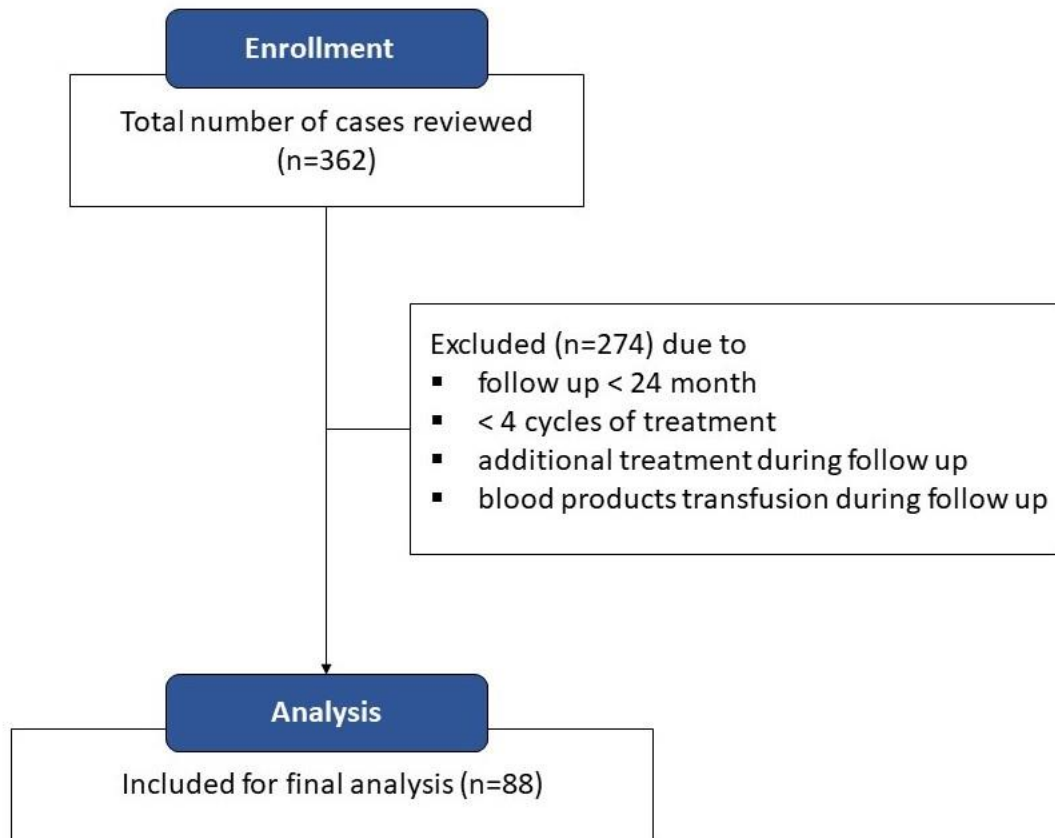
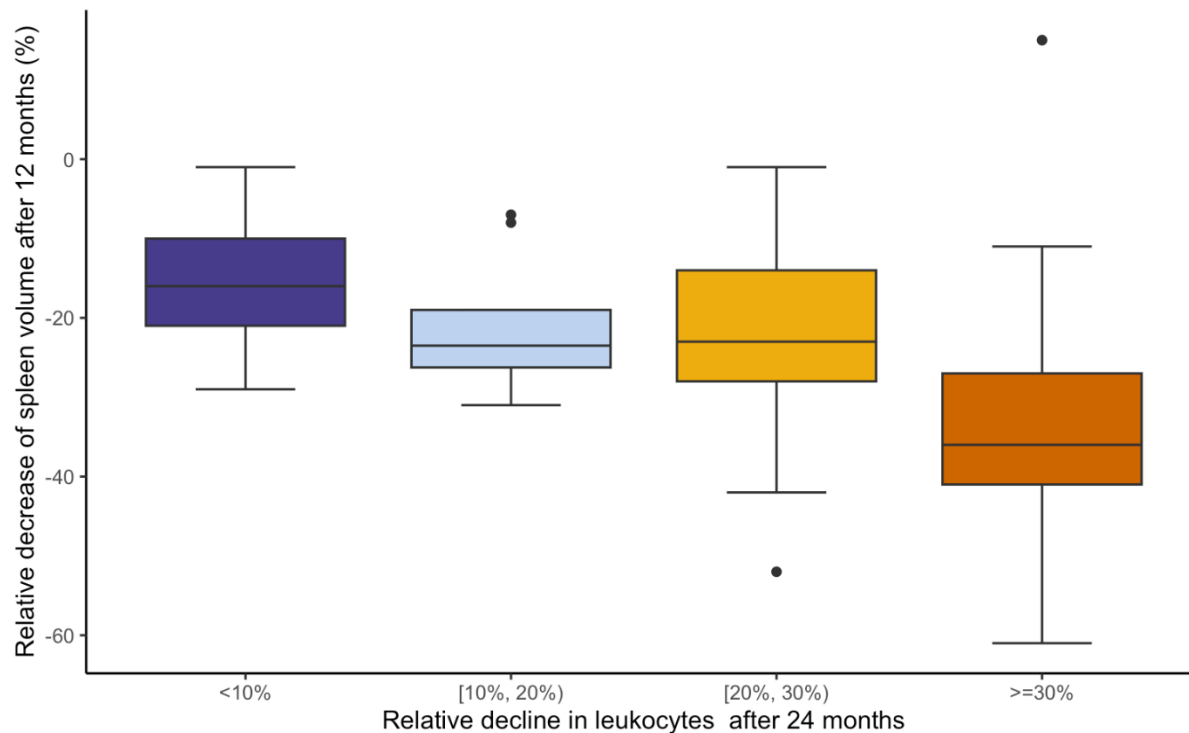


Supplemental Data



Supplemental Figure 1: Patient flow-chart.



Supplemental Figure 2: Relative decline in spleen volume after 12 months for patients stratified by their relative decline in leukocytes after 24 months. Here, we distinguished four different categories: A decline <10%, ≥10% and <20%, ≥20% and <30%, and ≥30%. As shown, the decline in spleen volume differs between the groups, with patients experiencing a higher decline in leukocytes after 24 months also showing a larger decline in spleen volume after 12 months.

| Feature | Patients with leukopenia (24 months) | Patients with normal WBC (24 months) | p-value |
|---|--------------------------------------|--------------------------------------|-------------------|
| Relative decline of spleen volume after 12 months | 0.36 ± 0.14 | 0.19 ± 0.10 | < 0.001 |
| Relative decline of WBC after 12 months | 0.07 ± 0.10 | 0.19 ± 0.17 | 0.002 |
| Weight (kg) | 73.1 ± 15.3 | 80.7 ± 15.4 | 0.03 |
| Relative decline of PLT after 12 months | 0.09 ± 0.15 | 0.17 ± 0.18 | 0.04 |
| PLT count after 12 months (x1.000 mm ³) | 206 ± 48 | 193 ± 58 | 0.30 |
| Hb after 12 months (g/dl) | 11.7 ± 1.8 | 12.1 ± 1.7 | 0.33 |
| Age at therapy onset (years) | 61.7 ± 11.9 | 63.2 ± 10.3 | 0.54 |
| Hb after 24 months (g/dl) | 12.2 ± 1.4 | 12.4 ± 1.7 | 0.58 |
| Baseline Hb (g/dl) | 13.2 ± 1.7 | 13.3 ± 1.7 | 0.74 |
| PLT count after 24 months (x1.000 mm ³) | 193 ± 49 | 190 ± 61 | 0.83 |

Supplemental Table 1: Results from the two-sided t-test for differing between patients developing leukopenia after 24 months and those maintaining normal WBC level. Features are displayed as mean ± standard deviation and decline of features is given relative to the baseline values. Following Bonferroni correction for multiple testing, a p-value of $p < 0.005$ was considered significant, yielding two significant parameters (decline of spleen volume after 12 months as well as reduction of WBC after 12 months).

| Feature | Patients with leukopenia (24 months) | Patients with normal WBC (24 months) | p-value |
|---|--|---|-------------------|
| Baseline WBC count (x1.000 mm ⁻³) | 5.75 ± 1.15 | 6.98 ± 1.79 | < 0.001 |
| Relative decline of PLT after 24 months | 0.14 ± 0.18 | 0.18 ± 0.23 | 0.36 |
| Number of cycles | 6 (4-8) | 6 (4-8) | 0.58 |
| Relative decline of Hb after 12 months | 0.12 ± 0.10 | 0.09 ± 0.12 | 0.62 |
| Baseline PLT count (x1.000 mm ⁻³) | 227 ± 46 | 238 ± 70 | 0.69 |
| Tumor grading | 2 (2-2) | 2 (2-2) | 0.73 |
| Decline of Hb after 24 months (decimal) | 0.07 ± 0.09 | 0.06 ± 0.12 | 0.76 |
| WBC after 12 months (1.000/mm ³) | 5.26 ± 0.91 | 5.47 ± 1.01 | 0.84 |
| Baseline spleen volume (ml) | 229 ± 107 | 243 ± 145 | 0.99 |

Supplemental Table 2: Mann-Whitney U test results comparing patients developing leukopenia after 24 months and those maintaining normal WBC levels. Continuous features are mean ± standard deviation, and for ordinary features, median (IQR) is provided. Feature decline is relative to baseline values. After Bonferroni correction for multiple testing, significance was set at $p < 0.0056$, revealing one significant feature: baseline WBC count.

| Feature | | Patients with leukopenia (24 months) | Patients with normal WBC (24 months) | p-value |
|--|-----|--|--|---------|
| Fisher's exact test, correlation significant if $p < 0.0125$ | | | | |
| SSA | yes | 17 (58.6 %) | 45 (76.3 %) | 0.14 |
| | no | 12 (41.4 %) | 14 (23.7 %) | |
| Primary surgery | yes | 16 (55.2 %) | 29 (49.2 %) | 0.65 |
| | no | 13 (44.8 %) | 30 (50.8 %) | |
| Diabetes mellitus | yes | 4 (13.8 %) | 16 (27.1 %) | 0.19 |
| | no | 25 (86.2 %) | 43 (72.9 %) | |
| Hypertension | yes | 12 (41.4 %) | 20 (33.9 %) | 0.64 |
| | no | 17 (58.4 %) | 39 (66.1 %) | |

Supplemental Table 3: Assessed binary features between the two patient groups at 24 months follow-up analysis. Bonferroni correction for multiple testing yielded a level of significance of $p < 0.0125$. No significant differences were found between the groups.

| <i>Feature</i> | Univariate Logistic Regression | | | Multivariate Logistic Regression | | |
|---|---------------------------------------|-----------|------------------|---|-----------|------------------|
| | <i>OR</i> | <i>CI</i> | <i>p</i> | <i>OR</i> | <i>CI</i> | <i>p</i> |
| Relative decline of spleen volume after 12 months | 1.15 | 1.09-1.23 | <0.001 | 1.16 | 1.09-1.26 | <0.001 |
| Baseline WBC count (x1.000 mm ⁻³) | 0.55 | 0.36-0.78 | 0.003 | 0.63 | 0.34-1.12 | 0.133 |
| Relative decline of WBC count after 12 months | 0.95 | 0.92-0.98 | 0.003 | 0.96 | 0.90-1.01 | 0.125 |

Supplemental Table 4: Results from the uni- and multivariate logistic regression including features significantly associated with patients developing leukopenia after 24 months. While WBC at baseline as well as their relative decline after 12 months are significant in the univariate analysis, only for the relative decline of spleen volume after 12 months the odds ratio remains significantly different from one in the multivariate analysis. Legend: OR = Odds Ratio, CI = Confidence Interval, p = p-value.