The Relationship Between Body Mass Index and Cytogenetic Abnormalities in Leukemia Patients with HIV: A Review

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Abstract

The interplay between Body Mass Index (BMI), cytogenetic abnormalities, and leukemia in HIV-infected patients presents a complex clinical scenario with significant implications for prognosis and treatment. This review synthesizes current knowledge on the relationship between BMI and cytogenetic abnormalities in leukemia patients with HIV, aiming to elucidate how these factors interact and impact disease progression and therapeutic outcomes. Given the dual burden of HIV and leukemia, understanding these relationships is crucial for developing effective, personalized treatment strategies. Cytogenetic abnormalities, such as translocations and deletions, are key drivers of leukemia progression and vary in their prognostic significance. BMI, a measure of body fat, influences overall health and has been associated with varying cancer prognoses, including leukemia. In HIV-infected individuals, the immunosuppressive effects of the virus complicate leukemia management, making the examination of BMI and cytogenetic interactions particularly pertinent. Preliminary evidence suggests that BMI may affect the prevalence and type of cytogenetic abnormalities, potentially due to differential immune responses and metabolic factors. Understanding these interactions may enable clinicians to optimize treatment plans based on individual patient profiles, ultimately improving outcomes for this vulnerable patient population.

Keywords: Body Mass Index, BMI, Cytogenetic Abnormalities, Leukemia, HIV, Co-infection, Prognosis, Personalized Treatment

Introduction

Leukemia, a type of blood cancer originating in the bone marrow, is characterized by the uncontrolled proliferation of abnormal white blood cells. This malignancy disrupts normal hematopoiesis and can present as acute or chronic forms, each with distinct clinical courses and prognoses. Understanding the underlying genetic and biological factors that influence leukemia progression is critical for developing effective treatment strategies. Among these factors, cytogenetic abnormalities play a pivotal role, with specific genetic alterations serving as markers for disease classification, prognostication, and therapeutic targeting.²⁻⁴ Cytogenetic abnormalities in leukemia include chromosomal translocations, deletions, duplications, and other structural variations. ⁵ These genetic alterations can lead to the activation of oncogenes, inactivation of tumor suppressor genes, and other molecular disruptions that drive leukemogenesis. For instance, the Philadelphia chromosome (t(9;22)(q34;q11)), which results in the BCR-ABL fusion gene, is a hallmark of chronic myeloid leukemia (CML) and is also observed in some cases of acute lymphoblastic leukemia (ALL).⁶ The presence and type of cytogenetic abnormalities significantly influence the prognosis and guide treatment decisions in leukemia patients. Body Mass Index (BMI), a measure calculated from a person's height and weight, is widely used to categorize individuals into various weight status groups: underweight, normal weight, overweight, and obese. BMI has been extensively studied in relation to overall health, and its impact on various diseases, including cancer, has garnered considerable attention. Both low and high BMI have been associated with adverse health outcomes, such as increased susceptibility to infections, poor wound healing, and altered pharmacokinetics of medications. In the context of cancer, BMI has been linked to variations in disease risk, progression, and response to therapy.⁷⁻⁹

In patients with leukemia, BMI may influence treatment outcomes and overall survival. Studies have shown that obesity can alter the pharmacokinetics and pharmacodynamics of chemotherapeutic agents, potentially leading to suboptimal drug efficacy or increased toxicity. Conversely, underweight patients may have diminished physiological reserves and impaired immune function, which can complicate treatment and recovery. Thus, maintaining an optimal BMI could be an important consideration in the management of leukemia patients. HIV infection adds another layer of complexity to the management of leukemia. HIV, the virus responsible for AIDS, severely compromises the immune system by targeting CD4+ T cells, leading to increased susceptibility to infections and malignancies. 10 HIV-infected individuals are at a higher risk of developing various cancers, including leukemia, due to chronic immune activation, inflammation, and impaired immune surveillance. The co-infection of HIV and leukemia presents unique clinical challenges, necessitating tailored treatment approaches that address both conditions simultaneously. The relationship between BMI and cytogenetic abnormalities in leukemia patients with HIV is an area of growing interest. Research in this domain seeks to understand how BMI influences the genetic landscape of leukemia cells and the clinical outcomes in this dual-affected patient population. Preliminary studies suggest that BMI may affect the prevalence and type of cytogenetic abnormalities observed in leukemia patients. These variations could be attributed to differences in metabolic and immune responses influenced by body weight. 11-13 In leukemia patients with HIV, the interplay between BMI and cytogenetic abnormalities may have significant Citation: Obeagu EI. The Relationship Between Body Mass Index and Cytogenetic Abnormalities in Leukemia Patients with HIV: A Review. Elite Journal of Haematology, 2024; 2(6): 1-15

implications for disease progression and treatment efficacy.¹⁴ For instance, underweight HIV-positive patients may exhibit distinct cytogenetic profiles compared to their overweight or obese counterparts. These differences could potentially impact the aggressiveness of the disease, response to treatment, and overall prognosis. Understanding these interactions could lead to more personalized and effective treatment strategies, ultimately improving patient outcomes.

Body Mass Index (BMI) and Health Outcomes

Body Mass Index (BMI) is a widely utilized measure to assess body fat and categorize individuals into different weight status groups: underweight, normal weight, overweight, and obese. 15 Calculated as weight in kilograms divided by the square of height in meters (kg/m²), BMI serves as a simple, non-invasive, and cost-effective tool for evaluating potential health risks associated with body weight. While BMI does not directly measure body fat, it correlates reasonably well with more direct methods of body fat measurement and is widely used in both clinical and research settings. High BMI, typically classified as overweight or obese, is associated with numerous adverse health outcomes. ¹⁶ Obesity is a well-established risk factor for various chronic conditions, including type 2 diabetes, cardiovascular diseases, hypertension, and certain cancers such as breast, colorectal, and pancreatic cancer. The excess adipose tissue in obese individuals can lead to metabolic dysregulation, insulin resistance, and chronic inflammation, which contribute to the pathogenesis of these diseases. Additionally, obesity can negatively impact respiratory function, joint health, and overall mobility, further diminishing quality of life. Conversely, low BMI, indicating underweight status, also poses significant health risks. Underweight individuals are at increased risk for malnutrition, osteoporosis, anemia, and compromised immune function. Malnutrition can lead to muscle wasting, reduced strength, and impaired wound healing, making underweight individuals more vulnerable to infections and other health complications. In the context of chronic diseases such as cancer, being underweight is often associated with poorer prognosis and reduced treatment tolerance.

In cancer patients, including those with leukemia, BMI has been linked to variations in disease risk, progression, and treatment outcomes.¹⁷ Obesity can alter the pharmacokinetics and pharmacodynamics of chemotherapeutic agents, potentially leading to suboptimal drug efficacy or increased toxicity. This can complicate treatment planning, as dosing regimens may need to be adjusted to account for body weight and composition. Moreover, obesity-related comorbidities, such as diabetes and cardiovascular diseases, can further complicate the management of cancer patients, increasing the risk of treatment-related complications and mortality. Underweight cancer patients face their own set of challenges. They may have diminished physiological reserves and impaired immune function, which can adversely affect their ability to tolerate and respond to aggressive cancer therapies. Malnutrition is common in cancer patients and can exacerbate treatment-related side effects, reduce the efficacy of treatment, and negatively impact overall survival. Nutritional support and interventions are often necessary to help underweight cancer patients maintain strength and resilience during treatment. In patients with leukemia, BMI's impact Citation: Obeagu EI. The Relationship Between Body Mass Index and Cytogenetic Abnormalities in Leukemia Patients with HIV: A Review. *Elite Journal of Haematology*, 2024; 2(6): 1-15

on health outcomes extends to influencing the biological behavior of the disease itself. ¹⁸ Studies have shown that obesity can promote a microenvironment conducive to cancer cell survival and proliferation, potentially leading to more aggressive disease. ¹⁹⁻²⁰ Conversely, underweight status and malnutrition can impair immune surveillance and increase susceptibility to infections, complicating leukemia management. In the context of HIV infection, BMI's influence on health outcomes becomes even more complex. HIV-infected individuals are at higher risk for both obesity and underweight status due to factors such as antiretroviral therapy, metabolic changes, and socioeconomic factors. The immunosuppressive effects of HIV, combined with the health risks associated with abnormal BMI, create a multifaceted challenge in managing comorbid conditions like leukemia. Optimizing BMI through nutritional and lifestyle interventions may help improve treatment outcomes and overall prognosis for HIV-infected leukemia patients. ²¹⁻²³

Cytogenetic Abnormalities in Leukemia

Cytogenetic abnormalities are crucial determinants in the diagnosis, classification, prognosis, and treatment of leukemia. These abnormalities involve changes in the number or structure of chromosomes within leukemia cells and are key drivers of leukemogenesis. They can include chromosomal translocations, deletions, duplications, inversions, and aneuploidies, each contributing to the disruption of normal cellular processes. 24-25 One of the most well-known cytogenetic abnormalities in leukemia is the Philadelphia chromosome, resulting from a translocation between chromosomes 9 and 22 (t(9;22)(q34;q11)). This translocation creates the BCR-ABL fusion gene, which encodes a constitutively active tyrosine kinase that drives the proliferation of leukemic cells. The Philadelphia chromosome is a hallmark of chronic myeloid leukemia (CML) and is also found in a subset of acute lymphoblastic leukemia (ALL) cases. The presence of this translocation has significant prognostic implications and has led to the development of targeted therapies, such as tyrosine kinase inhibitors (TKIs), which have revolutionized the treatment of CML. 26-28

In acute myeloid leukemia (AML), cytogenetic abnormalities are diverse and include a variety of translocations, inversions, and deletions. For instance, the t(15;17)(q22;q12) translocation, which produces the PML-RARA fusion gene, is characteristic of acute promyelocytic leukemia (APL), a subtype of AML. This particular translocation is associated with a unique clinical presentation and has been successfully targeted with all-trans retinoic acid (ATRA) and arsenic trioxide, leading to high remission rates. Other common cytogenetic abnormalities in AML include inv(16)(p13;q22) and t(8;21)(q22;q22), both of which are associated with relatively favorable prognoses when appropriate treatment regimens are applied. Acute lymphoblastic leukemia (ALL) also exhibits a range of cytogenetic abnormalities that influence disease classification and prognosis. In addition to the Philadelphia chromosome, other common abnormalities include hyperdiploidy (an increased number of chromosomes) and translocations such as t(12;21)(p13;q22), which results in the ETV6-RUNX1 fusion gene. These genetic alterations have distinct biological and clinical implications, guiding treatment decisions and risk stratification in Citation: Obeagu EI. The Relationship Between Body Mass Index and Cytogenetic Abnormalities in Leukemia Patients with HIV: A Review. *Elite Journal of Haematology*, 2024; 2(6): 1-15

ALL patients.³⁰⁻³¹ Chronic lymphocytic leukemia (CLL), another common leukemia type, is characterized by a variety of cytogenetic changes that affect prognosis and therapeutic approaches. Deletions of parts of chromosomes 13q, 11q, and 17p are frequently observed in CLL. The 17p deletion, which involves the loss of the TP53 tumor suppressor gene, is particularly associated with poor prognosis and resistance to conventional therapies. Identification of these deletions through cytogenetic analysis helps in tailoring more aggressive and targeted treatment strategies for affected patients.³²⁻³³

Cytogenetic analysis in leukemia is typically performed using techniques such as karyotyping, fluorescence in situ hybridization (FISH), and more recently, next-generation sequencing (NGS).³⁴ These techniques allow for the detection and characterization of chromosomal abnormalities at various levels of resolution. Karyotyping provides a broad overview of chromosomal changes, while FISH enables the identification of specific genetic alterations with high sensitivity. NGS offers a more detailed and comprehensive analysis of the genetic landscape, identifying not only known cytogenetic abnormalities but also novel mutations that may have clinical relevance. The presence and type of cytogenetic abnormalities in leukemia have profound implications for prognosis and treatment.³⁵ Certain genetic changes are associated with favorable outcomes and higher response rates to specific therapies, while others indicate a more aggressive disease course and poorer prognosis. For example, patients with the t(8;21) translocation in AML generally have a better prognosis and respond well to standard chemotherapy, whereas those with complex karyotypes or TP53 mutations typically have a worse prognosis and may require more intensive treatment regimens or experimental therapies. Advances in our understanding of cytogenetic abnormalities have led to the development of targeted therapies that specifically address the molecular mechanisms underlying these genetic changes. For instance, the success of TKIs in treating CML with the BCR-ABL fusion gene exemplifies the potential of precision medicine in leukemia. Similarly, therapies targeting specific genetic alterations in AML and ALL are continually being developed and refined, offering hope for improved outcomes in patients with these malignancies.

HIV and Its Impact on Leukemia

Human Immunodeficiency Virus (HIV) infection has a profound impact on the immune system, leading to acquired immunodeficiency syndrome (AIDS) in advanced stages. HIV targets and depletes CD4+ T cells, essential components of the immune response, resulting in immunosuppression and increased susceptibility to opportunistic infections and malignancies, including leukemia. The interplay between HIV and leukemia presents unique clinical challenges, influencing disease progression, treatment options, and overall patient outcomes. ³⁶⁻³⁹ Leukemia, a hematologic malignancy characterized by the proliferation of abnormal white blood cells, is classified into various subtypes, including acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), and chronic myeloid leukemia (CML). The development of leukemia in HIV-infected individuals is associated with both direct and Citation: Obeagu EI. The Relationship Between Body Mass Index and Cytogenetic Abnormalities in Leukemia Patients with HIV: A Review. *Elite Journal of Haematology*, 2024; 2(6): 1-15

indirect effects of the virus on hematopoietic cells and the bone marrow microenvironment. HIV-induced chronic immune activation and inflammation can contribute to genomic instability and the transformation of hematopoietic cells into malignant clones. HIV-infected individuals are at a higher risk of developing leukemia due to several factors. 40 Chronic immune activation and systemic inflammation, driven by ongoing HIV replication and co-infections, create a protumorigenic environment. Additionally, the immunosuppressive effects of HIV impair immune surveillance, reducing the ability of the body to detect and eliminate pre-malignant and malignant cells. Antiretroviral therapy (ART), while crucial for managing HIV infection, has also been implicated in altering cancer risk, potentially through metabolic changes and effects on the immune system.

The clinical presentation and progression of leukemia in HIV-infected patients can differ from those in the general population. 41 HIV-related immunosuppression may mask typical symptoms of leukemia, leading to delays in diagnosis and treatment. Moreover, HIV-infected individuals often present with more advanced stages of leukemia and may have a higher burden of cytogenetic abnormalities, which are known to influence prognosis and treatment response. Common cytogenetic abnormalities in leukemia, such as translocations and deletions, may occur more frequently or with greater complexity in the context of HIV infection. Treatment of leukemia in HIV-infected patients requires a multidisciplinary approach that addresses both malignancy and viral infection. 42 Antiretroviral therapy (ART) is essential to control HIV replication and improve immune function, but it must be carefully managed alongside chemotherapy and other cancer treatments to minimize drug-drug interactions and cumulative toxicity. HIV-infected leukemia patients often have comorbidities and a higher risk of treatment-related complications, necessitating close monitoring and supportive care. The impact of HIV on the bone marrow microenvironment further complicates leukemia treatment. HIV can infect bone marrow stromal cells, altering the production of hematopoietic growth factors and cytokines, which can disrupt normal hematopoiesis and support leukemic cell survival and proliferation. Additionally, HIVrelated myelosuppression can exacerbate the cytopenias associated with leukemia and its treatment, increasing the risk of infections and bleeding complications. 43-45

HIV-related factors, such as ART adherence and viral load control, significantly influence leukemia outcomes. Patients with well-controlled HIV infection, evidenced by undetectable viral loads and preserved CD4+ T cell counts, generally have better leukemia treatment outcomes compared to those with uncontrolled HIV. Effective management of HIV can enhance immune recovery, improve tolerance to cancer therapy, and reduce the risk of opportunistic infections, thereby improving overall survival. Despite advances in the treatment of both HIV and leukemia, research specifically focused on the intersection of these conditions remains limited. There is a need for more comprehensive studies to understand the unique biological interactions between HIV and leukemia, and to develop optimized treatment protocols that consider the dual burden of these diseases. Such research should aim to identify biomarkers that predict treatment

response and disease progression, as well as to evaluate the long-term outcomes of HIV-infected leukemia patients. 49-51

BMI and Cytogenetic Abnormalities in Leukemia Patients with HIV

The relationship between Body Mass Index (BMI) and cytogenetic abnormalities in leukemia patients with HIV is a complex and emerging area of research. Both BMI and cytogenetic abnormalities independently influence the prognosis and treatment outcomes in leukemia, and their interplay becomes even more critical in the context of HIV infection. Understanding how BMI impacts the cytogenetic landscape in HIV-infected leukemia patients could provide insights for developing personalized treatment strategies and improving patient outcomes. BMI, as a measure of body fat, affects overall health and disease outcomes, including in cancer.⁵² Obesity (high BMI) has been associated with an increased risk of developing various cancers, including leukemia, due to factors like chronic inflammation, insulin resistance, and altered levels of adipokines, which can promote tumorigenesis. Conversely, underweight status (low BMI) is often linked to malnutrition, weakened immune function, and poorer overall health, which can adversely affect cancer prognosis and treatment tolerance. Cytogenetic abnormalities are genetic changes within the chromosomes of leukemia cells that drive cancer progression.⁵³ These abnormalities can include translocations, deletions, duplications, and other structural changes. Specific cytogenetic profiles are associated with different leukemia subtypes and have significant prognostic implications. For instance, the presence of the Philadelphia chromosome (BCR-ABL fusion gene) in chronic myeloid leukemia (CML) or certain translocations in acute myeloid leukemia (AML) can guide treatment decisions and predict outcomes.

HIV infection complicates the management of leukemia due to the virus's impact on the immune system. HIV-induced immunosuppression and chronic inflammation can contribute to the development and progression of malignancies, including leukemia. HIV-infected individuals often experience more aggressive disease courses and may present with more advanced stages of leukemia. The management of these patients requires a careful balance of antiretroviral therapy (ART) to control HIV and chemotherapy to treat leukemia, along with the management of potential drug-drug interactions and cumulative toxicities. Feesearch suggests that BMI may influence the type and prevalence of cytogenetic abnormalities in leukemia patients with HIV. Obesity-related factors such as chronic inflammation and metabolic dysregulation could affect the genomic stability of hematopoietic cells, potentially leading to different cytogenetic profiles compared to those in normal-weight individuals. For example, obese leukemia patients might exhibit a higher frequency of specific genetic alterations that promote cancer cell survival and proliferation. Conversely, underweight patients may have a compromised immune system and metabolic environment, affecting the mutation landscape differently.

Clinical Implications

Personalized treatment strategies that consider BMI and cytogenetic profiles could improve outcomes. For instance, nutritional interventions to optimize BMI in underweight patients might enhance their resilience to treatment and reduce complications. In obese patients, targeting metabolic pathways involved in cancer progression could be beneficial. Despite the potential importance of this relationship, research in this specific area is limited.⁵⁷ Most studies focus on the general population of leukemia patients or the impact of HIV on cancer outcomes without explicitly considering the role of BMI. Comprehensive studies are needed to investigate how BMI influences cytogenetic abnormalities in HIV-infected leukemia patients. These studies should aim to elucidate the underlying mechanisms driving these interactions and identify biomarkers that could guide personalized treatment approaches. Several mechanisms could explain the influence of BMI on cytogenetic abnormalities in leukemia patients with HIV.⁵⁸ Obesity is associated with chronic low-grade inflammation, which can lead to increased oxidative stress and DNA damage, promoting genomic instability. Additionally, adipokines such as leptin and adiponectin, which are dysregulated in obesity, may directly affect hematopoietic cells and the bone marrow microenvironment. Conversely, malnutrition and low BMI could lead to immune suppression and increased susceptibility to genetic mutations due to a lack of essential nutrients required for DNA repair and cellular maintenance.

These insights can enhance the personalization of treatment strategies, improve patient outcomes, and optimize healthcare resource utilization. Integrating BMI assessment into the treatment planning for leukemia patients with HIV can help tailor therapies. ⁵⁹ For example, dose adjustments for chemotherapy may be necessary to account for the pharmacokinetic changes in obese or underweight patients. Nutritional interventions might also be important to support underweight patients, ensuring they have the physiological reserves to withstand intensive treatments. Detailed cytogenetic analysis should be a standard part of the diagnostic workup. Identifying specific genetic abnormalities can guide the use of targeted therapies, such as tyrosine kinase inhibitors for Philadelphia chromosome-positive CML, or all-trans retinoic acid for acute promyelocytic leukemia.

Effective antiretroviral therapy (ART) is critical for controlling HIV and improving immune function. ART regimens should be carefully selected to minimize interactions with chemotherapy drugs and manage potential toxicities. Continuous monitoring of HIV viral load and CD4+ T cell counts is essential to ensure that HIV remains well-controlled during leukemia treatment. HIV-infected patients often present with multiple comorbidities. Comprehensive management plans should address these conditions to reduce the risk of complications during leukemia treatment. This includes monitoring for cardiovascular diseases, diabetes, and other obesity-related conditions in overweight patients, and providing nutritional and immune support for underweight individuals. For underweight patients or those experiencing treatment-related weight loss, nutritional support is crucial. This might involve dietary modifications, supplementation, and potentially the involvement of a dietitian to create individualized nutrition plans. Encouraging appropriate physical activity can help manage weight, improve immune function, and enhance Citation: Obeagu EI. The Relationship Between Body Mass Index and Cytogenetic Abnormalities in Leukemia Patients with HIV: A Review. *Elite Journal of Haematology*, 2024; 2(6): 1-15

overall well-being. Exercise programs should be tailored to the patient's capabilities and health status, particularly for those with mobility limitations due to obesity or weakness from being underweight.⁶⁰

Future Research Directions

Despite the significant clinical relevance, research specifically addressing the relationship between BMI, cytogenetic abnormalities, and leukemia in HIV-infected patients remains limited. Future studies should aim to fill these gaps and provide a more comprehensive understanding of the interactions at play. Conducting large-scale, longitudinal studies to investigate how BMI influences the prevalence and type of cytogenetic abnormalities in leukemia patients with HIV. These studies should aim to include diverse patient populations to understand the impact of different genetic, lifestyle, and environmental factors. Investigating the underlying biological mechanisms that link BMI with cytogenetic changes in the context of HIV and leukemia. This could involve studying the effects of obesity-related inflammation, adipokines, and metabolic dysregulation on genomic stability and cancer progression.

Identifying biomarkers that predict treatment response and disease progression in leukemia patients with HIV. Biomarkers related to BMI, such as specific adipokines or inflammatory markers, could help guide personalized treatment strategies and improve prognostication. Designing and implementing clinical trials to evaluate the effectiveness of interventions aimed at optimizing BMI in leukemia patients with HIV. This could include nutritional support programs for underweight patients, weight management strategies for obese patients, and the integration of exercise and lifestyle modifications into standard care. Developing and testing integrative treatment models that combine ART, chemotherapy, targeted therapies, and supportive care tailored to the BMI and cytogenetic profile of each patient. These models should aim to enhance the coordination of care and improve overall treatment outcomes. Utilizing advanced genomic and proteomic technologies to perform detailed profiling of leukemia cells in HIV-infected patients. This can provide deeper insights into the molecular alterations associated with different BMI categories and help identify novel therapeutic targets.

Conclusion

The intricate relationship between Body Mass Index (BMI) and cytogenetic abnormalities in leukemia patients with HIV underscores the importance of personalized and comprehensive medical care. Both BMI and cytogenetic profiles independently influence disease progression, treatment response, and overall prognosis. In the context of HIV infection, these factors interplay in unique ways, posing additional challenges and complexities in the management of leukemia. High and low BMI each present distinct risks and complications that can affect the treatment and outcomes of leukemia patients. Obesity is associated with chronic inflammation and metabolic dysregulation, which can contribute to genomic instability and potentially lead to more aggressive Citation: Obeagu EI. The Relationship Between Body Mass Index and Cytogenetic Abnormalities in Leukemia Patients with HIV: A Review. *Elite Journal of Haematology*, 2024; 2(6): 1-15

disease phenotypes. Conversely, underweight patients often face malnutrition and weakened immune systems, impairing their ability to withstand intensive cancer treatments. Cytogenetic abnormalities, which are key drivers of leukemia pathogenesis, have significant prognostic implications and guide therapeutic decisions. In HIV-infected patients, the presence of such abnormalities may be influenced by the virus-induced immunosuppression and chronic inflammatory state, further complicating the disease landscape. The management of leukemia in these patients requires a nuanced approach that balances antiretroviral therapy (ART) for HIV control with chemotherapy and other cancer treatments, while also addressing potential drug-drug interactions and cumulative toxicities.

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