**Supplementary Table 1: Mixed effects linear regression analyses1 showing treatment response to four different treatment arms depending on pre-treatment white blood cell (WBC) count.**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Baseline | | | Estimated change per week | | | Difference compared to WBC 4.5-10 | |
|  | **WBC<4.5** | **WBC 4.5-10** | **WBC≥10** | **WBC<4.5** | **WBC 4.5-10** | **WBC≥10** | **WBC<4.5** | **WBC≥10** |
|  | Mean ±SD | Mean ±SD | Mean ±SD | β (95%-CI) | β (95%-CI) | β (95%-CI) | p-value | p-value |
| Lithium high-dose (from Bipolar CHOICE) | | | | | | | | |
| CGI-BP overall | 4.3 ±0.5 | 4.5 ±0.8 | 4.3 ±0.7 | -0.040 (-0.072; -0.009) | -0.047 (-0.056; -0.037) | -0.050 (-0.074; -0.002) | 0.35 | 0.38 |
| CGI-BP depression | 4.3±0.5 | 4.3±1.1 | 4.1±1.1 | -0.045 (-0.054; -0.035) | -0.039 (-0.072; -0.006) | -0.045 (-0.070; -0.019) | 0.69 | 0.45 |
| CGI-BP mania | 2.9±1.2 | 2.9±1.3 | 3.0±1.1 | -0.027 (-0.036; -0.018) | -0.036 (-0.067; -0.006) | -0.051 (-0.071; -0.030) | 0.82 | 0.86 |
| Quetiapine (from Bipolar CHOICE) | | | | | | | | |
| CGI-BP overall | 4.3±0.8 | 4.5±0.9 | 4.8±0.7 | -0.055 (-0.085; -0.026) | -0.053 (-0.062; -0.044) | -0.048 (-0.075; -0.021) | 0.94 | 0.19 |
| CGI-BP depression | 4.0±1.3 | 4.1±1.2 | 4.7±0.9 | -0.068 (-0.098; -0.038) | -0.050 (-0.060; -0.041) | -0.046 (-0.074; -0.018) | 0.53 | 0.06 |
| CGI-BP mania | 3.2±1.1 | 3.1±1.3 | 3.4±1.3 | -0.031 (-0.059; -0.003) | -0.030 (-0.038; -0.021) | -0.026 (-0.053; 0.001) | 0.82 | 0.26 |
| Lithium moderate-dose plus OPT (from LiTMUS) | | | | | | | | |
| CGI-BP overall | 4.3±0.5 | 4.3±0.9 | 4.3±1.1 | -0.040 (-0.071; -0.008) | -0.035 (-0.047; -0.024) | -0.034 (-0.068; -0.001) | 0.66 | 0.91 |
| CGI-BP depression | 3.8±0.7 | 3.7±1.3 | 3.7±1.5 | -0.034 (-0.067; -0.002) | -0.023 (-0.036; -0.011) | -0.033 (-0.071; 0.003) | 0.87 | 0.98 |
| CGI-BP mania | 3±1.4 | 2.9±1.4 | 3.3±1.5 | -0.018 (-0.046; 0.009) | -0.030 (-0.040; -0.019) | -0.036 (-0.067; -0.007) | 0.99 | 0.41 |
| OPT alone (from LiTMUS) | | | | | | | | |
| CGI-BP overall | 4.2±1.0 | 4.2±0.9 | 4.7±0.6 | -0.051 (-0.080; -0.022) | -0.047 (-0.058; -0.036) | -0.063 (-0.086; -0.039) | 0.94 | 0.12 |
| CGI-BP depression | 3.8±1.4 | 3.8±1.3 | 4.5±0.8 | -0.035 (-0.068; -0.002) | -0.034 (-0.046; -0.022) | -0.054 (-0.081; -0.026) | 0.63 | 0.99 |
| CGI-BP mania | 2.8±1.0 | 2.7±1.3 | 2.8±1.5 | -0.050 (-0.071; -0.030) | -0.035 (-0.044; -0.025) | -0.051 (-0.076; -0.026) | 0.82 | 0.04 |

Abbreviations: β: Regression coefficient; 95%-CI: 95% Confidence Interval; SD: Standard deviation; CGI-BP = Clinical Global Impression Scale for Bipolar Disorder.

A negative β indicates better treatment effect among users of NSAIDs or paracetamol, whereas a positive β indicates better treatment effect among non-users.

The analyses in each treatment arm were adjusted for multiple testing, i.e. p=0.05/6=0.0083.

1 All analyses were adjusted for: age, gender, body mass index (BMI), current smoking, and baseline CGI severity.