Supplemental Table. Comparison of individual serious adverse events (SAE) and their time to onset and resolution between treatment arms

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | MLC601 | Placebo | OR\*\* (95% CI) | p value |
|  | n/m (%) | n/m (%) |  |
| **Summary of individual SAEs** |  |  |  |  |
| SAE with ≥1 impact\*  | 52/64 (81.3) | 82/98 (83.7) | 0.85 (0.36, 1.97) | 0.70 |
| SAE with ≥2 impacts\* | 5/64 (7.8) | 15/98 (15.3) | 0.47 (0.16, 1.41) | 0.18 |
| **Time to onset of individual SAEs** | median  | median  |  | p *++* |
|   in subjects with any SAE (day) | 26.5  | 16.5 |  | 0.23 |
| in subjects surviving with any SAE (day) | 23.0  | 17.5  |  | 0.57 |
| in hospitalised subjects surviving with any SAE (day)## | 34.0  | 23.0  |  | 0.36 |
| SAE inducing new and/or prolonged hospitalisation in hospitalised subjects surviving with any SAE (day) | 34.0  | 22.0 |  | 0.30 |
| **Time to onset of first SAEs**  | median (95% CI) | median (95% CI) |  | p∞ |
| in subjects with any SAE (day) | 24.50 (11.0, 34.0) | 12.0 (8.0, 18.0) |  | 0.21 |
| in subjects surviving with any SAE (day) | 22.0 (10.0, 34.0) | 14.50 (8.0, 24.0) |  | 0.62 |
| in hospitalised subjects surviving with any SAE (day)## | 34.0 (16.0, 40.0) | 17.0 (8.0, 29.0) |  | 0.21 |
| SAE inducing new and/or prolonged hospitalisation in hospitalised subjects surviving with any SAE (day) | 34.0 (17.0, 40.0) | 17.0 (8.0, 29.0) |  | 0.23 |
| **Time to resolution of individual SAEs** | median (95% CI) | median (95% CI) | HR$ (95% CI) | p value*#* |
| in subjects with any SAE (day) | 13.0 (7.0, 34.0) | 11.0 (6.0, 18.0) | 0.96 (0.69, 1.33) | 0.81 |
| SAE inducing new and/or prolonged hospitalisation in hospitalised subjects surviving with any SAE (day) | 7.0 (5.0, 13.0) | 11.0 (5.0, 18.0) | 1.40 (0.96, 2.05) | 0.08 |
| SAE inducing prolonged hospitalisation in hospitalised subjects surviving with any SAE (day) | 7.0 (3.0, 32.0) | 20.0 (5.0, 61.0) | 2.46 (1.12, 5.43) | 0.03 |
| **Time to resolution of first SAE by onset** |  |  |  |  |
| in subjects with any SAE (day) | 14.0 (7.0, 43.0) | 14.0 (7.0, 27.0) | 0.95 (0.66, 1.37) | 0.78 |
| in hospitalised subjects surviving with any SAE (day)## | 7.0 (5.0, 13.0) | 11.0 (5.0, 18.0) | 1.28 (0.83, 1.96) | 0.26 |
| SAE inducing new and/or prolonged hospitalisation in hospitalised subjects surviving with any SAE (day) | 7.0 (5.0, 13.0) | 11.0 (5.0, 18.0) | 1.45 (0.97, 2.17) | 0.07 |
| SAE inducing prolonged hospitalisation in hospitalised subjects surviving with any SAE (day) | 7.0 (3.0, 32.0) | 18.0 (5.0, 52.0) | 2.37 (1.04, 5.38) | 0.04 |

n/m (%): number and percentages of SAEs where m is denominator. OR: odds-ratio. CI: confidence interval. HR: hazard ratio. For SAEs that had an outcome of death, time to resolution of SAE is censored at date of death. For SAEs that had an outcome of ongoing or unknown, time to resolution is censored at last contact with the subjects. 'Subjects surviving' in the table above means subjects did not die during study follow-up. \*SAE impacts: New and/or prolonged hospitalisation; Life-threatening event; Disability/Incapacity; Important medical events.

\*\* The odds ratio was estimated from a logistic regression model using the Generalized Estimating Equations (GEE) method for clustered binary data.

$ The hazard ratio was estimated from the marginal Cox model approach using a robust sandwich covariance estimate for clustered event data.

# p-value was based on Wald test of the parameter estimate from the model.

∞ Log-rank test.

## Analysis includes all SAEs in subjects who were surviving during study follow-up, and had an SAE that satisfied the SAE criterion of new and/or prolonged hospitalisation.

++ p-value for Clustered Wilcoxon Rank Sum Statistic.