10.4.1.2.4 Change in PR-DA chills/ fever score at weeks 9 to 12 and weeks 24 to 28, each compared to weeks -4 to -1 (baseline)

The PR-DA Chills/Fever Score declined from a mean value of 0.26 (SD = 0.53) at baseline (weeks -4 to -1), to a mean value of 0.00 (SD = 0.00) at weeks 9 to 12, and remained at that lower mean value of 0.01 (SD = 0.02) at weeks 25 to 28.

This is a change of -0.26 units (SD = 0.53, p-value = 0.500) from baseline to weeks 9 to 12, resp. a change of -0.25 units (SD = 0.51, p-value = 0.500) from baseline to weeks 25 to 28. Please see figure 10.4.1-1 below for the mean Chills/Fever Score over the study period.

10.4.1.2.5 Change in PR-DA headache score at weeks 9 to 12 and weeks 24 to 28, each compared to weeks -4 to -1 (baseline)

The PR-DA Headache Score declined from a mean value of 3.49 (SD = 1.33) at baseline (weeks -4 to -1), over a mean value of 0.65 (SD = 1.31) at weeks 9 to 12, to a mean value of 0.48 (SD = 0.96) at weeks 25 to 28.

This is a change of -2.83 units (SD = 1.40, p-value = 0.050) from baseline to weeks 9 to 12, resp. a change of -3.01 units (SD = 1.25, p-value = 0.050) from baseline to weeks 25 to 28. Please see figure 10.4.1-1. below for mean Headache Score over study period.

10.4.1.2.6 Change in PR-DA arthralgia score at weeks 9 to 12 and weeks 24 to 28, each compared to weeks -4 to -1 (baseline)

The PR-DA Arthralgia Score declined from a mean value of 3.93 (SD = 1.78) at baseline (weeks -4 to -1), over a mean value of 1.55 (SD = 3.05) at weeks 9 to 12, to a mean value of 0.57 (SD = 1.14) at weeks 25 to 28.

This is a change of -2.38 units (SD = 1.46, p-value = 0.050) from baseline to weeks 9 to 12, resp. a change of -3.35 units (SD = 0.78, p-value = 0.050) from baseline to weeks 25 to 28. Please see figure 10.4.1-1 below for mean Arthralgia Score over study period.

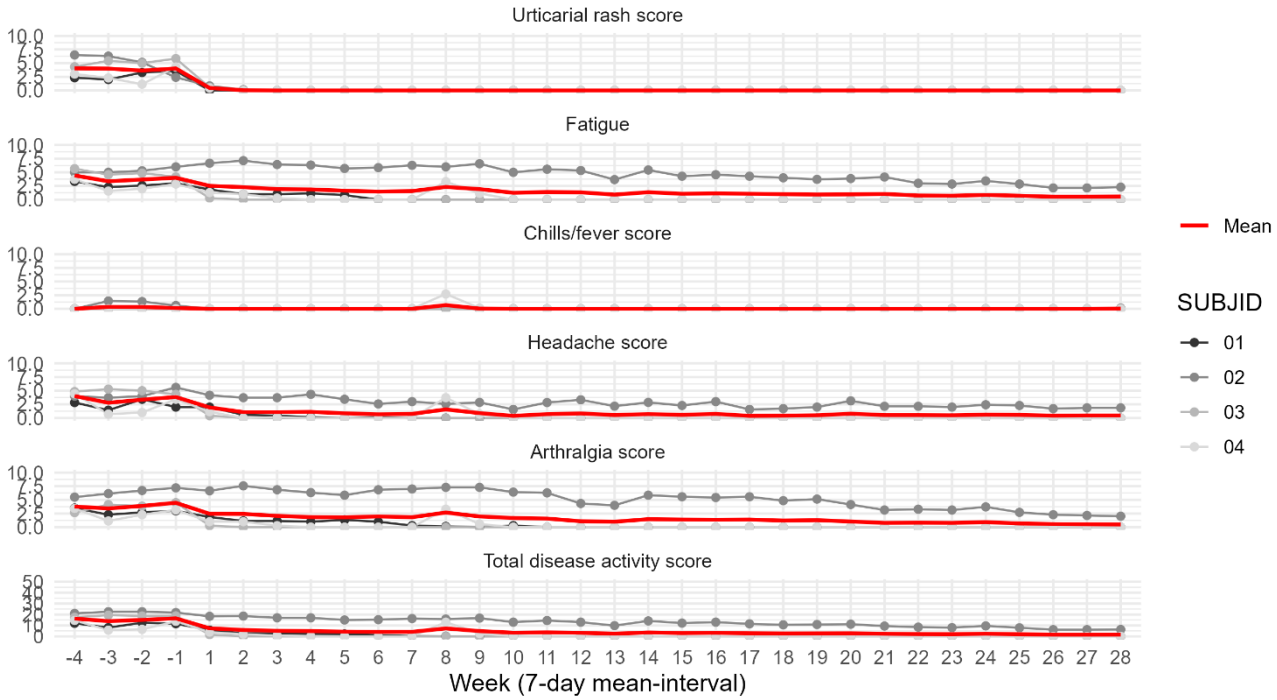


Figure 10.4.1-1: Mean PR-DA scores over study period. Mean Urticarail rash score, Fatique Score, Chills/Fever Score, headache Score, Arthralgia Score, Total disease activity score over time. Time = Weeks (7-day mean-interval).

#### 10.4.1.2.7 Change in disease-specific quality-of-life assessed by Dermatology Life Quality Index (DLQI) over the study (from Baseline to week 12 and week 28)

The DLQI Total Score declined from a mean value of 9.00 (SD = 5.77) at week 0 (Visit 2, Baseline), to a mean value of 0.00 (SD = 0.00) at week 12 (Visit 4), and to a mean value of 0.25 (SD = 0.50) at week 28 (Visit 6).

This is a change of -9.00 units (SD = 5.77, p-value = 0.053) from baseline (Visit 2/week 0) to Visit4/week 12, resp. a change of -8.75 units (SD = 5.38, p-value = 0.047) from baseline to Visit 6/week 28. Please see figure 10.4.1-2 below for DLQI Score over the study period.

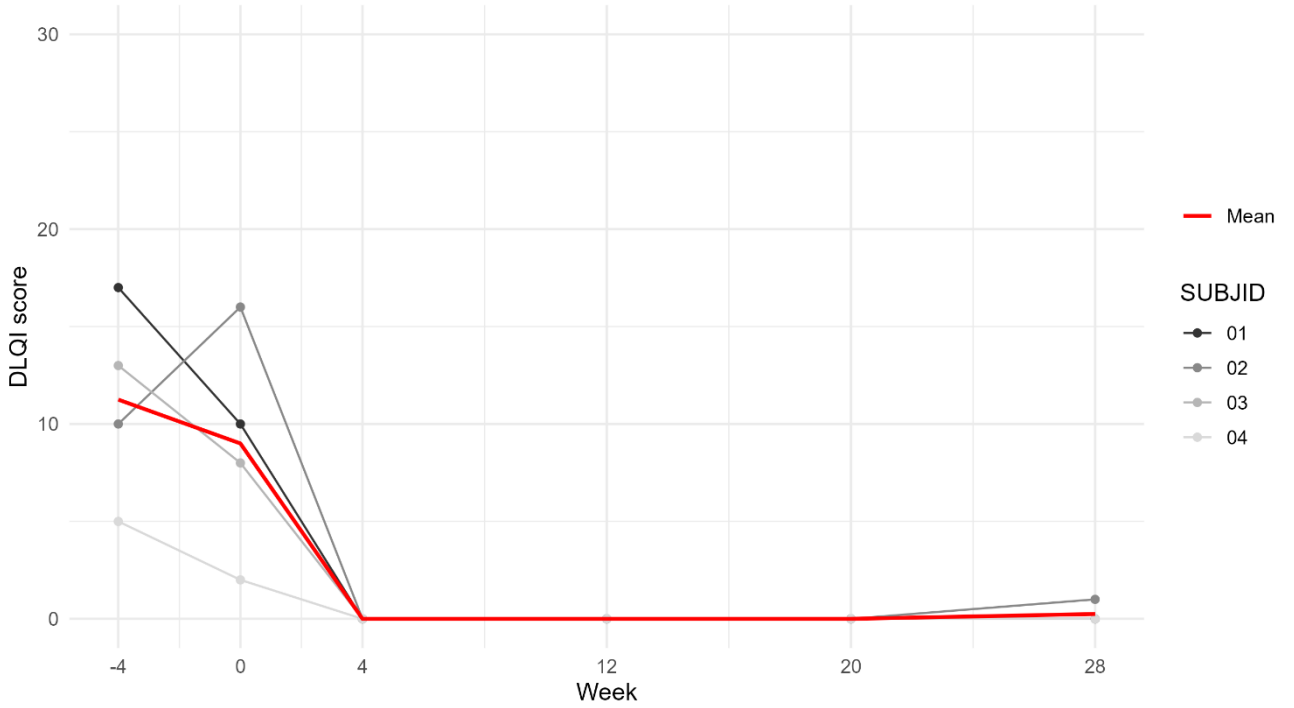


Figure 10.4.1-2: Mean DLQI score over study period.

10.4.1.2.8 Changes in generic quality-of-life assessed by 36-Item Short Form Health Survey (SF-36) (from Baseline to week 12 and week 28).

The SF-36 Mental component summary score increased from a mean value of 42.26 (SD = 15.09) at baseline (week 0/Visit 2), over a mean value of 48.30 (SD = 13.27) for week 12, to a mean value of 50.64 (SD = 7.09) at week 28/Visit 6.

This is a change of +6.04 units (SD = 7.11, p-value = 0.125) from baseline (week 0/Visit 2) to week 12/Visit 4, resp. a change of+8.38 units (SD = 8.93, p-value = 0.062) from baseline (week 0/Visit 2) to week 28/Visit 6.

The SF-36 Physical component summary score increased from a mean value of 41.96 (SD = 15.09) at baseline (week 0/Visit 2) over a mean value of 54.05 (SD = 5.94) for week 12, to a mean value of 55.70 (SD = 4.05) for week 28.

This is a change of +12.09 units (SD = 5.03, p-value = 0.062) from baseline (week 0/Visit 2) to week 12/Visit 4, resp. a change of+13.74 units (SD = 3.77, p-value = 0.062) from baseline (week 0/Visit 2) to week 28/Visit 6. Please see figure 10.4.1-3 below for SF-36 Score over study period.

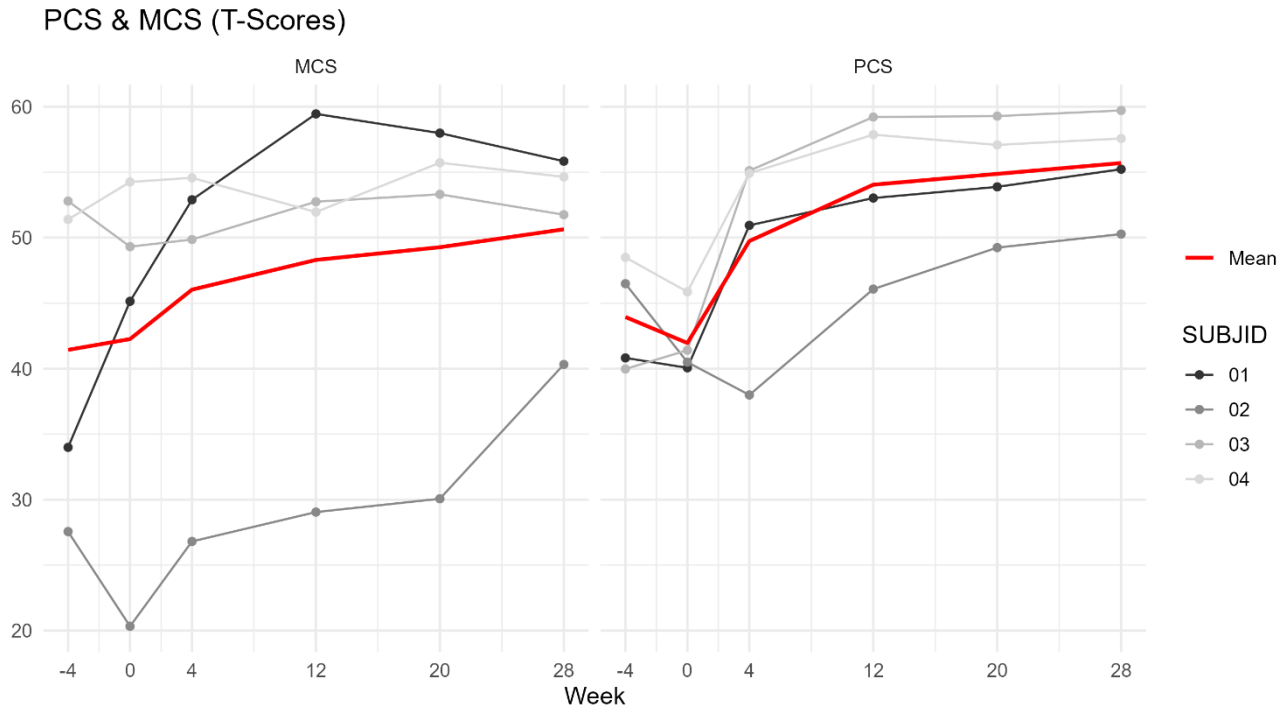


Figure 10.4.1-3: SF-36 score over study period. Physical component summary score (PCS) and Mental component summary score (MCS).

10.4.1.2.9 Change in physician global assessment as assessed by verbal rating scale from 0-10 (0=no symptoms; 10=very severe symptoms) over the study (from Baseline to week 12 and week 28)

The result of the Physician Global Assessment (PGA, where 0 means “no symptoms” and 10 means “very severe symptoms”) declined from 6.00 (SD = 0.96) at week 0 (Baseline/Visit 2), over 0.25 (SD = 0.50) at week 12/Visit 4 to 0.00 (SD = 0.00) at week 28/Visit 6.

This is a change of - 5.75 (SD = 2.63, p-value = 0.050) from baseline (week 0/Visit 2) to week 12/Visit 4, and a change of - 6.00 (SD = 2.83, p-value = 0.049) from baseline (week 0/Visit 2) to week 28/Visit 6. Please see figure 10.4.1-4 for PGA score during study period.

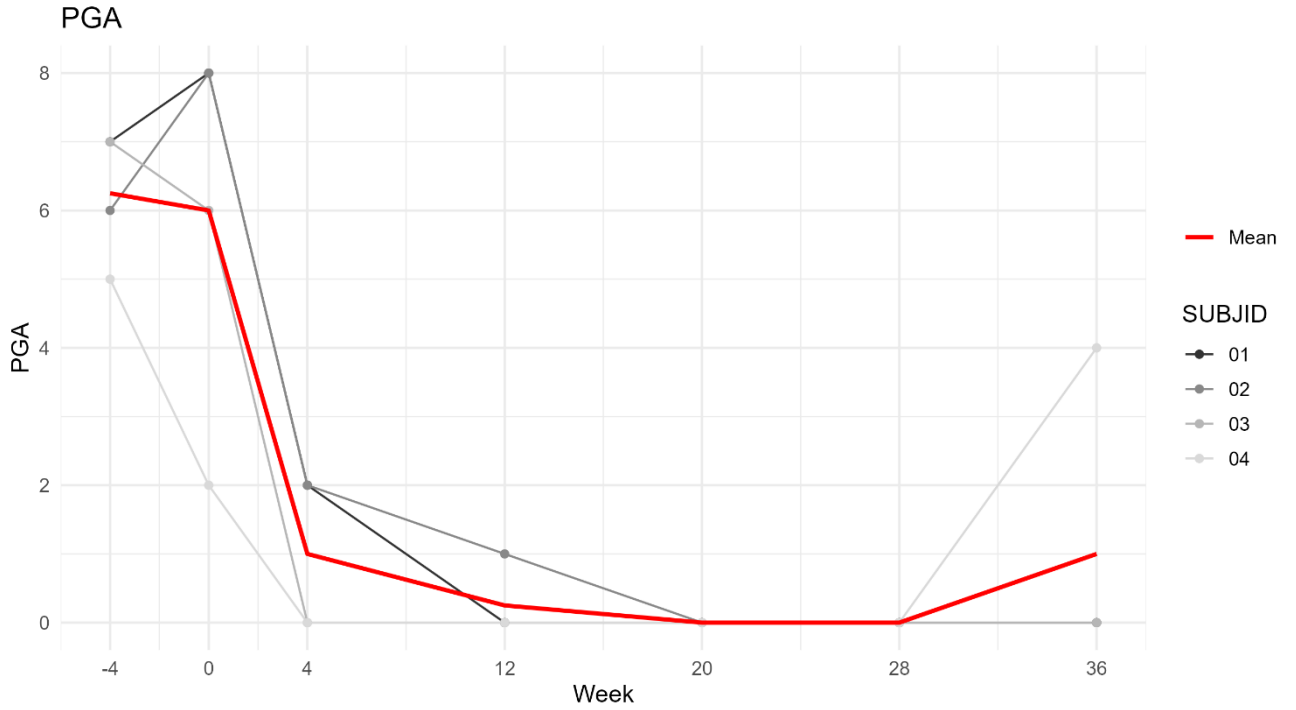


Figure 10.4.1-4: PGA score during study period.

10.4.1.2.10 Changes from Baseline to week 28 of plasma levels of potential biomarkers in Lanadelumab-treated patients

10.4.1.2.10.1 Bradykinin

Plasma levels of bradykinin decreased from 166.66 ng/ml (SD = 177.51) at baseline (week 0/Visit 2) to 30.29 ng/ml (SD = 22.16) at week 12/visit 4 and 19.66 ng/ml (SD = 13.72) at week 28/Visit 6. This is a change of -147.00 ng/ml (SD = 170.45, p-value = 0.125) from baseline (week 0/V2) to week 28/Visit 6. Please see figure 10.4.1-5 for plasma levels of Bradykinin over time.

10.4.1.2.10.2 FXII

Plasma levels of FXII decreased from 43.92 U/l (SD = 8.11) at baseline (week 0/Visit 2) to 20.60 U/l (SD = 6.72) at week 12/visit 4 and 25.03 U/l (SD = 5.64) at week 28/Visit 6. This is a change of -18.33 U/l (SD = 8.10, p-value = 0.125) from baseline to week 28/Visit 6. Please see figure 10.4.1-5 for plasma levels of FXII over time.

10.4.1.2.10.3 Prekallikrein

Plasma levels of prekallikrein increased from 3899.95 ng/ml (SD = 421.34) at baseline (Visit 2) to 5282.33 ng/ml (SD = 1017.64) at week 12/visit 4 and 5104.56 ng/ml (SD = 1493.30) at week 28/Visit 6.

This is a change of +1204.61 ng/ml (SD = 1365.77, p-value = 0.250) from baseline (V2) to week 28 (Visit 6). Please see figure 10.4.1-5 for plasma levels of Prekallikrein over time.

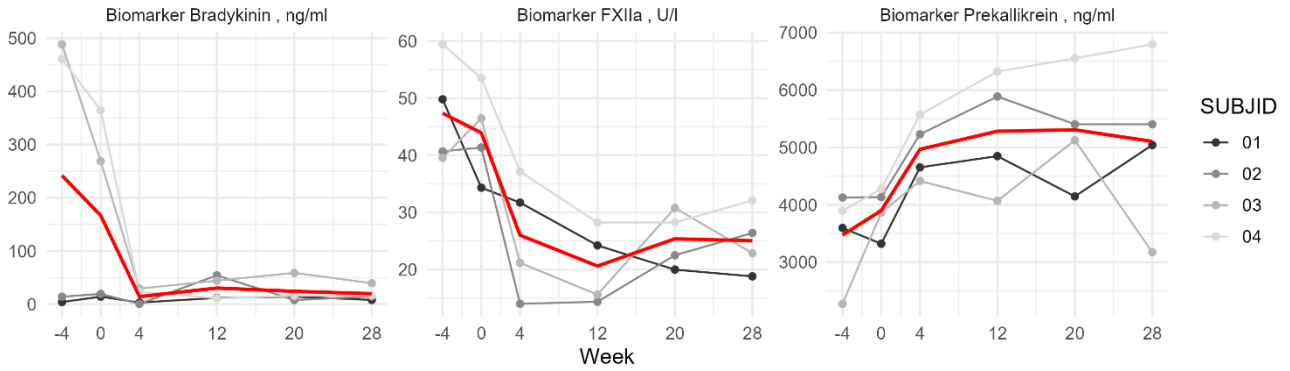


Figure 10.4.1-5: Plasma levels of biomarkers over time

10.4.1.2.11 Change in inflammation markers CRP, ESR, SAA, S100 A8/9 (from Baseline to week 12 and week 28)

10.4.1.2.11.1 hs-CRP

Mean serum levels of CRP changed, from 1.68 mg/L (SD = 2.15) at baseline (week 0/Visit 2), over 1.17 mg/L (SD = 1.08) at week 12/Visit 4, to 1.65 mg/L (SD = 2.10) at week 28/Visit 6. This is a change of -0.50 mg/L (SD = 1.07) from baseline (V2) to week 12 (V4) and a change of -0.03 mg/L (SD = 0.05, p-value = 1.000) from baseline (V2) to week 28 (V6). Upper reference range for hs-CRP is <= 5 mg/L. Please see figure 10.4.1-6 for plasma levels of hs-CRP over time.

10.4.1.2.11.2 ESR

The mean ESR changed, from 9.50 mm/h (SD = 8.89) at baseline (week 0/Visit 2), to 8.25 mm/h (SD = 3.10) at week 12/Visit 4, and to 10.00 mm/h (SD 6.68) at week 28/Visit 6. This is a change of -1.25 mm/h (SD = 9.11, p-value = 0.875) from baseline (V2) to week 12 (V4) and a change of 0.50 mm/h (SD = 9.68, p-value = 1.000) from baseline (V2) to week 28 (V6). Upper reference range for ESR is <= 20 mm/h. Please see figure 10.4.1-6 for plasma levels of ESR over time.

10.4.1.2.11.3 SAA

Mean serum levels of SAA changed, from 7.38 mg/L (SD = 6.66) at baseline (week 0/Visit 2), over 5.97 mg/L (SD = 3.24) at week 12/Visit 4, to 7.30 mg/L (SD 4.98) at week 28/Visit 6. That is a change of -1.40 mg/L (SD = 5.42, p-value = 0,625) from baseline (V2) to week 12 (V4) and a change of -0.07 mg/L (SD = 3.02, p-value = 1.000) from baseline (V2) to week 28 (V6). Upper reference range for SAA is < 6.4 mg/L. Please see figure 10.4.1-6 for plasma levels of SAA over time.

10.4.1.2.11.4 S100 A8/9

Mean serum levels of S100 A8/9 changed, from 0.93 mg/L (SD = 0.55) at baseline (week 0/Visit 2), over 2.38 mg/L (SD = 1.57) at week 12/Visit 4, to 2.43 mg/L (SD = 2.72) at week 28/Visit 6. This is a change of 1.45 mg/L (SD = 1.26, p-value = 0.250) from baseline (V2) to week 12 (V4) and a change of 1.50 mg/L (SD = 2.72, p-value = 0.375) from baseline (V2) to week 28 (V6). Upper reference range for S100 A8/9 is <= ´1.75 mg/L. Please see figure 10.4.1-6 for plasma levels of S100 A8/9 over time.

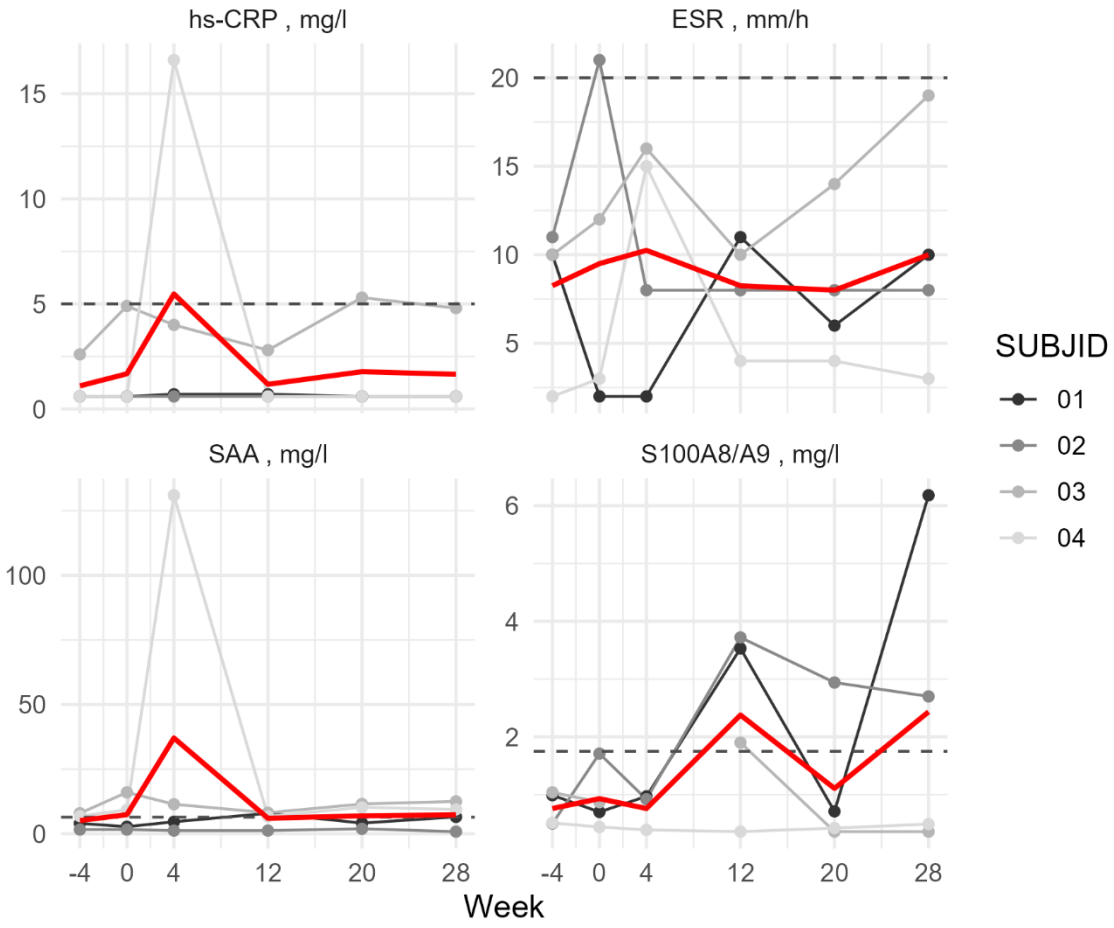


Figure 10.4.1-6: Plasma levels of inflammation markers over time. Upper reference ranges: for hs-CRP <= 5 mg/L; for ESR <= 20 mm/h; for SAA < 6.4 mg/L; for S100 A8/9 <= ´1.75 mg/L.

### 10.4.2 Statistical issues

There was no adjustment for covariates or for multiple comparisons, given the limited sample size; there were also no subgroup or sensitivity analyses performed. No missing value replacement was applied; patients with a missing value on a given measurement were removed from the comparison.

### 10.4.3 Tabulation of individual response data

Not applicable

### 10.4.4 Drug dose, drug concentration, and relationships to response