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Perspective

Characteristics and Prognosis of Cyclophosphamide

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DESCRIPTION

Cyclophosphamide is used to treat cancers of the ovaries, breast, blood and lymph system, and nerves (mainly in children). Cyclophosphamide is also used to cure retinoblastoma (a type of eye cancer that primarily affects children), multiple myeloma (bone marrow cancer), and mycosis fungoides (tumors on the skin). It belongs to the class of cancer medicines known as alkylating agents. Cyclophosphamide is also used to treat some types of kidney disease. Cyclophosphamide inhibits cancer cell growth, causing the body to kill the cancer cells. Since cyclophosphamide may affect the growth of normal body cells, other side effects may occur. Some of these may be serious and must be reported to the doctor. Other side effects, like as hair loss, may be minor yet cause concern. Some side effects may not appear for months or years after taking the medication.

Lymphomas, myelomas, leukemia, mycosis fungoides, neuroblastoma, ovarian adenocarcinoma, retinoblastoma, and breast cancer are all managed with cyclophosphamide is an antineoplastic and immunosuppressive alkylating nitrogen mustard precursor that must be activated in the liver to form active aldophosphamide. It has been used to treat lymphoma and leukemia. Cyclophosphamide can also cause sterility, birth defects, mutations, and cancer. Cyclophosphamide is used to treat malignant lymphomas, multiple myeloma, leukemia's, mycosis fungoides (advanced disease), neuroblastoma (disseminated disease), ovary adenocarcinoma, retinoblastoma, and breast cancer. It is also approved to treat of biopsy-proven minimal change nephrotic syndrome in patients.

Cyclophosphamide is an antineoplastic agent in the alkylating agent class that is used to treat various types of cancers. Alkylating agents get their name from their ability to add alkyl groups to many electronegative groups under cell conditions. They stop cancer growth by directly damaging DNA by cross-linking guanine bases in DNA double-helix strands. This stops the strands from unspooling and splitting. Cells can no longer divide as this is needed for DNA replication. As such, these drugs add methyl or other alkyl groups in molecules where they do not belong, preventing proper use by base pairing and leading in DNA miscoding. Alkylating agents have no effect on the cell cycle. Alkylating agents work through three separate mechanisms, all of which result in the same end result is disruption of DNA function and cell death.

Alkylating agents operate through 3 separate mechanisms: 1) Alkyl group attachment to DNA bases, resulting in strand breaks by repair enzymes in their attempts to replace the alkylated bases, preventing DNA synthesis and RNA transcription from the affected DNA; 2) DNA damage via cross-link formation (bonds between atoms in the DNA) which prevents DNA from being separated for synthesis or transcription, and 3) the induction of nucleotide mispairing, which leads in mutations. There are no dose-dependent changes in the protein bound cyclophosphamide at 20%. Some metabolites are protein bound to a greater than 60% extent. The liver is responsible for metabolism and activation. Cytochrome P450 isoforms CYP2A6, 2B6, 3A4, 3A5, 2C9, 2C18, and 2C19 activate 75% of the drug. The enzyme with the highest 4-hydroxylase activity is CYP2B6. Cyclophosphamide is activated, resulting in the formation of active metabolites such as phosphoramide mustard and acrolein. Following repeated treatment, cyclophosphamide appears to induce its own metabolism, resulting in an overall increase in clearance, increased formation of 4-hydroxyl metabolites, and lower t1/2 values. Cytochrome P450 3A4: Patients with this genotype have a high metabolism of cyclophosphamide to its active form and a lower disease-free survival time when using cyclophosphamide to treat node-positive breast cancer. Cytochrome P450 2B6: This genotype does have a reduced ability to convert cyclophosphamide to its active form.

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