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HIV: Current Research

Perspective

Exploring Drug-Drug Interactions between Cancer Treatments and Active Antiretroviral Therapy in Medicare

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DESCRIPTION

Patients with comorbid cancer and HIV face complex treatment challenges due to potential Drug-Drug Interactions (DDIs) between cancer therapies and Active Antiretroviral Treatments (ARTs). The growing population of Medicare-enrolled patients with dual diagnoses necessitates a deeper understanding of these interactions to optimize clinical outcomes. This article explores the prevalence, mechanisms, clinical implications, and management strategies for DDIs in this vulnerable group. Advances in ART have significantly increased life expectancy for People Living with HIV (PLWH), leading to a higher incidence of age-related comorbidities, including cancer. According to Medicare data, non-AIDS-defining cancers, such as lung, colorectal, and breast cancers, are increasingly diagnosed in this population. Cancer therapy in PLWH often involves multimodal treatments, including chemotherapy, targeted therapy, and immunotherapy, which are frequently administered alongside lifelong ART. The potential for DDIs arises from overlapping metabolic pathways and pharmacodynamics effects between ARTs and cancer therapies. Key mechanisms include:

Protease Inhibitors (PIs) and Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs) are metabolized *via* cytochrome P450 enzymes, particularly CYP3A4. Many chemotherapeutic agents, such as vinca alkaloids, taxanes, and Tyrosine Kinase Inhibitors (TKIs), also rely on CYP450 pathways, leading to competitive inhibition or induction. CYP3A4 induction by NNRTIs, such as efavirenz, can decrease the plasma concentrations of certain chemotherapeutic agents, compromising their efficacy. For example, the TKI erlotinib shows reduced activity when co-administered with efavirenz, potentially diminishing anti-cancer effects. Protease inhibitors, such as ritonavir, can inhibit CYP3A4, leading to elevated levels of cancer drugs and heightened toxicity. Paclitaxel, when co-administered with ritonavir, may result in severe neuropathy or myelosuppression. Immunotherapies, including Immune Checkpoint Inhibitors (ICIs), pose unique challenges in PLWH. ART-induced immune reconstitution may amplify immune-related Adverse Events (irAEs), complicating cancer treatment.

Complex regimens and overlapping toxicities can negatively impact adherence to both ART and cancer therapy, reducing overall treatment effectiveness and patient quality of life.

Conducting a detailed assessment of all medications, including ARTs, cancer therapies, and supportive treatments, is essential to identify potential DDIs. Clinical decision support tools, such as drug interaction databases, can aid in predicting and managing interactions. Tailoring cancer treatments to minimize interaction risks may involve selecting alternative agents with lower DDI potential. For instance, using capecitabine instead of fluorouracil in patients on CYP3A4 inhibitors. Regular monitoring of drug levels can help adjust dosages to maintain therapeutic efficacy while minimizing toxicity. TDM is particularly useful for TKIs and certain PIs. Engaging oncologists, infectious disease specialists, pharmacists, and primary care providers ensures a coordinated approach to managing DDIs. Educating patients about the importance of adherence and potential side effects can empower them to participate actively in their care. Integrase Strand Transfer Inhibitors (INSTIs), such as dolutegravir, have a lower DDI profile compared to PIs and NNRTIs, making them promising options for PLWH undergoing cancer treatment. The development of targeted therapies and antibody-drug conjugates offers potential for reduced DDI risk due to their unique mechanisms of action. Leveraging pharmacogenomic data to personalize treatment based on genetic variants affecting drug metabolism and transport may enhance safety and efficacy. Large-scale studies using Medicare data can provide insights into the prevalence and outcomes of DDIs in this population, guiding clinical practice and policy.

CONCLUSION

Managing DDIs between cancer therapies and ARTs among Medicare-enrolled patients with cancer and HIV is a multifaceted challenge requiring a proactive and personalized approach. By integrating pharmacological knowledge, clinical expertise, and patient-centered care, healthcare providers can navigate these complexities to improve outcomes. Future research and collaboration are essential to advance understanding and develop innovative strategies for this growing patient population.

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