

Chemotherapy of Cancer (Neoplasms)

Introduction

- Cancer chemotherapy refers to the use of cytotoxic drugs to kill or inhibit the growth of malignant (neoplastic) cells.
- These drugs act by interfering with cell division, DNA/RNA synthesis, or specific molecular targets essential for tumor growth.
- Cancer cells proliferate rapidly, often faster than normal cells.
- Chemotherapeutic agents exploit this difference but lack absolute selectivity, leading to toxicity in healthy rapidly dividing tissues (e.g. bone marrow, GI tract, hair follicles).
- Chemotherapy may be:
 - **Curative** (e.g., acute leukemia, testicular cancer)
 - **Adjuvant/Neoadjuvant** (before/after surgery)
 - **Palliative** (for symptom control in advanced disease)
 - Used in **combination** with radiation, immunotherapy, or targeted therapy.

Classification of Anticancer Drugs

A. Cell Cycle–Specific (CCS) Agents

Phase Targeted	Drug Classes
S-phase	Antimetabolites (e.g., methotrexate, 5-FU)
M-phase	Vinca alkaloids (vincristine), Taxanes

B. Cell Cycle–Non-Specific (CCNS) Agents

Drug Classes
Alkylating agents (e.g., cyclophosphamide)
Anthracyclines (e.g., doxorubicin)
Platinum compounds (e.g., cisplatin)

C. Other Major Categories

- **Antimetabolites:** Methotrexate, 5-Fluorouracil (5-FU), Cytarabine
- **Alkylating agents:** Cyclophosphamide, Ifosfamide, Busulfan
- **Antitumor antibiotics:** Doxorubicin, Bleomycin
- **Plant alkaloids:** Vincristine, Vinblastine, Paclitaxel
- **Topoisomerase inhibitors:** Etoposide, Irinotecan
- **Hormonal agents:** Tamoxifen, Anastrozole, Flutamide

- **Targeted therapy:** Imatinib, Erlotinib, Trastuzumab
- **Immunotherapy:** Nivolumab, Pembrolizumab (immune checkpoint inhibitors)

Mechanism of Action (Selected Examples)

Class	Mechanism
Alkylating agents	Form covalent DNA cross-links → strand breakage and apoptosis
Antimetabolites	Mimic DNA bases → inhibit enzymes in DNA synthesis (e.g., thymidylate synthase)
Topoisomerase inhibitors	Inhibit enzymes needed for DNA uncoiling → DNA strand breaks
Microtubule inhibitors	Disrupt mitotic spindle → mitosis arrest (e.g., vincristine)
Platinum compounds	Form intra/inter-strand DNA cross-links → inhibit replication
Anthracyclines	Intercalate into DNA + generate free radicals + topoisomerase inhibition
Monoclonal antibodies	Bind specific cancer cell receptors (e.g., HER2) → immune-mediated lysis
Checkpoint inhibitors	Block PD-1/PD-L1 → restore T-cell immune response

Pharmacokinetics (General Overview)

Feature	Characteristics
Absorption	Many agents are IV only (poor oral bioavailability); some oral forms exist (e.g., capecitabine)
Distribution	Some cross BBB (e.g., lomustine); many do not. High volume of distribution for lipophilic drugs
Metabolism	Most are hepatically metabolized (CYP450, conjugation)
Excretion	Renal and/or biliary excretion; dose adjustment may be needed in organ dysfunction
Half-life	Varies widely (minutes to hours); dosing schedules depend on cell cycle phase targeted

Pharmacodynamics

- **Narrow therapeutic index**
- **Effectiveness** often measured by tumor size reduction, remission rate
- **Cytotoxic effects** are more pronounced in rapidly dividing cells
- **Resistance** can develop (e.g., via efflux pumps like P-glycoprotein)

Adverse Effects (Classically Affecting Rapidly Dividing Cells)

Common General Toxicities

System/Tissue	Toxicity
Bone marrow	Myelosuppression (anemia, neutropenia, thrombocytopenia)
GI tract	Nausea, vomiting, mucositis, diarrhea
Hair follicles	Alopecia
Reproductive	Infertility, amenorrhea
Others	Fatigue, anorexia

Agent-Specific Toxicities

Drug/Class	Specific Toxicity
Doxorubicin	Cardiotoxicity (dose-dependent, irreversible)
Cyclophosphamide	Hemorrhagic cystitis (prevent with mesna)
Bleomycin	Pulmonary fibrosis
Vincristine	Peripheral neuropathy
Cisplatin	Nephrotoxicity, ototoxicity
Methotrexate	Hepatotoxicity, nephrotoxicity, mucositis
Paclitaxel	Neuropathy, hypersensitivity
Checkpoint inhibitors	Autoimmune reactions (e.g., colitis, pneumonitis)

Contraindications

Drug/Class	Contraindications
Most cytotoxics	Pregnancy, active infections, severe organ dysfunction
Cisplatin	Renal impairment
Bleomycin	Preexisting lung disease
Doxorubicin	Cardiac dysfunction
Methotrexate	Liver disease, pregnancy, pleural effusion (delayed clearance)

Therapeutic Uses (By Cancer Type)

Cancer Type	First-Line Chemotherapy Regimens
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Acute lymphoblastic leukemia (ALL)	Vincristine + prednisone + anthracyclines
Breast cancer	Cyclophosphamide + Doxorubicin + 5-FU; ± trastuzumab (HER2+)
Hodgkin lymphoma	ABVD (Adriamycin, Bleomycin, Vinblastine, Dacarbazine)
Non-Hodgkin lymphoma	CHOP (Cyclophosphamide, Doxorubicin, Vincristine, Prednisone)
Testicular cancer	BEP (Bleomycin, Etoposide, Cisplatin)
Lung cancer	Cisplatin + Paclitaxel or Etoposide (non-small cell)
Colorectal cancer	FOLFOX (5-FU + leucovorin + oxaliplatin)
Ovarian cancer	Paclitaxel + Carboplatin
CML (chronic myeloid leukemia)	Imatinib (BCR-ABL tyrosine kinase inhibitor)
Melanoma, NSCLC (PD-L1+)	Nivolumab, Pembrolizumab (immune checkpoint inhibitors)

Drug Interactions

Drug/Class	Common Interactions
Methotrexate	NSAIDs, sulfonamides, probenecid ↓ excretion → toxicity
Cyclophosphamide	Additive toxicity with nephrotoxic drugs
Doxorubicin	↑ cardiotoxicity with trastuzumab or other cardiotoxins
Vincristine	CYP3A4 inhibitors ↑ neurotoxicity risk
Checkpoint inhibitors	Avoid immunosuppressants unless managing toxicity

Dose and Route of Administration

Chemotherapy is usually individualized based on body surface area (BSA), cancer type, and patient factors.

Drug/Class	Typical Dose & Route
Cyclophosphamide	500–1000 mg/m ² IV q3 weeks (or oral in low doses)
Doxorubicin	60–75 mg/m ² IV q21 days
Methotrexate	Varies from 20 mg/m ² to >1000 mg/m ² IV/IM/oral (with leucovorin rescue for high dose)
Cisplatin	50–100 mg/m ² IV every 3–4 weeks



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