Table S1. Passing rate of originally superiority test

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Passing Rate of Superiority Test | Global | Region 1-2 | Region 3-4 | Region 5-6 | Region 7 | Region 8 | Region 9 | Region 10 |
| 0.900 | 0.155 | 0.222 | 0.286 | 0.549 | 0.374 | 0.116 | 0.050 |

Table S2. The rates of the original results falling into the categories

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Category | Category Rate | | | | | | | |
| Region 1-2 | Region 3-4 | Region 5-6 | Region 7 | Region 8 | Region 9 | Region 10 | All |
| All | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 1 | 0.500 | 0.499 | 0.500 | 0.841 | 0.690 | 0.311 | 0.162 | 0.500 |
| 2 | 0.139 | 0.183 | 0.215 | 0.083 | 0.140 | 0.188 | 0.155 | 0.164 |
| 3 | 0.138 | 0.163 | 0.175 | 0.051 | 0.102 | 0.204 | 0.208 | 0.152 |
| 4 | 0.223 | 0.155 | 0.110 | 0.025 | 0.068 | 0.297 | 0.475 | 0.184 |

Table S3. Consistency rate of the consistency test stratified by category\*region

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Approach | Category | Consistency Rate | | | | | | | |
| Region 1-2 | Region 3-4 | Region 5-6 | Region 7 | Region 8 | Region 9 | Region 10 | All |
| Shih Superiority | All | 0.884 | 0.925 | 0.949 | 0.989 | 0.969 | 0.839 | 0.687 | 0.900 |
| 1 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |
| 2 | 0.985 | 0.994 | 0.997 | 0.995 | 0.995 | 0.991 | 0.988 | 0.992 |
| 3 | 0.934 | 0.951 | 0.959 | 0.958 | 0.958 | 0.936 | 0.906 | 0.942 |
| 4 | 0.533 | 0.577 | 0.603 | 0.664 | 0.615 | 0.506 | 0.385 | 0.511 |
| Tse | All | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Tse Reference | All | 0.393 | 0.539 | 0.686 | 0.430 | 0.512 | 0.512 | 0.430 | 0.512 |
| 1 | 0.395 | 0.538 | 0.686 | 0.398 | 0.483 | 0.584 | 0.601 | 0.513 |
| 2 | 0.546 | 0.648 | 0.762 | 0.651 | 0.649 | 0.649 | 0.635 | 0.660 |
| 3 | 0.498 | 0.599 | 0.711 | 0.605 | 0.606 | 0.588 | 0.572 | 0.602 |
| 4 | 0.226 | 0.349 | 0.496 | 0.408 | 0.389 | 0.298 | 0.242 | 0.303 |
| Tse Sup | All | 0.004 | 0.000 | 0.000 | 0.005 | 0.001 | 0.000 | 0.000 | 0.002 |
| 1 | 0.009 | 0.001 | 0.000 | 0.007 | 0.002 | 0.000 | 0.000 | 0.003 |
| 2 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| 3 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| 4 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| Tse Sup Reference | All | 0.362 | 0.420 | 0.485 | 0.781 | 0.612 | 0.247 | 0.121 | 0.429 |
| 1 | 0.717 | 0.832 | 0.934 | 0.926 | 0.880 | 0.777 | 0.728 | 0.845 |
| 2 | 0.021 | 0.028 | 0.078 | 0.035 | 0.033 | 0.025 | 0.021 | 0.040 |
| 3 | 0.002 | 0.002 | 0.004 | 0.003 | 0.003 | 0.001 | 0.001 | 0.002 |
| 4 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| SenInd Simple | All | 0.595 | 0.609 | 0.624 | 0.895 | 0.779 | 0.418 | 0.243 | 0.599 |
| 1 | 0.996 | 0.998 | 0.999 | 0.999 | 0.999 | 0.997 | 0.997 | 0.998 |
| 2 | 0.612 | 0.562 | 0.543 | 0.610 | 0.591 | 0.526 | 0.486 | 0.559 |
| 3 | 0.086 | 0.051 | 0.042 | 0.078 | 0.065 | 0.041 | 0.031 | 0.053 |
| 4 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| RPspeP Reference | All | 0.554 | 0.606 | 0.641 | 0.416 | 0.553 | 0.553 | 0.418 | 0.554 |
| 1 | 0.553 | 0.607 | 0.639 | 0.345 | 0.484 | 0.713 | 0.792 | 0.554 |
| 2 | 0.974 | 0.962 | 0.949 | 0.979 | 0.974 | 0.953 | 0.935 | 0.959 |
| 3 | 0.781 | 0.695 | 0.636 | 0.789 | 0.739 | 0.649 | 0.594 | 0.683 |
| 4 | 0.156 | 0.092 | 0.056 | 0.170 | 0.114 | 0.066 | 0.043 | 0.088 |
| RPsupP Reference | All | 0.553 | 0.552 | 0.555 | 0.870 | 0.734 | 0.361 | 0.197 | 0.548 |
| 1 | 0.999 | 0.999 | 0.999 | 0.999 | 0.999 | 0.998 | 0.997 | 0.999 |
| 2 | 0.367 | 0.288 | 0.251 | 0.341 | 0.307 | 0.256 | 0.223 | 0.286 |
| 3 | 0.018 | 0.011 | 0.009 | 0.020 | 0.016 | 0.010 | 0.007 | 0.012 |
| 4 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| GenP | All | 0.685 | 0.652 | 0.648 | 0.897 | 0.790 | 0.526 | 0.463 | 0.664 |
| 1 | 0.991 | 0.995 | 0.997 | 0.998 | 0.997 | 0.993 | 0.991 | 0.995 |
| 2 | 0.586 | 0.572 | 0.574 | 0.616 | 0.591 | 0.547 | 0.520 | 0.571 |
| 3 | 0.051 | 0.026 | 0.021 | 0.038 | 0.034 | 0.023 | 0.016 | 0.028 |
| 4 | 0.454 | 0.299 | 0.204 | 0.178 | 0.237 | 0.367 | 0.461 | 0.374 |
| GenCB | All | 0.632 | 0.589 | 0.578 | 0.869 | 0.743 | 0.455 | 0.391 | 0.606 |
| 1 | 0.971 | 0.978 | 0.982 | 0.992 | 0.985 | 0.969 | 0.959 | 0.979 |
| 2 | 0.378 | 0.322 | 0.306 | 0.363 | 0.339 | 0.304 | 0.274 | 0.324 |
| 3 | 0.034 | 0.016 | 0.013 | 0.026 | 0.022 | 0.015 | 0.010 | 0.018 |
| 4 | 0.403 | 0.257 | 0.172 | 0.152 | 0.201 | 0.316 | 0.403 | 0.326 |
| GenP Sup | All | 0.599 | 0.627 | 0.652 | 0.902 | 0.791 | 0.440 | 0.264 | 0.615 |
| 1 | 0.995 | 0.998 | 0.999 | 0.999 | 0.998 | 0.997 | 0.997 | 0.998 |
| 2 | 0.674 | 0.676 | 0.686 | 0.715 | 0.693 | 0.655 | 0.632 | 0.675 |
| 3 | 0.063 | 0.036 | 0.028 | 0.050 | 0.045 | 0.031 | 0.022 | 0.037 |
| 4 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| GenCB Sup | All | 0.562 | 0.576 | 0.591 | 0.878 | 0.752 | 0.388 | 0.221 | 0.570 |
| 1 | 0.983 | 0.989 | 0.992 | 0.996 | 0.992 | 0.983 | 0.979 | 0.989 |
| 2 | 0.473 | 0.438 | 0.432 | 0.473 | 0.458 | 0.416 | 0.386 | 0.438 |
| 3 | 0.039 | 0.018 | 0.015 | 0.030 | 0.026 | 0.018 | 0.011 | 0.021 |
| 4 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| Bayesian Min Constant | All | 0.512 | 0.589 | 0.657 | 0.879 | 0.757 | 0.404 | 0.238 | 0.579 |
| 1 | 0.918 | 0.969 | 0.988 | 0.987 | 0.978 | 0.957 | 0.945 | 0.965 |
| 2 | 0.375 | 0.571 | 0.748 | 0.594 | 0.582 | 0.554 | 0.544 | 0.582 |
| 3 | 0.008 | 0.007 | 0.012 | 0.006 | 0.009 | 0.006 | 0.005 | 0.008 |
| 4 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| Bayesian Min Reference | All | 0.695 | 0.734 | 0.771 | 0.945 | 0.868 | 0.555 | 0.365 | 0.713 |
| 1 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |
| 2 | 0.967 | 0.969 | 0.981 | 0.985 | 0.980 | 0.961 | 0.953 | 0.971 |
| 3 | 0.441 | 0.355 | 0.345 | 0.439 | 0.395 | 0.310 | 0.263 | 0.355 |
| 4 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| Bayesian Mean Constant | All | 0.550 | 0.628 | 0.693 | 0.899 | 0.787 | 0.446 | 0.275 | 0.615 |
| 1 | 0.945 | 0.980 | 0.993 | 0.992 | 0.986 | 0.973 | 0.966 | 0.978 |
| 2 | 0.541 | 0.740 | 0.881 | 0.762 | 0.745 | 0.736 | 0.738 | 0.744 |
| 3 | 0.019 | 0.022 | 0.042 | 0.026 | 0.023 | 0.020 | 0.020 | 0.026 |
| 4 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| Bayesian Mean Reference | All | 0.722 | 0.762 | 0.797 | 0.954 | 0.885 | 0.591 | 0.401 | 0.739 |
| 1 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |
| 2 | 0.995 | 0.996 | 0.998 | 0.998 | 0.997 | 0.995 | 0.992 | 0.996 |
| 3 | 0.610 | 0.498 | 0.472 | 0.587 | 0.539 | 0.454 | 0.408 | 0.500 |
| 4 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| Bayesian Median Constant | All | 0.535 | 0.613 | 0.680 | 0.892 | 0.776 | 0.429 | 0.261 | 0.601 |
| 1 | 0.935 | 0.977 | 0.991 | 0.991 | 0.983 | 0.967 | 0.960 | 0.973 |
| 2 | 0.470 | 0.677 | 0.836 | 0.703 | 0.683 | 0.668 | 0.667 | 0.683 |
| 3 | 0.014 | 0.014 | 0.025 | 0.017 | 0.015 | 0.012 | 0.011 | 0.016 |
| 4 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| Bayesian Median Reference | All | 0.710 | 0.751 | 0.787 | 0.950 | 0.878 | 0.576 | 0.385 | 0.729 |
| 1 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |
| 2 | 0.986 | 0.989 | 0.994 | 0.996 | 0.993 | 0.986 | 0.981 | 0.990 |
| 3 | 0.532 | 0.436 | 0.419 | 0.526 | 0.476 | 0.390 | 0.342 | 0.436 |
| 4 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| Japan Simple | All | 0.561 | 0.582 | 0.601 | 0.885 | 0.759 | 0.389 | 0.219 | 0.574 |
| 1 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |
| 2 | 0.430 | 0.443 | 0.458 | 0.519 | 0.478 | 0.398 | 0.362 | 0.439 |
| 3 | 0.011 | 0.012 | 0.015 | 0.022 | 0.017 | 0.011 | 0.007 | 0.012 |
| 4 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |

Table E1. The results for the primary efficacy endpoint for selected sub-populations

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Population | Total # of Subjects, N | Drug A: # Subjects with events (Event rate), n (%/year) | Drug B: # Subjects with events (Event rate), n (%/year) | HR of Drug A /Drug B (95% CI) | Upper 95% CI based on Global CI | Category |
| Global | 15421 | 183 (1.13) | 230 (1.39) | 0.81 (0.68, 0.97) |  |  |
| Country C18 | 1609 | 18 (0.96) | 29 (1.52) | 0.63 (0.36, 1.10) | 0.75 | 1 |
| Country C22 | 1255 | 16 (1.13) | 16 (1.24) | 0.91 (0.49, 1.70) | 1.09 | 2 |
| Country C28 | 752 | 25 (3.47) | 23 (3.24) | 1.07 (0.63, 1.82) | 1.28 | 2 |
| Country C31 | 830 | 12 (1.35) | 9 (1.01) | 1.33 (0.59, 3.00) | 1.59 | 3 |
| Country C34 | 289 | 3 (0.80) | 2 (0.44) | 1.82 (0.30, 10.99) | 2.18 | 4 |

Table E2. Values of posterior probability (*Pc*) for various values of weight (γ) for Countries C28 and C31

|  |  |  |
| --- | --- | --- |
| **γ** | ***Pc*for C28** | ***Pc*for C31** |
| 0.0 | 1.00 | 1.00 |
| 0.1 | 0.98 | 0.90 |
| 0.2 | 0.96 | 0.83 |
| 0.3 | 0.94 | 0.77 |
| 0.4 | 0.92 | 0.72 |
| 0.5 | 0.91 | 0.68 |
| 0.6 | 0.89 | 0.65 |
| 0.7 | 0.88 | 0.62 |
| 0.8 | 0.86 | 0.59 |
| 0.9 | 0.85 | 0.57 |
| 1.0 | 0.84 | 0.55 |