Graft-Versus-Host Disease and Quality of Life: Can We Make a Difference?

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6.1 Introduction

Acute and chronic graft-versus-host disease (GVHD) are immune-mediated complications that occur after allogeneic hematopoietic cell transplantation (HCT) and contribute to the mortality and morbidity of the procedure. The clinical syndrome of GVHD is considered acute or chronic based on clinical features and not the temporal relationship to HCT (Filipovich et al. 2005). The incidence of acute GVHD ranges from 35 to 60% and that of chronic GVHD from 30 to 70% and is dependent on risk factors such as stem cell source, patient and donor age, conditioning, GVHD prophylaxis used, and prior acute GVHD specifically for chronic GVHD (Jacobsohn and Vogelsang 2007; Lee and Flowers 2008; Jagasia et al. 2012).

Both acute and chronic GVHD (chronic more than acute) have been shown in multiple studies to be associated with poor quality of life (QOL), impaired functional status, adverse psychological outcomes, and delayed recovery from HCT (Lee et al. 2006; Kiss et al. 2002; Hjermstad et al. 1999; Syrjala et al. 2004; Fraser et al. 2006; Sun et al. 2011). In the last few years, studies from chronic GVHD consortium have helped elucidate quite well the impact of chronic GVHD on patient reported outcomes (PROs).

This chapter provides an overview of the current literature on QOL associated with GVHD, specifically summarizing studies from Chronic GVHD Consortium. We briefly describe the considerations in developing endpoints and response

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measures that incorporate QOL aspects to test the efficacy of interventions used for prevention and treatment of GVHD. We conclude by describing interventions to help improve QOL in patients with GVHD, exploring the lacunae in the state of our current knowledge and outlining research priorities in the area.

6.2 Impact of Acute GVHD on QOL

In one of the earlier studies, Lee et al. reported grades II and IV acute and chronic GVHD to be associated with worse QOL after allogeneic HCT as measured by the Trial Outcome Index of the FACT-BMT (Lee et al. 2006). Acute GVHD led to a measurable decline in the QOL of patients who developed it, unlike those with no acute GVHD who had stable QOL over the first 6 months after HCT. Williams et al. have reported grade I–IV acute GVHD to be associated with greater symptom burden during 100 days after HCT than no acute GVHD (Williams et al. 2009).

6.3 Impact of Chronic GVHD on QOL

The impact of chronic GVHD on QOL is more profound and has been described by many more studies than for acute GVHD. Chiodi et al. examined the QOL in 244 patients undergoing an allogeneic HCT and found chronic GVHD to be one of the predictors for poor QOL (Chiodi et al. 2000). The BMT Survivor Study, a collaborative effort between City of Hope and University of Minnesota, reported that patients with active chronic GVHD were more likely to report adverse general health, mental health, functional impairments, activity limitation, and pain than were those with no history or those who had been optimally treated with the resolution of chronic GVHD (Fraser et al. 2006). Additionally patients with chronic GVHD have been reported to exhibit other poor psychosocial outcomes such as worse psychological, social, and spiritual well-being, higher depression, higher somatic distress, and lower likelihood of returning to work (Syrjala et al. 2004; Sun et al. 2011; Wong et al. 2010). In a large European Society for Blood and Marrow Transplantation (EBMT) registry study, chronic GVHD was an important predictor for a higher risk of committing suicide after allogeneic HCT (Tichelli et al. 2013).

6.4 Studies from Chronic GVHD Consortium

The Chronic GVHD Consortium is an integrated group of academic medical centers, patient support organizations, and clinical research resources that conducts clinical research in immune-mediated disorders after allogeneic HCT with the goal of improving the care and limiting the disability of patients affected by these disorders. Studies from the consortium have provided extensive information about impact of chronic GVHD on PROs. These studies are based on a cohort of allogeneic HCT recipients with chronic GVHD requiring systemic immunosuppressive therapy that was prospectively assembled in a multicenter observational study. Information

about symptoms, global ratings and perceptions of change, quality of life, and functional status was collected from the enrolled patients using the following well-validated instruments: SF-36, FACT-BMT trial outcome index, chronic GVHD symptom scale, and Human Activities Profile.

In one of the first studies from the consortium, Pidala et al. examined baseline QOL of HCT patients with chronic GVHD at the time of enrollment in the Chronic GVHD Consortium (Pidala et al. 2011a). They reported moderate and severe GVHD as defined by NIH global severity scoring system to be associated with poor patient-reported QOL, particularly in the physical domain, similar to some other systemic autoimmune diseases. In another analysis that compared the impact of overlap subtype and classic chronic GVHD, overlap subtype was associated not only with inferior clinical outcomes but also higher functional impairment and symptom burden (Pidala et al. 2012). Other consortium studies which have helped describe the influence of moderating factors such as age, the site of GVHD involvement and socioeconomic status on QOL in chronic GVHD patients are summarized in Table 6.1.

6.5 Consideration of QOL and Other PROs in Treatment and Prevention of GVHD

The use of PROs such as QOL, functional status, and symptom burden has been recognized as important for the drug approval process for products developed to treat chronic disabling conditions where the intent is not curative but to ameliorate symptoms, facilitate functioning, or improve QOL (Gnanasakthy et al. 2012). Challenges of including PRO end points in trials for acute GVHD include lack of instruments validated specifically for GVHD population, inability to tease out the impact of concurrent complications on QOL in a patient with severe acute GVHD, and patient burden associated with frequency and timing of data collection (Lee and Williams 2010).

Clinical Trials Working Group of 2014 NIH Consensus Conference on Chronic GVHD has proposed SWOPI (survival without progressive impairment) as a primary endpoint in chronic GVHD treatment trials (Martin et al. 2015). They also felt that PRO assessment might be reasonable to consider as a key secondary or co-primary endpoint to measure the core disease-related symptoms of chronic GVHD.

6.6 Use of QOL Endpoints in Treatment/Intervention Trials

QOL was examined as a secondary endpoint in a randomized trial of T-cell depleted bone marrow transplantation versus unmodified transplantation for unrelated transplants (Altmaier et al. 2006). Even though the incidence of acute GVHD was slightly higher in the unmodified arm, T-cell depletion did not have a differential impact on QOL at 1 year after transplantation indicating that acute GVHD may not have a notable impact on QOL. An ongoing multicenter trial that is evaluating the Outcomes of Second-line Therapy in Acute Graft-versus-Host Study including

Table 6.1 Summary of studies from chronic GVHD consortium

Author; number of patients	Aims of the study	Results
Pidala et al. (2011a) *N* = 298	• Examine association between cGVHD severity and QOL • Compare cGVHD cohort members' SF-36 mean scores to age- and gender-matched US population • Compare cGVHD cohort members' SF-36 mean scores to other chronic health conditions	• cGVHD severity was independently associated with QOL, adjusting for age • Compared with population normative data, SF-36 scores were lower for some domains but comparable for others • Moderate-to-severe cGVHD associated with significant compromise in multiple QOL domains, comparable to those for SS, SLE, and MS, but greater impairment compared with several common chronic health conditions including chronic lung disease, hypertension, diabetes, and arthritis
Pidala et al. (2011b) N = 336	• Examine association between changes in cGVHD severity over 6 months as assessed by NIH severity scale, clinicians, and patients with changes in patient-reported QOL	• No association between change in cGVHD severity evaluated by NIH criteria and change in QOL • Clinician-reported changes in severity were associated with changes in some QOL measures • Patient-reported changes in the severity of cGVHD were strongly associated with changes in all QOL measures
Inamoto et al. (2012) *N* = 283	• Assess correlation of the calculated response based on the provisional algorithm with symptom burden, QOL, and survival outcomes	• Clinical response at 6 months correlated with changes in symptom burden in patients with newly diagnosed cGVHD, but not with changes in quality of life or survival outcomes
Pidala et al. (2012) *N* = 427	• Examine clinical, functional, or prognostic significance of overlap subtype cGVHD	• Overlap syndrome (vs. classic cGVHD) was associated with: – Higher degrees of functional impairment – Higher symptom burden – Worse social functioning – Lower overall survival and higher non-relapse mortality rates
Pidala et al. (2013a) *N* = 567	• Examine whether the site of GI (esophageal, upper GI, lower GI) and type of hepatic (bilirubin, AP), ALT) involvement are associated with overall survival and non-relapse mortality, symptoms, QOL, and functional status measures	• Any esophageal involvement and NIH GI score greater than zero were associated with both symptoms and QOL • Elevated bilirubin was associated with QOL • No evidence that upper GI involvement, AP, ALT, or NIH liver score was associated with survival, overall symptom burden, or QOL

Table 6.1 (continued)

Author; number of patients	Aims of the study	Results
Pidala et al. (2013b) *N* = 584	• Examine relationship between hand grip strength (HGS) and 2-minute walk test (2 MWT) with patient-reported measures, cGVHD global severity, calculated and clinician-reported cGVHD response, and mortality	• Shorter 2MWT: – Associated with higher symptom burden, lower QOL, functional disability • Lower HGS: – Associated with lower QOL and functional disability
Inamoto et al. (2014)	• Evaluate 3 joint assessment scales and 10 other scales that assess symptoms, QOL, and physical functions • Examine longitudinal joint responses according to the validated scales and associations of joint/fascia manifestations with subsequent mortality	• Joint and fascia manifestations were associated with higher symptom burden, lower QOL
El-Jawahri et al. (2014) *N* = 522	• Examine the relationship between age group and QOL, physical functioning, functional status, non-relapse mortality, and overall survival	• More physical limitations in older patients with worse functional status relative to adolescent young adults (AYA) and middle-aged patients • Overall better QOL in older patients compared with middle-aged patients and similar to AYA patients
Palmer et al. (2014) *N* = 496	• Association of pulmonary measures with non-relapse mortality, overall survival, and patient-reported outcomes	• NIH symptom-based lung score was associated with non-relapse mortality and overall survival, patient-reported symptoms, and functional status
Sun et al. (2015) *N* = 342	• Describe the impact of ocular involvement in QOL	• Patients with ocular GVHD had worse QOL, and greater cGVHD symptom burden, compared with patients without ocular GVHD
Hamilton et al. (Abstract submitted to BMT Tandem Meetings 2017) *N* = 421	• Examine the association of SES parameters (income, education and work status) with survival and patient-reported outcomes	• Higher income was significantly associated with lower symptom burden • Ability to return to work was associated with lower symptom burden, better activity, and QOL • No association of SES with survival after cGVHD

Abbreviations: *cGVHD* chronic graft-vs.-host disease, *QOL* quality of life, *SS* systemic sclerosis, *SLE* systemic lupus erythematosus, *MS* multiple sclerosis, *NIH* National Institutes of Health, *AP* alkaline phosphatase, *ALT* alanine aminotransferase, *GI* gastrointestinal, *SES* socioeconomic status

extra corporeal photopheresis plans to examine the differences in QOL with different treatments (Personal communication: Madan Jagasia; PI of POSTAGE STUDY).

CBMTG 0801 was a randomized, multicenter study that examined whether the addition of Thymoglobulin (TG) to preparative regimens resulted in a decrease in the use of immunosuppression for chronic GVHD, leading to improvements in

QOL (Walker et al. 2014). Life Happiness was higher and chronic GVHD symptoms were lower in the TG group as compared to the no TG group ($p = 0.014$ and 0.017 respectively). The long-term follow-up data from BMT CTN 0201 study (peripheral blood vs. bone marrow for unrelated donor HCT) was recently published and showed better psychological well-being, less burdensome chronic GVHD symptoms, and increased likelihood of return to work for bone marrow recipients as compared to peripheral blood at 5 years after HCT (Lee et al. 2016).

QOL endpoints have recently been used in the case of treatment of organ-specific chronic GVHD. In a phase II trial of bandage contact lenses for ocular GVHD, eye symptoms were primary endpoint (Inamoto et al. 2015). All measures including the Lee eye subscale, ocular surface disease index, and 11-point eye symptom ratings showed statistically significant and clinically meaningful improvement in symptoms after the placement of these lenses. A prospective, multicenter, randomized, two-arm phase II crossover trial of imatinib or rituximab for the treatment of sclerotic chronic GVHD examined the correlation of changes in patient-reported outcomes (SHAQ standard disability index, Lee skin symptom scale, SF-36, FACT-BMT, or HAP) with significant clinical response as a secondary endpoint (Arai et al. 2016). Patients on imatinib arm showed a median 10-point decrease for the Lee skin symptom scale and a response to imatinib was associated with improvement in the SF-36 vitality score and the Lee lung symptom score. There were no differences in the other patient-reported measures, including skin bother, and no differences correlated with rituximab treatment successes. Williams et al. recently reported on the use of Fluticasone propionate, azithromycin, and montelukast (FAM therapy) with steroid pulse to be associated with stable lung function and improved functional and patient-reported outcomes (SF 36 social functioning score and mental component score, FACT emotional well-being, and Lee symptom scores in lung, skin, mouth, and the overall summary score) for newly diagnosed patients with bronchiolitis obliterans syndrome (Williams et al. 2016).

The BMT CTN 0801 was a phase II/III randomized, multicenter trial comparing sirolimus plus prednisone, and sirolimus/calcineurin inhibitor plus prednisone for the treatment of chronic GVHD. The trial examined the severity of chronic GVHD symptoms as reported by patients and QOL utilizing the FACT-BMT, SF-36, etc., as secondary endpoints and results of these secondary analyses are awaited.

6.7 Non-pharmacologic Interventions to Improve QOL in GVHD Patients

Interventions such as exercise, cognitive behavioral therapy, mindfulness-based practices for developing positive emotions, and educational efforts have been tried in HCT generally to help improve QOL (Baumann et al. 2009; DeFor et al. 2007; DuHamel et al. 2010; Jacobsen et al. 2014). The proportion of patients with GVHD in these studies is either not described optimally or very small to be able to make definitive conclusions about their benefits for chronic GVHD patients. While there have been some preclinical studies showing the benefits of exercise on survival,

clinical severity, physical fitness, and cytokine profile in a murine model, there is a paucity of clinical studies that have assessed the impact of exercise interventions on ameliorating the detrimental effects of both acute and chronic GVHD in humans (Fiuza-Luces et al. 2016). In a small retrospective study, pulmonary rehabilitation led to improvement in 6-minute walk distance, subjective symptoms of dyspnea, and exercise tolerance in ten patients with bronchiolitis obliterans syndrome (Tran et al. 2012). It is intuitive that aggressive physical therapy and a home-based exercise program, along with the provision of resources for regular strength training and aerobics, can help address the functional impairments due to fasciitis, contractures, and steroid myopathy commonly seen in chronic GVHD patients but have not been tested in a study or reported widely. Despite this, the Ancillary Therapy and Supportive Care Working Group of 2014 National Institutes of Health Consensus Development Project on Criteria for Clinical Trials in Chronic GVHD recommends more frequent screening for such issues and appropriate referrals for physical medicine and rehabilitation for intensive physical therapy, cognitive, behavioral interventions, or psychiatry assessment if indicated (Carpenter et al. 2015).

6.8 Gaps in Research and Recommendations

Survivors with acute and chronic GVHD have a different spectrum of issues that impact QOL. While acute GVHD is mostly about symptoms such as pain, diarrhea and itching, factors such as prolonged hospitalization, concurrent complications such as infections, and need for higher doses of immunosuppressive medications may contribute to the decline in QOL. Prospective collection of QOL and other PRO information in the context of large BMT CTN studies may provide us with better insights into the impact of different transplant strategies on the incidence and QOL impact of acute GVHD, though some of the challenges around measuring QOL in these patients such as intrinsic measurement variability and higher mortality/sicker patients leading to more missing data may influence the quality of such information. In that case, the hope will be that interventions directed toward decreasing the incidence and mortality associated with acute GVHD will have positive impact on QOL as well.

The psychological, functional, or adjustment difficulties have been much better characterized for chronic GVHD. The extensive work done by Chronic GVHD Consortium has contributed to our understanding of the PRO as endpoints and their sensitivity to clinical change in patients with chronic GVHD. One of the other areas that has recently been highlighted in HCT is the concept of financial toxicity and its impact on other psychosocial outcomes after HCT (Majhail et al. 2013; Khera et al. 2014; Hamilton et al. 2013; Abel et al. 2016). It is likely that chronic GVHD can result in increased financial burden for HCT patients even after a long time from HCT because of the need for intense medical follow-up/treatments and impaired functional status preventing return to work. Interestingly while chronic GVHD was shown to be associated with delayed return to work in one of the studies (Syrjala et al. 2004), it has not emerged as a predictor for return to work or overt financial

hardship in others (Khera et al. 2014; Abel et al. 2016; Kirchhoff et al. 2010). This is likely due to small sample size for patients with chronic GVHD in the overall study population. An ongoing Chronic GVHD Consortium study is examining financial burden and its determinants in chronic GVHD patients and will study the association of financial burden with quality of life as measured by FACT-BMT and SF-36.

6.9 Conclusion

There is a need to apply the knowledge that has been gathered in the area of QOL in chronic GVHD to start including validated measures of QOL in prevention/treatment trials for chronic GVHD. In addition to therapeutic trials for this disease, we must design and test non-medical interventions to help improve QOL for these patients while working toward decreasing its psychosocial and financial burden and increasing the social and professional reintegration of these patients. While advances are being made in the understanding of the pathobiology and targeted treatments for GVHD, it is important to include assessments of patient outcomes and experiences when testing approaches to contain this difficult complication of allogeneic HCT to be able to meet the goal of optimum patient centered care.

References

Abel GA, Albelda R, Khera N et al (2016) Financial hardship and patient-reported outcomes after hematopoietic cell transplantation. Biol Blood Marrow Transplant 22:1504–1510

Altmaier EM, Ewell M, McQuellon R et al (2006) The effect of unrelated donor marrow transplantation on health-related quality of life: a report of the unrelated donor marrow transplantation trial (T-cell depletion trial). Biol Blood Marrow Transplant 12:648–655

Arai S, Pidala J, Pusic I et al (2016) A randomized phase II crossover study of imatinib or rituximab for cutaneous sclerosis after hematopoietic cell transplantation. Clin Cancer Res 22:319–327

Baumann FT, Kraut L, Schule K, Bloch W, Fauser AA (2009) A controlled randomized study examining the effects of exercise therapy on patients undergoing haematopoietic stem cell transplantation. Bone Marrow Transplant 45:355–362

Carpenter PA, Kitko CL, Elad S et al (2015) National Institutes of Health consensus development project on criteria for clinical trials in chronic graft-versus-host disease: V. the 2014 ancillary therapy and supportive care working group report. Biol Blood Marrow Transplant 21:1167–1187

Chiodi S, Spinelli S, Ravera G et al (2000) Quality of life in 244 recipients of allogeneic bone marrow transplantation. Br J Haematol 110:614–619

DeFor TE, Burns LJ, Gold EM, Weisdorf DJ (2007) A randomized trial of the effect of a walking regimen on the functional status of 100 adult allogeneic donor hematopoietic cell transplant patients. Biol Blood Marrow Transplant 13:948–955

DuHamel KN, Mosher CE, Winkel G et al (2010) Randomized clinical trial of telephone-administered cognitive-behavioral therapy to reduce post-traumatic stress disorder and distress symptoms after hematopoietic stem-cell transplantation. J Clin Oncol 28:3754–3761

El-Jawahri A, Pidala J, Inamoto Y et al (2014) Impact of age on quality of life, functional status and survival in patients with chronic graft-versus-host disease. Biol Blood Marrow Transplant 20(9):1341–1348

Filipovich AH, Weisdorf D, Pavletic S et al (2005) National Institutes of Health consensus development project on criteria for clinical trials in chronic graft-versus-host disease: I. Diagnosis and staging working group report. Biol Blood Marrow Transplant 11:945–956

Fiuza-Luces C, Simpson RJ, Ramirez M, Lucia A, Berger NA (2016) Physical function and quality of life in patients with chronic GvHD: a summary of preclinical and clinical studies and a call for exercise intervention trials in patients. Bone Marrow Transplant 51:13–26

Fraser CJ, Bhatia S, Ness K et al (2006) Impact of chronic graft-versus-host disease on the health status of hematopoietic cell transplantation survivors: a report from the Bone Marrow Transplant Survivor Study. Blood 108:2867–2873

Gnanasakthy A, Mordin M, Clark M, DeMuro C, Fehnel S, Copley-Merriman C (2012) A review of patient-reported outcome labels in the United States: 2006 to 2010. Value Health 15:437–442

Hamilton JG, Wu LM, Austin JE et al (2013) Economic survivorship stress is associated with poor health-related quality of life among distressed survivors of hematopoietic stem cell transplantation. Psycho-Oncology 22:911–921

Hjermstad MJ, Evensen SA, Kvaløy SO, Fayers PM, Kaasa S (1999) Health-related quality of life 1 year after allogeneic or autologous stem-cell transplantation: a prospective study. J Clin Oncol 17:706

Inamoto Y, Martin PJ, Chai X et al (2012) Clinical benefit of response in chronic graft-versus-host disease. Biol Blood Marrow Transplant 18:1517–1524

Inamoto Y, Pidala J, Chai X et al (2014) Joint and fascia manifestations in chronic graft-versus-host disease and their assessment. Arthritis Rheumatol (Hoboken, NJ) 66:1044–1052

Inamoto Y, Sun Y-C, Flowers MED et al (2015) Bandage soft contact lenses for ocular graft-versus-host disease. Biol Blood Marrow Transplant 21:2002–2007

Jacobsen PB, Le-Rademacher J, Jim H et al (2014) Exercise and stress management training prior to hematopoietic cell transplantation: blood and marrow transplant clinical trials network (bmt ctn) 0902. Biol Blood Marrow Transplant 20(10):1530–1536

Jacobsohn DA, Vogelsang GB (2007) Acute graft versus host disease. Orphanet J Rare Dis 2:35–35

Jagasia M, Arora M, Flowers MED et al (2012) Risk factors for acute GVHD and survival after hematopoietic cell transplantation. Blood 119:296–307

Khera N, Chang YH, Hashmi S et al (2014) Financial burden in recipients of allogeneic hematopoietic cell transplantation. Biol Blood Marrow Transplant 20:1375–1381

Kirchhoff AC, Leisenring W, Syrjala KL (2010) Prospective predictors of return to work in the 5 years after hematopoietic cell transplantation. J Cancer Surviv 4:33–44

Kiss TL, Abdolell M, Jamal N, Minden MD, Lipton JH, Messner HA (2002) Long-term medical outcomes and quality-of-life assessment of patients with chronic myeloid leukemia followed at least 10 years after allogeneic bone marrow transplantation. J Clin Oncol 20:2334–2343

Lee SJ, Flowers ME (2008) Recognizing and managing chronic graft-versus-host disease. Hematol Am Soc Hematol Educ Program 2008:134–141

Lee SJ, Williams LA (2010) Patient-reported outcomes for acute graft-versus-host disease prevention and treatment trials. Biol Blood Marrow Transplant 16:295–300

Lee SJ, Kim HT, Ho VT et al (2006) Quality of life associated with acute and chronic graft-versus-host disease. Bone Marrow Transplant 38:305–310

Lee SJ, Logan B, Westervelt P et al (2016) Comparison of patient-reported outcomes in 5-year survivors who received bone marrow vs peripheral blood unrelated donor transplantation: long-term follow-up of a randomized clinical trial. JAMA Oncol 2:1583

Majhail NS, Rizzo JD, Hahn T et al (2013) Pilot study of patient and caregiver out-of-pocket costs of allogeneic hematopoietic cell transplantation. Bone Marrow Transplant 48:865–871

Martin PJ, Lee SJ, Przepiorka D et al (2015) National Institutes of Health consensus development project on criteria for clinical trials in chronic graft-versus-host disease: VI. The 2014 clinical trial design working group report. Biol Blood Marrow Transplant 21:1343–1359

Palmer J, Williams K, Inamoto Y et al (2014) Pulmonary symptoms measured by the National Institutes of Health lung score predict overall survival, nonrelapse mortality, and patient-reported outcomes in chronic graft-versus-host disease. Biol Blood Marrow Transplant 20:337–344

Pidala J, Kurland B, Chai X et al (2011a) Patient-reported quality of life is associated with severity of chronic graft-versus-host disease as measured by NIH criteria: report on baseline data from the Chronic GVHD Consortium. Blood 117:4651–4657

Pidala J, Kurland BF, Chai X et al (2011b) Sensitivity of changes in chronic graft-versus-host disease activity to changes in patient-reported quality of life: results from the Chronic Graft-versus-Host Disease Consortium. Haematologica 96:1528–1535

Pidala J, Vogelsang G, Martin P et al (2012) Overlap subtype of chronic graft-versus-host disease is associated with an adverse prognosis, functional impairment, and inferior patient-reported outcomes: a Chronic Graft-Versus-Host Disease Consortium study. Haematologica 97:451–458

Pidala J, Chai X, Kurland BF et al (2013a) Analysis of gastrointestinal and hepatic chronic GVHD manifestations on major outcomes: a chronic GVHD Consortium study. Biol Blood Marrow Transplant 19:784–791

Pidala J, Chai X, Martin P et al (2013b) Hand grip strength and 2-minute walk test in chronic graft-versus-host disease assessment: analysis from the chronic GVHD consortium. Biol Blood Marrow Transplant 19:967–972

Sun CL, Francisco L, Baker KS, Weisdorf DJ, Forman SJ, Bhatia S (2011) Adverse psychological outcomes in long-term survivors of hematopoietic cell transplantation: a report from the Bone Marrow Transplant Survivor Study (BMTSS). Blood 118:4723–4731

Sun Y-C, Chai X, Inamoto Y et al (2015) Impact of ocular chronic graft-versus-host disease on quality of life. Biol Blood Marrow Transplant 21:1687–1691

Syrjala KL, Langer SL, Abrams JR et al (2004) Recovery and long-term function after hematopoietic cell transplantation for leukemia or lymphoma. JAMA 291:2335–2343

Tichelli A, Labopin M, Rovó A et al (2013) Increase of suicide and accidental death after hematopoietic stem cell transplantation. Cancer 119:2012–2021

Tran J, Norder EE, Diaz PT et al (2012) Pulmonary rehabilitation for bronchiolitis obliterans syndrome after hematopoietic stem cell transplantation. Biol Blood Marrow Transplant 18:1250–1254

Walker I, Schultz KR, Toze CL et al (2014) Thymoglobulin decreases the need for immunosuppression at 12 months after myeloablative and nonmyeloablative unrelated donor transplantation: CBMTG 0801, a randomized, controlled trial. Blood 124:38–38

Williams LA, Giralt SA, Wang XS et al (2009) Measuring the symptom burden of allogeneic hematopoietic stem cell transplantation in patients with and without acute graft-versus-host disease. Biol Blood Marrow Transplant 15:20–21

Williams KM, Cheng G-S, Pusic I et al (2016) Fluticasone, azithromycin, and montelukast treatment for new-onset bronchiolitis obliterans syndrome after hematopoietic cell transplantation. Biol Blood Marrow Transplant 22:710–716

Wong FL, Francisco L, Togawa K et al (2010) Long-term recovery after hematopoietic cell transplantation: predictors of quality-of-life concerns. Blood 115:2508–2519