



BLOOD CANCERS: MANAGING SIDE EFFECTS



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WELCOMING REMARKS

BLOOD CANCERS: MANAGING SIDE EFFECTS



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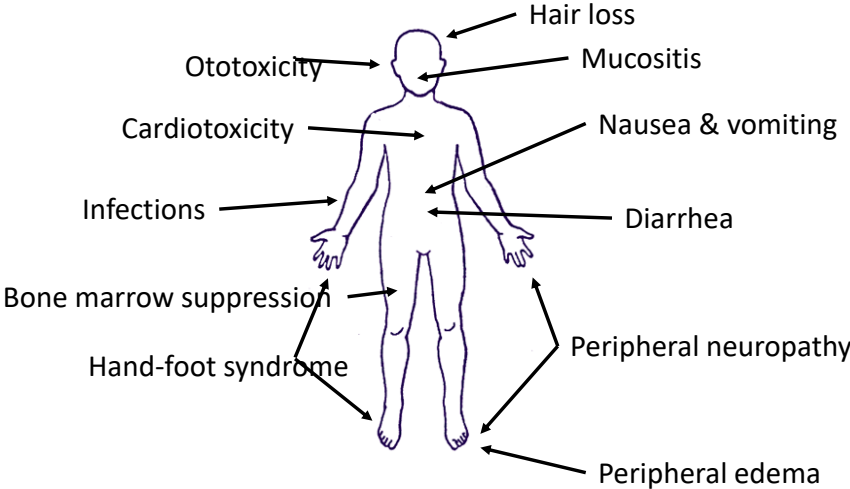
DISCLOSURE SLIDE

BLOOD CANCERS: MANAGING SIDE EFFECTS

- Peter Campbell, PharmD, BCOP, has no affiliations to disclose.



OVERVIEW OF CHEMOTHERAPY TOXICITIES



NOT ALL TREATMENTS ARE CREATED EQUALLY

Chemotherapy

Broadly kill all cells undergoing replication

Tyrosine Kinase Inhibitors

Inhibit specific receptors or enzymatic processes

Immunotherapy

Target specific malignant cells in the body

Unintended and undesired side effects



DRUG CLASSES AND ASSOCIATED SIDE EFFECTS

Anthracyclines	Vinca Alkaloids	Alkylating Agents	Antimetabolites	Topoisomerase Inhibitors	Hypomethylating Agents	Platinums
Doxorubicin Daunorubicin Idarubicin Mitoxantrone	Vincristine Vinblastine	Cyclophosphamide Ifosfamide Thiotepa Busulfan	Cytarabine Methotrexate Mercaptopurine Thioguanine Cladribine Fludarabine	Etoposide	Azacitidine Decitabine	Carboplatin Cisplatin
Cardiac effects Myelosuppression Hair loss Urine discoloration	Constipation Peripheral neuropathy	Myelosuppression Fatigue Bladder toxicity Neurotoxicity	Myelosuppression Fatigue Mucositis	Fatigue Mucositis Diarrhea Nausea/vomiting Myelosuppression	Myelosuppression Fatigue Injection site reactions Muscle pain	Myelosuppression Cardiac effects Hearing loss Mucositis

*List of drugs and side effects is not all-inclusive

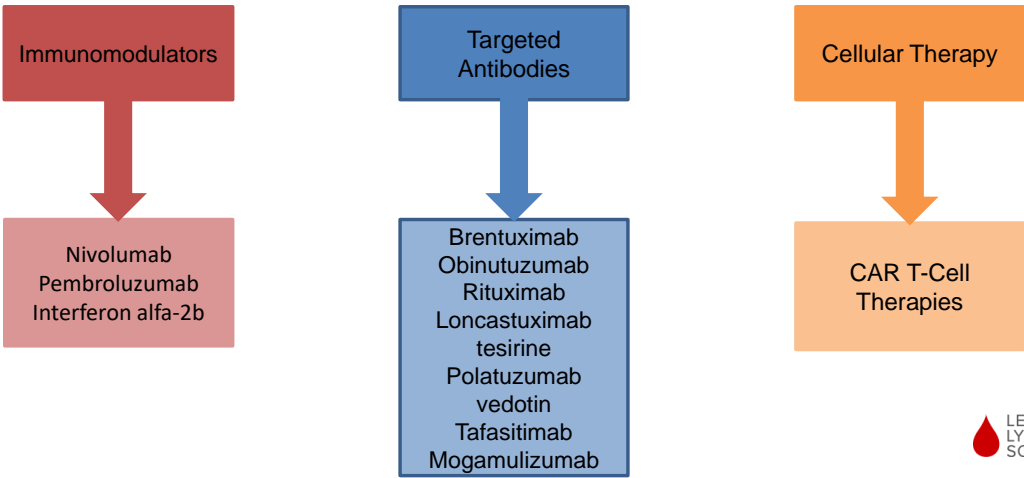


DRUG CLASSES AND ASSOCIATED SIDE EFFECTS

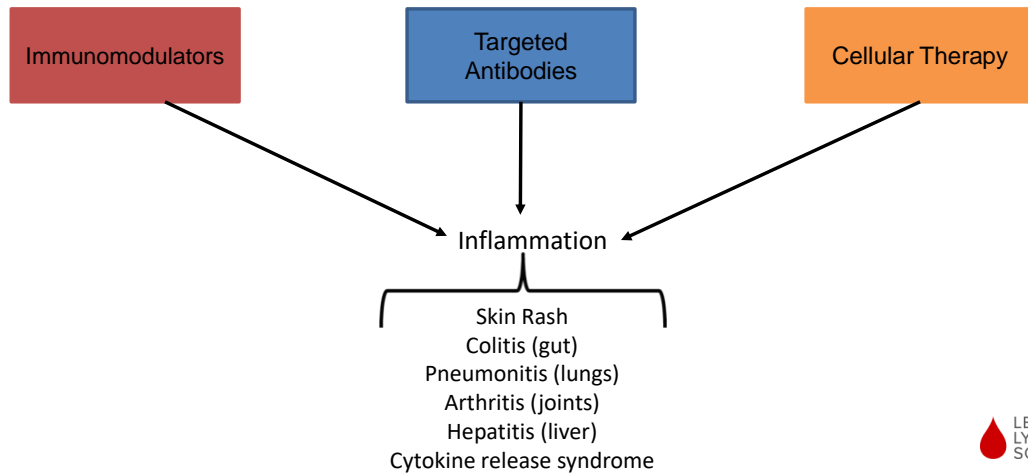
Monoclonal Antibodies	Enzymes	Tyrosine Kinase Inhibitors	BCL2 Inhibitors	IDH1/2 Inhibitors
Rituximab Obinutuzumab Polatuzumab Daratumumab	Asparaginase Pegaspargase	Each agent carries its own risks and side effects, for which patients should consult their care team for a detailed discussion	Venetoclax	Ivosidenib Enasidenib
Infusion reactions Fatigue Joint/muscle pain Infections	Liver test abnormalities Allergic reactions Hyperglycemia Pancreatitis		Myelosuppression Electrolyte abnormalities	Myelosuppression Fluid retention Fatigue Muscle pain Electrolyte abnormalities

*List of drugs and side effects is not all-inclusive

IMMUNOTHERAPY



IMMUNOTHERAPY SIDE EFFECTS



COMBINATION CHEMO/IMMUNOTHERAPY

While we know the side effects of medications, combinations can present new risks and challenges

- Some side effects are exacerbated when used in combination with other agents
- Many studies are small in scale and new information is discovered from “real-world” usage
- Just because we haven’t seen it doesn’t mean it can’t happen

A 5% chance of a side effect becomes 100% if it happens to you

- Know the toxicities associated with chemotherapy agents, but don’t go fishing

NAUSEA AND VOMITING

Nausea and vomiting can vary based on the drug and/or regimen that you are receiving

- Dose, schedule, and type of treatment change incidence of nausea and vomiting

Prevention is the best medicine

- Nausea and vomiting is very difficult to manage or stop once the symptoms are felt
- All chemotherapy regimens should include the appropriate antiemetics

Learn and understand your body and your triggers

- Certain sights, smells, or places can trigger nausea and vomiting



ANTIEMETIC DRUG CLASSES

Drugs from different classes can be utilized together for maximal effect

- Agents used for the management of breakthrough nausea and vomiting should be mechanistically different than those used for prevention
- Agents should be dosed appropriately for single-day versus multi-day chemotherapy regimens

Dopamine antagonists	Selective serotonin receptor antagonist	Neurokinin 1 receptor antagonist	Antipsychotics	Corticosteroids	Benzodiazepines
Metoclopramide Prochlorperazine	Ondansetron Granisetron Palonosetron Dolasetron	Fosaprepitant Rolapitant Netupitant	Olanzapine Haloperidol	Dexamethasone	Lorazepam Clonazepam

Not and all-inclusive list



NAUSEA AND VOMITING

Non-pharmacological treatment approaches

- Eat small, frequent meals throughout the day
- Eat slowly
- Avoid any trigger foods (spicy, fried, greasy, fatty)
- Avoid strong odors that may precipitate nausea and vomiting
- Don't lay down immediately after eating, try to stay upright for 20-30 minutes
- Wear loose fitting clothing, or clothing that is otherwise comfortable

Always let your care team know how you are feeling

- Your care team can play a large role in adjusting your prophylactic antiemetics, but only if they know how you are feeling

DIARRHEA

Can be associated with any chemotherapy regimen, but increased risk with certain agents

Patients and their care providers should assess the onset timing, frequency, and severity of diarrhea

- Treatment will vary based on the above factors, as well as the chemotherapy regimen that the patient is receiving
- Some cases of diarrhea will be self-limiting, while others may need more pharmacological intervention
- In some situations, infectious diarrhea will need to be ruled out

PERIPHERAL NEUROPATHY

Each patient is affected differently by associated agents, including at different times of onset and doses

- Symptoms may be present after a single dose or may be due to a cumulative dosing effect
- Symptoms can be permanent or resolve with time

Symptoms vary from patient to patient and in severity

- Tingling feeling in extremities
- Pain that is either persistent or fleeting
- Increased sensitivity to touch or to hot/cold stimulus
- Decreased hand/foot sensation or a feeling of extremity muscle weakness

PERIPHERAL NEUROPATHY

Pharmacologic treatment

- Very few pharmacologic agents have shown any benefit in the treatment of chemotherapy-induced peripheral neuropathy
- Lidocaine patches may be of benefit depending on the location affected
- Duloxetine, and SNRI, has shown promising results for some patients

Non-pharmacologic treatment

- Avoid triggers such as hot/cold stimulation
- Physical therapy/occupational therapy
- Make lifestyle alterations such as adjusting your home to limit trips, falls, etc

ITCHING/PRURITUS

Many chemotherapy agents can kill rapidly dividing cells, for which skin is a prime target

- Itching, dryness, burning, peeling

Treating dry skin should be the first step for nearly all patients

- Utilize a non-fragrant emollient, especially after bathing
- Wear non-irritating clothing that is loose
- Avoid any fragrances or dyes that trigger or exacerbate symptoms
- Try using a humidifier in your house, especially in the winter or in dry climates

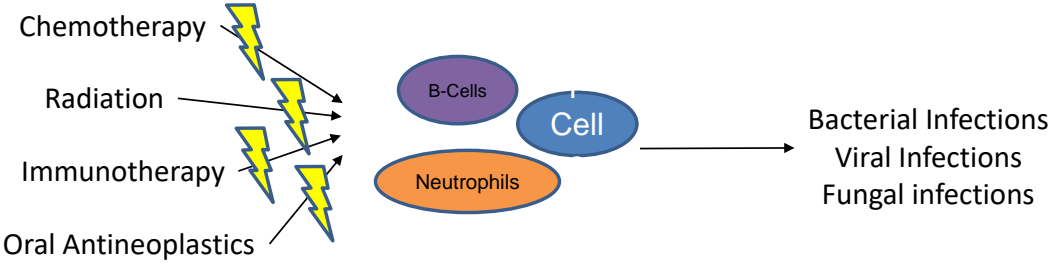
ITCHING/PRURITUS

Pharmacological treatments

- No single drug has been proven to be the most effective
- Patients should experiment to find what works best for them
 - Proxamine lotion has been proven to reduce itching in other patient populations and may be beneficial in malignancy-associated itching
 - Topical “cooling” agents such as menthol or camphor may be beneficial
 - Low strength lidocaine cream is beneficial for many patients but caution should be exercised as excessive quantities may result in increased absorption through the skin
- Topical agents with lacking data
 - Topical antihistamines such as diphenhydramine
 - Capsaicin
- Refractory pruritis
 - System agents such as antidepressants, anticonvulsants, and opioid antagonists have limited data in this setting

BONE MARROW SUPPRESSION/INFECTIONS

Many different chemotherapeutics agents/regimens, as well as oral antineoplastic agents, can suppress the immune system and increase the risk for infections



BONE MARROW SUPPRESSION/INFECTIONS

Bacterial Infections



Amoxicillin/clavulanate
Levofloxacin
Cefpodoxime

Viral Infections



Acyclovir
Valacyclovir
Letermovir

Fungal Infections



Nystatin
Fluconazole
Posaconazole

HAND-FOOT SYNDROME

Typically can manifest within the first 2 – 4 weeks after treatment starts

- Affects palms of hands and soles of feet, but can occur on any surface that is high impact or friction

Preventative measures are generally most affective

- Be aware of any potential area that could be affected
- Wear cotton gloves or socks to protect affected areas
- Avoid excessive friction/use
- Avoid excessive exercise (especially that which affects hands and feet)
- Avoid hot water
- Wear loose fitting shoes

HAND-FOOT SYNDROME

Prophylaxis

- Ammonium lactate cream twice daily
- “Thick” moisturizer, generally containing petroleum or lanolin twice daily or as needed

Treatment

- Varies depending on the grading/severity of symptoms
- Comprised of a combination of therapies
 - Urea 20% cream twice daily
 - Clobetasol 0.05% cream daily (or topical steroid equivalent)
 - Pain relievers
 - NSAIDs, GABA agonists, opioids

MUCOSITIS & STOMATITIS

Breakdown of the oral mucosal lining due to chemotherapy killing rapidly dividing cells

Typically manifests 5 – 10 days after chemotherapy

Pharmacologic treatment

- Magic Mouthwash (diphenhydramine, viscous lidocaine, & sodium bicarbonate) rinses every 6 hours or as needed

Non-pharmacologic treatment

- Rinse mouth frequently, particularly after meals
- Use a **non**-alcoholic mouth wash after meals and at bedtime
- Use a soft bristle toothbrush after meals
- Avoid irritating items such as spicy foods and alcoholic beverages

SAFE HANDLING OF CHEMOTHERAPEUTICS

There are several steps that patients and caregivers can take to minimize risk of exposure and toxicity of chemotherapeutics

- Intravenous agents
 - Reduce spread of bodily fluids such as vomit and urine
 - Close the lid of the toilet prior to flushing to reduce splashing
 - Clean toilet and/or seat after each use
 - Caregivers should wear gloves when handling any bodily fluids (such as a urinal or bedpan)
- Oral agents
 - When possible, oral agents should be self-administered
 - If not possible, caregivers should always wash hands thoroughly, put on disposable gloves, administer the medication, remove gloves and place in trash, then wash hands thoroughly
 - The above process should also be followed when filling pill boxes
 - Do not throw out unused medications, return to pharmacy for disposal if possible

BEING A GOOD ADVOCATE

Both patients and caregivers should understand the treatments that they are receiving, as well as what to expect from the treatments

Side effects and toxicities

Keep a list of all medications that you are taking, as some medications can have drug-drug interactions or side effects that can exacerbate chemotherapy toxicities

Ask Questions! Ask Questions! Ask Questions!

LEVERAGING YOUR TREATMENT TEAM

Always be open and communicative about side effects or toxicities that you are experiencing, even if you aren't sure if it is related to the treatment, you are receiving

- Caregivers may need to be advocates for patients
- General feeling of not wanting to be a “bother” to the treatment team

Utilize specialists on your treatment team

- Physicians, nurse practitioners, physician assistants, pharmacists, social workers, dieticians, nurses, physical therapists, occupational therapists, psychologists, and many more

Toxicities of Chemotherapy Treatment

What is and is not discussed with your physician

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27

DISCLOSURES

- **AbbVie Pharmaceuticals: advisory board**
- **Agios pharmaceuticals: advisory board**
- **Bristol Myers Squibb: advisory board and speakers bureau**
- **Incyte Pharmaceuticals: advisory board and speakers bureau**
- **Gilead: research funding, advisory board**
- **Jazz Pharmaceuticals: research funding**
- **Pfizer: research funding**



28

Leukemia Patients are my focus

What I tell my patients before chemotherapy treatment

CASE STUDY

61F publisher with a history of breast cancer in remission 10 years ago and otherwise in good health presents with syncope at work to the ER.

EKG and head CT are normal

CBC with wbc 65, hemoglobin 6.2 and platelets 10

Blood sent for analysis and is consistent with acute myeloid leukemia

She is given hydroxyurea (to lower her wbc) and transfusions

She needs immediate chemotherapy and plan for induction chemotherapy with daunorubicin and cytarabine is recommended.

Need for placement of a central line and echocardiogram before treatment can begin discussed with the patient

She is consented for chemotherapy and the following toxicities were discussed.

IMMEDIATE SIDE EFFECTS FROM CHEMOTHERAPY TREATMENT DISCUSSED

- Alopecia
- Pancytopenia with possible need for transfusion of blood products and the administration of growth factors
- Neutropenia: prophylactic antibiotics, antifungals and antiviral medication with the side effects of those treatments
- Neutropenic Fever: will require hospitalization and the need for a course of IV antibiotics
- Other infections: teeth, skin, pneumonia
- Gastrointestinal toxicities: Nausea, Vomiting, Constipation, Diarrhea, mucositis (sores in the mouth) and typhlitis (inflammation of the colon).
- Fatigue and weakness
- Need for prolonged hospitalization approximately 30 days after the start of treatment
- Need for bone marrow transplant or additional chemotherapy if remission is achieved depending on the chromosomes structure in the bone marrow report and what genes are mutated in her disease.

CASE HISTORY



Patient began to lose her hair two-and-one-half weeks after starting treatment

She developed neutropenic fever and started antibiotics

She had many bruises secondary to blood draws

Because of access problems, a central neckline was placed

She developed neutropenic colitis and a NGT was placed

After these interventions, she developed depression

She did not discuss her feelings with the primary team or her husband.

SIDE EFFECTS OF DISEASE AND CHEMOTHERAPY NOT FREQUENTLY DISCUSSED THAT CAN IMPACT OUTCOME

Changes in Body Image and Self Esteem

Dependence on a caregiver

Sleep disturbance, depression and anxiety

Sexual Dysfunction and Relationship changes

Cognitive Changes Associated with Chemotherapy

Financial Toxicities of Chemotherapy

Social Toxicities: Loneliness and alterations in social relationships

CHANGES IN BODY IMAGE

- Wounds and scars from biopsy sites, surgeries
- Bruises from phlebotomy sites
- Alopecia from chemotherapy
- Rashes from chemotherapy treatment or medications needed to tolerate chemotherapy treatment like allopurinol or antibiotics
- Presence of a central line
- Changes in body image led to a decrease in self esteem



ADJUSTMENTS TO ACCEPT THESE CHANGES IN BODY IMAGE AND TO IMPROVE SELF ESTEEM INCLUDE:

- Allow yourself to mourn what you have lost and discuss with loved ones, friends or support groups
- Wigs, scarves and new clothing to accommodate changes in appearance
- Take new risks with your appearance that "spark joy"
- Engage in a gentle exercise program—ie walking outdoors
- Maintain a healthy diet
- Be open about the changes that bother you with your physician. Drugs and dosages can potentially be adjusted to improve your sense of self

CHEMOTHERAPY TREATMENT REQUIRES A CAREGIVER

Caregiver is a necessity for successful treatment

- **Not feasible to give chemotherapy to a patient without an adequate caregiver**
- **Many toxicities of chemotherapy require assistance from others**
- **For some patients, the need for a caregiver causes guilt and concerns that they are a burden to their family and friends.**

Relationship between caregiver and patient can be important to outcome

- **Chemotherapy outcome is improved with adequate caregiver support**
- **Relationships deepen between patients and caregivers and can provide solace to both parties**
- **Counseling and support groups can allow for both patients and caregivers to discuss their feelings**

LONELINESS AND DEPRESSION



- Depression affects up to 25% of cancer patients
- This can significantly affect treatment outcome
- Depressed patients can't cope with the burden of the illness
- May decrease the acceptance of treatment options
- Can extend length of hospitalization
- Reduce overall quality of life
- Recent abstract at ASH shows that depression can influence prognosis and decrease OS in patients with MDS

(Pleyer et al, EQ-5D-5L Predicts Treatment Outcome, Ash abstract 0064)

ADDRESSING DEPRESSION

Important to discuss feelings with your oncologist as this can affect your overall outcome	Oncologist may prescribe antidepressants	May refer to psychiatrist devoted to oncology patients or to a support group
Consider alternative treatments: meditation, exercise	Adhere to a healthy diet	Maintain a social life and share your feelings with friends and family

SEXUAL DYSFUNCTION AND RELATIONSHIP CHANGES



Karacan et al, AP Journal of Nursing 2021, Jan-Feb;88(1)

Sexual dysfunction is prevalent in patients with hematologic malignancies

Observed at rate of 60% in patients with acute leukemia, 55% in patients with CLL and 73.3 in lymphoma. In patients undergoing stem cell transplant 71.4% of patients.

Many medications, including chemotherapy, can interfere with sex drive

Erectile dysfunction is the most common abnormality in men

Female dysfunction can be related to early ovarian failure

Fertility preservation may not be routinely discussed with oncologists

The psychologic burden of a cancer diagnosis can change the nature of relationships with spouses and other partners

There is a lack of validated interventions for sexual rehabilitation after cancer treatment

Cost effective strategies for addressing these problems are not readily available (ie fertility treatment)

For some patients, medical management can improve sexual function and it is important that this topic be discussed with the primary oncologist.

CASE HISTORY

- Patient's sister discussed with team her concerns about depression
- Team discussed the sister's suspicions with the patient who agreed to see a psychiatry consult
- An antidepressant was started, and she participated in a patient support group on the floor held weekly
- Her counts started to recover, and her mood improved
- Her NGT and central line were removed
- Bone marrow showed a remission
- The patient was sent home and started consolidation chemotherapy
- She tried to go back to work but was unable to concentrate on her projects and had some difficulty finding words and felt frustrated

CHEMOTHERAPY AND COGNITIVE FUNCTION

- Cognitive effects from chemotherapy treatment are common in hematologic and solid tumor malignancies.
- Numerous drugs used to treat hematologic malignancies and a deleterious effect on brain function
- Mechanisms include direct neurotoxicity of chemotherapeutic agents, oxidative stress, genetic predisposition to metabolizing chemotherapy drugs, histone modification, cytokine provoked damage, immune alternations and the direct action of chemotherapy drugs on structural proteins in brain cells.
- There are no efficient treatments for this syndrome, and it is a challenge in clinical practice
- Future studies are needed to determine which patients are vulnerable to this syndrome and evaluate ways to mitigate damage.
- Cognitive training and physical activity may be methods to improve dysfunction in patients.

Vitali et al, Crit Rev Onc/Hem,2017 (118): 7-14

Allegra et al, Exp Rev Hematol 2020 Apr;13(4):393.

CASE HISTORY

- Because of her difficulties with concentration, the patient was not able to resume her previous job at full capacity
- She was put on azacitidine maintenance treatment but her monthly copay for the drug was \$3000.00.
- In her current state of employment, this was not a feasible number. She had two children in college with tuitions to pay.
- Insurance did not cover the costs of some of the specialists that saw her during hospitalization, and these were surprise expenses.
- The patient became very worried about her financial situation and that of her family.

FINANCIAL TOXICITIES AND CANCER TREATMENT

Financial Toxicities describe problems related to the cost of chemotherapy treatment

Several studies show that cancer patients and survivors are more likely to have financial toxicity than are people without cancer

Cancer treatment can directly affect a patient or caregiver's ability to work and pay medical bills.

The degree of toxicity is dependent on many factors including amount of income earned, savings, and assets.



PROBLEM'S PATIENTS HAVE REGARDING COST OF TREATMENT



Copayments: amount you pay for each healthcare service such as a doctor's appt or prescription.

Deductibles: Amount you pay for your medical care before your health insurance plan begins to pay.

Coinsurance: percentage of costs you pay for a service that your health insurance covers after you have paid your deductible, for example you pay 20% and your insurance pays 80%.

Cancer survivors report higher out-of-pocket spending than those who do not have cancer. Some cancer survivors report spending more than 20% of their annual income on medical care.

CANCER PATIENTS AND SURVIVORS ARE MORE LIKELY TO HAVE FINANCIAL TOXICITY THAN ARE PEOPLE WITHOUT CANCER

Cancer is one of the most expensive medical conditions to to treat

Patients may have multiple types of treatment including surgery, radiation, chemotherapy and are more likely to require hospitalization

Compared to ten years ago, patients receive much more expensive treatment, namely chemotherapy and immunotherapy treatments.

Copayments for these more expensive treatments may cause severe financial toxicity even with good insurance coverage.

HOUSEHOLD FACTORS WHICH MAY AFFECT DEGREE OF FINANCIAL TOXICITY

- Who makes the most money in the household?
 - How much do others in the household make
 - How much debt was there before cancer diagnosis
 - What are the total assets
 - Costs related to the cancer treatment
 - Does the cancer diagnosis interfere with the ability to work
 - Whether there is health and disability insurance and degree of coverage
-
- Possible consequences
 - Less income and assets
 - Debt because of cost of cancer care
 - Trouble paying for food, clothing and shelter
 - Bankruptcy

EFFECTS OF FINANCIAL TOXICITY ON CANCER PATIENTS

Patients may not take their medicine as directed so they can save money on copayments

Patients who have financial toxicity may have a lower quality of life

Financial toxicity may lead to debt and bankruptcy

ASK A QUESTION

BLOOD CANCERS: MANAGING SIDE EFFECTS

Ask a question by **phone**:

Press star (*) then the number 1 on your keypad.

Ask a question by **web**:

Click "Ask a question"

Type your question

Click "Submit"

Due to time constraints, we can only take one question per person. Once you've asked your question, the operator will transfer you back into the audience line.

CLOSING REMARKS

BLOOD CANCERS: MANAGING SIDE EFFECTS



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LLS EDUCATION & SUPPORT RESOURCES



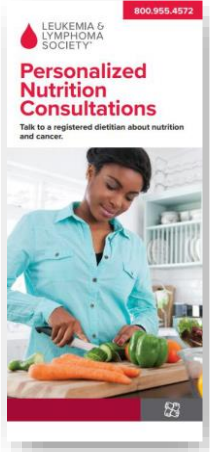
HOW TO CONTACT US:

To contact an **Information Specialist** about disease, treatment and support information, resources and clinical trials:

- Call: (800) 955-4572**
Monday to Friday, 9 a.m. to 9 p.m. ET
- Chat live online: www.LLS.org/InformationSpecialists**
Monday to Friday, 10 a.m. to 7 p.m. ET
- Email: www.LLS.org/ContactUs**
All email messages are answered within one business day.

CLINICAL TRIAL SUPPORT CENTER

Work one-on-one with an LLS Clinical Trial Nurse Navigator who will help you find clinical trials and personally assist you throughout the entire clinical-trial process.
www.LLS.org/Navigation



NUTRITION CONSULTATIONS
Our registered dietitian has expertise in oncology nutrition and provides free one-on-one consultations by phone or email.
www.LLS.org/Consult

LLS EDUCATION & SUPPORT RESOURCES



Online Chats

Online Chats are free, live sessions, moderated by oncology social workers. To register for one of the chats below, or for more information, please visit www.LLS.org/Chat.



Education Videos

View our free education videos on disease, treatment, and survivorship. To view all patient videos, please visit www.LLS.org/EducationVideos.



Patient Podcast

The Bloodline with LLS is here to remind you that after a diagnosis comes hope. To listen to an episode, please visit www.TheBloodline.org.

LLS EDUCATION & SUPPORT RESOURCES

LEUKEMIA & LYMPHOMA SOCIETY 877.557.2672

Help With Finances

The Leukemia & Lymphoma Society (LLS) offers financial assistance* to help individuals with blood cancer.

- The LLS Patient Aid Program** provides financial assistance to blood cancer patients in active treatment. Eligible patients will receive a \$100 stipend. Visit www.LLS.org/PatientAid
- The Urgent Need Program**, established in partnership with Moppie's Love, helps pediatric and young adult blood cancer patients, or adult blood cancer patients who are enrolled in clinical trials, with acute financial need. The program provides a \$500 grant to assist with non-medical expenses, including utilities, rent, mortgage, food, lodging, dental care, child care, elder care, and other essential needs. Visit www.LLS.org/UrgentNeed
- The Susan Lang Pay-It-Forward Patient Travel Assistance Program** provides blood cancer patients a \$500 grant to assist with transportation and lodging-related expenses. Visit www.LLS.org/Travel
- The Co-Pay Assistance Program** offers financial support toward the cost of insurance co-payments and/or insurance premiums for prescription drugs. Visit www.LLS.org/Copay

*Funding for LLS's Co-Pay Assistance Program is provided by pharmaceutical companies. Funding for other LLS financial assistance programs is provided by donations from individual donors, companies, and LLS employees.

The Leukemia & Lymphoma Society (LLS) offers the following financial assistance programs to help individuals with blood cancers: www.LLS.org/Finances



To order free materials: www.LLS.org/Booklets



THANK YOU

We have one goal: A world without blood cancers

