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INTERCEPT® Blood System for Platelets Pathogen Reduction System

Reducing the Risk of Cytomegalovirus (CMV) Transfusion Transmission

- The Centers for Disease Control and Prevention estimates that over 50% of adults in the United States are infected with cytomegalovirus (CMV), a member of the herpes virus family which can be transfusion transmitted.[1]
- While CMV disease is uncommon in healthy people, immunocompromised patients are at high risk of severe complications from CMV infection. CMV disease mortality rate in bone marrow transplant patients is 15-20%, and CMV pneumonia is associated with a mortality rate of 80-90%.[2]
- Recent data have shown that more serious CMV disease, requiring longer durations of antiviral treatment, can occur in patients who are infected with multiple strains of the virus.[3]
- To reduce the risk of transfusion transmitted CMV infection, mitigation steps are performed, which vary widely in the effectiveness of transfusion risk reduction. Mitigation strategies to reduce the risk of CMV transmission which meet AABB Standard 5.19.2[4] include:

Leukoreduction "CMV-Safe"

- A filtration process that removes some leukocytes from a blood product as a safety measure.[5]
- Filtration results in a 1.9 $\log_{10}$ reduction leukocytes.[6]
- Transfusion transmitted CMV disease has been reported in 2.4%[7] - 6.5%[8] of previously CMV negative patients undergoing transfusion of leukoreduced blood products (RBC and platelets).
- 44% of newly CMV infected donors have CMV in their plasma, it is not only in the leukocytes.[9]

CMV Serology "CMV-Negative"

- A serological test indicating anti-CMV antibody presence.
- Units are referred to as "CMV negative", however, CMV infection can have a long 'window' period (40-60 days)[10] between infection and the development of detectable antibody levels.
- Before the antibodies develop, serology results would appear to be negative, despite the presence of the virus.[11]

INTERCEPT® Blood System, Pathogen Reduction

- INTERCEPT treatment of platelets reduces CMV levels by ≥4.9 $\log_{10}$ (platelets in PAS) or ≥4.2 $\log_{10}$ (platelets in plasma*),[8] and are approved to reduce the risk of transfusion transmission by the FDA.
- AABB standards allow for pathogen reduction as a CMV risk mitigating strategy.[4]
- INTERCEPT treatment efficacy is independent of viral location in leukocytes and/or plasma, as well as antibody titers.

*For platelets in plasma, pseudorabies virus was used as a model for CMV

- Although CMV-safe and CMV-negative blood components are considered safe, meta-analysis comparing CMV serology and leukoreduction as techniques to reduce the risk of transfusion transmitted infection (TTI) of CMV in high-risk patients showed no difference in resulting CMV infection rates (relative risk reduction, 2.18; 95% CI, 0.96-4.98).[13] Patients transfused with leukoreduced or seronegative platelet units still have reported CMV TTI. There have been no reported cases of CMV TTI with the INTERCEPT® Blood System. Multiple large tertiary care hospitals have replaced their requirement for CMV serology with INTERCEPT pathogen-reduced platelets.[14]

References

1. CDC. Cytomegalovirus (CMV) and congenital CMV infection. 2017 January 10 2018]; Available from: https://www.cdc.gov/cmv/index.html.
2. Sable, C. and G. Donowitz, Infections in bone marrow transplant recipients. Clin Infec Dis, 1994. 18(3): p.273-281.
3. Vinuesa, V., et al., The impact of virus population diversity on the dynamics of cytomegalovirus DNAemia inallogeneic stem cell transplant recipients. J Gen Virol, 2017. 98(10): p. 2530-2542.
4. AABB, Standards for Blood Banks and Transfusion Services 33rd Edition. 2022, AABB: Bethesda, MD.
5. Preiksaitis, J.K., The cytomegalovirus-"safe" blood product: is leukoreduction equivalent to antibody screening? Transfus Med Rev, 2000. 14(2): p. 112-36.
6. Visconti, M.R., et al., Assessment of removal of human cytomegalovirus from blood components by leucocyte depletion filters using real-time quantitative PCR. Blood, 2004. 103: p. 1137-1139.
7. Bowden, R., et al., A comparison of filtered leukocyte-reduced and cytomegalovirus (CMV) seronegative blood products for the prevention of transfusion-associated CMV infection after marrow transplant. Blood, 1995. 86(9):p. 3598-603.
8. Wu, Y., et al., Direct assessment of cytomegalovirus transfusion-transmitted risks after universal leukoreduction.Transfusion, 2010. 50: p. 776-786.
9. Ziemann, M., et al., High prevalence of cytomegalovirus DNA in plasma samples of blood donors in connection with seroconversion. Transfusion, 2007. 47(11): p. 1972-83.
10. Seed, C.R., et al., Validation of an automated immunoglobulin G-only cytomegalovirus (CMV) antibody screening assay and an assessment of the risk of transfusion transmitted CMV from seronegative blood. Transfusion, 2009.49(1): p. 134-45.
11. Ziemann, M., et al., Window period donations during primary cytomegalovirus infection and risk of transfusion-transmitted infections. Transfusion, 2013. 53(5): p. 1088-94.
12. INTERCEPT Blood System for Platelets [Package Insert]. September 6, 2022. Cerus Corporation: Concord, CA.
13. Mainou, M., et al., Reducing the risk of transfusion-transmitted cytomegalovirus infection: a systematic review and meta-analysis. Transfusion, 2016. 56(6 pt 2): p. 1569-1580.
14. Healy, M., et al., Implementation of Psoralen-Treated Pathogen-Reduced Platelets: A US Transfusion Service Perspective [Poster]. 2016, Presented at AABB.

Contraindications[12]

Contraindicated for preparation of platelet components intended for patients with a history of hypersensitivity reaction to amotosalen or other psoralens. Contraindicated for preparation of platelet components intended for neonatal patients treated with phototherapy devices that emit a peak energy wavelength less than 425 nm, or have a lower bound of the emission bandwidth <375 nm, due to the potential for erythema resulting from interaction between ultraviolet light and amotosalen.

Warnings and Precautions[12]

Only INTERCEPT Processing Sets for platelets are approved for use with the INTERCEPT Blood System. Use only the INTERCEPT INT100 Illuminator for UVA illumination of amotosalen-treated platelet components. No other source of UVA light may be used. Please refer to the Operator's Manual for the INT100 Illuminator. Discard any platelet components not exposed to the complete INT100 illumination process. Tubing components and container ports of the INTERCEPT Blood System contain polyvinyl chloride (PVC). Di(2-ethylhexyl)phthalate (DEHP) is known to be released from PVC medical devices, and increased leaching can occur with extended storage or increased surface area contact. Blood components will be in contact with PVC for a brief period of time (approx. 15 minutes) during processing. The risks associated with DEHP released into the blood components must be weighed against the benefits of therapeutic transfusion.

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Rx only. See package insert for full prescribing information.