An Overview of Hematologic Cancers and Treatments

Nursing Practice Standards and Hematologic Cancer

Each year in the United States, it's estimated there will be 175,000 new cases of hematologic cancer and 68,000 deaths. Blood cancers account for 10% of new cancer diagnoses. Nurses in hematology/oncology and transplant settings provide high acuity care, delivering high-risk treatments to patients whose disease course is unpredictable and complicated, while addressing patients' and caregivers' psychosocial and educational needs, and ensuring accurate and thorough documentation. RNs and advanced practice RNs can refer to resources published by the Oncology Nursing Society (ONS), such as *Oncology Nursing: Scope and Standards of Practice,* for in-depth and up-to-date guidelines and best practices.

Etiology and Classification

Known risks for blood cancers include toxic environmental and workplace exposures, exposure to medical, occupational, or natural radiation, genetic and chromosomal abnormalities, and prior treatment with chemotherapy. Some viruses are associated with cancer, particularly the Epstein-Barr virus (EBV), which has been linked to lymphoma. Multiple myeloma is twice as common in Black people compared to White people, affects more men than women, and is four times more common in people who have a parent or sibling with the disease.

Hematologic malignancies originate from the blood-forming tissues in the bone marrow and lymphatic system. The blood cancers are classified into 4 groups: leukemias, lymphomas, multiple myeloma, and myelodysplastic syndrome (MDS). We will focus on the first 3, as these are the most common. The last, MDS, in some cases, is considered a "pre-cancer" and occurs in relatively low numbers, with about 10, 000 new cases diagnosed each year in the US. MDS often has mild symptoms of anemia and low platelets. About a third of MDS patients experience disease progression to acute myeloid leukemia.

Diagnosing Hematologic Malignancies

Diagnosis starts with a complete blood count (CBC) with differential, which shows the percentages of all the cell types, followed by bone marrow or lymph node tissue biopsy, for a closer look. Cell morphology and histology are viewed in the microscope, and the cell cycle stage and quantity of tumor cells can be determined using flow cytometry. Immunohistochemistry detects tumor-specific protein markers, or antigens, to help identify its type. Cytogenetics identifies chromosomal abnormalities, molecular genetics detects gene abnormalities, and gene expression profiling measures the activity of tumor cells. The ability to see the tumor cells in such detail has enabled scientists to define more than 135 subtypes of hematologic cancers. In some cases, very specific cell types have been found to respond especially well to treatments. For patients in clinical trials, stratifying them according to cell type provides information on the efficacy of the experimental treatment regimen. As specific cell types are found to respond to specific treatments, the arsenal of targeted treatments expands.

Hematopoiesis

Hematopoiesis is the process whereby stem cells develop into mature blood cells. In hematopoiesis, all blood cells originate from pluripotent stem cells in the bone marrow. Pluripotent stem cells are capable of both self-renewal and differentiation into any of the blood cell types. The pluripotent stem cell first divides to become either a myeloid stem cell or a lymphoid stem cell. Myeloid and lymphoid stem cells are multipotent, meaning they can become one of several types of cells in their line. These multipotent stem cells are also called precursor cells. Myeloid and lymphoid cells will progress through several stages, becoming progenitor cells. Progenitor cells are more highly differentiated than precursor cells and will continue to develop into one or more mature cell types. Myeloid precursor cells progress to become erythrocytes (red blood cells), platelets, neutrophils, monocytes, macrophages, dendritic cells, eosinophils, basophils, or mast cells. Lymphoid stem cells are destined to become T- cells, B-cells, natural killer (NK) cells, and plasma cells.

Cancer-causing gene mutations can occur anywhere along this cascade of development. The mutation causes the cell to develop abnormally, and to self-replicate, forming a clonal population of abnormal cells. Illness occurs when tumor cell proliferation crowds out and suppresses the development of healthy cells in the bone marrow.

Leukemia

The leukemias are “liquid” cancers that start in the bone marrow in the precursor myeloid or lymphoid stem cells. Leukemia can present as acute, developing rapidly over days or weeks, or chronic, remaining relatively stable or progressing slowly, even over years. Most leukemias are thus classified as acute or chronic myeloid (or myelogenous) leukemia (AML or CML), and acute or chronic lymphocytic (or lymphoblastic) leukemia (ALL or CLL). These groups differ in disease course, treatment, and prognosis, and the groups can be further subdivided based on molecular and genetic features.

Clinical Signs and Symptoms of Leukemia

Symptoms common to all leukemias include fatigue, weakness, and fever. These symptoms occur as the cancer cells proliferate and crowd out or suppress the manufacture of healthy cells. AML is more common in adults, while ALL usually affects children. As leukemia starts early in the hematopoietic cascade, it affects all the cells down the line. For instance, in myeloid leukemia, the cancerous mutation occurs in the myeloid precursor cells, which leads to a decrease in the cells in the myeloid family. The blood will show decreased mature erythrocytes, megakaryocytes (which produce platelets), and neutrophils, along with an abnormally high number of immature cells, or blasts. Symptoms result from these cytopenias---anemia causes shortness of breath, fatigue, weakness, and pallor; low platelets cause bleeding, bruising, and petechiae; and low neutrophils create a risk of infection. Patients may present with these as well as fever, bone and joint pain, lymph node swelling, loss of appetite and weight loss.

Lymphoma

Lymphomas develop in the lymphoid family of cells, but farther down the cascade, in the progenitor cells which would normally produce B-cells, T-cells, or natural killer (NK) cells. About 85% are B-cell lymphomas, and the remainder affect T-cells and NK cells. Lymphoma may

develop in just one place or in many sites in the body, usually originating in the lymph nodes, spleen, thymus, or bone marrow. However, it can also start in the lung, gastrointestinal tract, or skin. The cells are found in the blood, but also tend to form masses, so lymphoma is both a liquid and solid tumor.

There are more than 60 subtypes of lymphoma, and these are divided into Hodgkin's and non-Hodgkin's lymphoma (NHL). Hodgkin's lymphoma is one of the most curable cancers and occurs primarily in younger people between ages 16 and 24. It is characterized by the presence of Reed-Sternberg cells, which are large abnormal lymphocytes that often contain more than one nucleus. While there are several subtypes of Hodgkin's lymphoma, most lymphoma subtypes fall under the NHL umbrella. These cancers vary widely as to disease course, treatment, and prognosis; some are "indolent" or "smoldering," meaning they grow slowly, causing few or mild symptoms, while other types are aggressive (fast-growing).

Clinical Signs and Symptoms of Lymphoma

Lymphoma commonly presents as one or more enlarged, painless lymph nodes in the neck, upper chest, armpit, abdomen, or groin. Other signs and symptoms include night sweats, unexplained weight loss, unexplained fever, fatigue, cough and shortness of breath, itchy skin, decreased appetite, abdominal pain or swelling, and enlarged spleen and liver. Some lymphomas present with rashes or skin lumps. So-called "B-symptoms" ---fever, night sweats, and weight loss indicate more advanced disease and can suggest a poor prognosis.

Multiple Myeloma

Multiple myeloma (MM) is a group of malignancies of the mature antibody-producing plasma-B cells. Myeloma can be inactive and active, and active myeloma can be aggressive or non-aggressive. In MM cells, the abnormal plasma cells produce M-proteins instead of normal immunoglobulins---these non-functional proteins are so named because they are monoclonal. Large numbers of M-proteins can damage the functional units of the kidneys, causing kidney disease or failure. These, and other abnormal proteins secreted from the tumor can cause hyperviscosity in the blood, potentially damaging organs. The malignant plasma cells can also infiltrate organs, especially the bones, lymph nodes, liver, and spleen. Infiltration of the bones causes activation of osteoclasts and suppression of osteoblasts, producing bone lesions and releasing calcium into the blood. The "C.R.A.B symptoms" are classic signs of MM and include calcium elevation, renal insufficiency, anemia, and bone abnormalities. There can also be thrombocytopenia and leukopenia.

Clinical Signs and Symptoms of Multiple Myeloma

Patients with MM may experience bone pain due to the tiny lesions, which typically affect the skull, ribs, spine, shoulder, and pelvis. Abnormal proteins and calcium damage kidneys, which can cause fatigue, loss of appetite, nausea, vomiting, confusion, and restlessness. Patients may have symptoms secondary to cytopenias, such as weakness, bruising, and bleeding. MM patients are also at high risk for infection.

Treatments
The most common treatments for hematologic cancers are chemotherapy, targeted therapy, and allogeneic (from a donor) or autologous (from self) hematopoietic stem cell transplant (HSCT). In cases where there is a mass such as in lymphoma, radiation and surgery may be used to reduce the bulk of the solid tumor. For some indolent or inactive cancers, a wait and watch approach might be used, where patients are not treated but monitored frequently for disease progression.

Chemotherapy and HSCT
Patients with acute hematologic cancers are usually treated with several rounds of chemotherapy which may or may not be followed by HSCT. Chemotherapy protocols generally consist of several drugs that have different mechanisms of action to increase efficacy. This first phase of chemotherapy is called "conditioning." Depending on the age of the patient, disease risk, and performance status, conditioning may be myeloablative, reduced-intensity, or non-myeloablative.

Myeloablative conditioning uses high doses of chemotherapy and may also involve total body irradiation. The goal is to obtain complete remission of the cancer and then to follow this with HSCT. Myeloablative conditioning causes irreversible cytopenia. When the absolute neutrophil is below 500 cells/μL, this is called the "nadir." Patients receive the HSCT shortly after conditioning, but ANC remains low until the new cells "take" in the bone marrow, and hematopoiesis occurs. This process is called "engraftment", and it can take 2-6 weeks for the blood counts to reach normal levels. Older patients and those with comorbidities may be treated with reduced-intensity conditioning and with or without HSCT. Reduced-intensity regimens are less toxic but are also more likely to lead to graft rejection and disease relapse.

Targeted Therapies
Some cancers express antigens that can be targeted. This allows the patient to avoid the toxicity of traditional chemotherapy. Targeted therapies are designed to interfere with specific molecules and processes unique to the tumor cells. This contrasts with chemotherapy which attacks healthy cells along with tumor cells. Targeted therapies include immunotherapies, which exploit the abilities of the immune system to destroy cancer cells. These include monoclonal antibodies, checkpoint inhibitors, and chimeric antigen receptor T-cell therapies.

Monoclonal antibodies are manufactured by cloning mouse or human white blood cells to produce large amounts of a specific antibody, which are then delivered via intravenous infusion. Rituximab was the first monoclonal antibody approved, in 1997, for the treatment of certain cancers, including B-cell lymphomas. Rituximab targets and binds to the CD20 antigen which is expressed on B-cell lymphoma cells. There are now many more monoclonal antibodies used for treating cancer, but rituximab is still in use for lymphoma.

Checkpoint inhibitors are a newer class of drug, of which there are several, used to treat various solid cancers, as well as Hodgkin's lymphoma. In a normal immune system, T-cells express a "checkpoint protein", known as the programmed cell death protein 1 (PD-1), which binds to the

cell programmed death-ligand 1 (PD-L1), which is present on healthy host tissue cells. This binding action triggers the suppression of T-cell proliferation and cytokine production, protecting host cells from autoimmunity. The Reed-Sternberg cells of Hodgkin's disease overexpress PD-L1, exploiting the immune-suppressive activity of checkpoint protein binding. PD-1 inhibitors are monoclonal antibodies that block the binding of PD-1 to PD-L1, which then allow the host's T-cells to target and destroy the cancer cells.

Tyrosine-kinase inhibitors (TKIs) are another class of targeted drugs that are used in some hematologic cancers. TKIs target tumor epidermal growth factor receptor (EGFR) signaling pathways, (which regulate cell proliferation, survival, and differentiation), while leaving healthy cells intact.

Chimeric antigen receptor (CAR) T-cell therapy is a very new treatment that involves extracting the patient's own T cells, and then inserting a gene into the cell, which codes for a receptor that binds to a protein target on cancer cells. The CAR T-cells are then grown in the lab and reinfused into the patient, where they find and attack the cancer.

Nursing Considerations--Administering Treatments

Preventing central line-associated bloodstream infections

Chemotherapy, targeted treatments, stem cells, and blood products are delivered via intravenous route, and patients need central intravenous access, such as a PICC line, Hickman catheter, or port. These devices stay in place for a prolonged period and there is an increased risk for central line-associated bloodstream infection (CLABSI). To prevent this, nurses follow guidelines and hospital protocol, changing the sterile dressing at appropriate intervals or when it is soiled, bloody, or no longer intact. Lumens should be flushed as per protocol with heparin and normal saline. Antimicrobial soap, such as chlorhexidine [CHG]) should be used during daily bathing. Strict hand hygiene is essential. Patients often go home with a line in place, and they and their caregivers need to be educated on aseptic catheter care.

Precautions

Nurses administering chemotherapy should know whether the drug is a vesicant or irritant and should check the IV access for a robust blood return before infusing, to ensure that the catheter is in the vessel. During infusion, to prevent injury, the nurse should check the IV site frequently for signs of infiltration. Some chemotherapy drugs have an antidote, which, in case of extravasation into the subcutaneous and intradermal tissue, can be injected into the infiltrated tissue, where it neutralizes the caustic drug. Prior to starting the chemotherapy infusion, nurses should familiarize themselves with the antidote and procedure for administering it.

During infusion of chemotherapy, an anaphylactic kit should be kept at the bedside in case the patient reacts to the drug. Signs of anaphylaxis include lightheadedness, shortness of breath or dyspnea, wheezing, tachycardia, decreased blood pressure, clammy skin or rash, and mental status changes or loss of consciousness. Hemolytic transfusion reactions can occur with the infusion of blood products or stem cells. The nurse should watch for fever, chills, shortness of

breath, hypotension, back or flank pain, rigors, and fatigue, and renal failure. Patients should be instructed to notify the nurse if they feel anything unusual during the infusion.

Chemotherapy is toxic, and nurses handling and administering oral and IV chemotherapy should wear full PPE with double gloves. A special clean-up kit, designed to contain and dispose of accidental spills or drips, should be at the bedside. Empty medicine bags, tubing, and used PPE should be placed carefully in a yellow hazardous waste bin for disposal. Chemotherapy remains in the patient for 48-72 hours, and during this time, PPE should be worn when there is a chance of contact with body fluids. Patients should be instructed to avoid splashes when using the toilet. The toilet should be flushed twice with the lid down, and if possible, the patient should use a separate bathroom. Caregivers should wear double gloves when handling items that might have body fluid on them. Dirty clothes and linens should be sealed in a plastic bag and washed separately in hot water. Patients that take oral chemotherapy at home should be instructed to avoid touching the meds with their hands as they can irritate the skin. Caregivers should also avoid touching the pills, as some are carcinogenic.

Patients in nadir (when ANC is $< 500/\mu L$) should follow neutropenic precautions. To limit exposure to infectious microorganisms, flowers and fresh produce should not be allowed in the patient's room. Raw fish and shellfish, raw and undercooked eggs, as well as unpasteurized milk, cheese, eggnog, honey, juice, and cider, should also be avoided. The patient should stay away from sick contacts and patients and caregivers should always practice strict hand hygiene.

Monitoring Patients

Nurses caring for patients receiving treatment for hematologic cancer are tasked with monitoring a wide variety of parameters to ensure their patients remain safe. Patients with hematologic cancer receive frequent blood tests and physical assessments. Some chemotherapies have very narrow therapeutic ranges and require blood draws at intervals several times a day, to ensure serum levels remain in the range. Routine CBC and chemistry panels allow clinicians to monitor the effects of disease and treatments. Coagulation panels are ordered if there is thrombocytopenia or signs of bleeding. Blood, urine, stool, wound, and central line cultures are obtained if there is fever or other signs of infection.

Physical assessment should include checks for mental status, vision and gate changes, and cardiovascular, pulmonary, and neurovascular status. Patients should be examined for edema, and daily weights obtained. Intake and output should be measured, and nutritional status assessed. Patients should be asked about bowel movements and the consistency and frequency of stools. The skin and mucous membranes should be checked frequently for rashes and breakdown. Patients should be asked about nausea, vomiting, and pain, and these should be treated promptly, and even prophylactically. Patients should be supported psychologically and spiritually, and psychiatry and clerical services consulted as needed.

Complications of Disease and Treatments

Blast Crisis and Hyperviscosity

Patients with leukemia can find themselves in blast crisis, which is a life-threatening emergency. Blast crisis occurs when the number of circulating immature and nonfunctional leukocytes is so large (with > 50-100 WBC X 10^9) that the blast cells cause leukostasis, where the blood clogs the microvasculature, leading to tissue hypoxia and ischemia. Hyperviscous blood tends to affect the CNS, eyes, and lungs, causing symptoms such as headache, dizziness, ataxia, confusion, somnolence, and blurry vision, as well as those suggestive of pneumonia or volume overload, such as fever, dyspnea, lung crackles, and pulmonary infiltrates.

Hypercalcemia of Malignancy

Blood chemistry panels can alert clinicians to toxic effects of chemotherapy on the kidneys and liver, as well as to the onset of oncologic emergencies, such as hypercalcemia of malignancy and tumor lysis syndrome. Hypercalcemia of malignancy can occur due to osteolysis in multiple myeloma and aberrant secretion of PTHrP in T-cell lymphomas and myelomas. Symptoms include lethargy, confusion, anorexia, nausea and constipation, polyuria, and polydipsia. Severe and rapid onset of hypercalcemia may cause cardiac dysrhythmias such as bradycardia, shortening of the QT interval, and even cardiac arrest. All patients with severe hypercalcemia should undergo electrocardiography. Treatment of hypercalcemia includes IV boluses and maintenance fluids titrated to cardiovascular status. Bisphosphonates are the mainstay of treatment and are able to control hypercalcemia in most patients. Other treatments include calcitonin, and denosumab, a humanized monoclonal antibody, recently approved for use in hypercalcemia of malignancy. In some cases, hemodialysis might be required. (*Emergencies in Hematology and Oncology - Mayo Clinic Proceedings*, n.d.)

Adverse Effects of Treatment

Chemotherapy, because it attacks cells with rapid turnover, also affects healthy cells with rapid turnover, such as the skin, mucous membranes, and gut. Thus, it can cause alopecia, nausea and vomiting, diarrhea, skin rashes, and mucositis (oral lesions). Mucositis is a serious complication, and patients receiving chemotherapy should be on a prophylactic regimen to prevent or minimize it. They should receive and be taught proper mouth care. They should also receive oral (i.e., “swish-and-swallow”), or IV antifungal prophylaxis. Pain medicine and “magic mouthwash,” containing lidocaine, may be necessary as mucositis can be painful enough to impact nutrition. In some cases, patients may need to be put on total parenteral nutrition (TPN). Mucositis following an HSCT can also be a sign of graft-vs-host disease (GVHD), which is when the transplanted immune system attacks the host’s healthy tissues. GVHD is treated with steroids and other immunosuppressants.

Targeted therapies are designed to reduce the incidence of adverse events, but they are not risk-free. Adverse events associated with immunotherapies are called immune-related adverse events (irAEs), and the most common ones are rash, colitis, and endocrinopathies. Immune checkpoint inhibitors have been associated with pneumonitis, colitis, dermatitis, and

autoimmune hemolytic anemia. Depending on the type and severity, immune-related AEs may be treated with steroids, IVIG, or apheresis.

Febrile Neutropenia

Patients with neutropenia should be monitored closely for signs of infection. Febrile neutropenia is defined as a single oral or axillary temperature of ≥38.3°C (101°F), or a temperature of ≥ 38.0°C (100.4°F), sustained over a 1-hour period, in a neutropenic patient with an ANC < 500/µL. Febrile neutropenia is an emergency, as it is associated with increased morbidity and mortality. Patients with febrile neutropenia should receive sepsis workup, which includes pan cultures and prompt administration of broad-spectrum antibiotics. (*Oncologic Emergencies: Recognition and Initial Management - American Family Physician*, n.d.)

Tumor Lysis Syndrome

Tumor lysis syndrome (TLS) can occur after treatment causes lysis of a large number of tumor cells, leading to the massive release of cell contents, i.e., potassium, phosphate, and uric acids, into the circulation. Clinical symptoms are related to the severity of the electrolyte imbalances and kidney injury. A patient with early TLS may present with increased weakness and altered mental status. Hyperuricemia and hyperphosphatemia precipitate uric acid and calcium phosphate crystals in the renal tubules, causing acute kidney injury (AKI). Hyperuricemia also causes vasoconstriction, decreased renal blood flow, and release of pro-inflammatory mediators, also damaging to kidneys. Hyperphosphatemia and calcium phosphate formation lead to hypocalcemia. Hypocalcemia with hyperkalemia can cause cardiac dysrhythmias, sudden death, tetany, paresthesia, or seizure. Patients at risk for TLS should receive adequate hydration and daily oral allopurinol or rasburicase prophylaxis to prevent hyperuricemia. Patients with clinical TLS should be admitted to ICU with telemetry monitoring, and managed with aggressive hydration, rasburicase, Q 4-hour labs, and control of symptomatic electrolyte imbalances. Patients who don't adequately respond to phosphate-binding and/or potassium binding therapies may require renal replacement therapy. (Thandra et al., 2020)

Malignant Spinal Cord Compression

Malignant spinal cord compression (MSCC) is an oncologic emergency, with a poor prognosis especially if there is paralysis. Patients with multiple myeloma and non-Hodgkin lymphoma are, particularly at risk. In patients with known bone metastases and a high tumor burden, any recent onset of back pain should be considered secondary to MSCC until it is ruled out. Pain tends to be local, or radiate to legs, is usually progressive, and may be increased with certain movements, or with the Valsalva maneuver. In 5-15% of patients with MSCC, there's minimal or no pain, but they may have lower extremity numbness, weakness, or paralysis, and bowel and bladder dysfunction. Diagnosis is performed using magnetic resonance imaging (MRI), which should image the whole spine, as 40% of patients have multiple areas of compression or cord impingement. Patients may be treated with surgical decompression, steroids, and/or radiation. (*Emergencies in Hematology and Oncology - Mayo Clinic Proceedings*, n.d.)

Patient Education, Documentation, and Listening to the Patient

For patients with hematologic cancers, the disease and treatment trajectories are long, and in between cycles of treatment, patients go home. Nurses are responsible for educating patients and their caregivers so that they remain safe and have the best possible quality of life. Central line care, neutropenic and chemotherapy precautions, disease course, and side effects of treatments---these are all important topics for patient education. Nurses use teaching flowsheets so that they remember important points and so they can document that teaching was done. However, flowsheets are not enough, and it is essential that nurses listen to patients. Listening allows the nurse to assess the patient's teaching needs, but more importantly, it enhances the connection to the patient and caregivers on their journey.

References

1. *Acute leukemic blast crisis, Hyperleukocytosis, Leukostasis*. (2019, January 17). Cancer Therapy Advisor. https://www.cancertherapyadvisor.com/home/decision-support-in-medicine/critical-care-medicine/acute-leukemic-blast-crisis-hyperleukocytosis-leukostasis/
2. *Anaphylaxis—Symptoms and causes*. (n.d.). Mayo Clinic. Retrieved November 21, 2021, from https://www.mayoclinic.org/diseases-conditions/anaphylaxis/symptoms-causes/syc-20351468
3. Blood Cancer Statistics. (2018, October 10). *Leukemia Research Foundation*. https://allbloodcancers.org/statistics/
4. *Conditioning regimens for allogeneic hematopoietic stem cell transplants in acute myeloid leukemia | Bone Marrow Transplantation*. (n.d.). Retrieved November 21, 2021, from https://www.nature.com/articles/bmt201783
5. Dassonville, O., Bozec, A., Fischel, J. L., & Milano, G. (2007). EGFR targeting therapies: Monoclonal antibodies versus tyrosine kinase inhibitors. Similarities and differences. *Critical Reviews in Oncology/Hematology*, *62*(1), 53–61. https://doi.org/10.1016/j.critrevonc.2006.12.008
6. *Definition of CAR T-cell therapy—NCI Dictionary of Cancer Terms—National Cancer Institute* (nciglobal,ncienterprise). (2011, February 2). [NciAppModulePage]. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/car-t-cell-therapy
7. Fauer, A. J., Choi, S. W., & Friese, C. R. (2019). The Roles of Nurses in Hematopoietic Cell Transplantation for the Treatment of Leukemia in Older Adults. *Seminars in Oncology Nursing*, *35*(6), 150960. https://doi.org/10.1016/j.soncn.2019.150960
8. *Frontiers | Past, Present, and Future of Rituximab—The World's First Oncology Monoclonal Antibody Therapy | Oncology*. (n.d.). Retrieved November 21, 2021, from https://www.frontiersin.org/articles/10.3389/fonc.2018.00163/full
9. Halfdanarson, T. R., Hogan, W. J., & Madsen, B. E. (2017). Emergencies in Hematology and Oncology. *Mayo Clinic Proceedings*, *92*(4), 609–641. https://doi.org/10.1016/j.mayocp.2017.02.008
10. *Keytruda_pi.pdf*. (n.d.). Retrieved November 21, 2021, from https://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_pi.pdf
11. Moy, R. H., & Younes, A. (2018). Immune Checkpoint Inhibition in Hodgkin Lymphoma. *HemaSphere*, *2*(1), e20. https://doi.org/10.1097/HS9.0000000000000020

12. *Myelodysplastic Syndromes—MDS - Statistics*. (2012, June 25). Cancer.Net. https://www.cancer.net/cancer-types/myelodysplastic-syndromes-mds/statistics
13. *Myelosuppressive Chemotherapy and Low Neutrophil Levels*. (n.d.). Amgen, Inc. Retrieved November 21, 2021, from https://www.neupogenhcp.com/low-neutrophil-levels
14. NurseOEP. (2013, November 22). *Competence in Cancer Care: Hematologic Malignancies*. https://www.youtube.com/watch?v=NYzWqj_CDZU
15. *Scope and Standards of Oncology Nursing Practice | ONS*. (n.d.). Retrieved November 21, 2021, from https://www.ons.org/standards-and-reports/scope-and-standards-oncology-nursing-practice