Zidovudine (Retrovir)

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Drug Summary

Zidovudine, a thymidine analogue nucleoside reverse transcriptase inhibitor (NRTI), was approved in 1987 by the United States FDA as the first antiretroviral treatment for HIV infection. Zidovudine served as the cornerstone of HIV treatment in the early years of antiretroviral therapy, first as monotherapy and later as part of combination regimens. Due to toxicity, newer antiretroviral agents that cause fewer short-term and long-term side effects have replaced zidovudine and, unless there is a clear indication, patients taking this medication should be strongly encouraged to change it to a newer option. Zidovudine frequently causes gastrointestinal side effects, mitochondrial toxicity leading to lipodystrophy and lactic acidosis, and bone marrow suppression leading to anemia and neutropenia. According to the HHS Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents, zidovudine (with lamivudine) is designated as not recommended as initial therapy due to greater toxicity than recommended NRTIs. Zidovudine was the first antiretroviral medication shown to reduce mother-to-child transmission of HIV. In the mid 1990’s, the Centers for Disease Control and Prevention showed that zidovudine monotherapy significantly reduced the risk of HIV transmission in health care workers after percutaneous exposure to HIV; this study led to the widespread use of zidovudine for postexposure prophylaxis for years, but its use in this setting has now been supplanted by newer and better tolerated agents.

Key Clinical Trials

Early, double-blind, placebo-controlled trials that included individuals with advanced HIV infection demonstrated that, at least in the short term, zidovudine decreased mortality and opportunistic infections and increased CD4 count as compared to placebo [ACTG 002] and [ACTG 016]. Similarly, in asymptomatic individuals with CD4 count below 500 cells/mm$^3$, zidovudine use led to short term benefits (delayed progression to AIDS) as compared to placebo [ACTG 019]. Subsequent studies demonstrated more sustained benefits of combination therapy with zidovudine, first as part of dual therapy and later as part of triple therapy [ACTG 290], [ACTG 298], [ACTG 116], [ACTG 320], [START], and [ACTG 384]. Later trials that compared zidovudine-based triple therapy to triple therapy with newer NRTIs, such as tenofovir disoproxil fumarate, demonstrated reduced toxicity with the newer agents [GS-934]. In a landmark, randomized, placebo-controlled trial, investigators established that zidovudine treatment significantly reduced the risk of mother-to-child transmission of HIV in pregnant women with a CD4 count above 200 cells/mm$^3$; in this trial, the zidovudine treatment
consisted of oral zidovudine for the mother after week 14 of pregnancy, intrapartum intravenous zidovudine, and oral zidovudine postpartum for the infant [ACTG 076].

Use In Pregnancy

In the HHS Perinatal Guidelines section Recommendations for Use of Antiretroviral Drugs During Pregnancy (last updated October 19, 2017), zidovudine, as part of the fixed-dose combination tablet zidovudine-lamivudine, is listed as an Alternative Two-NRTI backbone combination in the category Alternative Initial Regimens in Pregnancy.

- For additional information regarding the safety and toxicity of zidovudine in pregnancy see the HHS Perinatal Guidelines summary on Zidovudine.

Resistance

For a listing of the most common clinically significant mutations associated with zidovudine (ZDV) resistance, see the NRTI Resistance Notes on the Stanford University HIV Drug Resistance Database.

Key Drug Interactions

For complete information on zidovudine-related drug interactions, see the Drug Interactions section in the Zidovudine (Retrovir) Prescribing Information.

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