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Guidance on Platelet Transfusion for Patients with Cancer

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The “Guidance on Platelet Transfusion for Patients with Hypoproliferative Thrombocytopenia” developed by the International Collaboration for Transfusion Medicine Guidelines (ICTMG) was endorsed by the COG Supportive Care Guideline Committee in April 2016. In October 2018, the evidence-based recommendations included in the “Platelet Transfusion for Patients with Cancer: American Society of Clinical Oncology (ASCO) Clinical Practice Guideline Update” were also endorsed by the Committee.

Both source guidelines are published (Nahirniak S, Slichter SJ, Tanael S, et al. *Transfus Med Rev.* 2015;29(1):3-13. doi.org/10.1016/j.tmr.2014.11.004; Schiffer CA, Bohlke K, Delaney M, et al. *J Clin Oncol.* 2018;36(3):283-299. doi:10.1200/JCO.2017.76.1734) and are available at: [http://www.tmreviews.com/article/S0887-7963\(14\)00095-9/pdf](http://www.tmreviews.com/article/S0887-7963(14)00095-9/pdf) and <http://ascopubs.org/doi/pdf/10.1200/JCO.2017.76.1734>

The purposes of the source guidelines are to provide evidence-based recommendations regarding the use of platelet transfusion in people with cancer. They are limited to people aged 4 months and older.

Recommendations from both endorsed clinical practice guidelines are presented in the table below. Recommendations deemed not to be generalizable to pediatric patients by the source clinical practice guideline panel have been omitted. Where the clinical practice guidelines address the same clinical question, the recommendation from the more current clinical practice guideline is presented.

Summary of Recommendations for Platelet Transfusion for Patients with Cancer

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
How should platelets for transfusion be prepared?	
<ul style="list-style-type: none"> Platelets for transfusion can be prepared either by separation of units of platelet concentrates (PCs) from whole blood using either the buffy coat (BC) or the platelet-rich plasma (PRP) method, which can be pooled before administration, or by apheresis from single donors. Comparative studies have shown that the post-transfusion increments, hemostatic benefit, and adverse 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. (ASCO Q1) 	<p>Evidence quality: High Strength of recommendation: Strong</p>

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
Should platelet transfusions be given prophylactically or therapeutically?	
<ul style="list-style-type: none"> 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. (ASCO Q4) 	<p>Evidence quality: High Strength of recommendation: Strong</p>
What platelet transfusion threshold should be used?	
<ul style="list-style-type: none"> Patients with Hematologic Malignancies: The Panel recommends a threshold of $<10 \times 10^9/L$ 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 (eg, 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 for outpatients who live at a distance from the treatment center. (ASCO Q5) 	<p>Evidence quality: High Strength of recommendation: Strong</p>
<ul style="list-style-type: none"> Patients in the Setting of Hematopoietic Stem Cell Transplant: The Panel recommends a threshold of $< 10 \times 10^9/L$ for prophylactic platelet transfusion in adult and pediatric patients undergoing allogeneic HSCT. Prophylactic platelet transfusion may be administered at higher counts based on clinician judgment. (ASCO Q6) 	<p>Evidence quality: High Strength of recommendation: Moderate</p>
<ul style="list-style-type: none"> Platelet Count at which Surgical or Invasive Procedures may be Performed: The Panel recommends a threshold of $40 \times 10^9/L$ to $50 \times 10^9/L$ for performing major invasive procedures in the absence of associated coagulation abnormalities. Certain procedures, such as bone marrow aspirations and biopsies, and removal of central venous catheters, can be performed safely at counts $< 20 \times 10^9/L$. 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 post-transfusion 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 post-operative bleeding occurs. For alloimmunized patients, histocompatible platelets must be available in these circumstances. (ASCO Q9) 	<p>Evidence quality: Low Strength of recommendation: Weak</p>

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
What platelet transfusion threshold should be used? (continued)	
<ul style="list-style-type: none"> Patients with hypoproliferative thrombocytopenia with clinically significant bleeding attributed to thrombocytopenia should probably receive platelet transfusions even if the platelet count is above $10 \times 10^9/L$. (ICTMG Q2, R3) 	Weak recommendation Very weak level of evidence
What platelet dose should be used?	
<ul style="list-style-type: none"> Low- or standard-dose platelet transfusion (i.e., $1.1 \times 10^{11}/m^2$ or $2.2 \times 10^{11}/m^2$, respectively), as opposed to high-dose platelet transfusion ($4.4 \times 10^{11}/m^2$), should be given to hospitalized patients with hypoproliferative thrombocytopenia who require prophylactic platelet transfusion. (ICTMG Q3, R4) Conversion to platelet units can be performed using estimates of 50×10^9 per unit of whole blood derived, random-donor platelet products or 300×10^9 per unit apheresis or buffy coat pooled products. (ICTMG Q3, R4) 	Strong recommendation High level of evidence
Implementation tips from the COG Supportive Care Guideline Committee: 1) In general, platelets that are collected via apheresis have a higher concentration (plt/mL) than pooled units collected as the platelet portion from whole blood donation. However, there is significant variability in platelet concentration within each type of platelet product (whole blood donation vs. apheresis collection) and between centers. The platelet doses recommended above can be converted to approximate platelet dose volumes after consultation with local transfusion medicine specialists. 2) For larger children or adolescents who require prophylactic platelet transfusion, the dose of transfused platelets should not exceed the usual adult dose.	
Should patients receive ABO-matched platelets?	
<ul style="list-style-type: none"> Platelet concentrates that are ABO identical should probably be used in patients with hypoproliferative thrombocytopenia, if available. (ICTMG Q4, R5) 	Weak recommendation Weak level of evidence
In what circumstances should providers take steps to prevent Rh alloimmunization resulting from platelet transfusion?	
<ul style="list-style-type: none"> 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 immune prophylaxis. These approaches may be used for female children and female adults of child-bearing potential being treated with curative intent. However, because of the low rate of RhD alloimmunization in patients with cancer, these approaches need not be applied universally. (ASCO Q2) 	Evidence quality: Intermediate Strength of recommendation: Moderate

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
How should refractoriness to platelet transfusion be managed?	
<p>Implementation tip from the COG Supportive Care Guideline Committee: The recommendation below applies to platelet refractoriness due to alloimmunization. Other causes of platelet refractoriness should be excluded.</p>	
<ul style="list-style-type: none"> Alloimmunization is usually due to antibody against HLA antigens and only rarely to platelet-specific antigens. Patients with alloimmune-refractory thrombocytopenia, as defined previously,[†] 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 (1) whose HLA type cannot be determined, (2) who have uncommon HLA types for whom suitable donors cannot be identified, or (3) 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. (ASCO Q11) <p>[†] A diagnosis of refractoriness to platelet transfusion should be made only when at least two transfusions of ABO-compatible units, stored for < 72 hours, result in poor increments. See: Schiffer CA, et al. J Clin Oncol. 2018; 36(3):283-99.</p> <ul style="list-style-type: none"> Patients with hypoproliferative thrombocytopenia who are refractory to platelet transfusions solely due to nonimmune factors should probably not receive HLA-selected or crossmatch-selected platelets. (ICTMG Q6, R10). Patients with hypoproliferative thrombocytopenia who are not refractory to platelet transfusion should probably not receive HLA-selected, HPA-selected, or crossmatch-selected platelets. (ICTMG Q6, R11) 	<p>Evidence quality: High Strength of recommendation: Strong</p> <p>Weak recommendation Weak level of evidence</p> <p>HLA and crossmatch selection: Weak recommendation Weak level of evidence</p> <p>HPA-selection: Weak recommendation Very weak level of evidence</p>

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
In what circumstances should providers use leukoreduced blood products to prevent alloimmunization?	
<ul style="list-style-type: none"> 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 patients with cancer who are receiving chemotherapy. There are fewer data in patients who are not receiving chemotherapy in the same time periods that the transfusions are being administered (eg, aplastic anemia, myelodysplasia), although the consensus would favor its use in these patients as well. In the United States and in 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 in transmission of cytomegalovirus infection. (ASCO Q3) 	<p>Evidence quality: High; Strength of recommendation: Strong</p>

*see Appendix 1

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Appendix 1: Systems for Classifying Recommendations and Evidence used by the Source Clinical Practice Guidelines

I. GRADE: used by Nahirniak S, Slichter SJ, Tanael S, et al. *Transfus Med Rev.* 2015; 29(1):3-13.

Strength of Recommendations:

Strong Recommendation	When using GRADE, panels make strong recommendations when they are confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects.
Weak Recommendation	Weak recommendations indicate that the desirable effects of adherence to a recommendation probably outweigh the undesirable effects, but the panel is less confident.

Strength of Recommendations Determinants:

Factor	Comment
Balance between desirable and undesirable effects	The larger the difference between the desirable and undesirable effects, the higher the likelihood that a strong recommendation is warranted. The narrower the gradient, the higher the likelihood that a weak recommendation is warranted
Quality of evidence	The higher the quality of evidence, the higher the likelihood that a strong recommendation is warranted
Values and preferences	The more values and preferences vary, or the greater the uncertainty in values and preferences, the higher the likelihood that a weak recommendation is warranted
Costs (resource allocation)	The higher the costs of an intervention—that is, the greater the resources consumed—the lower the likelihood that a strong recommendation is warranted

Quality of Evidence

High Quality	Further research is very unlikely to change our confidence in the estimate of effect
Moderate Quality	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low Quality	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very Low Quality	Any estimate of effect is very uncertain

Guyatt, GH, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ.* 2008;336(7650):924-926.

Guyatt, GH, et al. GRADE: going from evidence to recommendations. *BMJ.* 2008;336(7652):1049-1051.

II. American Society of Clinical Oncology: used by: Schiffer CA, Bohlke K, Delaney M, et al. Platelet Transfusion for Patients With Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update. J Clin Oncol.2018; 36(3):283-299.

Guide for Strength of Recommendations

Rating for Strength of Recommendation	Definition
Strong	There is high confidence that the recommendation reflects best practice. This is based on (1) strong evidence for a true net effect (eg, benefits exceed harms); (2) consistent results, with no or minor exceptions; (3) minor or no concerns about study quality; and/or (4) the extent of Expert Panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a strong recommendation.
Moderate	There is moderate confidence that the recommendation reflects best practice. This is based on (1) good evidence for a true net effect (eg, benefits exceed harms); (2) consistent results, with minor and/or few exceptions; (3) minor and/or few concerns about study quality; and/or (4) the extent of Expert Panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a moderate recommendation.
Weak	There is some confidence that the recommendation offers the best current guidance for practice. This is based on (1) limited evidence for a true net effect (eg, benefits exceed harms); (2) consistent results, but with important exceptions; (3) concerns about study quality; and/or (4) the extent of Expert Panelists' agreement. Other considerations (discussed in the guideline's literature review and analyses) may also warrant a weak recommendation.

Guide for Quality of Evidence

Rating for Strength of Evidence	Definition
High	High confidence that the available evidence reflects the true magnitude and direction of the net effect (i.e., balance of benefits v harms) and that further research is very unlikely to change either the magnitude or direction of this net effect.
Intermediate	Moderate confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research is unlikely to alter the direction of the net effect; however, it might alter the magnitude of the net effect.
Low	Low confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research may change either the magnitude and/or direction this net effect.
Insufficient	Evidence is insufficient to discern the true magnitude and direction of the net effect. Further research may better inform the topic. The use of the consensus opinion of experts is reasonable to inform outcomes related to the topic.

Schiffer CA, Bohlke K, Delaney M, et al. Platelet Transfusion for Patients With Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update. J Clin Oncol. 2018; 36(3):283-299. Data supplement.