

New Cancers after Transplant: Steps You Can Take to Reduce Your Risk

**Celebrating a Second Chance at Life
Survivorship Symposium**

April 27 – May 3, 2024



Saro Armenian DO, MPH

Director, Center for Survivorship and
Outcomes, Hematologic Malignancies Research
Institute, City of Hope Cancer Center

New Cancers after Transplant: Steps You Can Take to Reduce Your Risk

Saro Armenian, DO, MPH

Barron Hilton Chair and Professor of Pediatrics

Director, Division of Outcomes Research

Director, Center for Survivorship and Outcomes

Hematologic Malignancies and Stem Cell Transplantation Institute

Program Co-Leader, Cancer Control and Population Sciences

City of Hope Comprehensive Cancer Center

Following this workshop attendees will understand:

1. Potential secondary cancers that can occur following an allogeneic HCT
2. Potential secondary cancers that can occur following an autologous HCT
3. Incidence and risk of developing a secondary cancer after HCT
4. Medical tests and exams needed, and timing of same, to reduce the risk of developing a secondary cancer
5. Lifestyle modifications that can reduce the risk of a new cancer after HCT

Risk Factors Associated with Cancer Development

- Genetic predisposition
 - Family history
 - Syndromes (Telomere shortening)
- Aging
- Carcinogens
 - Smoking
 - Alcohol
 - Sun exposure
 - Viruses
- Cancer Treatment exposures
 - Chemotherapy
 - Radiation
 - Prolonged immunosuppression
- Immune deficiency syndrome/
disorder

Risk Factors for Cancer after Transplant

- Graft versus host disease
- Medications used to treat/prevent GvHD
- Underlying disease and associated prior treatments
- Transplant-related chemotherapy or radiation
- Donor (versus own stem cells)
- Maintenance therapies after transplant
- New lifestyle risk factors and their interaction with transplant factors

Patient Scenario 1 – Allogeneic transplant

- 47 year-old male, with a history of acute lymphoblastic leukemia (ALL), underwent matched unrelated bone marrow transplantation. Is now a 3-year survivor.
- Presents to clinic with a 2-month history of a skin lesion on his forehead
- Relevant history
 - Male pattern baldness
 - Race/ethnicity: non-Hispanic white
 - Past employment: construction worker
 - Conditioning exposures: Total body irradiation (TBI), Etoposide
 - Graft versus host disease (GvHD) that resolved by 6 months after transplant
 - GvHD treatment included CellCept® for >3 months



New Cancers after Allogeneic Transplant

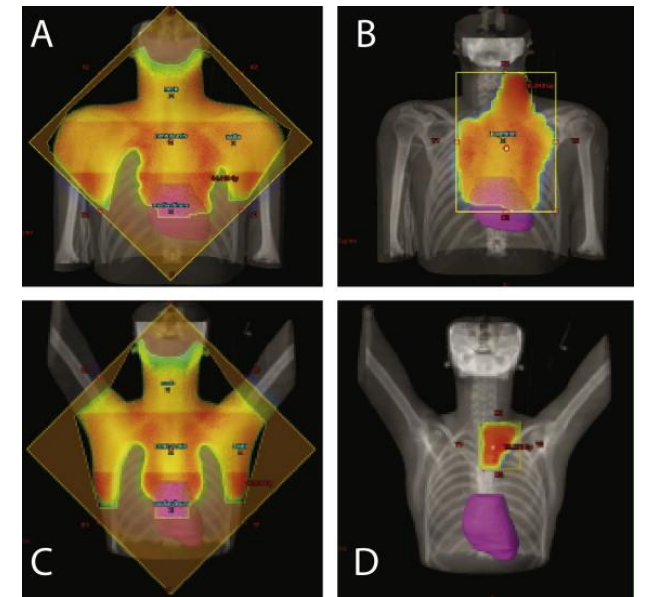
- In general, twice the expected risk of cancer compared to the general population
- The risk relative to the general population increases with time
- Highest relative risk of:
 - Skin, oral (lip, salivary gland, tongue), bone and soft tissue, liver
 - Specific to solid tumors: Lung, breast, colorectal, prostate, melanoma
- Patient and transplant-specific risk factors:
 - Older age, GvHD, radiation exposure

Lymphoproliferative Disorder after Transplant

- Presents within the first two years after transplant
- Associated with Epstein-Barr Virus activation
- Lymphoma clinical characteristics
- Associate with extent of immune suppression
 - T-cell depleted transplant
 - Severe GvHD
 - Cord blood stem cell source
- Treatment
 - Rituxan, chemotherapy

Patient Scenario 2 – Autologous Transplant

- 32 year-old female, with history of Hodgkin lymphoma (diagnosed at 17)
 - treated with ABVD x6 and chest radiation therapy
 - relapsed, and eventually underwent autologous transplant.
 - Is now a 15-year survivor.
- Feels a suspicious breast mass, and presents to her physician for work-up
- Relevant history
 - No family history of breast cancer
 - 10 pack-year smoking history
 - Original site of disease was the mediastinum
 - Received 20 Gy involved nodal chest radiotherapy (B)
 - Conditioning chemotherapy: BEAM



New Cancers after Autologous transplant- Risk Factors

- Older age
- Type cancer and associated therapies
- Post-transplant therapies, including maintenance
- Radiation therapy
 - Control of underlying disease
 - Used as part of conditioning (less often)

New Cancers after Transplant for Myeloma

- No overall increase in second cancers in myeloma patients who had a transplant compared to those who did not have a transplant.
- 50% increased risk of leukemia/lymphoma diagnoses compared to the general population
- New cancers do not impact overall mortality risk
 - *May be due to overall outcomes with baseline disease*
- Emerging concerns about Revlimid maintenance therapy

Myelodysplastic Syndrome and Acute Myeloid Leukemia

- Marrow injury from prior cancer therapies
- Increased risk after autologous transplant
- Associated treatment exposures
 - Alkylator chemotherapy (Cytosan, ifosfamide)
 - Topoisomerase inhibitors (Etoposide)
 - Radiation
- Usually develop within the first 5 years after transplant
- Outcomes generally poor, unless additional more aggressive therapies are implemented (e.g. another [allogeneic] transplant)

Outcomes after Second Cancers

- Factors that impact outcomes
 - Type of cancer
 - Age of the patients
 - Stage at diagnosis
 - Extent of localization
- Effectiveness of drug therapy
- Chronic health conditions
 - General health
 - Organ function
 - GvHD and associated immunocompromised status

Outcomes for Solid Tumors after Transplant

5-year survival rates %

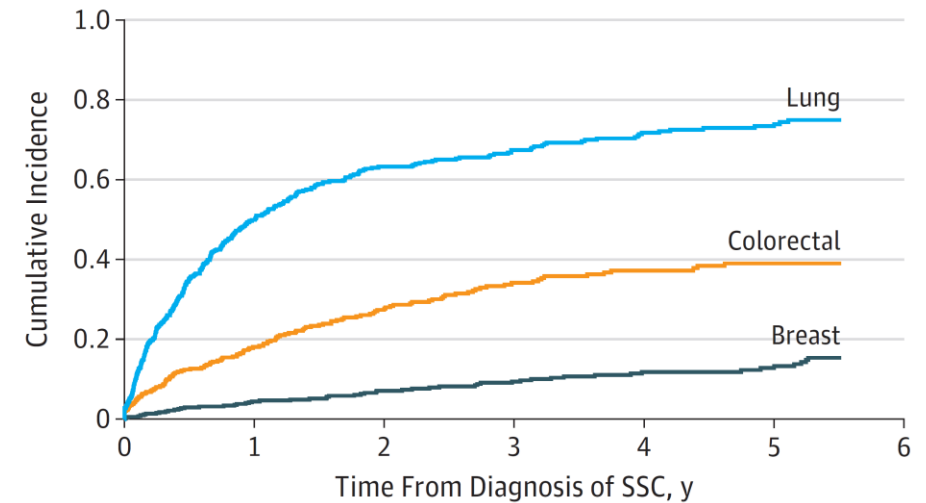
Favorable		
Thyroid		83 (76-92)
Cervix		70 (57-86)
Prostate		69 (64-75)
Breast		69 (64-74)
Melanoma		68 (62-74)

Intermediate		
Kidney		55 (47-65)
Oropharyngeal		53 (46-62)
Bladder		49 (39-62)
Ovarian		43 (32-58)
Sarcomas		42 (34-51)
Colorectal		41 (36-48)
Endometrial		40 (26-63)

JAMA Oncology February 2019 Volume 5, Number 2

Poor		
Gastric		29 (21-39)
Brain		21 (15-30)
Esophageal		21 (13-36)
Hepatobiliary		18 (11-31)
Lung		14 (11-19)
Pancreas		8 (3-18)

Incidence of deaths from second breast, colorectal, or lung cancer



What can survivors to do reduce their risk of new cancers after transplant?

- Reduce the factors that increase risk
 - Multi-hit process
 - Lifestyle modification (exercise, no smoking, low alcohol intake)
- Screening and close follow-up
 - Follow established guidelines for wellness
 - Increase surveillance that is personalized to risk/exposures
- Early detection
 - Optimize the outcomes associated with diagnosis

General Steps to Prevent Cancer

- No tobacco use
- Skin protection from UV/sun
- Maintain a healthy diet
- Keep a healthy weight and stay physically active
- Avoid risky behaviors
- Immunizations (HPV, Hepatitis vaccines)
- Empower yourself with your own and family's history



Signs and Symptoms that Could Be Concerning

- New lumps or bumps
- Unusual fatigue, fevers, sweats
- Cough, hoarseness, chest pain
- Easy bleeding/bruising
- Abdominal pain, loss of appetite, difficulty swallowing
- New blood clots
- Sores and skin infections
- Changes in neurologic status (seizures, severe headaches, etc.)





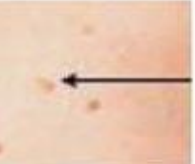




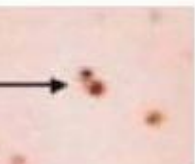
Skin Cancers

- One of the most common post-transplant cancer
- Allogeneic > autologous transplant
- Prevent with sun avoidance or sunscreen
- Regular dermatologic visits – full body examination
- Early detection is especially important to optimize outcomes
- Compared to skin cancers in non-transplant populations, tend to be more aggressive
- Important to be aware of suspicious lesions



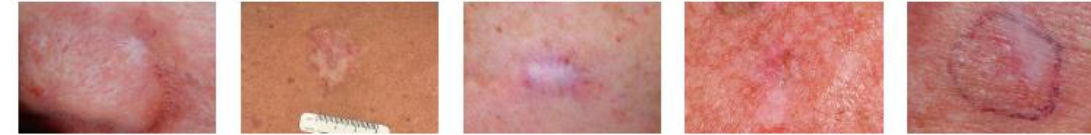
Suspicious Lesions

The ABCDEs of Detecting Melanoma

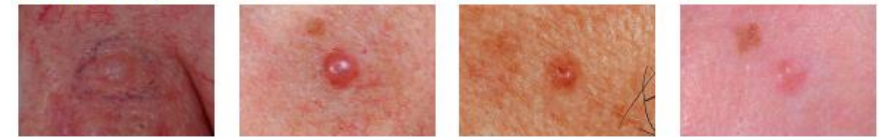
	A Asymmetry	B Border	C Color	D Diameter	E Evolving
NORMAL					
	Symmetrical	Borders Are Even	One Color	Smaller Than 1/4 Inch	Ordinary Mole
MELANOMA					
	Asymmetrical	Borders Are Uneven	Multiple Colors	Larger Than 1/4 Inch	Changing in Size, Shape and Color

Basal Cell Carcinoma

Unexplained whitish scar-like area



Shiny bump or nodule



Reddish patch or irritated area



Persistent non-healing sore



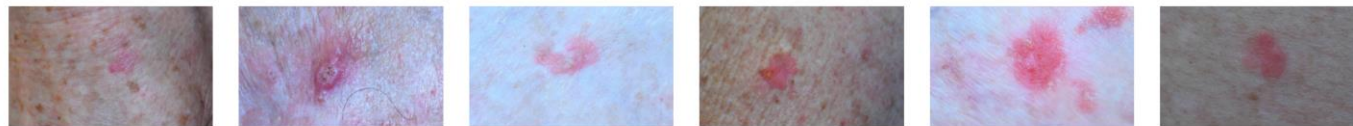
Pink growth with slightly elevated rolled border and a crusted indentation in the center



Squamous Cell Carcinoma

Images not to scale

SCCs tend to have a rough (keratotic) texture. While most grow slowly, there are variants that can grow rapidly over weeks to months.



How to check your skin

Step 1 Gather a hand mirror, hairdryer, two chairs or stools, and your partner, close friend, or family member, if you feel comfortable asking them for help. Go to a full-length mirror. Make sure you have plenty of light. The easiest time to do the check may be after a bath or shower.

Step 2



Stand in front of a full-length mirror and look at your whole face, including your nose, lips, mouth, ears, and behind the ears (use your hand mirror or ask your partner to help you see).

Step 3

Part your hair layer by layer and check your scalp in the mirror. You can use the hairdryer to help move your hair aside to see.



Step 4



Check your hands. Start with your palms and the back of your hands; look between your fingers and then under your fingernails. Take your shirt off, and continue to look down your wrists; look at the front and back of your forearms.

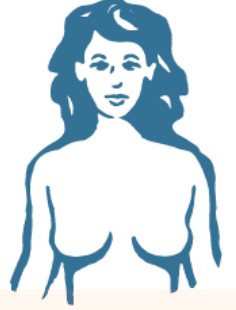
Step 5



Stand in front of the full-length mirror, bend your elbow, and check your upper arm and armpit. Now check the other side.

Step 6

Finish undressing and check your neck, chest, and the front of your upper body, including your stomach. Women should lift their breasts to see under the skin folds, and everyone should lift any folds of skin, as necessary.



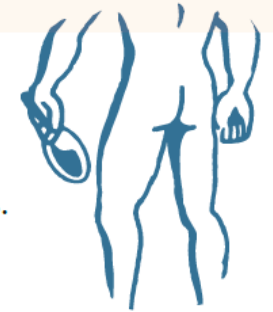
Step 7



Using a hand mirror or with help from your partner, check the back of your neck, shoulders, back of your upper arms, and back of your upper body.

Step 8

Continuing to use the hand mirror or with help from your partner, check your lower back, buttocks, and the backs of your legs.



Step 9



Lastly, sit down and prop your leg up on a stool. Examine your groin area with your hand mirror. Check the front and sides of both legs, the top of your feet, between your toes, under your toenails, your heels, and the soles of your feet.

Last step

Enjoy knowing that you did something important for yourself and your loved ones by doing your skin self-check this month.

Oral Cancer

- Associated with history of GvHD
- Regular dental visits for comprehensive screening
- Low threshold for consultation with oral surgeon if there are suspicious lesions



*Oral Surg Oral Med Oral Pathol Oral Radiol Endod
(PMID 15953918)*



Hematol Oncol Stem Cell Ther (PMID 20543542)

Breast Cancer

- Risk factors – prior chest radiation therapy or total body irradiation (TBI)
- Annual breast examination at age 25 years or 8 years after radiation therapy/TBI, whichever comes first, no later than age 40
 - Clinical breast examination
 - Mammogram
 - Breast MRI
- Average risk
 - Age 20-40 years: clinical breast exam every 1-3 years
 - Age >40 years: annual exam and mammogram



Cervical Cancer

- Major risk factor is human papilloma virus (HPV)
- HPV vaccine prevention in younger patients
- Pelvic examinations, cervical smears
- Annual Pap test and HPV DNA test

Liver Cancer

- Risk factors
 - Hepatitis B – vaccinate/treat
 - Hepatitis C – treat
 - Alcohol – limit intake
 - Cirrhosis – due to chemo/GvHD, or other associated risk factors
 - Iron overload – phlebotomy, Iron chelating medications
- Outcomes generally poor if not caught early

Colorectal Cancer

- Curable at early stage with surgery alone
- Risk factors: GI GvHD, radiation exposure
- Tests
 - Colonoscopy
 - Sigmoidoscopy
 - Stool blood and DNA testing
- First colonoscopy recommended at 45-years-old, screen up to 75-years-old
- More frequently/earlier if higher risk (pediatric patients treated with abdominal radiation therapy [RT])

Lung cancer

- Strong risk associated with smoking
- Exponentially high risk if smoker and there is a history of chest radiation exposure
- Screening with low-dose CT of chest for the following high-risk groups
 - >55y and >30 pack-year smoking history
 - $\geq 50y$ and $\geq 20y$ pack-year smoking history with another risk factor



Resources to Keep You Engaged



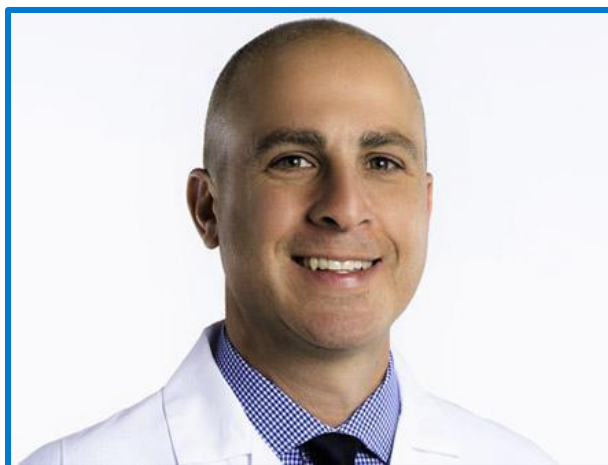
What We Encourage Survivors To Do

- Learn about the treatment you received
- Get regular check-ups focusing on the health risks related to your cancer treatment
- Work with healthcare providers to develop a long-term follow-up plan
- Make healthy choices

You are the most important member of your healthcare team!”



Questions?



Saro Armenian DO, MPH

Director, Center for Survivorship and Outcomes,
Hematologic Malignancies Research Institute,
City of Hope Cancer Center

Let Us Know How We Can Help You

Visit our website: bmtinfonet.org

Email us: help@bmtinfonet.org

Phone: 888-597-7674 or 847-433-3313

Find us on:

Facebook, facebook.com/bmtinfonet

X, twitter.com/BMTInfoNet

