

**Supplementary Table 1** Inclusion criteria

| Study                                              | Baseline BCVA                | Disease duration                      |
|----------------------------------------------------|------------------------------|---------------------------------------|
| <b>Battaglia Parodi <i>et al.</i></b> <sup>8</sup> | ≤ 74 letters*                | Not available                         |
| <b>BRAVO</b> <sup>9 23</sup>                       | 19–73 letters (20/400–20/40) | ≤ 52 weeks                            |
| <b>BRIGHTER</b> <sup>32</sup>                      | 19–73 letters (20/400–20/40) | ≤ 24 months                           |
| <b>COMRADE-B</b> <sup>33</sup>                     | 19–73 letters (20/400–20/40) | ≤ 6 months                            |
| <b>GENEVA</b> <sup>14 34</sup>                     | 34–68 letters (20/200–20/50) | Duration of macular oedema ≤ 52 weeks |
| <b>RABAMES</b> <sup>22</sup>                       | 24–73 letters (20/320–20/40) | > 3 to < 18 months                    |
| <b>Tan <i>et al.</i></b> <sup>27</sup>             | 19–68 letters (20/400–20/50) | 6 weeks to 9 months                   |
| <b>VIBRANT</b> <sup>12</sup>                       | 24–73 letters (20/320–20/40) | ≤ 52 weeks                            |

\*Decimal score converted into ETDRS letters.

BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study.

**Supplementary Table 2** Impact of adjusting inclusion criteria for BRIGHTER<sup>11</sup> on baseline characteristics.

| Baseline characteristic             | Before adjustment         |                                      |       |                | After adjustment          |                                      |       |                |
|-------------------------------------|---------------------------|--------------------------------------|-------|----------------|---------------------------|--------------------------------------|-------|----------------|
|                                     | Ranibizumab<br>0.5 mg PRN | Ranibizumab<br>0.5 mg PRN<br>+ laser | Laser | <i>p</i> value | Ranibizumab<br>0.5 mg PRN | Ranibizumab<br>0.5 mg PRN<br>+ laser | Laser | <i>p</i> value |
| <b>Patients (n)</b>                 | 180                       | 178                                  | 90    |                | 142                       | 143                                  | 72    |                |
| <b>Female (%)</b>                   | 49.2                      | 46.7                                 | 59.8  | 0.11           | 49.0                      | 42.7                                 | 60.8  | 0.04           |
| <b>Duration of disease (months)</b> | 10.3                      | 9.3                                  | 10.5  | 0.85           | 3.4                       | 3.2                                  | 2.8   | 0.44           |
| <b>Age (years)</b>                  | 64.7                      | 67.3                                 | 67.8  | 0.02           | 63.9                      | 66.7                                 | 67.1  | 0.03           |
| <b>BCVA (letters)</b>               | 59.5                      | 56.6                                 | 56.5  | 0.05           | 58.9                      | 56.7                                 | 58.3  | 0.28           |

*p* values calculated with an analysis of variance test for continuous variables (duration of disease, age, BCVA) and with a X-squared test for the categorical variable (gender).

BCVA, best-corrected visual acuity; PRN, *pro re nata* (as needed). Before adjustment, the number of patients is based on the full analysis set and the other demographics are based on the randomized set

**Supplementary Table 3** Outcomes before adjustment of baseline characteristics for BRAVO, BRIGHTER and COMRADE-B

| Study                          | Outcome | Treatment group           |            |             |                                 |                                      |
|--------------------------------|---------|---------------------------|------------|-------------|---------------------------------|--------------------------------------|
|                                |         | Ranibizumab<br>0.5 mg PRN | Laser      | Sham        | Dexamethasone<br>0.7 mg implant | Ranibizumab<br>0.5 mg PRN +<br>laser |
| <b>BRAVO</b> <sup>9</sup>      | n/N (%) | 80/131 (61)               |            | 38/132 (29) |                                 |                                      |
|                                | LG (SD) | 18.3 (13.2)               |            | 7.3 (13.0)  |                                 |                                      |
| <b>COMRADE-B</b> <sup>33</sup> | n/N (%) | 77/126 (61)               |            |             | 44/118 (37)                     |                                      |
|                                | LG (SD) | 17.3 (11.8)               |            |             | 9.2 (12.5)                      |                                      |
| <b>BRIGHTER</b> <sup>32</sup>  | n/N (%) | 81/180 (45)               | 25/90 (28) |             |                                 | 83/178 (47)                          |
|                                | LG (SD) | 14.8 (10.7)               | 6.0 (14.3) |             |                                 | 14.4 (12.0)                          |

BCVA, best-corrected visual acuity; LG, BCVA letters gained from baseline to month 6 or month 12; n, number of patients in treatment arm with adverse events; N, total number of patients in treatment arm; PRN, *pro re nata* (as needed); SD, standard deviation.

**Supplementary Table 4** Node-splitting (consistency between direct and indirect evidence): BCVA letters gained

| Comparison                                                    | Direct evidence estimates (95% CrI) | Indirect evidence estimates (95% CrI) | Difference between direct and indirect estimates (95% CrI) |
|---------------------------------------------------------------|-------------------------------------|---------------------------------------|------------------------------------------------------------|
| <b>Ranibizumab 0.5 mg PRN vs dexamethasone 0.7 mg implant</b> |                                     |                                       |                                                            |
| <b>Laser vs sham</b>                                          | 7.8 letters (1.8–13.8)              | 8.1 letters (0.8–15.5)                | –0.3 letters (–9.9–9.2)                                    |
| <b>Ranibizumab 0.5 mg PRN vs laser</b>                        | –1.4 letters (–9.0–6.0)             | –0.6 letters (–7.6–6.1)               | –0.7 letters (–11.0–9.5)                                   |
|                                                               | 9.6 letters (5.7–14.4)              | 12.2 letters (1.9–22.6)               | –2.5 letters (–13.4–9.1)                                   |

BCVA, best-corrected visual acuity; CrI, credible interval; PRN, *pro re nata* (as needed);

## Supplementary materials. Medline search strategy for RCTs published since 2010

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1 exp Randomized Controlled Trials as Topic/ (95562)  
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3 randomised controlled trial.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (11379)  
4 exp Random Allocation/ (81374)  
5 exp Double-Blind Method/ (127150)  
6 exp Single-Blind Method/ (19394)  
7 exp Clinical Trial/ (777973)  
8 1 or 2 or 3 or 4 or 5 or 6 or 7 (1046544)  
9 ((singl\$ or doubl\$ or treb\$ or tripl\$) adj (blind\$3 or mask\$3)).tw. (131376)  
10 (clinic\$ adj trial\$1).tw. (221207)  
11 exp Placebos/ (32810)  
12 placebo\$.tw. (161803)  
13 randomly allocated.tw. (17435)  
14 (allocated adj2 random).tw. (719)  
15 9 or 10 or 11 or 12 or 13 or 14 (428319)  
16 8 or 15 (1197477)  
17 case report.tw. (208126)  
18 exp Letter/ (850388)  
19 exp Historical Article/ (323716)  
20 review of reported cases.pt. (0)  
21 17 or 18 or 19 or 20 (1370515)  
22 16 not 21 (1167377)  
23 exp Macular Edema/ (4207)  
24 exp Edema/ (34634)  
25 (macular adj3 (edema or oedema or odema)).ti,ab. (6759)  
26 exp Retinal Vein/ (1824)  
27 exp Retinal Vein Occlusion/ (2858)  
28 ((vein or veins or veinous) adj5 (occlusion\$1 or occluded or obstruction\$1 or obstructed or closed or closure\$1 or stricture\$1 or stenosis or stenosed or block or blocks or blockage\$1 or blocking or embolism\$1 or emboli) adj5 retina\$1).ti,ab. (3391)

29 (crvo or cvo or rvo or brvo or bvo or crvome).ti,ab. (1587)  
30 (branch vein adj5 occlu\$).ti,ab. (245)  
31 (central vein adj5 occlu\$).ti,ab. (216)  
32 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 (46263)  
33 exp Antibodies, Monoclonal/ (181446)  
34 antibodies/tu (1951)  
35 exp Vascular Endothelial Growth Factors/ (37359)  
36 (vascular endothelial growth or vegf\$ or antivef\$2).ti,ab,rn. (59116)  
37 (ranibizumab or lucentis or rhufab v2 or 347396-82-1).ti,ab,rn. (1905)  
38 exp Angiogenesis Inhibitors/ (34530)  
39 triamcinolone acetonide.mp. or exp Triamcinolone Acetonide/ (5879)  
40 ivta.ti,ab,rn. (267)  
41 exp Dexamethasone/ (44286)  
42 ozurdex.ti,ab,rn. (109)  
43 exp Light Coagulation/ (10884)  
44 (photocoagulation or laser coagulation).ti,ab. (8545)  
45 aflibercept.mp. or Vascular Endothelial Growth Factor A/ (35162)  
46 Eylea.mp. (14)  
47 or/33-47 (324212)  
48 Animals/ (5361952)  
49 (editorial or letter or news).pt. (1376300)  
50 32 and 47 (4411)  
51 50 not (48 or 49) (3390)  
52 limit 51 to english language (2872)  
53 limit 52 to ed=20101101-20140803 (976)  
54 22 and 53 (284)