**Supplementary Table S1. Immunomodulators, immunosuppressants and cytostatic agents for the rescue of patients with multirefractory primary ITP**

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| **Drug** | **Dose** | **Route** | **Response after 1 month (%)** | **Sustained response (%)** | **Side effects** |
| Azathioprine | 50-300 mg/day | Oral | − | 51-64 | Neutropenia, nausea, infection, liver toxicity |
| Cyclosporine | 2.5-6 mg/kg/day | Oral | 38-57 | 23-44 | Asthenia, weakness, AHT, gingival hyperplasia, neuropathy, renal toxicity |
| Mycophenolate mofetil | 250-1,000 mg, twice daily | Oral | − | 57-62 | Diarrhea, cephalea |
| Danazol | 400-800 mg/day | Oral | 24-58 | 9.5-96 | Weight gain, hair loss, amenorrhea, virilization, liver toxicity |
| Dapsone | 50-100 mg/day | Oral | 36-63 | 0-55 | Hemolytic anemia, methemoglobinemia, skin affection |
| Cyclophosphamide | 1-2 mg/kg/day | Oral | 10-70 | 60 | Myelosuppression, infection, secondary neoplasm, infertility, hemorrhagic cystitis |
| Vinca alkaloids | 1-2 mg/wk VC; 5-10 mg/wk VB | i.v. | − | 0-42 | Myelosuppression, neuropathy, constipation |

AHT, arterial hypertension; ITP, immune thrombocytopenia; i.v., intravenous; VB, vinblastine; VC, vincristine; wk, week.

**Supplementary Table S2. A proposal for the progressive dose reduction and suspension of treatment with TPO-RA**

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| **Dose de-escalation proposal** |
| Eltrombopag |
| Reduce 30% dose in each step |
| Monitor patient each 2 weeks: with stable platelet counts >50x109/L, introduce a new dose-  reduction step each 2-4 weeks |
| Romiplostim |
| Reduce 1mg/kg/week in each step |
| Avatrombopag |
| Reduce dose progressively according to technical sheet |
| **Suitability** [59,62,63] |
| Candidate patients |
| Patients with platelet counts >100×109/L (complete response) which have been maintained for  ≥6 months without rescue treatment |
| Patients with platelet counts >50×109/L in 75% of controls during ≥6 months |
| Non-indicated patients |
| Patients with history of severe or life-threatening bleeding and poor response to rescue therapy |
| Patients with history of unsteady platelet count values |
| Patients with comorbidities increasing hemorrhagic risk |
| Patients in treatment with anticoagulant or antiplatelet agents |
| Patients with history of sharp drop of platelet count values after a slight dose modification |
| Patients with platelet count values in the range of 30-50x109/L |

TPO-RA, agonist of thrombopoietin receptor.