# Residual retinal fluid following intravitreal anti-VEGF treatment for neovascular age-related macular degeneration: a systematic review and meta-analysis

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### Purpose

- The relationship between the presence of residual subretinal fluid (SRF) and residual intraretinal fluid (IRF) with visual acuity following anti-vascular endothelial growth factor (VEGF) treatment is not well understood.
- The objective of this meta-analysis is to analyze the association of residual retinal fluid, SRF, and IRF on visual acuity following anti-VEGF treatment for neovascular age-related degeneration macular (nAMD).

### Methods

- A systematic literature search was performed from January 2005 to August 2021 on Ovid MEDLINE, EMBASE, and the Cochrane Library.
- Peer-reviewed articles reporting on visual acuity at last study observation stratified by the presence or absence of any residual SRF, IRF, and/or any retinal fluid after intravitreal injection of bevacizumab, ranibizumab, aflibercept, or brolucizumab in patients with nAMD were included.
- Studies that reported on other anti-VEGF agents, in fewer than 10 findings eyes, or were non-comparative, were excluded.
- Primary outcomes were BCVA at last study observation, change in BCVA from baseline, and retinal thickness at last study observation.
- Random-effects meta-analysis was conducted.

- analysis.
- eyes).
- GRADE=low, 7 studies, n=2114 eyes).

		SRF	No SRF			
Study or Subgroup	Mean	SD	Total	Mean	SD	1
Chatziralli 2016	65.4	19.3	129	62.8	16.7	
Dervenis 2016	61	18	42	52.5	26.5	
Holekamp 2021	69.39	19.49	163	62.26	17.94	
Khanani 2015	65.1	16.5	9	62.6	12	
Ohji 2021	61.81	15.46	51	63.1	16.86	
Saenz-de-viteri 2021	65.279	16.743	82	63.7	17.4	

Total (95% CI) 476 Heterogeneity: Tau<sup>2</sup> = 6.51; Chi<sup>2</sup> = 10.02, df = 5 (P = 0.07); l<sup>2</sup> = 50% Test for overall effect: Z = 1.99 (P = 0.05)

# Results

• 11 studies and 3092 eyes were included in our

• At last study observation, the BCVA of eyes with residual SRF was better than eyes with no SRF (WMD=3.1 letters, 95% CI=[0.05,6.18], p=.05, GRADE=low certainty of evidence, 6 studies, n=1931

• The BCVA of eyes with residual IRF at last study observation was worse than eyes with no IRF (WMD=-8.2 letters, 95% CI=[-11.79,-4.50], p<.001,

• In a leave-one-out sensitivity analysis, residual SRF was no longer associated with a better BCVA at last study observation relative to no residual SRF when Chatziralli et al. (p=.12), Dervenis et al. (p=.09), Holekamp et al. (p=.20), Khanani et al. (P=.07), or Saenz de Viteri et al. (p=.07) were excluded.



Figure 1. BCVA at final follow-up for eyes with residual SRF.

	IRF			No IRF				Mean Difference	Mean
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Ran
Chatziralli 2016	59	18	156	65.9	16.8	291	21.5%	-6.90 [-10.32, -3.48]	-
Dervenis 2016	56.5	22.5	32	63	14.5	30	9.7%	-6.50 [-15.86, 2.86]	
Holekamp 2021	58.91	21.77	246	65.32	16.67	649	22.5%	-6.41 [-9.42, -3.40]	
Khanani 2015	69.5	9.9	4	62.2	15.4	12	6.0%	7.30 [-5.74, 20.34]	
Ohji 2021	48.15	18.53	16	63.9	15.97	224	9.7%	-15.75 [-25.07, -6.43]	
Saenz-de-viteri 2021	58.771	18.691	63	65.6	16.5	207	17.4%	-6.83 [-11.96, -1.70]	
Wickremasinghe 2014	43	22.5	48	60.5	18.5	136	13.3%	-17.50 [-24.58, -10.42]	-
Total (95% CI)			565			1549	100.0%	-8.15 [-11.79, -4.50]	•
Heterogeneity: Tau <sup>2</sup> = 13	.07; Chi <sup>z</sup> :	= 16.35, 0	df = 6 (F	P = 0.01	); <b>I<sup>z</sup> = 6</b> 3	3%		2	
Test for overall effect: Z = 4.38 (P < 0.0001)								-20 -10 Favours No IF	

Figure 2. BCVA at final follow-up for eyes with residual ) IRF.

## Discussion

- The presence of residual SRF was associated with slightly better BCVA at last study observation, however, there was no significant difference between these two groups on leave-one-out sensitivity analysis and subgroup analysis based on study design.
- The presence of residual IRF was associated with substantially worse BCVA at last study observation and less improvement of BCVA from baseline.
- Our conclusions are limited by data observational studies, heterogeneity, and a low certainty of evidence.
- · While these findings support tolerance of residual SRF when treating nAMD, future clinical trials would be needed to confirm the association of residual SRF on BCVA outcomes.

### **Conflicts of Interest**

N.P: None Declared, A.M: None Declared, A.H: None Declared, M.P: PSI Foundation, P.K: Bayer, Roche, Novartis, ArcticDx, R.M: Bayer, Novartis













