## Supplementary Figure 2. Direct meta-analysis for TR erimental Control Odds Ratio

| Study or Subgroup   | Experimental<br>Events Tota          | Contro<br>L Events |                | Weight                   | Odds Ratio<br>M-H, Random, 95% CI                             | Odds Ratio<br>M-H, Random, 95% CI                           |
|---|--------------------------------------|--------------------|----------------|--------------------------|---|---|
| 2.1.1 TAC vs CTX<br>chen2010  | 33 39                                | 22                 | 34             | 3.3%                     | 3.00 [0.98, 9.18]   | <u> </u>  |
| He2013<br>Liang2017   | 25 28<br>24 30<br>25 30              | 23                 | 28<br>28       | 2.8%<br>2.9%<br>3.0%     | 4.63 [1.11, 19.26]<br>0.87 [0.23, 3.25]                       |   |
| Peng2016<br>Ramachandran2017<br>Xu2013  | 25 30<br>21 35<br>21 48              | 30                 | 30<br>35<br>52 | 3.2%                     | 1.82 [0.52, 6.38]<br>0.25 [0.08, 0.80]<br>0.26 [0.11, 0.61]   |   |
| Subtotal (95% CI) Total events  | 210<br>210                           |                    | 207            | 18.9%                    | 1.01 [0.36, 2.82]   | <b>*</b>  |
| Heterogeneity: Tau <sup>2</sup> = 1.28;<br>Test for overall effect: Z = 0     | Chi2 = 23.48, df =                   |                    | 003); I²       | = 79%                    |   |   |
| 2.1.2 TAC vs Control  | 10 25                                | , 7                | 23             | 3.1%                     | 1 52 10 48 5 041  |   |
| Praga2007<br>Subtotal (95% CI)<br>Total events                                | 10 25                                |                    | 23             | 3.1%                     | 1.52 [0.46, 5.04]<br>1.52 [0.46, 5.04]                        | -   |
| Heterogeneity: Not applicat<br>Test for overall effect: Z = 0                 | ole                                  | ·                  |                |                          |   |   |
| 2.1.3 MMF vs Control  |                                      |                    |                |                          |   |   |
| Dussol2008<br>Subtotal (95% CI)   | 7 19<br>19                           | 1                  | 17<br>17       | 2.9%<br>2.9%             | 0.83 [0.22, 3.19]<br>0.83 [0.22, 3.19]                        |   |
| Total events Heterogeneity: Not applicat Test for overall effect: Z = 0       |                                      | 7                  |                |                          |   |   |
| 2.1.4 MMF vs CTX  | .27 (P = 0.79)                       |                    |                |                          |   |   |
| Fu2012<br>Hayati2019  | 10 13<br>9 17                        |                    | 13<br>13       | 2.3%<br>1.2%             | 1.48 [0.26, 8.50]<br>0.04 [0.00, 0.81]                        | <u> </u>  |
| Peng2016<br>Senthil2008   | 21 30<br>7 11                        | 8                  | 30<br>10       | 3.2%<br>2.0%             | 0.85 [0.28, 2.61]<br>0.44 [0.06, 3.16]                        |   |
| Subtotal (95% CI) Total events  | 47                                   | 52                 | 66             | 8.8%                     | 0.59 [0.19, 1.83]   |   |
| Heterogeneity: Tau <sup>2</sup> = 0.50;<br>Test for overall effect: Z = 0     | .91 (P = 0.36)                       | 3 (P = 0.19        | );  - = 3      | 1%                       |   |   |
| 2.1.5 MMF vs Chlorambuo<br>Chan2007   | ill 5 11                             | 5                  | 9              | 2.3%                     | 0.67 [0.11, 3.92]   |   |
| Subtotal (95% CI)<br>Total events   | 5<br>5                               | 5                  | 9              | 2.3%                     | 0.67 [0.11, 3.92]   |   |
| Heterogeneity: Not applicate<br>Test for overall effect: Z = 0                | ole<br>i.45 (P = 0.65)               |                    |                |                          |   |   |
| 2.1.6 MMF vs CsA<br>Choi2018  | 16 21                                | 12                 | 18             | 2.8%                     | 1.60 [0.39, 6.51]   |   |
| Subtotal (95% CI) Total events  | 16                                   | 12                 | 18             | 2.8%                     | 1.60 [0.39, 6.51]   |   |
| Heterogeneity: Not applicat<br>Test for overall effect: Z = 0                 | ole                                  |                    |                |                          |   |   |
| 2.1.7 CsA vs Steroids   | 44 ***                               |                    | 20             | 2 001                    | 1311102 100.  |   |
| Cattran2001<br>Subtotal (95% CI)<br>Total events                              | 11 28<br>28                          | 3                  | 23<br>23       | 2.8%<br>2.8%             | 4.31 [1.03, 18.04]<br>4.31 [1.03, 18.04]                      |   |
| Heterogeneity: Not applicat<br>Test for overall effect: Z = 2                 | ole                                  | 3                  |                |                          |   |   |
| 2.1.8 CTX vs Control  |                                      |                    |                |                          |   |   |
| Donadio1974<br>Jha2007  | 3 11<br>34 47                        | 16                 | 11<br>46       | 2.0%<br>3.6%             | 1.69 [0.22, 12.81]<br>4.90 [2.03, 11.84]                      |   |
| Kosmadakis2010<br>Murphy1992<br>Subtotal (95% CI)                             | 8 8<br>9 19<br>85                    | 4                  | 10<br>21<br>88 | 2.8%<br>8.4%             | Not estimable<br>3.83 [0.93, 15.72]<br>4.06 [2.01, 8.19]      | -   |
| Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.00:                       | 54<br>Chi² = 0.90, df =              | 32                 |                |                          | 4.00 [2.01, 0.10]   |   |
| Test for overall effect: Z = 3  | .91 (P < 0.0001)                     | - (- 0.01          | ,,             |                          |   |   |
| 2.1.9 CTX vs Chlorambuc<br>Branten1998  | 11 17                                |                    | 15             | 2.3%                     | 11.92 [1.99, 71.41]   |   |
| Ponticeli1998<br>Reichert1994<br>Subtotal (95% CI)                            | 40 43<br>3 9                         | 4                  | 44<br>9<br>68  | 2.8%<br>2.1%<br>7.2%     | 2.96 [0.73, 12.03]<br>0.63 [0.09, 4.22]<br>2.89 [0.63, 13.27] |   |
| Total events<br>Heterogeneity: Tau <sup>2</sup> = 1.07;                       | 54                                   | 42                 |                |                          | 2.00 [0.00, 10.21]  |   |
| Test for overall effect: Z = 1  | .37 (P = 0.17)                       |                    |                |                          |   |   |
| 2.1.10 Steroids vs Contro<br>Cameron1990                                      | 7 52                                 |                    | 51             | 3.0%                     | 1.83 [0.50, 6.67]   | <u>+</u>  |
| Coggins1979<br>Subtotal (95% CI)<br>Total events                              | 12 34<br>86<br>19                    |                    | 38<br>89       | 3.3%<br>6.3%             | 2.42 [0.82, 7.12]<br>2.15 [0.94, 4.94]                        | •   |
| Heterogeneity: Tau <sup>2</sup> = 0.00;<br>Test for overall effect: Z = 1     | Chi² = 0.11, df =                    |                    | ); I² = 0      | %                        |   |   |
| 2.1.11 Chlorambucil vs St   | eroids                               |                    |                |                          |   |   |
| Ponticeli1992<br>Subtotal (95% CI)  | 28 45<br>45                          |                    | 47<br>47       | 3.7%<br>3.7%             | 2.65 [1.14, 6.16]<br>2.65 [1.14, 6.16]                        | •   |
| Total events Heterogeneity: Not applicat Test for overall effect: Z = 2       |                                      | 18                 |                |                          |   |   |
| 2.1.12 Chlorambucil vs Co   | ontrol                               |                    |                |                          |   |   |
| Ponticeli1983<br>Ponticeli1984  | 17 21<br>23 32                       | 9                  | 24<br>30       | 2.9%<br>3.3%             | 7.08 [1.80, 27.80]<br>5.96 [1.99, 17.86]                      |   |
| Ponticeli1995<br>Subtotal (95% CI)<br>Total events                            | 26 42<br>95<br>66                    |                    | 39<br>93       | 3.6%<br>9.8%             | 3.25 [1.31, 8.09]<br>4.65 [2.49, 8.68]                        | •   |
| Heterogeneity: Tau <sup>2</sup> = 0.00;<br>Test for overall effect: Z = 4     | Chi2 = 1.15, df =                    | 2 (P = 0.56        | ); I² = 0      | %                        |   |   |
| 2.1.13 Rituximab vs Contr   |                                      |                    |                |                          |   |   |
| Dahan2016<br>Subtotal (95% CI)  | 24 37<br>37                          |                    | 38<br>38       | 3.5%<br>3.5%             | 3.55 [1.37, 9.19]<br>3.55 [1.37, 9.19]                        | •   |
| Total events Heterogeneity: Not applicat Test for overall effect: Z = 2       | 24<br>ble                            | 13                 |                |                          |   |   |
| 2.1.14 TAC vs CsA   |                                      |                    |                |                          |   |   |
| Li 2017<br>Subtotal (95% CI)  | 14 16<br>16                          | i                  | 15<br>15       | 2.2%<br>2.2%             | 2.55 [0.39, 16.55]<br>2.55 [0.39, 16.55]                      |   |
| Total events Heterogeneity: Not applicat                                      |                                      | 11                 |                |                          |   |   |
| Test for overall effect: Z = 0<br>2.1.15 rituximab vs CsA                     | .oo (r = 0.33)                       |                    |                |                          |   |   |
| Fervenza 2019<br>Subtotal (95% CI)  | 39 65<br>65                          |                    | 65<br>65       | 3.8%<br>3.8%             | 6.00 [2.74, 13.15]<br>6.00 [2.74, 13.15]                      | -   |
| Total events<br>Heterogeneity: Not applicat                                   | 39<br>ole                            | 13                 |                |                          |   |   |
| Test for overall effect: Z = 4  | .48 (P < 0.00001)                    |                    |                |                          |   |   |
| 2.1.16 TAC vs MMF<br>Peng2016<br>Subtotal (95% CI)                            | 25 30<br>30                          | 21                 | 30<br>30       | 3.1%<br>3.1%             | 2.14 [0.62, 7.39]<br>2.14 [0.62, 7.39]                        |   |
| Total events Heterogeneity: Not applicat                                      | 25                                   | 21                 |                | 51.70                    | [0.04, 1.09]  |   |
| Test for overall effect: Z = 1  | .21 (P = 0.23)                       |                    |                |                          |   |   |
| 2.1.17 CSA vs Control<br>Cattran1995<br>Kosmadakis2010                        | 4 9                                  |                    | 8              | 1.1%                     | 13.91 [0.62, 312.60]  |   |
| Kosmadakis2010<br>Subtotal (95% CI)<br>Total events                           | 6 10<br>19                           |                    | 10<br>18       | 1.1%<br>2.3%             | 0.07 [0.00, 1.50]<br>0.97 [0.01, 177.01]                      |   |
| Heterogeneity: Tau <sup>2</sup> = 11.6i<br>Test for overall effect: Z = 0     | 0; Chi <sup>2</sup> = 5.65, df =     | 1 (P = 0.0         | 2); I² =       | 82%                      |   |   |
| 2.1.18 CSA vs CTX   |                                      |                    |                |                          | 0.5   |   |
| Kosmadakis2010<br>Subtotal (95% CI)   | 6 10<br>10                           |                    | 8              | 1.1%<br>1.1%             | 0.08 [0.00, 1.88]<br>0.08 [0.00, 1.88]                        |   |
| Total events<br>Heterogeneity: Not applicab<br>Test for overall effect: Z = 1 |                                      | 8                  |                |                          |   |   |
| 2.1.19 Rituximab vs CTX   | .50 (r = 0.12)                       |                    |                |                          |   |   |
| Fernández-Juárez G2021<br>Scolari2021   | 25 43<br>17 37                       | 16                 | 43<br>37       | 3.4%<br>3.6%             | 0.27 [0.10, 0.74]<br>1.12 [0.45, 2.79]                        |   |
| Subtotal (95% CI)<br>Total events   | 42                                   | 52                 | 80             | 7.0%                     | 0.56 [0.14, 2.24]   |   |
| Heterogeneity: Tau <sup>2</sup> = 0.76;<br>Test for overall effect: Z = 0     | .82 (P = 0.41)                       | ı (₽ = 0.04        | ); I* = 7      | 0%                       |   |   |
| Total (95% CI)<br>Total events  | 1022<br>626                          | 502                |                | 100.0%                   | 1.66 [1.13, 2.44]   | •   |
| Heterogeneity: Tau <sup>2</sup> = 0.84;<br>Test for overall effect: Z = 2     | Chi² = 107.76, df<br>.61 (P = 0.009) | = 35 (P < 0        |                |                          |   | 0.01 0.1 1 10 100  Favours [experimental] Favours [control] |
| Test for subgroup difference  |                                      | If = 18 (P =       | 0.007)         | , I <sup>2</sup> = 49.9% | 6   |   |