$Table \ S1-Univariate \ analysis \ of \ the \ association \ of \ the \ sTXB_2 \ levels \ with \ the \ clinical \ and \ hematologic \ features \ at \ Visit \ 2$

| Variable | Standardized B | Univariate p |
|-------------------------|----------------|--------------|
| Platelet Count | 0.35 | <0.0001 |
| Leukocyte Count | 0.13 | 0.046 |
| Age at enrollment | -0.20 | 0.002 |
| Female Sex | -0.21 | 0.198 |
| JAK2 mutation | 0.42 | 0.09 |
| Body mass index | -0.01 | 0.55 |
| Cytoreductive treatment | -0.73 | <0.0001 |

Table S2. Characteristics of ET patients overall and according to the absence (no) or presence (yes) of cytoreductive drugs at randomization.

| | [ALL] | No | Yes | P overall |
|---------------------------------|------------------------|------------------|------------------|-----------|
| | n=243 | n=98 | n=145 | |
| Sex: | | | | 0.044 |
| Male | 112 (46.1%) | 37 (37.8%) | 75 (51.7%) | |
| Female | 131 (53.9%) | 61 (62.2%) | 70 (48.3%) | |
| Age at enrollme | nt 60.0 [51.0;67.0] | 53.0 [45.0;59.0] | 66.0 [57.0;69.0] | < 0.001 |
| Diagnosis (Years) | 5.00 [2.00;10.0] | 4.00 [2.00;9.00] | 5.00 [3.00;10.0] | 0.034 |
| BMI (kg/m ²) | 25.0 [22.9;27.3] | 24.6 [21.9;26.6] | 25.2 [23.0;28.1] | 0.030 |
| Leukocytes (x10 ⁹ /I | ــ)7.00 [5.66;8.50] | 7.77 [6.73;9.17] | 6.41 [5.15;7.69] | < 0.001 |
| Hematocrit (%) | 41.7 [39.2;44.3] | 43.4 [40.5;45.1] | 40.7 [38.4;43.6] | < 0.001 |
| Platelets (x10 ⁹ /L) | 521 [422;641] | 631 [524;776] | 455 [391;536] | < 0.001 |
| TXB ₂ (ng/ml) | 19.0 [9.20;42.6] | 37.1 [16.0;64.0] | 14.0 [8.00;29.0] | < 0.001 |
| TXM (pg/m creatinine) | ng 428 [318;618] | 407 [303;611] | 438 [326;629] | 0.294 |
| <i>JAK2-V617F</i> ,n (%) |) † | | | 0.140 |
| Wild Type | 99 (40.7%) | 34 (34.7%) | 65 (44.8%) | |
| Mutated | 143 (58.8%) | 64 (65.3%) | 79 (54.5%) | |
| 'Missing' | 1 (0.41%) | 0 (0.00%) | 1 (0.69%) | |
| <i>CALR</i> , n (%): | | | | 0.258 |
| Type 1 | 19 (7.82%) | 6 (6.12%) | 13 (8.97%) | |
| Type 2 | 16 (6.58%) | 4 (4.08%) | 12 (8.28%) | |
| Other | 93 (38.3%) | 35 (35.7%) | 58 (40.0%) | |

| | [ALL] | No | Yes | P overall |
|----------------|-------------|------------|-------------|-----------|
| | n=243 | n=98 | n=145 | |
| 'Missing' | 115 (47.3%) | 53 (54.1%) | 62 (42.8%) | |
| MPL, n (%): | | | | 0.061 |
| Wild Type | 111 (45.7%) | 36 (36.7%) | 75 (51.7%) | |
| Mutated | 6 (2.47%) | 3 (3.06%) | 3 (2.07%) | |
| Not determined | 125 (51.4%) | 59 (60.2%) | 66 (45.5%) | |
| 'Missing' | 1 (0.41%) | 0 (0.00%) | 1 (0.69%) | |
| Microvascular | | | | 0.266 |
| symptoms | | | | 0.200 |
| No | 218 (89.7%) | 91 (92.9%) | 127 (87.6%) | |
| Yes | 25 (10.3%) | 7 (7.14%) | 18 (12.4%) | |
| Previous | | | | 0.000 |
| thrombosis**: | | | | 0.088 |
| No | 234 (96.3%) | 97 (99.0%) | 137 (94.5%) | |
| Yes | 9 (3.70%) | 1 (1.02%) | 8 (5.52%) | |

Quantitative values are reported as median (interquartile range), unless otherwise indicated. Significant differences between the different groups were tested based on the Kruskal-Wallis test or chi-square test for continuous or discrete variables.

Abbreviations: BMI: body mass index; TX: thromboxane.

^{**} Defined as any major thrombosis occurring within 2 years before diagnosis and at any time afterward .

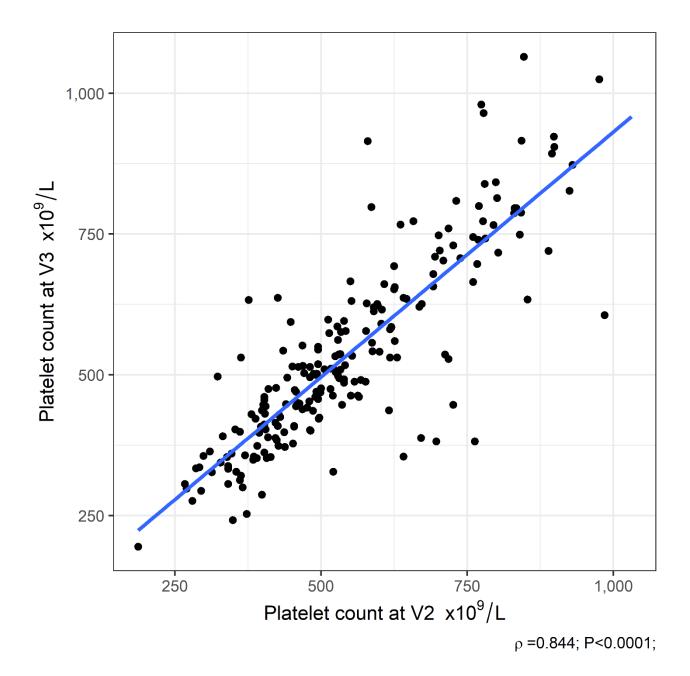


Figure S1. Correlation between platelet count at visit 2 and visit 3. The plots depict the correlation of platelet counts $(x10^9/L)$ at randomization visit 2 (V2) and at the end of the randomized treatment visit 3 (V3).