Common Chemotherapies used In Bone Cancer

Type of chemotherapy	Examples	Mode of action
Anthracycline antibiotics	Doxorubicin	• It binds with DNA and intercalate between the DNA nitrogenous bases. This causes the uncoiling of the structure of the DNA. • The DNA consists of two strands of genetic material (polynucleotides) coiled in a spiral way. • The RNA is one strand of genetic material. • Therefore, it affects the synthesis of DNA and RNA.
DNA Alkylating agents	Cisplatin Carboplatin Cyclophosphamide Ifosfamide (related to cyclophosphamide) Temozolomide	• It forms crosslinks with N7 guanine residues (type of base found in DNA and RNA). • It intercalates DNA and produces toxic (reactive oxygen species) • It cleaves the transcription factor (CREB1) – this affects the transcription of target genes involved in cellular processes. • This causes interstrand and intrastrand breaks in the DNA molecule. • It affects how cell divides, copy (replicate), grow and die (apoptosis)

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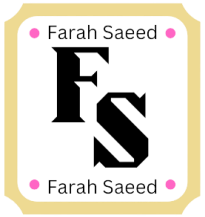
Topoisomerase I inhibitor	Irinotecan topotecan	• It stabilises topoisomerase 1 and DNA complexes. • This causes single strand breaks and progresses to double strand breaks leading to apoptosis (cell death). ***Role of Topoisomerase*** • Topoisomerase regulates supercoiling of DNA needed for transcription and replication. • Positive supercoiling causes the tightening and inhibits strand separation. • Negative supercoiling causes the extension of the DNA strand separation. This produces irregular nucleic acid structures and DNA double strand breaks. • The role of topoisomerase I is to cleave one strand of DNA through transient break.
Topoisomerase II inhibitor	Etoposide Doxorubicin	• This stabilises cleavage complex with DNA. • It creates transient double stranded breakage of DNA. • This causes DNA damage, DNA replication and transcription.



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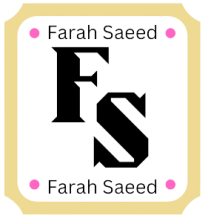
Microtubule- targeting agents	Vincristine (microtubule disruptor)	It commonly binds to tubulin. Tubulin is the building block/monomer of microtubule. The normal role of microtubule is in growth, motility/movement and cell division. Affecting the structure of microtubule prevents its production and causes cell arrest at metaphase stage in cell division. It also prevents cell replication and cell death. Cell death is achieved through the tumour suppressor protein p53 where it targets key checkpoints in the cell cycle: G1/S checkpoint - p53-independent death. G2/M checkpoint – p53 dependent death



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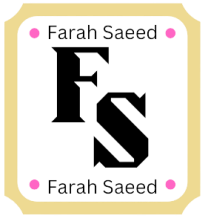
Microtubule-targeting agent	Docetaxel	A type of taxane chemical. It stabilises microtubule similar to paclitaxel. This is achieved by stimulating phosphorylation of proteins and inducing survival. Key targets: Bcl2. COX2 and Akt. This causes cell death. It also affects the production of blood vessels (angiogenesis) affecting the nutrients supply of the cancer cells.
Anti-metabolites	Gemcitabine	mimics a natural chemical and prevents its use in cells. It disrupts DNA formation by mimicking a DNA building block. This slows or stops the growth of cancer cells and other rapidly growing cells.



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Anti metabolite (di hydrofolate reductase inhibtiors)	methotrexate	It inhibits DHFR and THF production Folate needed to make nitrogenous bases. The nitrogenous bases form part of the DNA structure and therefore, the production of DNA will be affected. Dihydrofolate reductase (DHFR) is reduced to dihydrofolate and is further reduced to tetrahydrofolate (THF).
	capecitabine	It is metabolised to 5-flouracil. Capecitabine inhibits the enzyme thymidylate synthase which is involved in the production of thymidylate. This inhibits RNA synthesis.