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Prospective study of longitudinal geriatric assessment with risk-adapted interventions for older patients in allogeneic hematopoietic cell transplantation

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DATA SHARING STATEMENT

The study protocol and datasets generated and analyzed for this manuscript are available from the corresponding author upon request.

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Final approval of manuscript: All authors

DISCLOSURES

RJL reports serving on the IAC for Priothera Inc. and as a consultant for Kite Pharm. IP has received research funding from Merck and OrcaBio; and serves as a DSMB member for ExcellThera. BG reports serving as a paid DSMB chair for Theriva Biologics. MBG received research support from Amgen, Actinium Pharmaceuticals, and Tigen Pharma. He serves on the advisory boards of Amgen and Autolus. ADG received research grants from AbbVie, Aprea, Aptose, AROG, Celularity, Kura, Pfizer, and Prelude Therapeutics, received honoraria for consulting/advisory boards from AbbVie, Aptose, Astellas, Bristol Myers Squibb, Cardinal Health, Daiichi Sankyo, Geron, Genentech, Ikena Oncology, Kura Oncology, Molecular Partners, Pfizer, Remedy Plan Therapeutics, Rigel, Systimmune, Syndax Pharmaceuticals, honoraria from DAVA Oncology, and served on safety monitoring committees for AbbVie and Kura. MAP reports honoraria from Allogene, Cartesian, Celgene, Bristol-Myers Squibb, Incyte, Kite/ Gilead, Merck, Miltenyi Biotec, Nektar Therapeutics, Novartis, Omeros, OrcaBio, Ossium Health, Pierre Fabre, Sanofi, and Takeda. He serves on DSMBs for Cidara Therapeutics/ Mundipharma and Sellas Life Sciences. He has ownership interests in Omeros and OrcaBio. He has received institutional research support for clinical trials from Allogene, Genmab, Incyte, Kite/Gilead, Miltenyi Biotec, Novartis, and Tr1x. PBD has financial interest in Atara Biotherapeutics and has served on Advisory Board for Pierre Fabre Pharmaceuticals. SAG

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ABSTRACT

Older patients are increasingly considered for higher-intensity, potentially curative therapy such as allogeneic hematopoietic cell transplantation (alloHCT). While comprehensive geriatric assessment (GA) can help identify important vulnerabilities, it remains unknown whether GA-guided management interventions could improve outcomes in alloHCT. We conducted a single center, phase II study of a comprehensive, GA-driven, risk-adapted strategy for older patients (≥60 years old) undergoing first alloHCT. Based on pre-transplant GA, robust patients received myeloablative while vulnerable patients received reduced-intensity conditioning. The geriatrics team followed patients longitudinally and provided individualized, GA-directed management. The primary endpoint was one-year non-relapse mortality (NRM) of 10% compared to historical rates of 25%, for a cohort of 32 patients with median age of 69.3 years. The study met the primary endpoint with one-year NRM of 6.3% with no unexpected toxicities attributable to the intervention. With a median follow-up of 28.1 months, the two-year overall and progression-free survival was 72% (95% CI 57-89) and 56% (95% CI 41 – 76), respectively. Both patient reported and objective functioning outcomes were stable to improved by 6 to 12 months after alloHCT. We demonstrate here for the first time that a GA-driven, risk-adapted alloHCT approach that incorporates longitudinal GA-directed management may lead to promising, low NRM and patient-centered outcomes important for older patients.

INTRODUCTION

Advanced myeloid malignancies including acute myelogenous leukemia (AML), myelodysplastic syndromes (MDS), and myeloid proliferative neoplasms (MPN), predominantly affect older adults in their late sixties and early seventies and commonly present with higher risk disease.[1,2] Despite recent advances in combination chemotherapy and targeted agents, allogeneic hematopoietic cell transplantation (alloHCT) remains the only curative option for most of these patients,[3] and vastly underutilized among older patients.[4] Given the intensive, high-risk nature of alloHCT and the intrinsic, aging-related vulnerabilities among older patients, appropriate selection and optimization of older patients for alloHCT and meticulous post-transplant care are essential for expanding access to this curative treatment modality and improving its outcomes.[5,6] Moreover, older patients are at increased risk for exaggerated burden of toxicities and functional decline from alloHCT, and many prioritize quality of life (QOL) and independence.[5,7] All these considerations represent an area of urgent, unmet need in the current era of broadly increased transplant consideration, expanded donor availability across human leukocyte antigen barrier, and rapidly improving transplant supportive care.[8,9]

Older patients traditionally have inferior outcomes following alloHCT as compared to younger patients, mostly driven by increased NRM due to pre-existing comorbidities and functional/cognitive limitations.[6,10,11] Moreover, many older transplant recipients develop functional deterioration, loss of independence, and geriatric syndromes such as delirium and falls during the recovery phase, resulting in ongoing increase of NRM over the subsequent years.[12,13] Geriatric assessment (GA) is a comprehensive, holistic approach to evaluate and optimize an older patient's functional and cognitive status and identify prognostically relevant geriatric vulnerabilities.[14,15] Importantly, leveraging information generated from GA to appropriately manage non-oncologic, geriatric-related issues during cancer treatment can avoid both over- and under-treatment of older adults.[16] In both solid tumors and hematologic

malignancies, GA-identified deficits have been shown to be associated with overall survival (OS) and treatment related toxicities.[15,17] Importantly, GA-guided treatment intensity modification and interventions have been shown to improve treatment tolerance, toxicities, and quality-of-life (QOL) among patients with solid tumors.[18-21] More specifically to the field of alloHCT, multiple GA domains including comorbidities, functional impairment, and cognitive deficits have been shown to be associated with important transplant outcomes including non-relapse mortality (NRM), overall survival (OS), toxicities, and functional decline.[6,22-24] However, GA-guided management interventions have not been studied prospectively in alloHCT, and their impact on survival, treatment-related toxicities, and QOL outcomes remains unknown. Given these considerations and the rapidly increasing number of older transplant recipients in recent years,[8] there is a critical need to develop effective approaches to select appropriate older candidates, to adapt the transplant strategy to account for identified geriatric deficits, and to properly manage non-oncologic, geriatric issues prior to and following alloHCT to improve patient outcomes.

We conducted a phase II study to assess the impact of a GA-directed, longitudinal, comprehensive management intervention study for older patients (≥60 years old) with advanced myeloid malignancies undergoing first alloHCT (NCT04761770). As the first study of this kind, we sought to use a GA-based criterion prior to transplant to determine if a patient is fit/robust for higher intensity, myeloablative (MA) conditioning; or vulnerable and more suitable for reduced intensity (RIC) or nonmyeloablative (NMA) conditioning. Most importantly, all patients in the study received concurrent, longitudinal, comprehensive GA-directed management intervention and education throughout the transplant course with up to 5-year follow-up. Our hypothesis was that this GA-informed approach will reduce 1-year NRM as compared to historical rates published in registry and single center studies of heterogenous cohorts of older patients,[25-28] to ameliorate treatment-related toxicities and functional decline, and to maintain QOL among older transplant recipients.

METHODS

Study Population and Transplant Platform:

This investigator-initiated, single center, phase II study is registered at clinicaltrial.gov as NCT 04761770 (protocol available upon request). Eligible patients 60 years or older with a diagnosis of advanced myeloid malignancies including AML, MDS, or MPN receiving a first alloHCT were referred from transplant clinicians at our institution. The transplant platform was agnostic to any donor types except for cord blood, conditioning regimens, graft sources, and graft-versus-host disease (GVHD) prophylaxis regimen. In total, 34 patients were enrolled from 2021-2024 and 32 patients were eventually evaluable. Two patients had relapsed disease prior to conditioning and did not receive intervention. The data cutoff date was Dec. 31, 2025. Transplant care was conducted according to standard, National Comprehensive Cancer Network (NCCN) and institutional guidelines. The intensity of transplant conditioning regimen followed the standard definition.[29] CTCAE v5.0 was used to grade treatment-related toxicities. The study was conducted in accordance with the precepts established by the Helsinki Declaration and was approved by the Institution Review Board at the Memorial Sloan Kettering Cancer Center.

GA and GA-directed Management Interventions:

Geriatrics consultation and GA were performed according to standard guidelines.[15,30] GA components included Katz Index of Independence in Activities of Daily Living (ADL), the Lawton Instrumental Activities of Daily Living (iADL) Scale, and assessment of comorbidities, polypharmacy, functional, nutritional, and psychosocial impairment. These self-reported components were completed electronically via the Electronic Rapid Fitness Assessment (eRFA) prior to the geriatrics visit and geriatricians confirmed all findings during the outpatient GA visit using validated cutoff values.[31] Mobility and muscle strength were assessed during geriatrics visit using walking speed, Timed Up & Go (TUG), and grip strength.[32] Cognition was assessed

using the Montreal Cognitive Assessment (MoCA), Mini-Mental State Examination (MMSE) and/or Mini-Cog©.[31,32] All GA assessment outcomes are dichotomized scores to facilitate longitudinal comparison. Patients who were deemed suitable to proceed to first alloHCT with an available donor were consented and underwent pre-transplant GA within 30 days of admission for conditioning. The fitness criterion for conditioning intensity is defined as below based on previous findings of prognostically important GA domains[6,10]. Patients with functional impairment by IADL based on previous findings[28,33], and/or high comorbidity burden (hematopoietic cell transplant comorbidity index, age adjusted, HCT-CI-age >4) were categorized as vulnerable and received reduced intensity conditioning. Patients without functional impairment by IADL or high comorbidity burden were categorized as robust and received myeloablative conditioning (Table S1). All patients received an individually tailored, longitudinal, comprehensive supportive care and education plan based on identified deficits at the time of initial geriatrics evaluation and management. During the transplant admission, the inpatient geriatrics team sees each patient at least weekly and more frequently if clinically appropriate. All interventions including referrals and consultations were requested by the geriatrics team in collaboration with the transplant team. These supportive care interventions and optimization are consistent with national standards and may be carried out at our center or locally.[15]

Statistical Analysis:

Patient demographics are presented using descriptive statistics, including frequencies, medians, and interquartile ranges (IQRs). The primary endpoint was one-year NRM, with a target of 10% or less, and an estimated study size of 32 patients. The GA-driven, risk-adapted transplant strategy was to be considered unpromising if the 1-year NRM was greater than historical controls of approximately 25% in heterogenous chorts of older transplant patients,[25-28] and promising if it was 10% or less using point estimate with one-sided alpha level of 0.10 and 80% power. Important secondary endpoints included overall survival (OS); progression free

survival (PFS); grade 2-4 acute GVHD; moderate-severe chronic GVHD; and longitudinal changes in GA deficits and QOL measured by FACT-BMT.[34] To avoid confounding impact from relapsed disease and subsequent anti-neoplastic therapy, all patients who relapse will come off the study and will no longer receive GA or QOL evaluation. OS and PFS were estimated using Kaplan Meier methods and compared across groups using the log-rank test. Incidence of NRM, acute and chronic GVHD were estimated using the standard cumulative incidence function and compared using Gray's test. Changes in GA deficits over time were summarized descriptively among patients with complete data. Longitudinal changes in QOL were evaluated using linear mixed models. To account for correlated repeated measures, a random intercept for patient ID was used. All statistical analysis was performed using R (version 4.3.2).

RESULTS

Baseline Characteristics:

Patient and transplant characteristics are described in Table 1. The median age of the cohort was 69.3 years (range 61.8 – 79.5). Twelve patients (38%) were females, and five (18%) were ethnic minorities. AML was the primary diagnosis in 56% of patients while MDS/MPN accounted for the rest. Most patients, 26 (81%), had high or very high-risk disease by standard disease risk criteria (Table 1),[35-37] including 8 (25%) patients with mutation/alterations in TP53 gene. Most patients, 27 (84%), had active disease (for MDS/MPN patients), or measurable residual disease (MRD) for AML patients in complete remission prior to transplant. The comorbidity burden was high with a median HCT-CI of 5. Most patients, 72%, however, had Karnofsky performance status (KPS) of 90 or 100. Most patients, 23 (72%), had matched related or unrelated donors, while the rest had mismatched donors. Donors included matched related and unrelated (72%); mismatched unrelated (22%); and haploidentical donors (6%). Graft-versus-host-disease (GVHD) prophylaxis regimen included post-transplant cyclophosphamide (PTCy)

in 13 patients (41%), calcineurin inhibitor-based in 13 (41%), and CD34+ selection in 6 patients (19%).

Transplant Outcomes:

According to the GA fitness criteria, 8 patients (25%, median age 67.9, range 63.6 – 79.5) underwent MA, and 24 patients (75%, median age 69.7, range 61.8 – 78.7) underwent RIC/NMA conditioned alloHCT. All patients received GA-guided, longitudinal geriatrics supportive care throughout transplant admission and the required follow-up period. The study met the primary endpoint with one-year NRM of 6.25% by point estimate. Two patients died of NRM before 1-year; one patient died of sepsis during transplant admission and the second died of immune-mediated cytopenia and hemorrhage at 9-month post-transplant. Both patients had received reduced intensity conditioning. One additional patient died of chronic GVHD at 20-month post-transplant during the extended study follow-up period. With a median follow-up of 28.1 months among survivors (IQR, 22.8, 33.5), the 2-year OS was 72% (95% CI, 57 – 89) and the 2-year PFS was 56% (95% CI, 41 –76) (Figure 1A, 1B). Eleven patients relapsed for 2-year cumulative incidence of relapse of 34.4% (95% CI, 18.5 - 50.9), including 5 of 8 patients with TP53 mutation/alterations. The cumulative incidence of grade 2-4 acute GVHD by day 100 was 50% (95% CI, 31.4 - 66) (Figure 1C). There was no difference in OS, PFS, or cumulative incidence of relapse among patients who received either MA or RIC/NMA conditioning regimen (Supplemental Figure 1A, 1B, 1C). The cumulative incidence of moderate/severe chronic GVHD by 1 year was 18.8% (95% CI, 7.39 - 34.1), with most events, 5 out of 6, occurring in the patients who received CNI-based GVHD prophylaxis (Figure 1D). CTCAE (version 5.0) grade 3 and 4 non-hematologic toxicities were typical of early post-transplant care with the majority being infections, organ toxicities, and metabolic/electrolyte abnormalities. All toxicity events were attributed to the transplantation process, not to the GA or GA-guided interventions (Table S2).

Longitudinal trajectories in GA deficits:

All patients received an individually tailored, longitudinal, comprehensive supportive care and education plan based on identified deficits (Table 2). At the baseline pre-transplant evaluation, many patients had deficits in one or more GA domains (Figure 2A). These included physical and functional impairments in ADL (16%), IADL (22%), fall (16%), and mobility (3.1%); cognitive impairment (17%); and significant psychosocial impairments in social activities (87%); social support (33%); depression (59%); and distress (36%). In addition, 50% patients had polypharmacy and 3.1% had malnutrition. During the transplant admission, the geriatrics consult team saw all patients at least weekly or more frequently as clinically appropriate. All patients were scheduled for outpatient, follow-up GA at 3-, 6-, and 12-month post-transplant and continued all GA-directed, individually tailored supportive care interventions as appropriate. Nearly all patients who remained in remission post-transplant completed required, outpatient follow-up evaluation and GA visits within the 12-month period, resulting in an overall GA visit compliance rate of 97% with only one patient missing his 6-month visit due to hospitalization. We present descriptively the impact of GA-guided, longitudinal management intervention on GA deficits based on each individual domain in Figure 2 (B, C, D). We found largely stable GA deficits with some gradual improvement in IADL, cognition, depression, and social activities over the period of 12-month post-transplant.

Longitudinal trajectories in QOL:

Finally, we evaluated trajectory in QOL and the impact of longitudinal GA-guided management. Overall, QOL declined early after transplant and returned toward baseline by 6-12 months among evaluable, relapse-free patients. As measured by the FACT-BMT questionnaire, we observed an initial decline in physical/function outcomes and overall wellbeing following transplant, followed by improvement at 6-month and 12-months mark to return to the pre-transplant baseline (Figure 3). The initial decline at the 3-month mark as compared to the

baseline was statistically significant for FACT-BMT-TOI (mean change: -5.50, 95% CI [-10.91, -0.09], p=0.046) and FACTG (mean change: -4.92, 95% CI [-9.75, -0.09], p=0.046), while was approaching statistical significance for FACT-BMT-TOTAL (mean change: -6.18, 95% CI [-12.68, 0.28], p=0.061). This pattern of initial decline followed by improvement was seen within each individual domain of FACT-BMT except for social well-being which did not return to pre-transplant baseline by one-year mark (data not shown).

DISCUSSION

Given the curative potential of alloHCT for myeloid malignancies and recent advances in transplant technology, improving alloHCT outcomes for older patients represents an essential step to expand access of these patients to the life-saving therapy.[6,10] Our study is the first to leverage GA tools to appropriately select, optimize, and facilitate the high-intensity treatment of alloHCT for older patients with high comorbidities and high-risk disease. Most importantly, we show here that an individually tailored, longitudinal, comprehensive approach could potentially avoid both over- and under-treatment of older patients in alloHCT, and lead to favorable, clinically meaningful outcomes of survival, toxicities, functional recovery, and QOL.[15,16]

GA has emerged as an important prognostic tool to identify geriatric vulnerabilities associated with transplant outcomes, validated prospectively by the recent, large observational CHARM study.[22,23] In addition, both geriatric consultation and multidisciplinary supportive care programs have been shown to be feasible in hematologic malignancies and transplantation.[38-40] Our study builds upon these findings and further leverages GA to help guide the selection of treatment intensity (conditioning chemotherapy), to longitudinally remedy identified geriatric vulnerabilities, and to provide timely patient, caregiver, and provider education and awareness. While in general, increased conditioning intensity is associated with increased treatment-related toxicities, conditioning intensity, especially in fit patients, is crucial for disease control and elimination of measurable residual disease in alloHCT.[41,42] This type of comprehensive,

longitudinal, GA-guided intervention package has not been prospectively evaluated in hematologic malignancies and alloHCT, although it has been shown to be associated with a wide range benefits in patients with solid tumors.[18,21] We show in this prospective study that this intervention package achieved the primary endpoint of lower one-year NRM comparing to historical rates of NRM for older patients undergoing alloHCT, with favorable toxicity profiles and timely recovery of overall functioning and QOL. This is especially impressive considering our cohort's older age with the median age close to 70 years who have higher comorbidities burden (median HCT-CI of 5), as well as many pre-existing deficits including functional, cognitive, and psychosocial impairments.

The mechanisms by which our GA-guided management intervention leads to favorable clinical outcomes are likely multifaceted. First, we conducted GA to determine whether the patient is fit/robust or vulnerable based on the combination of functional impairment and comorbidities. This fitness level appropriately allowed the patient to receive either more intensive or less intensive conditioning chemotherapy. This beneficial strategy could potentially avoid both over- and under-treatment of older cancer patients, and it has been supported by previous studies in lung and other solid cancer patients demonstrating reduction of treatment-related toxicities and improved patient-centered care.[19,21] Second, our GA-guided management intervention is multidisciplinary, comprehensive, longitudinal, and encompasses both inpatient and outpatient components over the course of years (Table 2). It is conceivable that this intensive, co-management strategy minimized the adverse impact of non-oncologic, geriatric issues resulting improved outcomes for these vulnerable older patients. This is a logical extension of using GA to identify vulnerabilities that are associated with treatment outcomes.[15] Finally, we incorporated significant amount of dedicated teaching and education for patients, caregivers, and clinicians on GA and GA-guided interventions throughout. It is likely that awareness education may have resulted in concerted efforts to streamline and optimize the care of these older patients among

the intensive peri-transplant period. Similar benefits of educational awareness have been described in a recent study of using GA-guided management in solid tumor patients.[20,43]

Our study has several limitations. First, this is a single institution, prospective study of a small cohort of patient comparing to historical rates, rather than a randomized study or direct comparison with a propensity-matched cohort. Although promising, our findings require validation via a multicenter randomized controlled study. Second, all enrolled patients were already deemed suitable by their transplant physicians to proceed and GA was not used to screen or exclude patients, although it presumably could be beneficial in this setting for a larger number of older patients.[44] Third, the GA-guided interventional package, although highly effective, is resource and labor intensive and may not be readily adoptable to other settings. In addition, within each GA visit, there are likely variations in survey completion rates, management interventions, and/or patient compliance. We are examining individual components of our intervention package to identify key interventions that drive potential benefits. Fourth, this is a heterogenous cohort of patient regarding their disease and treatment, transplant platform, conditioning, donor, and GVHD prophylaxis, and missing elements of GA/QOL surveys as well as survivorship bias, all of which may have compounded our analyses. However, we designed the intervention to be applicable across various transplant platforms to mimic real world population of transplant patients. Finally, an important finding from our study is significant risk of relapse despite one-quarter of patients having received myeloablative conditioning. Most of relapses were driven by TP53-mutated myeloid neoplasia, which is enriched among older patients especially those who were treated for solid cancer. The higher risk of relapse may compromise the effectiveness of GA and GA-guided intervention post-transplant for these patients. TP53-mutated MDS/AML remains an area of unmet need and novel intervention targeting this population of ultra-high-risk patients are urgently needed.[45]

Despite these limitations, our study is the first of its kind to show that it is feasible to conduct GA-guided intervention throughout the continuum of alloHCT, and more importantly, to show favorable outcomes comparing to historical cohorts. Our study went beyond outcome prognostication with GA and showed that a comprehensive, GA-guided intervention package, delivered by a multidisciplinary team longitudinally, could lead to favorable outcomes relevant to older cancer patients including survival, functional recovery, and QOL. Our GA-guided intervention delivered fitness-appropriate treatment intensity, comprehensive prehabilitation and optimization, longitudinal reassessment and rehabilitation, and patient, caregiver, and provider awareness education. Our study added to the growing literature of GA-guided management interventions for older cancer patients to avoid both over- and under-treatment; and these findings support further testing of GA-guided risk-adapted alloHCT in multicenter studies to improve outcomes and to expand access for older patients.

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Table 1. Baseline Characteristics.

Patient Characteristics	**N=32**
Age at transplant (median, range)	69.3 (61.8 – 79.5)
Female gender (n, %)	12 (38%)
Non-white race (n, %)	5 (16%)
Comorbidities (HCT-CI-age, median, range)	6 (1 – 10)
Karnofsky Performance Status (KPS) < 90 (n, %)	9 (28%)
Disease indication (n, %)	
- AML (de novo, secondary, or treatment-related)	18 (56%)
- MDS	9 (28%)
- MPN	5 (16%)
High/very high disease risk* (n, %)	26 (81%)
TP53 mutation/17p deletion (n, %)	8 (25%)
Donor type (n, %)	
- Matched related or unrelated	23 (72%)
- Mismatched unrelated	7 (22%)
- Haploidentical related	2 (6%)
Graft-versus-host disease (GVHD) prophylaxis (n, %)	
- Calcineurin inhibitor based	13 (41%)
- Post-transplant cyclophosphamide based	13 (41%)
- CD34+ selection platform	6 (19%)

***Risk defined by ELN2022 for AML, IPSS-M for MDS, or MIPSS70+ for MPN.**[35-37]

Table 2. GA-guided, Supportive Management Plans.

1. Targeted, Longitudinal Geriatric Interventions at Each Visit	
Geriatric Assessment Domain Deficits	**Additional Assessment and Intervention**
Impairment in ADL/IADL	• Consultation with social worker or case manager • Consultation with physical and occupational therapists (PT/OT) • Consider blister packing of medications for patient to safely take medications
Slow gait speed (Timed Up & Go > 10 seconds)	• Consultation with PT/OT • Encourage use of appropriate assistive devices.
History of fall (one or more)	• Consultation with PT/OT • Encourage use of appropriate assistive devices • Evaluating neurological symptoms, muscle strength, and coordination. Check orthostatics. • Assess if patient has cognitive impairment, vision difficulties, and review medications list.
Cognitive impairment	• Consider workup and referral to psychiatry • Provide frequent reorientation to time, place and person after transplant • Avoid sedatives such as benzodiazepines, anticholinergics, and antihistamines as much as possible
Depression (Geriatric depression scale ≥1) or Distress score ≥4	• Consider workup and referral to psychologist/psychiatrist • Consider referral to support group • Assess caregiver's burnout
Polypharmacy (5 medications or more	• Consider consulting with pharmacist • Review each medication for its appropriateness
Weight loss (10 pounds or more)	• Consider consultation with the nutritionist • Assess dentition, fitting of dentures
Hearing difficulties	• Recommend use of hearing aide, if the patient has one • Provide white boards for written communication
Vision difficulties	• Encourage use of eye glasses • Consider home safe evaluation
2. Inpatient Geriatrics Consultation	
Essential components	• Weekly follow-up or more frequently as need • Multidisciplinary rounding • Pharmacist medication review • Collaboration with the transplant team and consultants • Collaboration with floor nursing staff and PT/OT

3. GA-based Education and Awareness	
Patients and caregivers	• Review GA findings and recommendations • Preparation for inpatient admission • Education on polypharmacy and potentially inappropriate medication use • Education on non-oncologic, geriatric related issues • Education on common medical comorbidities
Transplant team/clinicians	• Review GA findings and recommendations • Education on common geriatric syndromes in either inpatient or outpatient settings • Education on polypharmacy and potentially inappropriate medication use • Education on strategies on managing non-oncologic, geriatric related issues in the peri-transplant period
Ancillary staff (nursing, rehabilitation, social work, etc.)	• Review GA findings and recommendations • Education on signs and symptoms of common geriatric syndromes in either inpatient or outpatient settings • Education on strategies to support older patients' overall function and wellbeing in the peri-transplant period

Figure legends

Figure 1. Transplant outcomes.

A. Overall survival and at-risk table
B. Progression-free survival and at-risk table
C. Cumulative incidence of grade 2-4 acute GVHD and at-risk table
D. Cumulative incidence of chronic GVHD and at-risk table

Figure 2. Impairment of GA domains and their trajectories with evaluable patients [baseline (n=32); 3-month (n=28); 6-month (n=23); 12-month (n=20)].

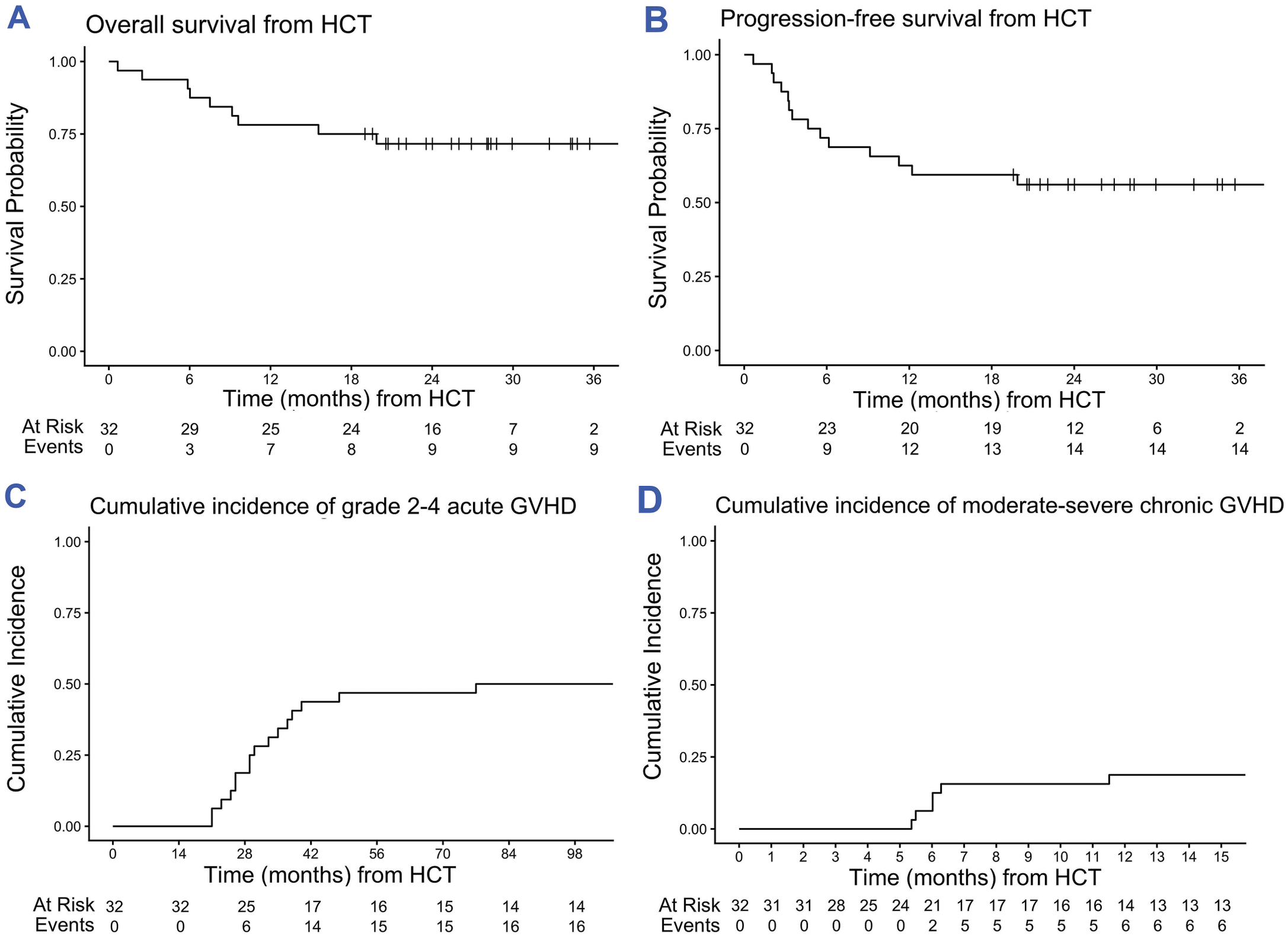
A. Percentages of impairment in each individual domain at baseline, represented by the bar graph
B. Percentage changes in each individual domain at the 3-month mark as compared with baseline (Green: improvement; Yellow: no change; Red: decline; Gray: missed item)
C. Percentage changes in each individual domain at the 6-month mark as compared with baseline (Green: improvement; Yellow: no change; Red: decline; Gray: missed item)
D. Percentage changes in each individual domain at the 12-month mark as compared with baseline (Green: improvement; Yellow: no change; Red: decline; Gray: missed item)

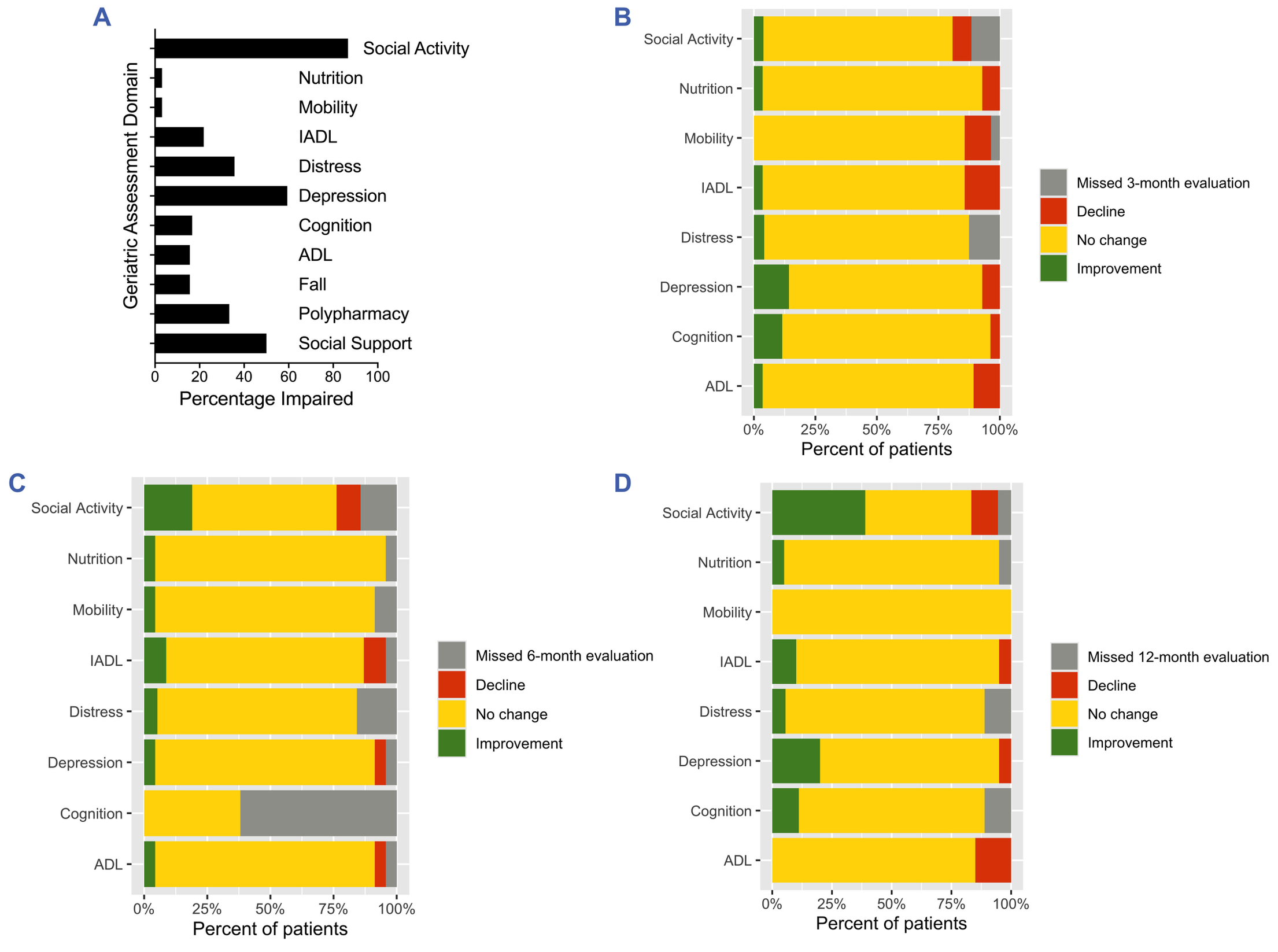
Figure 3. Trajectories of quality-of-life measures with evaluable patients [baseline (n=25); 3-month (n=18); 6-month (n=19); 12-month (n=17)].

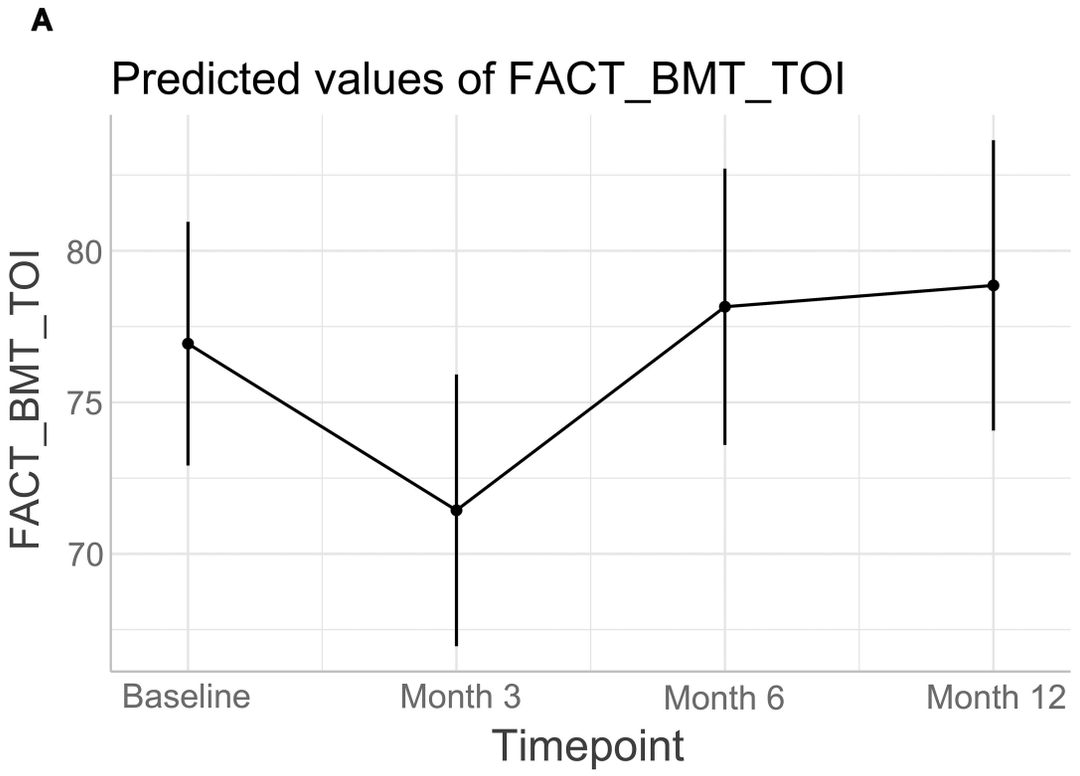
A. Trejectory in the subdomain score of FACT-BMT-TOI (Functional Assessment of Cancer Therapy – Bone Marrow Transplant Trial Outcome Index) over the study period

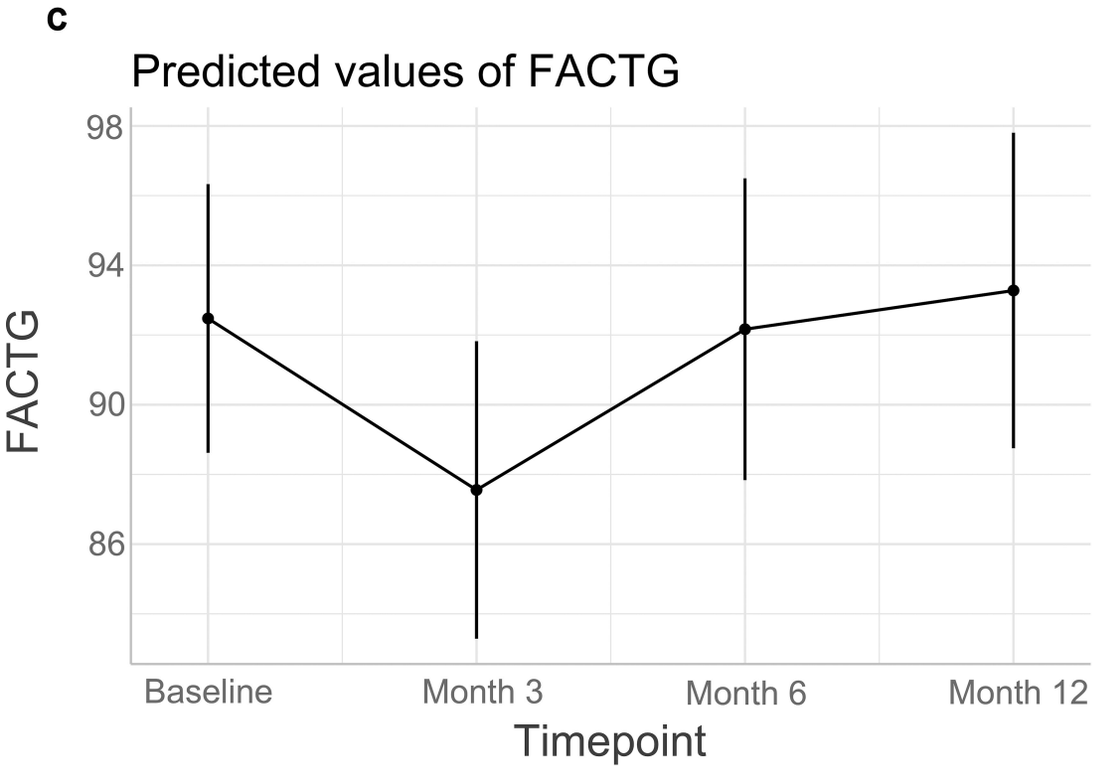
B. Trejectory in the subdomain score of FACT-G (Functional Assessment of Cancer Therapy - General) over the study period

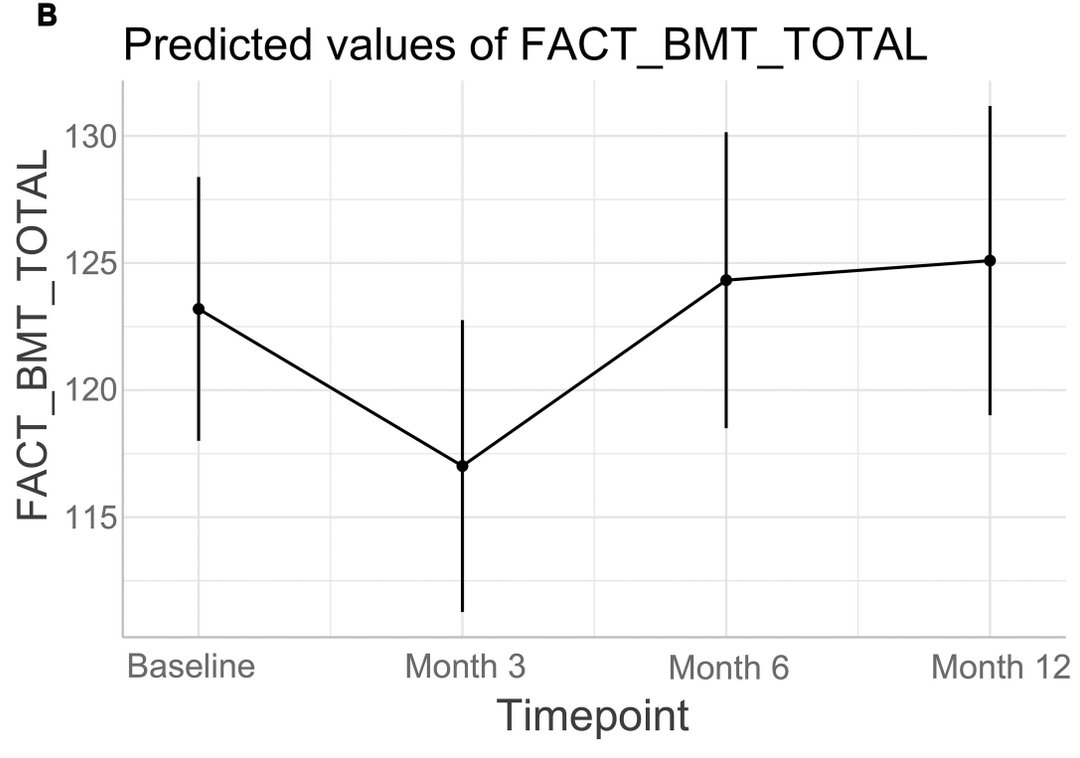
C. Trejectory in the total score of FACT-BMT over the study period


A
Overall survival from HCT
Survival Probability
1.00
0.75
0.50
0.25
0.00
0
6
12
18
24
30
36
Time (months) from HCT
At Risk 32 29 25 24 16 7 2
Events 0 3 7 8 9 9 9
B
Progression-free survival from HCT
Survival Probability
1.00
0.75
0.50
0.25
0.00
0
6
12
18
24
30
36
Time (months) from HCT
At Risk 32 23 20 19 12 6 2
Events 0 9 12 13 14 14 14
C
Cumulative incidence of grade 2-4 acute GVHD
Cumulative Incidence
1.00
0.75
0.50
0.25
0.00
0
14
28
42
56
70
84
98
Time (months) from HCT
At Risk 32 32 25 17 16 15 14 14
Events 0 0 6 14 15 15 16 16
D
Cumulative incidence of moderate-severe chronic GVHD
Cumulative Incidence
1.00
0.75
0.50
0.25
0.00
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Time (months) from HCT
At Risk 32 31 31 28 25 24 21 17 17 17 16 16 14 13 13 13
Events 0 0 0 0 0 0 2 5 5 5 5 5 6 6 6 6


A
Geriatric Assessment Domain
Social Activity
Nutrition
Mobility
IADL
Distress
Depression
Cognition
ADL
Fall
Polypharmacy
Social Support
0
20
40
60
80
100
Percentage Impaired
B
Social Activity
Nutrition
Mobility
IADL
Distress
Depression
Cognition
ADL
0%
25%
50%
75%
100%
Percent of patients
Missed 3-month evaluation
Decline
No change
Improvement
C
Social Activity
Nutrition
Mobility
IADL
Distress
Depression
Cognition
ADL
0%
25%
50%
75%
100%
Percent of patients
Missed 6-month evaluation
Decline
No change
Improvement
D
Social Activity
Nutrition
Mobility
IADL
Distress
Depression
Cognition
ADL
0%
25%
50%
75%
100%
Percent of patients
Missed 12-month evaluation
Decline
No change
Improvement


A
Predicted values of FACT_BMT_TOI
FACT_BMT_TOI
80
75
70
Baseline
Month 3
Month 6
Month 12
Timepoint


C
Predicted values of FACTG
FACTG
98
94
90
86
Baseline
Month 3
Month 6
Month 12
Timepoint


B
Predicted values of FACT_BMT_TOTAL
FACT_BMT_TOTAL
130
125
120
115
Baseline
Month 3
Month 6
Month 12
Timepoint

Supplement Table 1. Conditioning Regimens.

Myeloablative (MA) Conditioning Regimen
Busulfan/Melphalan/Fludarabine
Busulfan/Fludarabine (Bu4/Flu or Bu3/Flu)
Clofarabine/Melphalan/Thiotepa
Melphalan/Thiotepa/Fludarabine
Cyclophosphamide/Thiotepa/Fludarabine/Low dose TBI (4Gy)
Busulfan/Cyclophosphamide
Reduced intensity (RIC)/ Nonmyeloablative (NMA) Regimen
Melphalan/Fludarabine
Treosulfan/Fludarabine +/- Low dose TBI (2-4 Gy)
Busulfan/Fludarabine (Bu2/Flu)
Cyclophosphamide/Fludarabine/Low dose TBI (2-4 Gy)
Fludarabine/Low dose TBI (2-4 Gy)
Fludarabine/Cyclophosphamide

Supplemental Table 2. CTCAE (v5) Grade 3-4 Non-hematologic Toxicities

Categories of Toxicity#	**Grade 3 (n*, %)**	**Grade 4 (n*, %)**
Infection, bacterial	9, 28.1%	1, 3.1%
Infection, viral	1, 3.1%	1, 3.1%
Infection, febrile neutropenia (no proven organism)	7, 21.9%	
Infection, sepsis (no proven organism)	6, 18.8%	
Organ, cardiac	8, 25%	
Organ, gastrointestinal	10, 31.3%	1, 3.1%
Organ, pulmonary	1, 3.1%	1, 3.1%
Organ, others	3, 9.4%	
Electrolyte/Renal/Metabolic	32, 100%	3, 9.4%
Infusion related reaction		1, 3.1%
Others, not related to intervention	5, 15.6%	1, 3.1%

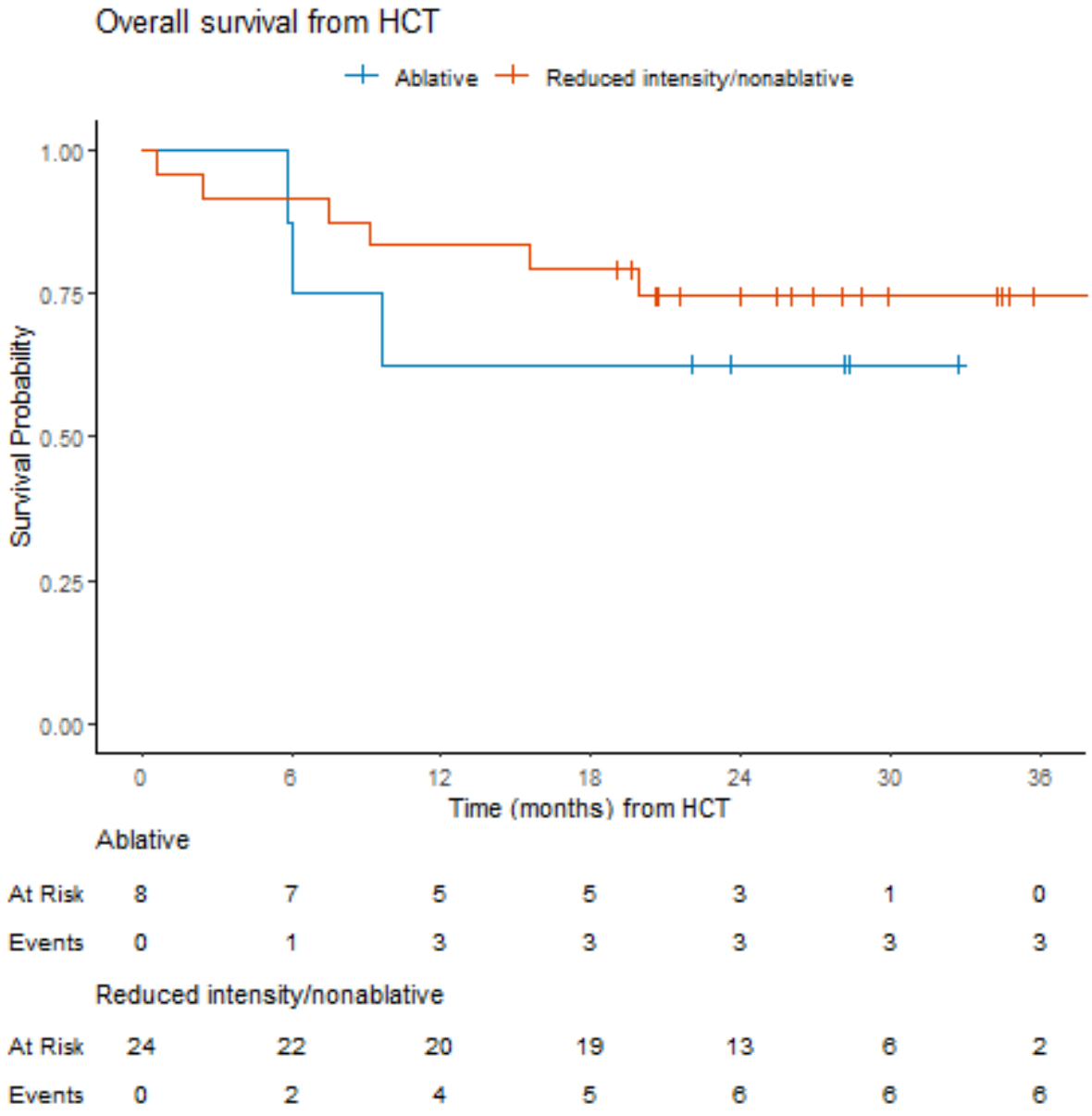
***n = number of patients**

 # All toxicities were attributed to transplantation, not GA and GA-guided interventions

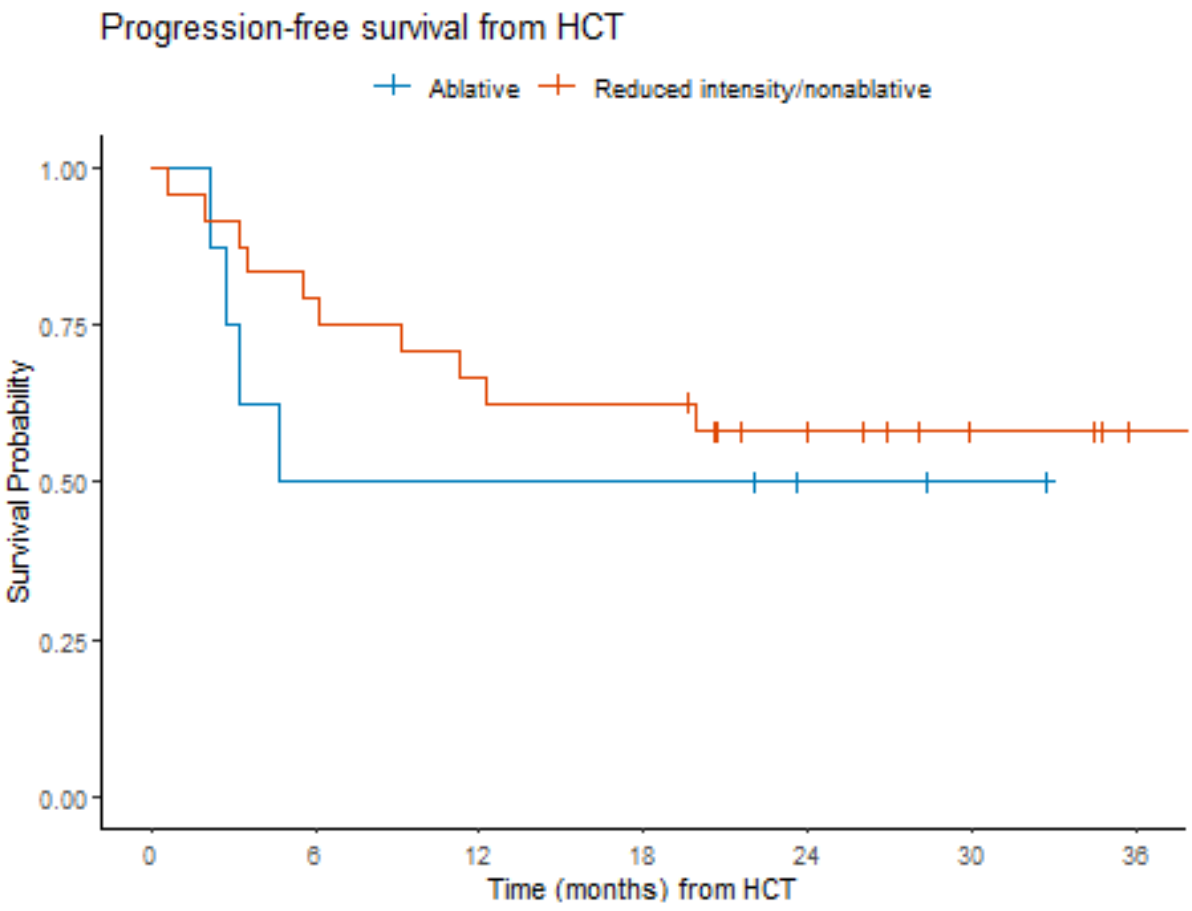
Supplemental Figure 1.

Overall Survival (A), Progression-Free Survival (B), and Cumulative Incidence of Relapse (C) according to Conditioning Intensity

A.

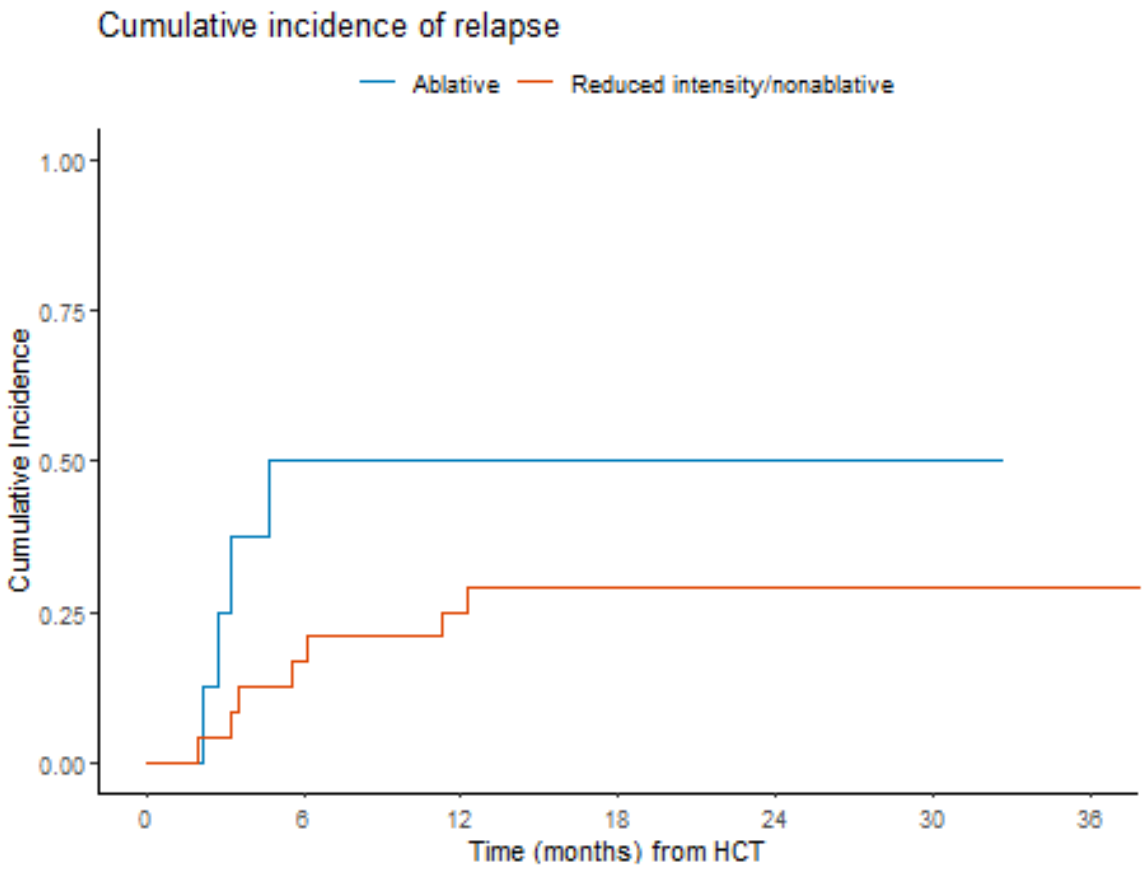


B.



Ablative							
At Risk	8	4	4	4	2	1	0
Events	0	4	4	4	4	4	4
Reduced intensity/nonablative							
At Risk	24	19	16	15	10	5	2
Events	0	5	8	9	10	10	10

C.



Ablative							
At Risk	8	4	4	4	2	1	0
Events	0	4	4	4	4	4	4
Reduced intensity/nonablative							
At Risk	24	19	16	15	10	5	2
Events	0	4	6	7	7	7	7