ANTI VEGF AGENTS IN DIABETIC RETINOPATHY

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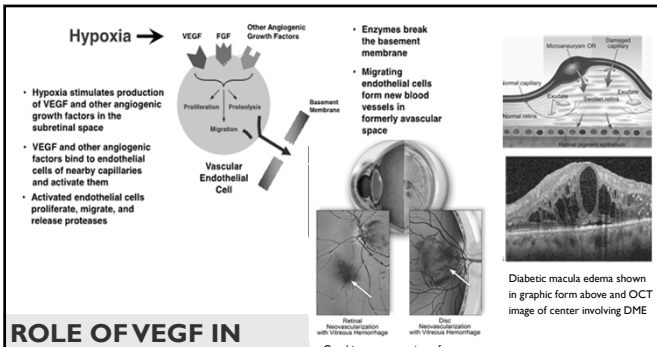
OUTLINE

- Role of VEGF in Diabetic retinopathy
  – Diabetic Macula Edema and Proliferative Diabetic Retinopathy
- Types of Anti VEGF
- How Anti VEGF work in DR
- How we use Anti VEGF in clinical practice- evidence from the landmark studies
- Real world outcomes and treatment burden implications

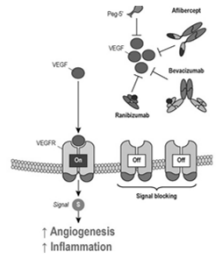
ROLE OF VEGF IN DIABETIC

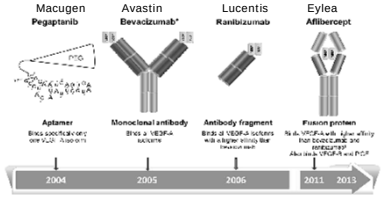


Graphic representation of proliferative diabetic retinopathy

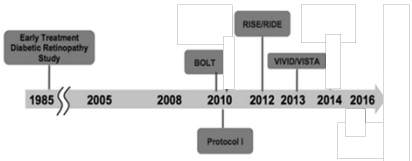
Diabetic macula edema shown in graphic form above and OCT image of center involving DME

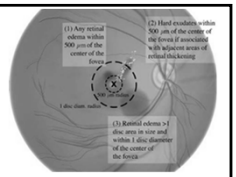
ANTI VEGF AGENTS



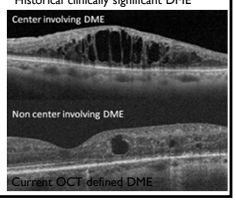


HISTORY OF ANTI VEGF IN DR





Historical clinically significant DME



Current OCT defined DME

THE RECENT/ONGOING STUDIES FROM DRCR.NET

Protocol I 2007-2013	Protocol S 2012-2018	Protocol T 2012-2018	Protocol V 2013-2018	Protocol W 2016-2022	Protocol AC 2017-ongoing
•Intravitreal Ranibizumab or Triamcinolone Acetonide in Combination with Laser Photocoagulation for Diabetic Macular Edema	•Prompt Panretinal Photocoagulation versus Intravitreal Ranibizumab with Deferred Panretinal Photocoagulation for Proliferative Diabetic Retinopathy	•A Comparative Effectiveness Study of Intravitreal Aflibercept, Bevacizumab and Ranibizumab for Diabetic Macular Edema	•Treatment for Central-Involved Diabetic Macular Edema in Eyes with Very Good Visual Acuity	•Intravitreous Anti-VEGF Treatment for Prevention of Vision Threatening Diabetic Retinopathy in Eyes at High Risk	•Randomized Trial of Intravitreous Aflibercept versus Intravitreous Bevacizumab + Deferred Aflibercept for Treatment of Central-Involved Diabetic Macular Edema

PROTOCOL I

INTRAVITREAL RANIBIZUMAB OR TRIAMCINOLONE ACETONIDE IN COMBINATION WITH LASER PHOTOCOAGULATION FOR DIABETIC MACULAR EDEMA

compared four treatment strategies:

- (1) sham injection and focal laser,
- (2) intravitreal triamcinolone plus prompt focal laser,
- (3) intravitreal lucentis plus prompt focal laser, and
- (4) intravitreal lucentis plus deferred focal laser (after 6months).

RESULTS

- Anti-VEGF was highly effective for treatment of DME.
- Vision improved an average of 8/ 9 letters in the Lucentis groups compared to laser only (3 letters)
- 5 year follow up –sustained improvement in mean and median VA in Lucentis treated groups.
- median of 0–1 injection in the 4th and 5th years of follow-up.

PROTOCOL T

A COMPARATIVE EFFECTIVENESS STUDY OF INTRAVITREAL AFLIBERCEPT, BEVACIZUMAB AND RANIBIZUMAB FOR DIABETIC MACULAR EDEMA

660 eyes with DMEand reduced VA 6/12 or worse randomised

- Avastin
- Lucentis
- Eylea

Rescue laser @ 24 weeks if persistent DME after at least 2 injections

Injection every 4 weeks until VA and structural stabilisation is achieved and resume injections if the VA or OCT worsens.

RESULTS

- All three drugs resulted in significantly improved visual acuity. (ave 8 letters over 2 years)
- When baseline VA was 6/12 or better VA improvement was similar in all groups
- Eyes with VA of 6/15 or worse has less VA improvement with Avastin and more with Eylea at 1 year but this was no longer present at 2 years.
- In all three groups average 10 injections in 1st year and 5 in 2nd year
- through out the trial Avastin resulted in less improvement in OCT CMT compared to Lucentis and Eylea but the differences were less pronounced by year 2.

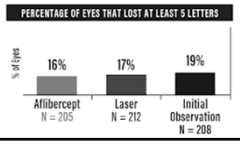
PROTOCOL V

TREATMENT FOR CENTRAL-INVOLVED DIABETIC MACULAR EDEMA IN EYES WITH VERY GOOD VISUAL ACUITY

702 patients with VA of 6/7.5 or better randomly assigned

- **monthly Eylea** (until improvement on 2 consecutive visits with VA of at least 6/6 and OCT better than baseline threshold defer treatment and monitor)
- **focal laser therapy with deferred Eylea** (seen 8 weekly then 16 weekly unless VA dropped)
- **observation with deferred Eylea** (seen 8 weekly then 16 weekly unless VA dropped)

Observation/focal laser group receive Eylea if vision drops 10 letters compared with baseline at any visit or by 5 to 9 letters on two consecutive visits



PROTOCOL S

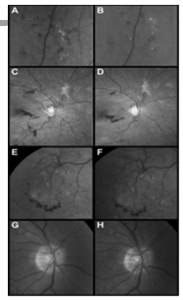
PROMPT PANRETINAL PHOTOCOAGULATION VERSUS INTRAVITREAL RANIBIZUMAB WITH DEFERRED PANRETINAL PHOTOCOAGULATION FOR PROLIFERATIVE DIABETIC RETINOPATHY

394 eyes from patients with Proliferative Diabetic retinopathy (PDR)

- **Pan retinal Photocoagulation Laser (PRP) (1,200-1,600 spots)**
- **Lucentis** 4 weekly or until vessels had regressed or stabilized over 2 consecutive visits.

RESULTS

- Lucentis was non-inferior to PRP for VA at 2 and 5 years.
- Less visual field loss in Lucentis group compared to PRP, but continued field loss was seen in both groups up to 5 years.
- Lucentis group had less new onset DME and less vitrectomy surgery.



A, **B**, Resolved: neovascularization @1 week after ANTI VEGF
C, **D**, Improved: neovascularization decreased @ 1 week after ANTI VEGF
E, **F**, Stable: neovascularization @ 1year
G, **H**, Worsened: neovascularization of the disc over 32

REAL WORLD VA OUTCOMES AND TREATMENT BURDEN

Real world results show VA gains are not equal to the studies.

Patients with DME have a mean 12 extra clinical appt per year compared with diabetic patients with no DME.

DME patients have higher rates of appointment cancellations (10.01%) and no-shows (14.32%) compared nAMD patients.

SUMMARY

- VEGF plays a central role in the development of DME and PDR
- Anti VEGFs are highly effective at blocking the effects of VEGF
- Anti VEGFs have become the treatment of choice for center involving DME rather than laser with a vision gain of about 11 letters.
- Avastin, Lucentis and Eylea are equally effective in patients with VA of 6/12 but Eylea is more effective for patients with VA 6/15 or worse.
- For DME patients with very good vision of 6/7.5 or better, anti VEGF treatment no better than observation.
- PRP remains the gold standard of care for PDR but anti VEGFs are a useful tool in patients with good compliance.
- Real world VA outcomes are lower than the study results suggest and treatment burden is high in the diabetic population with DME and PDR.