

Supplementary Online Content

Lunetta C, Lizio A, Maestri E, et al. Serum C-reactive protein as a prognostic biomarker in amyotrophic lateral sclerosis. *JAMA Neurol*. Published online April 3, 2017. doi:10.1001/jamaneurol.2016.6179

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This supplementary material has been provided by the authors to give readers additional information about their work.

| eTable 1. Survival Analysis in Discovery and Validation Cohorts | | | | |
|--|---------------------------------------|----------------|--|----------------|
| | Discovery Cohort (n = 394) | P Value | Validation Cohort (n = 122) | P Value |
| HR of survival per unit of score [95% CI] | 1.129 [1.033-1.234] | .0071* | 1.044 [1.016-1.056] | .0009* |

Abbreviation: HR, Hazard Ratio

**adjusted for age, sex, body mass index and smoke*

| eTable 2. Demographic and Clinical Characteristics at Baseline of the Patients in Each Group of Treatment | | | | |
|--|--|--|----------------------------|----------------|
| | NP001 1 mg/kg/dose Group (n=42) | NP001 2 mg/kg/dose Group (n=36) | Placebo Group (n=35) | <i>P</i> Value |
| Age, y | 53.71±12.65 | 53.67±10.99 | 53.68±9.68 | .9998 |
| Age at onset, y | 51.83±12.49 | 52.23±11.07 | 52.28±9.57 | .9816 |
| ALS Duration, mo | 22.52±9.40 | 17.23±8.36 | 16.85±8.26 | .0069 |
| Baseline CRP, mg/dL* | 1.41 [0.83-2.27] | 0.96 [0.54-3.47] | 1.03 [0.59-2.86] | .2265 |
| ALSFRS-R score at baseline | 38.02±5.10 | 38.47±5.07 | 39.68±3.51 | .2855 |
| Sex, No. (%) | | | | .9001 |
| • Male | 30 (71.43) | 24 (66.67) | 24 (68.57) | |
| • Female | 12 (28.57) | 12 (33.33) | 11 (31.43) | |
| Type of ALS, No. (%) | | | | .0835 |
| • Familial | 0 (0) | 2 (5.56) | 4 (11.43) | |
| • Sporadic | 42 (100) | 34 (94.44) | 31 (88.57) | |
| Site of ALS onset, No. (%) | | | | .9578 |
| • Bulbar | 8 (19.05) | 6 (16.67) | 6 (17.14) | |
| • No-Bulbar | 34 (80.95) | 30 (83.33) | 29 (82.86) | |

All values are reported as mean ± SD unless otherwise indicated

Abbreviations: No., number of patients; y, year; mo, month; CRP, C-reactive protein; ALSFRS-R,

Amyotrophic Lateral Sclerosis Functional Rating Scale - Revised

* *Median and range are reported*

| eTable 3. Changes of ALSFRS-R From Baseline Through the End of the Treatment Period and Follow-up in Each Group of Treatment | | | | | | | | | |
|--|--------------------------|----------------|----------------|--------------------------|----------------|----------------|----------------|----------------|----------------|
| | NP001 1 mg/kg/dose group | | | NP001 2 mg/kg/dose group | | | Placebo group | | |
| Time of evaluation | CRP≤0.20 mg/dL | CRP>0.20 mg/dL | <i>P</i> Value | CRP≤0.20 mg/dL | CRP>0.20 mg/dL | <i>P</i> Value | CRP≤0.20 mg/dL | CRP>0.20 mg/dL | <i>P</i> Value |
| W 1 | 0.00 | 0.00 | . | 0.00 | 0.00 | . | 0.00 | 0.00 | . |
| W 5 | -0.03 | -0.64 | .3483 | -0.81 | -1.10 | .8286 | -0.60 | -1.50 | .0556 |
| W 9 | -1.37 | -0.73 | .5689 | -1.35 | -0.80 | .7346 | -0.96 | -1.70 | .2636 |
| W 13 | -2.67 | -1.55 | .1965 | -2.46 | -1.50 | .8870 | -1.60 | -1.70 | .8684 |
| W 17 | -3.27 | -2.36 | .4493 | -2.88 | -1.60 | .5462 | -3.08 | -2.80 | .9123 |
| W 21 | -3.63 | -2.64 | .4858 | -3.92 | -1.80 | .3115 | -3.52 | -3.80 | .5813 |
| W 25 | -5.00 | -2.82 | .1884 | -4.69 | -2.00 | .1661 | -4.28 | -4.60 | .6993 |
| W 29 | -5.70 | -3.36 | .0837 | -5.62 | -2.10 | .0601 | -4.76 | -6.70 | .1864 |
| W 33 | -7.43 | -5.18 | .2150 | -7.31 | -3.00 | .0454 | -5.64 | -8.00 | .1995 |
| W 37 | -7.90 | -6.55 | .4169 | -7.88 | -3.70 | .0996 | -6.88 | -9.00 | .4521 |

Abbreviations: ALSFRS-R, Amyotrophic Lateral Sclerosis Functional Rating Scale – Revised; W, week;

CRP, C-reactive protein

eTable 4. Changes of ALSFRS-R From Baseline Through the End of the Treatment Period and Follow-up in Each Group of Treatment According to the CRP Serum Level at Baseline

| Time of evaluation | CRP ≤ 0.20 mg/dL | | | | | | CRP > 0.20 mg/dL | | | | | |
|--------------------|------------------|---------|----------------|---------|---------|----------------|------------------|---------|----------------|---------|---------|----------------|
| | Placebo | 1 mg/kg | <i>P</i> Value | Placebo | 2 mg/kg | <i>P</i> Value | Placebo | 1 mg/kg | <i>P</i> Value | Placebo | 2 mg/kg | <i>P</i> Value |
| W 1 | 0.00 | 0.00 | . | 0.00 | 0.00 | . | 0.00 | 0.00 | . | 0.00 | 0 | . |
| W 5 | -0.60 | -0.03 | .6441 | -0.60 | -0.81 | .6271 | -1.50 | -0.64 | .2631 | -1.50 | -1.1 | .4419 |
| W 9 | -0.96 | -1.37 | .6010 | -0.96 | -1.35 | .8342 | -1.70 | -0.73 | .2644 | -1.70 | -0.8 | .4917 |
| W 13 | -1.60 | -2.67 | .1658 | -1.60 | -2.46 | .7472 | -1.70 | -1.55 | .9425 | -1.70 | -1.5 | .9392 |
| W 17 | -3.08 | -3.27 | .8452 | -3.08 | -2.88 | .5389 | -2.80 | -2.36 | .8309 | -2.80 | -1.6 | .4697 |
| W 21 | -3.52 | -3.63 | .7082 | -3.52 | -3.92 | .9395 | -3.80 | -2.64 | .4757 | -3.80 | -1.8 | .2824 |
| W 25 | -4.28 | -5.00 | .4815 | -4.28 | -4.69 | .9547 | -4.60 | -2.82 | .3349 | -4.60 | -2 | .1699 |
| W 29 | -4.76 | -5.70 | .3640 | -4.76 | -5.62 | .7765 | -6.70 | -3.36 | .0756 | -6.70 | -2.1 | .0098 |
| W 33 | -5.64 | -7.43 | .2598 | -5.64 | -7.31 | .2899 | -8.00 | -5.18 | .2420 | -8.00 | -3 | .0294 |
| W 37 | -6.88 | -7.90 | .4974 | -6.88 | -7.88 | .7331 | -9.00 | -6.55 | .4156 | -9.00 | -3.7 | .0277 |

Abbreviations: ALSFRS-R, Amyotrophic Lateral Sclerosis Functional Rating Scale – Revised; W, week;

CRP, C-reactive protein.

eFigure. Correlation Between ALSFRS-R Total Score Slopes and CRP Serum Level Slopes

