

A Phase 2, Double-Blinded, Randomized study with a proprietary amino acid mixture as diarrhea prevention in patients undergoing autologous stem cell transplantation (AST) for Multiple Myeloma (MM) and Non-Hodgkin lymphoma (NHL)

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AMINO ACID ORAL REHYDRATION SOLUTION

enterade is an amino acid-based, glucose-free medical food/beverage with electrolytes. It comprises of 5 amino acids (Valine, Aspartic Acid, Serine, Threonine, Tyrosine) selected to rebuild villi, protect the GI tract and promote hydration. I. These nutrients facilitate retention of the absorbing capacity of the small intestine by rebuilding the villi and reduce antigenic translocation by tightening the mucosal barrier. In a study of irradiated mice, enterade improved survival and improved body weight following irradiation. On electron microscopy of the ileum, there was loss of cell-to-cell contact after irradiation, which was restored after the introduction of enterade.

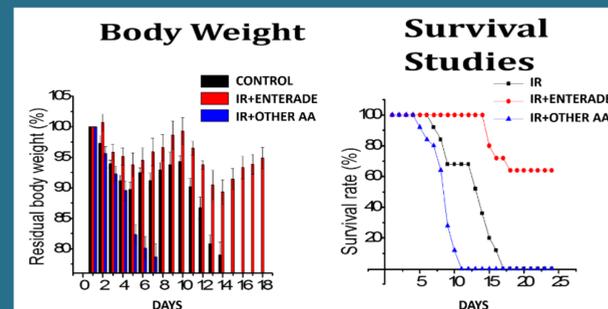


Figure 1. enterade® improved mouse survival and improved body weight following irradiation.

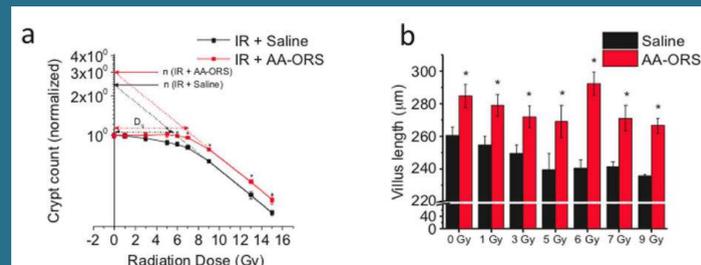


Figure 2. enterade® increased crypt count & villus length following irradiation

INTRODUCTION

The alkylating agent, melphalan, remains the mainstay of conditioning for autologous hematopoietic stem cell transplantation (HSCT) in multiple myeloma (MM) and non-Hodgkin lymphoma (NHL) patients. The mucosal sequelae of Melphalan and the subsequent enteritis are similar to those induced by total body irradiation, with approximately 40% of patients experiencing CTCAE grade 2 or higher diarrhea following conditioning regimens containing Melphalan. This study was to assess the effectiveness of enterade in reducing grade >2 diarrhea associated with high dose Melphalan chemotherapy.

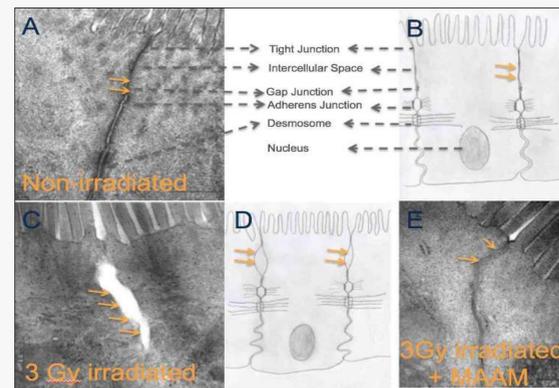


Figure 3: Electron microscopy of ileal sections show the formation of a normal cell junction complex

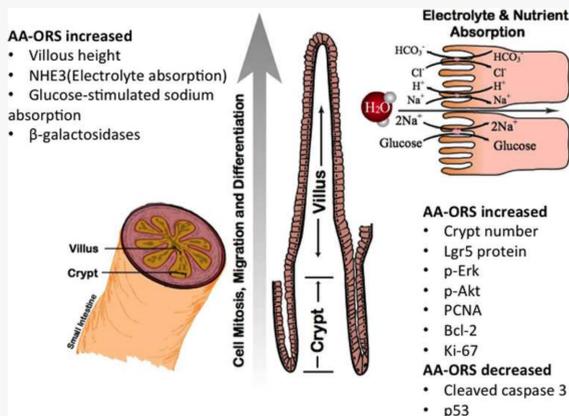
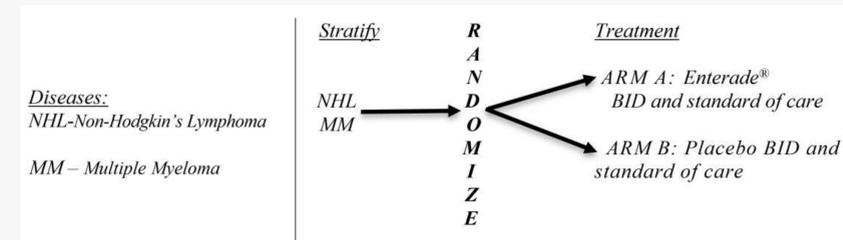


Figure 4. Schematic figure of small intestinal villus and enterocytes: AA-ORS treatment increases rapidly dividing stem cells that are Lgr5+, as well as proliferation markers p-Erk, p-Akt and PCNA.

METHODS

The trial was designed as a Phase 2, multi-center, double blinded, 2-arm randomized study. 114 MM or NHL patients were enrolled between October 2016 and October 2017. Patients were randomized 1:1 to receive either two 8oz bottles of enterade or Placebo starting on the day of admission through Day +14. GI toxicity was scored by the CT-CAE 4.0 system from admission through Day + 14. Compliance was arbitrarily set at consumption of 2 bottles daily for 11+ days.

Schema:

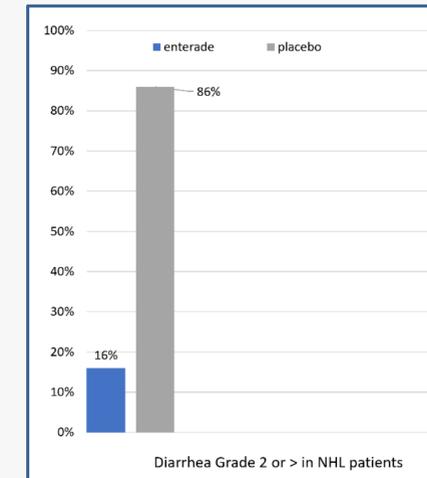


DEMOGRAPHIC/RESULTS

Compliance overall was much lower than anticipated; with no MM patients achieving compliance compared to 34.2% in the NHL group. Compliance in NHL patients was 31.6% in the enterade group versus 36.8% in the placebo group.

	Enterade (N=6)	Placebo (N=7)		
	CTCAE v4.0 Grade			p-value
	2	2	3	
NHL (>=11 days of intake)				
Diarrhea	1	3	3	0.02*

DEMOGRAPHIC/RESULTS



Analysis of primary endpoint in NHL patients showed a 16% incidence of diarrhea ≥ grade 2 in enterade@ compliant patients versus 86% in the placebo group (p= 0.02).

CONCLUSIONS

- 11 Days of two 8oz bottles of liquid is a difficult task during ASCT, especially for MM with nausea, altered taste and poor appetite.
- For those NHL patients, compliant per protocol (who consumed ≥11 days), enterade significantly reduced diarrhea.
- At ≥7 days of treatment there was also a signal for effect.
- The use of enterade to prevent high dose chemotherapy associated diarrhea should be explored further in populations capable of reasonable oral intake.

REFERENCES

Yin L, Vijaygopal P, Menon R, Vaught LA, Zhang M, Zhang L, Okunieff P, Vidyasagar S. An amino acid mixture mitigates radiation-induced gastrointestinal toxicity. *Health Phys.* 2014 Jun; 106(6):734-44.