9 ± 12.8 (n=25)

DEX = dexamethasone intravitreal implant; DME = diabetic macular edema

Mean Change in CRT From Baseline After Each DEX Injection



Error bars indicate 95% CI

Other Key Efficacy Endpoints

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Outcome Measure	Result	*P* Value
Percentage of study eyes with ≥15-letter improvement in BCVA from baseline during the study	36.0% (62/172)	
Mean average improvement in BCVA from baseline during the study using the AUC approach (95% CI)	3.6 letters (2.3, 5.0)	
Mean maximum change in BCVA from baseline during the study (95% CI)	11.7 letters (10.0, 13.5)	<.0001
Mean maximum change in CRT from baseline during the study (95% CI)	−137.7 µm (−158.2, −117.3)	<.0001
Percentage of study eyes achieving BCVA of 20/40 or better and CRT ≤300 µm at the same visit[a]	19.4% (19/98)	

[a] Percentage calculated among study eyes that had baseline BCVA worse than 20/40 and baseline CRT >300 µm.

AUC = area-under-the-curve; BCVA = best-corrected visual acuity; CI = confidence interval; CRT = central retinal thickness.

IOP Parameters

Parameter, n (%)	Study Eyes (N=180)[a]
At any time during the study	
IOP ≥25 mm Hg	22 (12.2)
IOP ≥35 mm Hg	5 (2.8)
IOP increase of ≥10 mm Hg from baseline	23 (12.8)

[a] Percentages calculated based on the total number of study eyes; 9 study eyes had missing baseline and/or follow-up IOP data.
IOP = intraocular pressure.

- 41 (22.8%) patients used IOP-lowering medication during the study
- No glaucoma surgeries were reported

Incidence of Adverse Events

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All Adverse Events Reported in 3 or More Patients

Adverse Event, n (%)	Patient Population (N=177)
Any adverse event	69 (39.0)
IOP increased	11 (6.2)
Conjunctival hemorrhage	8 (4.5)
Vitreous floaters	7 (4.0)
Dry eye	6 (3.4)
Ocular hypertension	6 (3.4)
Posterior capsule opacification	6 (3.4)
Glaucoma	5 (2.8)
Macular fibrosis	4 (2.3)
Vision blurred	4 (2.3)
Cataract	3 (1.7)
Eye pain	3 (1.7)
Photopsia	3 (1.7)
Vitreous detachment	3 (1.7)
Vitreous hemorrhage	3 (1.7)

IOP = intraocular pressure.

CONCLUSIONS

- In real-world clinical practice, DEX monotherapy and adjunctive therapy improved BCVA and CRT in patients with DME
- Consistent with other observational studies performed throughout the world such as the Reldex study which showed increased vision of 9.5 letters, and Mozart study which showed improvement of 8.7 letters
- No new safety concerns were identified

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THANK YOU