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Early Administration of the Dexamethasone Implant After Anti-VEGF Therapy for the Treatment of Diabetic Macular Edema

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Disclosures

- Consultant or Speaker's Bureau
 - Allergan
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 - Alimera Sciences
 - Novartis
 - Spark
 - Biogen
 - Graybug
 - Regeneron

Summary

- Post-hoc analyses find a significant number of patients with DME who receive anti-VEGF monotherapy show a suboptimal response within the first 12 weeks of therapy
- This retrospective, real-world analysis evaluated treatment-naïve patients with DME who were treated with 1-3 anti-VEGF injections
- Switching patients who have received few anti-VEGF injections (≤ 3) earlier to the 0.7mg Dexamethasone Implant improved BCVA from 61 after anti-VEGF treatment to 75 letters and reduced central retinal thickness from 377 microns after anti-VEGF treatment to 289 microns



Background

- The two most common current treatments for DME are anti-VEGFs and intravitreal corticosteroids¹
- Anti-VEGF use in DME stems from their proven record in improving visual acuity and decreasing macular fluid
 - BUT... not all patients respond equally or consistently
- Pivotal studies found similar results:
 - RIDE/RISE found 66% were not 3-line gainers²
 - VIVID/VISTA found 58%-69% were not 3-line gainers³

1. Schmidt-Erfurth et al. *Ophthalmologica* 2017;237(4): 185–222. 2. Brown et al. *Ophthalmology* 2013;120:2013-22. 3. Korobelnik et al. *Ophthalmology*. 2014;21:2247-2254.



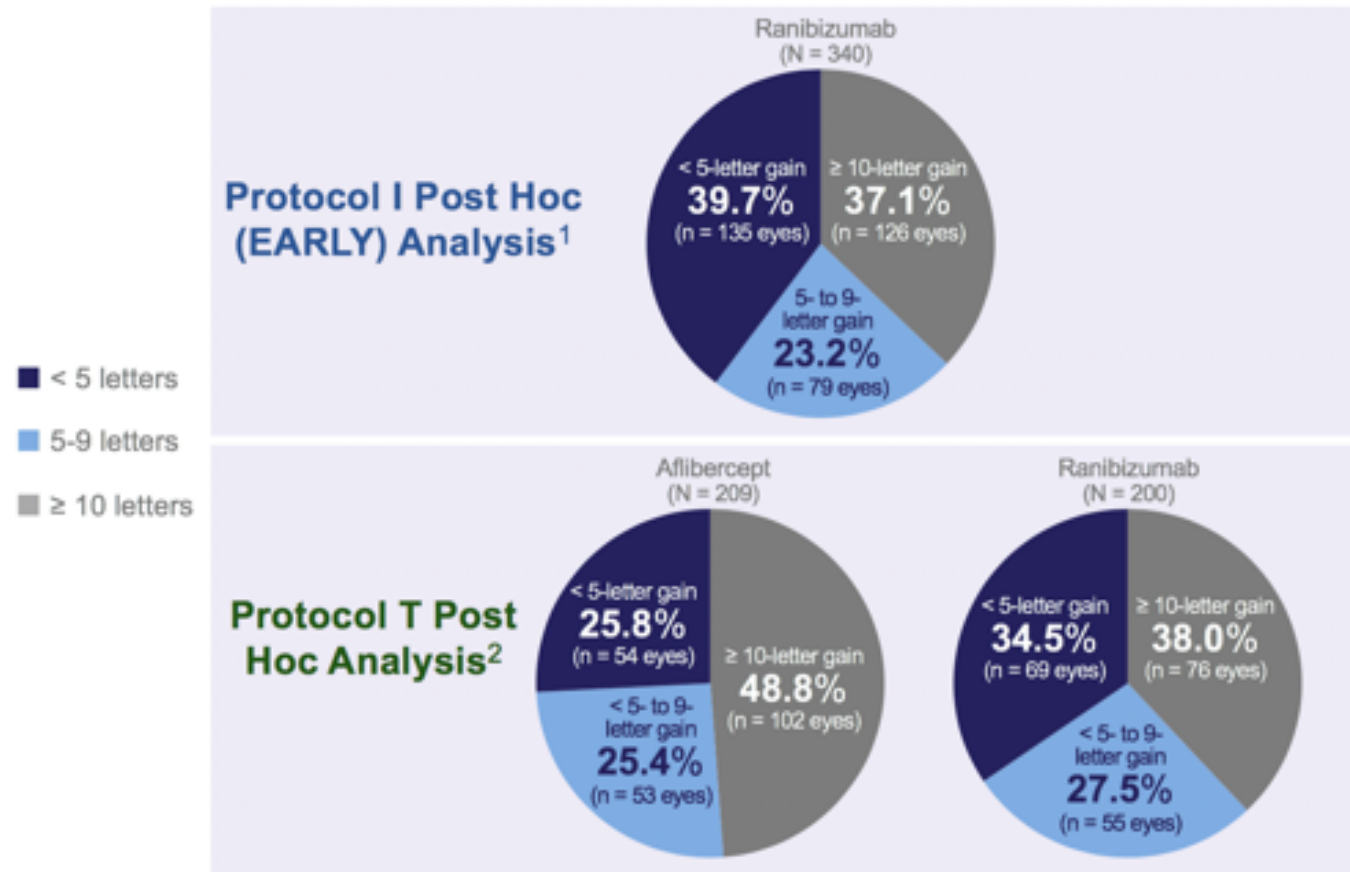
Background

- Post-hoc analysis of anti-VEGF *suboptimal responders* reported that longer duration and greater magnitude of edema resulted in fewer letters gained¹⁻⁵
- The Protocol I EARLY analysis also showed best-corrected visual acuity (BCVA) response after 3 months was a telltale harbinger of longer term vision gains^{4,5}
 - Three magnitudes of patient responses to anti-VEGF therapy were observed
 - Maximum, moderate and suboptimal responders
 - 40% were <5-letter gainers at 12 weeks⁵
- The outcomes from Protocol T were the same
 - Vision gains at 12 weeks were similar to vision at 3 years, regardless of treatment.³

1. Gonzalez et al. *Am J Ophthalmol*. 2016;172:72-79. 2. Dugel P. AAO Subspecialty Day. 2015. 3. Bressler et al. *Am J Ophthalmol*. 2018;195:93.100. 4. Dugel et al. *Retina*. 2019;39:88-97.
5. Gonzalez et al. *Am J Ophthalmol* 2016; 172: 72–79.



Protocol I (EARLY) and Protocol T Post Hoc Analysis: Percentages of suboptimal responders

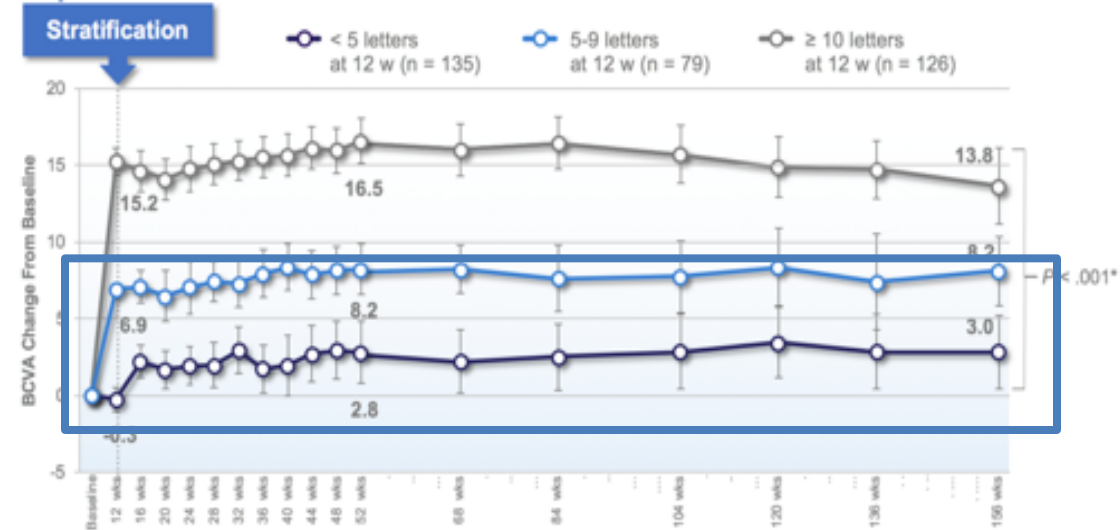


1. Gonzalez et al. *Am J Ophthalmol.* 2016;172:72-79. 2. Bressler et al. *Am J Ophthalmol.* 2018;195:93-100



Protocol I (EARLY) Post-Hoc Analysis*

In each group, mean BCVA through year 3 was within 5 letters of the response at week 12

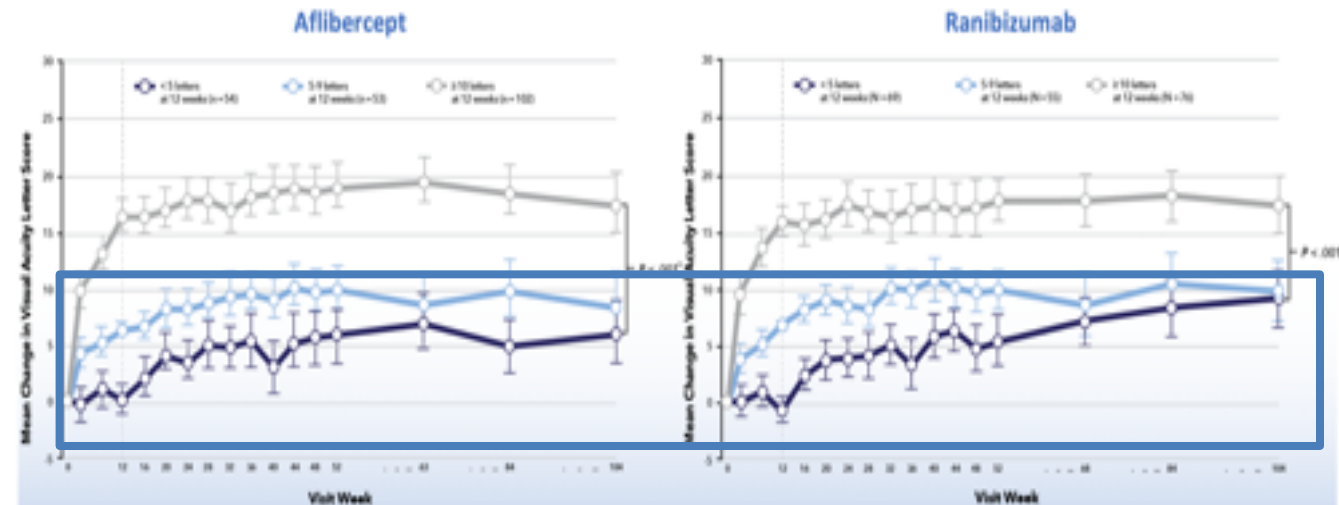


*P value for comparing among all 3 BCVA categories (for each visit) is based on analysis of variance. 95% confidence intervals.

* Ranibizumab only

Protocol T Post-Hoc Analysis**

Mean change in BCVA from baseline through year 2



** Aflibercept on the left; ranibizumab on the right

1. Gonzalez et al. *Am J Ophthalmol.* 2016;172:72-79. 2. Bressler et al. *Am J Ophthalmol.* 2018;195:93-100



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Purpose

- Real-world outcomes rarely match clinical study findings¹⁻⁴
- Worse outcomes in real-world settings — suggests that an unmet need exists to address a large number of suboptimal responders

Can switching from anti-VEGF therapy to the Dexamethasone 0.7mg Implant produce better visual and anatomic outcomes if patients are switched early?



Methods

- Retrospective, real-world analysis of 38 treatment-naïve DME patients confirmed with optical coherence tomography (OCT) from 4 clinics
- Clinicians treated patients with intravitreal bevacizumab or aflibercept (no patient was treated with ranibizumab):
 - 11% received 1 injection
 - 8% received 2 injections
 - 81% received 3 injections
- Patients were deemed poor responders based on minimal VA gain or poor anatomic response
- Patients were switched to a single intravitreal Dexamethasone 0.7mg Implant
- Main outcome measures included changes in BCVA and central retinal thickness (CRT)

Methods

- There were 38 unique patients included
 - One patient received two bevacizumab and one aflibercept before switch

Anti-VEGF medication	Number of times used	Number of patients	Total
Bevacizumab	1	4	4
	2	3	6
	3	21	63
Aflibercept	1	1	1
	3	10	30

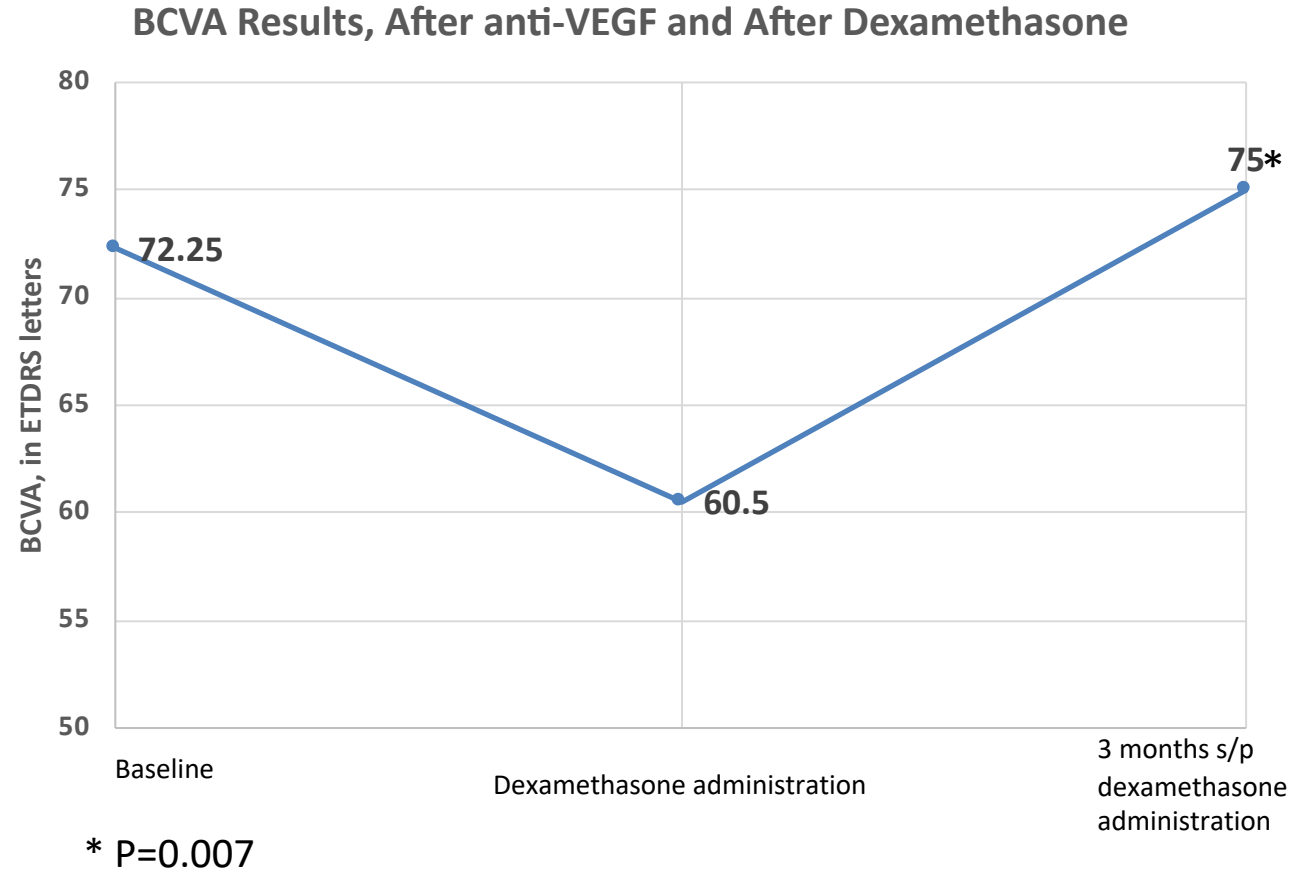
VEGF=vascular endothelial growth factor



Visual Acuity Results

Parameters	Mean BCVA, in letters
Baseline (N=38)	72.25 (± 13.36)
After anti-VEGF*	61 (± 11.74)
P-value	$P=0.50^*$
3 months s/p dexamethasone 0.7mg	75 (± 12.53)
P-value	$P=0.007^*$

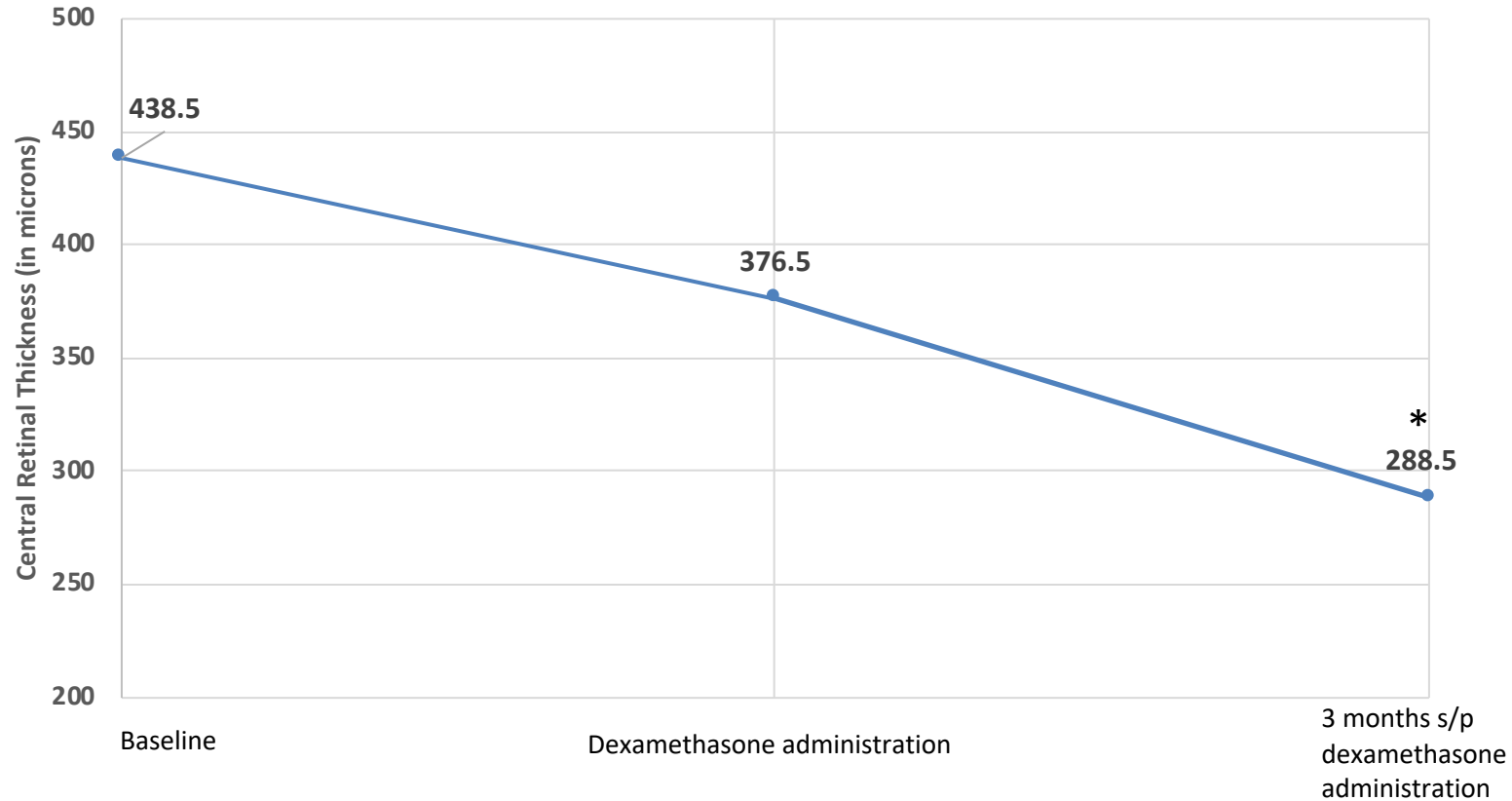
* 2-tailed, unpaired t-test



OCT Results

Parameters	CRT
Baseline (N=38)	439 microns (± 152.35)
After anti-VEGF*	377 microns (± 121.6)
P-value	$P=0.09$
3 months s/p dexamethasone 0.7mg	289 microns (± 47.38)
P-value	$P=0.00007$

CRT, After anti-VEGF and After Dexamethasone



Suboptimal Responder After 3 Anti-VEGF Injections

1 st Visit Afibercept Injection 6/09/2016	OD 20/60 -2 OS 20/50 IOP OD:19 OS:17	 C.C. - RPE	Central Subfield Thickness (µm) 488	Cube Volume (mm³) 12.1	Cube Average Thickness (µm) 240	
2 nd Visit Afibercept Injection 8/25/2016	OD 20/50 OS 20/80 IOP OD:19 OS:15	 C.C. - RPE	Central Subfield Thickness (µm) 278	Cube Volume (mm³) 11.2	Cube Average Thickness (µm) 208	
3 rd Visit Afibercept Injection 9/22/2016	OD 20/70 OS 20/80 IOP OD:22 OS:18	 C.C. - RPE	Central Subfield Thickness (µm) 380	Cube Volume (mm³) 10.8	Cube Average Thickness (µm) 235	
Date of Dexamethasone Injection Visit 3/23/2017 OD	OD 20/40 -2 OS 20/50 IOP OD:14 OS:11	 C.C. - RPE	Central Subfield Thickness (µm) 257	Cube Volume (mm³) 8.5	Cube Average Thickness (µm) 215	
Follow up Visit 7/6/2017	OD 20/30 - OS 20/30 IOP OD:14 OS:11	 C.C. - RPE	Central Subfield Thickness (µm) 245	Cube Volume (mm³) 8.5	Cube Average Thickness (µm) 208	

Images courtesy of M. Singer, MD



Conclusions

- Post-hoc analyses find a significant number of DME patients receiving anti-VEGF monotherapy show a suboptimal response within the first 12 weeks of therapy
 - Addressing the multifactorial mechanism(s) of DME may yield superior outcomes
- An opportunity may exist to improve outcomes in these patients with early introduction of the 0.7mg Dexamethasone Implant
- A larger, prospective study may be warranted to validate this treatment paradigm based on the results of this real-world study





THANK YOU