

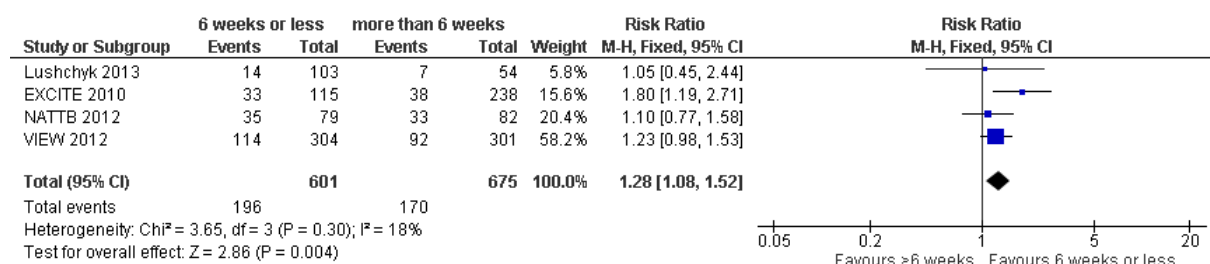
## H.6.1.7 Treatment frequency: ≤6 weeks vs &gt;6 weeks treatment intervals

| Number of studies  | Risk of bias         | Inconsistency        | Indirectness | Imprecision          | Sample size | Effect (95%CI)               | Quality  |
|--|----------------------|----------------------|--------------|----------------------|-------------|------------------------------|----------|
| <b>PRN vs (6 and/or 12 weeks) interval injections</b>  |                      |                      |              |                      |             |                              |          |
| <b>Gain of ≥15 letters at one year</b>   |                      |                      |              |                      |             |                              |          |
| 1 study (GMAN 2015)  | Serious <sup>1</sup> | N/A                  | Not serious  | Serious <sup>2</sup> | 231         | RR 0.55<br>(0.34 to 0.88)    | LOW      |
| <b>Loss of &lt;15 letters at one year</b>  |                      |                      |              |                      |             |                              |          |
| 1 study (GMAN 2015)  | Serious <sup>1</sup> | N/A                  | Not serious  | Not serious          | 231         | RR 0.91<br>(0.84 to 0.99)    | MODERATE |
| <b>Mean change in BCVA in ETDRS letters at one year (higher values indicate better vision)</b> |                      |                      |              |                      |             |                              |          |
| 1 study (GMAN 2015)  | Serious <sup>1</sup> | N/A                  | Not serious  | Serious <sup>2</sup> | 231         | MD -4.40<br>(-8.39 to -0.41) | LOW      |
| <b>Adverse events (serious systemic events at one year)</b>                                    |                      |                      |              |                      |             |                              |          |
| 1 study (GMAN 2015)  | Serious <sup>1</sup> | N/A                  | Not serious  | Serious <sup>2</sup> | 231         | RR 1.39<br>(0.82 to 2.37)    | LOW      |
| <b>Adverse events (serious ocular events at one year)</b>                                      |                      |                      |              |                      |             |                              |          |
| 1 study (GMAN 2015)  | Serious <sup>1</sup> | N/A                  | Not serious  | Serious <sup>2</sup> | 231         | RR 1.25<br>(0.85 to 1.84)    | LOW      |
| <b>Routine injections (interval 6 weeks or less vs more than 6 weeks)</b>                      |                      |                      |              |                      |             |                              |          |
| <b>Gain of ≥15 letters at one year</b>   |                      |                      |              |                      |             |                              |          |
| 4 studies (Lushchyk 2013, NATTB 2012, VIEW 2012, EXCITE)                                       | Serious <sup>3</sup> | Not serious          | Not serious  | Serious <sup>2</sup> | 1276        | RR 1.28<br>(1.08, 1.52)      | LOW      |
| <b>Loss of &lt;15 letters at one year</b>  |                      |                      |              |                      |             |                              |          |
| 3 studies (Lushchyk 2013, NATTB 2012, EXCITE)  | Serious <sup>3</sup> | Serious <sup>4</sup> | Not serious  | not serious          | 671         | RR 0.99<br>(0.92, 1.06)      | LOW      |
| <b>Mean change in BCVA in ETDRS letters at one year (higher scores indicate better vision)</b> |                      |                      |              |                      |             |                              |          |

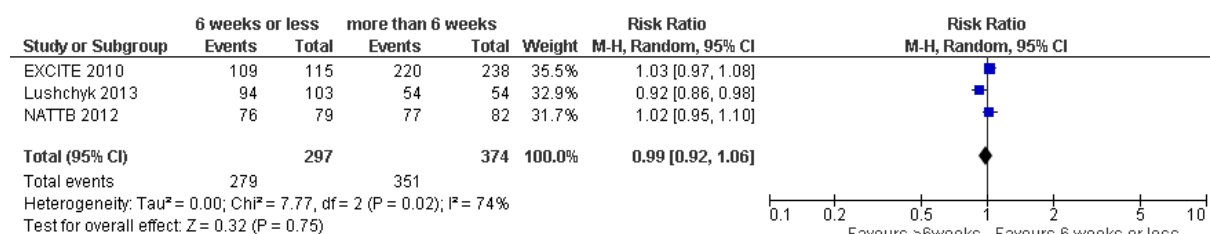
| Number of studies   | Risk of bias         | Inconsistency        | Indirectness | Imprecision          | Sample size | Effect (95%CI)          | Quality |
|---|----------------------|----------------------|--------------|----------------------|-------------|-------------------------|---------|
| 4 studies (Lushchik 2013, NATTB 2012, VIEW 2012, EXCITE 2010)   | Serious <sup>3</sup> | Serious <sup>4</sup> | Not serious  | Not serious          | 1276        | MD 1.87<br>(0.36, 3.39) | LOW     |
| <b>Adverse events (serious systemic events at one year)</b>   |                      |                      |              |                      |             |                         |         |
| 2 studies (Lushchik 2013, VIEW 2012)  | Serious <sup>5</sup> | Not serious          | Not serious  | Serious <sup>2</sup> | 798         | RR 0.77<br>(0.53, 1.11) | LOW     |
| <b>Adverse events (serious ocular events at one year)</b>   |                      |                      |              |                      |             |                         |         |
| 3 studies (Lushchik 2013, NATTB 2012, VIEW 2012)  | Serious <sup>3</sup> | Not serious          | Not serious  | Serious <sup>2</sup> | 983         | RR 1.52<br>(0.86, 2.69) | LOW     |
| <ol style="list-style-type: none"> <li>Downgraded one level for risk of bias due to masking of participants (patients, treating clinicians, and other staff involved in the study were not masked)</li> <li>Downgraded one level for imprecision due to 95%CI of estimated effect crossing of 1 line of defined minimal important difference</li> <li>Downgrade one level for risk of bias due to open label study design (Lushchik 2013 and NATTB 2012) and selection bias (randomisation sequence were unclear in EXCITE and VIEW study)</li> <li>Downgraded one level for inconsistency due to heterogeneity (<math>i^2 &gt; 50\%</math>)</li> <li>Downgraded one level for risk of bias due to open label study design (Lushchik 2013)</li> </ol> |                      |                      |              |                      |             |                         |         |

**Treatment frequency: ≤6 weeks vs >6 weeks treatment intervals**

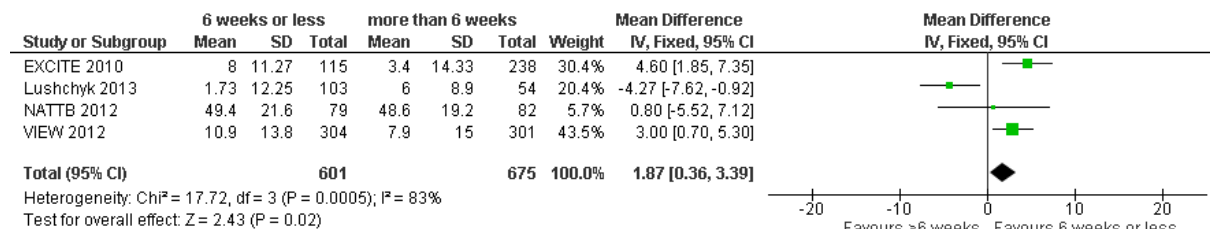
**Gain of 15 or more letters of visual acuity**



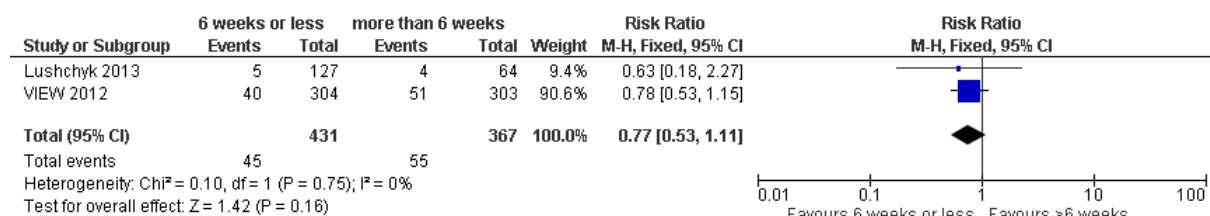
**Loss of fewer than 15 letters of visual acuity**



**Mean visual change in BCVA (EDTRS letters)**



**Serious systemic events**



**Serious ocular events**

