TITLE: The Myelodysplasia Transplantation-Associated Outcomes (MDS-TAO) Study

NCT NUMBER: NCT02390414

DOCUMENT DATE: 05/18/2018

Status Page

PROTOCOL 11-056

Permanent
Closed to New Accrual

Closure Effective Date: 05/18/2018
No new subjects may be enrolled in the study as described above.
Any questions regarding this closure should be directed to the study's Principal Investigator

DANA-FARBER CANCER INSTITUTE
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Office for Human Research Studies

Protocol Front Sheet

DFCI Protocol No.: 11-056

1. PROTOCOL TITLE AND VERSION

Title: The Myelodysplasia Transplantation-Associated Outcomes (MDS-TAO) Study
Protocol Version No./ Date: No. 5, 7/9/2014 **Sponsor Study Number:** N/A

2. DF/HCC STUDY CONTACT INFORMATION

Primary Study Contact: Maxwell Teschke **Email:** maxwellp_teschke@dfci.harvard.edu **Phone:** 617-582-7396

INVESTIGATORS: (List only those under DFCI IRB, *i.e.*, from institutions listed in Section 6 below)

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3. DRUG / DEVICE INFORMATION N/A:

☐ **Drug(s), Biologic(s)**:
Provided by:
IND Exempt: ☐ -or-
IND#: **Holder Type:** [pull down]
IND Holder Name:

☐ **Device(s) Name**:
Provided by:
IDE Exempt: ☐ -or-
IDE #: **Holder Type:** [pull down]
IDE Holder Name:

4. PROTOCOL COORDINATION, FUNDING, PHASE, MODE, TYPE ETC.

Regulatory Sponsor:
DF/HCC Investigator

Cancer Related: Yes If yes:
Primary Disease Program:
Leukemia
or
Primary Discipline Based Program:
Outcomes Research

Funding/Support (check all that apply):
☐ Industry:
☐ Federal Organization:
Grant #:
☒ Internal Funding: DFCI
☐ Non-Federal:
☐ Other:

CTEP Study: No

Phase: N/A

Multi-Center (i.e., non-DF/HCC site participation):
No

Protocol Type: Other
If Ancillary, provide parent protocol #:

Protocol Involves (check all that apply as listed in the protocol document, even if not part of the research but is mandated by the protocol document):

☐ Chemotherapy	☐ Hormone Therapy	☒ Medical Record Review
☐ Immunotherapy	☐ Vaccine	☒ Questionnaires/Surveys/Interviews
☐ Surgery	☐ Data Repository	☐ Radiological Exams
☒ Bone Marrow/Stem Cell Transplant	☐ Exercise/Physical Therapy	☐ Required Biopsy Study
☐ Cell Based Therapy	☐ Genetic Studies	☐ Human Embryonic Stem Cell
☐ Gene Transfer (use of recombinant DNA)	☐ Human Material Banking	☐ Quality of Life
☐ Radiation Therapy	☐ Human Material Collection	☐ Other:

5. SUBJECT POPULATION (also applies to medical record review and specimen collection studies)

Total Study-Wide Enrollment Goal: 290 **Greater than 25% of the overall study accrual will be at DF/HCC:** ☒ Yes ☐ No

Total DF/HCC Estimated Enrollment Goal: 290 **Adult Age Range:** 60-75 **Pediatric Age Range:** N/A

Will all subjects be recruited from pediatric clinics? ☐ Yes ☒ No

If enrolling both adults and pediatric subjects, anticipated percent of pediatric subjects: N/A

Retrospective Medical Record Reviews only (Please provide date range): from to

6. DF/HCC PARTICIPANTS UNDER DFCI IRB (check all that apply)

☒ Beth Israel Deaconess Medical Center (BIDMC)
☐ Beth Israel Deaconess Medical Center – Needham (BIDMC-Needham)
☐ Boston Children's Hospital (BCH)
☐ Brigham and Women's Hospital (BWH)
☒ Dana-Farber Cancer Institute (DFCI)
☐ Dana-Farber/New Hampshire Oncology-Hematology (DFCI @ NHOH)
☐ DF/BWCC in Clinical Affiliation with South Shore Hospital (DFCI @ SSH)
☐ Dana-Farber at Milford Regional Cancer Center (DFCI @ MRCC)
☐ Dana-Farber at Steward St. Elizabeth's Medical Center (DFCI @ SEMC)
☒ Massachusetts General Hospital (MGH)
☐ Mass General/North Shore Cancer Center (MGH @ NSCC)
☐ Mass General at Emerson Hospital – Bethke (MGH @ EH)
☐ New England Cancer Specialists (NECS)

7. NON-DF/HCC PARTICIPANTS UNDER DFCI IRB (check all that apply)

☐ Cape Cod Healthcare (CCH)
☐ Lowell General Hospital (LGH)
☐ New Hampshire Oncology-Hematology-P.A. (NHOH)
☐ Newton-Wellesley Hospital (NWH)
☐ Broad Institute
☐ Lawrence & Memorial Cancer Center in affiliation with Dana-Farber Community Cancer Care (LMCCC)

8. DF/HCC INITIATED STUDIES ONLY - INSTITUTIONAL PARTICIPANTS UNDER OTHER IRB (N/A:)

DF/HCC Multi-Center Protocols: (list institution/location)

DF/PCC Network Affiliates: (list institution/location)

Protocol Number: 11-056

Approval Date: 04/01/11 (IRB meeting date when protocol/consent approved or conditionally approved)

Activation Date: 04/07/11 (Date when protocol open to patient entry)

Approval signatures are on file in the Office for Human Research Studies, tel. 617-632-3029.

Date Posted	Revised Sections	IRB Approval Date	OHRS Version Date
05/31/11	Front Sheet replaced due to Amendment #1	05/25/11	-
06/06/11	Protocol and Front Sheet replaced due to Amendment #2	05/31/11	-
06/06/11	Protocol replaced due to Amendment #3	06/02/11	-
07/15/11	Front Sheet replaced due to Amendment #4	06/29/11	-
12/07/11	Protocol and Front Sheet replaced due to Amendment #5	12/05/11	-
03/08/12	Study renewal/ Consent Form footer replaced due to Continuing Review #1	02/15/12	-
05/29/12	Consent Form and Front Sheet replaced due to Amendment #6	05/15/12	-
02/14/13	Study renewal/ Consent Form footer replaced due to Continuing Review #2	02/14/13	N/A
08/09/13	Correction: Front Sheet replaced due to incorrect version previously provided	n/a	n/a
10/28/13	Consent Form and Front Sheet replaced due to Amendment #7	10/22/13	10/23/13
01/09/14	Study renewal/ Consent Form footer replaced due to Continuing Review #3	01/07/14	n/a
08/04/14	Consent Form, Protocol and Front Sheet replaced; Appendix C added (as a Local Appendix)	07/21/14	07/23/14
12/23/14	Study renewal/ Consent Form footer replaced due to Continuing Review #4	12/23/14	N/A
06/18/15	Consent Form and Front Sheet replaced due to Amendment #9	06/15/15	06/16/15
Date Posted	**Revised Sections**	**IRB Approval Date**	**OnCore Version Date**
12/21/15	Study renewal/ Consent Form footer replaced due to Continuing Review #5	12/21/15	12/21/15
Date Posted	**Revised Sections**	**Approved Date**	**Version Date (OnCore)**
12/12/16	Study renewal/ Consent Form footer replaced due to Continuing Review #6	12/02/2016	12/05/2016
11/29/17	Study renewal/ Consent Form footer replaced due to Continuing Review #7	11/29/2017	11/29/2017
05/21/2018	Study Closed – Study Accrual Goal Met	05/18/2018	N/A
10/17/2018	Study renewal/Consent Form footer replaced per Continuing Review #8	10/10/2018	10/17/2018

The Myelodysplasia Transplantation-Associated Outcomes (MDS-TAO) Study

Revised July 9, 2014

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The Myelodysplasia Transplantation-Associated Outcomes (MDS-TAO) Study

1.0 ABSTRACT

Although hematopoietic stem cell transplantation (HSCT) is the only therapy that can cure patients with the myelodysplastic syndrome (MDS), and HSCT has long been the standard of care for younger patients with high-risk disease, the procedure has been traditionally withheld from older patients due to concerns about excessive toxicity and limited underlying overall survival. More recently, however, HSCT with reduced-intensity conditioning (RIC) has been increasingly offered to older patients with the syndrome, a clinical picture that is complicated by the introduction of non-HSCT disease-modifying treatments for MDS such as the DNA methyltransferase inhibitors. We propose an observational study enrolling high-risk MDS patients who are fit enough to undergo RIC HSCT but whose HLA and donor status is unknown at baseline. Whether or not enrollees eventually go on to HSCT—indeed, many will not, due to factors such as lack of a suitable donor or rapid progression of disease—all will be followed for outcomes such as overall survival, progression free survival, and quality of life. Our protocol will generate much-needed comparative outcomes data for older patients with high-risk MDS, and has the potential to greatly influence how the disorder is treated in the United States.

2.0 BACKGROUND AND SIGNIFICANCE

The myelodysplastic syndromes (MDS) are a group of hematopoietic stem cell disorders characterized by ineffective hematopoiesis and a tendency to transform to leukemia. They range in clinical severity from incidentally-found cases manifesting with mild anemia, to highly symptomatic cases characterized by severe anemia, neutropenia and/or thrombocytopenia. These latter cases are often accompanied by hemorrhage, infection and rapid mortality, and are thus the focus of most MDS treatments, including HSCT. Despite recent advances in treatment and classification, until recently little was known about the epidemiology and patterns of care for patients with MDS in the United States.[1] Indeed, MDS was only added to the National Cancer Institute's Surveillance Epidemiology and End Results (SEER) program in 2001, and reliable incidence rates (2001-2003) were only recently reported: 3.4 cases per 100,000, with a male predominance (4.5 for males versus 2.7 for females) and three-year overall survival of 45%.[2-3] Data on patterns of care for MDS patients is also limited, although it is known that the newer WHO classification system[4] (as compared to the older FAB system) has become widely-adopted in clinical pratice.[5] One study reported the results of a survey among US hematologists,[6] finding that fewer MDS patients with lower-risk disease were transfusion-dependent, a majority received erythropoiesis-stimulating agents (ESAs), and only a small percentage of patients had had or were being considered for HSCT.[7]

This last finding is provocative, as HSCT remains the only curative option for MDS. Indeed, HSCT has a long and successful history in management of these hematologic disorders, using both ablative and RIC regimens.[8-24] A recent evidence-based review published under the aegis of the American Society of Blood and Marrow Transplantation was supportive of the role of HSCT in the management of MDS.[25] Moreover, the introduction of RIC regimens has greatly expanded the utility of HSCT in older and sicker patients by reducing the risk of regimen-related toxicity.[26-32] For example, Kroger and associates reported on 26 patients with MDS or secondary AML (median age = 60; range 44 to 70) who were transplanted with RIC with cells from related (n=6) or unrelated (n=20) donors. Transplant-related mortality was 28%, and the two-year

estimate overall survival rate was 36%.[29] A Spanish trial reported results on 37 patients (median age = 57; range 22 to 66) with MDS or AML transplanted from HLA-identical siblings following a RIC regimen. The one-year transplant-related mortality and relapse-free survival were 5% and 66%, respectively. In our group, we have found similar outcomes in patients treated with RIC and myeloablative regimens. For example, we reviewed 136 patients with advanced AML and MDS undergoing allogeneic HSCT, comparing 39 patients receiving RIC HSCT to 97 patients receiving myeloablative HSCT. Patients receiving RIC were at high risk for treatment-related complications given that they were older, 57 vs 43 years ($P < .001$), and more likely had received previous or myeloablative transplantation (54% vs 2%; $P < .0001$). Still, Cox regression analysis showed that the intensity of the conditioning regimen had no effect on either overall survival or progression free survival, suggesting that RIC is a reasonable alternative for patients with advanced MDS or AML at high risk for complications with myeloablative HSCT.[33]

Despite these promising preliminary results, until recently, concerns regarding morbidity and mortality related to even RIC HSCT limited its application in older patients (60 to 75) with MDS, especially given the lack of rigorous comparative outcomes data from a study including patients both with and without HSCT. Perhaps due to this fact, earlier this year, the Centers for Medicare & Medicaid Services (CMS)—the main health insurer for adults 65 and older in the United States—posted their controversial decision on coverage of HSCT for Medicare patients with MDS. In the decision, CMS disallowed coverage for HSCT, but stated that the current data from younger patients, especially with regard to RIC HSCT, is promising enough to provide for some coverage under the Coverage with Evidence Development process (§1862(a) (1) (E) of the Social Security Act. This allows for Medicare patients with MDS to receive HSCT provided that the HSCT is performed in the context of a prospective clinical study comparing Medicare patients with MDS who receive HSCT to similar Medicare patients with MDS who do not. In part to address this challenge, the aim of this current protocol is to prospectively examine post-RIC HSCT outcomes in those patients aged 60 to 75 with MDS (which would include Medicare beneficiaries aged 65 to 75) to determine whether these outcomes are similar to those patients with MDS aged 60 to 75 who do not undergo HSCT, but who both have disease severe enough as well as a health status good enough they would also be eligible for RIC HSCT.

3.0 STUDY OBJECTIVES

3.1 Primary Objective

To prospectively compare the overall survival (OS) of patients aged 60-75 who undergo HSCT for MDS (Group A) to that of patients aged 60-75 who do not undergo HSCT (Group B) but who have disease of sufficiently high enough risk to warrant HSCT and who are also fit enough to undergo the procedure (**primary outcome**).

3.2 Secondary Objectives

1. To prospectively compare the progression-free survival (PFS) of patients in Group A to that of patients in Group B as defined above (**secondary outcome**).
2. To prospectively compare changes in the quality of life (QoL) from baseline to two years of patients in Group A to that of patients in Group B as defined above (**secondary outcome**).

3. To assess the potential association of patient- and disease-specific factors—including International Prognostic Scoring System (IPSS) score, WHO-based Prognostic Scoring System (WPSS) score, number of cytopenias, transfusion dependence, disease duration at baseline, prior therapies and age at HSCT—with the primary and secondary outcomes.

4.0 STUDY POPULATION

Eligible patients will be 60 to 75 years old with a diagnosis of MDS or related disorder (eg, MDS/MPD or CMML) who have disease that is advanced enough to warrant RIC HSCT (defined by high-risk cytogenetics,[34] int-2 or high-risk on IPSS[35] or transfusion dependence as defined by WPSS[36]) and who are physically fit enough to undergo RIC HSCT as assessed by pre-determined measures of organ function. Patients whose baseline donor status is known will be excluded; however, knowledge of HLA status is allowed as long as a donor search has not been performed.

4.1 Inclusion Criteria

1. Histologically-confirmed diagnosis of:
    a. Primary or secondary MDS using the World Health Organization (WHO) 2008 classification:
        i. Refractory cytopenia with unilineage dysplasia
            1. Refractory Anemia (RA)
            2. Refractory Neutropenia (RN)
            3. Refractory Thromobucytopenia (RT)
        ii. Refractory Anemia with Ring Sideroblasts (RARS)
        iii. Refractory Cytopenia with Multilineage Dysplasia (RCMD)
        iv. Refractory Anemia with Excess Blasts-1 (RAEB-1)
        v. Refractory Anemia with Excess Blasts-2 (RAEB-2)
        vi. MDS with isolated del (5q)
        vii. MDS-Unclassified (MDS-U)

    b. Another of the following related disorders:
        i. Chronic Myelomonocytic leukemia (CMML)
        ii. Myelodysplastic/myeloproliferative neoplasm, unclassifiable (MDS/MPD-U)

2. Age 60 to 75 years

3. Intermediate-2 or High-Risk IPSS

    OR

    Secondary MDS (any karyotype)

    OR

    Documented non-IPSS intermediate- or poor-prognosis karyotype[43] including:
        i. del(11q)

ii. +8
iii. t(11q23)
iv. Rea 3q
v. +19
vi. 3 or greater abnormalities
vii. del(7q)
viii. -5
ix. t(5q)

OR

Documented significant cytopenia for at least four months prior to enrollment, defined by the following criteria:

a. *Red Blood Cell (RBC) Transfusion Dependence*: four or more units of RBC transfusions within an eight-week period for symptomatic anemia with hemoglobin of ≤ 9.0 g/dL; **OR**

b. *Severe Anemia*: average of two or more hemoglobin values ≤ 8 g/dL within an eight-week period not influenced by RBC transfusions (i.e., must be seven days post transfusion); **OR**

c. *Severe Thrombocytopenia:* average of two or more platelet counts ≤ 50 × 10^9/L within an eight-week period not influenced by platelet transfusions (i.e., must be at least three days post- transfusion) or a clinically significant hemorrhage requiring platelet transfusions within the prior four months; **OR**

d. *Severe Neutropenia:* average of two or more absolute neutrophil counts (ANC) ≤ 500 within an eight-week period, or a clinically significant infection requiring IV antibiotics in the setting of ANC ≤ 1000 within the prior four months.

4. Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1 or 2.

5. Adequate organ function to permit RIC HSCT as indicated by the following:
   a. Serum bilirubin ≤ 2.5 mg/dL (except when Gilbert's syndrome or MDS-related hemolysis suspected).
   b. AST and ALT ≤ 2.5 times the upper limit of normal (ULN).
   c. Serum creatinine ≤ 2.0 mg/dL
   d. Seemingly sufficient baseline cardiac function to undergo HSCT (no echocardiogram required).
   e. Seemingly sufficient baseline pulmonary function to undergo HSCT (no pulmonary function tests required).
   f. Seemingly sufficient neuro-psychiatric function to undergo HSCT (no specific neuro-psychiatric evaluation required).

6. Willingness to undergo HLA-typing and consider subsequent HSCT.

7. Willingness and ability to give informed consent.

4.2 Exclusion Criteria

1. Known baseline conversion to AML (eg, ≥ 20% peripheral or marrow blasts).

2. Knowledge of potential donor status at study entry. Of note, knowledge of HLA status WITHOUT a related or unrelated search is allowed.

3. History of prior malignancy within the past year, except for adequately-treated carcinoma in situ of uterine cervix, basal cell or squamous cell skin cancer.

4. Any severe concurrent disease, infection, or comorbidity that, in the judgment of the principal investigator, would make the patient inappropriate for HSCT at the time of study entry.

5. Psychiatric disorders including dementia that would preclude obtaining informed consent or the ability to participate in an ongoing research study.

5.0 STUDY DESIGN AND METHODS

5.1 Data Collection

Data for this study will be collected using the existing mechanisms of the Dana-Farber/Harvard Cancer Center (DF/HCC) Leukemia Clinical Research Information Systems (Leukemia CRIS) for baseline data (all study participants). For patients who do not go on to HSCT, Leukemia CRIS will be used to collect their outcomes, while HSCT patients will have outcomes collected in the Center for International Blood and Marrow Transplant Research Stem Cell Therapeutic Outcomes Database (CIBMTR SCTOD). Leukemia CRIS is a state-of-the-art information infrastructure for hematologic oncology at the DF/HCC, developed to link clinical outcomes to blood and tissue samples, and to lay the foundation for innovative pilot studies and health services research. The database has been accruing data since January of 2006. Patients in Leukemia CRIS have baseline information and a new patient survey entered at 3 months; they are then assessed for outcomes every 6 months for 3 years. After 3 years, their records are updated for outcomes once per year. Note that baseline IPSS, WPSS and entry criterion (eg, histology, cytogenetics, or transfusion requirements), or as well as eventual HLA status and donor status will be added to Leukemia CRIS data screens and captured for MDS-TAO patients. Also, QoL will be assessed at baseline and two years with the EORTC-30,[37] a validated quality of life instrument, as well as the QUALMS-1, an MDS-specific quality of life instrument being validated by Dr. Abel under OHRS protocol 13-346.

5.2 Methods of Procedure

A dedicated clinical research assistant will work with the hematologic oncology new patient coordinators at the DF/HCC member institutions (Dana-Farber Cancer Institute (DFCI), Beth

Israel Deaconess Medical Center (BIDMC) and Massachusetts General Hospital (MGH)) to identify high-risk MDS patients that may be eligible for the study. The transplant and non-transplant MDS physicians will be ultimately responsible for identifying patients who are eligible for MDS-TAO; in addition, as all MDS patients followed at the DF/HCC are eligible for the Leukemia CRIS database, the research assistant and the Principal Investigator will also perform periodic reviews of MDS patients seen at the DF/HCC to retroactively assess eligibility and contact the appropriate physician to encourage that physician to enroll appropriate patients. Of note, the point of contact for patient enrollment will always be the treating physician.

Once enrolled, all study patients will be followed for the primary and secondary outcomes listed above, with assessments in step with those in the Leukemia CRIS system (baseline and every 6 months for 3 years; then yearly). A difference is that MDS-TAO patients will be followed on the same schedule whether or not they continue to receive their care at DF/HCC (Leukemia CRIS does not follow patients that are only seen for one-time consultation at DF/HCC). The investigators understand that this will require a different informed consent, and more resources (eg, another clinical research assistant) to obtain and abstract outside hospital records. Also, all MDS-TAO enrollees will be given the EORTC-30 to take home and mail back (if they have not already done it as part of their Leukemia CRIS new patient survey) at baseline and again at two years, regardless of HSCT status or whether or not they continue to be followed at DF/HCC. All enrollees will also be asked to complete the QUALMS-1 instrument. Finally, as above, if any patient goes on to RIC HSCT, his or her data—including outcomes—will be collected in the CIBMTR SCTOD.

6.0 STATISTICAL CONSIDERATIONS

6.1 Study Design

MDS-TAO is a prospective, observational study comparing OS between patients aged 60-75 who undergo RIC HSCT for MDS (Group A) and patients 60-75 who do not undergo HSCT but who have disease of sufficiently high enough risk to warrant HSCT and who are also fit enough to undergo the procedure (Group B).

6.2 Sample Size

290 eligible patients will be enrolled between the two groups over a period of 5 years and followed for an additional 5 years. Based on our current practice, we anticipate that the enrollment will be 1:2 ratio for Group A (HSCT) to Group B (no HSCT). This design will give approximately 85% power to detect a 15% difference in 5-year OS between the two study groups.

6.3 Accrual

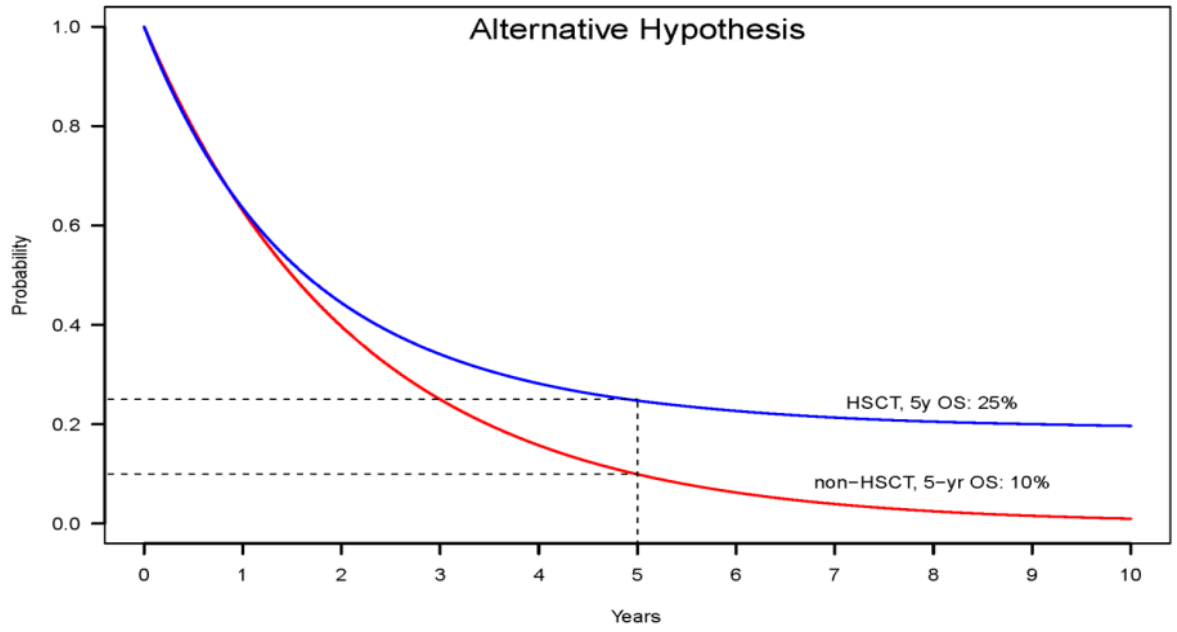
In 2009, the DFCI performed 18 RIC HSCTs in patients similar to the ones who will be eligible for the MDS-TAO study. Given the addition of the other members of the DF/HCC (BIDMC and MGH), we anticipate that we will accrue 20 patients per year for the HSCT group (Group A). There were also 50 patients seen at DFCI in 2009 with MDS of sufficiently high risk by WHO category (RAEB-1, RAEB-2, RCMD, and RCMD-RS) to be considered for HSCT but who did not ultimately receive HSCT. Thus, we project that we will accrue at least 40 patients per year who will enter MDS-TAO but not go on to HSCT (Group B). With 60 patients per year, we anticipate that accrual will be complete in 5 years.

6.4 Primary Outcome

The primary endpoint of this study is 5-year OS. OS is defined as time from study entry to death from any cause. Alessandro et al[39] recently reported the impact of WPSS on the outcome of MDS patients who underwent allogeneic HSCT. According to their report, the 5-year OS after HSCT was 51% in RAEB-1 and 28% in RAEB2 with an indication of plateau after 5-6 years post transplant. This observation resembles our experience at DFCI with RIC HSCT for older patients with MDS. Malcovati et al[36] reported that 5-year OS was 3% in the RAEB-1 group and 14% in the RAEB-2 group among 426 MDS patients who did not undergo HSCT. Most of the patients in these studies, however, were treated prior to the wide use of DNA-methyltransferase inhibitors. Thus, extrapolating this information and based on our experience at DFCI, we hypothesize that a small portion of patients will be cured with HSCT from the underlying disease and the 5-year OS will be 25%, whereas the 5-year OS will be 10% for the non-HSCT patients and the survival distribution of these patients will follow an exponential distribution. In addition, we expect that there will be an approximately 4-6 month wait time for patients in Group A from enrollment to actual RIC HSCT, thus no difference in OS between the two groups is expected for some period after the start of the study. Based on this information and assumptions, we propose an alternative hypothesis as: H_a: $S_A > S_B$, where S_A denotes the survival distribution of Group A and S_B denotes the survival distribution of Group B. Specifically:

$S_A = 0.19 + 0.4*\exp(t*(\log 2/10)) + 0.41*\exp(-t*(\log(2)/20)$; and $S_B = \exp(-t*(\log(2)/18)$.

The figure depicts these two survival distributions graphically. With this design, 290 patients



will be required to achieve 85% power with one-sided significance level of 0.025. This power calculation is calculated using the R program *Powlgrnk* (developed by Dr. Robert Gray at DFCI), which computes power of the two-group log-rank test for arbitrary failure time distributions.

6.5 Interim Analyses

The study will be monitored using standard procedures and processes. Interim inspections will occur annually; however, as this is an observational study and no new treatment is proposed, it is important to note that these interim analyses will not have an effect in terms of stopping accrual to the study or to terminate the study early in favor of alternative or null hypothesis.

6.6 Secondary Outcomes

Secondary outcomes include PFS and changes in self-reported QoL. PFS is defined as time from enrollment until evidence of progression to acute leukemia (time until increase in marrow or peripheral blasts to >20%). QoL will be assessed via changes between baseline and two-year assessments on the EORTC-30 and QUALMS-1. We also plan baseline assessment of IPSS and WPSS, number of cytopenias, transfusion dependence, disease duration at baseline, prior therapies and age at HSCT. Of note, we have not based our power calculations on these outcomes and covariates due to their exploratory nature.

6.7 Statistical Analysis Plan

As a patient's status in Group A may be changed during the study from waiting for HSCT to being a HSCT recipient, the effect of HSCT will be assessed in a various ways. Our first approach will be using the Mantel-Byer method.[40] Mantel and Byer (1974) proposed a modified life table to avoid 'time-to-treatment' bias and to accommodate the transient nature of transplant status. The second approach is to treat patient's transplant status as a time-dependent function, X=X(t), as proposed by Crowley and Hu.[41] In this approach, X(t) is an indicator variable at time *t*, that is, X(t)=0 if the patient has not received the transplant at time *t,* and 1 if the patient has received the transplant at time *t.* Age at HSCT will be constructed in a similar manner. Another approach is a landmark analysis at one year after study entry.[42] We will also explore a combination of a pointwise comparison of survival curves at specified time *t* and a log-rank test after *t,* using the method proposed by Logan et al.[42] The last two approaches are particularly suitable as the overall survival between the two groups is not expected to be different during the first year of study, but instead start to separate after approximately one year.

QoL will be assessed using the EORTC-30[37]and the QUALMS-1, a disease-specific measure developed by Dr. Abel and colleagues at DFCI which is currently undergoing validation.[38] The predictability of IPSS or WPSS score on survival outcome will be assessed using the time-dependent ROC curve estimation for censored survival data (survival ROC), proposed by Heagerty et al.[44-45] The predictability of these two scoring systems will be compared in each group. In addition, a subset analysis will be performed for Group A (HSCT) to prospectively determine if disease- or patient-related factors predict outcomes of HSCT for MDS in patients aged 60-75. These factors include baseline age at HSCT, IPSS score, WPSS score, number of cytopenias, transfusion dependence, disease duration, prior therapies, and Sorror co-morbidity index. In this subset analysis, standard time-to-event analysis as well as competing risks data analysis[46] will be performed.

7.0 COMMITMENT OF INSTITUTIONAL RESOURCES

MDS-TAO will be a long-term study, with at least 5 years of active accrual, and likely several more years of follow-up. The DFCI has invested a substantial commitment to the success of this effort. The current Leukemia CRIS program has a dedicated 100% FTE clinical research assistant, and is overseen by a disease-specific Principal Investigator, as well as a Population Scientist (2.5% FTE). MDS-TAO will call on these existing resources; in addition, the DFCI has committed support for another 50% FTE research assistant—who will be housed and supervised at the McGraw-Patterson Center for Outcomes and Policy Research—as well as 20% FTE programmer (to start in year 2 of the study) to assist the project biostatistician with interim analyses. Finally, the DFCI will fund or assist with the ascertainment of grant funding for 10%

FTE of the Principal Investigator, who will work to assure the quality of the data collected as well as the scientific integrity of the data and any resulting manuscripts.

8.0 POTENTIAL CLINICAL AND POLICY IMPACT

To our knowledge, our planned analysis will be the first large study of comparative outcomes associated with RIC HSCT versus non-HSCT for older patients with MDS—crucial information for our health care system as our country becomes increasingly concerned with the costs of health care and comparative effectiveness. Our results will provide essential insight to patients and practicing oncologists regarding the advisability of HSCT for MDS patients in this largely understudied age group, as well as help policymakers and funding sources such as CMS understand if the procedures truly lead to improved outcomes. Next, the data we plan to collect regarding potential changes in quality of life associated with HSCT in this age group promise to address an important gap in the current HSCT literature. Finally, MDS-TAO would also provide a long-overdue source of primary and prospective data for MDS researchers as to the usefulness of the IPSS and WPSS in prognosticating for transplantation-related outcomes.

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APPENDIX A: Sample of Baseline Data Abstracted in Leukemia CRIS

1. Data from the New Patient Survey
    - Reason for Seeking Care
    - Other Therapies
    - Quality of Life
    - Medical Hx
    - Demographics
    - Pt Status
    - Cancer Hx
    - Tobacco Hx
    - Social History
    - Household Members
    - Family Hx

2. Data abstracted from Medical Record
    - Demographics
    - Patient Disease and morphology
    - Episode
    - Diagnosis Detail
    - Pt Status
    - Sites of Involvement
    - Lab Results and tests
        - *BCR-ABL:*
        - *FLT-3 AL (D835 mutation)*
        - *FLT-3 ITD*
        - *Hematocrit*
        - *JAK-2*
        - *Malignant Cells in Blood*
        - *Malignant Cells in BM aspirate*
        - *Malignant Cells in BM Biopsy*
        - *NPM-1:*
        - *Platelet Count*
        - *RAR-Alpha*
        - *White Blood Cell Count*
    - Cytogenetics
        - *t (1;19)*
        - *t (4;11)*
        - *t (6;9)*
        - *t (8;14)*
        - *t (8;21)*
        - *t (9;11)*
        - *t (9;22)*
        - *t (11;14)*
        - *t (14;18)*
        - *t (15;17*

t (16;16)
Hyperdiploid
abn 3q:
abn 13q

abn 17p
abn 21q
del 5q:
monosomy 5
del 7q/monosomy 7
del 9q
del 11q
del 12p
del 17 p
del 20q
inv 16
trisomy 6
trisomy 8
trisomy 12
trisomy 21
trisomy 22
Normal karyotype
Other: other cytogenetic events not listed above
Other abnormalities: other chromosomal abnormalities not listed
Multiple complex abnormalities:
Not Performed
Inconclusive Results

Hospitalizations
Treatments

APPENDIX B: New Patient Survey for Leukemia CRIS, including EORTC-30

APPENDIX C: QUALMS-1 Quality of Life Instrument

APPENDIX D: Consent Form for MDS-TAO

MDS-TAO Appendix B

Hematologic Oncology New Patient Survey

Dana-Farber Cancer Institute

Patient Name	**Age**	**D.O.B.**
DFCI MRN	**BWH MRN**	**MGH MRN**
Appt Provider	**Appt Date/Time**	

Please fill out this form and return it to the
MAIN RECEPTION DESK

Please complete this form as thoroughly as possible. This information will help your health care providers to develop a plan of care tailored to your needs.

Thank you.

REASON FOR SEEKING CARE

Where were you first diagnosed with your blood disorder?

Select **ONE.**
- O Emergency Room
- O Hospital
- O Hematologist/Oncologist's office
- O Primary Care Physician
- O Other physician office
- O Other

Have you seen another physician for your current blood disorder?

O No O Yes

If yes, what type of physician(s) have you seen previously for the treatment or evaluation of your current blood disorder?

Select **ALL** that apply.
- ☐ Medical oncologist (treats with chemotherapy / medicines)
- ☐ Primary care physician
- ☐ Radiation oncologist (treats with radiation)
- ☐ Other (Please specify: _____)

REASON FOR SEEKING CARE (continued)

Have you received any prior treatments for your blood disorder?

○ No ○ Yes

If yes, what prior treatments have you received?

Select **ALL** that apply.

- ☐ Chemotherapy
- ☐ Radiation therapy
- ☐ Surgery
- ☐ Vaccine therapy
- ☐ Other (Please specify: _____)

Who recommended that you to come to DFCI/MGH for consultation?

Select **ALL** that apply.

- ☐ Children
- ☐ Friend
- ☐ Internet
- ☐ My oncologist
- ☐ My primary care physician
- ☐ Self
- ☐ Spouse
- ☐ Other family
- ☐ Other (Please specify: _____)

Why are you coming to clinic today?

Select **ALL** that apply.

- ☐ To find out whether I have a blood disorder
- ☐ To see if I'm eligible for a clinical trial
- ☐ To find out if there are any new treatments available
- ☐ Other (Please specify: _____)

Do you expect to receive your ongoing care at DFCI/MGH?

Select **ONE.**

- ○ No- I'm here for a second opinion
- ○ Yes
- ○ Not sure

REASON FOR SEEKING CARE (continued)

Outside of a multivitamin do you REGULARLY do other complementary/nontraditional/alternative therapies?

○ No ○ Yes

If yes, which therapies? Select **ALL** that apply.

☐ Acupressure	☐ Macrobiotics	☐ Tai Chi or Chi Gong
☐ Acupuncture	☐ Massage	☐ Yoga
☐ Biofeedback	☐ Meditation	☐ Other (please specify
☐ Body Work	☐ Megavitamins	_____)
☐ Herbal and botanical remedies	☐ Reiki	
☐ Hypnosis	☐ Spiritual healing	

QUALITY OF LIFE

We are interested in some things about you and your health. Please answer all of the questions by circling the number that applies to you.

	Not at All	A Little	Quite a Bit	Very Much
Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	1	2	3	4
Do you have any trouble taking a long walk?	1	2	3	4
Do you have any trouble taking a short walk?	1	2	3	4
Do you need to stay in bed or a chair during the day?	1	2	3	4
Do you need help with eating, dressing, washing yourself or using the toilet?	1	2	3	4

QUALITY OF LIFE (continued)

During the past week:	Not at All	A Little	Quite a Bit	Very Much
Were you limited in doing either your work or other daily activities?	1	2	3	4
Were you limited in pursuing your hobbies or other leisure time activities?	1	2	3	4
Were you short of breath?	1	2	3	4
Have you had pain?	1	2	3	4
Did you need to rest?	1	2	3	4
Have you had trouble sleeping?	1	2	3	4
Have you felt weak?	1	2	3	4
Have you lacked appetite?	1	2	3	4
Have you felt nauseated?	1	2	3	4
Have you vomited?	1	2	3	4
Have you been constipated?	1	2	3	4
Have you had diarrhea?	1	2	3	4
Were you tired?	1	2	3	4
Did pain interfere with your daily activities?	1	2	3	4
Have you had difficulty in concentrating on things, like reading a newspaper or watching television?	1	2	3	4
Did you feel tense?	1	2	3	4
Did you worry?	1	2	3	4
Did you feel irritable?	1	2	3	4
Did you feel depressed?	1	2	3	4
Have you had difficulty remembering things?	1	2	3	4
Has your physical condition or medical treatment interfered with your family life?	1	2	3	4
Has your physical condition or medical treatment interfered with your social activities?	1	2	3	4
Has your physical condition or medical treatment caused you financial difficulties?	1	2	3	4

For the following questions please circle the number between 1 and 7 that best applies to you.

How would you rate your overall health during the past week?

1 2 3 4 5 6 7
Very poor Excellent

How would you rate your overall quality of life during the past week?

1 2 3 4 5 6 7
Very poor Excellent

QUALITY OF LIFE (continued)

Which option below describes your level of physical activity OVER THE PAST WEEK?

Select **ONE**
- ○ Fully active, able to carry on all usual activities without restriction
- ○ Restricted in strenuous activity; can walk; able to carry out light housework
- ○ Can walk and care for self; up more than ½ day
- ○ Need some help taking care of self; spend more than ½ day in bed or chair
- ○ Cannot take care of self at all and spend all of my time in bed or chair

MEDICAL HISTORY

Have you ever had a heart attack?	O No	O Yes
Have you ever been treated for heart failure (you may have been short of breath and the doctor may have told you that you had fluid in your lungs or that your heart was not pumping well)?	O No	O Yes
Have you ever had an operation to unclog or bypass the arteries in your legs?	O No	O Yes
Have you had a stroke, cerebrovascular accident, blood clot or bleeding in the brain, or transient ischemic attack (TIA)?	O No	O Yes
If yes, do you have difficulty moving an arm or leg as a result of a stroke or cerebrovascular accident?	O No	O Yes
Do you have asthma, emphysema, chronic bronchitis, or chronic obstructive lung disease?	O No	O Yes
If yes, do you take medicine for your condition (either on a regular basis or just for flare-ups)?	O No	O Yes
Do you have stomach ulcers or peptic ulcer disease?	O No	O Yes
If yes, was this condition diagnosed by endoscopy (where a doctor looks into your stomach through a scope) or an upper GI or barium swallow study (where you swallow chalky dye and then x-rays are taken)?	O No	O Yes
Do you have diabetes or high blood sugar?	O No	O Yes
If yes, answer all of the following four questions:		
is it treated by modifying your diet?	O No	O Yes
is it treated by medications taken by mouth?	O No	O Yes
is it treated by insulin injections?	O No	O Yes
has your diabetes caused problems with your kidneys or problems with your eyes (treated by an opthalmologist)?	O No	O Yes

MEDICAL HISTORY (continued)

Have you ever had problems with your kidneys?	O No	O Yes
If yes, have you had poor kidney function with blood tests showing:		
high creatinine levels?	O No	O Yes
have you used hemodialysis or peritoneal dialysis?	O No	O Yes
have you received a kidney transplant?	O No	O Yes
Do you have rheumatoid arthritis?	O No	O Yes
If yes, do you take medications for it regularly?	O No	O Yes
Do you have lupus (systemic lupus erythematosus) or polymyalgia rheumatica?	O No	O Yes
Do you have any of the following conditions?		
Alzheimer's Disease or another form of dementia?	O No	O Yes
Cirrhosis or serious liver damage?	O No	O Yes
AIDS? (This question is optional.)	O No	O Yes
Leukemia or polycythemia vera?	O No	O Yes
Lymphoma?	O No	O Yes
Cancer (other than skin cancer, leukemia or lymphoma)?	O No	O Yes
If yes, has the cancer spread or metastasized to other parts of your body?	O No	O Yes
Have you received a heart, lung, liver or pancreas transplant?	O No	O Yes
Do you have any other autoimmune disease (besides lupus or polymyalgia rheumatica)? **If so, what kind?**_____	O No	O Yes
Do you have a history of immunodeficiency?	O No	O Yes
If yes, please elaborate_____		
Have you ever tested positive for HIV? (This question is optional)	O No	O Yes
If yes, have you ever received antiviral treatment?	O No	O Yes
Have you ever tested positive for hepatitis B?	O No	O Yes
If yes, have you ever received treatment?	O No	O Yes
Have you ever tested positive for hepatitis C?	O No	O Yes
If yes, have you ever received treatment?	O No	O Yes
Were you told that you have Heliobacter pylori (either during an endoscopy or by blood test)?	O No	O Yes
Do you have either Crohn's disease or ulcerative colitis?	O No	O Yes
Do you have celiac sprue?	O No	O Yes

PATIENT BACKGROUND INFORMATION

For research purposes only, we would like to know the following information.

Are you of Spanish / Hispanic origin?

○ No
○ Yes
○ Not sure

What best describes your racial background? Select ALL that apply.

Definitions from Federal Government's Office of Management and Budget

☐	American Indian or Alaskan Native	Have origins in any of the original peoples of North and South America (including Central America) and maintain tribal affiliation or community attachment
☐	Asian	Have origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent including for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand and Vietnam
☐	Black or African American	Have origins in any of the original peoples of Africa: includes Haitian
☐	Native Hawaiian or Other Pacific Islander	Have origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Island
☐	White	Have origins in any of the original peoples of Europe, the Middle East or North Africa

What best describes your educational status?

Select **ONE**

○ Some grade school
○ Some high school
○ High school graduate
○ Vocational or technical school beyond high school
○ Some college or associate's degree
○ College
○ Graduate or professional school
○ Other (Please specify _____)

What is your current employment status?

Select **ONE**

○ Disabled
○ Employed 32 hours or more per week
○ Employed less than 32 hours per week
○ Full time student
○ Homemaker
○ On medical leave
○ Part time student
○ Part time student and also employed less than 32 hours per week
○ Retired
○ Unemployed and/or seeking work
○ Other (Please specify _____)

PATIENT BACKGROUND INFORMATION(continued)

What is your current weight? ☐ pounds

What was your weight 6 months ago? ☐ pounds

What is your current height? ☐ feet ☐ inches

PAST CANCER HISTORY

In the past, have you ever had any of the following types of cancer listed below? Check ALL that apply (do not include basal cell skin cancer).

For each of the cancers checked, what type of treatment did you receive for it? Check ALL that apply.

Cancer diagnosis	Approximate diagnosis date	Chemotherapy	Surgery	Radiation Therapy	Hormone Therapy
☐ Bladder		☐	☐	☐	☐
☐ Brain		☐	☐	☐	☐
☐ Breast		☐	☐	☐	☐
☐ Colon		☐	☐	☐	☐
☐ Colorectal		☐	☐	☐	☐
☐ Hodgkin's lymphoma		☐	☐	☐	☐
☐ Invasive cervical		☐	☐	☐	☐
☐ Kidney		☐	☐	☐	☐
☐ Leukemia		☐	☐	☐	☐
☐ Liver		☐	☐	☐	☐
☐ Lung		☐	☐	☐	☐
☐ Lymphoma, type unknown		☐	☐	☐	☐
☐ Melanoma		☐	☐	☐	☐
☐ Mouth/throat		☐	☐	☐	☐
☐ Multiple Myeloma		☐	☐	☐	☐
☐ Non-hodgkin's lymphoma		☐	☐	☐	☐
☐ Ovarian		☐	☐	☐	☐
☐ Pancreatic		☐	☐	☐	☐
☐ Prostate		☐	☐	☐	☐
☐ Rectal		☐	☐	☐	☐
☐ Stomach		☐	☐	☐	☐
☐ Thyroid		☐	☐	☐	☐
☐ Uterine/Endometrial		☐	☐	☐	☐
☐ Other (Please Specify_____)		☐	☐	☐	☐

TOBACCO HISTORY

Have you ever smoked more than 100 cigarettes in your lifetime? O No O Yes

If Yes…

How old were you when you started smoking cigarettes? ☐☐ Age started

Throughout the time that you smoked cigarettes, what is the average number of cigarettes per day that you smoked? ☐☐☐ Number cigarettes per day

Do you currently smoke cigarettes (within the past month)? O No O Yes

If No…

What was the date that you stopped smoking cigarettes? ☐☐ /☐☐ /☐☐☐☐

SOCIAL HISTORY

Have you ever or do you currently drink alcohol?

Select **ONE**
- ○ No, never
- ○ Yes, but only in the past
- ○ Yes, currently

How many alcoholic beverages (beer, wine, mixed drinks, etc) do you consume weekly?

Select **ONE**
- ○ None
- ○ Less than 1 drink per week
- ○ 1- 4 drinks per week
- ○ 5-9 drinks per week
- ○ 10-19 drinks per week
- ○ More than 19 drinks per week

If your alcohol intake in the past was different from now, how many alcoholic beverages (beer, wine, mixed drinks, etc) did you consume weekly?

Select **ONE**
- ○ None
- ○ Less than 1 drink per week
- ○ 1- 4 drinks per week
- ○ 5-9 drinks per week
- ○ 10-19 drinks per week
- ○ More than 19 drinks per week

HOUSEHOLD MEMBERS

Please list the age of all the people who live with you and their relationship to you. Please include all people who share your household, whether they are blood relatives or not (see key below). If there is more than one person with a particular relationship to you, please assign each a number (e.g. Son 1 Son 2).

☐ **No household members**

Household Member	Age

Key: Household Members

Aunt	Grandson	Personal Care Assistant
Brother	Housekeeping Staff	Roommate
Cousin	Husband	Significant Other
Daughter	Mother	Sister
Father	Nanny	Son
Granddaughter	Nephew	Tenant
Grandfather	Niece	Uncle
Grandmother	Nurse	Wife

Other (Please Specify _____)

FAMILY HISTORY

Please include only blood relatives, both living and deceased.

How many sisters do you have?	
How many brothers?	
How many daughters?	
How many sons?	

FAMILY HISTORY (continued)

Do you have any blood related relatives who have been diagnosed with cancer? If yes, please use the chart below to indicate their relationship to you, the type of cancer they have, their age at diagnosis, and whether or not they are still living.

NOTE: If you have more than one relative of a particular type who has been diagnosed with cancer, please assign each a number in the relative column. E.g. Sister 1 and Sister 2

*For example if your mother was diagnosed with stomach cancer at age 63 and she is still living, you would print Mother in the Relative column, Stomach in the Cancer Type column, 63 in the Age at Diagnosis column and check off Yes in the Alive column. If you only know that she was diagnosed sometime in her 60's, you would print 60 in the Age at Diagnosis column and check off Yes in the Age Estimated to the Decade Column.

Blood Relative	Maternal/ Paternal/Both	Cancer Type	Age at Diagnosis	Is Age Estimated to the decade?	Alive?
Sample Mother	M	Stomach Cancer	63	☐ Yes	○ Yes ○ No ○ Not Sure

*** Relatives**

Aunt
Brother
Cousin
Daughter
Father
Grandfather
Grandmother
Mother
Sister
Son
Uncle
Other (Please specify_____)

**** Cancer Types**

Bladder
Brain
Breast
Colon
Colorectal
Hodgkin's lymphoma
Invasive Cervical
Kidney
Leukemia
Liver
Lung
Lymphoma, type unknown
Melanoma
Mouth/throat
Multiple Myeloma
Non-Hodgkin's Lymphoma
Ovarian
Pancreatic
Prostate
Rectal
Stomach
Thyroid
Uterine/Endometrial
Unknown
Other (Please specify_____)

In order to facilitate correspondence with you and your physicians please confirm the following information and correct if necessary.

Patient:

Name: _____

Address: _____

_____

Home Phone: ( )_____

Work Phone: ( )_____

Marital Status: _____

Name: _____

Address: _____

_____

Home Phone: (_____)_____

Work Phone: (_____)_____

Marital Status: _____

Referring physician:

Name: _____

Address: _____

_____

Phone: ( )_____

Name: _____

Address: _____

_____

Phone: (_____)_____

Primary Care physician:

Name: _____

Address: _____

_____

Phone: ( )_____

Name: _____

Address: _____

_____

Phone: (_____)_____

Q.U.A.L.M.S.-1© Dana-Farber Cancer Institute, Boston, MA

The Quality of Life in Myelodysplasia Scale

Patients often have different experiences over the course of their illness; however, please limit your responses to your experience **over the past week only**. The information you provide will remain strictly confidential.

	During the past week, how often…	Never	Rarely	Sometimes	Often	Always
1	…did you feel as though there was a lack of clear information about your disease?	☐	☐	☐	☐	☐
2	…have you felt there was limited emotional support available for patients with MDS beyond their families?	☐	☐	☐	☐	☐
3	…did you feel as though you couldn't do anything about your disease?	☐	☐	☐	☐	☐
4	…did you feel the course of your disease was unpredictable?	☐	☐	☐	☐	☐
5	…did you have difficulty explaining MDS to your friends or family?	☐	☐	☐	☐	☐
6	…did you have trouble concentrating?	☐	☐	☐	☐	☐
7	…have you considered changing long-term plans due to health concerns?	☐	☐	☐	☐	☐
8	…have you experienced shortness of breath?	☐	☐	☐	☐	☐
9	…did low energy levels cause you to change your schedule?	☐	☐	☐	☐	☐
10	…did you feel as though your life was organized around medical appointments?	☐	☐	☐	☐	☐
11	…have you felt a sense of hopelessness?	☐	☐	☐	☐	☐
12	…have you been worried about getting an infection?	☐	☐	☐	☐	☐
13	…have you had sufficient energy for routine tasks?	☐	☐	☐	☐	☐
14	…were you afraid of dying?	☐	☐	☐	☐	☐
15	…did you feel angry about your diagnosis?	☐	☐	☐	☐	☐
16	…were you worried about bleeding?	☐	☐	☐	☐	☐
17	…did you feel a sense of gratitude for a part of life that you took for granted before?	☐	☐	☐	☐	☐
18	…did you feel nauseated?	☐	☐	☐	☐	☐
19	…did you worry about your MDS progressing or developing into leukemia?	☐	☐	☐	☐	☐
20	…did you take into account that you might be fatigued when planning your activities?	☐	☐	☐	☐	☐

Please continue on to the next page →

For the following questions, please again mark the answer choice that best represents your experiences and feelings **over the past week**. The information you provide will remain strictly confidential.

	During the past week, how often…	Never	Rarely	Sometimes	Often	Always
21	…were you concerned that your MDS caused a financial burden for you or your family?	☐	☐	☐	☐	☐
22	…did you feel your family relationships were strained by your disease?	☐	☐	☐	☐	☐
23	…have you felt weak?	☐	☐	☐	☐	☐
24	…have you been too tired to take on the responsibilities you used to have?	☐	☐	☐	☐	☐
25	…did you worry about becoming a burden to your friends or family?	☐	☐	☐	☐	☐
26	…were you unable to participate in activities you are used to doing?	☐	☐	☐	☐	☐
27	…have you felt anxious about test or lab results?	☐	☐	☐	☐	☐
28	…did you avoid crowds because of fear of getting an infection?	☐	☐	☐	☐	☐
29	…did you find yourself grateful for tomorrow?	☐	☐	☐	☐	☐
30	…did you feel you were able to find quality information about MDS treatments?	☐	☐	☐	☐	☐
31	…were you concerned about bruising?	☐	☐	☐	☐	☐
32	…did you feel as though there were a lack of concrete answers about what will happen with your MDS?	☐	☐	☐	☐	☐
33	…did you experience a change in bowel habits?	☐	☐	☐	☐	☐

For the following questions, **you may select "not applicable"** if the question does not apply to you.

	During the past week, how often…	Never	Rarely	Sometimes	Often	Always
34	…were you afraid of losing your job? (**check here** ☐ if not applicable because you are unemployed/retired)	☐	☐	☐	☐	☐
35	…did you feel too tired to drive? (**check here** ☐ if not applicable because you do not drive)	☐	☐	☐	☐	☐
36	…were you afraid to have sex due to your blood counts? (**check here** ☐ if not applicable because you are not currently sexually active)	☐	☐	☐	☐	☐
37	…were you afraid that your MDS treatment would stop working? (**check here** ☐ if not applicable because you are not currently being treated)	☐	☐	☐	☐	☐
38	…have you been too tired to take care of a family member or loved one? (**check here** ☐ if not applicable because you are not providing such care)	☐	☐	☐	☐	☐

Thank you for completing the QUALMS-1.