Optimizing Cryopreservation of Hematopoietic Stem Cells Collected for Autologous Stem Cell Transplantation in Patients with Multiple Myeloma

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Background

- Cryopreservation is required prior to storage of hematopoietic stem cells (HSC) used to reconstitute hematopoiesis for autologous stem cell transplantation.
- Cryopreservation techniques should be optimized to ensure adequate recovery of viable progenitor cells while minimizing variability in the field.
- Limitations with current cryopreservation methods include:
  - Inconsistency in components used to formulate media at various institutions,
  - Increased risk for technical error,
  - Risk for contamination.
- This study explored a reduction in DMSO content at cryopreservation with goals of decreasing infusion-related Adverse Events (AE) while maintaining, or improving, engraftment and CD34+ cell recovery.

Methods

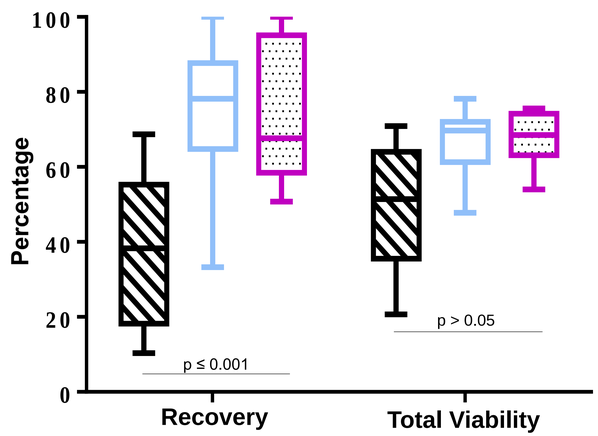
- Ten products, collected after standard mobilization of multiple myeloma patients, were cryopreserved with a pre-formulated cryoprotectant: PRIME-XV FreezIS (Irvine Scientific ISPN: 91139) and compared to products previously cryopreserved with two standard use cryoprotectants: Std10 and Std5.
  - Std10 and Std5 are cryoprotectant media formulated in-house to achieve a final DMSO concentration of 10% and 5% respectively.

Endpoints

- CD34+ recovery and total viability.
- Adverse events during, and for 4 hours following completion of the infusion.
- Time to neutrophil and platelet engraftment
  - Neutrophil recovery ≤ 14 days and platelet recovery ≤ 28 days from day of transplant.

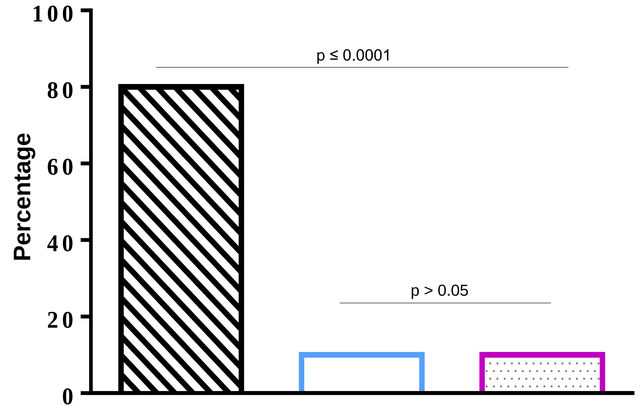
Results

Prime-XV FreezIS Results in Increased CD34+ Recovery



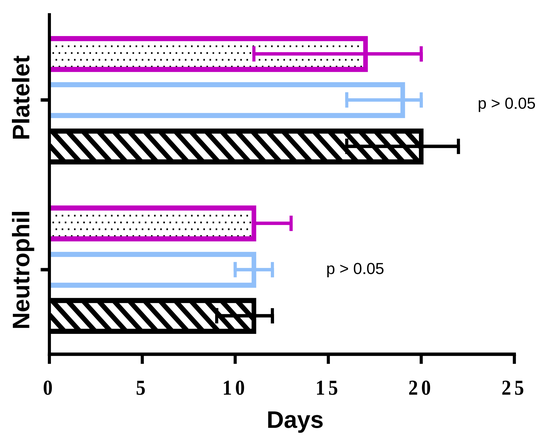
*Flow Analysis at thaw indicates a **significant increase** in **CD34+ recovery** with Std5 and FreezIS when compared to Std10 and **no significant change** in **total viability.** Average (SD) recovery of CD34+ cells for Std10, Std5 and FreezIS were 39 (19.95), 74.7 (18.99) and 73.6 (18) respectively. Average (SD) Total Viability (%) was 48.5 (17.75), 67 (8.90), and 67.9 (6.98), respectively.*

Frequency of Adverse Events Decreased Significantly with Prime-XV FreezIS

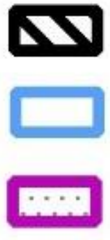


8 (80%) patients who received products containing 10% DMSO experienced an AE as opposed to only 1 patient (10%) who received Std5 and 1 patient (10%) who received FreezIS.

Comparable HSC Engraftment when Utilizing Prime-XV FreezIS



*There was **no significant change in the time to ANC or PLT Engraftment** when comparing cells cryopreserved with the three different freezing solutions. The median (range) time to ANC & PLT engraftment for Std10, Std5 and FreezIS were as followed, ANC: 11 (9-12), 11 (10-12), and 11 (11-13), respectively and PLT: 20 (16-22), 19 (16-20), and 17 (11-20), respectively.*



Standard Solution, 10% DMSO

Standard Solution, 5% DMSO

Prime-XV FreezIS (Irvine Scientific)

Prime-XV FreezIS ISPN (Irvine Scientific Product Number): 91139

Conclusion

- This study validated what is now our standard institutional practice for cryopreservation of hematopoietic stem cell products.
- We demonstrated that the reduction of DMSO concentration from 10% to 5% significantly decreased the frequency of AEs, without impairing the functionality of the HSC graft.
- Additionally, we detected improvement in CD34+ recovery and viability, which in the small cohorts analyzed, did not translate to a significant change in time to engraftment.
- We present data supporting the use of a pre-constituted cryopreservative media, FreezIS, that results in recovery and preserved functionality of HSC similar to our in-house, constituted media.
- The advantage of PRIME-XV FreezIS compared with our current standard is that its use would:
  - Minimize processor handling during constitution of the media,
  - Decrease processing time,
  - Reduce the risk of product contamination,
  - Ensure consistency and reproducibility across different processors within the same laboratory and across the field.
- With an increasing number of cellular therapies being offered for different diseases, the entire cellular therapy field would benefit from continued improvement in methods and materials used for cryopreservation of these products.

Acknowledgements

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