Pattern lasers

Laser	Wavelength (nm)	Duration (ms)	Power (mW)	Diameter (µm)	Number
Argon ion	488 & 514.5	100	~150-250	500	1600
Laser diode	532/577/other	20 - 50	~300 - 650	400	~2800

Seymenoglu KJMS 2016 32: 22-26

Pattern lasers with short pulses need on average 75% more burns of same nominal diameter to be effective:

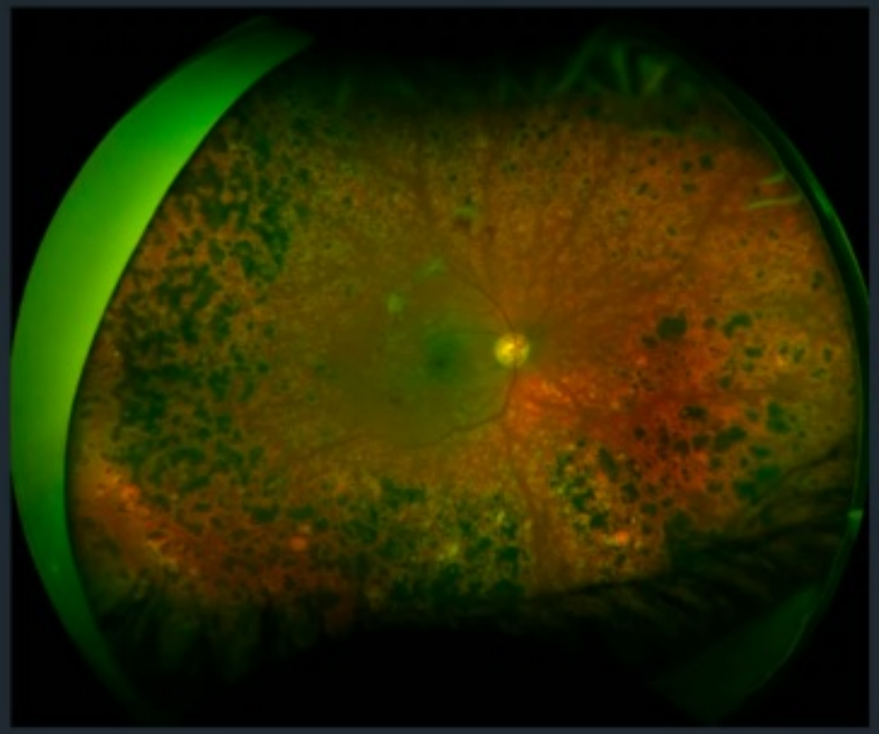
2885 vs 1642 burns

Do PRP properly

Conventional

Denser burn

Burn expansion



Pattern

Lighter burn

Burn contraction

Surely we can treat PDR with anti-VEGF?

Surely we can treat PDR with anti-VEGF?

Protocol S

- Ranibizumab *vs* PRP
- DRCR Network JAMA 2015 314: 2137-46

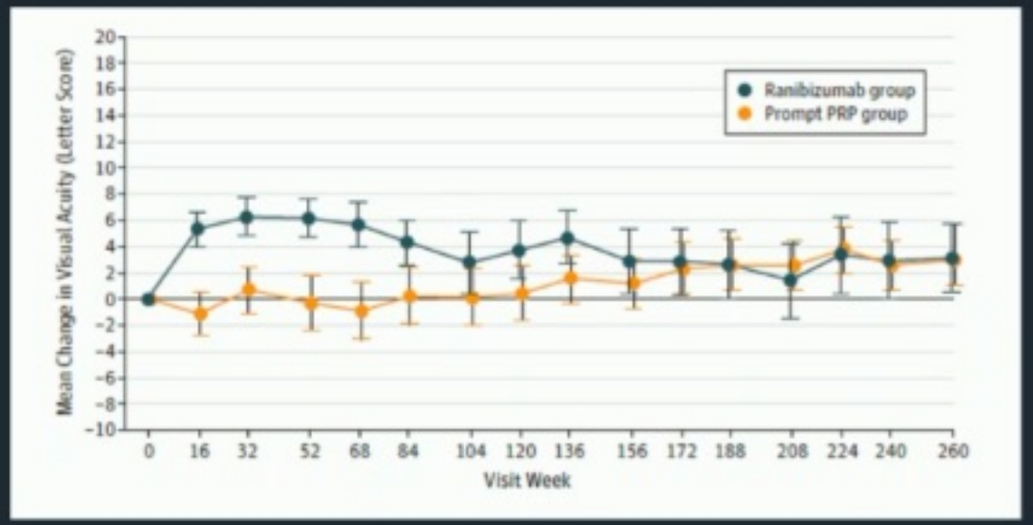
- Eyes with PDR ± DMO
- No previous ocular treatments

Surely we can treat PDR with anti-VEGF?

Protocol S	CLARITY
• Ranibizumab *vs* PRP	Aflibercept *vs* PRP
• DRCR Network JAMA 2015 314: 2137-46	Sivaprasad et al. Lancet 2017 389: 2193-5
• Eyes with PDR ± DMO	Eyes with PDR without DMO
• No previous ocular treatments	Untreated or previously treated with PRP (but still active)

Protocol S: 5 year outcomes – new vessels

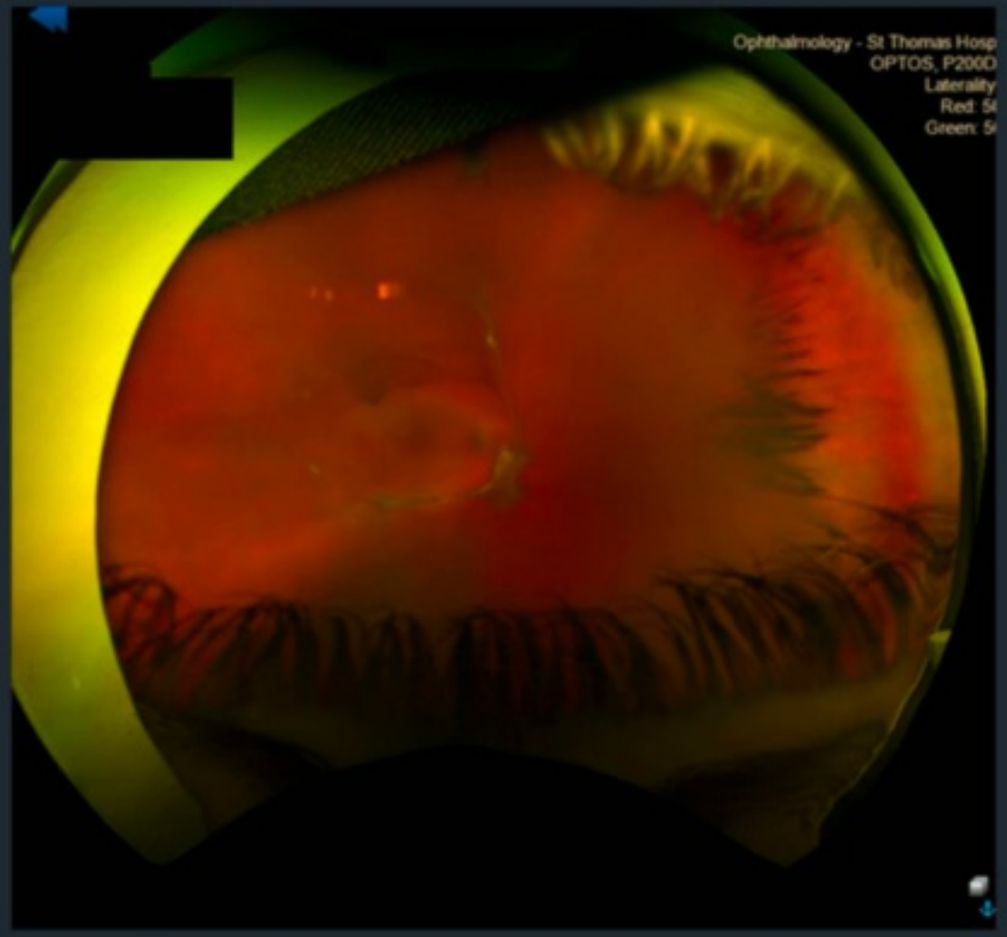
Ranibizumab group		PRP group	
No PDR	43 %	No PDR	37 %
Regressed NV	28 %	Regressed NV	33 %
Active NV	29 %	Active NV	30 %
Vitreous haem	48 %	Vitreous haem	46 %



Lost to follow up

Patients lost to follow up do badly:
Obeid A et al Ophthalmology. 2018 Aug 2. pii: S0161-6420(18)31079-0

PRP	reasonable outcome
Anti VEGF	poor outcome



Cochrane review of RCTs

Martinez-Zapata MJ, Salvador I, Martí-Carvajal AJ, Pijoan JI, Cordero JA, Ponomarev D, Kernohan A, Solà I, Virgili G. Anti-vascular endothelial growth factor for proliferative diabetic retinopathy. Cochrane Database Syst Rev. 2023 Mar 20;3(3):CD008721.

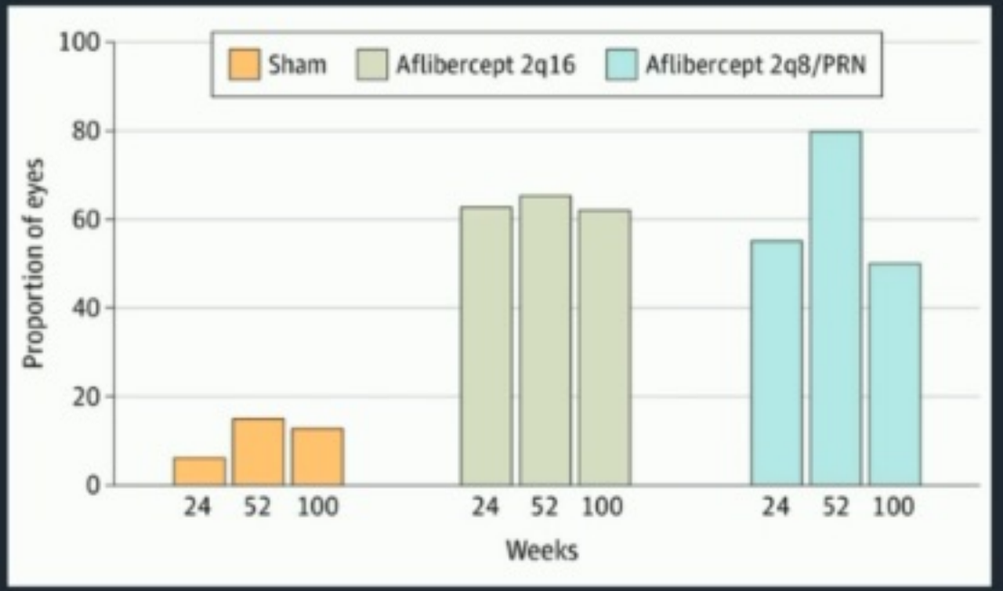
23 RCTs 2334 eyes of 1755 patients

Parameter	Anti VEGF ± PRP *vs* PRP			Evidence level
Visual acuity	Mean difference	-0.08 logMAR	95% CI -0.12 to -0.04	Moderate
New vessel regression	Mean difference	-4.14 mm^2	95% CI -6.84 to -1.43	Low
Vitreous haemorrhage	Relative risk	0.72	95% CI 0.57 to 0.90	Low
Vitrectomy	Relative risk	0.67	95% CI 0.49 to 0.93	Low
Quality of life	Mean difference	0.62	95% CI -3.99 to 5.23	Low

Anti-VEGF also reduces appearance of NPDR

Brown DM, et al. Evaluation of Intravitreal Aflibercept for the Treatment of Severe Nonproliferative Diabetic Retinopathy: Results From the PANORAMA Randomized Clinical Trial. JAMA Ophthalmol. 2021 Sep 1;139(9):946-955.

2 years: Aflibercept 16 weeks *vs* Aflibercept 8 weekly then prn *vs* sham



RECOVERY study

Wykoff et al. (2019). Intravitreal aflibercept for retinal nonperfusion in proliferative diabetic retinopathy: outcomes from the randomized recovery trial. *Ophthalmology Retina*, *3*(12), pp.1076-1086.

DRSS severity scores improved in 74%
Retinal non-perfusion increased from 235mm^2 to 266 mm^2

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Proliferative retinopathy improved and a reduction in number of microaneurysms

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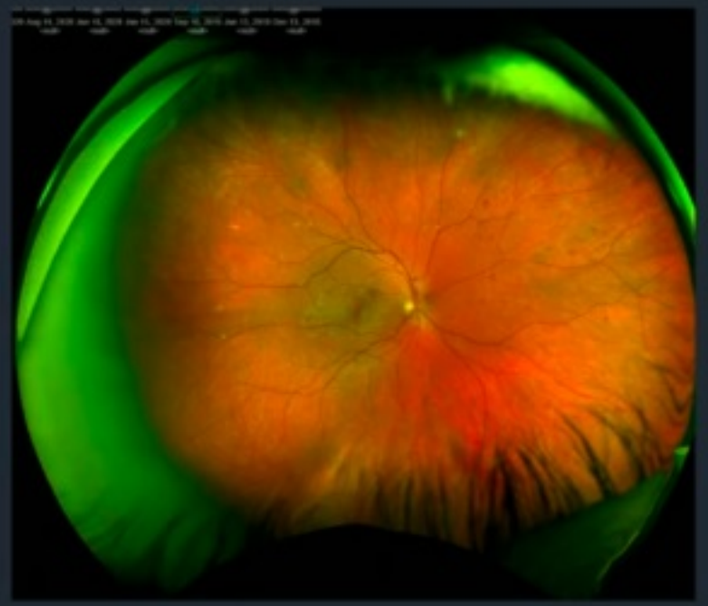
Wykoff et al. (2022) Final Outcomes from the Randomized RECOVERY Trial of Aflibercept for Retinal Nonperfusion in Proliferative Diabetic Retinopathy. Ophthalmol Retina Jul;6(7):557-566.

DRSS severity scores improved in 82%
Retinal non-perfusion increased 235mm^2 to 402 mm^2 yes, 402mm^2 !!

What is all this telling us?

Ongoing microvascular damage

No retinopathy	Non-proliferative retinopathy	Proliferative retinopathy



What is all this telling us?

Ongoing microvascular damage

Proliferative retinopathy	PRP (done properly)	Stable treated Proliferative retinopathy

Proliferative retinopathy	PRP (done properly)	Stable	Reactivation	More PRP/ other

What is all this telling us?

Ongoing microvascular damage

Proliferative retinopathy	Anti VEGF	Stable	Anti VEGF	Stop	Reactivate

Non-proliferative retinopathy	Anti VEGF	Clinical regression	Stop	Reactivate or proliferate

This might mean

Not only is proliferative retinopathy driven by VEGF

Clinical signs of NPDR are driven in part by presence of VEGFs

Anti-VEGF treatment allows these signs to regress

But the capillary damage continues and non-perfusion increases

Increased risk of proliferation or worse proliferation if treatment stops

Summary

Panretinal photocoagulation remains gold standard

No convincing evidence that anti-VEGF has a place in all PDR patients

The area of non-perfusion increases despite improvement of clinical signs

Beware the ‘featureless retina’

Be very careful in patients treated for DME with anti-VEGF

If their initial images show severe NPDR at the outset, consider wide field FFA to assess peripheral circulation