| **Study, Year** | **Study DesignPurpose of Study** | **Patients** | **InterventionDuration of Followup** | **Results** |
| --- | --- | --- | --- | --- |
| **AMD (Dry)** |
| AREDS Research Group, 200197 and Johnson 2007135*AREDS Report No. 8* | To evaluate the effect of high-dose vitamins C and E, beta carotene and zinc supplements on AMD progression and visual acuity PCT | n=3640Median age 56 years56% female 96% white, 3% black, <1% other Mean BCVA at baseline better than 20/32 for all participants | Antioxidant multivitamin: 500 mg vitamin C + 400 IU vitamin E + 5 mg beta carotene/dayZinc 80 mg/dayAntioxidant multivitamin + zincPlacebo 7 years | Progression to advanced AMD: Antioxidants vs. placebo: OR 0.77 (0.56 to 1.05; p=0.03) Zinc vs placebo: OR 0.71 (0.51 to 0.98; p=0.005) Antioxidants + zinc vs placebo: adjusted OR 0.66 (0.47 to 0.93)Loss of ≥15 letters of VA: Antioxidants vs. placebo: OR 0.87 (0.67 to 1.15; p=0.20)Zinc vs. placebo: OR 0.82 (0.63 to 1.08; p=0.07) Antioxidants + zinc vs. placebo: adjusted OR 0.75 (0.55 to 1.02) ORs adjusted for age, sex, race, baseline AMD category and smoking statusIncreased risk for hospitalization due to genitourinary causes versus non-use (RR 1.47, 95% CI 1.19 to 1.80) |
| **AMD (Wet)** |
| *VEGF inhibitors* |
| Gragoudas, 2004122(VISION; 2 trials) | To test the short-term safety and effectiveness of pegaptanib  | n=1208Mean age NRAge range 50-64 years: 6%; 65-74 years: 32%; 75-84 years: 52%; ≥85 years: 10%58% female96% white; 4% otherMean visual acuity, study eye: 51.8 letters (SD 12.8) | 0.3, 1.0, or 3.0 mg pegaptanib every 6 weeks up to 48 weeks (9 treatments) vs. sham injection | Pegaptanib (all doses) vs sham:Visual acuity, gain ≥15 letters: 5.7% (51/890) vs. 2.0% (6/296); RR 2.83 (95% CI 1.23 to 6.52)Visual acuity, loss <15 letters: 68.8% (612/890) vs. 55.4% (164/296)Visual acuity, 20/200 or better: 58.7% (522/890) vs. 44.3% (131/296)Withdrawals due to adverse events: 1% (9/890) vs. 1% (3/296); RR 1.00 (95% CI 0.27 to 3.66)Endophthalmitis: 1.3% (12/890) vs. 0% (0/296); RR 8.33 (95% CI 0.50 to 140)Traumatic lens injury: 0.6% (5/890) vs. 0% (0/296); RR 3.67 (95% CI 0.20 to 66)Retinal detachment 0.6% (5/890) vs. 0% (0/296); RR 3.67 (95% CI 0.20 to 66)Severe (>30 letters) vision loss: 0.1% (1/890) vs. 0% (0/296); RR 1.00 (95% CI 0.04 to 24) |
| Regillo, 2008123*PIER study year 1* | To evaluate the effectiveness and safety of ranibizumab for treatment of minimally classic or occult with no classic choroidal neovasculatization associated with AMD. Prospective, double-blind RCT. | n=184Mean age ~78 years60% femaleNeovascular AMD | 0.3 or 0.5 mg ranibizumab vs sham injection; dosing 1x/month for 3 months followed by 1x every 3 months12 months | Ranibizumab (all doses) vs. sham:Visual acuity, gain ≥15 letters: 12.4% (15/121) vs. 9.5% (6/63); RR 1.30 (95% CI 0.53 to 3.19)Visual acuity, loss <15 letters: 86.8% (105/121) vs. 49.2% (31/63)Visual acuity, 20/200 or better: 73.6% (89/121) vs. 44.4% (28/63)Mortality and CV events: No deaths, MI or CVA in either groupWithdrawals: 0.8% (1/121) vs. 0% (0/63); RR 1.57 (95% CI 0.07 to 38)Ocular hemorrhage: 1.6% (2/121) vs. 3.2% (2/63); RR 0.52 (95% CI 0.08 to 3.61)Macular edema: 0.8% (1/121) vs. 3.2% (2/63); RR 0.26 (95% CI 0.02 to 2.82) |
| Rosenfeld et al, 2006121*MARINA Trial* | To evaluate the effectiveness and safety of ranibizumab for treatment of minimally classic or occult with no classic choroidal neovasculatization associated with AMD. Double-blind PCT. | n=716Mean age 77 years (SD 8)65% femaleAMD | 0.3 or 0.5 mg ranibizumab 1x/month (range 23-37 days) for 2 years vs. sham injection2 years | *Ranibizumab (all doses) vs. sham:* Visual acuity, gain ≥15 letters: 29.2% (140/478) vs. 5.0% (12/238); RR 5.81 (95% CI 3.29 to 10.26)Visual acuity, loss <15 letters: 94.6% (452/478) vs. 62.2% (148/238)Visual acuity, 20/200 or better: 88.1% (421/478) vs. 57.1% (136/238)All-cause mortality: 2.3% (11/478) vs. 2.5% (6/238); RR 0.91, 95% CI 0.34 to 2.44Vascular mortality: 1.3% (6/478) vs. 1.7% (4/236); RR 0.74, 95% CI 0.21 to 2.60MI: 1.9% (9/478) vs. 1.7% (4/238); RR 1.12, 95% CI 0.35 to 3.60CVA: 1.9% (9/478) vs. 0.8% (2/238); RR 2.24, 95% CI 0.49 to 10Withdrawals: 13.2% (63/478) vs. 28.6% (68/238); RR 0.46 (95% CI 0.34 to 0.63)Withdrawals due to adverse events: 4.8% (23/478) vs. 5.5% (13/238); RR 0.88 (95% CI 0.45 to 1.70)Serious, nonocular hemorrhage: 1.7% (8/478) vs. 0.8% (2/236); RR 1.97 (95% CI 0.42 to 9.23)Endophthalmitis: 5/478 vs 0/238; RR 5.49 (95% CI 0.30 to 99)Uveitis: 1.3% (6/478) vs. 0% (0/238); RR 6.49 (95% CI 0.37 to 115)Retinal detachment: 0% (0/478) vs. 0.4% (1/238); RR 0.17 (95% CI 0.01 to 4.07)*Ranizumab 0.3 mg vs. 0.5 mg vs. sham*Vision related quality of life (NEI-VFQ), mean change from baseline: 1-year followup, composite score (95% CI): 5.2 (3.5 to 6.9) vs. 5.6 (3.9 to 7.4) vs. −2.8 (−4.6 to −1.1); ranibizumab vs. sham p<0.01General health score: −2.6 (−5.0 to 0.2) vs. −5.1 (−7.6 to −2.6) vs. −6.9 (−9.6 to −4.3); ranibizumab vs. sham p=NSMental health score: 12.0 (9.4 to 14.6) vs. 13.1 (10.0 to 16.2) 3.3 (0.5 to 6.1); ranibizumab vs. sham p<0.01Social functioning score: 3.1 (0.3 to 5.9) vs. 3.8 (1.2 to 6.3) vs. −5.1 (−7.7 to −2.5); ranibizumab vs. sham p<0.01Driving score: −2.1 (−5.9 to 1.7) vs. −0.4 (− 3.8 to 3.0) vs. −12.4 (−16.0 to −8.7); ranibizumab vs. sham p<0.012-year followup, composite score: 4.8 (2.9 to 6.8) vs. 4.5 (2.5 to 6.5) vs. −6.5 (−8.4 to −4.6); ranibizumab vs. sham p<0.01General health score: −5.7 (−8.6 to −2.8) vs. −6.7 (−9.6 to −3.8) vs −9.0 (−12.0 to −6.2); ranibizumab vs. sham p=NSMental health score: 11.9 (8.9 to 14.9) v.s 12.6 (9.4 to 15.8) vs. −0.7 (−3.7 to 2.4); ranibizumab vs. sham p<0.01Social functioning score: 1.9 (−1.1 to 4.9) vs. 1.4 (−1.6 to 4.3) vs. −9.5 (−12.0 to −6.5); ranibizumab vs. sham p<0.01Driving score: −1.6 (−5.7 to 2.5) vs. −2.7 (−6.3 to 0.9) vs. −17.1 (−21.0 to −13.0); ranibizumab vs. sham p<0.01 |

**Abbreviations:** AMD = age-related macular degeneration; BCVA = best-corrected visual acuity; CI = confidence interval; NR = not reported; NS = not significant; OR = odds ratio; PCT = placebo controlled trial; RCT = randomized controlled trial; RR = risk ratio; SD = standard deviation; VEGF = vascular endothelial growth factor.