

**LABORATORY PREDICTORS OF BLEEDING, AND EFFECT OF PLATELET AND  
RBC TRANSFUSIONS ON BLEEDING OUTCOMES, IN THE PLADO TRIAL**

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**Supplemental Table 1.** Definitions of WHO bleeding grades.

	Grade 1	Grade 2	Grade 3
<b>Oral and nasal</b>	<ul style="list-style-type: none"> <li>➤ Oropharyngeal bleeding – total duration of all episodes in previous 24 hours <math>\leq</math> 30 minutes*</li> <li>➤ Petechiae of oral mucosa</li> <li>➤ Epistaxis – total duration of all episodes in previous 24 hours <math>\leq</math> 30 minutes*</li> </ul>	<ul style="list-style-type: none"> <li>➤ Oropharyngeal bleeding – total duration of all episodes in previous 24 hours <math>&gt;</math> 30 minutes*</li> <li>➤ Epistaxis – total duration of all episodes in previous 24 hours <math>&gt;</math> 30 minutes*</li> </ul>	<ul style="list-style-type: none"> <li>➤ Any bleeding requiring RBC transfusion over routine transfusion needs**</li> </ul>
<b>Skin, soft tissue, musculoskeletal</b>	<ul style="list-style-type: none"> <li>➤ Petechiae of skin</li> <li>➤ Purpura <math>\leq</math> 1 inch diameter</li> <li>➤ One or more spontaneous hematomas in the soft tissue or muscle <math>&gt;</math> 1"</li> </ul>	<ul style="list-style-type: none"> <li>➤ Purpura <math>&gt;</math> 1 inch diameter</li> <li>➤ Spontaneous hematoma in deeper tissues</li> <li>➤ Joint bleeding (confirmed by aspiration, imaging study or other accepted technique)</li> </ul>	<ul style="list-style-type: none"> <li>➤ Any bleeding requiring RBC transfusion over routine transfusion needs**</li> </ul>
<b>Gastrointestinal</b>	<ul style="list-style-type: none"> <li>➤ Positive stool occult blood test</li> </ul>	<ul style="list-style-type: none"> <li>➤ Melanotic stool</li> <li>➤ Hematochezia – visible red blood mixed in stool, not requiring a transfusion</li> <li>➤ Hematemesis – Grossly visible blood in emesis or in nasogastric drainage tube (not related or secondary to swallowed blood)</li> </ul>	<ul style="list-style-type: none"> <li>➤ Any bleeding requiring RBC transfusion over routine transfusion needs**</li> </ul>
<b>Genitourinary</b>	<ul style="list-style-type: none"> <li>➤ Any biochemical or microscopic Hb/RBCs without red urine</li> <li>➤ Abnormal vaginal bleeding (Unexpected bleeding out of normal cycle <b>OR</b> Bleeding heavier than normal <b>OR</b> Breakthrough bleeding (patient on hormonal therapy to prevent bleeding)) with spotting</li> </ul>	<ul style="list-style-type: none"> <li>➤ Gross/visible hematuria without need for transfusion</li> <li>➤ Abnormal vaginal bleeding (Unexpected bleeding out of normal cycle <b>OR</b> Bleeding heavier than normal <b>OR</b> Breakthrough bleeding (patient on hormonal therapy to prevent bleeding)) more than spotting</li> </ul>	<ul style="list-style-type: none"> <li>➤ Any bleeding requiring RBC transfusion over routine transfusion needs**</li> </ul>
<b>Pulmonary</b>		<ul style="list-style-type: none"> <li>➤ Hemoptysis – Visible blood</li> <li>➤ Blood in broncho-pulmonary lavage, or blood tinged sputum (excluding those with nose or oropharyngeal bleeding)</li> </ul>	<ul style="list-style-type: none"> <li>➤ Any bleeding requiring RBC transfusion over routine transfusion needs**</li> </ul>

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Supplemental Table 1, Continued

	Grade 1	Grade 2	Grade 3
<b>Body Cavity</b>		<ul style="list-style-type: none"> <li>➤ Visible blood in body cavity fluid (e.g. red cells apparent in fluid aspirate) short of criteria for Grade 3 or 4</li> </ul>	<ul style="list-style-type: none"> <li>➤ Grossly bloody body cavity fluids and organ dysfunction with symptoms, and/or need to intervene (e.g. to aspirate), and/or need for transfusion</li> </ul>
<b>Central Nervous System</b>		<ul style="list-style-type: none"> <li>➤ Retinal bleeding without visual impairment</li> <li>➤ Lumbar puncture with blood (&gt;5 RBC/μL in CSF on microscopic analysis and non-traumatic tap), no symptoms and no visible red color</li> </ul>	<ul style="list-style-type: none"> <li>➤ Lumbar puncture with visible red color in absence of symptoms, and non-traumatic tap</li> </ul>
<b>Invasive Sites</b>		<ul style="list-style-type: none"> <li>➤ Bleeding at invasive sites (venipuncture sites, intravenous lines or catheter exit sites): active oozing at site for a cumulative total of &gt; 1 hour in the previous 24 hours</li> </ul>	<ul style="list-style-type: none"> <li>➤ Any bleeding requiring RBC transfusion over routine transfusion needs**</li> </ul>
<b>Hemodynamic Instability</b>			<ul style="list-style-type: none"> <li>➤ Any bleeding associated with moderate hemodynamic instability (hypotension; &gt;30mmHg fall or &gt;30% decrease in either systolic or diastolic blood pressure) and requiring RBC transfusion over routine transfusion needs**</li> </ul>

\*Count actual bleeding (i.e. "running out" or need for basin, Kleenex, towel, etc.) not minor bleeding

\*\*Red cell transfusion must be specifically related to treatment of bleeding within 24 hours of onset of bleeding

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**Supplemental Table 1**, continued**GRADE 2A:** Grade 2 bleeding not due solely to purpura > 1 inch in diameter**GRADE 4:**

- ◆ Any bleeding associated with severe hemodynamic instability (hypotension; >50mm/Hg fall or >50% decrease in either systolic or diastolic blood pressure, with associated tachycardia (heart rate increase of  $\geq 20\%$  for 20 minutes) and requiring RBC transfusion over routine transfusion needs
- ◆ Fatal bleeding from any source
- ◆ Retinal bleeding with visual impairment (Visual impairment is defined as a field deficit, and patients with suspected visual impairment require an ophthalmologic consult for documentation)
- ◆ CNS symptoms with non-traumatic bloody lumbar puncture
- ◆ CNS bleeding on imaging study with or without dysfunction