

Predicting circulating biomarker response and its impact on the survival of advanced melanoma patients treated with adjuvant therapy

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Supplementary Tables

Table S1. Median value (5–95th) of different outcomes obtained after 1000 simulation of different dosing schedules.

| <i>Standard dosing regimen</i> *: induction: 20 MU/m^2 5 days a week + maintenance: 10 MU/m^2 3 days a week | | | | |
|-----------------------------------------------------------------------------------------------------------------|----------------------|---------------------|--------------------|---------------------|
| | 1-year | 2-year | 5-year | 10-year |
| LDHrel | -0.127 (-0.29-0.095) | -0.242 (-0.52-.019) | -0.062 (-0.61-1) | 0.138 (-0.6-1.79) |
| Overall Survival | 91.5 (89.7-93.2) | 83.6 (81.3-85.9) | 58.5 (55.5-61.6) | 29.5 (26.8-32.4) |
| Absolut neutrophil count ($10^9/L$) | 2.14 (1.04-4.07) | 3.21 (1.94-5.36) | 3.17 (1.93-5.66) | 3.92 (2.37-6.15) |
| <i>Regimen 2</i> *: induction: 40 MU/m^2 5 days a week + maintenance: 10 MU/m^2 3 days a week | | | | |
| LDHrel | -0.133 (-0.3-0.088) | -0.247 (-0.53-.018) | -0.07 (-0.62-0.99) | 0.129 (-0.619-1.74) |
| Overall Survival | 91.6 (89.9-93.3) | 83.7 (81.4-86) | 58.8 (55.8-61.9) | 29.7 (27-32.7) |
| Absolut neutrophil count ($10^9/L$) | 2.14 (1.03-4.07) | 3.21 (1.94-5.36) | 3.17 (1.93-5.66) | 3.92 (2.36-6.14) |
| <i>Regimen 3</i> *: induction: 20 MU/m^2 5 days a week + maintenance: 20 MU/m^2 3 days a week | | | | |
| LDHrel | -0.132 (-0.3-0.09) | -0.266 (-0.53-.016) | -0.1 (-0.66-0.94) | 0.134 (-0.66-1.62) |
| Overall Survival | 91.5 (89.8-93.2) | 83.6 (81.3-86) | 59.8 (56.8-62.9) | 31.5 (28.7-34.5) |
| Absolut neutrophil count ($10^9/L$) | 1.4 (0.4-3.27) | 3.21 (1.93-5.36) | 3.15 (1.93-5.66) | 3.87 (2.3-6.1) |

*The treatment started 6 weeks after diagnosis for all the regimens simulated. The treatment was administered to an individual with a body surface area of 1.8 m^2 . LDHrel is the relative change of LDH from the baseline value.

Supplementary Figures

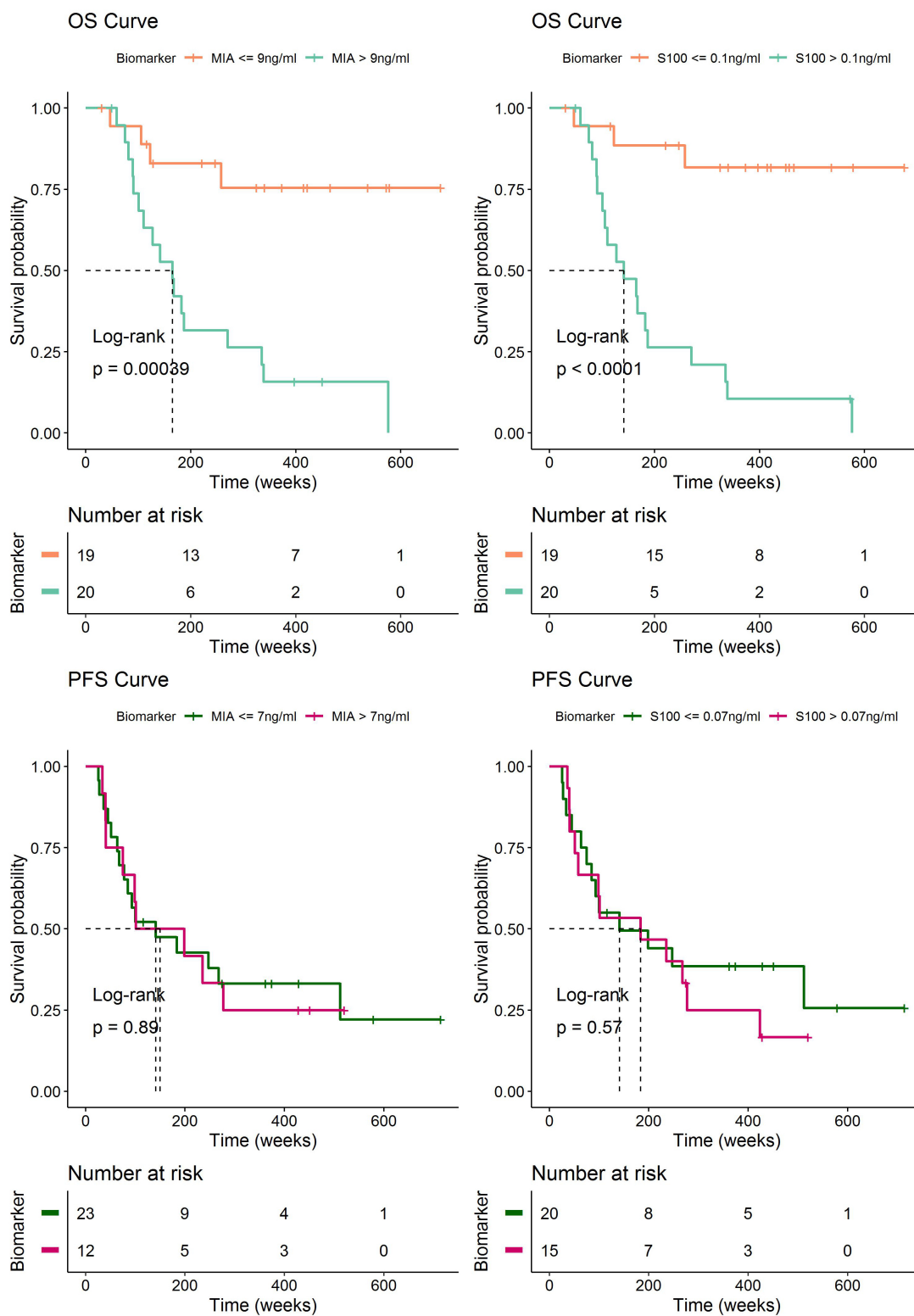


Figure S1. Evaluation of the overall survival (OS) and progression-free survival (PFS) of the patients with high and low MIA and S100B concentrations at the end of the study.

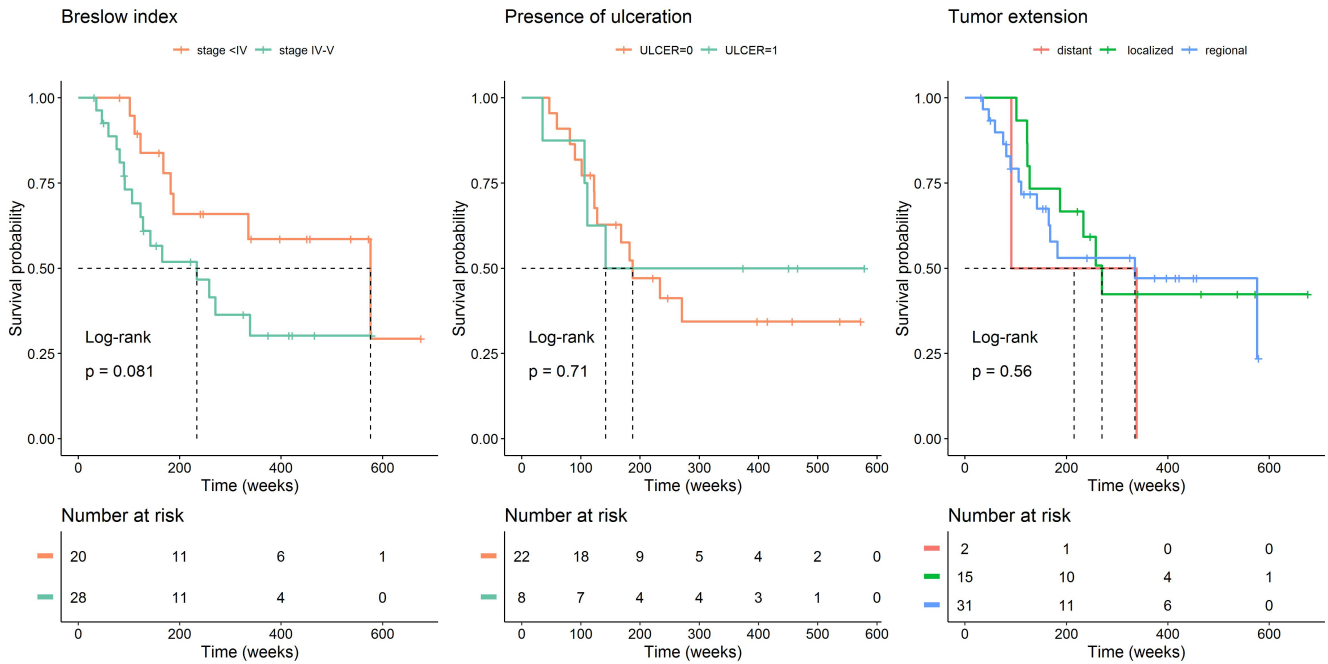


Figure S2. Kaplan-Meier curves of the overall survival stratified by different baseline covariates: Breslow index, the presence of ulceration and the tumor extension.

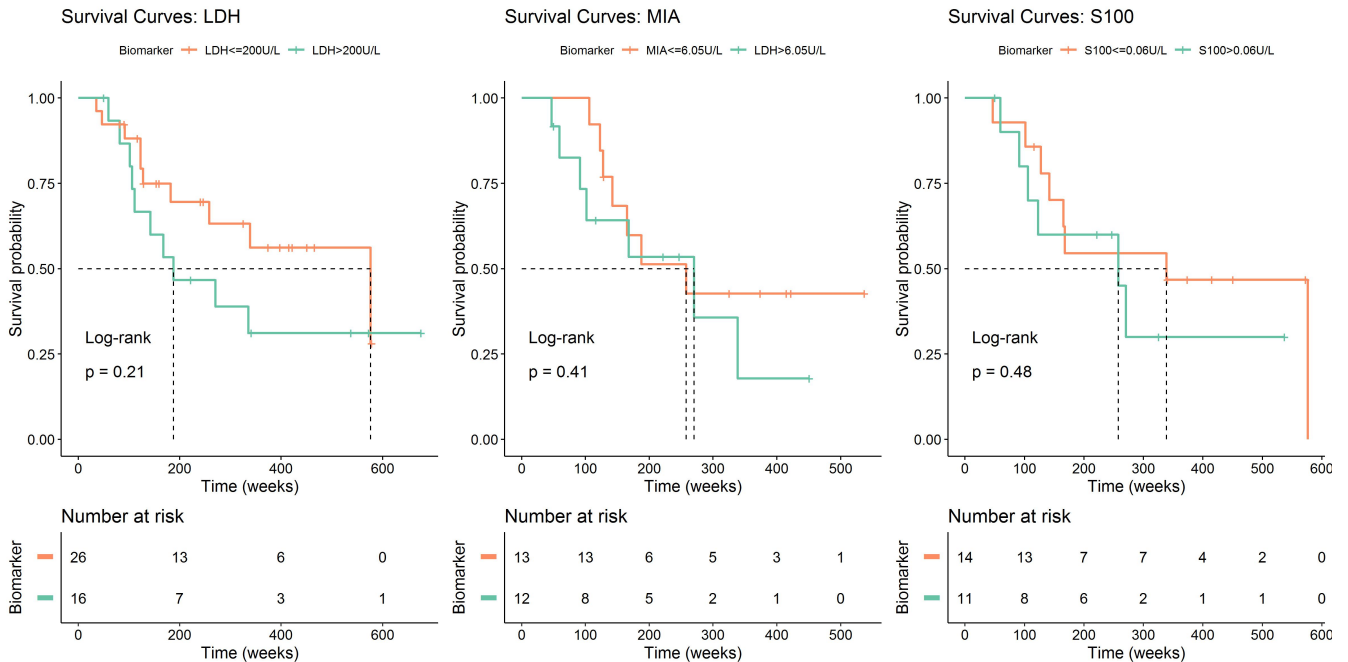


Figure S3. Kaplan-Meier curves of the overall survival stratified by baseline biomarker values (before treatment initiation).

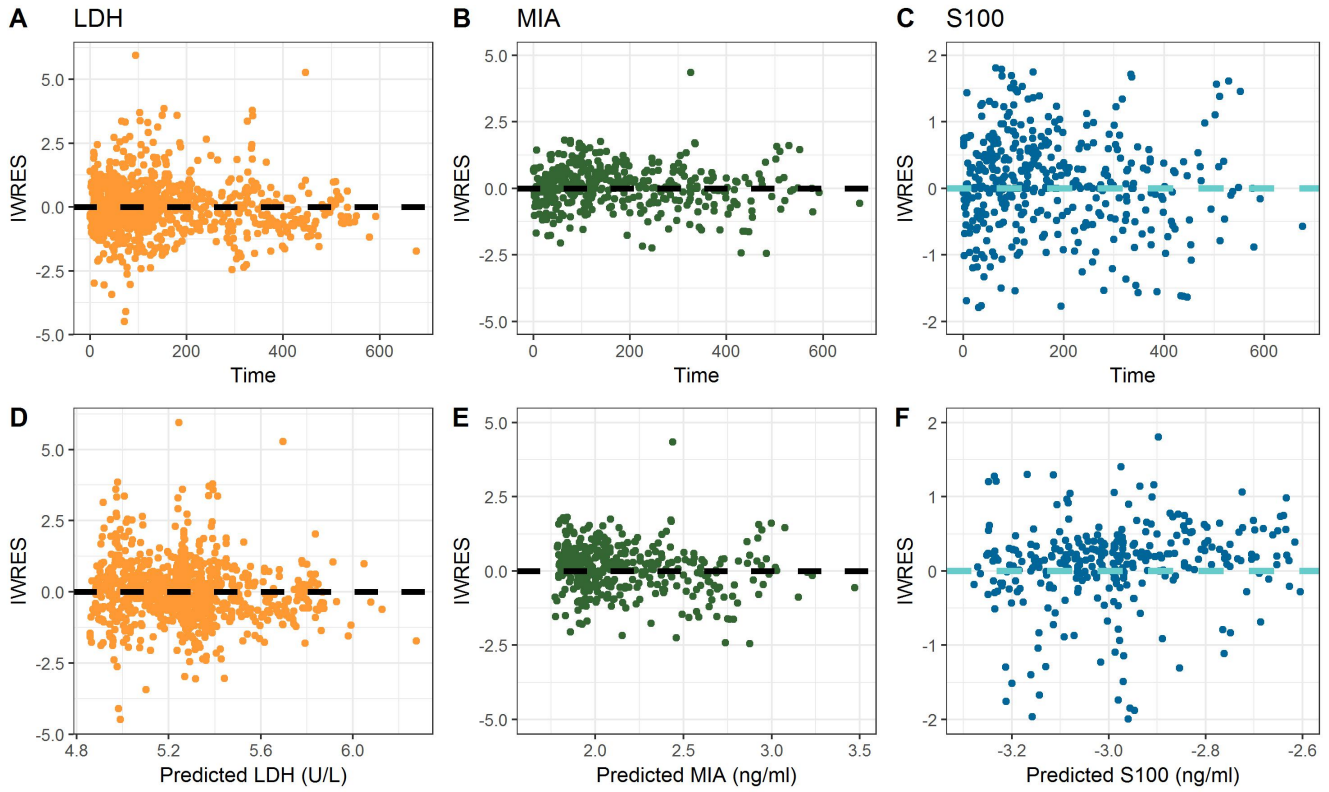


Figure S4. Residual error model diagnostics: Individual Weighted Residuals (IWRES) over time and vs model predictions.

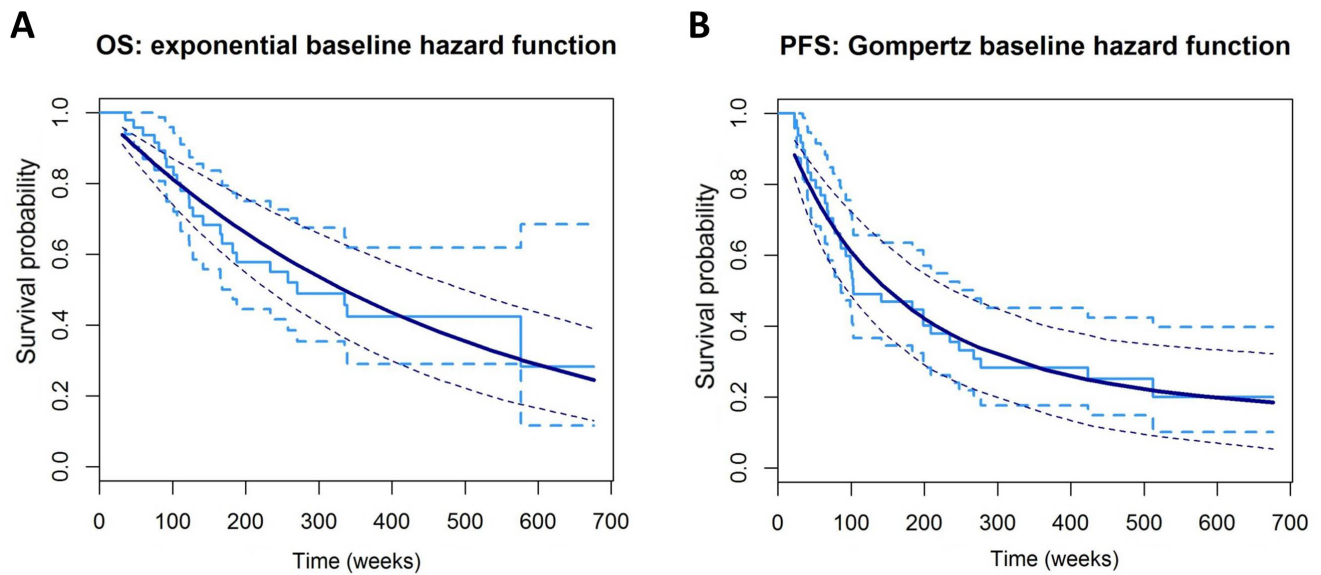


Figure S5. Best fitted models for the baseline hazard function of the overall survival (OS) and progression-free survival (PFS) of the patients. Light blue lines represent raw data and dark blue lines indicate the output of the model (the solid lines represent the median tendency and the dashed lines represent the 95% confidence interval)

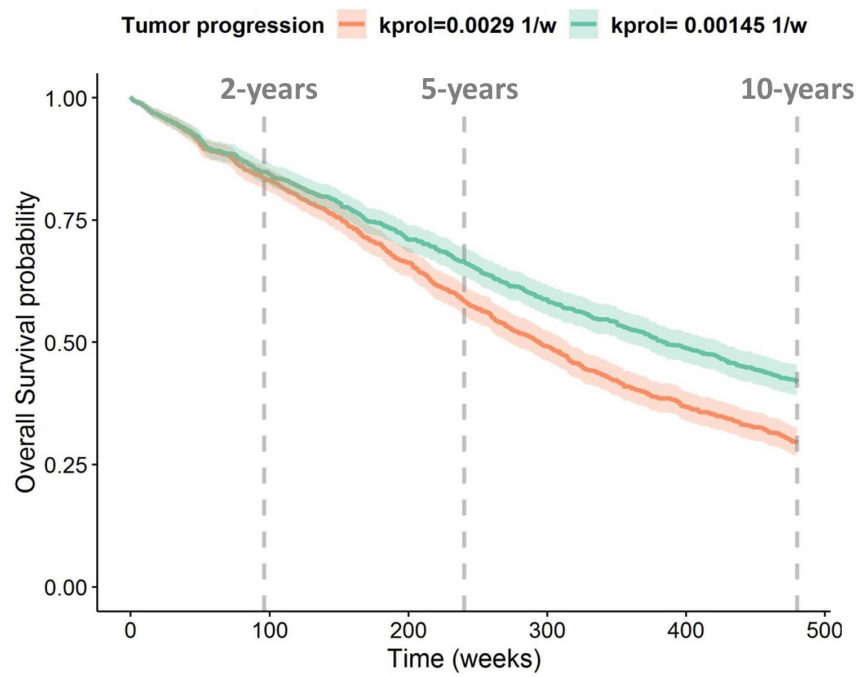


Figure S6. Kaplan Meier overall survival stratified by different values of the tumor proliferation rate constant parameter (k_{prol}). The plot is the result of the simulation of 1000 individuals receiving the treatment in the same time period.