

Supplementary Table 1. Summary of Outcomes in Real-World Studies of Anti-VEGF Treatment (Not Including Treat-and-Extend Regimens) in Patients With nAMD*

Study	Study design	Patient population	Anti-VEGF therapy	Dosing regimen	Patients, N	Eyes, n	Outcomes during the previous 12 months
PrONTO[1]	Open-label prospective	nAMD	Ranibizumab	PRN, following loading doses	40	–	At 12 months: Mean injections: 5.6 Mean visual acuity change: +9.3 letters (p<0.001)
CATT[2]	Single-blind, randomised, prospective	nAMD	Ranibizumab	Every 28 days	284	–	At 12 months: Mean injections: 11.7 Mean visual acuity change: +8.5 letters
				PRN, following first mandatory injection	285	–	At 12 months: Mean injections: 6.9 Mean visual acuity change: +6.8 letters
			Bevacizumab	Every 28 days	265		At 12 months: Mean injections: 11.9 Mean visual acuity change: +8.0 letters
				PRN, following first mandatory injection	271		At 12 months: Mean injections: 7.7 Mean visual acuity change: +5.9 letters
SECURE[3]	Phase 4, open-label extension study	nAMD	Ranibizumab	PRN	234	–	At 24 months: Mean injections: 6.1 Mean visual acuity change: -4.3 letters
HORIZON[4]	Open-label extension study	nAMD	Ranibizumab	PRN (initially treated with ranibizumab)	600	–	At 24 months: Mean injections: 4.4 Mean visual acuity change: -7.0 letters
				PRN (crossover to ranibizumab)	190	–	At 24 months: Mean injections: 4.8

							Mean visual acuity change: -2.2 letters
TWIN[5]	Retrospective observational study	nAMD	Ranibizumab	PRN, following loading doses	881	–	At 12 months: Mean injections: 5.6 Mean visual acuity change: +4.3 letters
AURA[6]	Retrospective observational study	nAMD	Ranibizumab	PRN, following loading doses	2227	–	At 24 months: Mean injections: 7.2 Mean visual acuity change: +0.6 letters
LUMINOUS[7, 8]	Prospective observational study	nAMD	Ranibizumab	PRN, following loading doses	2701	–	At 12 months: Mean injections: 5.3 Mean visual acuity change: +3.6 letters
					372		Mean visual acuity change with <3 injections: +2.1 letters
					1499		Mean visual acuity change with 3–6 injections: +3.6 letters
					830		Mean visual acuity change with >6 injections: +4.3 letters
IRIS[9]	Retrospective, non-randomised, comparative registry study	nAMD	Ranibizumab	PRN	2749	–	At 12 months: Mean injections: 6.4 Mean visual acuity change: -0.05 logMAR
			Aflibercept	PRN	4387	–	At 12 months: Mean injections: 6.2 Mean visual acuity change: -0.04 logMAR
			Bevacizumab	PRN	6723	–	At 12 months: Mean injections: 5.9 Mean visual acuity change: -0.05 logMAR

Talks et al.[10]	Retrospective review of medical records	nAMD	Aflibercept	Fixed bimonthly, following loading doses	1682	1840	At 12 months: Mean injections: 7.0 Mean visual acuity change: +5.1 letters
PERSEUS[11]	Prospective, non-interventional, non-controlled, multicentre, observational cohort study	nAMD	Aflibercept	Fixed bimonthly (treatment-naïve), following loading doses	447	–	At 12 months: Mean injections: 7.4 Mean visual acuity change: +8.0 letters
				PRN (treatment-naïve)			At 12 months: Mean injections: 5.1 Mean visual acuity change: +4.0 letters
				Fixed bimonthly (previously treated), following loading doses	355	–	At 12 months: Mean injections: 7.5 Mean visual acuity change: +3.1 letters
				PRN (previously treated)			At 12 months: Mean injections: 5.3 Mean visual acuity change: -1.1 letters
Lee et al.[12]	Retrospective review of medical records	nAMD	Aflibercept	Fixed bimonthly, following loading doses	–	942	At 12 months: Mean injections: 7.0 Mean visual acuity change: +6.1 letters (p<0.001)
			Ranibizumab	PRN	–	942	At 12 months: Mean injections: 5.8 Mean visual acuity change: +1.6 letters
Airody et al.[13]	Single-centre cohort	nAMD	Ranibizumab	PRN, following loading doses	68	–	At 60 months: Median injections: 6, 4, 4, 4, 7 in Year 1–5, respectively Mean visual acuity change: +5.7 letters

Almuhtaseb et al.[14]	Retrospective review of medical records	nAMD	Aflibercept	Fixed bimonthly, following loading doses	223	255	At 12 months: Mean injections: 7.0 Mean visual acuity change: -0.16 logMAR
Almuhtaseb et al.[15]	Retrospective review of medical records	nAMD	Aflibercept	Fixed bimonthly in Year 1, PRN in Year 2, following loading doses	1083	1180	At 12 months: Mean visual acuity change: +5.0 letters From 12 to 24 months: Mean injections: 3.7 Mean visual acuity change: +2.8 letters
Arias et al.[16]	Prospective, non-comparative, consecutive case series study	nAMD	Ranibizumab	PRN, following loading doses	88	90	At 12 months: Mean injections: 4.4 Mean visual acuity change: +7 letters
Barthelmes et al.[17]	Registry study	Exudative nAMD switching treatment after ≥12 months (mean 39.8 months) treatment with ranibizumab	Aflibercept	PRN, following loading doses	–	384	At 12 months after switch: Mean injections: 3.2 Mean visual acuity change: -0.1 letters
Berg et al.[18]	Retrospective review of medical records	nAMD	Bevacizumab	PRN, following monthly dosing until there were	40		At Year 8: Mean injections: 5.4 Mean visual acuity change: -2.1 letters

				no signs of active nAMD			
Biarnés et al.[19]	Retrospective, consecutive case series	nAMD	Ranibizumab	PRN	71	67	At 12 months: Mean injections: 3.5 Mean visual acuity change: +1.3 letters
Böhni et al.[20]	Retrospective review of medical records	nAMD	Ranibizumab	PRN, following loading doses	15	16	At 12 months: Mean injections: 8.3 Mean visual acuity change: +15.0 letters
			Aflibercept	PRN, following loading doses	9	11	At 12 months: Mean injections: 8.5 Mean visual acuity change: +5.6 letters
Braimah et al.[21]	Retrospective review of medical records	Patients with nAMD switched from bevacizumab and ranibizumab	Aflibercept	PRN	14	16	At 12 months: Mean injections: 5.9 Mean visual acuity change: No change
UNCOVER[22]	Retrospective cohort study	nAMD	Ranibizumab	–	3241	3725	At mean 22.3 months: Mean injections: 4.2 per year Mean visual acuity change: -0.7 letters
Elwes et al.[23]	Retrospective review of medical records	nAMD	Aflibercept, switching from ranibizumab	PRN, following loading doses	182	207	At 85 weeks: Mean injections: 10 Mean visual acuity change: -8.9 letters

WAVE[24]	Prospective observational study	nAMD	Ranibizumab	PRN, following loading doses	2587	–	At 12 months: Mean injections: 4.3 Mean visual acuity change: +0.02 logMAR
Gabai et al.[25]	Retrospective review of patient records	nAMD	Ranibizumab	PRN, following loading doses	92	100	At 12 months: Mean injections: 4.8 Mean visual acuity change: -2.0 letters
Garweg et al.[26]	Retrospective review of medical records	nAMD	Any anti-VEGF therapy	PRN, following loading doses	104	104	At Years 3–10: Mean injections: 2.8 annually Mean visual acuity change: -7.3 to -11.9 letters
Gerding et al.[27]	Retrospective review of medical records	nAMD	Ranibizumab	PRN, following loading doses	–	104	At 12 months: Mean injections: 5.8 Mean visual acuity change: +5.0 letters
Giacomelli et al.[28]	Retrospective review of medical records	nAMD	Ranibizumab	PRN, following loading doses	31	–	At 12 months: Mean injections: 5.1 Mean visual acuity change: +0.14 logMAR At 24 months: Mean injections: 7.6 Mean visual acuity change: +0.25 logMAR

Giannou et al.[29]	Prospective cohort study	nAMD	Ranibizumab	Observe-and-plan	104	115	At 12 months: Mean injections: 7.8 Mean visual acuity change: +9.7 letters At 24 months: Mean injections: 13.6 Mean visual acuity change: +9.2 letters
Fight Retinal Blindness! Study[30]	Prospective observational study	nAMD	Ranibizumab	–	–	197	At 12 months: Mean injections: 8.1 Mean visual acuity change: +2.9 letters
			Aflibercept	–	–	197	At 12 months: Mean injections: 8.0 Mean visual acuity change: +5.4 letters
Heimes et al.[31]	Prospective observational study	nAMD	Ranibizumab	PRN, following loading doses	–	152	At 12 months: Mean injections: 5 Mean visual acuity change: 0 logMAR
Kang and Roh[32]	Retrospective review of medical records	nAMD	Ranibizumab	PRN (without a loading dose)	41	41	At 12 months: Mean injections: 4.1 Mean visual acuity change: -0.078 logMAR (p<0.05)
Lala et al.[33]	Retrospective review of medical records	Exudative AMD	Ranibizumab	PRN, following loading doses	284	284	At 12 months: Mean injections: 7.1 Mean visual acuity change: +7.5 letters
					208	208	At 24 months:

					152	152	Mean injections: 5.0 Mean visual acuity change: +9.1 letters At 36 months: Mean injections: 5.2 Mean visual acuity change: +8.3 letters
Liew et al.[34]	Retrospective review of medical records	nAMD	Ranibizumab	PRN, following loading doses	–	5811	At 12 months: Median injections: 6.0 Mean visual acuity change: +2.5 letters
Lotery et al.[35]	Retrospective, comparative, non-randomised cohort study	nAMD	Ranibizumab	Regimen not defined	–	3350	At 12 months: Median injections: 6.7 Mean visual acuity change: -0.30 letters
			Aflibercept	Regimen not defined	–	4300	At 12 months: Median injections: 7.0 Mean visual acuity change: -0.19 letters
Marques et al.[36]	Retrospective review of medical records	nAMD	Ranibizumab	PRN	77	84	At 36 months: Mean injections: 8.6 Mean visual acuity change: +0.19 letters
Muftuoglu et al.[37]	Prospective interventional study	Patients with nAMD who failed treatment with ranibizumab or bevacizumab or aflibercept every 8 weeks	Aflibercept	PRN	39	43	At 12 months: Mean injections: 8 Mean visual acuity change: +0.02 logMAR
Muniraju et al.[38]	Retrospective review of medical records	nAMD	Ranibizumab	PRN, following loading doses	156	174	At 12 months: Mean injections: 4.8

							<p>Mean visual acuity change: +3.0 letters (p<0.05)</p> <p>At 24 months: Mean injections: 2.9 Mean visual acuity change: +2.2 letters</p> <p>At 36 months: Mean injections: 2.4 Mean visual acuity change: +0.9 letters</p>
Ozkaya et al.[39]	Retrospective review of medical records	nAMD	Ranibizumab	PRN, following loading doses	37	44	<p>At 12 months: Mean injections: 3.9 Mean visual acuity change: -0.02 logMAR</p> <p>At 24 months: Mean injections: 2.6 Mean visual acuity change: +0.09 logMAR</p> <p>At 36 months: Mean injections: 2.1 Mean visual acuity change: +0.23 logMAR</p> <p>At 48 months: Mean injections: 2.0 Mean visual acuity change: +0.27 logMAR</p> <p>At 60 months: Mean injections: 2.3 Mean visual acuity change: +0.29 logMAR</p>

Parvin et al.[40]	Prospective non-comparative case series	nAMD	Aflibercept	Observe-and-plan, following loading doses	102	112	At 12 months: Mean injections: 8.7 Mean visual acuity change: +8.0 letters (p<0.001) At 24 months: Mean injections: 6.3 Mean visual acuity change: +6.2 letters (p<0.001)
Peden et al.[41]	Retrospective review of medical records	Exudative AMD	Any anti-VEGF therapy	Continuous fixed dosing every 4–8 weeks (mean 10.5 injections/year)	109	–	At 60 months: Mean visual acuity change: +14.0 letters (p<0.001)
					75	–	At 72 months: Mean visual acuity change: +12.2 letters (p<0.001)
					44	–	At 84 months: Mean visual acuity change: +12.1 letters (p<0.001)
Rasmussen et al.[42]	Retrospective review of medical records	nAMD	Ranibizumab	PRN, following loading doses	559	616	At 12 months: Mean injections: 6.9 Mean visual acuity change: +0.08 Snellen (p<0.001)
			Aflibercept		468	527	At 12 months: Mean injections: 5.9 Mean visual acuity change: +0.08 Snellen (p<0.001)

Rasmussen et al.[43]	Retrospective review of medical records	nAMD	Ranibizumab	PRN, following loading doses	192	192	At 12 months: Mean injections: 5.2 Mean visual acuity change: +0.05 Snellen ($p<0.001$) At 24 months: Mean injections: 5.0 At 36 months: Mean injections: 5.5 At 48 months: Mean injections: 6.4 Mean visual acuity change: +0.02 Snellen
Ricci et al.[44]	Retrospective review of medical records	nAMD switched from ranibizumab	Aflibercept	PRN, following loading doses	–	36	At 12 months: Mean injections: 3.5 Mean visual acuity change: -3 letters
				Fixed dosing bimonthly, following loading doses	–	36	At 12 months: Mean injections: 7.0 Mean visual acuity change: +3 letters ($p<0.01$; $p=0.01$ versus PRN)
Saleh et al.[45]	Prospective cohort study	Exudative AMD	Aflibercept	PRN, following loading doses	60	66	At 24 months: Mean injections: 5/year Mean visual acuity change: +1.0 letters
LUEUR[5]	Prospective cohort study	nAMD (total study population)	Ranibizumab	PRN, following loading doses	517	592	At 12 months: Mean injections: 2.9 Mean visual acuity change: +0.1 letters At 24 months:

							Mean injections: 2.2 Mean visual acuity change: -2.0 letters
		nAMD (treatment-naïve population)		PRN, following loading doses	–	90	At 12 months: Mean injections: 3.4 Mean visual acuity change: +2.1 letters At 24 months: Mean injections: 1.6 Mean visual acuity change: -0.2 letters
Westborg et al.[46]	Retrospective registry study	nAMD	Any anti-VEGF therapy	Regimen not defined	–	–	At 84 months: Mean injections: 3/year Mean visual acuity change: -1.0 letters
PACORES[47, 48]	Retrospective review of medical records	nAMD	Bevacizumab	PRN	63	63	At 12 months: Mean injections: 3.5 Mean visual acuity change: -0.2 logMAR (p<0.001)
					247	292	At 60 months: Mean injections: 10.9 over 5 years Mean visual acuity change: +0.2 logMAR (p<0.001)
Axer-Siegel et al.[49]	Retrospective review of medical records	Exudative AMD	Bevacizumab	PRN, following loading doses	130	150	At 20.2 months: Mean injections: 11.3 Mean visual acuity change: No change
Bashshur et al.[50]	Prospective, open-label, non-randomised clinical study	CNV resulting from nAMD	Bevacizumab	PRN, following loading doses [51]	51	51	At 24 months: Mean injections in Year 2: 1.5 Mean visual acuity change: +8.6 letters (p=0.001)
Bellerive et al.[52]		nAMD	Bevacizumab	PRN, following loading doses	–	142	At 12 months: Mean injections: 4.8

	Retrospective review of medical records		Ranibizumab	PRN, following loading doses	–	50	Mean visual acuity change: -0.03 logMAR At 12 months: Mean injections: 4.9 Mean visual acuity change: -0.06 logMAR
Beykin et al.[53]	Retrospective review of medical records	CNV resulting from nAMD	Bevacizumab (with second line ranibizumab therapy for patients experiencing treatment failure)	PRN, following loading doses	128	142	Mean injections per year: 5.4 At 12 months: Mean visual acuity change: +8.8 letters (p<0.05) At 24 months: Mean visual acuity change: +7.8 letters (p<0.05) At 36 months: Mean visual acuity change: -1.2 letters At ≥48 months (mean 60 months): Mean visual acuity change: -1.7 letters
Calvo et al.[54]	Retrospective review of medical records	nAMD	Ranibizumab	PRN, following loading doses	51	51	Mean injections over 3 years: 6.98 At 12 months: Mean visual acuity change: -0.17 logMAR
Chang et al.[55]	Retrospective review of medical records	Exudative AMD in eyes with initial visual acuity of 20/25 or better	Ranibizumab or bevacizumab	PRN, following loading doses	18	18	At 12 months: Mean injections: 4.4 Mean visual acuity change: +0.08 logMAR (p=0.009)
LUMIERE[56]	Retrospective review of medical records	nAMD	Ranibizumab	PRN, following loading doses	551	–	At 12 months: Mean injections: 5.1 Mean visual acuity change: +3.2 letters
De Bats et al.[57]	Retrospective case-control study	nAMD	Bevacizumab	PRN, following loading doses	30	–	At 12 months: Mean injections: 4.8 Mean visual acuity change: -0.23 logMAR

			Ranibizumab		28	–	At 12 months: Mean injections: 5.8 Mean visual acuity change: -0.01 logMAR
Eleftheriadou et al.[58]	Retrospective case series	nAMD (treatment-naïve)	Aflibercept	Fixed dosing in Year 1, following loading doses, then treat-and-extend	139	148	At 12 months: Mean injections: 7.2 Mean visual acuity change: +5.9 letters At 24 months: Mean injections: 12 Mean visual acuity change: +6.4 letters At 36 months: Mean injections: 15.9 Mean visual acuity change: +6.6 letters
Gupta et al.[59]	Retrospective review of medical records	nAMD and CND (treatment naïve)	Ranibizumab	PRN, following loading doses	47	47	At 12 months: Mean injections: 6.0 Mean visual acuity change: +4.4 letters
				PRN, following one injection at baseline	31	31	At 12 months: Mean injections: 4.5 Mean visual acuity change: +4.0 letters
Hjelmqvist et al.[60]	Open-label, prospective and retrospective observational study	Wet AMD	Ranibizumab	PRN, following loading doses	370	-	At 12 months: Mean injections: 7.7 Mean visual acuity change: +1.0 letter
HELIX[61]	Retrospective review of medical records	nAMD	Ranibizumab	PRN, following loading doses	69	88	At 12 months: Mean injections: 5.2 Mean visual acuity change: +3.7 letters At 24 months: Mean injections in Year 2: 3.2 Mean visual acuity change: +2.4 letters

							<p>At 36 months: Mean injections in Year 3: 3.1 Mean visual acuity change: +1.1 letters</p> <p>At 48 months: Mean injections in Year 4: 3.2 Mean visual acuity change: +2.6 letters</p> <p>At 60 months: Mean injections in Year 5: 3.1 Mean visual acuity change: -1.1 letters</p> <p>At 72 months: Mean injections in Year 6: 2.5 Mean visual acuity change: -1.6 letters</p>
Krüger et al.[62]	Retrospective review of medical records	nAMD	Ranibizumab	PRN (according to Danish Guidelines), following loading doses	855	855	<p>At 48 months (mean follow-up): Mean injections: 8.7 over 48 months Mean visual acuity change: -2.7 letters</p>
Lalwani et al.[63]	Open-label prospective study	nAMD	Ranibizumab	PRN, following loading doses	40	-	<p>At 24 months: Mean injections: 9.9 over 24 months Mean visual acuity change: +11.1 letters (p<0.001)</p>
Mantel et al.[64]	Open-label prospective study	nAMD and CNV (treatment-naïve)	Ranibizumab	Observe-and-plan, following loading doses	104	115	<p>At 12 months: Mean injections: 7.8 injections Mean visual acuity change: +8.7 letters</p>
Mekjavic et al.[65]	Retrospective review of medical records	nAMD and CNV	Ranibizumab	PRN, following loading doses	147	149	<p>At 12 months: Mean injections: 5.1 injections Mean visual acuity change: +6 letters (p<0.0001)</p>

Messenger et al.[66]	Retrospective review of medical records	nAMD previously treated with bevacizumab or ranibizumab for at least 12 months	Aflibercept	PRN, following loading dose	109	109	At 12 months: Mean injections: 7.2 injections Mean visual acuity change: No change
Muether et al.[67]	Open-label prospective study	nAMD	Ranibizumab	PRN, following loading dose	89	–	At 12 months: Mean injections: 6.9 injections Mean visual acuity change: -0.66 letters
Ohnaka et al.[68]	Retrospective review of medical records	nAMD	Aflibercept	Modified treat-and-extend	36	36	At 12 months: Mean injections: 4.5 injections Mean visual acuity change: -0.08 logMAR (p<0.01)
HELIOS (Belgium)[69]	Prospective, observational, open-label study	Wet AMD	Ranibizumab	PRN	267	309	At 12 months: Mean injections: 5.0 Mean visual acuity change: +1.6 letters At 24 months: Mean injections: 7.6 Mean visual acuity change: -2.4 letters
HELIOS (The Netherlands)[70]					243	–	At 12 months: Mean injections: 5.5 Mean visual acuity change: +4.4 letters At 24 months: Mean injections: 7.8 Mean visual acuity change: +1.0 letters
Suzuki et al.[71]	Retrospective review of medical records	nAMD and CNV	Bevacizumab	PRN	47		At 12 months: Mean injections: 3.4

							Mean visual acuity change: +0.04 logMAR
Warwick et al.[72]	Retrospective review of medical records	nAMD (Treatment-naïve)	Aflibercept	3 monthly loading doses followed by injection every 2 months	51	58	At 12 months: Mean injections: 7.1 Mean visual acuity change: +4.7 letters (p<0.001)
		nAMD (Treatment-experienced)			88	107	At 12 months: Mean injections: 7.5 Mean visual acuity change: +3.3 letters (p<0.01)
RAINBOW[73]	Observational, retrospective and prospective	Wet AMD	Aflibercept	Fixed (bimonthly)	012		At 12 months: Mean injections: 7.2 Mean visual acuity change: +7.1 letters (p<0.001; p<0.001 versus PRN without loading dose)
				PRN (with loading dose)	266		At 12 months: Mean injections: 6.1 Mean visual acuity change: +5.6 letters (p<0.001; p=0.003 versus PRN without loading dose)
				PRN (without loading dose)	60		At 12 months: Mean injections: 5.2 Mean visual acuity change: +5.0 letters (p<0.001)
Lovestam Adrian et al.[74]	Observational, retrospective	nAMD	Aflibercept	PRN, following loading dose	2312	12 months: 2478 24 months: 831	At 12 months: Mean visual acuity change from baseline overall: +3.2 letters At 24 months:

							Mean visual acuity change from baseline overall: +3.8
Barakat et al.[75]	Observational, retrospective	nAMD	Aflibercept	Loading phase, PRN (Weeks 12 to 32), then treat-and-extend	38	48	At 12 months: Mean injections: 6 Mean visual acuity change: +6.0 letters At 24 months: Mean injections: 3.2 Mean visual acuity change: +5.2 letters
Ono et al.[76]	Interventional, case series, prospective	Exudative AMD	Aflibercept	3 monthly loading doses followed by injection every 2 months	48	48	At 12 months: Total injections: 7 Mean overall visual acuity change: LogMAR -0.13 (p=0.008; vs baseline)
Chatziralli et al.[77]	Observational, retrospective	nAMD	Aflibercept	Bimonthly dosing in Year 1, following loading dose	-	2506 (<90 years of age)	At 12 months: Mean visual acuity: +4.6 letters At 24 months: Mean visual acuity: +2.1
Brand et al.[78]	Observational, retrospective	nAMD	Ranibizumab monotherapy	3 month loading doses then PRN	50	-	At 12 months: Mean injections: 5.6 Mean visual acuity change: -0.3 letters
			Ranibizumab + stereotactic radiotherapy	Stereotactic therapy during 3-month loading dose then PRN	132	-	At 12 months: Mean injections: 4.5 Mean visual acuity change: +3.0 letters

*All visual acuity changes are relative to baseline. Mean injections are the number of injections in the preceding 12-month period.
p-values are versus baseline unless otherwise stated.

AMD, age-related macular degeneration; CNV, choroidal neovascularisation; logMAR, log of the Minimum Angle of Resolution; nAMD, neovascular AMD; PRN, pro re nata; VEGF, vascular endothelial growth factor.

Supplementary Table 2. Summary of Outcomes in Real-World Studies of Anti-VEGF Treatment (Including Treat-and-Extend Regimens) in Patients With nAMD*

Study	Study design	Patient population	Anti-VEGF therapy	Dosing regimen	Patients, N	Eyes, n	Outcomes during the previous 12 months
Oubraham et al.[79]	Retrospective consecutive case series	Exudative AMD	Ranibizumab	PRN, following loading doses	52	–	At 12 months: Mean injections: 5.2 Mean visual acuity change: +2.3 letters
				Treat-and-extend, following loading doses	38	–	At 12 months: Mean injections: 7.8 Mean visual acuity change: +10.8 letters (p<0.05)
Hatz and Prünke[80]	Retrospective, consecutive, comparative case series of treatment-naïve patients	nAMD	Ranibizumab	PRN (mean duration: 17 months), following loading doses	134	146	Mean BCVA (\pm SD) increased from 0.39 \pm 0.23 to 0.55 \pm 0.22 (p<0.001) during the PRN loading regimen, then declined to 0.49 \pm 0.22 (p<0.001)
				Treat-and-extend			BCVA improved from 0.49 \pm 0.22 to 0.55 \pm 0.23 and 0.56 \pm 0.24 by 6 and 12 months, respectively (p<0.001)
Fight Retinal Blindness! Study[81]	Observational registry	nAMD	Predominantly ranibizumab	Treat-and-extend, following loading doses until CNV activity had resolved	1101	1198	At 24 months: Mean injections: 13.0 (7.5 in Year 1 and 5.5 in Year 2) Mean visual acuity change: +5.3 letters

Fight Retinal Blindness! Study[82]	Observational registry	nAMD	Aflibercept	Treat-and-extend, following loading doses	123	136	At 24 months: Mean injections: 13.6 (7.8 in Year 1 and 5.7 in Year 2) Mean visual acuity change: +6.0 letters
Abedi et al.[83]	Prospective cohort study	nAMD	Ranibizumab or bevacizumab	Treat-and-extend, following loading doses	120	–	At 12 months: Mean injections: 8.6 Mean visual acuity change: +9.5 letters At 24 months: Mean injections: 5.6 Mean visual acuity change: +8.0 letters
Castro-Navarro et al.[84]	Retrospective review of medical records	Exudative nAMD	Aflibercept	Treat-and-extend, following loading doses	30	30	At 12 months: Mean injections: 7.4–8.7 Mean visual acuity change: -0.23 logMAR
Castro-Navarro et al.[85]	Retrospective review of medical records	Exudative nAMD with secondary CNV and retinal angiomatous proliferation	Aflibercept	Treat-and-extend, following loading doses	–	37	At 12 months: Mean injections: 7.3–8.0 Mean visual acuity change: -0.20 logMAR
Chen et al.[86]	Retrospective review of medical records	nAMD	Ranibizumab	Treat-and-extend, following loading doses	79	–	At 12 months: Mean injections: 8.6 Mean visual acuity change: +7.9 letters
Garweg et al.[87]	Retrospective review of medical records	nAMD	Ranibizumab	PRN, following loading doses	61	68	At 12 months: Mean injections: 5.5 Mean visual acuity change: +0.66 letters At 24 months:

							Mean injections in Year 2: 1.9 Mean visual acuity change: -3.67
				Treat-and-extend, following loading doses	35	39	At 12 months: Mean injections: 6.8 Mean visual acuity change: +2.65 letters At 24 months: Mean injections in Year 2: 3.8 Mean visual acuity change: +1.43 letters
Giannakaki-Zimmerman et al.[88]	Retrospective observational study	AMD and CNV switch from PRN to treat-and-extend	Aflibercept	PRN	32	-	12 months prior to crossover: Mean injections: 6.0 Mean visual acuity change: -0.0 letters
				Treat-and-extend			At 12 months: Mean injections: 7.5 Mean visual acuity change: -0.65 letters
Gupta et al.[89]	Retrospective review of medical records	nAMD	Ranibizumab	Treat-and-extend, following loading doses	92	92	At 12 months: Mean injections: 8.4 Mean Snellen visual acuity: 20/77 (from 20/135 at baseline;p<0.001) At 24 months: Mean injections: 7.5 Mean Snellen visual acuity: 20/83 (p=0.002)
Hatz and Prünfte[90]	Retrospective study consisting of two consecutive, comparative	nAMD	Ranibizumab	PRN, following loading doses	70	70	At 12 months: Mean injections: 6.0 Mean visual acuity change: +0.07 letters
				Treat-and-extend, following loading doses	70	70	At 12 months: Mean injections: 8.6 Mean visual acuity change: +0.18 letters

	case series						
Ito et al.[91]	Retrospective review of medical records	nAMD	Aflibercept	Treat-and-extend, following loading doses	–	61	At 24 months: Mean injections: 13.6 Mean visual acuity change: -0.13 logMAR
Makjevic and Benda[92]	Retrospective review of medical records	nAMD	Ranibizumab or bevacizumab	Treat-and-extend, following loading doses	101	101	At 12 months: Mean injections: 8.0 Mean visual acuity change: +6.8 letters
							At 24 months: Mean injections: 6.3 Mean visual acuity change: +5.9 letters
							At 36 months: Mean injections: 5.9 Mean visual acuity change: +4.0 letters
							At 48 months: Mean injections: 5.4 Mean visual acuity change: +0.9 letters
							At 60 months: Mean injections: 4.0 Mean visual acuity change: -1.9 letters
Jørstad et al.[93]	Prospective observational study	Exudative AMD and persistent macular fluid despite monthly treatment with ranibizumab or bevacizumab	Aflibercept	Treat-and-extend, following loading doses until no signs of active AMD	47	50	At 12 months: Mean injections: 9.2 Mean visual acuity change: -0.01 logMAR At 24 months: Mean injections: 8.0 Mean visual acuity change: +0.07 logMAR (p=0.005)

Rahimy et al.[94]	Retrospective observational case series	nAMD with initial vision better than 20/40	Ranibizumab or bevacizumab	Treat-and-extend, following monthly dosing until no signs of CNV were detectable	40	42	At 12 months: Mean injections: 7.8 Mean visual acuity change: +0.031 logMAR At 24 months: Mean injections: 6.1 Mean visual acuity change: +0.041 logMAR
Rayess et al.[95]	Retrospective, consecutive case series	nAMD	Ranibizumab or bevacizumab	Treat-and-extend, following loading doses	189	212	At 12 months: Mean injections: 7.6 Mean visual acuity change: +11.6 letters At 24 months: Mean injections: 5.7 Mean visual acuity change: +10.7 letters At 36 months: Mean injections: 5.8 Mean visual acuity change: +13.6 letters
Vardarinos et al.[96]	Retrospective review of medical records	nAMD	Ranibizumab	Treat-and-extend, following loading doses	60		At 12 months: Mean injections: 7.8 Mean visual acuity change: +8.3 letters At 24 months: Mean injections: 12.1 Mean visual acuity change: +5.2 letters
Westborg et al.[46]	Retrospective registry study	nAMD	Any anti-VEGF therapy	Regimen not defined	–	–	At 84 months: Mean injections: 3/year Mean visual acuity change: -1.0 letters

Yamamoto et al.[97]	Retrospective review of medical records	nAMD	Aflibercept	Treat-and-extend, following loading doses	67	67	At 12 months: Mean injections: 8.3 Mean visual acuity change: -0.15 logMAR (p<0.001)
Engelbert et al.[98]	Retrospective case-control study	Type 1 AMD	Bevacizumab and/or ranibizumab	Modified treat-and-extend, following loading doses	16	18	At 24 months: Mean injections: 12 Mean visual acuity change: -0.01 logMAR At 36 months: Mean injections: 20 Mean visual acuity change: -0.01 logMAR
Garweg et al.[99]	Retrospective comparative case series	Exudative AMD	Aflibercept	Treat-and-extend, following loading doses	99	106	At 12 months: Mean injections: 7.5 Mean visual acuity change: Stable At 24 months: Mean injections: 11.8 Mean visual acuity change: Stable
			Ranibizumab		43	47	At 12 months: Mean injections: 6.9 Mean visual acuity change: Stable At 24 months: Mean injections: 10.3 Mean visual acuity change: Stable
Rush et al.[100]	Retrospective review of medical records	nAMD	Bevacizumab	Treat-and-extend	–	230	At 12 months: Mean injections: 9.2 injections Mean visual acuity change: -0.09 logMAR (p<0.001)

Sakamoto et al.[101]	Prospective, interventional, open-label study	Exudative AMD	Aflibercept	Fixed (bimonthly), following loading dose Treat-and-extend (in Year 2)	47	47	At 12 months: Mean injections: 6.7 Mean visual acuity change: -0.04 logMAR (p<0.05) At 24 months: Mean injections: 4.8 Mean visual acuity change: -0.03 logMAR
Shienbaum et al.[102]	Retrospective review of medical records	nAMD	Bevacizumab	Treat-and-extend	73	74	At 12 months: Mean injections: 7.9 Mean Snellen visual acuity: 20/109 (20/230 at baseline; p<0.05)

AMD, age-related macular degeneration; BCVA, best corrected visual acuity; CNV, choroidal neovascularisation; logMAR, log of the Minimum Angle of Resolution; nAMD, neovascular AMD; PRN, pro re nata; VEGF, vascular endothelial growth factor.

*All visual acuity changes are relative to baseline.

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