WELCOMING REMARKS
BLOOD CANCERS: MANAGING SIDE EFFECTS

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

OVERVIEW OF CHEMOTHERAPY TOXICITIES

- Mucositis
- Hair loss
- Ototoxicity
- Nausea & vomiting
- Cardiotoxicity
- Diarrhea
- Infections
- Peripheral neuropathy
- Bone marrow suppression
- Peripheral edema
- Hand-foot syndrome
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

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<td>Fludarabine</td>
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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**

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<td>Each agent carries its own risks and side effects, for which patients should consult their care team for a detailed discussion</td>
<td>Venetoclax</td>
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<td>Infusion reactions</td>
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<td>Fatigue</td>
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<tr>
<td>Joint/muscle pain</td>
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<td>Infections</td>
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<td>Pancreatitis</td>
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<td>Electrolyte abnormalities</td>
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**IMMUNOTHERAPY**

- **Immunomodulators**
  - Nivolumab
  - Pembroluzumab
  - Interferon alfa-2b

- **Targeted Antibodies**
  - Brentuximab
  - Obinutuzumab
  - Rituximab
  - Loncastuximab
  - tesirine
  - Polatuzumab
  - vedotin
  - Tafasitimab
  - Mogamulizumab

- **Cellular Therapy**
  - CAR T-Cell Therapies
IMMUNOTHERAPY SIDE EFFECTS

- Immunomodulators
- Targeted Antibodies
- Cellular Therapy

Inflammation
- Skin Rash
- Colitis (gut)
- Pneumonitis (lungs)
- Arthritis (joints)
- Hepatitis (liver)
- Cytokine release syndrome

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

<table>
<thead>
<tr>
<th>Dopamine antagonists</th>
<th>Selective serotonin receptor antagonist</th>
<th>Neurokinin 1 receptor antagonist</th>
<th>Antipsychotics</th>
<th>Corticosteroids</th>
<th>Benzodiazepines</th>
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<tr>
<td>Metoclopramide</td>
<td>Ondansetron</td>
<td>Granisetron</td>
<td>Olanzapine</td>
<td>Dexamethasone</td>
<td>Lorazepam</td>
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<td>Prochlorperazine</td>
<td>Palonosetron</td>
<td>Rolapitant</td>
<td>Haloperidol</td>
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<td>Clonazepam</td>
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<td>Dolasetron</td>
<td>Netupitant</td>
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Not 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

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**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

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

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.

Chemotherapy
Radiation
Immunotherapy
Oral Antineoplastics

B-Cells
Neutrophils

Bacterial Infections
Viral Infections
Fungal 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

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 diving 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 mouthwash 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 toiled 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

Ellen K. Ritchie MD
Assistant Director of the Leukemia Program
Associate Professor of Clinical Medicine
Weill Cornell Medicine

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
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

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<td>Cognitive Changes Associated with Chemotherapy</td>
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<td>Financial Toxicities of Chemotherapy</td>
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<td>Social Toxicities: Loneliness and alterations in social relationships</td>
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### 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—i.e., 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**

Sexual dysfunction is prevalent in patients with hematologic malignancies. Observed at a 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 (e.g., fertility treatment).

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

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**CASE HISTORY**

- Patient's sister discussed with the 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 alterations 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

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 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

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

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

The Leukemia & Lymphoma Society (LLS) offers financial assistance to help individuals with blood cancers:

Help With Finances
The Leukemia & Lymphoma Society (LLS) offers financial assistance programs to help individuals with blood cancers:

The LLS Patient Aid Program provides financial assistance to help cancer patients and their families with out-of-pocket expenses, such as medication, housing, transportation, and more. Visit www.LLS.org/Aid

The Urgent Need Program, established in partnership with the Leukemia & Lymphoma Society (LLS), provides financial assistance to help individuals with blood cancers. Visit www.LLS.org/Need

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.
We have one goal: A world without blood cancers