**Keppra Study Report R-168**

1. **Patient demographics**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Stratified by Behavioral Event | | P-Value |
| Variable | No (N=550) | Yes (N=415) |  |
| Age (mean (SD)) | 59.53 (18.33) | 60.84 (18.86) | 0.277 |
| Ethnicity (%) |  |  | 0.646 |
| White | 267 (48.5) | 217 (52.3) |  |
| Black or African American | 250 (45.5) | 174 (41.9) |  |
| Other | 24 ( 4.4) | 19 ( 4.6) |  |
| Unknown | 9 ( 1.6) | 5 ( 1.2) |  |
| Gender (%) |  |  | 0.454 |
| Male | 281 (51.1) | 223 (53.7) |  |
| Female | 269 (49.9) | 192 (46.3) |  |
| Diagnosis (%) |  |  |  |
| CEREBRAL INFARCTION | 151 (27.5) | 101 (24.3) |  |
| INTRACEREBRAL HEMORRHAGE | 166 (30.2) | 136 (32.8) |  |
| SUBARACHNOID HEMORRHAGE | 84 (15.3) | 53 (12.8) |  |
| Traumatic intracranial injury | 149 (27.1) | 125 (30.1) | 0.475 |
| GCS (mean (SD)) | 11.23 (4.32) | 11.02 (4.36) | <0.001 |
| Discharge.Disposition (%) |  |  |  |
| Disch to Rehab Unit/Facility | 87 (15.8) | 98 (23.6) |  |
| Disch to SNF | 79 (14.4) | 123 (29.6) |  |
| Expired | 114 (20.7) | 46 (11.1) |  |
| Home | 224 (40.7) | 98 (23.6) |  |
| Hospice | 18 ( 3.3) | 29 ( 7.0) |  |
| Other | 28 ( 5.1) | 21 ( 5.1) | <0.001 |
| Length of Stay Hospital (mean (SD)) | 12.25 (13.41) | 20.57 (30.05) | <0.001 |
| Length of Stay ICU (mean (SD)) | 8.21 (10.07) | 13.47 (26.81) | <0.001 |
| Total Keppra Doses (mean (SD)) | 13.21 (13.24) | 20.68 (21.19) | <0.001 |
| Keppra Duration (mean (SD)) | 6.38 (7.59) | 10.98 (15.74) | <0.001 |
| log Length of Stay Hospital (mean (SD)) | 0.89 (0.44) | 1.13 (0.39) | <0.001 |
| log Length of Stay ICU (mean (SD)) | 0.67 (0.47) | 0.88 (0.45) | <0.001 |
| log Total Keppra Doses (mean (SD)) | 0.95 (0.41) | 1.16 (0.38) | <0.001 |
| log Keppra Duration (mean (SD)) | 0.72 (0.36) | 0.92 (0.36) | <0.001 |
| Rass less than -3 (%) |  |  | <0.001 |
| Yes | 236 (42.9) | 238 (57.3) |  |
| No | 314 (57.1) | 177 (42.7) |  |
| Median Keppra Dose (%) |  |  | NaN |
| 250 | 9 ( 1.6) | 7 ( 1.7) |  |
| 500 | 359 (65.3) | 251 (60.5) |  |
| 750 | 80 (14.5) | 68 (16.4) |  |
| 1000 | 74 (13.5) | 58 (14.0) |  |
| 1250 | 0 ( 0.0) | 2 ( 0.5) |  |
| 1500 | 23 ( 4.2) | 19 ( 4.6) |  |
| 1750 | 0 ( 0.0) | 1 ( 0.2) |  |
| 2000 | 4 ( 0.7) | 9 ( 2.2) |  |
| 3000 | 1 ( 0.2) | 0 ( 0.0) |  |
| Missing | 0 ( 0.0) | 0 ( 0.0) |  |
| Received Benzo (%) |  |  | <0.001 |
| Yes | 181 (32.9) | 210 (50.6) |  |
| No | 369 (67.1) | 205 (49.4) |  |
| CIWA Orders (%) |  |  | <0.001 |
| Yes | 58 (10.5) | 111 (26.7) |  |
| No | 492 (89.5) | 304 (73.3) |  |
| Pain Scores (%) |  |  | 0.27 |
| 0-3 | 162 (29.5) | 108 (26.0) |  |
| 4-10 | 388 (71.5) | 307 (74.0) |  |
| Received IV opioid (%) |  |  | 0.143 |
| Yes | 417 (75.8) | 332 (80.0) |  |
| No | 133 (24.2) | 83 (20.0) |  |
| AED Received while on Keppra (%) |  |  | <0.001 |
| Yes | 58 (10.5) | 81 (19.5) |  |
| No | 492 (89.5) | 334 (81.5) |  |
| Times RASS less neg3 (mean (SD)) | 29.72 (47.04) | 21.02 (26.97) | 0.014 |
| Times RASS evaluated (mean (SD)) | 83.66 (86.84) | 141.90 (121.69) | <0.001 |
| Percent RASS less neg3 (mean (SD)) | 49.98 (39.14) | 20.71 (28.02) | <0.001 |

1. Multiple Logistic Regression

|  |  |  |  |
| --- | --- | --- | --- |
| **Potential Confounder** | **Estimate** | **Std. Error** | **P-Value** |
| Intercept | -0.82511 | 0.16625 | <0.0001 |
| Rass < -3 (Yes) | 0.44526 | 0.15008 | 0.00301 |
| Received Benzo (Yes) | 0.60455 | 0.13926 | <0.0001 |
| Pain Score (4-10) | -0.03888 | 0.15693 | 0.80431 |
| Received IV opioid (Yes) | -0.03454 | 0.1734 | 0.84213 |
| Concurrent AED (Yes) | 0.57265 | 0.19292 | 0.003 |
| Median Keppra Dose (>500) | 0.06692 | 0.14159 | 0.63648 |

Odds Ratios:

|  |  |
| --- | --- |
| **Potential Confounder** | **Odds Ratio (95% CI)** |
| Intercept | 0.438 (0.315, 0.605) |
| Rass < -3 (Yes) | 1.561 (1.164, 2.097) |
| Received Benzo (Yes) | 1.830 (1.394, 2.406) |
| Pain Score (4-10) | 0.962 (0.707, 1.308) |
| Received IV opioid (Yes) | 0.966 (0.688, 1.359) |
| Concurrent AED (Yes) | 1.773 (1.216, 2.595) |
| Median Keppra Dose (>500) | 1.069 (0.809, 1.410) |

1. Multiple linear regression (log transformed)

Hospital length of stay:

|  |  |  |  |
| --- | --- | --- | --- |
| Parameter | Estimate | Std. Error | P-Value |
| Intercept | 0.53027 | 0.03033 | < 0.0001 |
| Behavioral Event (Yes) | 0.17419 | 0.025 | < 0.0001 |
| Rass < -3 (Yes) | 0.08399 | 0.02728 | 0.002135 |
| Received Benzo (Yes) | 0.15454 | 0.02572 | < 0.0001 |
| Pain Scores (4-10) | 0.01013 | 0.02811 | 0.718656 |
| Received IV opioid (Yes) | 0.31914 | 0.03089 | < 0.0001 |
| Concurrent AED (Yes) | 0.12441 | 0.03515 | 0.000421 |
| Median Keppra Dose cat (>500 mg) | 0.03893 | 0.02557 | 0.128192 |

ICU length of stay

|  |  |  |  |
| --- | --- | --- | --- |
| Parameter | Estimate | Std. Error | P-Value |
| Intercept | 0.25513 | 0.03254 | < 0.0001 |
| Behavioral Event (Yes) | 0.12314 | 0.02682 | < 0.0001 |
| Rass < -3 (Yes) | 0.15731 | 0.02926 | < 0.0001 |
| Received Benzo (Yes) | 0.21791 | 0.0276 | < 0.0001 |
| Pain Scores (4-10) | 0.01358 | 0.03016 | 0.653 |
| Received IV opioid (Yes) | 0.33929 | 0.03314 | < 0.0001 |
| Concurrent AED (Yes) | 0.09287 | 0.03771 | 0.014 |
| Median Keppra Dose cat (>500 mg) | 0.02343 | 0.02744 | 0.393 |

1. Cox proportional hazards model

Time to antipsychotic administration:

* Cox Proportional Hazard Ratio Estimates:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Parameter | HR | Lower 95% CI | Lower 95% CI | P-Value |
| Rass < -3 (Yes) | 0.7486 | 0.5372 | 1.0431 | 0.0871 |
| Received Benzo (Yes) | 1.3081 | 0.9697 | 1.7645 | 0.0786 |
| Pain Score (4-10) | 0.9789 | 0.6988 | 1.3712 | 0.9012 |
| Received IV opioid (Yes) | 0.66 | 0.4503 | 0.9673 | 0.0332 |
| Concurrent AED (Yes) | 1.2134 | 0.864 | 1.7041 | 0.2644 |
| Median Keppra Dose (>500) | 0.8971 | 0.6655 | 1.2093 | 0.4759 |

Time to positive CAM:

* Cox Proportional Hazard Ratio Estimates:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Parameter | HR | Lower 95% CI | Lower 95% CI | P-Value |
| Rass < -3 (Yes) | 2.3332 | 1.4172 | 3.8414 | 0.0009 |
| Received Benzo (Yes) | 0.8294 | 0.5668 | 1.2137 | 0.3356 |
| Pain Score (4-10) | 0.8309 | 0.5136 | 1.3443 | 0.4505 |
| Received IV opioid (Yes) | 0.5041 | 0.2919 | 0.8707 | 0.0140 |
| Concurrent AED (Yes) | 0.7438 | 0.4585 | 1.2067 | 0.2306 |
| Median Keppra Dose (>500) | 1.0613 | 0.7247 | 1.5543 | 0.7598 |