

Seven patients died from disease relapse and were excluded from outcome analysis. Of the remaining 28 patients, five HSCT recipients (4 allo and 1 auto) have died (18%). All patients who died were in the lower respiratory tract infection group and their death was directly attributed to pulmonary complications as a result of respiratory virus infections. Two patients died from adenovirus pneumonitis and ARDS. Two patients died from severe parainfluenza infection with deterioration of symptoms and respiratory failure despite treatment with ribavirin and the last patient had ARDS from RSV infection. No chronic pulmonary complication or allo-immune lung syndrome was observed among the remaining 23 survivors with a median follow-up time of 3.8 years (8 months–10.3 years).

This study supports the significant TRM from respiratory virus infection diagnosed within the first 100 days post HSCT particularly in patients presented with lower respiratory tract infection. Higher mortality was observed among allo recipients. Every effort should be made to prevent respiratory virus infections early post HSCT.

295

Risk Factors for Falls with Injury for Patients Admitted for Hematopoietic Stem Cell Transplant

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Introduction: Falls are a common cause of morbidity and mortality among hospitalized patients in the United States. Patients with cancer are vulnerable to falls with injury as a result of complex medical regimens, impaired performance status, and chemotherapy toxicities such as neuropathy. Predictors of falls in the general oncology population include abnormal gait, presence of metastasis, antidepressant and antipsychotic medication use, and blood product use. Risk factors for falls in the hematopoietic stem cell transplant (HSCT) population are not as well understood.

Methods: We performed a retrospective review of patients admitted to Dana-Farber/Brigham and Women's Cancer Center from 01/2011 to 12/2012, who had a fall during their admission to a HSCT service. Patients were classified as either fall or fall with injury (FWI). Our primary objective was to describe characteristics of hospitalized HSCT patients who experience a FWI, including medications administered in the 24 hours prior to the fall.

Results: There were 91 falls identified in 81 patients. One patient was excluded from the analysis due to incomplete electronic medical records. Nine patients had more than one fall. Thirty-two falls resulted in FWI. Fifty-seven falls (62.6%) occurred during an index admission for HSCT. This represents 5.48% of our index admissions. Patients had a history of HSCT or were undergoing myeloablative HSCT (n=25), reduced intensity conditioning HSCT (n=19) or autologous HSCT (n=36). Patient and transplant characteristics were compared between patients who had falls without injury and patients who had FWI. There was no significant difference in age (p=0.99), gender (p=0.65), cancer diagnosis (p=0.84), hospital admission team (p=0.99), admission type (p=0.14) or transplant type (p=0.80) between patients with falls and FWI. In

multivariate analysis, benzodiazepine use (p=0.016) and Morse Fall score ≥ 45 (p=0.031) were associated with increased risk of FWI, whereas diuretic use (p=0.029), presence of heart disease (p=0.023) and prior fall (p=0.015) were associated with decreased risk of FWI.

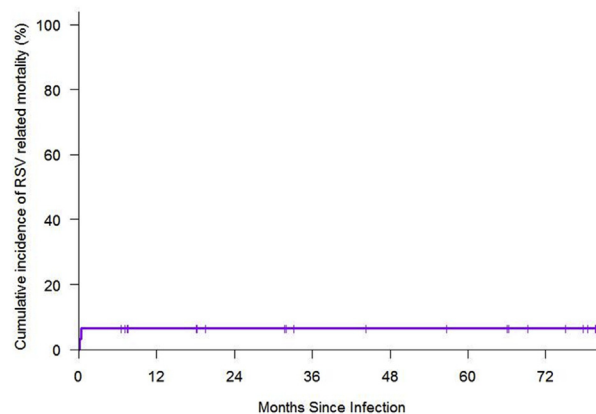
Conclusions: Falls are common in patients hospitalized for HSCT. Benzodiazepine use and high Morse Fall score predict for an increased risk of injury after a fall event. Adequate assessment and management of these modifiable fall risk factors, including decreasing our benzodiazepine use and early identification of at risk patients may help prevent FWI in our HSCT population.

296

Early Use of Inhaled Ribavirin Can Improve Outcomes in High Risk Hematopoietic Stem Cell Transplant and Leukemia Patients with RSV Infection

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Respiratory syncytial virus (RSV) in the immunocompromised adult can lead to significant morbidity and mortality. Most immunocompromised patients with RSV pneumonia present to a health care facility with an upper respiratory tract infection ~ 1 week prior to the onset of pneumonia. Overall, 40%–50% of RSV upper respiratory tract infections (URTI) in HCT recipients will progress to pneumonia. RSV pneumonia in HCT recipients is associated with fatality rates as high as 70–80%. Treatment of RSV pneumonia is primarily supportive. The role of specific antiviral therapy remains uncertain. We retrospectively reviewed RSV-infected patients with upper or lower respiratory tract infection (LRTI) diagnosed by antigen testing, polymerase chain reaction and/or culture from January 2007 through March 2013. In general, clinically stable URTI patients with an absolute lymphocyte count (ALC) > 300 received only supportive care. Patients presenting with URTI and lymphopenia (ALC ≤ 300) were preferentially treated with a course of inhaled ribavirin (IR) alone. Those presenting with LRTI were preferentially treated with IR in combination with the RSV-specific humanized monoclonal antibody, Palivizumab. We identified 60 consecutive patients who were diagnosed with RSV (median age 52 [21 - 72]) - 35 had URTI and 25 had LRTI. Forty-one (71%) of the patients had received an allogeneic transplant, seven (12%) were post autologous transplant, while 10 (17%) were receiving treatment for acute leukemia. Of the allogeneic transplant patients, 31 (51.6%) were receiving immunosuppressants and 24 (40%) were being



actively treated for graft-versus-host disease (GVHD). The median (range) ANC and ALC at the time of RSV diagnosis was 1.6 (0 - 11) and 0.8 (0 - 7.3), respectively. Among the 35 patients with URTI, 12 received IR while 23 did not. None of the 12 patients treated with IR progressed to LRTI. In contrast, 6 of the 23 untreated patients (24%) with URTI progressed to LRTI. Of the 31 patients with LRTI (25 initially diagnosed with LRTI and 6 patients who progressed from URTI to LRTI), there were four deaths occurring within 60 days of RSV diagnosis (two deaths directly from RSV, one from disease relapse, and one from GVHD). In patients with LRTI (25 patients with LRTI at diagnosis plus 6 patients who progressed from URTI to LRTI), RSV-related mortality was (6.4%). On univariate analysis, only the presence of GVHD significantly predicted the development of LRTI in patients with URTI ($P = .028$); however, the use of inhaled ribavirin had a protective effect that was marginally significant ($P = .074$). Early use of IR in high-risk transplant and leukemia patients can both reduce the progression from URTI to LRTI and improve the historically dismal outcomes of patients with RSV pneumonia.

297

Physical Therapy during the Hemopoietic Stem Cell Transplant Process to Improve Quality of Life

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Clinical Question (in PICO format)

Background / Purpose of BEST Development

Hemopoietic stem cell transplant can have profound and lasting adverse effects on an individual's physical and psychological well-being (Wolin 2010 [1a], Tsimicalis 2005 [1a], Baumann 2011 [2b], Jarden 2009 [2b]). The HSCT treatment results in a decline in physical function functioning related to loss of muscle mass and muscle strength and muscle atrophy is associated with several transplant related problems, including immunosuppressive therapy, bed rest, and drug toxicities (Wolin 2010 [1a], Knols 2005 [1a], Wiskemann 2008 [1b], Baumann 2011 [2b]). The experience of the isolated environment and the stress of a life threatening illness, resulting in fatigue, anxiety, depression, and fear, may also contribute to negative effects on physical function and QoL (Tsimicalis 2005 [1a]).

Chemotherapy results in anemia, which can affect cardiorespiratory fitness and cause skeletal muscle atrophy and weakness. Chemotherapy toxicities can impede adequate nutrition needed to maintain muscle mass. Radiation therapy can lead to lung fibrosis, resulting in decreased pulmonary function. Cranial radiation in childhood has been strongly linked to physical inactivity during adulthood (Wolin 2010 [1a]). Individuals being treated for pediatric cancers, in particular, tend to experience adverse effects of treatment including impaired growth, decreased neurological and/or cardiac function, endocrine complications, osteoporosis and obesity (Wolin 2010 [1a]). All of these side effects can lead to a decline in physical functioning and contribute to experiences of fatigue, anxiety, and depression (Wolin 2010 [1a]).

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| P: | Among school aged children and adolescents receiving hemopoietic stem cell transplant (HSCT) |
| I: | does physical therapy (PT) intervention (active participation in mobility, endurance, strength exercise) |
| C: | compared to no intervention |
| O: | improve the patient's quality of life (QoL)? |

In addition to the symptoms and side effects, the treatment requires prolonged isolation, which can also impede functional activity and impair psychological well-being (*Tremolada 2009 [1b]*). Activity restrictions and limited exercise options hinder the individual's ability to sustain physical function throughout this process. Mentally, the challenges pediatric patients experience while undergoing HSCT may have a long lasting impact on QoL (*Tremolada 2009 [1b]*). Because survival rates have increased, the need to address these quality of life issues and the impact of functional impairment has grown significantly. It is important to consider not only immediate survival, but also long term recovery of this patient population. The purpose of developing this BEST was to identify interventions that can improve function and positively impact outcomes improving HSCT pediatric patients' QoL.

298

Nephrotoxicity of Co-Administration of Tacrolimus and Teicoplanin in Allogeneic Hematopoietic Stem Cell Transplant Recipients

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Backgrounds: Both tacrolimus and glycopeptide antibiotics are nephrotoxic, and are frequently co-administered after hematopoietic stem cell transplantation (HSCT). The aim of this study is to evaluate the nephrotoxicity of co-administration of tacrolimus and glycopeptide antibiotic, teicoplanin, in HSCT recipients.

Patients and Methods: Sixty-seven patients who received intravenous tacrolimus and teicoplanin concomitantly for more than four days after allogeneic HSCT were retrospectively examined. Therapeutic drug monitoring (TDM) was performed in all patients both for tacrolimus and teicoplanin.

Results: The median duration of the co-administration of tacrolimus and teicoplanin was 11 days (range: 4-40). The mean serum creatinine (sCr) level tended to be elevated after the co-administration of tacrolimus and teicoplanin (from 0.69 ± 0.26 to 0.75 ± 0.30 mg/dL; $P = 0.08$); however, a two-fold or greater increase of sCr was observed only in 2 (3.0%) patients. Increased sCr was tolerable and reversible.

Conclusion: These results suggest that the nephrotoxicity of the co-administration of tacrolimus and teicoplanin is minimal after allogeneic HSCT if the TDM of each drug is properly applied.

299

Immunogenicity of a Lived-Attenuated Japanese Encephalitis Vaccine in Children after Hematopoietic Stem Cell Transplantation

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Japanese encephalitis (JE) virus is one of the most widespread causes of viral encephalitis in Asia and western Pacific. JE causes long-term neurological morbidities and mortality. National implementation of JE vaccine effectively reduces incidences of JE in Asian countries. A live-attenuated