2020

Comparison of Function, Fatigue, Frailty in Patients with Malignant Hematology, Pre-Bone Marrow Transplant and Solid Tumors

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Citation
Biology of Blood and Marrow Transplantation (2020) 26 (3 Suppl):S362

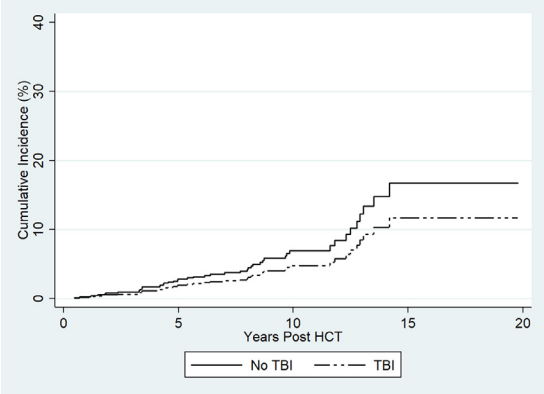

Figure 1. Cumulative incidence of subsequent malignancy after conditioning with myeloablative fludarabine/busulfan (No TBI group) versus myeloablative fludarabine/busulfan plus 400 cGy total body irradiation in 2 fractions (TBI group).

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Introduction: Impaired physical function, fatigue and frailty are commonly seen in patients undergoing cancer treatment as well as in cancer survivors. These can have a significant adverse effect on the quality of life of the affected individuals.
Objectives: To compare the prevalence of impairment of physical function, fatigue and frailty in three populations of cancer patients-malignant hematology, patients with malignant hematology (MH) selected to undergo bone marrow transplant (pre-BMT) and patients with solid tumors (ST).
Methods: Retrospective chart review of patients referred to a cancer rehabilitation clinic in a cancer institute. The medical charts of 355 patients with ST (Breast-264; prostate-20; lung-34 and GI- 37), 48 patients with MH (AML/ALL-5, Lymphoma-23, Myeloma-18, other:2) and 29 patients pre-BMT (AML/ALL-4, Lymphoma-11 and myeloma 14) were reviewed. Mean age: ST-67, MH-67 and Pre-BMT-55. Gender: ST-305 female; 50male; MH-25 female and 23 male; Pre-BMT-12 female and 17 male. Information reviewed: a) Patient Reported Outcome Measure Information System (PROMIS) Physical Function short form and Fatigue short form b) Timed Up and Go (TUG) test c) Sit to stand in 30 seconds test d) Grip Strength (in Kg), e) weight loss. Frailty or pre-frailty was determined by using modified Fried frailty criteria. Elements included: a) exhaustion (PROMIS-Fatigue score) b) low physical activity (PROMIS-Physical Function score) c) slowness (TUG) d) weakness (Grip strength) and e) weight loss. If person had 3/5 elements present, they were considered “frail” and if 1-2/5 elements were present, they were considered “pre-frail”.
Results: Impaired physical function: 198/348 of ST patients (57%), 35/48 of MH patients (72.9%) and 9/28 pre-BMT (32%). Significant Fatigue: 122/349 ST patients (35%), 24/46 of MH patients (52%) and 6/28 pre-BMT patients (21%). Frail and Pre-frail: 137/315 (44%) of ST patients met “pre-frail” criteria and 143/315 (45%) ST patients met frail criteria. 14/43 (33%) of MH patients were “pre-frail” and 27/43 (63%) MH patients were frail. 16/28 (57%) of pre-BMT patients were “pre-frail” and 7/28 (25%) pre-BMT patients were frail.
Conclusion: Malignant hematology patients are more likely to have impaired self-reported physical function, significant fatigue and be frail compared to patients selected to undergo BMT and those with solid tumors at time of initial presentation to a cancer rehabilitation clinic. Physical impairments, fatigue and frailty should be identified early at time of diagnosis, during active treatment and during survivorship period and appropriate rehabilitation interventions initiated to maximize function and quality of life.

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Ibrutinib for Pure Red Cell Aplasia after Allogeneic Hematopoietic Stem Cell Transplant with Major ABO Incompatibility

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Introduction: Since Human leukocyte antigen (HLA) and ABO blood group system are inherited independently and with up to 50% of allogeneic hematopoietic cell transplantations (HCT) are performed with donor-recipient ABO incompatibility, recipients are at increased risk for acute and delayed hemolytic reaction and delayed RBC precursors engraftment; i.e. pure RBC aplasia (PRCA). PRCA is a sever consequence of major and bi-directional ABO mismatch after alloHCT, leading to frequent transfusions, iron overload and secondary complications. Risk factors for PRCA after Major ABO incompatibility include; stem cell source, conditioning intensity, and titer of iso-agglutinins. Treatment is mostly supportive with transfusions and growth factors as well as withdrawing immunosuppressive therapy (IS). Targeting recipient immune system with high-dose steroids, DLI, and rituximab have been reported with variable results. Here we report a case series of a novel method of targeting recipient iso-agglutinins-producing B cells by Ibrutinib.
Methods: We report 3 cases of PRCA refractory to conventional therapy who responded to ibrutinib, a BTK inhibitor targeting recipient B cells to allow engraftment of donor RBCs. Patient, transplant and disease characteristic including prior therapies, time to transfusion independence, and switch of blood group (BG) are summarized in Table 1. First patient’s day 30 post-transplant bone marrow biopsy (BMBx) showed complete remission (CR) with full donor chimera, but BG remained O. He developed severe anemia requiring transfusions and Day 100 BMBx showed CR with markedly decreased number of erythroid progenitors. He did not respond to IS withdrawal, prednisone, rituximab or bortezomib. But BMBx 4 weeks after starting ibrutinib showed trilineage hematopoiesis. Second patient remained