2017 Cochrane Systematic Review:
Pathogen reduced platelets for prevention of bleeding

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The updated systematic review by the Cochrane Group summarized and analyzed results of clinical trials that studied patients who received transfusions of pathogen-reduced platelets.[1] The report is of remarkable depth and scope, as it summarized clinical trial results with pathogen reduction technologies from Europe and the US. Almost all participants in the trials had hematological or oncological disease. The observations are not necessarily applicable to other patient populations for which there is insufficient evidence. In this White Paper we will address selected findings of the report. Specifically, we will consider trials that compared the transfusion of multiple units of Intercept-treated platelets to standard platelets.[2-7]

Findings include the following:

- The number of patients experiencing platelet refractoriness was significantly greater in those receiving Intercept-treated platelets (93/605) compared to standard platelets (33/616) Risk ratio 2.85 [95% CI:1.96-4.15). (References 2,3,4,5,6,7)
- The number of patients experiencing platelet refractoriness and platelet alloimmunization was also significantly greater in those receiving Intercept-treated platelets (36/605) compared to standard platelets 19/616) Risk ratio 1.90 [95% CI:1.11-3.26]. (References 2,3,4,5,6,7)
- One-hour post-transfusion platelet count increments were significantly lower among recipients of Intercept-treated platelets compared to recipients of standard platelets. -10.08 $x10^9$/L [95%CI - 11.67 to -8.48]. (References 2,3,4,6,7)
- Twenty-four-hour post-transfusion platelet count increments were also significantly lower among recipients of Intercept-treated platelets compared to recipients of standard platelets. -8.39$x10^9$/L [95% CI -9.82 to -6.96]. (References 2,3,4,6,7)
- One-hour post-transfusion platelet corrected count increments (CCIs) were significantly lower among recipients of Intercept-treated platelets compared to recipients of standard platelets. - 4,110 [95% CI -4,870 to -3,350]. (References 2,3,4,6,7)
  (The CCI is an index calculated from the recipient's body surface area, platelet recovery post-transfusion, and the number of platelets transfused. As an index, it has no meaningful units. The Cochrane report is incorrect is assigning a unit value to the CCI.)
- Twenty-four-hour post-transfusion platelet CCIs were also significantly lower among recipients of Intercept-treated platelets compared to recipients of standard platelets. - 3,500 [95% CI - 4,180 to - 2,820. (References 2,3,4,6,7)
- Recipients of Intercept-treated platelets received 30% more platelet transfusions than recipients of standard platelets. This represented a strong statistical trend: 1.3 [95% CI 0.84-1.77}. (References 2,3,4,6,7).
- Recipients of Intercept-treated platelets had a statistically significant shorter time interval between transfusions compared to recipients of standard platelets: -0.50 days [95% CI -0.61 to - 0.38]. (References 2,3,4,6,7)
- In an analysis of patients who had any bleeding event (WHO grade 1 to 4 or equivalent) with follow-up more than 7 days, there was a slightly but statistically significant increase in bleeding among recipients of Intercept-treated platelets (374/477) compared to standard platelets (361/498). Relative risk 1.07 [95% CI 1.01-1.13]. (References 2,3,4,6)

- The number of patients who developed an infection while receiving transfusions was greater in recipients of Intercept-treated platelets (181/477) compared to recipients of standard platelets (141/498). Risk ratio 1.36 [95% CI 1.14-1.62]. (References 2,3,4,6)
  (It should be noted that none of the infections was due to the transmission of bacteria by transfusion.)

The Cochrane report does not discuss the reasons for the reported findings. No explanations are offered for any of the results. Additionally, costs were not systematically evaluated in the trials and were not included in the Cochrane report. The results cited above, however, influence the costs of Intercept-treated platelets compared to standard platelets. Increased refractoriness with and without accompanying alloimmunization, decreased platelet recoveries post-transfusion, increased number of transfusions, a shorter time interval between transfusions, bleeding events, and infections may each contribute to increased costs associated with the transfusion of Intercept-treated platelets compared to standard platelets. Another publication developed a model to compare the costs to a hospital of adopting an all Intercept-treated apheresis platelet inventory to using standard platelets tested using the Verax Biomedical Platelet PGD test.[8] Using reasonable assumptions, costs for Intercept-treated platelet were calculated to be substantially more expensive than standard platelets. Taken together, the results in the Cochrane report substantiate this finding.

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