plained heterogeneity weakens our inference (Table1).

Table 1. *Estimate of Risk for Developing VOD*

Subgroup	Investigations Contributing data	OR with 95% Confidence Interval	I^2
All trials	Ohashi, Ruutu, Essell 92, and 98, Carerras, Thompson	0.33 [0.12, 0.90]	67.6%
Clinical trial	Ohashi, Ruutu, Essell 98	0.30 [0.03, 2.80]	70.5%
Observational study	Thompson, Carerras, Essell 92	0.36 [0.11, 1.23]	80.4%
Busulfan conditioned patients	Essell 92, Essell 98, Ohashi	0.19 [0.06, 0.59]	41%
TBI conditioned patients	Ohashi, Ruutu	0.37 [0.03, 4.84]	67%
Seattle criteria	Essell 92, Essell 98, Ruutu, Thompson	0.40 [0.12, 1.37]	76%
modified Seattle criteria	Carerras, Ohashi	0.17 [0.04, 0.64]	0%
Allogeneic transplant recipients	Essell 92, Essell 98, Ohashi, Ruutu, Thompson	0.33 [0.11, 0.99]	73.7%

I^2 represents the precentage of unexplained heterogeneity.

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A RETROSPECTIVE ANALYSIS OF THE IMPACT OF ERYTHROPOEITIC GROWTH FACTOR UTILIZATION ON TRANSFUSION REQUIREMENTS IN PATIENTS WITH AL AMYLOIDOSIS UNDERGOING AUTOLOGOUS SCT

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Introduction: The benefit of the addition of erythropoietin-derived growth factors (EPOs) to neutrophil growth factors to hasten engraftment and decrease transfusion requirements in patients undergoing hematopoietic stem cell transplantation is uncertain. We previously reported the equivalence between erythropoetin alfa and long-acting darbepoetin alfa in patients with AL amyloidosis undergoing autologous stem cell transplantation (ASCT). To further evaluate EPOs in this patient population, we examined the time to neutrophil engraftment and transfusion requirements in all patients undergoing ASCT for AL amyloidosis over a 10 year period. **Methods:** A retrospective review was conducted of all patients undergoing ASCT between July 1994 and July 2005. Three groups were compared. Group A consisted of patients treated with darbepoetin alfa at 200 mcg weekly (n = 64), Group B consisted of patients treated with epoetin alfa at either 150 u/kg thrice weekly or 40,000 units weekly (n = 151), and Group C consisted of those patients not treated with EPOs (n = 161). All groups were treated with GCSF to promote neutrophil engraftment. Primary endpoints evaluated were mean number of units of PRBCs transfused and time to neutrophil engraftment. A secondary endpoint was the proportion of patients requiring PRBC transfusion. Groups were stratified by intensity of conditioning regimen as well as for life-threatening bleeding events and reanalyzed. A nonparametric analysis of variance was conducted utilizing the Kruskal-Wallis test with plans for a Dunn comparison of all three groups in the event of a P value < 0.05. **Results:** The mean number of PRBC units transfused was 3.23, 4.5, and 3.92 for Groups A, B, and C, respectively; $P = .1591$. The mean number of days to engraftment was 9.87, 10.3, and 10.4 for the groups; $P = .0956$. When life threatening bleeding events were excluded, there was still no significant difference, $P = .12$. In the subgroup of patients receiving the highest dose (200 mg/m2) of melphalan, the proportion of patients not requiring RBC transfusion was higher in the group receiving EPOs (38% versus 23%, $P = .0512$, χ^2). **Discussion:** In this analysis, we were unable to demonstrate a benefit for EPOs in the entire patient group, which is heterogenous in terms of chemotherapy dosing and bleeding complications. However, when we examined those patients receiving the highest dose of chemotherapy, an increase in the percentage of patients not requiring RBC transfusion support was seen.

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MELPHALAN-INDUCED SEVERE ORAL MUCOSITIS IS PREVENTED BY ORAL CRYOTHERAPY IN AUTOLOGOUS HEMATOPOIETIC CELL TRANSPLANT RECIPIENTS

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Background: Oral mucositis is an expected complication of high dose mephalan chemotherapy due to its cytotoxic effects. Severe mucositis leads to complications of severe pain requiring narcotic management, difficulty or inability to eat and take oral medications, and prolonged hospital stays. Melphalan has a very short plasma half-life making it an ideal candidate for cryotherapy intervention.

Objective: Primary objective is to evaluate whether the cryotherapy intervention will reduce mucositis in patients receiving high dose melphalan compared to historical controls. Secondary objectives included determining the tolerance of the procedure and comparing the need for intravenous narcotics to historical controls. **Methods:** The program assessed a modified version of cytotherapy intervention protocols reported previously by two institutions. Patients and staff were given written and verbal instructions describing the oral cryotherapy intervention. The procedure included holding cold medium (ice, popsicle, cold fluid) in the mouth beginning 10 minutes before the melphalan infusion and continuing until 1 hour after the infusion was completed. **Results:** Consecutive patients (multiple myeloma 18, NHL 13, other 3) being conditioned with melphalan were eligible. The cryotherapy intervention was used 04/04&ndash09/05, (n = 20). A retrospective review of previous consecutive transplants provided the melphalan matched controls (03/02–03/04), n = 14. Most (90%) of the patients were able to complete the entire procedure for oral cryotherapy. Two patient (10%) intermittently followed the procedure because they felt too full from drinking cold fluid. Subsequently, cold fluid has been eliminated as an option for treatment. Forty-three percent of historical controls had severe mucositis compared to none of the patients who received cryotherapy (Table). Additionally, a dramatic difference in the amount of opiate used was noted. In the historical control group 47% of patients required IV PCA (cummulative dose MSO4 937mg and Fentanyl 11,850 mcg) compared to 10% in the cryotherapy group (cumulative 68 mg MSO4) (Table 1). **Summary:** Cryotherapy was well tolerated and appeared to decrease mucositis in high dose melphalan recipients. Additionally, there was a decrease in IV pain medication use resulting in less overall morbidity.

Table 1. *Mucositis in Melphalan Recipients*

Intervention	Patients	None/Mild	Moderate	Severe
No cryotherapy	14	6 (43%)	2 (14%)	6 (43%)*
Cryotherapy	20	17 (85%)	3 (15%)	0

*Two intubated for airway protection.

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PHASE III TRIAL OF VALACYCLOVIR FOR THE PREVENTION OF SHINGLES AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Despite advances in antiviral therapy, reactivation of latent varicella-zoster virus (VZV) infections remains a significant cause of morbidity following stem cell transplantation (SCT). Twenty-five percent or more of patients undergoing SCT will reactivate VZV in the form of zoster (shingles) within the first year after transplant. Short course (6–12 months) prophylactic therapy with acyclovir has been shown effective, but compliance with administration up to 5 times daily has been problematic, and outbreaks resumed following completion. We undertook a phase III, randomized, double-blind, placebo-controlled trial of valacyclovir (VACV, 1000 mg

twice daily) from 4 months through 2 years following SCT for the prevention of zoster. VACV is readily converted to acyclovir in vivo following oral administration, has potent activity against VZV, and can be dosed twice daily. Fifty-three VZV-seropositive transplant recipients (17 autologous, 36 allogeneic SCT) were randomized at a median of 163 days following SCT. Using an intent-to-treat analysis, the rate of VZV in the VACV arm was 3 of 27 versus 6 of 26 in the placebo arm ($P = .21$). All three cases in the VACV arm occurred after randomization but prior to starting VACV. Using a modified intent-to-treat analysis comprised of those subjects randomized who took any study drug, 49 subjects started the planned therapy with VACV or placebo (4 subjects never started: 2 developed zoster and 2 dropped blood counts prior to the time they were supposed to start; a fifth subject started drug following resolution of zoster starting after randomization). The rate of zoster was 6 of 26 in the placebo arm versus 0 of 23 in the VACV arm ($P = .03$). Thirty subjects completed the planned therapy through the second year after transplant or first episode of zoster. Reasons for discontinuation in the placebo group included adverse reactions (nausea/vomiting/dehydration in 2 subjects; elevated transaminases, low platelets, and joint pains in 1 subject each) and relapse (4). Reasons in the VACV group included withdrawal of consent (4), relapse (3), and adverse reactions (1 leukopenia, 1 cramping abdominal pain). The 6 episodes of zoster were recorded at a median of 122 days after randomization (278 days after BMT) and were complicated by 3 episodes of post-herpetic neuralgia. Valacyclovir at a dose of 1000 mg twice daily through the second year after transplant is well tolerated and effective in preventing the outbreak of shingles after SCT.

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TREATMENT OF ZYGOMYCOSIS: POSACONAZOLE AS A TREATMENT OPTION IN 91 CASES

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Background: Zygomycosis is an emerging opportunistic mycosis for which few therapies exist and can occur in hematopoietic stem cell transplant (HSCT) recipients and patients with hematologic malignancies. We evaluated the use of posaconazole (POS) as salvage therapy in patients with zygomycosis enrolled in a Schering-Plough compassionate-use program. **Methods:** A retrospective analysis was conducted using questionnaires completed by investigators treating patients with zygomycosis. Patients were required to have proven or probable zygomycosis (EORTC/MSG criteria) and have disease refractory (R) to and/or be intolerant (I) of prior antifungal therapy. Outcome at 12 weeks was assessed.

Results: The majority (69/91) of patients had proven infection, and most (48/91) were R or R + I (33/91) to prior therapy. Most (85%) failed lipid amphotericin B (LAB) therapy, and about half had ≤1 month of prior antifungal therapy. Overall success (complete response [CR] + partial response [PR]) was 60% (14% CR, 46% PR). Another 21% of patients had stable disease (SD). Success by predisposing risk factor (subjects could have had more than 1 risk factor) occurred in 28/48 (60%) patients with hematologic malignancy, 14/27 (52%) HSCT recipients, and 18/30 (60%) patients with GVHD. Duration of POS therapy (800 mg/day oral suspension) ranged from 6 days to nearly 3 years. Success was also generally similar by site of infection: 23/42 (54%) sinus, 24/37 (65%) pulmonary, 8/13 (62%) cutaneous, 8/11 (73%) brain, and 5/11 (46%) orbital infections. Success was observed for various species of Zygomycetes. Combination therapy (POS + LAB) for >10 days in 15 heavily immunosuppressed patients resulted in similar response (7% CR, 47% PR, 27% SD). Sixty-four patients (70%) had adjunct surgical debridement (38 patients before POS, 9 patients during POS, 17 patients both before and during POS); 26 patients had no surgery. Thirty-five patients died while on POS or within 1 month of follow-up, though only 15 deaths were considered related to zygomycosis.

Conclusions: Overall success with POS was high, including patients with hematologic malignancies and HSCT recipients. The favorable survival rate in this case series provides encouraging data regarding POS as an alternative to LAB. Further well-controlled clinical studies are warranted.

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CREATING A CULTURE OF SUPPORT ON A BONE MARROW TRANSPLANT UNIT: IT TAKES A VILLAGE

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The Bone Marrow Transplant Unit at Cincinnati Children's Hospital Medical Center (CCHMC) is an 18 bed unit that serves children from all over the country and internationally for transplants. The usual range of stay in the hospital is about 30–60 days, but can be much longer. We have found the patients and families bring not only their medical needs, but many social issues must be understood and addressed. These include issues related to being away from home, loss of normal resources, financial stress, family conflicts, health and/or behavioral problems of family members, transportation problems, insurance difficulties, and the list continues. The community of patients and families forms somewhat of a village. The instant village of the BMT unit requires much attention and support from a vast array of staff in addition to the medical team. The needs of the patient and families are as varied and complicated as are the diseases which brought them to our hospital. An interdisciplinary and family-centered approach called the Family Support Network (FSN) has been developed in the Division of Hematology and Oncology at CCHMC to address the needs of the patients and families. The social worker, school intervention specialist, child life specialist, massage therapist, chaplain, and financial counselor have become essential personnel to the transplant process. Every member of the FSN uses a supportive, family-centered, and solution-focused approach which becomes the new culture for the families. Families are offered support groups, individual counseling, educational opportunities, and various self-care interventions (massages, family meals, make-overs, movies). The patients and families, in turn, utilize services and begin to support themselves and each other in more adaptive ways. The acclimation process for patients and families into the culture begins before they ever come to the hospital, through telephone contacts and written materials. This process continues in person during treatment and after-care phases. The FSN staff also provides support for the nursing and medical team to reduce stress caused by working with high-acuity patients through de-briefing sessions, massages, supportive counseling, and educational interventions (Table 1).

Table 1. *Services of the Family Support Network (FSN)*

Social Work	School Intervention	Child Life	Pastoral Care	Financial Service
Emotional support and crisis counseling	Facilitate home instruction	Creative and innovative medical play	Liaison with community clergy	Customer service for financial issues
Family support and diagnosis onward	Individualized Education Plans	Sibling support	Spiritual and emotional support	Pre-authorizations
Resource connections/ advocacy	School reintegration	Support and distraction	Visitation and prayer	Pre-certifications
Teaching, education, and consulting	Pre-school through college	Therapeutic play	Reflection	Verification of financial eligibility

The FSN is committed to helping patients and families through BMT process.