**ROLE OF VEGF IN DIABETIC RETINOPATHY**

- Hypoxia stimulates production of VEGF and other angiogenic growth factors.
- VEGF and other angiogenic factors bind to endothelial cells of new blood vessels and activate them.
- Activated endothelial cells proliferate, migrate, and release proteins.

**ROLE OF VEGF IN DIABETIC RETINOPATHY**

- Diabetic macula edema shown in graphic form above and OCT image of center involving DME.
- Graphic representation of proliferative diabetic retinopathy.

**HISTORY OF ANTI-VEGF IN DR**

- Early use of anti-VEGF agents for diabetic macula edema.
- Determination of treatment efficacy.

**THE RECENT/ONGOING STUDIES FROM DRCR.NET**


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**Title: Anti-VEGF agents in diabetic retinopathy**

**REAL WORLD VA OUTCOMES AND TREATMENT BURDEN**

- Real world results show VA gains are not equal in the diabetic population.
- Patients with DME have a mean 13 letters visual gain per year compared with diabetic patients with no DME.
- DME patients have higher rate of appointments cancellations (50%) and no-appearances (40%) compared to AMD 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-involved 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 Lucentis was non-inferior to PRP for VA at 2 and 5 years.
- Lucentis was more effective for patients with VA 6/15 or worse.
- 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 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 I**

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

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

**RESULTS**
- Anti-VEGF was highly effective for treatment of DME.
- Vision improved an average of 9-11 letters in the Lucentis groups compared to laser only (3 letters).
- Median of 0–1 injection in the 4th and 5th years of follow-up.
- All three drugs resulted in significantly improved visual acuity (i.e., 8 letters over 2 years).
- Eyes with VA of 6/15 or worse have 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 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 T**

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

- Injection every 4 weeks until VA and structural stabilization is achieved and resume injection if the VA or OCT worsens.

- **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.
  - Less visual field loss in Lucentis group compared to PRP, but no statistical difference.
  - Lucentis was non-inferior to PRP for VA at 2 and 5 years.
  - Avastin, Lucentis and Eylea are equally effective in patients with VA of 6/12 but Lucentis was more effective for patients with VA of 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.