



Secondary Cancers after Transplant

Celebrating a Second Chance at Life
Survivorship Symposium

April 30 - May 6, 2022



Madhuri Vusirikala MD
UT Southwestern Simmons
Comprehensive Cancer Center

Secondary Cancers After Stem Cell Transplant

Madhuri Vusirikala, M.D.
Professor of Medicine
University of Texas at Southwestern Medical Center
Dallas, Texas

BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium

Learning Objectives

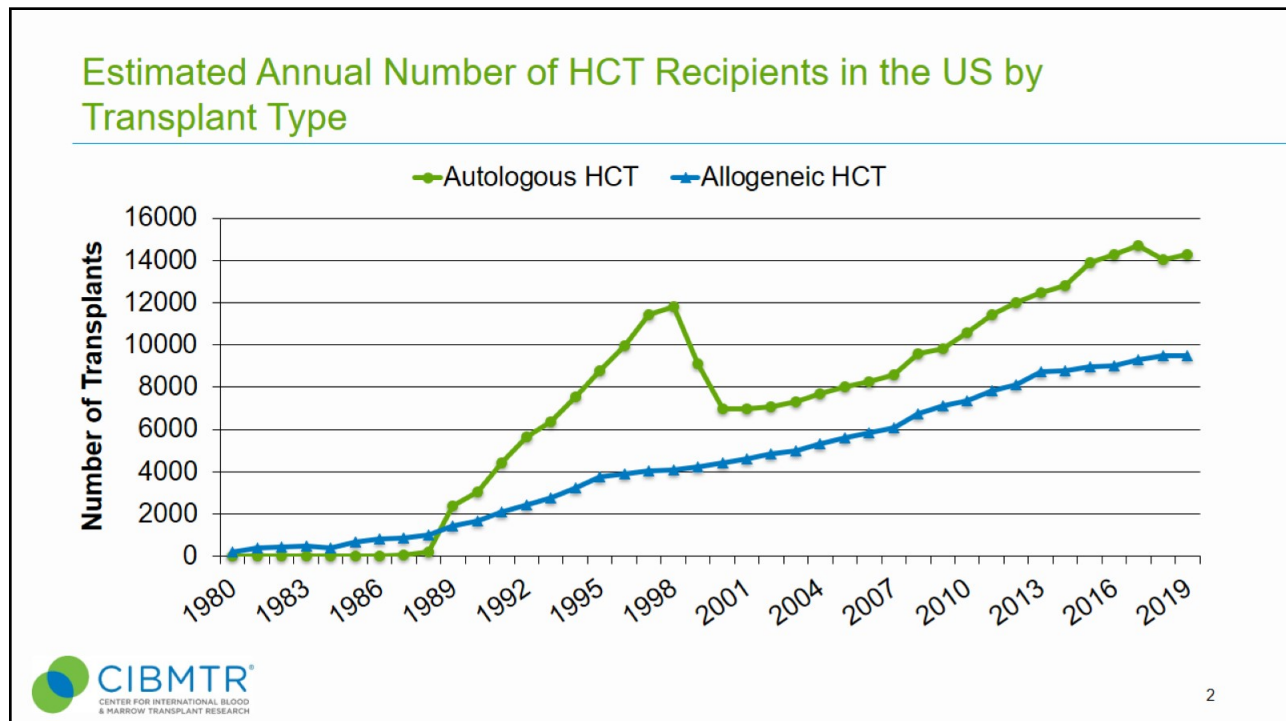
- Potential secondary cancers that can occur following an allogeneic transplant
- Potential secondary cancers that can occur following an autologous transplant
- Risk factors for developing a secondary cancer after a stem cell transplant
- Strategies to mitigate the risk of developing a secondary cancer after stem cell transplant
- Recommendations for screening for secondary cancers

BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium

Relevant Topics

- What are secondary cancers?
- Different types of secondary cancers
- Risk factors leading to development of secondary cancers
- How can we reduce the risks of developing these cancers?
- Prevention strategies
- Screening procedures for early detection

BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium



Secondary Cancers

- Cancer that occurs after the stem cell transplant, different from the original cancer or condition that the transplant was done for
- Typically occur several years (>5 years) after the stem cell transplant
- Rare but responsible for 5-10% of late deaths after transplant
- Types:
 - Solid tumors
 - Cancers involving the bone marrow
 - Post transplant lymphoproliferative disorders

Contributing Factors

Patient-Related

- Age
- Family history
- Genetic (Fanconi)
- Infections
- Social history
 - Smoking
 - Alcohol
 - Sun exposure

Transplant-Related

- Radiation exposure
- Chemotherapy
- Underlying cancer (lymphoma)
- Duration of immune suppression
- Infections related to transplant

BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium

Transplant Related Factors

- Chemotherapy and radiation given for initial treatment of the disease
- Chemotherapy and radiation given for the transplant
- Maintenance therapy used after transplant
- Infections: Epstein-Barr Virus (EBV), Human Papilloma Virus (HPV)
- Graft-versus-Host Disease (GvHD)-related medications (immunosuppressive drugs)
- GvHD by itself
- Condition for which transplant performed (Lymphoma, CLL, Fanconi anemia)

BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium

Secondary Cancers after Autologous Transplants

(transplant using patient's own stem cells)

BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium

Typical indications for autologous stem cell transplantation

- Multiple myeloma
- Lymphomas
- Germ Cell tumors
- Autoimmune disorders
 - Lupus
 - Rheumatoid arthritis
 - Multiple Sclerosis

BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium

Factors contributing to risk of secondary cancers after autologous transplant

- Age of the patient
- Type of cancer (patients with lymphoma and CLL are at a higher risk for secondary cancers)
- Treatments given prior to transplant (chemotherapy and radiation)
- Post transplant maintenance therapies

- Incidence of all secondary cancers
 - 5 years after autologous stem cell transplant, is ~ 4.3%
 - 15 years after autologous stem cell transplant, is ~ 8-15%

BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium

Does autologous transplant, by itself, increase the risk for second cancers?

- Several clinical trials in Multiple myeloma and Lymphomas
- Risk of increased second cancers is due to the treatments given prior to transplant rather than transplant itself.
- In general, patients with Lymphoma are at higher risk of developing second cancers

BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium

Risk of second cancers in patients with Hodgkin Disease

- 1700 patients with Hodgkin Disease analyzed
- 1500 patients received conventional treatment alone (no transplant)
- 200 patients underwent autologous transplant

- Overall risk of developing second cancer after 15 years ~9%
- No difference in second cancers between two groups
- Only risk factor noted to increase risk of second cancer was age >35

BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium

Forrest DL et al. J Clin Oncol. 2005 Nov
1;23(31):7994-8002

Risk of second cancers in Myeloma patients +/- Lenalidomide

- Lenalidomide DOES improve overall survival and progression when given as maintenance
- Lenalidomide exposure increases risk of secondary cancers irrespective of transplant
- Large analysis of 3200 myeloma patients
 - 5-year risk of second cancers was 6.9% with lenalidomide versus 4.8% without
 - Risk was higher if lenalidomide was given with melphalan

BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium

Palumbo A et al. Lancet Oncol. 2014;15:333-342

Types of second cancers after autologous transplant – Solid Tumors

- Skin cancers
- Cancers of oral cavity
- Brain
- Bone
- Thyroid
- Breast and uterine cervix

Risk continues to increase 15 years and beyond

BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium

Types of second cancers after autologous transplant – MDS/AML

- MDS=Myelodysplastic Syndrome; AML=Acute Myeloid Leukemia
- Due to damage to bone marrow from chemo-radiation given for treatment of the cancer **before** stem cell collection and transplant
- Worse prognosis than de-novo MDS/AML
- Best treatment is allogeneic transplant
- Risk continues to increase as time goes by
 - 1% in 30 months
 - 11.7% in 6 years
 - continues to rise for as long as 12–15 years after autologous stem cell transplant

BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium

Secondary Cancers after Allogeneic Transplants (transplant using donor cells)

BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium

Risk factors for second cancers after allogeneic transplants

- Use of total body radiation
- Immune-suppression drugs
- Graft versus host disease
- Advanced age
- Infections
- Underlying genetic predisposition
- Intensity of the preparative regimen used for the transplant (?)

BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium

Types of second cancers after allogeneic transplant – Solid Tumors, MDS/AML

- Solid tumors
 - 1.2 to 1.6% at 5 years post-transplantation
 - 2.2 to 6.1% at 10 years post-transplantation
 - 3.8 to 14.9% at 15 years post-transplantation
- MDS/AML
 - Rare after allogeneic transplants

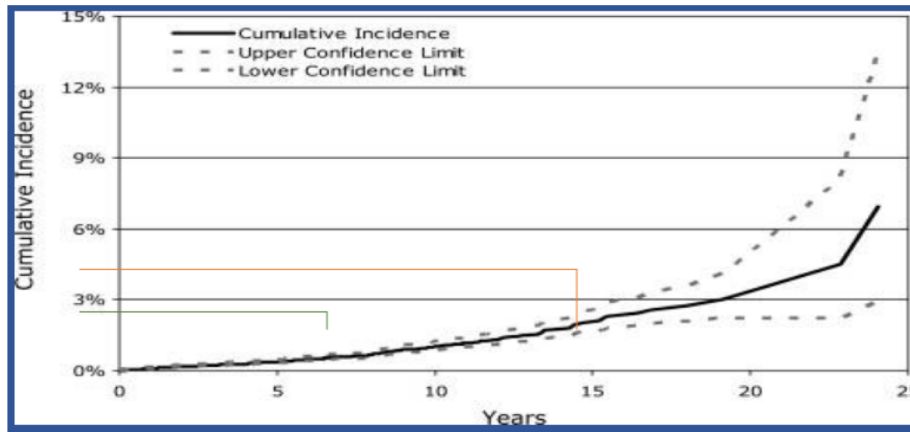
BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium

Types of second cancers after allogeneic transplant – PTLD

- PTLD = Post transplant lymphoproliferative disorders
- Most common second cancer in the first year of transplant
- Incidence ranges from 0.2 to 11% depending on type of donor, use of strong immune suppressing chemotherapy, T-cell depletion
- Due to Epstein Barr Virus (EBV) infection and strong immune-suppression
- Typically, donor derived

BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium

Incidence of second solid cancers after allogeneic transplant



BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium

Rizzo JD et al. Blood. 2009;113(5):1175–83

Donor-cell derived Second Cancers

- Post transplant lymphoproliferative disorder (PTLD)
- Late occurring lymphoma
 - Different from PTLD (not associated with Epstein-Barr Virus)
 - Occurs in patients with severe chronic GvHD
 - Relatively good prognosis
- Donor cell leukemia
 - Very rare entity, occurs late in the course of transplant (>2 years)
 - No clear cause
 - Presumed to be due to already “damaged” donor stem cells that developed additional mutations due to transplant process (medications, infections)

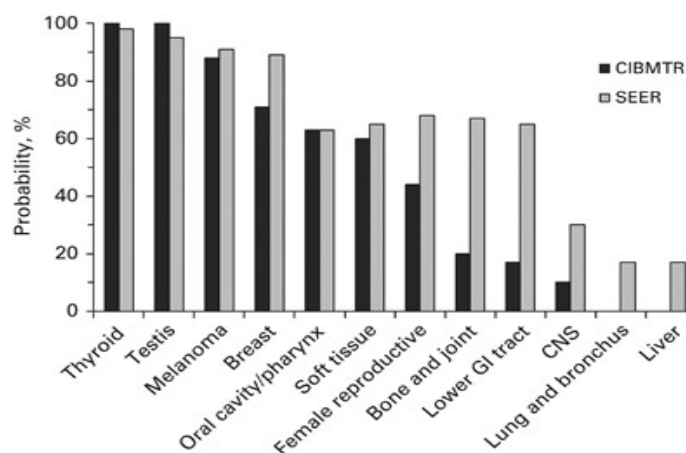
BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium

Outcomes of Secondary Cancers

- Secondary cancers account for 5-10% of deaths among transplant recipients who survive 2 years or longer
- Outcome depends on several factors
 - Type of cancer
 - Age of the patient
 - Fitness level of the patient
 - Stage of the cancer at diagnosis
 - Availability of effective treatments

BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium

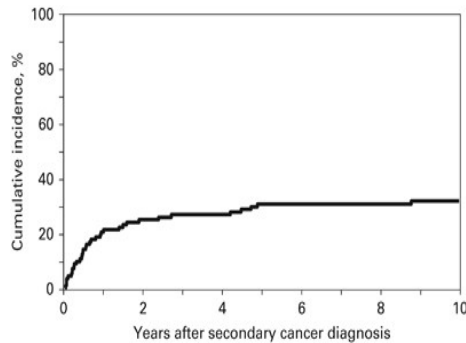
Outcomes of Secondary Cancers



Observational comparison of the probability of 5-year overall survival for secondary and *de novo* solid cancers (Surveillance, Epidemiology and End Results (SEER) data)

BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium

Outcomes of Secondary Cancers



Cumulative incidence of death because of secondary solid cancer.

- 10- and 15-year overall survival estimates of 46% and 40%, respectively
- Survival particularly poor for cancers of CNS (central nervous system), liver and lung
- Better outcomes noted for male reproductive, thyroid, breast and skin (melanoma) cancers

Prevention Strategies

- Reduce risk factors
 - Smoking cessation
 - Sun protection
 - Reduce infection risk (HPV, Hepatitis C)
 - Diet and exercise
- Regular Screening
 - Recommended screening procedures
 - Self examination (skin, breast, genitalia)
 - Early reporting of symptoms (cough, bleeding, pain, rashes, weight loss)

Prevention Strategies – Treatment Changes

- Avoid total body irradiation
- Reduce exposure to certain chemotherapies
- Donor choices (younger versus older)
- Thorough screening bone marrows for underlying mutations prior to autologous transplant

BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium

Cancer Screening Recommendations

- CIBMTR and EBMT working group recommendations
([Secondary solid cancer screening following hematopoietic cell transplantation - PubMed \(nih.gov\)](#))
- CIBMTR guidelines for long term follow up
([After Transplant Guidelines for Patients \(bethematch.org\)](#))

BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium

Specific Cancers

BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium

Skin Cancer

- Most common secondary cancer after stem cell transplant
- Squamous cell cancer, basal cell carcinoma, melanoma
- Cumulative incidence at 20 years:
 - Basal cell ~6.5%
 - Squamous cell ~3.4%
- Important:
 - Regular self exam
 - Sun protection
 - Dermatology visits

BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium

Breast Cancer

- Female survivors of SCT are at increased risk for developing breast cancer,
- Risk Factors
 - Younger age at diagnosis
 - Increased time since transplantation
 - Use of TBI
- Screening
 - Self breast exams
 - Annual mammogram starting age 40 (earlier age if radiation received ~25)

BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium

Head and Neck Cancers

- Oropharyngeal cancer most common
- Risk factors:
 - Increased in patients with chronic GvHD and long-term immunosuppressive drugs (greater than 2 years)
 - Radiation another risk factor
 - Risk higher in males
- Avoid chewing tobacco
- Routine dental visits

BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium

Gastro-intestinal Cancer

- Esophageal
 - Risk increased in patients with extensive chronic GvHD and long-term immunosuppression (>2 years)
 - Higher risk in patients with Fanconi Anemia
- Colorectal
 - Early detection important
 - Routine colonoscopy (start age 50 for regular risk, 40 if high risk)
 - Stool testing if regular risk

BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium

Cervical Cancer

- Human Papilloma Virus (HPV) important risk factor
- Routine gynecologic exams
- HPV vaccinations

BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium

Lung Cancer

- Tobacco use pre and post transplant highest risk
- TBI not considered major risk factor
- One study using busulfan and cyclophosphamide showed higher risk of lung cancer in the survivors
- Smoking Cessation of utmost importance!!!
- Screening recommendations not very clear

BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium

Long Term Follow Up and Survivorship

- Routine transplant and disease follow up
- Revaccinations for preventable infections
- Cancer screening
 - Mammograms
 - Pap smears
 - Dental exams
 - Colonoscopy
 - Prostate exam/PSA
 - Routine dermatology care

BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium

Summary

- Secondary cancers after stem cell transplant are a rare but a well-defined complication
- Solid tumors and PTLN more common after allogeneic transplants
- Bone marrow cancers (MDS and AML) more common after autologous transplants
- Risk continues to increase over the years after transplant
- Prevention strategies and routine screening are vital to reduce risk of fatal outcomes

BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium

BMT *infonet.org*
BLOOD & MARROW TRANSPLANT INFORMATION NETWORK
SURVIVORSHIP SYMPOSIUM

Questions?



Madhuri Vusirikala MD

Celebrating a Second Chance at Life Survivorship Symposium 2022

bmtinfonet.org ♦ help@bmtinfonet.org ♦ 847-433-3313



Let Us Know How BMT InfoNet Can Help YOU!



Visit our website: bmtinfonet.org

Email us: help@bmtinfonet.org

Give us call: 888-597-7674

We're here to help every step of the way!

BMT InfoNet Celebrating a Second Chance at Life Survivorship Symposium