**Online Supplemental Table S1.** Patient baseline characteristics in studies including at least 10 eyes treated with brolucizumab (26 studies).

| **Publication *(study)*** | **Country** | **Study dates** | **Inclusion criteria (diagnostic criteria)** | **Exclusion criteria** | **Naïve/ switch patients (eyes) (n)** | **Age (years)**a | **M/F (%)** | **Baseline clinical characteristics** | **Baseline fluid status** | **History of ocular AEs** | **Pretreated for AEs** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Abdin 2021 (Abdin et al. 2021) | Germany | – | Refractory macular oedema due to nAMD | – | Switch: 19 (21) | 76 (SD: 8) | – | – | – | – | – |
| Aziz 2021 (Aziz et al. 2021) (*REBEL)* | USA | – | nAMD | – | Naïve and switch: – (21/263) | 81.2 (SEM: 0.5; range: 51–99) | 41/59 | – | Fluid localization:b IRF: 35% SRF: 50% PED: 60% | – | – |
| Baumal 2020 (Baumal et al. 2020) | USA | Dec 2019 to Mar 2020 | nAMD with retinal vasculitis after brolucizumab | – | Switch: 12 (15) | 77.6 (SD: 7.2; range: 65–85) | 0/12 | History of HTN: 50%; HLD: 33%; breast cancer: 25%; arthritis: 25% | – | – | – |
| Bilgic 2021 (Bilgic et al. 2021a) (*REBA)* | Germany, India | – | MNV. Switch patients: prior treatment via treat-and-extend protocol | PCV, RAP | Naïve: 23 (25) | 69.2 (SD: 4.4) | 39/61 | MNV subtype: Type 1: 56% Type 2: 28% Mixed: 16%  MNV localization: SF: 60% JF: 16% EF: 4% IP: 20% | Fluid localization:b IRF: 92% SRF: 48% PED: 40% None: 8% | – | – |
|  |  |  | Switch: 55 (80) | 74.3 (SD: 5.8) | 47/53 | MNV subtype: Type 1: 70%; Type 2: 18 Mixed: 12%  MNV localization: SF: 70% JF: 15% EF: 3% IP: 12%  IOP-lowering medication: 49% of patients | Fluid localization:b IRF: 71% SRF: 39% PED: 30% None: 0% | – | – |
| Sudhalkar 2021 (Sudhalkar et al. 2021) *(REBA PCV)* |  |  | PCV | – | Naïve: 17 (17) | – | – | – | – | – | – |
| Bilgic 2021 (Bilgic et al. 2021b) *(PROBE)* | India | – | MNV (type 1: NVM under RPE layer; type 2: NVM above RPE) | PCV or RAP | Naïve: 27 (27) | 65.1 (SD: 3.4) | 44/56 | MNV subtype: Type 1: 59% Type 2: 30% Mixed: 11% | Fluid localization:b IRF: 67% SRF: 30% PED: 59% | – | – |
| Book 2022 [Epub 2021] (Book et al. 2022) | Germany | – | Refractory nAMD (persistent IRF, SRF and/or sub-RPE fluid) | BCVA >1.3 LogMAR | Switch: 20 (21) | 75.8 (SD: 7.8) | – | MNV subtype: Aneurysmal Type 1: 29% Type 1: 57% Type 2: 10% Type 3: 5% | Fluid localization:b IRF: 52% SRF: 81% PED: 67% | – | – |
| Bulirsch 2021 (Bulirsch et al. 2021) *(SHIFT)* | Germany | Mar 2020 to Oct 2020 | Exudative AMD (persistent fluid despite anti-VEGF treatment) | – | Switch: 57 (63) | 79.5 (SD: 6.7; range: 58–94) | 47/53 | – | Fluid localization:b IRF: 44% SRF: 69% None: 3% | – | – |
| Chakraborty 2021 (Chakraborty et al. 2021) *(BRAILLE)* | India | Oct 2020 to Feb 2021 | nAMD (clinical findings, fundus fluorescein angiography [areas of stippled hyperfluorescence with progressive leakage or late leakage of undetermined source or presence of early well-defined hyperfluorescence network with progressive leakage in late phase], indocyanine green angiography [to rule out PCV]) | Co-existing vitreoretinal pathology other than nAMD, CNV due to any other aetiology, significant media opacities precluding observation of ocular fundus, history of retinal surgery, coexisting diabetic retinopathy, history of systemic vasculitis or autoimmune disease, history of anterior or posterior segment inflammation | Naïve and switch: 20/74 (20/74) | 67.6 (SD: 10.3) | 68/32 | – | Fluid localization:b IRF: 89% SRF: 76% PED: 22% | – | Topical moxifloxacin 0.5% administered for 1 week after brolucizumab IVI |
| Cristian 2021 (Cristian et al. 2021) | UK | Apr 2020 to NR | nAMD, prior anti-VEGF treatment via treat-and-extend regimen | – | Switch: 40 (–) | 81c (range: 66–93) | 48/52 | – | Fluid localization:b SRF: 67% PED: 92% | – | – |
| Eandi 2021 (Eandi & Montesel 2021), Montesel 2021 (Montesel et al. 2021) | Switzerland | Mar 2020 to Dec 2020 | nAMD (any type of choroidal neovascularization involving the foveal region) | Macular diseases other than nAMD, history of IOI | Naïve and switch: 4/15 (4/15) | 78.0 (SD: 8.4; range: 63–92) | 26/74 | Geographic atrophy and/or retinal fibrosis affecting the central foveal area: 21%; clinically relevant  cataract: 16%;  amblyopic eye: 5%; epiretinal membrane: 5%; pseudophakic eye: 37%; received  verteporfin photodynamic therapy for nAMD: 5% | Fluid localization:b IRF: 63% SRF: 89% PED: 84% | No IOI (exclusion criterion) | – |
| Enríquez 2021 (Enríquez et al. 2021) | USA | Oct 2019 to Apr 2020 | nAMD as primary indication for treatment, ≥1 follow-up visit | – | Naïve and switch: NR/NR (4/166)d | 80.0 (SD: 8.0) | 43/57 | Comorbid DM: 19%, HTN: 74%, HLD: 49%; prior surgery in study eye: 73% (cataract surgery: 71%) | Fluid localization:b IRF: 21% SRF: 55% None: 34% | Prior IOI: 4.1% | – |
| Fossataro 2021 (Fossataro et al. 2021) | Italy | – | nAMD with non-responder PED to previous anti-VEGF treatment | – | Switch: 10 (10) | 73 (8) | – | – | – | – | – |
| Fukuda 2021 (Fukuda et al. 2021) | Japan | Sep 2020 to Feb 2021 | PCV (polypoidal lesion(s), regardless of presence of branching vascular networks) | History of uveitis, other maculopathy without evidence of PCV | Naïve: 14 (14) | 74.7 (SD: 7.3; range: 69–81) | 71/29 | Mean number of polyps: 2.3; mean maximum diameter of polyp(s): 280.2 | Fluid localization: SRF: 100% | – | – |
| Haensli 2021 (Haensli et al. 2021b, a) | Switzerland | Start Feb to May 2020 | nAMD (MNV), persisting IRF and/or SRF with previous anti-VEGF treatment | Macular scarring preventing change in visual function, other causes of IRF or SRF | Switch: 12 (12) | 80.3 (range: 65–89) | 42/58 | – | –e | – | – |
| Hamou 2021 (Hamou et al. 2021) | USA | Nov 2019 to Nov 2020 | nAMD | – | Naïve and switch: – (10/89) | 82.0 | 33/67 | – | – | – | – |
| Hussain 2021 (Hussain 2021) | USA | Start Nov 2019 to Feb 2020 | Wet AMD, persisting IRF and/or SRF with previous anti-VEGF treatment | Other causes of exudation, <2 IVI brolucizumab, <3 follow-up visits after switch | Switch: 0/– (0/58) | 82 (SD: 7) | 51/49 | Lens status pseudophakic: 81%; presence of geographic atrophy: 34% | – | – | – |
| Kilani 2021 (Kilani et al. 2021) | Germany | – | Exudative AMD | – | Switch: 0/32 (0/36) | 78.1 (range: 66–91) | 41/59 | – | Fluid localization:b IRF: 58% SRF: 78% | – | – |
| Maruko 2021 (Maruko et al. 2021) | Japan | May 2020 to Nov 2020 | Exudative AMD, ≥1 follow-up visit | – | Naïve and switch: 43/84 (43/84) | – | 86/14 | – | – | – | – |
| Matsumoto 2021 (Matsumoto et al. 2021) | Japan | Jun 2020 to Jan 2021 | nAMD with type 1 CNV (CNV detected beneath RPE) | – | Naïve: 40/0 (42/0) | 74.9 (SD: 8.6) | 83/17 | Polypoidal lesions: 55% | – | – | – |
| Rave 2021 (Rave et al. 2021), Sharma 2021 (Sharma et al. 2021b) | USA | Nov 2019 to Dec 2020 | Wet AMD, treat-and-extend regimen, eye exam every visit, OCT every other visit | – | Switch: 0/144 (0/144) | 77.6 (SD: 11.8) | 44/56 | – | – | – | – |
| Reyes-Capo 2021 (Reyes-Capo et al. 2021) | USA | Jan 2018 to Dec 2020 | Microbial endophthalmitis after anti-VEGF IVI | Did not receive vitreous tap and inject | –f | – | – | – | – | – | – |
| Rispoli 2021 (Rispoli et al. 2021) | Italy | – | Exudative AMD with PED, not responsive to prior anti-VEGF treatment | Ophthalmological diseases potentially able to confound image interpretation, lack of high-quality images, exudation regression following prior anti-VEGF treatments | Switch: 12 (12) | 78.4 (SD: 4.8) | 33/67 | – | Fluid localization: None: 0% | – | – |
| Sharma 2021 (Sharma et al. 2021a) *(BREW)* | USA | Dec 2019 to Feb 2020 | nAMD, ≥1 brolucizumab IVI, ≥4 weeks’ follow-up | Structural changes other than nAMD, vitreoretinal interface diseases | 0/42 (0/42) | 79.2 (SD: 7.0) | 43/57 | – | Fluid localization:b IRF: 45% SRF: 90% PED: 74% | – | – |
| Walter 2021 (Walter & Saba 2021b, a) | USA | Oct 2019 to May 2020 | nAMD | – | – (61g/ 530g) | 80.8 (SD: 9.4) | 40/60 | – | Fluid localization:b IRF: 31% SRF: 43% serous PED: 11% | – | – |
| Witkin 2020 (Witkin et al. 2020) | USA | NR to Apr 2020 | Retinal vasculitis after brolucizumabh | Likely to be related to infectious endophthalmitis | 0/25 (0/26) | 79.1 (range: 58–92) | 12/88 | Autoimmune history: 20%; pseudophakic lens: 81% | – | Iritis: 4% | – |
| Witkin 2021 (Witkin et al. 2021) | USA | NR to Jun 2020 | IOI without retinal vasculitis after brolucizumabh | No follow-up data, treated with intraocular antibiotics, retinal vasculitis | 4/41 (4/45) | 76 (range: 56–90) | 36/64 | Autoimmune history: 24%; pseudophakic lens: 59% | – | IOI: 6% | – |

All applicable information was reported when available. Empty cells containing only dashes indicate that the information was not reported or is not applicable.

aMean unless otherwise indicated.

bPatients could have fluid in more than one compartment.

cMedian.

dNaïve vs switch not specified for two eyes.

eReported for 7 of 12 eyes only.

f766 eyes treated with brolucizumab (naïve vs switch NR).

gn numbers differ by outcome.

hReports submitted to American Society of Retina Specialists Research and Safety in Therapeutics Committee.

AE = adverse event; AMD = age-related macular degeneration; BCVA = best corrected visual acuity; CNV = choroidal neovascularization; DM = diabetes mellitus; EF = extrafoveal; F = female; HLD = hyperlipidaemia; HTN = hypertension; IOI = intraocular inflammation; IOP = intraocular pressure; IP = interpapillomacular; IRF = intraretinal fluid; IVI = intravitreal injection; JF = juxtafoveal; M = male; MNV = macular neovascularization; nAMD = neovascular age-related macular degeneration; NR = not reported; NVM = neovascular membrane; OCT = optical coherence tomography; PCV = polypoidal choroidal vasculopathy; PED = pigment epithelial detachment; RAP = retinal angiomatous proliferation; RPE = retinal pigment epithelium; SD = standard deviation; SEM = standard error of the mean; SF = subfoveal; SRF = subretinal fluid; VEGF = vascular endothelial growth factor.

**Online Supplemental Table S2.** anatomical parameters at baseline and follow-up in studies including at least 10 eyes treated with brolucizumab (19 studies).

| **Publication *(study)*** | **Naïve/ switch eyes (%)** | **Eyes (n)** | **Time point(s)a** | **CST (μm)a** | **Presence of fluid overall (%)** | **Presence of fluid in eyes with baseline fluid (%)** | **Presence of IRF (%)** | **Presence of IRF in eyes with baseline IRF (%)** | **Presence of SRF (%)** | **Presence of SRF in eyes with baseline SRF (%)** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Abdin 2021 (Abdin et al. 2021) | 0/100 | Switch (n = 21) | Baseline | 373b | – | – | – | – | – | – |
| 4 weeks | 340;b p = 0.2 | – | – | – | – | – | – |
| 8 weeks | 333;b p = 0.6 | – | – | – | – | – | – |
| 16 weeks | 315;b p = 0.3 | – | – | – | – | – | – |
| 20 weeks | 309;b p = 0.3 | – | – | – | – | – | – |
| 24 weeks | 310;b p = 0.3 | – | – | – | – | – | – |
| 28 weeks | 291;b p = 0.06 | – | – | – | – | – | – |
| 32 weeks | 251;b p = 0.02 | – | – | – | – | – | – |
| 36 weeks | 290;b p = 0.03 | – | – | – | – | – | – |
| 40 weeks | 239;b p = 0.01 | – | – | – | – | – | – |
| 44 weeks | 257;b p = 0.05 | – | – | – | – | – | – |
| 48 weeks | 247;b p = 0.02 | – | – | – | – | – | – |
| 52 weeks | 258;b p = 0.04 | – | – | – | – | – | – |
| Aziz 2021 (Aziz et al. 2021) (*REBEL)* | 7/93 | Naïve and switch  (n = 284) | Baseline | 312.4 | – | – | 34.5 | – | 49.8 | – |
|  | 44 days | 272.4d | – | – | 20.9d | – | 27.8d | – |
|  | 89 daysc | 269.8d | – | – | 27.2d | – | 31.6d | – |
| Bilgic 2021 (Bilgic et al. 2021a)(*REBA)* | 24/76 | Naïve  (n = 25) | Baseline | 428.1 | 92.0 | – | 92.0 | – | 48.0 | – |
| 10.4 monthse | 278.0; p = 0.021 | – | – | – | – | – | – |
|  | Switch  (n = 80) | Baseline | 483.2 | 100.0 | – | 71.3 | – | 38.8 | – |
|  | 10.4 monthse | 297.5; p = 0.01 | – | – | – | – | – | – |
| Sudhalkar 2021 (Sudhalkar et al. 2021) *(REBA PCV)* | 100/0 | Naïve  (n = 17) | Baseline | 399 | – | – | – | – | – | – |
| 10 months | 248d | – | – | – | – | – | – |
| Bilgic 2021 (Bilgic et al. 2021b) *(PROBE)* | 100/0 | Naïve  (n = 27) | Baseline | 398.1 | – | – | 66.7 | – | 29.6 | – |
| 11.2 monthsf | 283.0; p = 0.021 | 85.2g | – | – | – | – | – |
| Book 2022 [Epub 2021] (Book et al. 2022) | 0/100 | Switch  (n = 21) | Baseline | 399.0 | – | – | 52.4 | – | 81.0 | – |
| 14 weeks | 326.5; p = 0.0001 | – | – | 37.5d | – | 37.5; p = 0.004 | – |
| Bulirsch 2021 (Bulirsch et al. 2021) *(SHIFT)* | 0/100 | Switch  (n = 63) | Baseline | 409.4 | 96.8 | – | 44.3h | – | 68.9h | – |
| 4.3 weeks | 342.7; p < 0.001 | – | 70.5h | – | 59.3h | – | 42.9h |
| Chakraborty 2021 (Chakraborty et al. 2021) *(BRAILLE)* | 21/79 | Naïve and switch  (n = 94) | Baseline | 408.45 | – | – | 89.4 | – | 75.5 |  |
| 7.3 weeks | 281.14; p < 0.00001 | – | – | – | 60.7 | – | 84.5 |
|  | Naïve  (n = 20) | Baseline | 398.53 | – | – | –j | – | –j | – |
|  | –i | 285.16; p < 0.00001 | – | – | –j | – | –j | – |
|  | Switch  (n = 74) | Baseline | 410.96 | – | – | –j | – | –j | – |
|  | –i | 280.12; p < 0.00001 | – | – | –j | – | –j | – |
| Cristian 2021 (Cristian et al. 2021) | 0/100 | Switch  (n = 40) | Baseline | 337k | – | – | – | – | 67 | – |
| 6 weeksk | 436d,k | – | – | – | – | 40 | – |
| Eandi 2021 (Eandi & Montesel 2021), Montesel 2021(Montesel et al. 2021) | 21/79 | Naïve and switch (n = 19) | Baseline | 470b | – | – | 63 | – | 89 | – |
| 14.4 weeks | 360; p = 0.001 | – | – | 16; p = 0.065 | – | 16; p = 0.011 | – |
| Enríquez 2021 (Enríquez et al. 2021) | 2/98 | Naïve and switch  (n = 172) | Baseline | 296.7 | 65.7 | – | 20.9 | – | 54.7 | – |
| 35 daysk (after 1 IVI) | 269.7; p = 0.002 (158 eyes) | – | 55.8 | 12.8 | – | 29.7 | – |
| NR (after 2 IVIs) | 275.4; p = 0.10 (57 eyes) | – | 50.4 | 4.7 | – | 13.4 | – |
| 59 daysk (final examination after 1–3 IVIs) | 269.8; p = 0.003 (144 eyes) | – | 50.4 | – | – | – | – |
| Fossataro 2021 (Fossataro et al. 2021) | nAMD | Switch (n = 11) | Baseline | – | 100 | – | – | – | – | – |
| 15 days | – | – | – | 37 | – | 46 | – |
| 1 month | – | – | – | 9 | – | 9 | – |
| 2 months | – | – | – | 9 | – | 18 | – |
| Fukuda 2021 (Fukuda et al. 2021) | 100/0 | Naïve  (n = 14) | Baseline | 280.5 | – | – | – | – | 100 | – |
| 1 month | 170.1; p = 0.0001 | – | – | – | – | 35.7 | – |
| 2 months | 147.6; p = 0.0026 | – | – | – | – | 14.3 | – |
| 3 months | 155; p = 0.001 | – | – | – | – | 0 | – |
| Hussain 2021 (Hussain 2021) | 0/100 | Switch from aflibercept  (n = 48) | Baseline | 336 | – | – | – | – | – | – |
| ~45 daysl | 300m | 69 | – | – | – | – | – |
| ~90 daysl | 310m | 75 | – | – | – | – | – |
|  | Switch from bevacizumab  (n = 10) | Baseline | 401 | – | – | – | – | – | – |
|  | ~45 daysl | 325m | 70 | – | – | – | – | – |
|  | ~90 daysl | 335m | 70 | – | – | – | – | – |
| Kilani 2021 (Kilani et al. 2021) | 0/100 | Switch  (n = 36) | Baseline | 312 | – | – | 58.3 | – | 77.8 | – |
| 32 weeks | 260; p NR | – | – | 25.0 | – | 30.6 | – |
| Matsumoto 2021 (Matsumoto et al. 2021) | 100/0 | Naïve  (n = 42) | Baseline | 301b | – | – | – | – | – | – |
| 1 month | 187;b p < 0.001 | 52.8n | – | – | – | – | – |
| 2 months | 166;b p < 0.001 | 13.9n | – | – | – | – | – |
| 3 months | 160;b p < 0.001 | 5.6n | – | – | – | – | – |
| Rave 2021 (Rave et al. 2021), Sharma 2021 (Sharma et al. 2021b) | 0/100 | Switch  (n = 144) | Baseline | 282 | – | – | – | – | – | – |
| NR | Change NS (actual data NR) | – | – | – | – | – | – |
| Rispoli 2021 (Rispoli et al. 2021) | 0/100 | Switch  (n = 12) | Baseline | – | 100 | – | – | – | – | – |
| 1 month | – | – | – | 0 | – | 0 | – |
| Sharma 2021 (Sharma et al. 2021a) *(BREW)* | 0/100 | Switch  (n = 42) | Baseline | 314 | – | – | 45.2 | – | 90.4 | – |
| 7.2 weeks | 263; p = 0.0027 | – | – |  | 63.2 |  | 60.6 |
| Walter 2021 (Walter & Saba 2021b, a) | 12/88 | Naïve and switch  (n = 591o) | Baseline | 342.1 | – | – | 30.5 | – | 42.7 | – |
| NR (after last IVI) | 294.2; p < 0.001 | – | – | 12.0; p < 0.001 | – | 14.1; p < 0.001 | – |
| Naïve (n = 61o) | Baseline | 420.28 | – | – | –j | – | –j | – |
|  | NR (after last IVI) | 295.5; p < 0.001 | – | – | –j | – | –j | – |
|  | Switch (n = 530o) | Baseline | 334.5 | – | – | –j | – | –j | – |
|  | NR (after last IVI) | 294.1; p < 0.001 | – | – | –j | – | –j | – |

All applicable information was reported when available. Empty cells containing only dashes indicate that the information was not reported or is not applicable.

Note: Haensli 2021(Haensli et al. 2021b, a) reports on efficacy outcomes for seven patients only and is thus not included here.

aMean unless otherwise indicated.

bCentral macular thickness.

cThis follow-up time was calculated by adding the mean days between the first and second injections and the second and third injections. However, because n numbers decreased this value is an approximation only.

d*p* value or other measure of statistical significance not reported.

ePatients had to be followed up for at least 9 months to be included in the study.

fPatients had to be followed up for at least 10 months to be included in the study.

gRecurrence of exudation prior to the end of follow-up.

hThe analysis reported by Bulirsch et al. excluded two patients who had no fluid present at baseline.

iFollow-up was 7.3 weeks overall; not reported separately for naïve and switch groups.

jData not reported separately for naïve and switch groups.

kMedian.

lValues read off graph.

mStatistically significant improvement; p values not reported.

nStudy reports proportion with dry macula and the difference to 100% is shown here.

on numbers differ by outcome.

CST = central subfield thickness; IRF = intraretinal fluid; IVI = intravitreal injection; NR = not reported; NS = not statistically significant; PCV = polypoidal choroidal vasculopathy; SRF = subretinal fluid.

**Online Supplemental Table S3.** Treatment intervals in studies including at least 10 eyes treated with brolucizumab (9 studies).

| **Publication *(study)*** | **Naïve/ switch (%)** | **Naïve/ switch patients (eyes)** | **Treatment protocol** | **Previous therapy** | |  | **Brolucizumab** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of injectionsa** | **Treatment interval** |  | **Follow-upa** | **Number of injectionsa** | **Treatment interval** | | | | |
| Aziz 2021 (Aziz et al. 2021) (*REBEL)* | 7/93 | – (21/263) | – | – | – |  | 89 daysb | 2.4 | First to second IVI: mean 44 days (SEM: 1; range: 25–141) Second to third IVI: mean 45 days (SEM: 1; range: 24–113) | | | | |
| Bilgic 2021 (Bilgic et al. 2021a) (*REBA)* | 24/76 | 23/55 (25/80) | Treat and extend | 32.4 | – |  | 10.4 months | Naïve: 5.1;c switch: 4.2 |  | **Naïve, end of loading phase** | **Naïve, end of follow-up** | | **Switch, end of follow-up** |
| **q8w** | 6/25 (24.0%) | 9/25 (36.0%) | | 55/80 (68.7%) |
| **q12w** | 19/25 (76.0%) | 16/25 (64.0%) | | 25/80 (31.3%) |
| Chakraborty 2021 (Chakraborty et al. 2021) *(BRAILLE)* | 21/79 | 20/74 (20/74) | Pro-re-nata | 8.6 | – |  | 7.3 weeks | 1.4 | For 29 eyes (30.9%) that received >1 IVI: mean (SD) 10.2 (2.1) weeks | | | | |
| Cristian 2021 (Cristian et al. 2021) | 1. /100 | 0/40 (0/NR) | Treat and extend | 16d | Maximal median: 6 weeks (range: 4–10 weeks) |  | 6 weeksd | 3.7e | Maximal median increased by a median of 3 weeks (range: 1–10 weeks) | | | | |
| Enríquez 2021 (Enríquez et al. 2021) | 2/98 | – (4/166)f | – | 18d | – |  | 59 daysd | 1.5 | First to second IVI: median 35 days Second to third IVI: median 35 days | | | | |
| Hamou 2021 (Hamou et al. 2021) | 10/90 | – (10/89) | – | 27 | Injection maintenance, average 88 days |  | 1 year | – | Injection maintenance, average 109 days (extension from previous: 23 days); *p* NR | | | | |
| Rave 2021 (Rave et al. 2021), Sharma 2021 (Sharma et al. 2021b) | 0/100 | 0/144 (0/144) | Treat and extend | – | Average: 34 days |  | – | 4.4 | Average treatment interval was extended to 60 days; *p* < 0.001 | | | | |
| Sharma 2021 *(BREW)* (Sharma et al. 2021a) | 0/100 | 0/42 (0/42) | – | 19d | – |  | 7.2 weeks | 1.4 | For 13 eyes (31.0%) that received >1 IVI, the treatment interval was 4–6 weeks | | | | |
| Walter 2021 (Walter & Saba 2021b, a) | 12/88 | NR/NR (61g/530g) | – | – | **Overall:** mean 6.3 weeks |  | – | 2.3 | **Previous therapy treatment interval** | | | **Brolucizumab treatment interval** | |
| **Overall** | | | Mean 6.8 weeks; *p* = 0.001 | |
| **Subgroup ≤4 weeks (mean 3.8 weeks)** | | | Mean 5.9 weeks; *p* ≈ 10-9 | |
| **Subgroup 4.1–6 weeks (mean 5.2 weeks)** | | | Mean 6.2 weeks; *p* ≈ 10-8 | |
| **Subgroup 6.1–8 weeks (mean 7.3 weeks)** | | | Mean 7.5 weeks; *p* = 0.26 | |
| **Subgroup >8 weeks (mean 9.9 weeks)** | | | Mean 7.6 weeks; *p* ≈ 10-9 | |

All applicable information was reported when available. Empty cells containing only dashes indicate that the information was not reported or is not applicable.

Note: Haensli 2021(Haensli et al. 2021b, a) reports on treatment intervals for seven patients only and is thus not included here. Studies reporting only on 1-monthly treatment intervals with brolucizumab as a loading phase are not included here.

aMean unless otherwise indicated.

bThis follow-up time was calculated by adding the mean days between the first and second injections and the second and third injections. However, because n numbers decreased this value is an approximation only.

cMean 2.1 injections after three loading injections.

dMedian.

eCalculated from 40 patients having had 147 injections.

fNaïve vs switch not specified for two eyes.

gn numbers differ by outcome.

IVI = intravitreal injection; NR = not reported; q8w = once every 8 weeks; q12w = once every 12 weeks; SD = standard deviation; SEM = standard error of the mean.

**Online Supplemental Table S4.** Overview of studies including fewer than 10 eyes treated with brolucizumab (19 studies).

| **Publication** | **N patients (eyes)** |
| --- | --- |
| **Angerer MPM**, Neuburger M, Hille K, Horn PC. [Vaso-occlusive retinitis following intravitreal injection of brolucizumab]. *Ophthalmologe.* 2021;118(10):1048–1050. | 1 (1) |
| **Antaki F**, Vadboncoeur J. Retinal vasculitis after intravitreal injection of brolucizumab. *Can J Ophthalmol.* 2021 [Epub ahead of print]. | 1 (1) |
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aEpub 2021.

PRISMA checklist

| **Section and topic** | **Item #** | **Checklist item** | **Location where item is reported** |
| --- | --- | --- | --- |
| **TITLE** | | |  |
| Title | 1 | Identify the report as a systematic review. | Page 1 |
| **ABSTRACT** | | |  |
| Abstract | 2 | See the PRISMA 2020 for Abstracts checklist. | Pages 3–4 |
| **INTRODUCTION** | | |  |
| Rationale | 3 | Describe the rationale for the review in the context of existing knowledge. | Pages 5–6 |
| Objectives | 4 | Provide an explicit statement of the objective(s) or question(s) the review addresses. | Page 6 |
| **METHODS** | | |  |
| Eligibility criteria | 5 | Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses. | Pages 6 and 8 |
| Information sources | 6 | Specify all databases, registers, websites, organizations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted. | Pages 6–7 |
| Search strategy | 7 | Present the full search strategies for all databases, registers and websites, including any filters and limits used. | Page 7 |
| Selection process | 8 | Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently and, if applicable, details of automation tools used in the process. | Pages 6–7 |
| Data collection process | 9 | Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators and, if applicable, details of automation tools used in the process. | Page 8 |
| Data items | 10a | List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses) and, if not, the methods used to decide which results to collect. | Page 8 |
| 10b | List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information. | Page 8 |
| Study risk of bias assessment | 11 | Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and, if applicable, details of automation tools used in the process. | Page 8 |
| Effect measures | 12 | Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results. | Page 8 |
| Synthesis methods | 13a | Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis [item #5]). | NA |
| 13b | Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions. | NA |
| 13c | Describe any methods used to tabulate or visually display results of individual studies and syntheses. | NA |
| 13d | Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used. | NA |
| 13e | Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression). | NA |
| 13f | Describe any sensitivity analyses conducted to assess robustness of the synthesized results. | NA |
| Reporting bias assessment | 14 | Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases). | Page 8 |
| Certainty assessment | 15 | Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome. | NA |
| **RESULTS** | | |  |
| Study selection | 16a | Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram. | Page 9, Fig. 1 |
| 16b | Cite studies that might appear to meet the inclusion criteria but which were excluded, and explain why they were excluded. | NA |
| Study characteristics | 17 | Cite each included study and present its characteristics. | Tables 1–3, Tables S1–S3 |
| Risk of bias in studies | 18 | Present assessments of risk of bias for each included study. | NA |
| Results of individual studies | 19 | For all outcomes, present for each study: (a) summary statistics for each group (when appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots. | Tables 1–3, Tables S1–S3 |
| Results of syntheses | 20a | For each synthesis, briefly summarize the characteristics and risk of bias among contributing studies. | Pages 10–17 |
| 20b | Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect. | NA |
| 20c | Present results of all investigations of possible causes of heterogeneity among study results. | NA |
| 20d | Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results. | NA |
| Reporting biases | 21 | Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed. | NA |
| Certainty of evidence | 22 | Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed. | NA |
| **DISCUSSION** | | |  |
| Discussion | 23a | Provide a general interpretation of the results in the context of other evidence. | Pages 17–20 |
| 23b | Discuss any limitations of the evidence included in the review. | Page 20 |
| 23c | Discuss any limitations of the review processes used. | Page 20 |
| 23d | Discuss implications of the results for practice, policy and future research. | Pages 17–19 |
| **OTHER INFORMATION** | | |  |
| Registration and protocol | 24a | Provide registration information for the review, including register name and registration number, or state that the review was not registered. | Page 6 |
| 24b | Indicate where the review protocol can be accessed, or state that a protocol was not prepared. | Page 6 |
| 24c | Describe and explain any amendments to information provided at registration or in the protocol. | NA |
| Support | 25 | Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review. | Page 21 |
| Competing interests | 26 | Declare any competing interests of review authors. | Page 20–21 |
| Availability of data, code and other materials | 27 | Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review. | NA |

NA = not applicable.

*From:* Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71.

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