

## Supplemental material

**Table S1.** Descriptions of each outcome.

| Outcome                                   | Definition   | Reasons censored  |
|---|--|---|
| <b>Platelet-Based Endpoints</b>           |  |   |
| Proportion with durable platelet response | ≥ 75% of all recorded platelet count measurements are $\geq 50 \times 10^9/L$ during weeks 14 through 24 after index date, in the absence of rescue therapy. Rescue therapy is assessed at any point following index and is considered a treatment failure if it occurs.                       | <ul style="list-style-type: none"> <li>• End of follow-up at 24 weeks</li> <li>• Date associated with end of study (ineligibility, consent withdrawn, administrative decision, lost to follow-up, other)</li> <li>• Receipt of splenectomy, eltrombopag, platelet transfusion</li> <li>• Death</li> <li>• No platelet measurement during weeks 14-16</li> <li>• No platelet measurement during weeks 22-24</li> <li>• Less than 4 total platelet measurements during weeks 14-24</li> </ul> |
| Overall platelet response                 | The probability that any platelet count measurement is $\geq 50 \times 10^9/L$ during weeks 2 through 24 after index date, in the absence of rescue therapy. All platelets occurring before rescue therapy will be included in the analysis. Follow-up will be censored on the date of rescue. | <ul style="list-style-type: none"> <li>• End of follow-up at 24 weeks</li> <li>• Date associated with end of study (ineligibility, consent withdrawn, administrative decision, lost to follow-up, other)</li> <li>• Receipt of splenectomy, eltrombopag, platelet transfusion</li> <li>• Death</li> <li>• At least 5 continuous weeks with no platelet measurement during weeks 2-24</li> <li>• Receipt of rescue therapy</li> </ul>  |
| Median overall platelet count             | The median of all platelet count measurements during weeks 2 through 24 after index date, in the absence of rescue therapy. All platelets occurring before rescue therapy will be included in the analysis. Follow-up will be censored on the date of rescue.                                  | <ul style="list-style-type: none"> <li>• End of follow-up at 24 weeks</li> <li>• Date associated with end of study (ineligibility, consent withdrawn, administrative decision, lost to follow-up, other)</li> <li>• Receipt of splenectomy, eltrombopag, platelet transfusion</li> <li>• Death</li> <li>• At least 5 continuous weeks with no platelet measurement during weeks 2-24</li> <li>• Receipt of rescue therapy</li> </ul>  |

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|------------------------------------|--|--|
| First platelet response by week 24 | The time to first platelet count $\geq 50 \times 10^9/L$ during weeks 2 through 24 after index date, in the absence of rescue therapy. All platelets occurring before rescue therapy will be included in the analysis. Follow-up will be censored on the date of rescue.   | <ul style="list-style-type: none"> <li>• End of follow-up at 24 weeks</li> <li>• Date associated with end of study (ineligibility, consent withdrawn, administrative decision, lost to follow-up, other)</li> <li>• Receipt of splenectomy, eltrombopag, platelet transfusion</li> <li>• At least 5 continuous weeks with no platelet measurement during weeks 2-24</li> <li>• Receipt of rescue therapy</li> </ul>  |
| <b>Rescue Therapy Use</b>          |  |  |
| Any rescue                         | Patients were defined as receiving rescue therapy if the therapy was received after 1) an initial platelet response and subsequent loss of platelet response; or 2) if the therapy represents a new type of therapy after no platelet response was observed (treatment switch); or 3) if therapies are introduced for active bleeding. | <ul style="list-style-type: none"> <li>• End of follow-up at 24 weeks</li> <li>• Date associated with end of study (ineligibility, consent withdrawn, administrative decision, lost to follow-up, other)</li> <li>• Receipt of splenectomy, eltrombopag, platelet transfusion</li> <li>• Loss of response definition: <ul style="list-style-type: none"> <li>• One platelet <math>\geq 50 \times 10^9/L</math> followed by;</li> <li>• One platelet <math>\leq 30 \times 10^9/L</math> followed by or on the same day as;</li> <li>• Administration or receipt of one of the following: <ul style="list-style-type: none"> <li>• oral steroid, IV steroid, IVIg, IV anti-D, azathioprine, cyclophosphamide, cyclosporin[e], danazol, dapsone, eltrombopag, mycophenolate mofetil, platelet transfusion, rituximab, splenectomy, vinblastine, and/or vincristine</li> </ul> </li> </ul> </li> <li>• Treatment switch definition: <ul style="list-style-type: none"> <li>• One platelet <math>\leq 30 \times 10^9/L</math> (the anchor platelet qualifies) followed by:</li> <li>• No platelets <math>\geq 50 \times 10^9/L</math></li> <li>• Administration or receipt of one of the following that was <b>not present at index</b>: <ul style="list-style-type: none"> <li>• oral steroid, IV steroid, IVIg, IV anti-D, azathioprine, cyclophosphamide, cyclosporin[e], danazol, dapsone, eltrombopag, mycophenolate mofetil, platelet transfusion, rituximab, splenectomy, vinblastine, and/or vincristine</li> </ul> </li> </ul> </li> </ul> |

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|---|---|--|
|   |   | <ul style="list-style-type: none"> <li>• Treatment received for active bleeding: A bleeding event where medication and/or transfusion was performed in response. Bleeding events include: <ul style="list-style-type: none"> <li>• Abnormal vaginal bleeding, CNS bleeding with neurologic symptoms, hematemesis, hematochezia, hematuria, melena</li> </ul> </li> </ul> |
| Oral steroids as rescue   | <p>Loss of response: At least one platelet count measurement of <math>\geq 50 \times 10^9/L</math>, followed by a platelet count measurement of <math>\leq 30 \times 10^9/L</math>, followed by administration of any oral steroid; OR</p> <p>Treatment switch: at least one platelet count measurement of <math>\leq 30 \times 10^9/L</math> and no platelet count measurement of <math>\geq 50 \times 10^9/L</math>, followed by administration of any oral steroid if any no oral steroid was present at romiplostim initiation.</p>   | <ul style="list-style-type: none"> <li>• End of follow-up at 24 weeks</li> <li>• Date associated with end of study (ineligibility, consent withdrawn, administrative decision, lost to follow-up, other)</li> <li>• Receipt of splenectomy, eltrombopag, platelet transfusion</li> </ul>   |
| IV anti-D, IVIg, IV steroids &/or platelet transfusions as rescue | <p>Loss of response: at least one platelet count measurement of <math>\geq 50 \times 10^9/L</math>, followed by a platelet count measurement of <math>\leq 30 \times 10^9/L</math>, followed by receipt of therapeutic platelet transfusion or administration of any of the following non-romiplostim ITP treatments: IV steroid, IVIg, and/or IV anti-D; OR</p> <p>Treatment switch: at least one platelet count measurement of <math>\leq 30 \times 10^9/L</math> and no platelet count measurement of <math>\geq 50 \times 10^9/L</math>, followed receipt of therapeutic platelet transfusion or administration of any of the following non-romiplostim ITP treatments that WERE NOT PRESENT at romiplostim initiation: IV steroid, IVIg, and/or IV anti-D.</p> | <ul style="list-style-type: none"> <li>• End of follow-up at 24 weeks</li> <li>• Date associated with end of study (ineligibility, consent withdrawn, administrative decision, lost to follow-up, other)</li> <li>• Receipt of splenectomy, eltrombopag, platelet transfusion</li> </ul>   |
| <b>Bleeding</b>   |   |  |

|  |   |   |
|--|---|---|
| Any bleeding                             | Any bleeding event, assessed from the day after index date through week 24 after romiplostim initiation   | <ul style="list-style-type: none"> <li>• End of follow-up at 24 weeks</li> <li>• Date associated with end of study (ineligibility, consent withdrawn, administrative decision, lost to follow-up, other)</li> <li>• Receipt of splenectomy, eltrombopag, platelet transfusion</li> </ul>                  |
| Hospitalized bleeding                    | Any ITP-related hospitalization from a bleeding event, assessed from the day after index date through week 24 after romiplostim initiation  | <ul style="list-style-type: none"> <li>• End of follow-up at 24 weeks</li> <li>• Date associated with end of study (ineligibility, consent withdrawn, administrative decision, lost to follow-up, other)</li> <li>• Receipt of splenectomy, eltrombopag, platelet transfusion</li> </ul>                  |
| Bleeding leading to emergent treatment   | Any bleeding event, assessed from the day after index date and IVIg, IV anti-D, or IV steroids or transfusion was implemented as treatment within seven days after the start of the bleeding event  | <ul style="list-style-type: none"> <li>• End of follow-up at 24 weeks</li> <li>• Date associated with end of study (ineligibility, consent withdrawn, administrative decision, lost to follow-up, other)</li> <li>• Receipt of splenectomy, eltrombopag, platelet transfusion</li> </ul>                  |
| Specific types of bleeding               | Any bleeding event categorized as abnormal vaginal bleeding, central nervous system bleeding with neurologic symptoms, hematemesis, hematochezia, hematuria, and/or melena, assessed from the day after index date through week 24 after romiplostim initiation   | <ul style="list-style-type: none"> <li>• End of follow-up at 24 weeks</li> <li>• Date associated with end of study (ineligibility, consent withdrawn, administrative decision, lost to follow-up, other)</li> <li>• Receipt of splenectomy, eltrombopag, platelet transfusion</li> </ul>                  |
| <b>Discontinuation of ITP Treatments</b> |   |   |
| Discontinuation of ITP treatment         | No administration of any type of non-romiplostim ITP medication that was present at romiplostim initiation (including cyclosporin, mycophenolate mofetil, oral steroid, IV steroid, IVIg, IV anti-D, danazol, vinca alkaloids, azathioprine, rituximab, Campath-1H, dapsone, cyclophosphamide) during weeks 14 through 24 after index date. | <ul style="list-style-type: none"> <li>• End of follow-up at 24 weeks</li> <li>• Date associated with end of study (ineligibility, consent withdrawn, administrative decision, lost to follow-up, other)</li> <li>• Receipt of splenectomy, eltrombopag, platelet transfusion</li> <li>• Death</li> </ul> |

|   |   |  |
|---|---|--|
| Discontinuation of any concomitant ITP treatments                   | No administration of any type of non-romiplostim ITP medication that was present at romiplostim initiation (including cyclosporin, mycophenolate mofetil, oral steroid, IV steroid, IVIg, IV anti-D, danazol, vinca alkaloids, azathioprine, rituximab, Campath-1H, dapsone, cyclophosphamide) during weeks 14 through 24 after index date. | <ul style="list-style-type: none"> <li>• End of follow-up at 24 weeks</li> <li>• Date associated with end of study (ineligibility, consent withdrawn, administrative decision, lost to follow-up, other)</li> <li>• Receipt of splenectomy, eltrombopag, platelet transfusion</li> </ul> |
| Discontinuation of oral steroids, IV steroids, IVIg, &/or IV anti-D | No administration of any of the following that were present at romiplostim initiation during weeks 14 through 24 after index date: oral steroids, IV steroid, IVIg, and / or IV anti-D.   | <ul style="list-style-type: none"> <li>• End of follow-up at 24 weeks</li> <li>• Date associated with end of study (ineligibility, consent withdrawn, administrative decision, lost to follow-up, other)</li> <li>• Receipt of splenectomy, eltrombopag, platelet transfusion</li> </ul> |
| <b>Splenectomy</b>  |   |  |
| Receipt of splenectomy  | Receipt of splenectomy, assessed from the day after index date through week 24 after romiplostim initiation   | <ul style="list-style-type: none"> <li>• End of follow-up at 24 weeks</li> <li>• Date associated with end of study (ineligibility, consent withdrawn, administrative decision, lost to follow-up, other)</li> <li>• Receipt of eltrombopag, platelet transfusion</li> </ul>              |
| <b>Adverse Drug Reactions</b>                                       |   |  |
| Any ADR   | Any adverse drug reaction, assessed from the day after index date through week 24 after romiplostim initiation  | <ul style="list-style-type: none"> <li>• End of follow-up at 24 weeks</li> <li>• Date associated with end of study (ineligibility, consent withdrawn, administrative decision, lost to follow-up, other)</li> <li>• Receipt of splenectomy, eltrombopag, platelet transfusion</li> </ul> |
| Thrombotic ADRs   | Thrombotic adverse drug reaction, assessed from the day after index date through week 24 after romiplostim initiation   | <ul style="list-style-type: none"> <li>• End of follow-up at 24 weeks</li> <li>• Date associated with end of study (ineligibility, consent withdrawn, administrative decision, lost to follow-up, other)</li> <li>• Receipt of splenectomy, eltrombopag, platelet transfusion</li> </ul> |
| Bone Marrow ADRs  | Bone marrow fibrosis adverse drug reaction, assessed from the day after index date through week 24 after romiplostim initiation   | <ul style="list-style-type: none"> <li>• End of follow-up at 24 weeks</li> <li>• Date associated with end of study (ineligibility, consent withdrawn, administrative decision, lost to follow-up, other)</li> <li>• Receipt of splenectomy, eltrombopag, platelet transfusion</li> </ul> |

**Table S2.** MedDRA search terms used for thrombotic events.

|    |                                    |
|----|------------------------------------|
| 1  | Acute aortic syndrome              |
| 2  | Acute myocardial infarction        |
| 3  | Amaurosis                          |
| 4  | Amaurosis fugax                    |
| 5  | Angioplasty                        |
| 6  | Aortic bypass                      |
| 7  | Aortic embolus                     |
| 8  | Aortic surgery                     |
| 9  | Aortic thrombosis                  |
| 10 | Aortogram abnormal                 |
| 11 | Arterectomy                        |
| 12 | Arterectomy with graft replacement |
| 13 | Arterial bypass operation          |
| 14 | Arterial graft                     |
| 15 | Arterial occlusive disease         |
| 16 | Arterial stent insertion           |
| 17 | Arterial therapeutic procedure     |
| 18 | Arterial thrombosis                |
| 19 | Arteriogram abnormal               |
| 20 | Arteriogram carotid abnormal       |
| 21 | Atherectomy                        |
| 22 | Basal ganglia infarction           |
| 23 | Basilar artery occlusion           |
| 24 | Basilar artery thrombosis          |
| 25 | Blindness transient                |
| 26 | Brachiocephalic artery occlusion   |
| 27 | Capsular warning syndrome          |
| 28 | Carotid angioplasty                |
| 29 | Carotid arterial embolus           |

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|----|-----------------------------------|
| 30 | Carotid artery bypass             |
| 31 | Carotid artery occlusion          |
| 32 | Carotid artery stent insertion    |
| 33 | Carotid artery thrombosis         |
| 34 | Carotid endarterectomy            |
| 35 | Cerebellar artery occlusion       |
| 36 | Cerebellar artery thrombosis      |
| 37 | Cerebral artery embolism          |
| 38 | Cerebral artery occlusion         |
| 39 | Cerebral artery thrombosis        |
| 40 | Cerebral hypoperfusion            |
| 41 | Cerebrovascular insufficiency     |
| 42 | Cerebrovascular stenosis          |
| 43 | Coeliac artery occlusion          |
| 44 | Coronary angioplasty              |
| 45 | Coronary arterial stent insertion |
| 46 | Coronary artery bypass            |
| 47 | Coronary artery embolism          |
| 48 | Coronary artery occlusion         |
| 49 | Coronary artery reocclusion       |
| 50 | Coronary artery thrombosis        |
| 51 | Coronary endarterectomy           |
| 52 | Coronary revascularisation        |
| 53 | Coronary vascular graft occlusion |
| 54 | Embolia cutis medicamentosa       |
| 55 | Embolism arterial                 |
| 56 | Endarterectomy                    |
| 57 | Femoral artery embolism           |
| 58 | Femoral artery occlusion          |
| 59 | Hepatic artery embolism           |

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| 60 | Hepatic artery occlusion                 |
| 61 | Hepatic artery thrombosis                |
| 62 | Hypothenar hammer syndrome               |
| 63 | Iliac artery embolism                    |
| 64 | Iliac artery occlusion                   |
| 65 | Intra-aortic balloon placement           |
| 66 | Intraoperative cerebral artery occlusion |
| 67 | Ischaemic cerebral infarction            |
| 68 | Ischaemic stroke                         |
| 69 | Lacunar infarction                       |
| 70 | Leriche syndrome                         |
| 71 | Mesenteric arterial occlusion            |
| 72 | Mesenteric arteriosclerosis              |
| 73 | Mesenteric artery embolism               |
| 74 | Mesenteric artery stenosis               |
| 75 | Mesenteric artery stent insertion        |
| 76 | Mesenteric artery thrombosis             |
| 77 | Myocardial infarction                    |
| 78 | Myocardial necrosis                      |
| 79 | Papillary muscle infarction              |
| 80 | Penile artery occlusion                  |
| 81 | Percutaneous coronary intervention       |
| 82 | Peripheral arterial occlusive disease    |
| 83 | Peripheral arterial reocclusion          |
| 84 | Peripheral artery angioplasty            |
| 85 | Peripheral artery bypass                 |
| 86 | Peripheral artery stent insertion        |
| 87 | Peripheral artery thrombosis             |
| 88 | Peripheral embolism                      |
| 89 | Peripheral endarterectomy                |



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| 90  | Popliteal artery entrapment syndrome   |
| 91  | Post procedural myocardial infarction  |
| 92  | Postinfarction angina                  |
| 93  | Precerebral artery occlusion           |
| 94  | Precerebral artery thrombosis          |
| 95  | Pulmonary artery therapeutic procedure |
| 96  | Pulmonary artery thrombosis            |
| 97  | Pulmonary endarterectomy               |
| 98  | Renal artery angioplasty               |
| 99  | Renal artery occlusion                 |
| 100 | Renal artery thrombosis                |
| 101 | Renal embolism                         |
| 102 | Retinal artery embolism                |
| 103 | Retinal artery occlusion               |
| 104 | Retinal artery thrombosis              |
| 105 | Silent myocardial infarction           |
| 106 | Spinal artery embolism                 |
| 107 | Spinal artery thrombosis               |
| 108 | Splenic artery thrombosis              |
| 109 | Splenic embolism                       |
| 110 | Stress cardiomyopathy                  |
| 111 | Stroke in evolution                    |
| 112 | Subclavian artery embolism             |
| 113 | Subclavian artery occlusion            |
| 114 | Subclavian artery thrombosis           |
| 115 | Superior mesenteric artery syndrome    |
| 116 | Thromboembolectomy                     |
| 117 | Thrombotic microangiopathy             |
| 118 | Thrombotic thrombocytopenic purpura    |
| 119 | Transient ischaemic attack             |

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| 120 | Truncus coeliacus thrombosis         |
| 121 | Vertebral artery occlusion           |
| 122 | Vertebral artery thrombosis          |
| 123 | Visual acuity reduced transiently    |
| 124 | Adrenal thrombosis                   |
| 125 | Angiogram abnormal                   |
| 126 | Angiogram cerebral abnormal          |
| 127 | Angiogram peripheral abnormal        |
| 128 | Arteriovenous fistula occlusion      |
| 129 | Arteriovenous fistula thrombosis     |
| 130 | Atrial thrombosis                    |
| 131 | Basal ganglia stroke                 |
| 132 | Bone infarction                      |
| 133 | Brain stem embolism                  |
| 134 | Brain stem infarction                |
| 135 | Brain stem stroke                    |
| 136 | Brain stem thrombosis                |
| 137 | Cardiac ventricular thrombosis       |
| 138 | Cerebellar embolism                  |
| 139 | Cerebellar infarction                |
| 140 | Cerebral infarction                  |
| 141 | Cerebral infarction foetal           |
| 142 | Cerebral ischaemia                   |
| 143 | Cerebral septic infarct              |
| 144 | Cerebral thrombosis                  |
| 145 | Cerebrospinal thrombotic tamponade   |
| 146 | Cerebrovascular accident             |
| 147 | Cerebrovascular accident prophylaxis |
| 148 | Cerebrovascular disorder             |
| 149 | Cerebrovascular operation            |

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|-----|---|
| 150 | Choroidal infarction                              |
| 151 | Collateral circulation                            |
| 152 | Coronary bypass thrombosis                        |
| 153 | Device embolisation                               |
| 154 | Device occlusion                                  |
| 155 | Diplegia  |
| 156 | Directional Doppler flow tests abnormal           |
| 157 | Disseminated intravascular coagulation            |
| 158 | Disseminated intravascular coagulation in newborn |
| 159 | Embolic cerebral infarction                       |
| 160 | Embolic pneumonia                                 |
| 161 | Embolic stroke                                    |
| 162 | Embolism  |
| 163 | Foetal cerebrovascular disorder                   |
| 164 | Graft thrombosis                                  |
| 165 | Haemorrhagic cerebral infarction                  |
| 166 | Haemorrhagic infarction                           |
| 167 | Haemorrhagic stroke                               |
| 168 | Haemorrhagic transformation stroke                |
| 169 | Haemorrhoids thrombosed                           |
| 170 | Hemiparesis                                       |
| 171 | Hemiplegia  |
| 172 | Heparin-induced thrombocytopenia                  |
| 173 | Hepatic infarction                                |
| 174 | Hepatic vascular thrombosis                       |
| 175 | Implant site thrombosis                           |
| 176 | Infarction  |
| 177 | Infusion site thrombosis                          |
| 178 | Injection site thrombosis                         |

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| 179 | Inner ear infarction              |
| 180 | Instillation site thrombosis      |
| 181 | Intestinal infarction             |
| 182 | Intracardiac mass                 |
| 183 | Intracardiac thrombus             |
| 184 | Mesenteric vascular insufficiency |
| 185 | Mesenteric vascular occlusion     |
| 186 | Microembolism                     |
| 187 | Monoparesis                       |
| 188 | Monoplegia                        |
| 189 | Optic nerve infarction            |
| 190 | Pancreatic infarction             |
| 191 | Paradoxical embolism              |
| 192 | Paraparesis                       |
| 193 | Paraplegia                        |
| 194 | Paresis                           |
| 195 | Peripheral revascularisation      |
| 196 | Pituitary infarction              |
| 197 | Placental infarction              |
| 198 | Pneumatic compression therapy     |
| 199 | Portal shunt                      |
| 200 | Post procedural stroke            |
| 201 | Prosthetic vessel implantation    |
| 202 | Quadriparesis                     |
| 203 | Quadriplegia                      |
| 204 | Renal infarct                     |
| 205 | Renal vascular thrombosis         |
| 206 | Retinal infarction                |
| 207 | Retinal vascular thrombosis       |
| 208 | Shunt occlusion                   |

|     |                                 |
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| 209 | Shunt thrombosis                |
| 210 | Spinal cord infarction          |
| 211 | Splenic infarction              |
| 212 | Splenic thrombosis              |
| 213 | Stoma site thrombosis           |
| 214 | Surgical vascular shunt         |
| 215 | Testicular infarction           |
| 216 | Thalamic infarction             |
| 217 | Thrombectomy                    |
| 218 | Thromboangiitis obliterans      |
| 219 | Thrombolysis                    |
| 220 | Thrombosis                      |
| 221 | Thrombosis in device            |
| 222 | Thrombosis mesenteric vessel    |
| 223 | Thrombosis prophylaxis          |
| 224 | Thrombotic cerebral infarction  |
| 225 | Thrombotic stroke               |
| 226 | Thyroid infarction              |
| 227 | Tumour embolism                 |
| 228 | Tumour thrombosis               |
| 229 | Ultrasonic angiogram abnormal   |
| 230 | Ultrasound Doppler abnormal     |
| 231 | Umbilical cord thrombosis       |
| 232 | Vascular graft thrombosis       |
| 233 | Vascular operation              |
| 234 | Vascular stent insertion        |
| 235 | Vasodilation procedure          |
| 236 | Vessel puncture site thrombosis |
| 237 | Visual midline shift syndrome   |
| 238 | Axillary vein thrombosis        |

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|-----|--------------------------------------|
| 239 | Budd-Chiari syndrome                 |
| 240 | Catheterisation venous               |
| 241 | Cavernous sinus thrombosis           |
| 242 | Central venous catheterisation       |
| 243 | Cerebral venous thrombosis           |
| 244 | Compression stockings application    |
| 245 | Deep vein thrombosis                 |
| 246 | Deep vein thrombosis postoperative   |
| 247 | Embolism venous                      |
| 248 | Hepatic vein occlusion               |
| 249 | Hepatic vein thrombosis              |
| 250 | Homans' sign positive                |
| 251 | Iliac vein occlusion                 |
| 252 | Inferior vena cava syndrome          |
| 253 | Inferior vena caval occlusion        |
| 254 | Intracranial venous sinus thrombosis |
| 255 | Jugular vein thrombosis              |
| 256 | Mahler sign                          |
| 257 | May-Thurner syndrome                 |
| 258 | Mesenteric vein thrombosis           |
| 259 | Mesenteric venous occlusion          |
| 260 | Obstetrical pulmonary embolism       |
| 261 | Obstructive shock                    |
| 262 | Ophthalmic vein thrombosis           |
| 263 | Ovarian vein thrombosis              |
| 264 | Paget-Schroetter syndrome            |
| 265 | Pelvic venous thrombosis             |
| 266 | Penile vein thrombosis               |
| 267 | Phlebectomy                          |
| 268 | Portal vein cavernous transformation |

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|-----|------------------------------------|
| 269 | Portal vein occlusion              |
| 270 | Portal vein thrombosis             |
| 271 | Post procedural pulmonary embolism |
| 272 | Post thrombotic syndrome           |
| 273 | Postoperative thrombosis           |
| 274 | Postpartum venous thrombosis       |
| 275 | Pulmonary embolism                 |
| 276 | Pulmonary infarction               |
| 277 | Pulmonary microemboli              |
| 278 | Pulmonary thrombosis               |
| 279 | Pulmonary vein occlusion           |
| 280 | Pulmonary veno-occlusive disease   |
| 281 | Pulmonary venous thrombosis        |
| 282 | Renal vein embolism                |
| 283 | Renal vein occlusion               |
| 284 | Renal vein thrombosis              |
| 285 | Retinal vein occlusion             |
| 286 | Retinal vein thrombosis            |
| 287 | SI QIII TIII pattern               |
| 288 | Splenic vein occlusion             |
| 289 | Splenic vein thrombosis            |
| 290 | Subclavian vein thrombosis         |
| 291 | Superior sagittal sinus thrombosis |
| 292 | Superior vena cava occlusion       |
| 293 | Superior vena cava syndrome        |
| 294 | Thrombophlebitis                   |
| 295 | Thrombophlebitis migrans           |
| 296 | Thrombophlebitis neonatal          |
| 297 | Thrombophlebitis superficial       |
| 298 | Thrombosed varicose vein           |

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| 299 | Thrombosis corpora cavernosa   |
| 300 | Transverse sinus thrombosis    |
| 301 | Vascular graft                 |
| 302 | Vena cava embolism             |
| 303 | Vena cava filter insertion     |
| 304 | Vena cava filter removal       |
| 305 | Vena cava thrombosis           |
| 306 | Venogram abnormal              |
| 307 | Venoocclusive disease          |
| 308 | Venoocclusive liver disease    |
| 309 | Venous occlusion               |
| 310 | Venous operation               |
| 311 | Venous recanalisation          |
| 312 | Venous repair                  |
| 313 | Venous stent insertion         |
| 314 | Venous thrombosis              |
| 315 | Venous thrombosis in pregnancy |
| 316 | Venous thrombosis limb         |
| 317 | Venous thrombosis neonatal     |

**Table S3.** MedDRA search terms used for liver events.

|   |  |
|---|--|
| 1 | Accessory liver lobe                     |
| 2 | Acquired antithrombin III deficiency     |
| 3 | Acquired hepatocerebral degeneration     |
| 4 | Acquired protein S deficiency            |
| 5 | Acute fatty liver of pregnancy           |
| 6 | Acute graft versus host disease in liver |
| 7 | Acute hepatic failure                    |
| 8 | Acute hepatitis B                        |
| 9 | Acute hepatitis C                        |



|    |                                      |
|----|--------------------------------------|
| 10 | Acute on chronic liver failure       |
| 11 | Acute yellow liver atrophy           |
| 12 | Adenoviral hepatitis                 |
| 13 | Alagille syndrome                    |
| 14 | Alanine aminotransferase abnormal    |
| 15 | Alanine aminotransferase increased   |
| 16 | Alcoholic liver disease              |
| 17 | Allergic hepatitis                   |
| 18 | Alloimmune hepatitis                 |
| 19 | Ammonia abnormal                     |
| 20 | Ammonia increased                    |
| 21 | Anti factor X activity abnormal      |
| 22 | Anti factor X activity decreased     |
| 23 | Anti factor X activity increased     |
| 24 | Antithrombin III decreased           |
| 25 | Ascites                              |
| 26 | Aspartate aminotransferase abnormal  |
| 27 | Aspartate aminotransferase increased |
| 28 | Asterixis                            |
| 29 | Asymptomatic viral hepatitis         |
| 30 | Autoimmune hepatitis                 |
| 31 | Bacterascites                        |
| 32 | Benign hepatic neoplasm              |
| 33 | Benign hepatobiliary neoplasm        |
| 34 | Bile output abnormal                 |
| 35 | Bile output decreased                |
| 36 | Biliary ascites                      |
| 37 | Biliary cirrhosis                    |
| 38 | Biliary fibrosis                     |

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|----|--|
| 39 | Bilirubin conjugated abnormal              |
| 40 | Bilirubin conjugated increased             |
| 41 | Bilirubin excretion disorder               |
| 42 | Bilirubin urine present                    |
| 43 | Biopsy liver abnormal                      |
| 44 | Blood bilirubin abnormal                   |
| 45 | Blood bilirubin increased                  |
| 46 | Blood bilirubin unconjugated increased     |
| 47 | Blood fibrinogen abnormal                  |
| 48 | Blood fibrinogen decreased                 |
| 49 | Blood thrombin abnormal                    |
| 50 | Blood thrombin decreased                   |
| 51 | Blood thromboplastin abnormal              |
| 52 | Blood thromboplastin decreased             |
| 53 | Bromosulphthalein test abnormal            |
| 54 | Cardiohepatic syndrome                     |
| 55 | Cerebrohepatorenal syndrome                |
| 56 | Child-Pugh-Turcotte score abnormal         |
| 57 | Child-Pugh-Turcotte score increased        |
| 58 | Cholaemia                                  |
| 59 | Cholangiosarcoma                           |
| 60 | Cholestasis                                |
| 61 | Cholestasis of pregnancy                   |
| 62 | Cholestatic liver injury                   |
| 63 | Cholestatic pruritus                       |
| 64 | Chronic graft versus host disease in liver |
| 65 | Chronic hepatic failure                    |
| 66 | Chronic hepatitis                          |
| 67 | Chronic hepatitis B                        |

|    |   |
|----|---|
| 68 | Chronic hepatitis C                     |
| 69 | Cirrhosis alcoholic                     |
| 70 | Coagulation factor IX level abnormal    |
| 71 | Coagulation factor IX level decreased   |
| 72 | Coagulation factor V level abnormal     |
| 73 | Coagulation factor V level decreased    |
| 74 | Coagulation factor VII level abnormal   |
| 75 | Coagulation factor VII level decreased  |
| 76 | Coagulation factor X level abnormal     |
| 77 | Coagulation factor X level decreased    |
| 78 | Coagulation factor decreased            |
| 79 | Coma hepatic                            |
| 80 | Computerised tomogram liver             |
| 81 | Computerised tomogram liver abnormal    |
| 82 | Congenital absence of bile ducts        |
| 83 | Congenital cystic disease of liver      |
| 84 | Congenital hepatic fibrosis             |
| 85 | Congenital hepatitis B infection        |
| 86 | Congenital hepatobiliary anomaly        |
| 87 | Congenital hepatomegaly                 |
| 88 | Cryptogenic cirrhosis                   |
| 89 | Cystic fibrosis hepatic disease         |
| 90 | Cytomegalovirus hepatitis               |
| 91 | Diabetic hepatopathy                    |
| 92 | Dilatation intrahepatic duct congenital |
| 93 | Drug-induced liver injury               |
| 94 | Duodenal varices                        |
| 95 | Fatty liver alcoholic                   |
| 96 | Focal nodular hyperplasia               |

|     |   |
|-----|---|
| 97  | Foetor hepaticus                              |
| 98  | Galactose elimination capacity test abnormal  |
| 99  | Galactose elimination capacity test decreased |
| 100 | Gallbladder varices                           |
| 101 | Gamma-glutamyltransferase abnormal            |
| 102 | Gamma-glutamyltransferase increased           |
| 103 | Gastric variceal injection                    |
| 104 | Gastric variceal ligation                     |
| 105 | Gastric varices                               |
| 106 | Gastric varices haemorrhage                   |
| 107 | Glycogen storage disease type I               |
| 108 | Glycogen storage disease type III             |
| 109 | Glycogen storage disease type IV              |
| 110 | Glycogen storage disease type VI              |
| 111 | Graft versus host disease in liver            |
| 112 | Guanase increased                             |
| 113 | HBV-DNA polymerase increased                  |
| 114 | Haemangioma of liver                          |
| 115 | Haemorrhagic hepatic cyst                     |
| 116 | Hepaplastin abnormal                          |
| 117 | Hepaplastin decreased                         |
| 118 | Hepatectomy                                   |
| 119 | Hepatic adenoma                               |
| 120 | Hepatic amoebiasis                            |
| 121 | Hepatic angiosarcoma                          |
| 122 | Hepatic artery flow decreased                 |
| 123 | Hepatic atrophy                               |
| 124 | Hepatic calcification                         |
| 125 | Hepatic cancer                                |

|     |                                    |
|-----|------------------------------------|
| 126 | Hepatic cancer metastatic          |
| 127 | Hepatic cancer recurrent           |
| 128 | Hepatic cancer stage I             |
| 129 | Hepatic cancer stage II            |
| 130 | Hepatic cancer stage III           |
| 131 | Hepatic cancer stage IV            |
| 132 | Hepatic candidiasis                |
| 133 | Hepatic cirrhosis                  |
| 134 | Hepatic congestion                 |
| 135 | Hepatic cyst                       |
| 136 | Hepatic cyst infection             |
| 137 | Hepatic cyst ruptured              |
| 138 | Hepatic echinococcosis             |
| 139 | Hepatic encephalopathy             |
| 140 | Hepatic encephalopathy prophylaxis |
| 141 | Hepatic enzyme abnormal            |
| 142 | Hepatic enzyme decreased           |
| 143 | Hepatic enzyme increased           |
| 144 | Hepatic failure                    |
| 145 | Hepatic fibrosis                   |
| 146 | Hepatic function abnormal          |
| 147 | Hepatic gas gangrene               |
| 148 | Hepatic haemangioma rupture        |
| 149 | Hepatic hamartoma                  |
| 150 | Hepatic hydrothorax                |
| 151 | Hepatic hypertrophy                |
| 152 | Hepatic infection                  |
| 153 | Hepatic infection bacterial        |
| 154 | Hepatic infection fungal           |

|     |                                       |
|-----|---------------------------------------|
| 155 | Hepatic infection helminthic          |
| 156 | Hepatic infiltration eosinophilic     |
| 157 | Hepatic lesion                        |
| 158 | Hepatic mass                          |
| 159 | Hepatic necrosis                      |
| 160 | Hepatic neoplasm                      |
| 161 | Hepatic pain                          |
| 162 | Hepatic sequestration                 |
| 163 | Hepatic steato-fibrosis               |
| 164 | Hepatic steatosis                     |
| 165 | Hepatic vascular resistance increased |
| 166 | Hepatitis                             |
| 167 | Hepatitis A                           |
| 168 | Hepatitis A antibody abnormal         |
| 169 | Hepatitis A antibody positive         |
| 170 | Hepatitis A antigen positive          |
| 171 | Hepatitis A virus test positive       |
| 172 | Hepatitis B                           |
| 173 | Hepatitis B DNA assay positive        |
| 174 | Hepatitis B DNA increased             |
| 175 | Hepatitis B antibody abnormal         |
| 176 | Hepatitis B antibody positive         |
| 177 | Hepatitis B core antibody positive    |
| 178 | Hepatitis B core antigen positive     |
| 179 | Hepatitis B e antibody positive       |
| 180 | Hepatitis B e antigen positive        |
| 181 | Hepatitis B reactivation              |
| 182 | Hepatitis B surface antibody positive |
| 183 | Hepatitis B surface antigen positive  |

|     |                                    |
|-----|------------------------------------|
| 184 | Hepatitis B virus test positive    |
| 185 | Hepatitis C                        |
| 186 | Hepatitis C RNA increased          |
| 187 | Hepatitis C RNA positive           |
| 188 | Hepatitis C antibody positive      |
| 189 | Hepatitis C core antibody positive |
| 190 | Hepatitis C virus test positive    |
| 191 | Hepatitis D                        |
| 192 | Hepatitis D RNA positive           |
| 193 | Hepatitis D antibody positive      |
| 194 | Hepatitis D antigen positive       |
| 195 | Hepatitis D virus test positive    |
| 196 | Hepatitis E                        |
| 197 | Hepatitis E antibody abnormal      |
| 198 | Hepatitis E antibody positive      |
| 199 | Hepatitis E antigen positive       |
| 200 | Hepatitis E virus test positive    |
| 201 | Hepatitis F                        |
| 202 | Hepatitis G                        |
| 203 | Hepatitis H                        |
| 204 | Hepatitis acute                    |
| 205 | Hepatitis alcoholic                |
| 206 | Hepatitis cholestatic              |
| 207 | Hepatitis chronic active           |
| 208 | Hepatitis chronic persistent       |
| 209 | Hepatitis fulminant                |
| 210 | Hepatitis infectious mononucleosis |
| 211 | Hepatitis mumps                    |
| 212 | Hepatitis neonatal                 |

|     |                                    |
|-----|------------------------------------|
| 213 | Hepatitis non-A non-B              |
| 214 | Hepatitis non-A non-B non-C        |
| 215 | Hepatitis post transfusion         |
| 216 | Hepatitis syphilitic               |
| 217 | Hepatitis toxic                    |
| 218 | Hepatitis toxoplasmal              |
| 219 | Hepatitis viral                    |
| 220 | Hepatitis viral test positive      |
| 221 | Hepato-lenticular degeneration     |
| 222 | Hepatobiliary cancer               |
| 223 | Hepatobiliary cancer in situ       |
| 224 | Hepatobiliary cyst                 |
| 225 | Hepatobiliary disease              |
| 226 | Hepatobiliary infection            |
| 227 | Hepatobiliary neoplasm             |
| 228 | Hepatobiliary scan abnormal        |
| 229 | Hepatoblastoma                     |
| 230 | Hepatoblastoma recurrent           |
| 231 | Hepatocellular carcinoma           |
| 232 | Hepatocellular damage neonatal     |
| 233 | Hepatocellular foamy cell syndrome |
| 234 | Hepatocellular injury              |
| 235 | Hepatomegaly                       |
| 236 | Hepatopulmonary syndrome           |
| 237 | Hepatorenal failure                |
| 238 | Hepatorenal syndrome               |
| 239 | Hepatosplenic abscess              |
| 240 | Hepatosplenic candidiasis          |
| 241 | Hepatosplenomegaly                 |



|     |  |
|-----|--|
| 242 | Hepatosplenomegaly neonatal              |
| 243 | Hepatotoxicity                           |
| 244 | Hereditary haemochromatosis              |
| 245 | Herpes simplex hepatitis                 |
| 246 | Hyperammonaemia                          |
| 247 | Hyperbilirubinaemia                      |
| 248 | Hypercholia                              |
| 249 | Hyperfibrinolysis                        |
| 250 | Hypertransaminasaemia                    |
| 251 | Hypocoagulable state                     |
| 252 | Hypofibrinogenaemia                      |
| 253 | Hypoprothrombinaemia                     |
| 254 | Hypothrombinaemia                        |
| 255 | Hypothromboplastinaemia                  |
| 256 | Icterus index increased                  |
| 257 | Immune-mediated hepatitis                |
| 258 | International normalised ratio abnormal  |
| 259 | International normalised ratio increased |
| 260 | Intestinal varices                       |
| 261 | Intestinal varices haemorrhage           |
| 262 | Ischaemic hepatitis                      |
| 263 | Jaundice                                 |
| 264 | Jaundice cholestatic                     |
| 265 | Jaundice hepatocellular                  |
| 266 | Kayser-Fleischer ring                    |
| 267 | Liver abscess                            |
| 268 | Liver carcinoma ruptured                 |
| 269 | Liver dialysis                           |
| 270 | Liver disorder                           |

|     |  |
|-----|--|
| 271 | Liver function test abnormal                               |
| 272 | Liver function test decreased                              |
| 273 | Liver function test increased                              |
| 274 | Liver induration   |
| 275 | Liver injury   |
| 276 | Liver operation  |
| 277 | Liver palpable   |
| 278 | Liver scan abnormal  |
| 279 | Liver tenderness   |
| 280 | Liver transplant   |
| 281 | Lupoid hepatic cirrhosis                                   |
| 282 | Lupus hepatitis  |
| 283 | Magnetic resonance proton density fat fraction measurement |
| 284 | Minimal hepatic encephalopathy                             |
| 285 | Mitochondrial aspartate aminotransferase increased         |
| 286 | Mixed hepatocellular cholangiocarcinoma                    |
| 287 | Mixed liver injury   |
| 288 | Molar ratio of total branched-chain amino acid to tyrosine |
| 289 | Neonatal cholestasis                                       |
| 290 | Neonatal hepatomegaly                                      |
| 291 | Nodular regenerative hyperplasia                           |
| 292 | Non-alcoholic steatohepatitis                              |
| 293 | Non-cirrhotic portal hypertension                          |
| 294 | Nonalcoholic fatty liver disease                           |
| 295 | Nuclear magnetic resonance imaging liver abnormal          |
| 296 | Ocular icterus   |
| 297 | Oedema due to hepatic disease                              |
| 298 | Oesophageal varices haemorrhage                            |
| 299 | Parenteral nutrition associated liver disease              |

|     |   |
|-----|---|
| 300 | Perihepatic discomfort                        |
| 301 | Perinatal HBV infection                       |
| 302 | Peripancreatic varices                        |
| 303 | Polycystic liver disease                      |
| 304 | Porphyria acute                               |
| 305 | Portal fibrosis                               |
| 306 | Portal hypertension                           |
| 307 | Portal hypertensive colopathy                 |
| 308 | Portal hypertensive enteropathy               |
| 309 | Portal hypertensive gastropathy               |
| 310 | Portal vein cavernous transformation          |
| 311 | Portal vein dilatation                        |
| 312 | Portal venous system anomaly                  |
| 313 | Portopulmonary hypertension                   |
| 314 | Primary biliary cholangitis                   |
| 315 | Progressive familial intrahepatic cholestasis |
| 316 | Protein C decreased                           |
| 317 | Protein S abnormal                            |
| 318 | Protein S decreased                           |
| 319 | Prothrombin level abnormal                    |
| 320 | Prothrombin level decreased                   |
| 321 | Prothrombin time abnormal                     |
| 322 | Prothrombin time prolonged                    |
| 323 | Prothrombin time ratio abnormal               |
| 324 | Prothrombin time ratio increased              |
| 325 | Radiation hepatitis                           |
| 326 | Regenerative siderotic hepatic nodule         |
| 327 | Renal and liver transplant                    |
| 328 | Retrograde portal vein flow                   |

|     |                                  |
|-----|----------------------------------|
| 329 | Reye's syndrome                  |
| 330 | Reynold's syndrome               |
| 331 | Schistosomiasis liver            |
| 332 | Splenic varices                  |
| 333 | Splenic varices haemorrhage      |
| 334 | Steatohepatitis                  |
| 335 | Subacute hepatic failure         |
| 336 | Sustained viral response         |
| 337 | Thrombin time abnormal           |
| 338 | Thrombin time prolonged          |
| 339 | Total bile acids increased       |
| 340 | Transaminases abnormal           |
| 341 | Transaminases increased          |
| 342 | Ultrasound liver abnormal        |
| 343 | Urine bilirubin increased        |
| 344 | Varices oesophageal              |
| 345 | Varicose veins of abdominal wall |
| 346 | Viral hepatitis carrier          |
| 347 | White nipple sign                |
| 348 | Withdrawal hepatitis             |
| 349 | X-ray hepatobiliary abnormal     |
| 350 | Zieve syndrome                   |

**Table S4.** Effectiveness outcomes during 24-week follow-up period stratified by duration of ITP.

|  | ITP duration (months) |              |                |                |
|--|-----------------------|--------------|----------------|----------------|
|  | Overall<br>(n=340)    | <3<br>(n=64) | 3-12<br>(n=50) | >12<br>(n=226) |

|   |                     |                      |                     |                     |
|---|---------------------|----------------------|---------------------|---------------------|
| Proportion with durable platelet response*, % (95% CI)                        | 45.6<br>(38.8-52.4) | 31.9<br>(18.3-45.5)  | 52.6<br>(36.9-68.4) | 49.2<br>(41.9-56.5) |
| Overall platelet response, % (95% CI)   | 81.8<br>(78.0-85.6) | 92.9<br>(82.5-100)   | 80.1<br>(70.1-90.1) | 80.0<br>(75.5-84.6) |
| Median overall platelet response, 10 <sup>9</sup> /L (95% CI)                 | 90<br>(81.2-98.8)   | 131<br>(102.2-159.8) | 90<br>(60-120)      | 88<br>(79.7-96.3)   |
| First platelet response by week 24, % (95% CI)                                | 97.0<br>(92.3-100)  | 96.3<br>(89.5-100)   | 99.6<br>(99-100)    | 95.1<br>(92-98.2)   |
| Any rescue, % (95% CI)  | 25.8<br>(20.9-30.7) | 45.1<br>(32.3-57.8)  | 22.8<br>(12.2-33.4) | 20.4<br>(15.1-25.7) |
| Oral steroids as rescue, % (95% CI)   | 14.2<br>(10.3-18.1) | 22.3<br>(11.9-32.7)  | 8.7<br>(1.3-16.1)   | 12.7<br>(7.9-17.5)  |
| IV anti-D, IVIg, IV steroids &/or platelet transfusions as rescue, % (95% CI) | 15.8<br>(11.9-19.8) | 24.7<br>(14.7-34.7)  | 20.7<br>(10.6-30.8) | 11.7<br>(7.2-16.2)  |
| Any bleeding, % (95% CI)  | 22.5<br>(17.7-27.3) | 22.1<br>(10.7-33.5)  | 21.2<br>(9.1-33.2)  | 22.3<br>(16.3-28.3) |
| Hospitalized bleeding, % (95% CI)   | 7.4<br>(4.3-10.5)   | 7.3<br>(0.2-14.3)    | 6.2<br>(0-12.5)     | 7.4<br>(3.7-11.2)   |
| Bleeding leading to emergent treatment, % (95% CI)                            | 9.8<br>(6.3-13.3)   | 15.2<br>(5.4-24.9)   | 10.5<br>(2-18.9)    | 7.9<br>(4.3-11.5)   |

|   |                     |                     |                     |                     |
|---|---------------------|---------------------|---------------------|---------------------|
| Specific types of bleeding, % (95% CI)  | 4.0<br>(1.8-6.2)    | 7.2<br>(0-14.4)     | 2.5<br>(0-7.6)      | 3.3<br>(1-5.5)      |
| Discontinuation of all concomitant ITP treatments, % (95% CI)                   | 58<br>(49.7-66.2)   | 74.4<br>(57.6-91.3) | 68.8<br>(45.4-92.1) | 51.1<br>(40.6-61.7) |
| Discontinuation of oral steroids, IV steroids, IVIg, &/or IV anti-D, % (95% CI) | 56.9<br>(48.8-65.1) | 77.3<br>(62.7-92)   | 68.8<br>(44.1-93.4) | 48.1<br>(38.3-58)   |
| Receipt of splenectomy, % (95% CI)  | 3.7<br>(1.6-5.9)    | 1.8<br>(0-5.1)      | 12.8<br>(3.6-22)    | 2.3<br>(0.2-4.4)    |

ITP, immune thrombocytopenia; CI, confidence interval; IV, intravenous

\* $\geq 75\%$  of all recorded platelet count measurements  $\geq 50 \times 10^9/L$  during weeks 14 through 24 after the index date

**Table S5.** Demographic and clinical characteristics of patients at romiplostim initiation, among patients with refractory ITP

|  | ITP duration (months) |              |                |                |
|--|-----------------------|--------------|----------------|----------------|
|  | Overall<br>(n=231)    | <3<br>(n=29) | 3-12<br>(n=30) | >12<br>(n=172) |
| <b>Age, median (min, max)</b>                | 59 (18, 91)           | 75 (19, 87)  | 58 (21, 79)    | 59 (18, 91)    |
| <b>Age at romiplostim initiation (years)</b> |                       |              |                |                |
| 18-64  | 135 (58.4%)           | 13 (44.8%)   | 18 (60.0%)     | 104 (60.5%)    |
| 65-74  | 48 (20.8%)            | 1 (3.4%)     | 7 (23.3%)      | 40 (23.3%)     |
| 75+  | 48 (20.8%)            | 15 (51.7%)   | 5 (16.7%)      | 28 (16.3%)     |
| <b>Male Sex</b>                              | 101 (43.7%)           | 12 (41.4%)   | 19 (63.3%)     | 70 (40.7%)     |
| <b>Year of Romiplostim initiation</b>        |                       |              |                |                |
| 2009   | 50 (21.6%)            | 4 (13.8%)    | 6 (20.0%)      | 40 (23.3%)     |
| 2010   | 106 (45.9%)           | 18 (62.1%)   | 13 (43.3%)     | 75 (43.6%)     |

|  |                |                 |               |               |
|--|----------------|-----------------|---------------|---------------|
| 2011   | 45 (19.5%)     | 6 (20.7%)       | 8 (26.7%)     | 31 (18.0%)    |
| 2012   | 30 (13.0%)     | 1 (3.4%)        | 3 (10.0%)     | 26 (15.1%)    |
| <b>Weight in Kilograms at baseline, median (min, max)</b>            | 77 (24, 160)   | 79 (45, 130)    | 75 (24, 120)  | 76 (43, 160)  |
| Missing  | 1 (0.4%)       | 0 (0%)          | 0 (0%)        | 1 (0.6%)      |
| <b>History of thrombotic events</b>                                  | 25 (10.8%)     | 4 (13.8%)       | 2 (6.7%)      | 19 (11.0%)    |
| <b>History of myocardial infarction</b>                              | 5 (2.2%)       | 0 (0%)          | 0 (0%)        | 5 (2.9%)      |
| <b>History of liver event *</b>                                      | 7 (3.0%)       | 0 (0%)          | 0 (0%)        | 7 (4.1%)      |
| <b>History of splenectomy</b>  | 116 (50.2%)    | 5 (17.2%)       | 4 (13.3%)     | 107 (62.2%)   |
| <b>Baseline platelet count x 10<sup>9</sup>/L, median (min, max)</b> | 20 (1.0, 380)  | 17 (1.0, 190)   | 19 (1.0, 150) | 20 (1.0, 380) |
| Missing  | 3 (1.3%)       | 0 (0%)          | 0 (0%)        | 3 (1.7%)      |
| <b>Baseline platelet count</b>                                       |                |                 |               |               |
| ≤15  | 90 (39.0%)     | 13 (44.8%)      | 13 (43.3%)    | 64 (37.2%)    |
| >30  | 73 (31.6%)     | 4 (13.8%)       | 12 (40.0%)    | 57 (33.1%)    |
| 16-30  | 65 (28.1%)     | 12 (41.4%)      | 5 (16.7%)     | 48 (27.9%)    |
| Missing  | 3 (1.3%)       | 0 (0%)          | 0 (0%)        | 3 (1.7%)      |
| <b>Duration of ITP, months, median (Min, Max)</b>                    | 53 (0.18, 670) | 1.2 (0.18, 3.0) | 6.4 (3.0, 12) | 87 (12, 670)  |
| <b>History of bleeding</b>   | 112 (48.5%)    | 28 (96.6%)      | 16 (53.3%)    | 68 (39.5%)    |
| <b>Hospitalized bleeding</b>   | 68 (29.4%)     | 15 (51.7%)      | 13 (43.3%)    | 40 (23.3%)    |
| <b>Active bleeding</b>   | 35 (15.2%)     | 7 (24.1%)       | 4 (13.3%)     | 24 (14.0%)    |
| <b><u>Prior ITP therapies</u></b>                                    |                |                 |               |               |
| <b>Oral steroid</b>  | 196 (84.8%)    | 23 (79.3%)      | 27 (90.0%)    | 146 (84.9%)   |
| <b>IV anti-D</b>   | 11 (4.8%)      | 0 (0%)          | 0 (0%)        | 11 (6.4%)     |

|  |                |                |                |                |
|--|----------------|----------------|----------------|----------------|
| <b>IVIg</b>  | 189 (81.8%)    | 28 (96.6%)     | 28 (93.3%)     | 133 (77.3%)    |
| <b>IV steroid</b>  | 89 (38.5%)     | 20 (69.0%)     | 15 (50.0%)     | 54 (31.4%)     |
| <b>Platelet transfusion</b>  | 49 (21.2%)     | 17 (58.6%)     | 8 (26.7%)      | 24 (14.0%)     |
| <b>History of splenectomy</b>  | 116 (50.2%)    | 5 (17.2%)      | 4 (13.3%)      | 107 (62.2%)    |
| <b>AHSCT</b>   | 1 (0.4%)       | 0 (0%)         | 0 (0%)         | 1 (0.6%)       |
| <b>Azathioprine</b>  | 27 (11.7%)     | 0 (0%)         | 5 (16.7%)      | 22 (12.8%)     |
| <b>Alemtuzumab</b>   | 0 (0%)         | 0 (0%)         | 0 (0%)         | 0 (0%)         |
| <b>Cyclophosphamide</b>  | 21 (9.1%)      | 0 (0%)         | 1 (3.3%)       | 20 (11.6%)     |
| <b>Cyclosporine</b>  | 31 (13.4%)     | 0 (0%)         | 4 (13.3%)      | 27 (15.7%)     |
| <b>Danazol</b>   | 33 (14.3%)     | 0 (0%)         | 3 (10.0%)      | 30 (17.4%)     |
| <b>Dapsone</b>   | 19 (8.2%)      | 0 (0%)         | 3 (10.0%)      | 16 (9.3%)      |
| <b>Mycophenolate</b>   | 6 (2.6%)       | 0 (0%)         | 1 (3.3%)       | 5 (2.9%)       |
| <b>Rituximab</b>   | 114 (49.4%)    | 6 (20.7%)      | 18 (60.0%)     | 90 (52.3%)     |
| <b>Vinca alkaloids</b>   | 25 (10.8%)     | 3 (10.3%)      | 3 (10.0%)      | 19 (11.0%)     |
| <b>Number of previous ITP treatments received, median (min, max)</b> | 3.0 (0.0, 9.0) | 3.0 (1.0, 5.0) | 4.0 (0.0, 6.0) | 3.0 (0.0, 9.0) |
| <b>Number of previous ITP treatments received, category</b>          |                |                |                |                |
| 0  | 9 (3.9%)       | 0 (0%)         | 1 (3.3%)       | 8 (4.7%)       |
| 1  | 13 (5.6%)      | 1 (3.4%)       | 1 (3.3%)       | 11 (6.4%)      |
| 2  | 21 (9.1%)      | 2 (6.9%)       | 0 (0%)         | 19 (11.0%)     |
| 3+   | 188 (81.4%)    | 26 (89.7%)     | 28 (93.3%)     | 134 (77.9%)    |

ITP, immune thrombocytopenia; IV, intravenous; AHSCT, Autologous haematopoietic stem cell transplantation

\*Measured in the 5 years before romiplostim initiation



**Table S6.** Concomitant treatments at romiplostim initiation, among patients with refractory ITP

|   | ITP duration (months) |                |                |                |
|---|-----------------------|----------------|----------------|----------------|
|   | Overall<br>(n=231)    | <3<br>(n=29)   | 3-12<br>(n=30) | >12<br>(n=172) |
| <b>Oral steroid</b>   | 90 (39.0%)            | 15 (51.7%)     | 11 (36.7%)     | 64 (37.2%)     |
| <b>IV anti-D</b>  | 0 (0%)                | 0 (0%)         | 0 (0%)         | 0 (0%)         |
| <b>IVIg</b>   | 18 (7.8%)             | 3 (10.3%)      | 3 (10.0%)      | 12 (7.0%)      |
| <b>IV steroid</b>   | 6 (2.6%)              | 1 (3.4%)       | 1 (3.3%)       | 4 (2.3%)       |
| <b>Azathioprine</b>   | 4 (1.7%)              | 0 (0%)         | 1 (3.3%)       | 3 (1.7%)       |
| <b>Alemtuzumab</b>  | 0 (0%)                | 0 (0%)         | 0 (0%)         | 0 (0%)         |
| <b>Cyclophosphamide</b>                                     | 0 (0%)                | 0 (0%)         | 0 (0%)         | 0 (0%)         |
| <b>Cyclosporine</b>   | 3 (1.3%)              | 0 (0%)         | 1 (3.3%)       | 2 (1.2%)       |
| <b>Danazol</b>  | 3 (1.3%)              | 0 (0%)         | 0 (0%)         | 3 (1.7%)       |
| <b>Dapsone</b>  | 4 (1.7%)              | 0 (0%)         | 0 (0%)         | 4 (2.3%)       |
| <b>Mycophenolate</b>  | 2 (0.9%)              | 0 (0%)         | 0 (0%)         | 2 (1.2%)       |
| <b>Rituximab</b>  | 3 (1.3%)              | 1 (3.4%)       | 0 (0%)         | 2 (1.2%)       |
| <b>Vinca alkaloids</b>                                      | 2 (0.9%)              | 1 (3.4%)       | 0 (0%)         | 1 (0.6%)       |
| <b>AHSCT</b>  | 0 (0%)                | 0 (0%)         | 0 (0%)         | 0 (0%)         |
| <b>Platelet transfusion</b>                                 | 11 (4.8%)             | 5 (17.2%)      | 2 (6.7%)       | 4 (2.3%)       |
| <b>Number of ITP treatments received, median (min, max)</b> | 0.0 (0.0, 5.0)        | 1.0 (0.0, 3.0) | 0.0 (0.0, 3.0) | 0.0 (0.0, 5.0) |
| <b>Number of ITP treatments received category</b>           |                       |                |                |                |
| 0   | 116 (50.2%)           | 10 (34.5%)     | 16 (53.3%)     | 90 (52.3%)     |
| 1   | 89 (38.5%)            | 13 (44.8%)     | 10 (33.3%)     | 66 (38.4%)     |
| 2   | 23 (10.0%)            | 5 (17.2%)      | 3 (10.0%)      | 15 (8.7%)      |

|    | ITP duration (months) |              |                |                |
|----|-----------------------|--------------|----------------|----------------|
|    | Overall<br>(n=231)    | <3<br>(n=29) | 3-12<br>(n=30) | >12<br>(n=172) |
| 3+ | 3 (1.3%)              | 1 (3.4%)     | 1 (3.3%)       | 1 (0.6%)       |

ITP, immune thrombocytopenia; IV, intravenous; AHSCT, Autologous haematopoietic stem cell transplantation

\*Medications were flagged as concomitant if the index romiplostim date fell between or on the start or end date of the medication.

**Table S7.** Romiplostim usage and dosing during 24-week follow-up period, among patients with refractory ITP.

|  | ITP duration (months) |                 |                 |                 |
|--|-----------------------|-----------------|-----------------|-----------------|
|  | Overall<br>(n=231)    | <3<br>(n=29)    | 3-12<br>(n=30)  | >12<br>(n=172)  |
| <b>Duration of exposure (weeks)</b>          |                       |                 |                 |                 |
| Mean (SD)                                    | 22 (5.3)              | 20 (6.9)        | 23 (3.4)        | 22 (5.2)        |
| Median (min, max)                            | 24 (1.0, 24)          | 24 (4.9, 24)    | 24 (10, 24)     | 24 (1.0, 24)    |
| <b>Number of romiplostim administrations</b> |                       |                 |                 |                 |
| Mean (SD)                                    | 18 (7.6)              | 17 (7.4)        | 18 (7.0)        | 19 (7.8)        |
| Median (min, max)                            | 22 (1.0, 46)          | 21 (4.0, 25)    | 23 (3.0, 24)    | 22 (1.0, 46)    |
| <b>Cumulative dose (µg/kg)</b>               |                       |                 |                 |                 |
| Mean (SD)                                    | 65 (56)               | 46 (24)         | 75 (57)         | 66 (59)         |
| Median (min, max)                            | 48 (1.0, 440)         | 43 (10, 120)    | 59 (4.0, 210)   | 51 (1.0, 440)   |
| <b>Average weekly dose (µg/kg)</b>           |                       |                 |                 |                 |
| Mean (SD)                                    | 3.0 (2.3)             | 2.5 (1.2)       | 3.3 (2.4)       | 3.0 (2.5)       |
| Median (min, max)                            | 2.4 (0.042, 18)       | 2.1 (0.66, 6.5) | 2.5 (0.17, 8.6) | 2.5 (0.042, 18) |
| <b>Initial romiplostim dose, n(%)</b>        |                       |                 |                 |                 |
| 1  | 161 (69.7%)           | 16 (55.2%)      | 18 (60.0%)      | 127 (73.8%)     |

|                                      |             |            |            |            |
|--------------------------------------|-------------|------------|------------|------------|
| 2                                    | 31 (13.4%)  | 4 (13.8%)  | 7 (23.3%)  | 20 (11.6%) |
| ≥3                                   | 39 (16.9%)  | 9 (31.0%)  | 5 (16.7%)  | 25 (14.5%) |
| <b>Maximum dose category (µg/kg)</b> |             |            |            |            |
| ≤3                                   | 108 (46.8%) | 15 (51.7%) | 10 (33.3%) | 83 (48.3%) |
| 4-9                                  | 98 (42.4%)  | 13 (44.8%) | 14 (46.7%) | 71 (41.3%) |
| 10                                   | 25 (10.8%)  | 1 (3.4%)   | 6 (20.0%)  | 18 (10.5%) |
| >10                                  | 0 (0%)      | 0 (0%)     | 0 (0%)     | 0 (0%)     |

\*SD, standard deviation

**Table S8.** Effectiveness outcomes during 24-week follow-up period for patients with refractory ITP.

|   | Overall<br>(n=231)  | ITP duration (months) |                     |                     |
|---|---------------------|-----------------------|---------------------|---------------------|
|   |                     | <3<br>(n=29)          | 3-12<br>(n=30)      | >12<br>(n=172)      |
| <b>Platelet-Based Endpoints</b>                 |                     |                       |                     |                     |
| Proportion with durable platelet response,<br>% | 43.5<br>(36-51)     | 31.8<br>(16.3-47.3)   | 43.5<br>(25.3-61.7) | 45.6<br>(36.6-54.6) |
| Overall platelet response, %                    | 79.6<br>(75.2-83.9) | 93.2<br>(85.5-100)    | 76.5<br>(64.9-88.2) | 78.9<br>(73.2-84.5) |
| Median overall platelet count                   | 85<br>(77.2-92.8)   | 126<br>(103.8-148.2)  | 83<br>(53.4-112.6)  | 84<br>(73.8-94.2)   |

|  |                     |                     |                     |                     |
|--|---------------------|---------------------|---------------------|---------------------|
| First platelet response by week 24, %                                | 96.2<br>(93.5-98.9) | 94.6<br>(86.2-100)  | 99.1<br>(96.8-100)  | 95.2<br>(92-98.5)   |
| <b>Rescue Therapy Use</b>  |                     |                     |                     |                     |
| Any rescue, %  | 27.4<br>(22.1-32.7) | 51.8<br>(35.6-68)   | 26.8<br>(11.1-42.6) | 23.4<br>(17.1-29.8) |
| Oral steroids as rescue, %   | 15.9<br>(11.1-20.7) | 26.8<br>(9-44.7)    | 10.3<br>(0-22.2)    | 15<br>(9.6-20.4)    |
| IV anti-D, IVIg, IV steroids &/or platelet transfusions as rescue, % | 17.5<br>(12.8-22.1) | 30.4<br>(13.9-47)   | 26.8<br>(11.1-42.6) | 13.6<br>(8.3-19)    |
| <b>Bleeding</b>  |                     |                     |                     |                     |
| Any bleeding, %  | 27.2<br>(21.4-33.1) | 34.4<br>(14.3-54.6) | 24.5<br>(8.4-40.5)  | 26.5<br>(20.2-32.8) |
| Hospitalized bleeding, %   | 8.8<br>(5.1-12.5)   | 8.2<br>(0-18.5)     | 6.9<br>(0-15.7)     | 9.2<br>(5.2-13.3)   |
| Bleeding leading to emergent treatment, %                            | 11.9<br>(7.3-16.6)  | 22.8<br>(5.4-40.2)  | 13.8<br>(0.1-27.5)  | 9.9<br>(5.4-14.3)   |
| Specific types of bleeding, %  | 4.7<br>(2.3-7.1)    | 12.3<br>(0-26.2)    | 3.8<br>(0-11.4)     | 3.7<br>(0.5-6.9)    |
| <b>Discontinuation of Concomitant ITP Treatments</b>                 |                     |                     |                     |                     |
| Discontinuation of any concomitant ITP treatments, %                 | 53.2<br>(43.3-63)   | 64.9<br>(43.6-86.2) | 72.7<br>(44.2-100)  | 47.9<br>(35.5-60.3) |

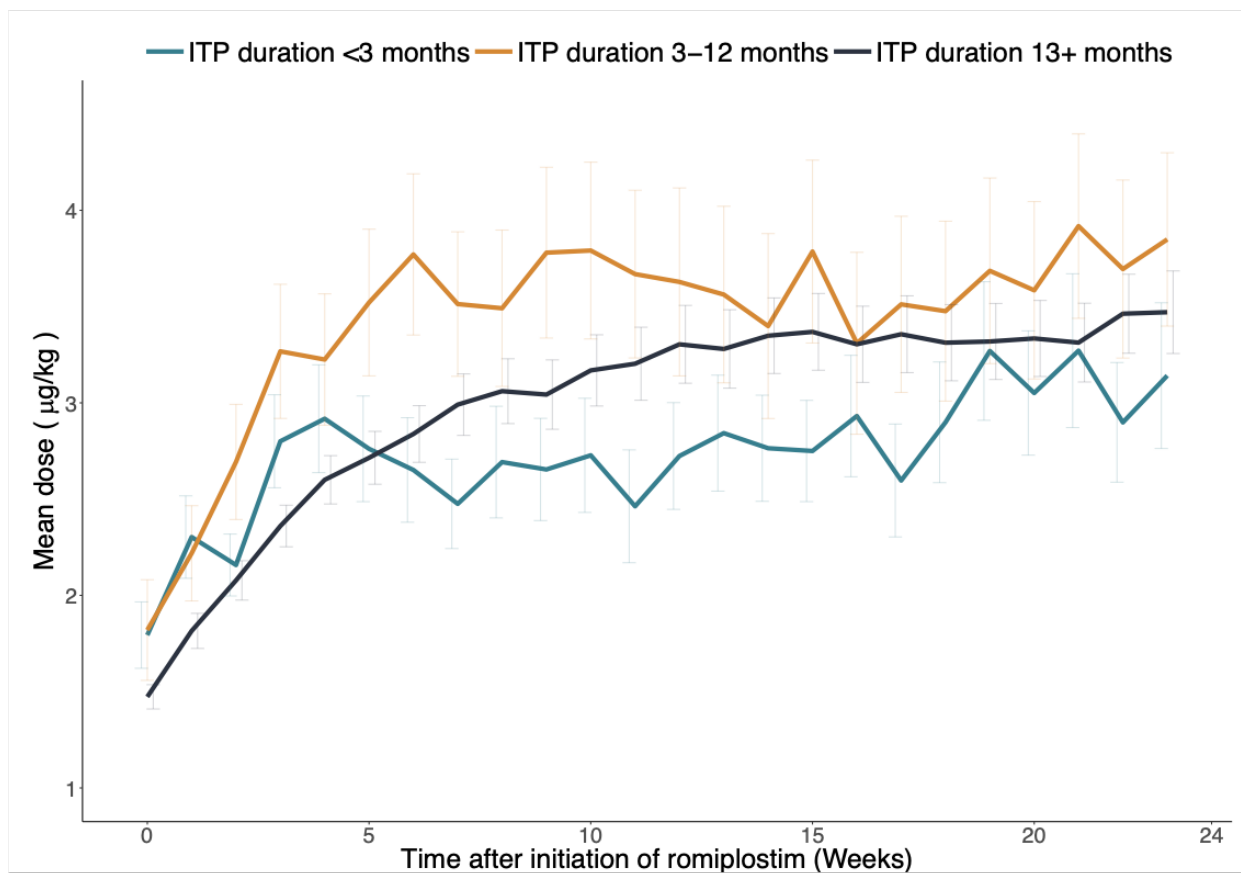
|  |                     |                     |                    |                     |
|--|---------------------|---------------------|--------------------|---------------------|
| Discontinuation of oral steroids, IV steroids, IVIg, &/or IV anti-D, % | 52.8<br>(41.4-64.2) | 72.1<br>(46.3-97.9) | 72.7<br>(44.2-100) | 45.5<br>(33.5-57.4) |
|--|---------------------|---------------------|--------------------|---------------------|

ITP, immune thrombocytopenia; IV, intravenous

**Table S9.** Adverse drug reactions during 24-week follow-up period

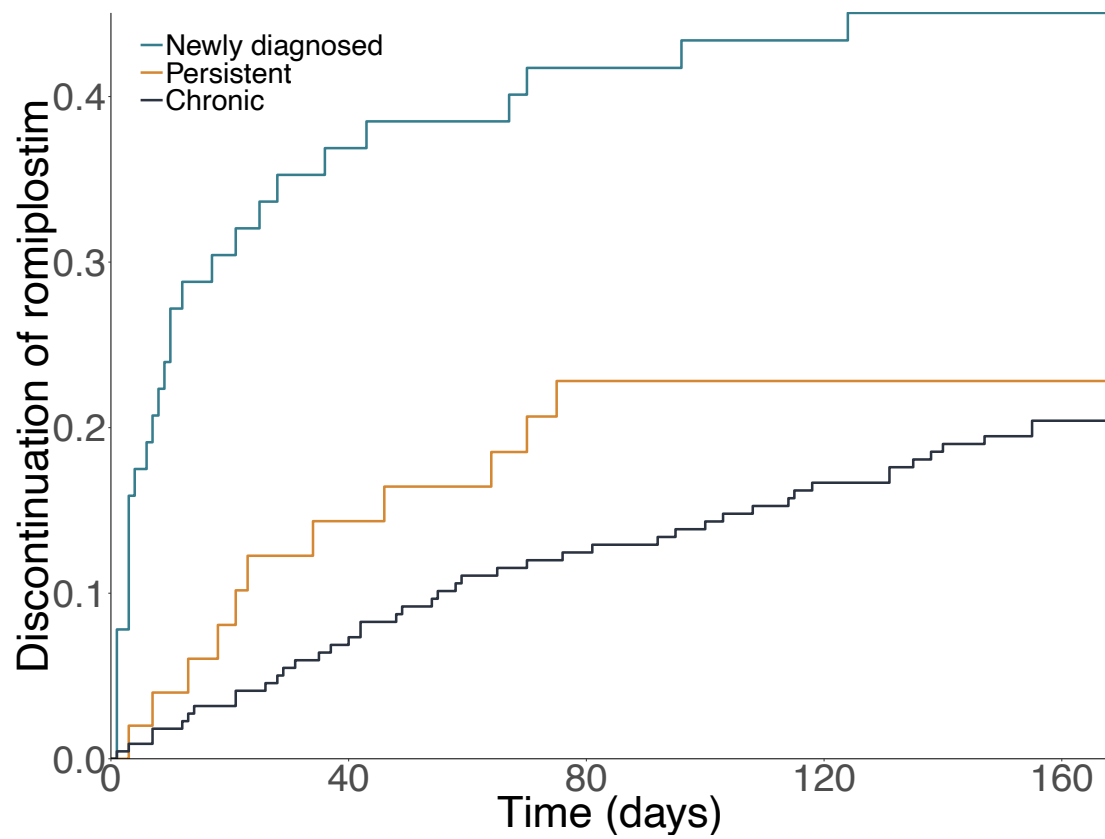
|                              | Overall<br>(n=231)  | ITP duration (months) |                  |                   |
|------------------------------|---------------------|-----------------------|------------------|-------------------|
|                              |                     | <3<br>(n=29)          | 3-12<br>(n=30)   | >12<br>(n=172)    |
| Any ADR, % (95% CI)          | 17.6<br>(12.5-22.7) | 25.2<br>(6.9-43.6)    | 20.6<br>(6.3-35) | 16<br>(10.8-21.2) |
| Thrombotic ADRs, % (95% CI)  | 1.9<br>(0.1-3.8)    | 4.2<br>(0-12.6)       | 0<br>(0-0)       | 1.9<br>(0.2-3.7)  |
| Bone Marrow ADRs, % (95% CI) | 0<br>(0-0)          | 0<br>(0-0)            | 0<br>(0-0)       | 0<br>(0-0)        |

ADR, adverse drug reaction; CI, 95% confidence interval



| <b>N Patients</b> | <b>Week 0</b> | <b>Week 12</b> | <b>Week 24</b> |
|-------------------|---------------|----------------|----------------|
| <3 months         | 64            | 47             | 42             |
| 3-12 months       | 50            | 43             | 41             |
| 13+ months        | 226           | 198            | 185            |

**Figure S1.** Unweighted mean dose over the 24-week study period.



**Figure S2.** Cumulative incidence of romiplostim discontinuation, by duration of ITP at romiplostim initiation.

**Appendix 1:** R packages and versions used in analyses.

| Package               | Version |
|-----------------------|---------|
| causalRisk (internal) | 0.26    |

|           |        |
|-----------|--------|
| tidyverse | 1.2.1  |
| drake     | 7.12.0 |
| table1    | 1.2    |
| htmlTable | 1.13.1 |
| survival  | 3.1.12 |
| glmnet    | 2.0.18 |