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| **Supplemental Table 1.** Mean values of oxidative stress biomarkers by important genetic and clinical ALS characteristics | | | | | | | | | | |
|  |  |  | **Creatinine** |  | **Uric Acid** |  | **Isoprostane** |  | **8-oxo-dG** |  |
|  |  | **N** | **Mean (SD)** | **P value** | **Mean (SD)** | **P value** | **Mean (SD)** | **P value** | **Mean (SD)** | **P value** |
| C9orf72 mutation | |  |  |  |  |  |  |  |  |  |
|  | Positive | 21 | 0.79 (0.21) | 0.82 | 5.02 (1.66) | 0.83 | 1.62 (0.98) | 0.96 | 5.26 (2.75) | 0.62 |
|  | Negative/Unknown | 333 | 0.80 (0.20) |  | 5.09 (1.31) |  | 1.63 (0.98) |  | 4.85 (3.83) |  |
| Cognitive Impairment | |  |  |  |  |  |  |  |  |  |
|  | Dementia | 91 | 0.80 (0.23) | 0.85\* | 4.83 (1.24) | 0.01\* | 1.53 (1.04) | 0.44\* | 5.03 (2.85) | 0.11\* |
|  | ALSci | 151 | 0.79 (0.18) |  | 5.09 (1.36) |  | 1.66 (0.92) |  | 4.81 (2.68) |  |
|  | Normal cognition | 113 | 0.81 (0.21) |  | 5.29 (1.34) |  | 1.65 (1.01) |  | 4.85 (5.36) |  |
| Riluzole | |  |  |  |  |  |  |  |  |  |
|  | Yes | 178 | 0.79 (0.20) | 0.20 | 5.04 (1.40) | 0.51 | 1.76 (1.02) | 0.0083 | 5.12 (4.59) | 0.22 |
|  | No | 168 | 0.81 (0.21) |  | 5.13 (1.26) |  | 1.48 (0.91) |  | 4.62 (2.61) |  |
| Region of Onset | |  |  |  |  |  |  |  |  |  |
|  | Bulbar | 105 | 0.83 (0.21) | 0.05 | 4.77 (1.36) | 0.0037 | 1.51 (0.99) | 0.13 | 4.80 (2.63) | 0.80 |
|  | Spinal/other | 241 | 0.79 (0.20) |  | 5.22 (1.30) |  | 1.68 (0.97) |  | 4.91 (4.19) |  |
| \*P value from spearman correlation | | | | | | | | | | |
| ALSci = ALS cognitive impairment | | | | | | | | | | |

**Supplemental Table 2.** Associations between baseline quartiles of the ALSFRS-R, PCr, and principal component 1 (PC1) with time to death

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| --- | --- | --- | --- | --- |
| **ALSFRS-R** | **ALSFRS-R Values** | **N** | **Hazard Ratio (95% CI)** | **p-value** |
| Quartile 4 | >41 | 75 | 0.35 (0.24, 0.50) | <0.0001 |
| Quartile 3 | 37-41 | 95 | 0.51 (0.38, 0.71) | <0.0001 |
| Quartile 2 | 32-37 | 92 | 0.65 (0.47, 0.90) | <0.01 |
| Quartile 1 | <32 | 93 | 1.0 (ref.) | ref. |
| **Creatinine** | **Creatinine Values** |  |  |  |
| Quartile 4 | >0.90 | 78 | 0.58 (0.39, 0.86) | <0.01 |
| Quartile 3 | 0.80 - 0.90 | 60 | 0.73 (0.50, 1.07) | 0.10 |
| Quartile 2 | 0.60 - 0.8 | 119 | 0.94 (0.69, 1.28) | 0.68 |
| Quartile 1 | <0.60 | 89 | 1.0 (ref.) | ref. |
| **PC1\*** | **PC1 Values** |  |  |  |
| Quartile 4 | >0.90 | 81 | 0.35 (0.24, 0.51) | <0.0001 |
| Quartile 3 | 0.20 - 0.90 | 81 | 0.44 (0.31, 0.62) | <0.0001 |
| Quartile 2 | -0.83 - 0.20 | 80 | 0.71 (0.50, 1.00) | 0.05 |
| Quartile 1 | < -4.28 | 81 | 1.0 (ref.) | ref. |
| \*PC1 is the first principal component from principal components analysis at baseline using the ALSFRS-R, %FVC, and PCr as input variables | | | | |

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| **Supplemental Table 3.** Joint models for longitudinal biomarkers and time to death | | | |
| **Exposure** | **Hazard Ratio** | **95% CI** | **P value** |
| Creatinine (0.1 mg/dL) | 0.62 | (0.51, 0.77) | <0.0001 |
| Uric Acid (0.1 mg/dL) | 0.96 | (0.94, 0.97) | <0.0001 |
| ALSFRS-R (1 unit) | 0.94 | (0.92, 0.94) | <0.0001 |
| Adjusted for sex, race, region of onset, age at case ascertainment, education, Latin ancestry, months between onset and baseline, and BMI at baseline.  CI = confidence interval. | | | |
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