Treatment of Hematopoietic Malignancy

	Drug	MOA	Uses	Side Effects	Notes
Antitumor Antibiotics	Bleomycin	-Induces free radical formation → breaks DNA strand	-Testicular cancer -Hodgkin lymphoma	-Pulmonary fibrosis -Flagellate erythema -**Minimal** myelosuppression	
	Doxorubicin & Daunorubicin	-Intercalates into DNA → preventing RNA synthesis	-Solid tumors, leukemias, lymphomas	- Cardiotoxicity (dilated cardiomyopathy) -Myelosuppression -Alopecia	- Dexrazoxane (iron chelating agent) is used to prevent cardiotoxicity, but it decreases the effect
Antimetabolites	Cladribine	-Purine analog → multiple mechanisms (e.g. inhibition of DNA polymerase, DNA strand breaks)	Hairy cell leukemia	- Myelosuppression -Nephrotoxicity -Neurotoxicity	
	Cytrabine	-Pyrimidine analog → DNA chain termination -At higher concentrations, inhibits DNA Polymerase	- Leukemias (AML), lymphomas	- Myelosuppression with megaloblastic anemia. -**CYT**arabine causes pan**CYT**openia.	
	Methotrexate	- Folic acid analog that competitively inhibits dihydrofolate reductase → decreases dTMP → decreases DNA synthesis	- Cancers: leukemias (ALL), lymphomas, choriocarcinoma, sarcomas. -Non-neoplastic: ectopic pregnancy, medical abortion (with **misoprostol**), rheumatoid arthritis, psoriasis, IBD, vasculitis	- Myelosuppression, which is reversible with leucovorin "rescue." -Hepatotoxicity -Mucositis (e.g. mouth ulcers) -Pulmonary fibrosis -Folate deficiency, which may be **teratogenic** (neural tube defects) without supplementation -Nephrotoxicity	
Alkylating Agents	Busulfan	-Cross-links DNA	- Used to ablate patient's bone marrow before bone marrow transplantation	- Severe myelosuppression (in almost all cases), pulmonary fibrosis, hyperpigmentation	

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	Drug	MOA	Uses	Side Effects	Notes
Alkylating Agents	Procarbazine	- Cell cycle phase–nonspecific alkylating agent, mechanism not yet defined	- Hodgkin lymphoma, brain tumors	- Bone marrow suppression -Pulmonary toxicity -Leukemia, -Disulfiram-like reaction	
	Cyclo-phosphamide Ifosfamide	- Cross-link DNA at guanine. (Require bioactivation by liver)	- Solid tumors, leukemia, lymphomas, rheumatic disease (e.g. SLE, granulomatosis with polyangiitis).	- Myelosuppression -SIADH -Fanconi syndrome (ifosfamide) -Hemorrhagic cystitis and bladder cancer, **prevented** with **Mesna** and adequate hydration	- A nitrogen mustard ***Mesna**: (sulfhydryl group of mesna binds toxic metabolites)
Microtubule Inhibitors	Vincristine	-Vinca alkaloids bind β-tubulin and inhibit its polymerization into microtubules → prevent mitotic spindle formation **(M-phase arrest)** → cell-cycle specific	-Solid tumors, leukemias, Hodgkin and non-Hodgkin lymphomas	-**Vincristine**: neurotoxicity (areflexia, peripheral neuritis), constipation (including paralytic ileus). Crisps the nerves **-Vinblastine**: bone marrow suppression → blasts the BM	
	Vinblastine				
Miscellaneous	Hydroxyurea	- Inhibits ribonucleotide reductase → DNA Synthesis (S-phase specific)	-Myeloproliferative disorders (e.g., CML, polycythemia vera), sickle cell (**increases HbF**).	- **Severe** myelosuppression	
	Imatinib & Dasatinib	- Inhibitor of Tyrosine Kinase domains of Bcr-Abl oncoprotein (encoded by Philadelphia chromosome fusion gene in CML), PDGFR, and c-kit (common in GI stromal tumors)	- Chronic myelogenous leukemia, GI stromal tumors (GIST)	- Safe drugs but can cause fluid retention	
	Rituximab	- Monoclonal antibody against CD20, which is found on most B-cell neoplasms	-Non-Hodgkin lymphoma, CLL, ITP, rheumatoid arthritis	- Neurotoxic: carries the risk of progressive multifocal leukoencephalopathy (by reactivation of JC virus) and opportunistic infections	- Must screen for Hepatitis B and C before giving Rituximab **(Risk for Hepatitis B reactivation)**

❋ Check slide (14) for key chemotoxicities

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