



Vascular Endothelial Growth Factor in Diabetic Retinopathy

Victor H. Gonzalez, M.D.
Director
Valley Retina Institute
Valley Retina Research
McAllen, Texas

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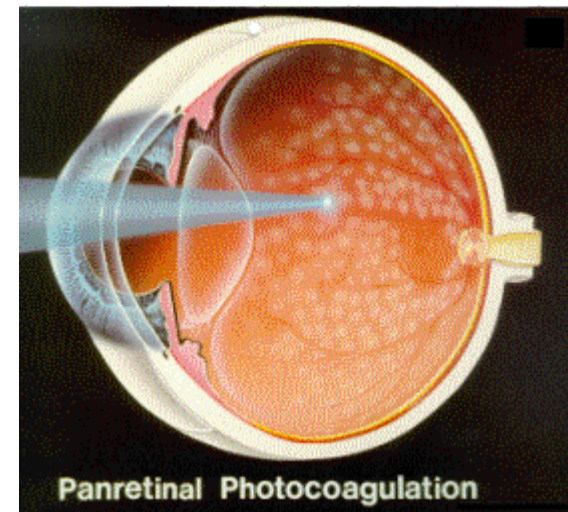
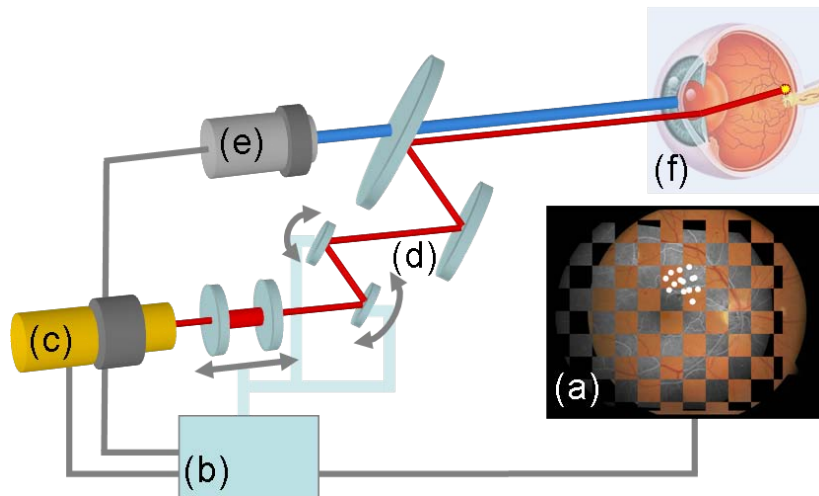
Diabetic Retinopathy Treatment

Based on NEI Trials

- 1- Diabetic Retinopathy Study (DRS)
- 2- Early Treatment Diabetic Retinopathy Study (ETDRS)
- 3- Diabetic Retinopathy Vitrectomy Study (DRVS)
- 4- Diabetic Control and Complications Trial (DCCT)

Photocoagulation

- Standard of treatment
- Decrease vitreous levels of VEGF *



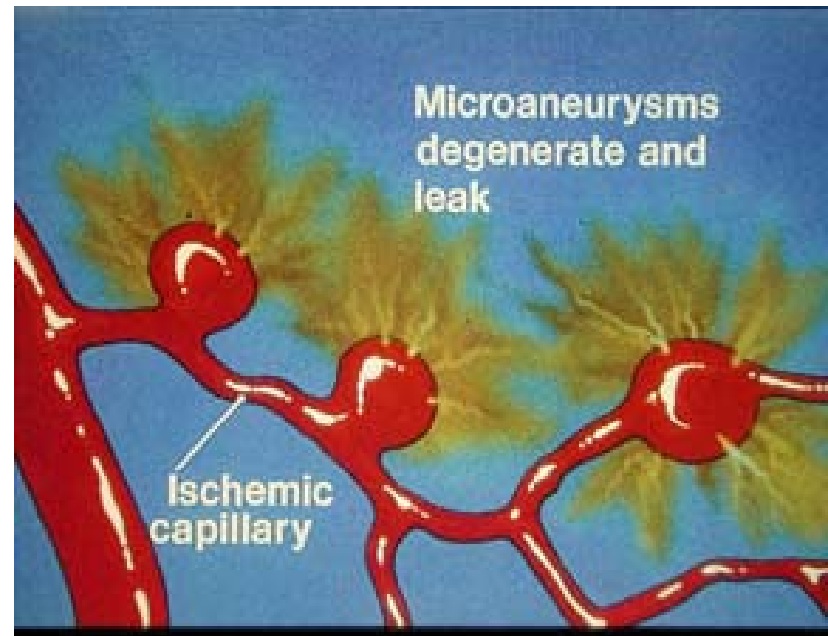
Limitations and Possible Side Effects

- Limited visual gain
 - Mostly avoid moderate vision loss
- Central vision loss
 - Distortion, scotomas, color vision disturbances
- Peripheral vision loss
 - Visual field constriction, night blindness

[illegible]

Pathophysiology of Diabetic Retinopathy

- Genetic
- Environmental
- Immunological
 - HLA-DR phenotypes 4/0, 3/0, and neither 3 nor 4¹ all with higher risk of PDR
- Long term hyperglycemia
 - Most important factor at present



Frank RN: Etiologic mechanisms in diabetic retinopathy. In Ryan SJ, ed: Retina, Schachat AP and Murphy RP, eds vol. 2 Medical Retina,, St. Louis, 1994, Mosby, p. 1245-1246

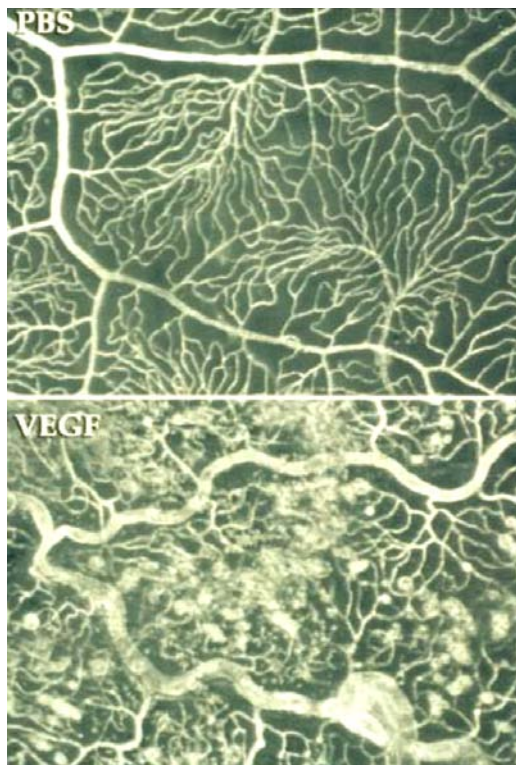
Pathophysiology of Diabetic Retinopathy

- Vascular Endothelial Growth Factor (VEGF)
 - Functions:
 - » Potent mitogen for vascular endothelial cells
 - » Increases vascular permeability
 - » Vasodilator
 - » Promoter of endothelial cell migration
 - » Anti-apoptotic, endothelial cell survival factor



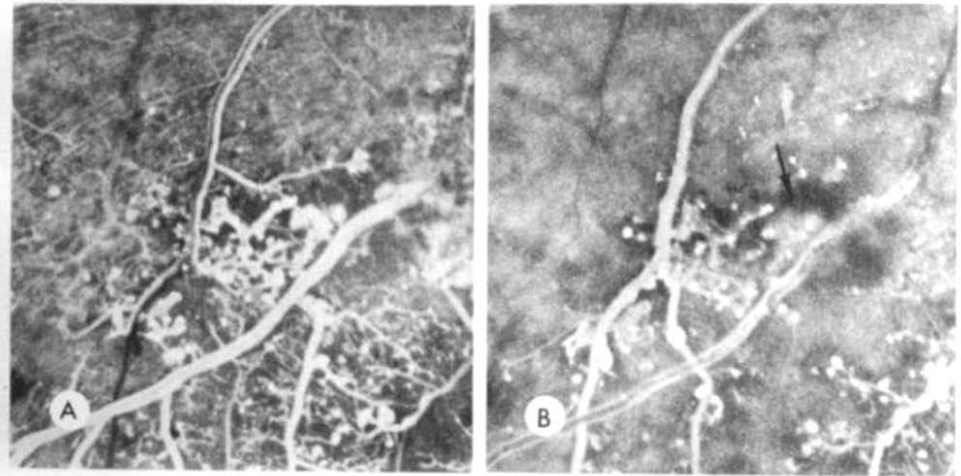
Diabetes Metab Res Rev
2003;19:442-455

Exogenous VEGF₁₆₅ Induces a Diabetic Retinopathy Phenotype in Primates



Post-VEGF₁₆₅ injection in
the primate

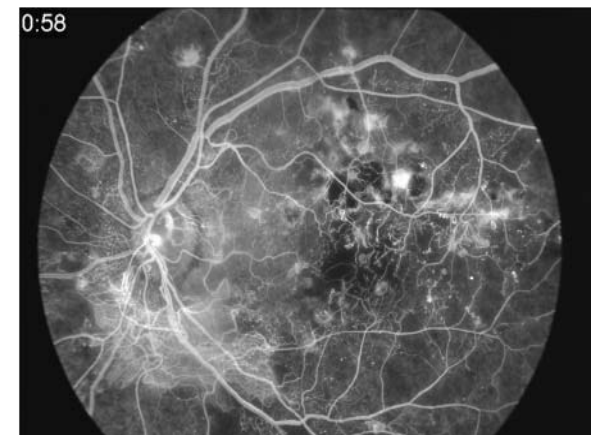
Fig. 15-12. A, Capillary-phase fluorescein angiogram of a diabetic patient shows microaneurysms. B, In the late venous phase the position of the aneurysms can be seen because of leakage of dye through their walls.



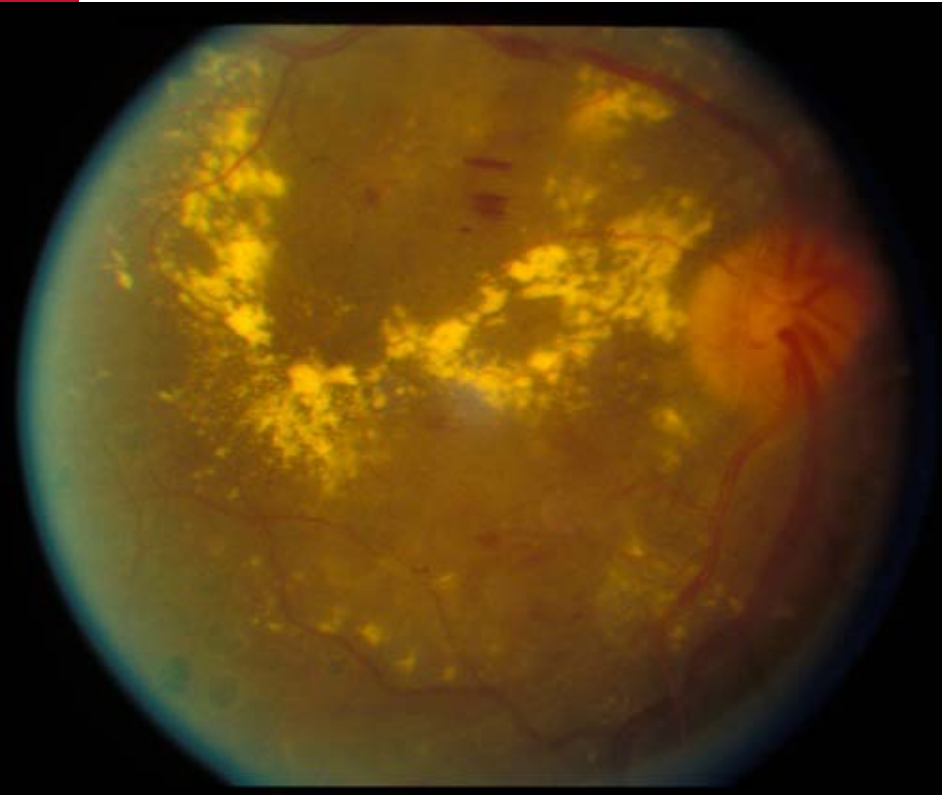
Human diabetic
retinopathy

VEGF₁₆₅ in Diabetic Retinopathy

- Retinal VEGF₁₆₅ levels elevated in experimental diabetes
- Increased VEGF₁₆₅ levels found in vitreous of eyes with proliferative DR
- DR patients have higher VEGF₁₆₅ levels in the aqueous



Anti-VEGF-Induced Improvement on Diabetic Retinopathy Severity Scale Indices



Baseline



Week 36

Regression of NVE with Anti-VEGF

... recurrence when but...

Pegaptanib

// Stop Therapy

Baseline

Week 36

Week 52

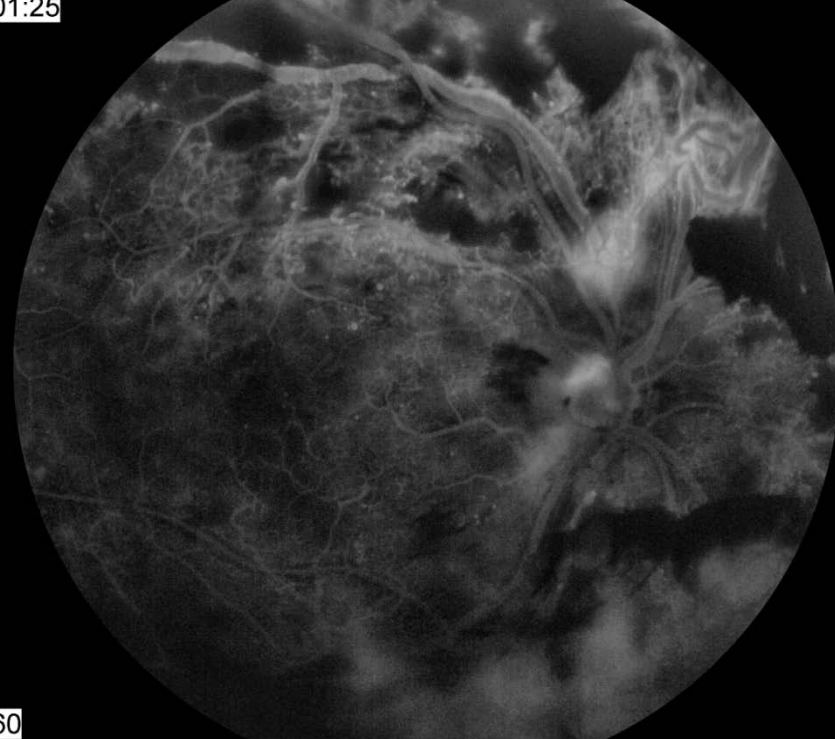
Regression

Recurrence

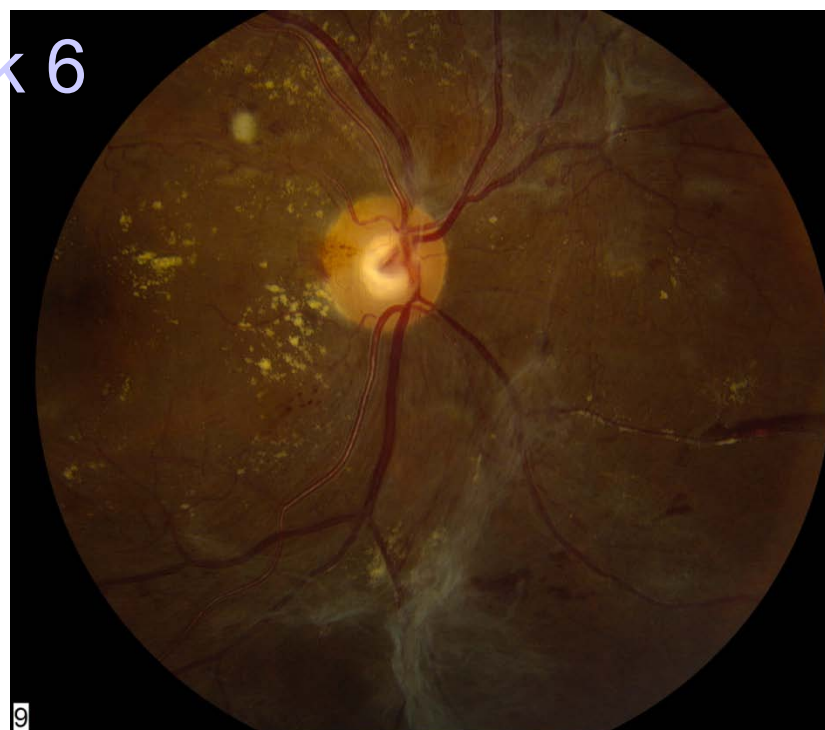
Baseline



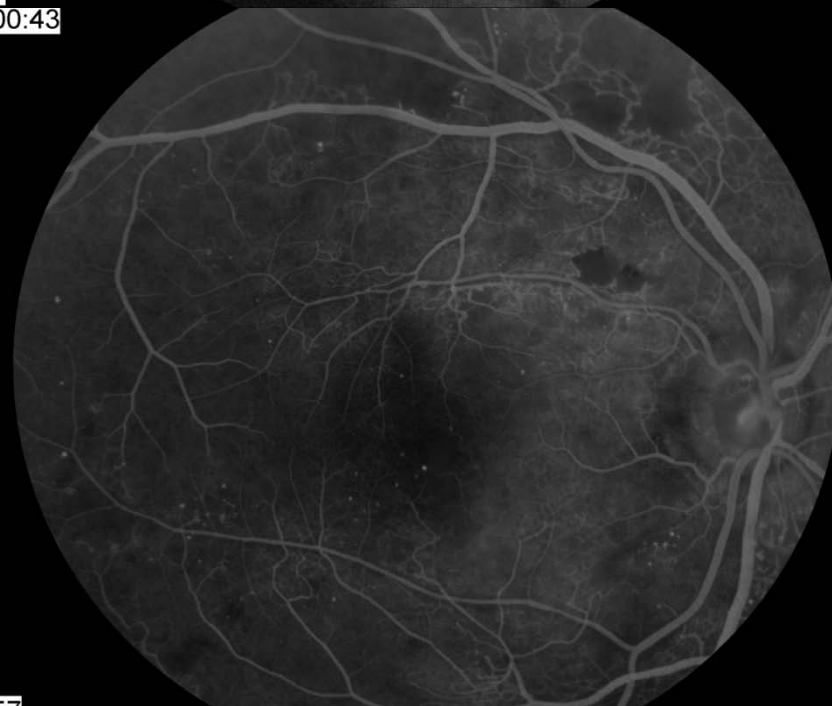
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Week 6

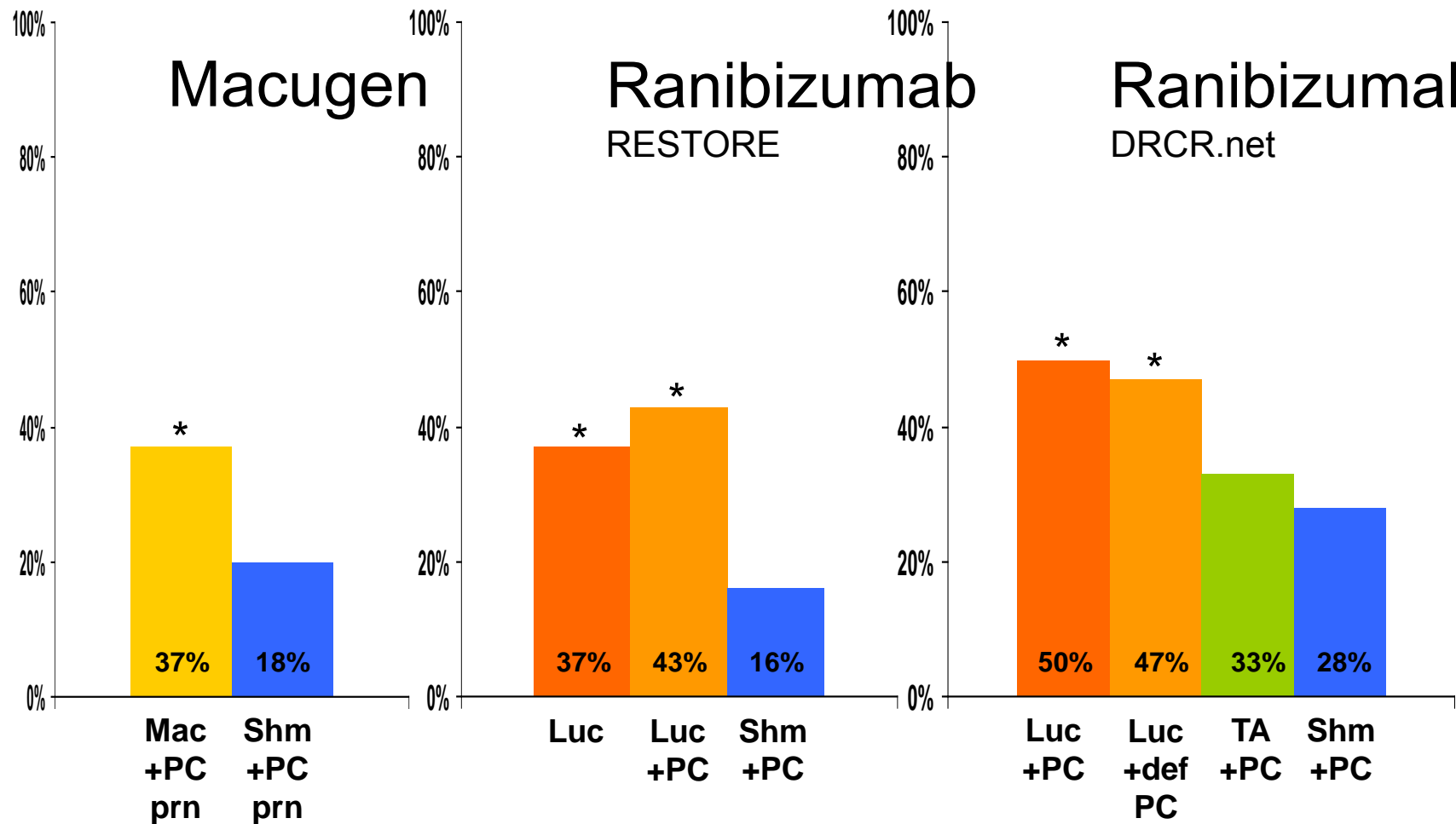


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Comparative Phase 3 Data in DME Proportion Gaining ≥ 10 Letters at Week 54



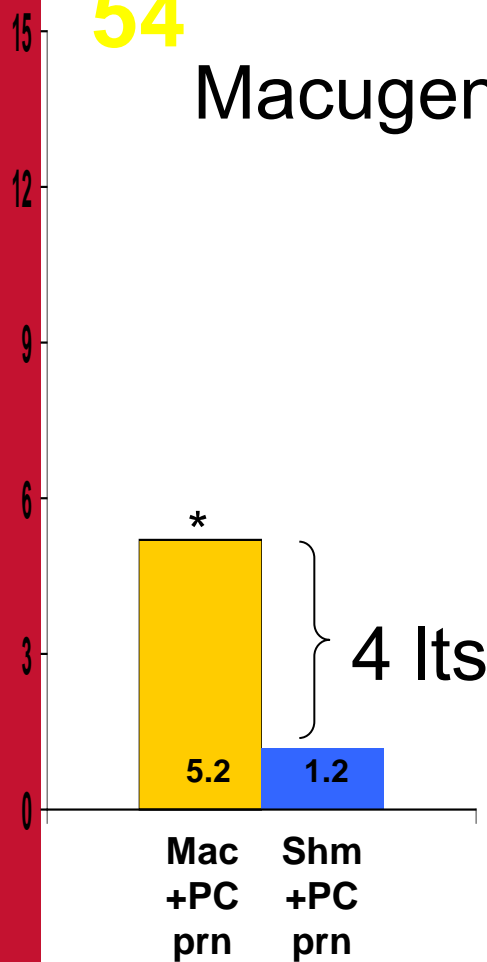
* P value <0.05 compared to control group

Anti-VEGF for DME Trials

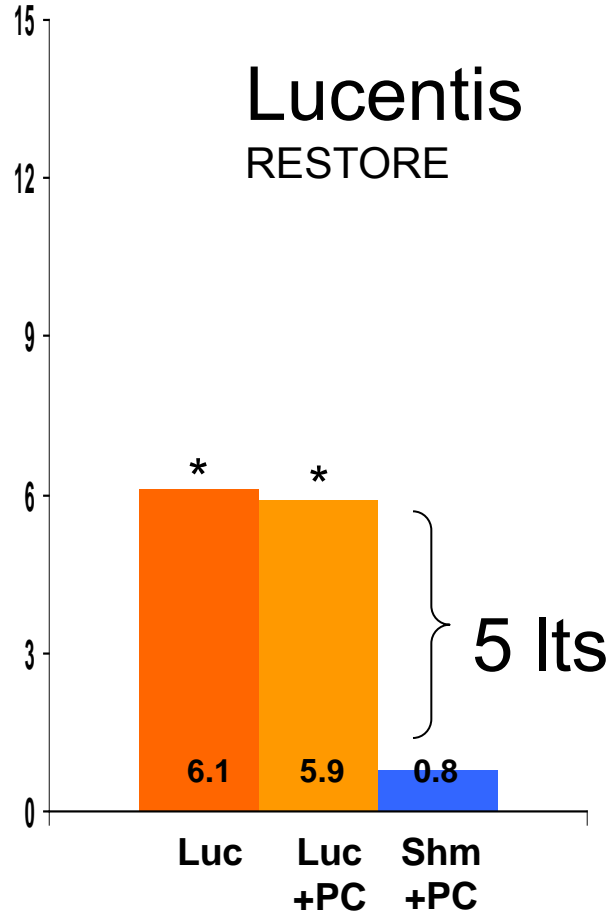
Mean Change in VA from Baseline to Week

54

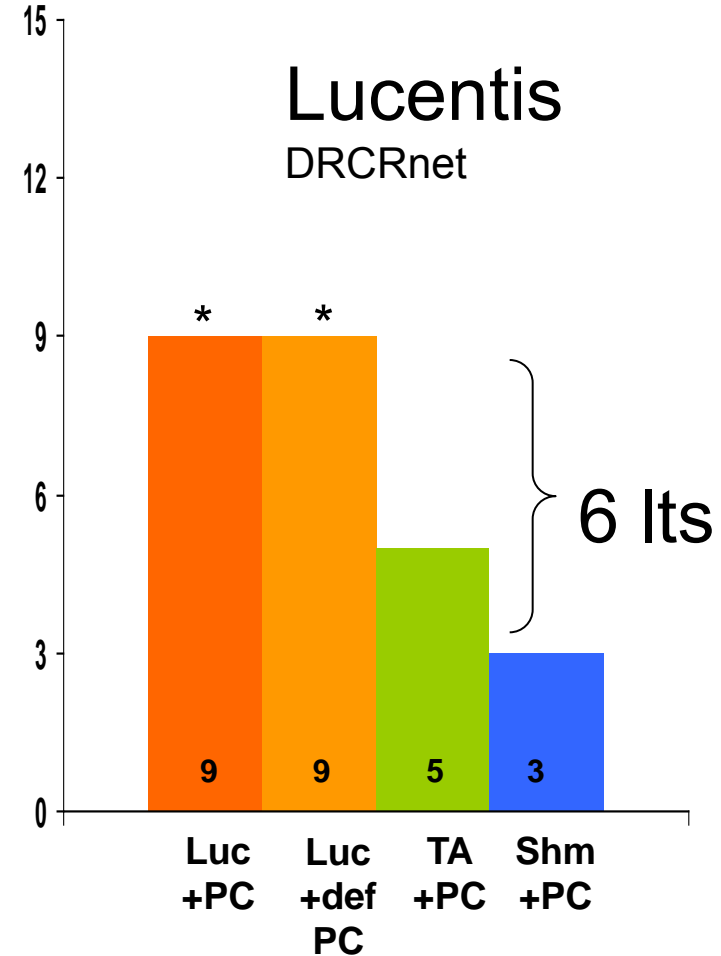
Macugen



Lucentis RESTORE



Lucentis DRCRnet



Conclusions

- Anti-VEGF agents are effective in the treatment of DR
 - Diabetic Macular Edema
 - Proliferative Diabetic Retinopathy
- Do not result in tissue loss
- Patients are more likely to improve vision
- More functional

