

# DMÖ ilk 3 dozda switch yapılmalı mı?

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# Finansal İlinti Beyanı

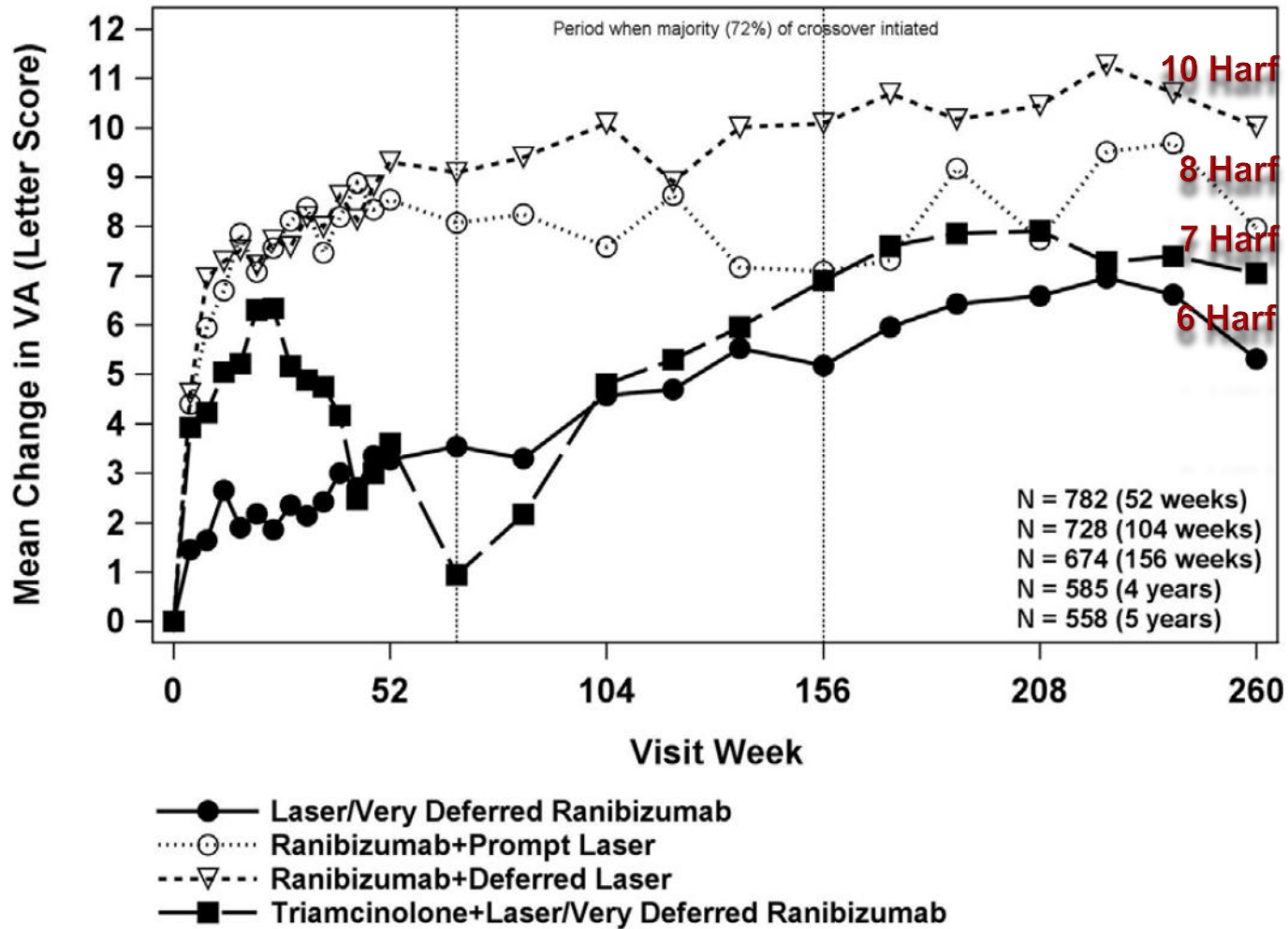
Sunumda adı geçen ürünlerle  
herhangi bir finansal ilintim yoktur.

# DMÖ Tedavisi

## **Guidelines for the Management of Diabetic Macular Edema by the European Society of Retina Specialists (EURETINA)**

nomically efficient manner. Laser treatment has found a less destructive competitor in pharmacological treatments. As a consequence of recent rigorous clinical trials, laser photocoagulation is no longer recommended for the treatment of diabetic macular edema (DME), and anti-vascular endothelial growth factor therapy has emerged as first-line therapy. Steroids have maintained a role in the management of

# Protokol I -5 yıl



RBZ+ geç lazer  
RBZ+ erken lazer  
Triamsolon  
Lazer

# Protokol I

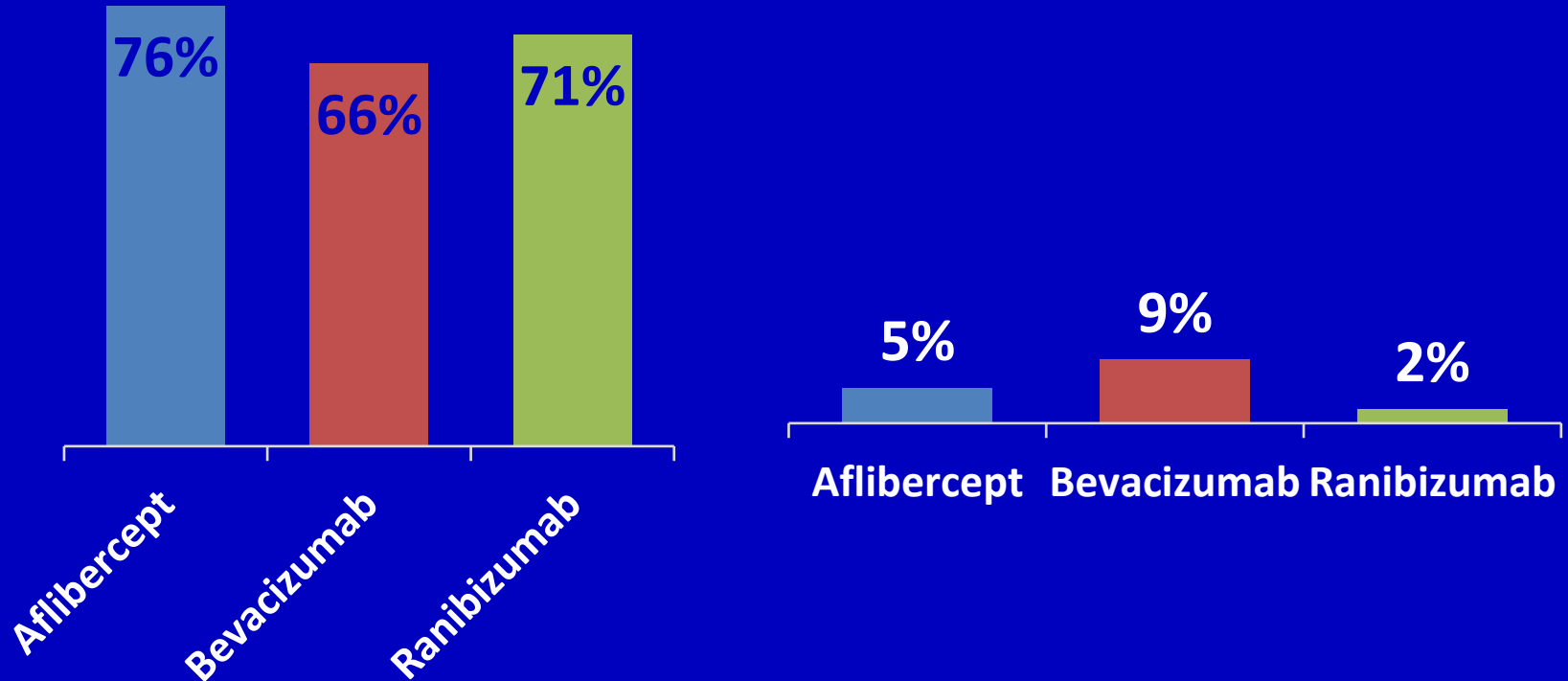
**Table 2.** DRCR.net Protocol I study: visits and treatments before 5-year visit

	Ranibizumab + prompt laser treatment ( <i>n</i> = 124)	Ranibizumab + deferred laser treatment ( <i>n</i> = 111)
Visit history, number of visits		
Year 1	13 (12–13)	13 (12–13)
Year 2	8 (6–11)	10 (7–12)
Year 3	7 (4–10)	8 (5–11)
Year 4	5 (4–9)	6 (4–9)
Year 5	4 (3–7)	5 (3–7)
Before 5-year visit	38 (31–47)	40 (34–49)
Intravitreal injection history, number of injections		
Year 1	8 (7–11)	9 (6–11)
Year 2	2 (0–5)	3 (1–6)
Year 3	1 (0–4)	2 (0–5)
Year 4	0 (0–3)	1 (0–4)
Year 5	0 (0–3)	0 (0–3)
Eyes that received ≥1 injections in year 4	57 (46)	61 (55)
Eyes that received ≥1 injections in year 5	47 (38)	53 (48)
Before 5-year visit	13 (9–24)	17 (11–27)
Focal/grid laser history		
Focal/grid laser treatments before the 5-year visit	3 (2–5)	0 (0–2)
Eyes that did not receive focal/grid laser treatment before the 5-year visit	0 (0)	62 (56)
Eyes that did not receive focal/grid laser treatment in year 5	112 (90)	108 (97)



Data are presented as median (quartiles) or *n* (%). Data are limited to study participants completing the 5-year visit. Reprinted from Elman et al. [48] with permission from Elsevier.

# 2 yılda 0.4'ten daha kötü gören olgularda ≥10 Haftan Daha Fazla Kazanç ve Kayıp Oranı Protokol T

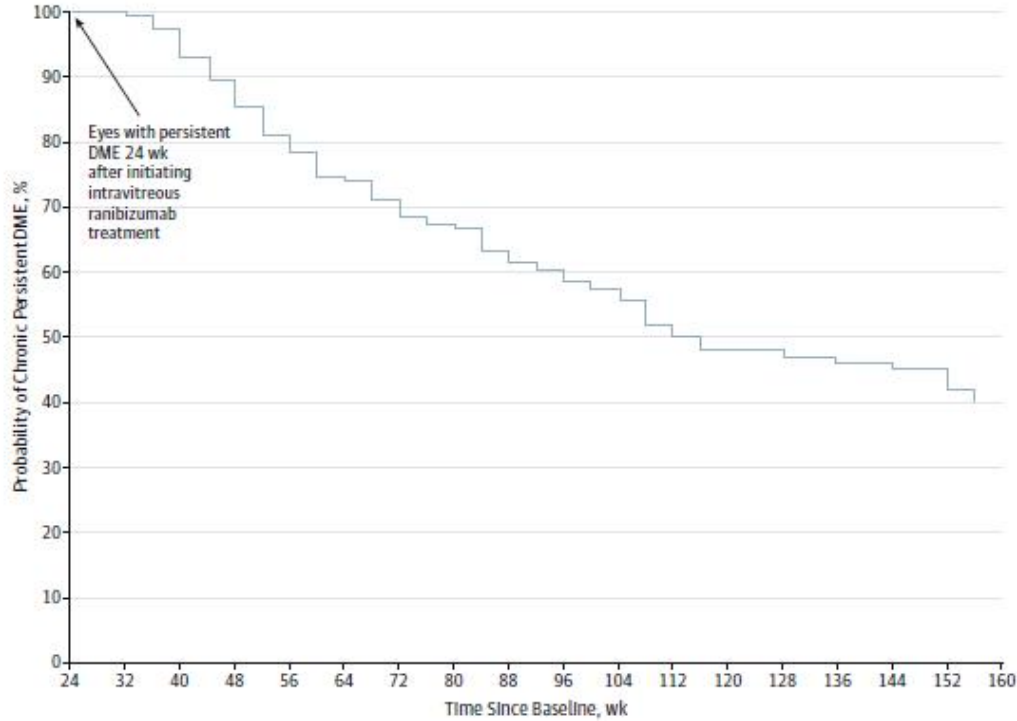


# Protokol I Alt Analizi- Yanıt Şekilleri

Erken ve tutarlı	Erken ama tutarsız	Yavaş ve deęişken	Yanıtsız
16., 32. hf ve 1. yıl vizitlerinde iyi	16. hf vizitinde iyi ancak 32. hf ve 1. yılda kötü	16. haftada kötü ancak 32. hf ve/veya 1. yıl vizitinde iyi	16., 32. hf ve 1. yıl vizitlerinde kötü
n=143 göz (%49.7)	n=43 (%14.9)	N=36 (%12.5)	N=66 (%25.9)
+13 harf	+9 harf	+7 harf	+4 harf

## 3. yılda ne oluyor?

Figure. Probability of Chronic Persistent Diabetic Macular Edema (DME)



3. yılda kronik  
persistan DMÖ %40,  
tüm gözlerin %16'sı

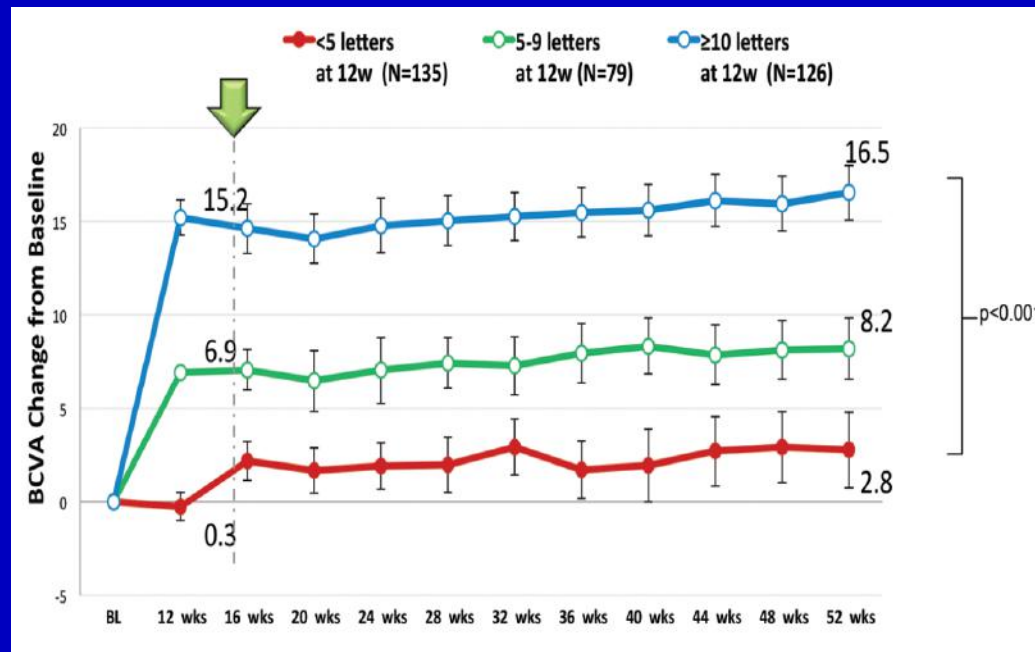
# Ne Zaman Switch

- Tedaviye yanıt alamadığımızda
- Komplikasyon geliştiğinde

## Rationale for the Diabetic Retinopathy Clinical Research Network Treatment Protocol for Center-involved Diabetic Macular Edema

After the 4 to 6 required injections in the DRCR.net protocol, retreatment continued every 4 weeks until one of three outcomes occurred: 1) "success" (defined above); 2) there had been "no further improvement" defined as <10% decrease in central subfield thickness and < 5 letter increase in visual acuity since the most recent injection, and, in the opinion of the treating ophthalmologist, it seemed unlikely that additional treatment would provide any further benefit; or 3) the result of treatment was considered a treatment "failure", defined as definite worsening despite treatment, or serious side effects associated with treatment precluding additional treatment.

# Protokol I EARLY Analizi



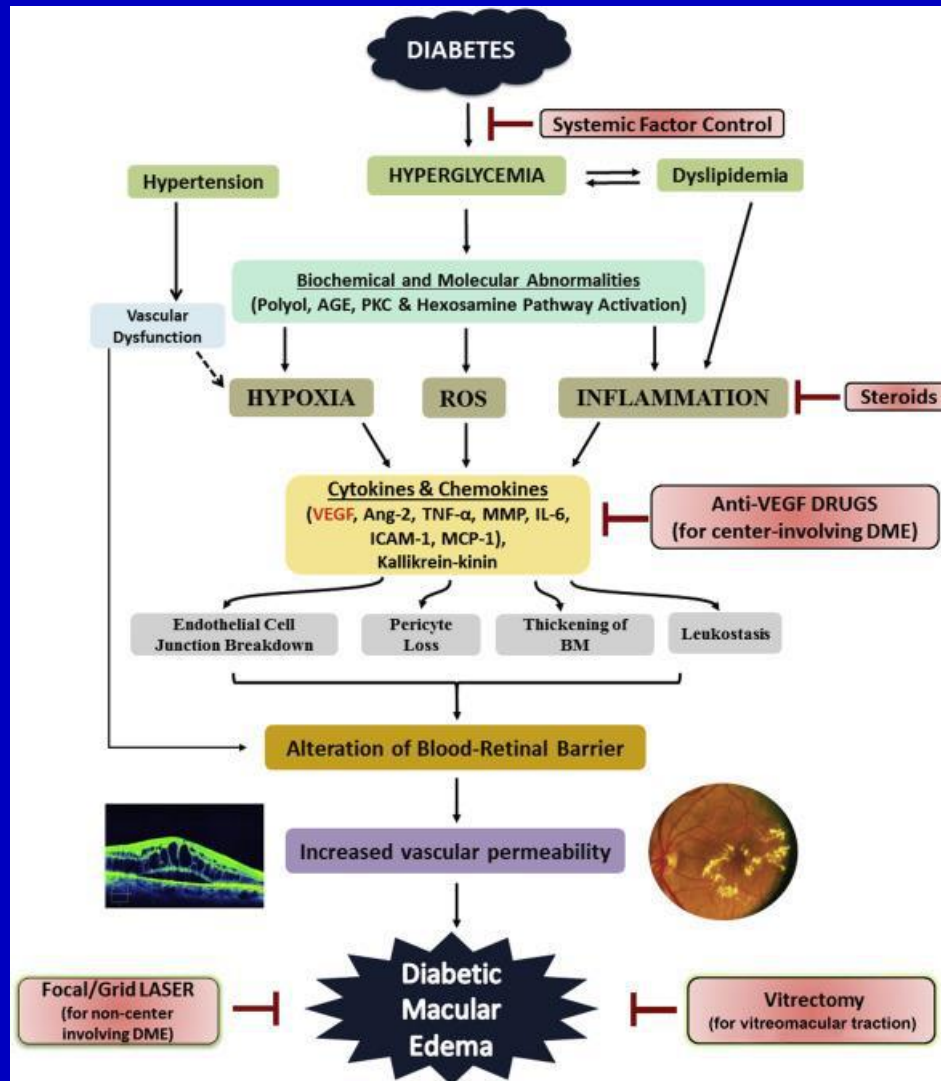
## DEX İMPLANT STUDY GROUP

- Çok merkezli (8 merkez) retrospektif, 102 göz
- 18 ay takip
- 3 aydaki yanıt ile 18 ay sonundaki yanıt karşılaştırılmış
- $\geq 10$  Harften fazla kazanç oranı : 3 ayda %37.3, 18 ayda %29'u korumuş
- 5-9 Harf kazanç oranı: 3 ayda %18.1
- $< 5$  kazanç oranı: 3 ayda %44.1
  
- **Dex İmplant Study Group. Early Response to Intravitreal Dexamethasone Implant Therapy in Diabetic Macular Edema May Predict Visual Outcome. Am J Ophthalmol, 2017 Oct 13. pii: S0002-9394(17)30427-0.**

- Hangi ajanla tedavi edersek

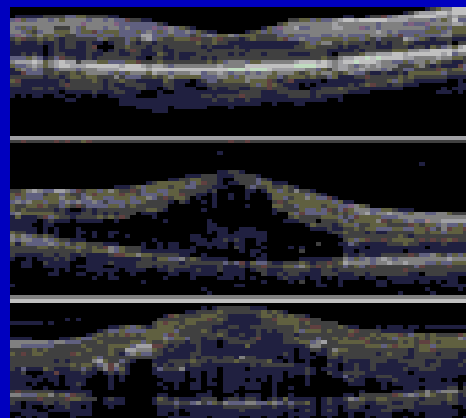
edelim olguların  $1/3$ -  $1/4$ 'ünde ilk 3 ayda

beklenen yanıt alınamayabilir.



Variable	Control group (n=12)	DME group			P value		
		DRT group (n=19)	CME group (n=17)	SRD group (n=14)	Control vs DME	Control vs DRT vs CME vs SRD	DRT vs CME vs SRD
IL-6	17.7	39.4	20.9	47.1	<0.001	0.001	0.014
IL-8	10.8	21.0	29.5	31.8	<0.001	<0.001	0.038
IP-10	239.5	390.0	398.0	479.0	<0.001	<0.001	0.021
MCP-1	1166.1	2495.0	3123.2	4211.8	<0.001	<0.001	0.205
PDGF-AA	71.7	68.3	77.7	86.5	0.055	0.004	0.041
VEGF	<u>38.4</u>	<u>68.5</u>	<u>79.2</u>	<u>94.4</u>	<0.001	<0.001	0.062

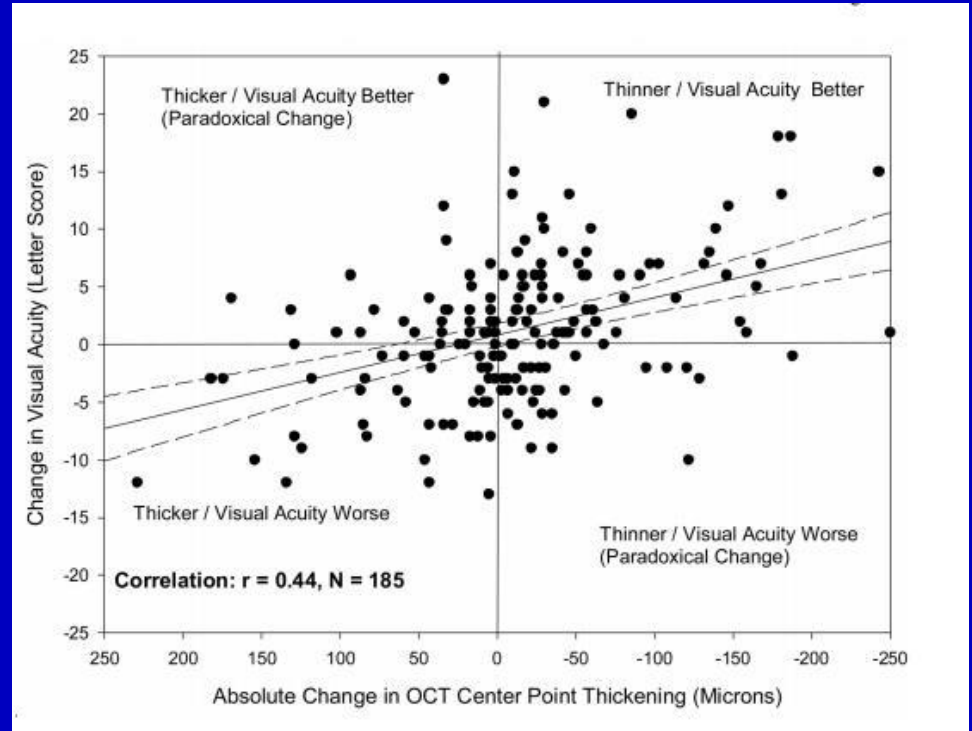
MCP: Monocyte chemotactic protein, PDGF: Platelet-derived growth factor, VEGF: Vascular endothelial growth factor, DME: Diabetic macular edema, DRT: Diffuse retinal thickening, SRD: Serous retinal detachment, CME: Cystoid macular edema



Kim M, Kim Y, Lee SJ. Comparison of aqueous concentrations of angiogenic and inflammatory cytokines based on optical coherence tomography patterns of diabetic macular edema. Indian J Ophthalmol. 2015 Apr;63(4):312-7. doi: 10.4103/0301-4738.158069.

# Tedaviye Yanıt Şekilleri

- Anatomik (MMK-OKT)
- Fonksiyonel (GK)
- Anatomik  $\neq$  Fonksiyonel



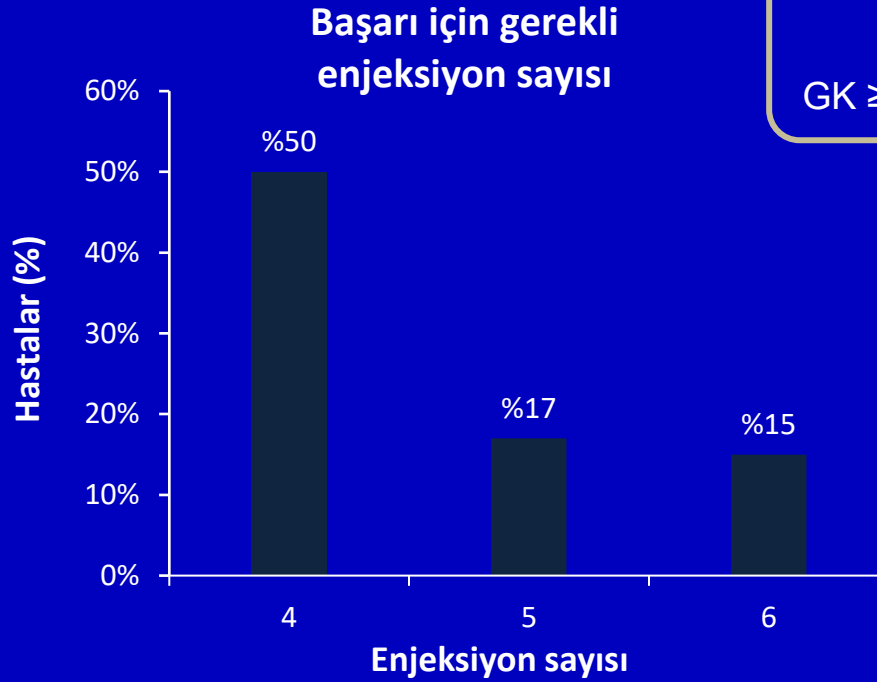
# Yanıt için Belirteçler

- Demografik Özellikler
  - Hasta yaşı, başlangıç GK, başlangıç MMK
- OCT Özellikleri
  - DRİL, DPT, IRS
- OCTA Özellikleri
  - Derin kapiller pleksusta
    - Mikroanevrizma sayısı
    - Daha geniş FAZ alanı
  - Subretinal fibrozis
  - Makulada laser skarı
  - Dejeneratif değişiklikler



3 enjeksiyonda yanıt alınamayan olgularda  
tedaviye devam edildiğinde neler oluyor?

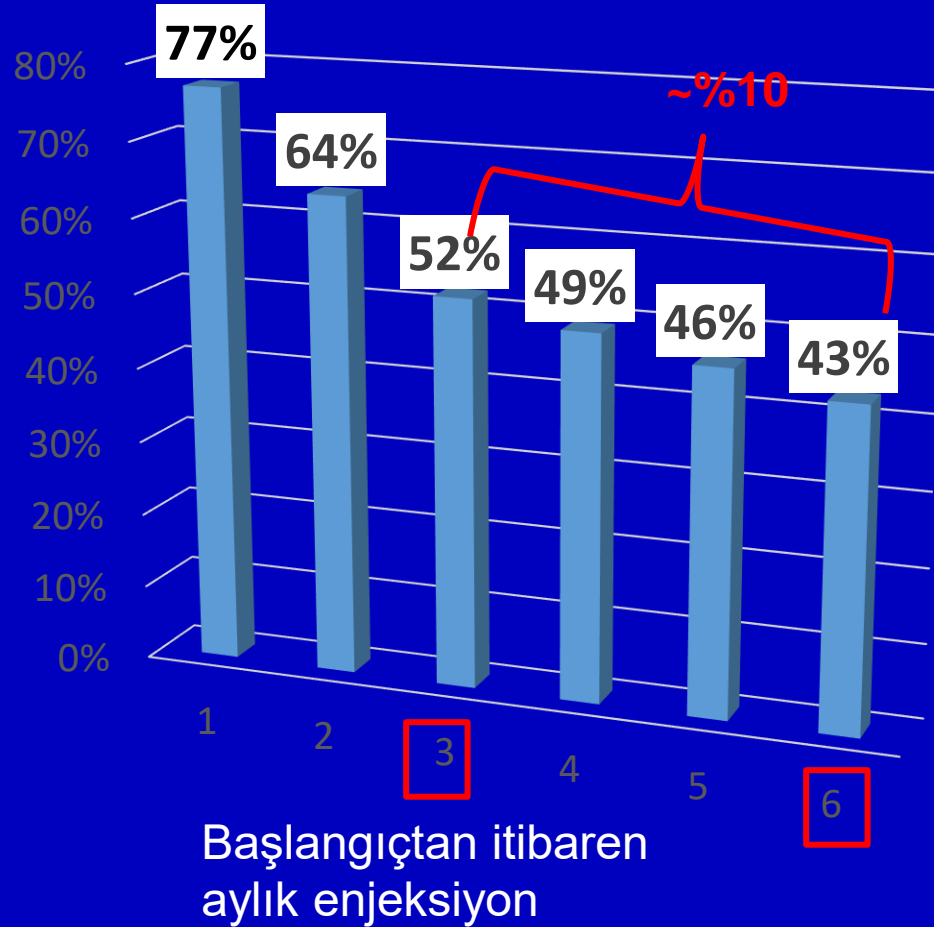
# Protokol I



**Başarı kriterleri şu şekilde tanımlanmıştır:**  
GK  $\geq 84$  harf (20/20) ya da CST  $< 250$   $\mu\text{m}$

# Protokol I Neden İlk 6 Ay Ranibizumab'a Devam Edilmiştir?

Persistan DMÖ'lü Hasta Oranı

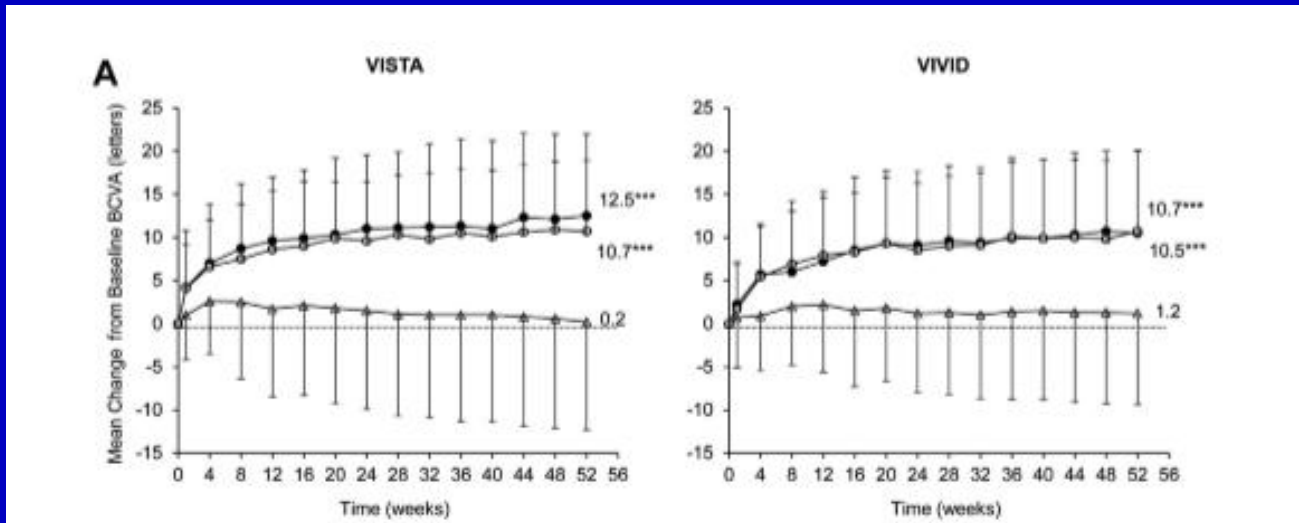


# RISE/RIDE: Ranibizumab'a 3. Aydan Sonra Morfolojik Ge Yanıt

- Hastalar Ranibizumab tedavisine verdikleri anatomik yanıt aısından 2 gruba ayrılmıřtır:
  - 1.Grup : İlk 3 enj sonrası SRK <%10 ( Ge Yanıt verenler)
  - 2.Grup : İlk 3 enj sonrası SRK >%10 ( Erken Yanıt verenler )

RIDE-RISE alıřmalarında %9-10 DMÖ hastası Ge Yanıt veren grupta bulunuyor.

- VIVID ve VISTA alıřmaları ile aflibercept
- 2014 te Avrupa'da
- 2015'te de Amerikada FDA onayı aldı.
- 5 aylık ykleme dozu nerildi.



## DEX İMPLANT STUDY GROUP

- Çok merkezli (8 merkez) retrospektif, 102 göz
- 18 ay takip
- 3 aydaki yanıt ile 18 ay sonundaki yanıt karşılaştırılmış
- <5 kazanç oranı: 3 ayda %44.1

Bu olguların %6.7 si 18. ayda  $\geq 10$  harf üzerinde kazanç sağlamış

- **Dex İmplant Study Group. Early Response to Intravitreal Dexamethasone Implant Therapy in Diabetic Macular Edema May Predict Visual Outcome.** Am J Ophthalmol, 2017 Oct 13. pii: S0002-9394(17)30427-0.

# Protokol I Alt Grup Analizi: Tedavi Değiştirmek Yerine Aynı Ajanla Devam Etmek

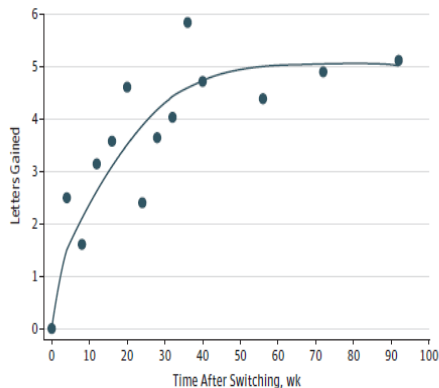
Research

JAMA Ophthalmology | **Brief Report**

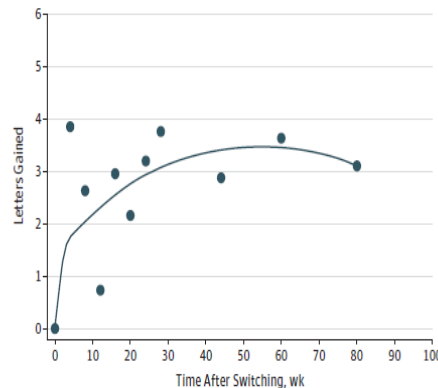
## Evaluating Effects of Switching Anti-Vascular Endothelial Growth Factor Drugs for Age-Related Macular Degeneration and Diabetic Macular Edema

Frederick L. Ferris III, MD; Maureen G. Maguire, PhD; Adam R. Glassman, MS;  
Gui-shuang Ying, PhD; Daniel F. Martin, MD

**C** Diabetic macular edema, 3 mo (n=59)



**C** Diabetic macular edema, 6 mo (n=54)



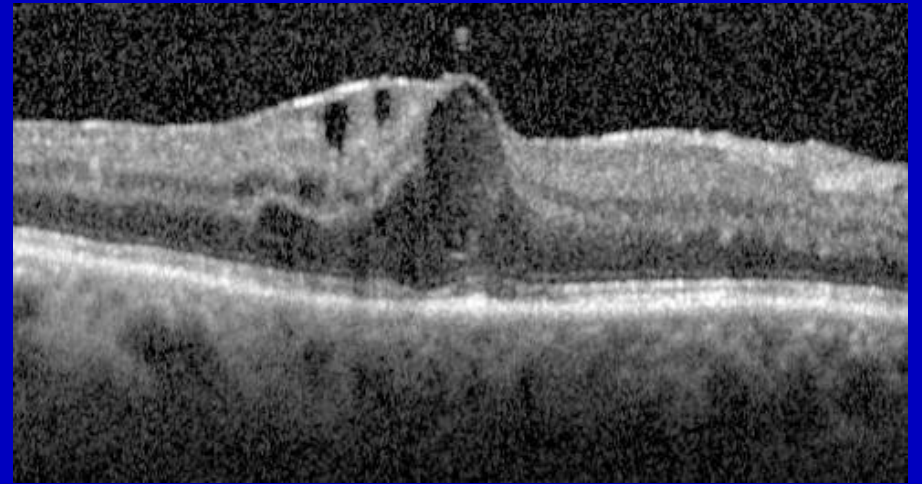
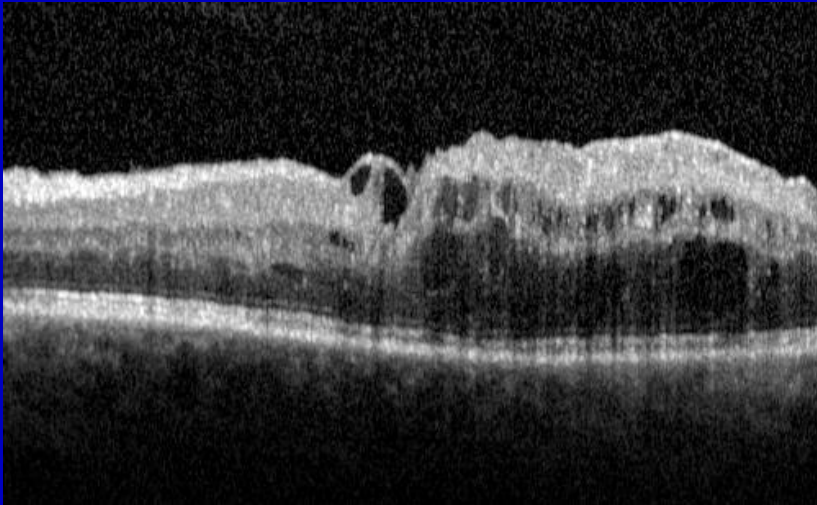
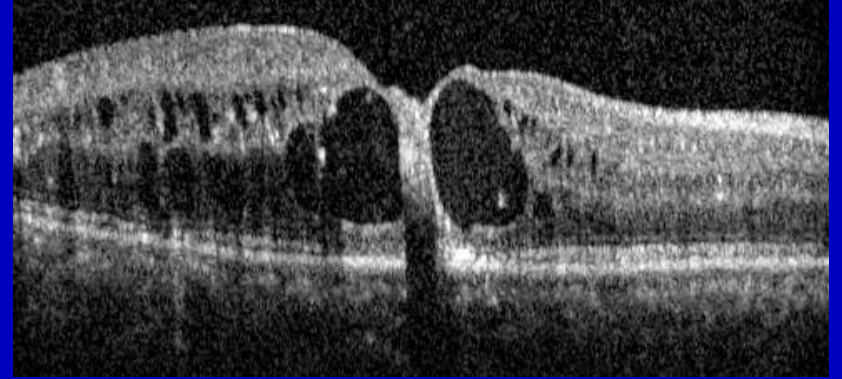
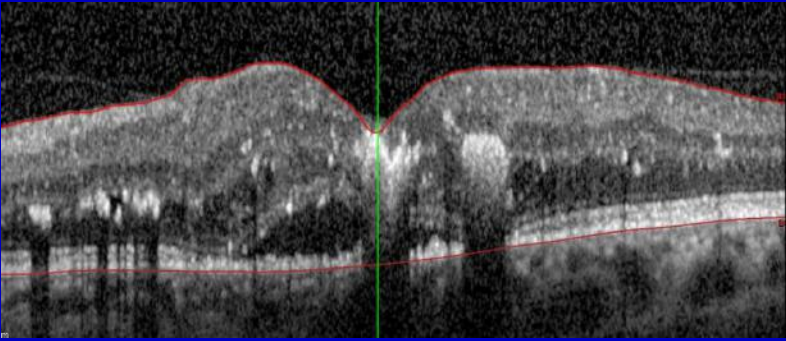
### Key Points

**Question** In studies of effects of switching anti-vascular endothelial growth factor agents after poor initial response, can it be assumed that there will be no future improvement if there is no switching?

**Findings** In eyes meeting criteria for switching but maintained on the original agent, improvements in visual acuity and retinal thickness were observed.

**Meaning** A control group maintained on the original agent should be included in studies of switching agents to make valid conclusions.

# Hangi Olgular Geç Yanıt Verir?



- Rehberler ne diyor?

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## The Royal College of Ophthalmologists



## Diabetic Retinopathy Guidelines

- **Anti-VEGF treatment regime:** Initial loading phase of monthly injections for 4-6 months, followed by PRN phase with continued treatment until the macula is dry or until there is no further improvement.

# Guidelines for the Management of Diabetic Macular Edema by the European Society of Retina Specialists (EURETINA)

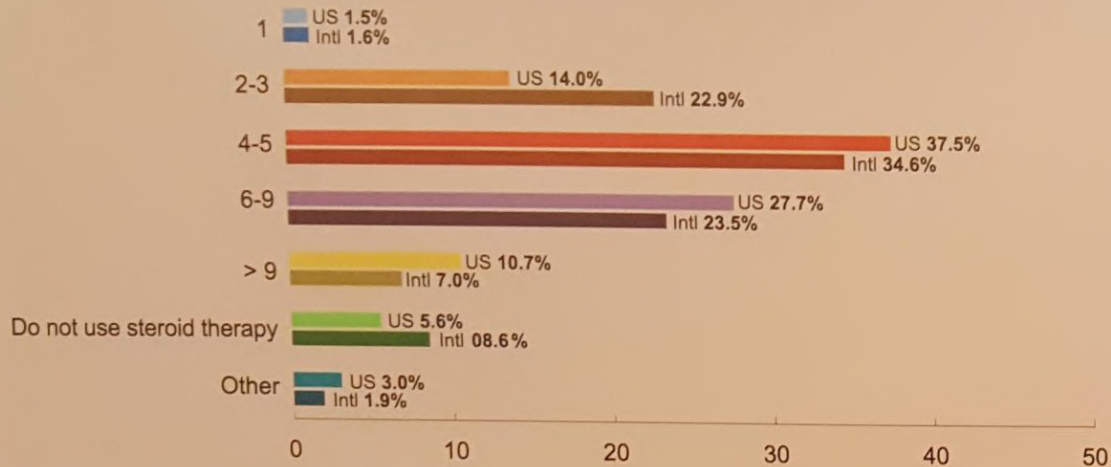
## Recommendation

Based on the data that exist thus far, corticosteroids are important in our armamentarium of drugs for treating DME patients, but largely on a second choice level. In nonresponders who have already been treated with anti-VEGF (after 3–6 injections, depending on the specific response of each patient), it is reasonable to switch to a steroid.

Ophthalmologica 2017;237:185–222  
DOI: 10.1159/000458539

# Retinal Vascular Diseases/Diabetes

After how many anti-VEGF injections do you consider incorporating steroid therapy?



27. After how many anti-VEGF injections do you consider incorporating steroid therapy?

*n* = 1070

27

# Sonuç Olarak

- VEGF düzeyinin farklılık gösterdiği DMÖ'de
- Anti-VEGF tedaviye yanıtta farklılık gösterir.
- Her olguda 3 enjeksiyon yeterli olmayabilir.
- Anti-VEGF tedavisine başarısız demek için 3'ten fazla enjeksiyon gereklidir.
- Uluslar arası rehberlerde en az 4-6 enjeksiyon önerilmektedir.