Platelet Transfusion for Patients with Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update
Introduction

• The purpose of this guideline is to provide updated recommendations regarding the use of platelet transfusion in people with cancer.

• ASCO first published a guideline on platelet transfusion in people with cancer in 2001.

• The guideline recognized the important role of platelet transfusion in the prevention and treatment of bleeding in patients with treatment-related thrombocytopenia, but also sought to avoid the overuse of platelet transfusions by identifying patients who are most likely to benefit.

• This guideline update reaffirms several of the earlier recommendations, but includes some important changes, such as reconsideration of the need for prophylactic platelet transfusion in adult patients undergoing autologous stem cell transplantation at experienced centers.
ASCO Guideline Development Methodology

The ASCO Clinical Practice Guidelines Committee guideline process includes:

- a systematic literature review by ASCO guidelines staff
- an expert panel provides critical review and evidence interpretation to inform guideline recommendations
- final guideline approval by ASCO CPGC

The full ASCO Guideline methodology supplement can be found at:

www.asco.org/supportive-care-guidelines
Clinical Questions

This clinical practice guideline addresses the following clinical questions:

(1) How should platelets for transfusion be prepared?

(2) In what circumstances should providers take steps to prevent Rh alloimmunization resulting from platelet transfusion?

(3) In what circumstances should providers use leukoreduced blood products to prevent alloimmunization?

(4) Should platelet transfusions be given prophylactically or therapeutically?

(5) What is the appropriate threshold for prophylactic platelet transfusion in patients with hematologic malignancies?
Clinical Questions

(6) What is the appropriate threshold for prophylactic platelet transfusion in the setting of hematopoietic cell transplantation?

(7) Is there a role for prophylactic platelet transfusion in patients with chronic, stable, severe thrombocytopenia who are not receiving active treatment?

(8) What is the appropriate threshold for prophylactic platelet transfusion in patients with solid tumors?

(9) At what platelet count can surgical or invasive procedures be performed?

(10) When and how should patients be monitored for refractoriness to platelet transfusion?

(11) How should refractoriness to platelet transfusion be managed?
Target Population

Adults and children (≥ 4 months of age) with hematologic malignancies, solid tumors or hypoproliferative thrombocytopenia.

Target Audience

Clinicians administering intensive therapies to patients with cancer
Summary of Recommendations

CLINICAL QUESTION 1
How should platelets for transfusion be prepared?

Recommendation 1
Platelets for transfusion can be prepared either by separation of units of platelet concentrates (PCs) from whole blood using either the buffy coat or platelet-rich plasma method, which can be pooled before administration, or by apheresis from single donors. Comparative studies have shown that the posttransfusion increments, hemostatic benefit, and side effects are similar with any of these platelet products. Thus, in routine circumstances, they can be used interchangeably. In most centers, pooled PCs are less costly. Single-donor platelets from selected donors are necessary when histocompatible platelet transfusions are needed. (Type: Evidence based; Evidence quality: High; Strength of recommendation: Strong.)

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CLINICAL QUESTION 2
In what circumstances should providers take steps to prevent Rh alloimmunization resulting from platelet transfusion?

Recommendation 2
Prevention of RhD alloimmunization resulting from platelet transfusions to RhD-negative recipients can be achieved either through the exclusive use of platelet products collected from RhD-negative donors or via anti-D immunoprophylaxis. These approaches may be used for female children and female adults of childbearing potential being treated with curative intent. However, because of the low rate of RhD alloimmunization in cancer patients, these approaches need not be applied universally. (Type: Evidence based; Evidence quality: Intermediate; Strength of recommendation: Moderate.)
Summary of Recommendations

CLINICAL QUESTION 3
In what circumstances should providers use leukoreduced blood products to prevent alloimmunization?

Recommendation 3
The incidence of alloantibody mediated refractoriness to platelet transfusion can be decreased in patients with acute myeloid leukemia (AML) receiving induction chemotherapy when both platelet and RBC products are leukoreduced before transfusion. It is therefore appropriate to provide leukoreduced blood products to patients with AML from the time of diagnosis to ameliorate this important clinical problem. Although randomized trials have not been conducted in other patient groups, it is likely that alloimmunization can also be decreased in patients with other types of leukemia and in other cancer patients receiving chemotherapy. There are less data in patients who are not receiving chemotherapy in the same time periods that the transfusions are being administered (for example, aplastic anemia, myelodysplasia), although the consensus would favor its use in these patients as well. In the United States and several other countries, the overwhelming majority of blood products are now leukoreduced at the time of blood collection and component preparation. Other advantages of prestorage leukoreduction include a substantial reduction in transfusion reactions and transmission of cytomegalovirus (CMV) infection. (Type: Evidence based; Evidence quality: High; Strength of recommendation: Strong.)

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CLINICAL QUESTION 4
Should platelet transfusions be given prophylactically or therapeutically?

Recommendation 4
Prophylactic platelet transfusion should be administered to patients with thrombocytopenia resulting from impaired bone marrow function to reduce the risk of hemorrhage when the platelet count falls below a predefined threshold level. This threshold level for transfusion varies according to the patient’s diagnosis, clinical condition, and treatment modality.(Type: Evidence based; Evidence quality: High; Strength of recommendation: Strong)
CLINICAL QUESTION 5
What is the appropriate threshold for prophylactic platelet transfusion in patients with hematologic malignancies?

Recommendation 5
The Panel recommends a threshold of < 10 X 10⁹/L for prophylactic platelet transfusion in patients receiving therapy for hematologic malignancies. Transfusion at higher levels may be advisable in patients with signs of hemorrhage, high fever, hyperleukocytosis, rapid fall of platelet count, or coagulation abnormalities (for example, acute promyelocytic leukemia) and in those undergoing invasive procedures or in circumstances in which platelet transfusions may not be readily available in case of emergencies, as might be the case in outpatients who live at a distance from the treatment center. (Type: Evidence based; Evidence quality: High; Strength of recommendation: Strong.)
Summary of Recommendations

CLINICAL QUESTION 6
What is the appropriate threshold for prophylactic platelet transfusion in the setting of hematopoietic cell transplantation (HSCT)?

Recommendation 6
The Panel recommends a threshold of < 10 X 10^9/L for prophylactic platelet transfusion in adult and pediatric patients undergoing allogeneic HSCT. Prophylactic platelet transfusion may be administered at higher counts based on clinician judgement. In adult recipients of autologous HSCT, randomized trials have demonstrated similar rates of bleeding with decreased platelet usage when patients are transfused at the first sign of bleeding rather than prophylactically, and this approach may be used in experienced centers. This recommendation is not generalizable to pediatric patients. (Type: Evidence based; Evidence quality: High; Strength of recommendation: Moderate.)
Summary of Recommendations

CLINICAL QUESTION 7

Is there a role for prophylactic platelet transfusion in patients with chronic, stable, severe thrombocytopenia who are not receiving active treatment?

Recommendation 7

Patients with chronic, stable, severe thrombocytopenia, such as individuals with myelodysplasia or aplastic anemia, who are not receiving active treatment may be observed without prophylactic transfusion, reserving platelet transfusions for episodes of hemorrhage or during times of active treatment. (Type: Informal consensus; Evidence quality: Intermediate; Strength of recommendation: Moderate.)
CLINICAL QUESTION 8
What is the appropriate threshold for prophylactic platelet transfusion in patients with solid tumors?

Recommendation 8
The risk of bleeding in patients with solid tumors during chemotherapy-induced thrombocytopenia is related to the depth and duration of the platelet nadir, although other factors contribute as well. The Panel recommends a threshold of $< 10 \times 10^9/L$ for prophylactic platelet transfusion, based on extrapolation from studies in hematologic malignancies. Platelet transfusion at higher levels is appropriate in patients with active localized bleeding which can sometimes be seen in patients with necrotic tumors.

(Type: Informal consensus; Evidence quality: Low; Strength of recommendation: Moderate.)
CLINICAL QUESTION 9
At what platelet count can surgical or invasive procedures be performed?

Recommendation 9
The Panel recommends a threshold of 40 × 10⁹/L to 50 × 10⁹/L for performing major invasive procedures, in the absence of associated coagulation abnormalities. Certain procedures, such as bone marrow aspirations and biopsies, and insertion or removal of central venous catheters can be performed safely at counts ≥ 20 × 10⁹/L. There are sparse data, and no randomized trials, addressing the safety of other invasive procedures at much lower count levels. If platelet transfusions are administered before a procedure, it is critical that a posttransfusion platelet count be obtained to prove that the desired platelet count level has been reached. Platelet transfusions should also be available on short notice, in case intraoperative or postoperative bleeding occurs. For alloimmunized patients, histocompatible platelets must be available in these circumstances. (Type: Evidence based; Evidence quality: Low; Strength of recommendation: Weak.)
CLINICAL QUESTION 10
When and how should patients be monitored for refractoriness to platelet transfusion?

Recommendation 10
Although there are no empirical data to suggest that monitoring and acting on the post-platelet-transfusion count decreases the incidence of hemorrhagic events, the Panel consensus is that platelet counts performed 10 to 60 minutes posttransfusion should be obtained after all transfusions, when refractoriness is suspected. Because patients may have a poor increment to a single transfusion yet have excellent platelet increments with subsequent transfusions, a diagnosis of refractoriness to platelet transfusion should only be made when at least two transfusions of ABO-compatible units, stored < 72 hours, result in poor increments, as defined in the supporting text of the recommendation. (Type: Informal consensus; Evidence quality: Insufficient; Strength of recommendation: Moderate)
Summary of Recommendations

CLINICAL QUESTION 11
How should refractoriness to platelet transfusion be managed?

Recommendation 11
Alloimmunization is usually due to antibody against HLA antigens and only rarely to platelet specific antigens. Patients with alloimmune refractory thrombocytopenia, as defined above, are best managed with platelet transfusions from histocompatible donors matched for HLA-A and HLA-B antigens. Many blood suppliers have access to computerized lists of such donors. For patients (a) whose HLA type cannot be determined, (b) who have uncommon HLA types for whom suitable donors cannot be identified, or (c) who do not respond to HLA matched platelets, histocompatible platelet donors can often be identified using platelet cross-matching techniques. In many patients, these two techniques are complementary. (Type: Evidence based; Evidence quality: High; Strength of recommendation: Strong.)
Patient and Clinician Communication

• Treatment decision-making should be a process that is shared between clinicians and their patients.

• Clinicians must communicate evidence-based options for treatment, inclusive of their benefits and risks, and patients must be allowed to express their goals and preferences.

• It is important to recognize that patients are no longer reliant solely upon their medical team for information, and often access other sources online, in print, or through social media and support groups.

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Limitation of the Research and Future Research

- There are relatively few compelling studies addressing thresholds for prophylactic platelet transfusions in patients with solid tumors.

- Similarly, the paucity of information about the safety of certain invasive procedures in thrombocytopenic patients is disappointing.

- It is difficult to do randomized trials in these populations, in part because the incidence of serious bleeding is so low and hence the numbers of patients to be included would be very large.

- Nonetheless, careful assessment of the incidence of bleeding in a series of markedly thrombocytopenic patients undergoing different procedures can be quite informative and such research should be encouraged.

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Additional Resources

More information, including a Data Supplement, a Methodology Supplement, slide sets, and clinical tools and resources, is available at

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Patient information is available at www.cancer.net
# ASCO Guideline Panel Members

<table>
<thead>
<tr>
<th>Member</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Charles A. Schiffer, MD, Co-Chair</td>
<td>Karmanos Cancer Institute, Wayne State University School of Medicine, Detroit, MI</td>
</tr>
<tr>
<td>Kenneth C. Anderson, MD, Co-Chair</td>
<td>Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA</td>
</tr>
<tr>
<td>Meghan Delaney, DO, MPH</td>
<td>Children’s National Medical System &amp; George Washington University, Washington DC</td>
</tr>
<tr>
<td>Heather Hume, MD</td>
<td>CHU Sainte-Justine, University of Montreal, Quebec, Canada</td>
</tr>
<tr>
<td>Anthony J. Magdalinski, DO</td>
<td>Alliance Cancer Specialists, Sellersville, PA; PGIN Representative</td>
</tr>
<tr>
<td>Jeffrey J. McCullough, MD</td>
<td>University of Minnesota, Minneapolis, MN</td>
</tr>
<tr>
<td>James L. Omel, MD</td>
<td>Patient Representative, Grand Island, NE</td>
</tr>
<tr>
<td>John M. Rainey, MD</td>
<td>University Health Center, Lafayette, LA</td>
</tr>
<tr>
<td>Paolo Rebulla, MD</td>
<td>Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, Milan, Italy</td>
</tr>
<tr>
<td>Scott D. Rowley, MD</td>
<td>Hackensack University Medical Center, Hackensack, NJ</td>
</tr>
<tr>
<td>Michael B. Troner, MD</td>
<td>Miami Cancer Institute, Miami, FL</td>
</tr>
<tr>
<td>Kari Bohlke, ScD, Staff, Health Research Methodologist</td>
<td>American Society of Clinical Oncology, Alexandria, VA</td>
</tr>
</tbody>
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