💊 Other Cancer Drugs

🧬 Anticancer Monoclonal Antibodies (mAbs)

🔑 Key Concept

- Target extracellular molecules (receptors/ligands) 🎯
- Work by:
  - Blocking signaling pathways
  - Triggering immune destruction (ADCC by NK cells)
- Eliminated by macrophages (NOT liver/kidney) ❗

💡 Core Mechanism

Monoclonal antibodies bind specific targets → either:

- Directly inhibit tumor growth
- OR tag tumor cells for immune destruction

🔄 Flowchart: General Mechanism of mAbs

Monoclonal antibody → Binds specific extracellular target → Blocks receptor signaling (↓ tumor growth) + Activates immune system (ADCC via NK cells) → Tumor cell destruction 💀

📊 High-Yield Master Table

Drug	Target	Clinical Use	Adverse Effects
Alemtuzumab	CD52	CLL, MS	Infections, autoimmunity

Bevacizumab	VEGF	CRC, RCC, NSCLC	Bleeding, thrombosis
Cetuximab, Panitumumab	EGFR	CRC (RAS WT), H&N cancer	Rash, diarrhea
Rituximab	CD20	NHL, CLL, RA, ITP	Infusion reaction
Trastuzumab	HER2	Breast, gastric cancer	Cardiomyopathy
Pembrolizumab, Nivolumab	PD-1	Multiple cancers	Autoimmune toxicity
Atezolizumab, Durvalumab	PD-L1	Multiple cancers	Autoimmune toxicity
Ipilimumab	CTLA-4	Melanoma	Autoimmune toxicity

🧪 Drug-by-Drug Notes

🅰️ Alemtuzumab

💡 Mechanism

- Targets CD52 on lymphocytes → Causes cell lysis

📌 Clinical Uses

- CLL 🎯
- Multiple sclerosis

❗ Adverse Effects

- ↑ Risk of infections 🦠
- Autoimmunity (e.g., ITP)

2️⃣ Bevacizumab

💡 Mechanism

- Binds VEGF → Inhibits angiogenesis (blood vessel formation)

🔄 Flowchart: Anti-VEGF Action

Bevacizumab → Inhibits VEGF → ↓ new blood vessel formation → ↓ tumor blood supply → Tumor starvation → death

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📌 Clinical Uses

- Colorectal cancer 🎯
- RCC, NSCLC
- Retinopathy (angioproliferative)

❗ Adverse Effects

- Hemorrhage 🩸
- Thrombosis
- Impaired wound healing ⚠️

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- Avoid before/after surgery → poor healing

3️⃣ EGFR Inhibitors

(Cetuximab, Panitumumab)

💡 Mechanism

- Block EGFR signaling → ↓ cell proliferation

📌 Clinical Uses

- Metastatic CRC (RAS wild-type only ⚠️)
- Head & neck cancers

❗ Adverse Effects

- Acneiform rash (very common 💡)
- Diarrhea
- Elevated LFTs

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- RAS mutation → drug WON'T work ❗

4️⃣ Rituximab

💡 Mechanism

- Targets CD20 on B cells → Causes B-cell destruction

🔄 Flowchart: Rituximab Action

Rituximab → Binds CD20 on B cells → Immune activation (ADCC) → B-cell lysis → ↓ disease activity

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📌 Clinical Uses

- Non-Hodgkin lymphoma 🎯
- CLL
- Autoimmune diseases (RA, ITP, TTP, AIHA, MS)

❗ Adverse Effects

- Infusion reaction → Cytokine release → fever, chills, hypotension

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- Pre-treat with antihistamines to reduce reaction

S Trastuzumab

💡 Mechanism

- Targets HER2 receptor

📌 Clinical Uses

- HER2+ breast cancer 🎯
- Gastric cancer

❗ Adverse Effects

- Dilated cardiomyopathy ❤️ (often reversible)

🎯 Mnemonic

"Don't Trast HER, she will break your heart" ❤️

6️⃣ Immune Checkpoint Inhibitors

🔑 Key Concept

- Remove "brakes" on immune system → enhance T-cell activity ⚡

🔄 Flowchart: Checkpoint Inhibition

Tumor expresses PD-L1 → Binds PD-1 on T cells → Inhibits immune response

Checkpoint inhibitor given → Blocks PD-1/PD-L1 or CTLA-4 → T cells activated → Tumor cell destruction 💀

🟢 PD-1 Inhibitors

(Pembrolizumab, Nivolumab, Cemiplimab)

- Block PD-1 receptor on T cells

🔵 PD-L1 Inhibitors

(Atezolizumab, Durvalumab, Avelumab)

- Block PD-L1 on tumor cells

🟣 CTLA-4 Inhibitor

(Ipilimumab)

- Blocks CTLA-4 → ↑ T-cell activation early

📌 Clinical Uses

- Many cancers → NSCLC, RCC, melanoma, urothelial carcinoma

❗ Adverse Effects

- Autoimmune toxicity:
  - Dermatitis
  - Enterocolitis
  - Hepatitis
  - Pneumonitis 🫁
  - Endocrinopathies

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- Side effects = immune system attacking body

🔥 Comparison Table

Drug	Target	Key Effect	Signature Toxicity
Bevacizumab	VEGF	↓ angiogenesis	Bleeding
Rituximab	CD20	B-cell depletion	Infusion reaction
Trastuzumab	HER2	↓ tumor growth	Cardiomyopathy
EGFR inhibitors	EGFR	↓ proliferation	Rash
Checkpoint inhibitors	PD-1/PD-L1/CTLA-4	↑ immunity	Autoimmunity

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🔑 Must-Know Points

- mAbs target extracellular molecules
- Bevacizumab → anti-VEGF → ↓ angiogenesis

- Rituximab → CD20 → B-cell destruction
- Trastuzumab → HER2 → cardiotoxicity
- EGFR inhibitors → rash + require RAS wild-type
- Checkpoint inhibitors → autoimmune side effects

🧠 Quick Recall

mAbs → Target receptors → Types:

- VEGF → ↓ blood supply
- EGFR → ↓ proliferation
- CD20 → B-cell kill
- HER2 → ↓ tumor growth
- Checkpoints → ↑ immune response

→ Side effects = target-related toxicity ⚠️

🧪 Anticancer Small Molecule Inhibitors

🔑 Key Concept

- Target intracellular signaling pathways (unlike monoclonal antibodies 🎯)
- Usually inhibit tyrosine kinases or key enzymes
- Many are orally active 💊

💡 Core Mechanism (Big Picture)

Cancer cells rely on abnormal signaling pathways → these drugs block those signals → inhibit growth & induce apoptosis 💀

🔄 Flowchart: General Mechanism

Growth factor binds receptor → Activates intracellular signaling (kinases) → Cell proliferation

Small molecule inhibitor → Blocks kinase/enzyme → Signal stops → Cell cycle arrest → Apoptosis

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📊 Master Table

Drug/Class	Target	Clinical Use	Adverse Effects
Alectinib, Crizotinib	ALK	NSCLC	Edema, rash, diarrhea
Erlotinib, Gefitinib, Afatinib	EGFR	NSCLC	Rash, diarrhea
Imatinib, Dasatinib, Nilotinib	BCR-ABL	CML, ALL, GIST	Myelosuppression

Ruxolitinib	JAK1/2	Polycythemia vera	Bruising, ↑ LFTs
Bortezomib, Carfilzomib	Proteasome	Multiple myeloma	Neuropathy, zoster
Vemurafenib, Dabrafenib	BRAF	Melanoma	Rash, fatigue
Palbociclib	CDK4/6	Breast cancer	Myelosuppression
Olaparib	PARP	Breast, ovarian cancer	Myelosuppression

🧪 Drug-by-Drug Notes

1️⃣ ALK Inhibitors

(Alectinib, Crizotinib)

💡 Mechanism

- Inhibit ALK (anaplastic lymphoma kinase) → Blocks tumor growth signaling

📌 Clinical Use

- Non-small cell lung cancer (NSCLC) 🎯

❗ Adverse Effects

- Edema
- Rash
- Diarrhea

2️⃣ EGFR Inhibitors

(Erlotinib, Gefitinib, Afatinib)

💡 Mechanism

- Inhibit EGFR tyrosine kinase → ↓ cell proliferation

📌 Clinical Use

- NSCLC 🎯

❗ Adverse Effects

- Acneiform rash 💡
- Diarrhea

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- Rash = drug is working (marker of response)

3️⃣ BCR-ABL Inhibitors

(Imatinib, Dasatinib, Nilotinib)

💡 Mechanism

- Inhibit BCR-ABL tyrosine kinase → Blocks Philadelphia chromosome signaling

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🔄 Flowchart: CML Pathway

Philadelphia chromosome → BCR-ABL fusion protein → Constitutive tyrosine kinase activity → Uncontrolled proliferation

Imatinib → Inhibits BCR-ABL → Stops proliferation → Disease control

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📌 Clinical Uses

- CML (VERY high-yield 💯)
- ALL
- GIST (via c-KIT inhibition)

❗ Adverse Effects

- Myelosuppression 💉
- ↑ LFTs

- Edema
- Myalgias

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- First-line for CML

4️⃣ JAK Inhibitor

(Ruxolitinib)

💡 Mechanism

- Inhibits JAK1/2 → Blocks cytokine signaling

📌 Clinical Use

- Polycythemia vera 🎯

❗ Adverse Effects

- Bruising
- ↑ LFTs

🇸 Proteasome Inhibitors

(Bortezomib, Carfilzomib, Ixazomib)

💡 Mechanism

- Inhibit proteasome → Accumulation of abnormal proteins → Cell stress → apoptosis

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🔄 Flowchart: Proteasome Inhibition

Proteasome inhibited → Misfolded proteins accumulate → Cellular stress → G2-M arrest → Apoptosis

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📌 Clinical Uses

- Multiple myeloma 🎯
- Mantle cell lymphoma

❗ Adverse Effects

- Peripheral neuropathy 🧠
- Herpes zoster reactivation 🦠 → ↓ cell-mediated immunity

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- Give antiviral prophylaxis (e.g., acyclovir)

6️⃣ BRAF Inhibitors

(Vemurafenib, Dabrafenib, Encorafenib)

💡 Mechanism

- Inhibit BRAF kinase (MAPK pathway)

📌 Clinical Use

- Melanoma 🎯

⚠️ Important Note

- Often combined with MEK inhibitors (e.g., trametinib)

  → Prevent resistance

❗ Adverse Effects

- Rash
- Fatigue
- Diarrhea

7️⃣ CDK4/6 Inhibitor

(Palbociclib)

💡 Mechanism

- Inhibits CDK4/6 → Blocks transition from G1 → S phase

🔄 Flowchart: CDK Inhibition

CDK4/6 active → G1 to S progression → Cell division

Palbociclib → Inhibits CDK4/6 → Cell cycle arrest at G1 → Apoptosis

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📌 Clinical Use

- Breast cancer 🎯

❗ Adverse Effects

- Myelosuppression

- Pneumonitis

8️⃣ PARP Inhibitor

(Olaparib)

💡 Mechanism

- Inhibits PARP enzyme → ↓ DNA repair

🔄 Flowchart: PARP Inhibition

DNA damage occurs → Normally repaired by PARP

Olaparib → Inhibits PARP → DNA damage accumulates → Tumor cell death 💀

📌 Clinical Uses

- BRCA-associated cancers 🎯 → Breast, ovarian, pancreatic, prostate

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❗ Adverse Effects

- Myelosuppression
- Edema
- Diarrhea

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- Works best in BRCA mutation (defective DNA repair)

🔥 Comparison Table

Pathway	Drug	Key Idea	Classic Use
BCR-ABL	Imatinib	CML driver	CML
Proteasome	Bortezomib	Protein buildup	Myeloma
BRAF	Vemurafenib	MAPK pathway	Melanoma
CDK4/6	Palbociclib	Cell cycle arrest	Breast CA
PARP	Olaparib	DNA repair block	BRCA cancers

🔑 Must-Know Points

- Small molecule inhibitors → intracellular targets
- Imatinib → CML (BCR-ABL)
- Bortezomib → multiple myeloma + neuropathy

- Vemurafenib → melanoma (BRAF)
- Palbociclib → G1 arrest
- Olaparib → PARP inhibition (BRCA cancers)

🧠 Quick Recall

Cancer signaling → Kinase activation → Drugs block pathways:

- BCR-ABL → CML
- EGFR/ALK → lung cancer
- BRAF → melanoma
- Proteasome → myeloma
- PARP → DNA repair block

→ Result: cell death 💀

-> The End <-