**Supplemental Data**

# Elevated serum creatine kinase in the early stage of sporadic amyotrophic lateral sclerosis

Daisuke Ito, MD, Atsushi Hashizume, MD, PhD, Yasuhiro Hijikata, MD, PhD, Shinichiro Yamada, MD, PhD, Yohei Iguchi, MD, PhD, Madoka Iida, MD, PhD, Yoshiyuki Kishimoto, MD, Hideyuki Moriyoshi, MD, Akihiro Hirakawa, PhD, Masahisa Katsuno, MD, PhD

**Contents:**

**Supplementary Table 1. Muscle-related biomarkers in male and female subjects**

| Male | Baseline | | | Change at 48 weeks | | |
|---|---|---|---|---|---|---|
| | ALS | HC | p-value | ALS | HC | p-value |
| **Blood test** | **ALS (n = 25)** | **HC (n = 13)** | | **ALS (n = 25)** | **HC (n = 13)** | |
| **CK (U/L)** | 266.0 ± 269.9 | 111.1 ± 61.3 | 0.011 | -81.4 ± 158.1 | -4.9 ± 58.3 | 0.039 |
| **log CK** | 2.26 ± 0.39 | 1.99 ± 0.22 | 0.032 | -0.16 ± 0.31 | -0.02 ± 0.14 | 0.065 |
| **Cr (mg/dL)** | 0.75 ± 0.22 | 0.84 ± 0.15 | 0.199 | -0.10 ± 0.15 | 0.03 ± 0.10 | 0.010 |
| **Body composition** | **ALS (n = 25)** | **HC (n = 13)** | | **ALS (n = 25)** | **HC (n = 13)** | |
| **ALST mass (kg)** | 18.46 ± 3.75 | 21.97 ± 2.73 | 0.005 | -2.70 ± 2.41 | -0.62 ± 1.48 | 0.007 |

| Female | Baseline | | | Change at 48 weeks | | |
|---|---|---|---|---|---|---|
| | ALS | HC | p-value | ALS | HC | p-value |
| **Blood test** | **ALS (n = 14)** | **HC (n = 7)** | | **ALS (n = 14)** | **HC (n = 7)** | |
| **CK (U/L)** | 147.4 ± 61.9 | 100.6 ± 38.5 | 0.084 | -69.2 ± 92.3 | 15.3 ± 26.8 | 0.006 |
| **log CK** | 2.13 ± 0.19 | 1.97 ± 0.18 | 0.075 | -0.24 ± 0.30 | 0.05 ± 0.14 | 0.006 |
| **Cr (mg/dL)** | 0.56 ± 0.10 | 0.64 ± 0.06 | 0.060 | -0.08 ± 0.14 | 0.01 ± 0.03 | 0.032 |
| **Body composition** | **ALS (n = 14)[a]** | **HC (n = 7)** | | **ALS (n = 10)** | **HC (n = 7)** | |
| **ALST mass (kg)** | 13.4 ± 1.8 | 14.1 ± 1.5 | 0.412 | -2.20 ± 1.96 | -0.04 ± 0.36 | 0.012 |

[a]Longitudinal data of body compositions was not available in 4 subjects with ALS.

ALS, amyotrophic lateral sclerosis; ALST, appendicular lean soft tissue; CK, creatine kinase; Cr, creatinine; HC, healthy control. Data represent mean ± standard deviation.

**Supplementary Table 2. Correlation between ALSFRS-R and each parameter**

| | Correlation between baseline values and baseline ALSFRS-R | | Correlation between annualized changes and ΔALSFRS-R | |
|---|---|---|---|---|
| | r | p-value | r | p-value |
| **Blood test** | **ALS (n = 39)** | | **ALS (n = 39)** | |
| **CK (U/L)** | 0.233 | 0.154 | 0.327 | 0.042 |
| **log CK** | 0.371 | 0.020 | 0.427 | 0.007 |
| **Cr (mg/dL)** | -0.018 | 0.914 | 0.456 | 0.004 |
| **CysC (mg/L)** | -0.327 | 0.042 | 0.141 | 0.399 |
| **UN (mg/dL)** | -0.229 | 0.160 | 0.201 | 0.220 |
| **UA (mg/dL)** | -0.221 | 0.176 | -0.021 | 0.900 |
| **AST (U/L)** | 0.062 | 0.709 | 0.179 | 0.274 |
| **ALT (U/L)** | -0.078 | 0.638 | 0.359 | 0.025 |
| **T-Bil (mg/dL)** | 0.087 | 0.613 | 0.083 | 0.629 |
| **ALP (U/L)** | -0.107 | 0.517 | 0.129 | 0.441 |
| **γ-GTP (U/L)** | -0.163 | 0.321 | -0.005 | 0.974 |
| **TP (g/dL)** | 0.182 | 0.269 | 0.262 | 0.108 |
| **Alb (g/dL)** | 0.341 | 0.034 | 0.144 | 0.382 |
| **LDH (U/L)** | 0.424 | 0.007 | 0.337 | 0.039 |
| **LDL-C (mg/dL)** | 0.111 | 0.507 | 0.004 | 0.980 |
| **HDL-C (mg/dL)** | 0.266 | 0.107 | 0.154 | 0.362 |
| **HbA1c (%)** | -0.341 | 0.034 | 0.451 | 0.005 |
| **WBC ($10^3$/μL)** | 0.028 | 0.864 | -0.790 | 0.633 |
| **Hb (g/dL)** | 0.042 | 0.801 | -0.052 | 0.753 |
| **Plt ($10^3$/μL)** | 0.120 | 0.467 | -0.197 | 0.228 |
| **Body composition** | **ALS (n = 39)[a]** | | **ALS (n = 35)** | |
| **ALST mass (kg)** | -0.069 | 0.677 | 0.381 | 0.024 |
| **BMC (kg)** | -0.138 | 0.403 | 0.436 | 0.009 |
| **Total fat mass(kg)** | -0.084 | 0.613 | 0.562 | <0.001 |

[a]Longitudinal data of body compositions was not available in 4 subjects with ALS.

Alb, albumin; ALP, alkaline phosphatase; ALS, amyotrophic lateral sclerosis; ALST, appendicular lean soft tissue; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMC, bone mineral content; CK, creatine kinase; Cr, creatinine; CysC, cystatin C; γ-GTP, gamma glutamyl transpeptidase; Hb, hemoglobin; HbA1c, hemoglobin A1c; HC, healthy control; HDL-C, high-density lipoprotein cholesterol; LDH, lactate dehydrogenase; LDL, low-density lipoprotein

cholesterol; Plt, platelet count; T-Bil, total bilirubin; TP, total protein; UA, uric acid; UN, uric nitrate; WBC, white blood cell count. Data represent mean ± standard deviation.