Oral Anticancer Therapy

Oncology Nursing Symposium

Saturday, May 3rd 2025

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Outline

- Oral anticancer therapy logistics
- Cytotoxic chemotherapy
- Tyrosine Kinase Inhibitors (TKIs)
- Immunomodulating drugs (IMiDs) in multiple myeloma
- Hormone suppressing therapy in breast and prostate cancer

Treating Cancer: A Brief History

Hippocrates (Greek)
"Carcinos"
Galen (Greek)
"oncos"
Celsus (Roman)
"Cancer"

Theodor Bilroth
Sampson Handley
William Halstead
Stephen Paget

1896 Wilhelm Conrad Roentgen
X ray's discovered

1917 Mustard gas used in WWI

2001 Imatinib on the front cover of TIME

2004 first VEGF-targeted therapy approval (bevacizumab)

B.A. (Before Anesthesia) | 19th century: Surgery | 20th century: radiation and chemotherapy | 1990s – present: targeted and immune therapy

1840's General anesthesia

1940 Charles Huggins
Orchiectomy in prostate cancer

1956 First metastatic cancer cure from chemotherapy alone (choriocarcinoma)

1990s first approval of monoclonal antibody therapy (rituximab, trastuzumab)

2010 first approval of cellular therapy (Sipuleucel-T)

2011 first checkpoint inhibitor approval (ipilimumab)

Oral therapy logistics

And why nurses are so critical

IV vs PO

	IV	PO
Insurance Coverage	Medical benefit (e.g. Part B)	Pharmacy benefit (e.g. Part D)
Cost	Visit-based cost-sharing (co-pays, etc.)	Drug-tier based; often higher out-of-pocket
Administration	Healthcare provider in clinic/hospital	Self-administered at home

Specialty Pharmacy

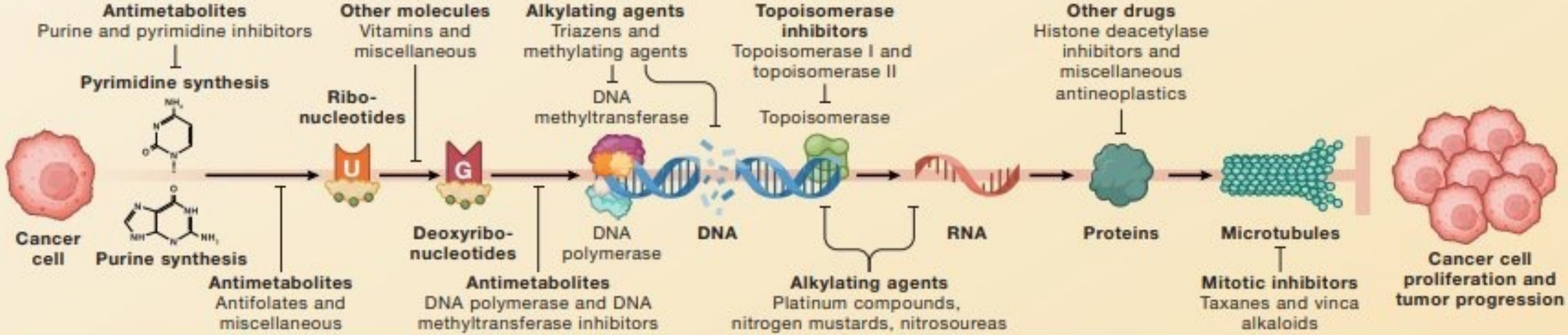
- Dispenses complex and high-cost medications that are not available at retail pharmacies
- Provides patient support (education, adherence, prior authorizations)
- Ships medications directly to the patient's home

IV vs PO

- Benefits
  - No need for central venous access
  - No need to spend time in infusion – less time off work, less transportation needs, travel flexibility
- Drawbacks
  - Efficacy depends on patient/family administration
  - Assessments prior to starting
    - Ability to swallow pills (few can be crushed)
    - Cognitive capacity and ability to adhere to medication schedule
  - Fewer interactions with healthcare = less direct monitoring for toxicity

Cytotoxic Chemotherapy

Killing cells that grow fast



ANTIMETABOLITES

	Drug	Mechanism of action	Therapeutic applications
Pyrimidine antagonists	Fluorouracil	Purine antagonists / Pyrimidine antagonists	Colorectal, breast, stomach, pancreatic, head and neck cancer
	Capecitabine		Colorectal, breast and gastric cancer
	Floxuridine		Digestive system cancers
Purine antagonists	6-mercaptopurine	DNA incorporation / HGPRT and thymidylate synthase / RNA incorporation	Acute lymphoblastic or lymphocytic leukemia
	Thioguanine		Acute myeloblastic or lymphoblastic leukemia
Antifolates	Methotrexate	Antifolates: Inosine synthesis, Dihydrofolate reductase, Thymidylate synthase / Nucleotide synthesis	Leukemia, breast, skin, head and neck, lung, uterine cancer
	Pemetrexed		Non-squamous non-small cell lung cancer, malignant pleural mesothelioma
	Pralatrexate		T-cell lymphoma
Enzyme inhibitors	Cladribine	Thymidylate synthase / Ribonucleotide reductase / Gemcitabine / Cladribine / Cytarabine / Clofarabine / Fludarabine / Nelarabine / DNA polymerase / DNA crosslinks / DNA terminator	Hairy cell leukemia
	Fludarabine		B-cell chronic lymphocytic leukemia
	Gemcitabine		Pancreatic, lung, ovarian, breast cancer
	Clofarabine		Acute lymphoblastic leukemia
	Nelarabine		T-cell lymphoblastic leukemia and lymphoma
	Cytarabine		Acute myeloid and other leukemias

ALKYLATING AGENTS

	Drug	Mechanism of action	Therapeutic applications
Platinum compounds	Cisplatin	① Alkylating agents / Alkyl group	Bladder, testicular, ovarian, head and neck, uterus, lung cancer
	Carboplatin		Lung cancer, ovarian cancer
	Oxaliplatin		Colorectal cancer
Nitrosoureas	Carmustine		Brain tumor, lymphoma, multiple myeloma
	Lomustine		Brain and lung tumor, malignant melanoma, Hodgkin's lymphoma
	Streptozocin		Pancreatic cancer
Nitrogen mustards	Bendamustine	② DNA alkylation / DNA crosslink	Chronic lymphocytic leukemia, B-cell non-Hodgkin's lymphoma, multiple myeloma
	Chlorambucil		Hodgkin's lymphoma, chronic lymphocytic leukemia, giant follicular lymphoma
	Cyclo-phosphamide		Multiple solid tumors
	Ifosfamide		Sarcoma, testicular, ovarian, bronchial, breast, pancreatic, endometrial cancer, lymphoma
	Mechlorethamine	③ Multiple DNA strand breaks	T-cell lymphoma, B-cell lymphoma, chronic leukemia, lung cancer, medulloblastoma
	Melphalan		Multiple myeloma, ovarian cancer, neuroblastoma, melanoma, sarcoma
Triazenes	Dacarbazine	④ Cell cycle arrest and death	Malignant melanoma, Hodgkin's lymphoma, sarcoma
	Temozolomide		Brain tumors
	Procarbazine		Hodgkin's lymphoma

TOPOISOMERASE INHIBITORS

	Drug	Mechanism of action	Therapeutic applications
TOP1 Inhibitors	(Liposomal) Irinotecan	TOP1 inhibitors / TOP2 inhibitors / Block of DNA unfolding and replication	Colorectal, small-cell lung, pancreatic cancer
	Topotecan		Ovarian cancer, small cell lung cancer, cervical cancer
TOP2 Inhibitors	Etoposide (VP-16)		Lung, testicular and ovarian cancer, lymphoma, acute myeloid leukemia
	Mitoxantrone		Prostate, liver and breast cancer, leukemia, non-Hodgkin's lymphoma
	Teniposide		Leukemia

MITOTIC INHIBITORS

	Drug	Mechanism of action	Therapeutic applications
Taxanes	Cabazitaxel	Microtubule polymerization / Vinca alkaloids / Microtubule degradation / Taxanes / Mitosis block and cell death	Metastatic castration-resistant prostate cancer
	Docetaxel		Breast, lung, prostate, stomach, head and neck cancer
	(Nab) Paclitaxel		Breast, ovarian, lung and pancreatic cancer, AIDS-related Kaposi's sarcoma
Vinca alkaloids	Vinblastine		Hodgkin's lymphoma, testicular and breast cancer, Kaposi's sarcoma
	(Liposome) Vincristine		Leukemia,lymphoma, neuroblastoma, sarcomas
	Vinorelbine		Lung cancer and breast cancer

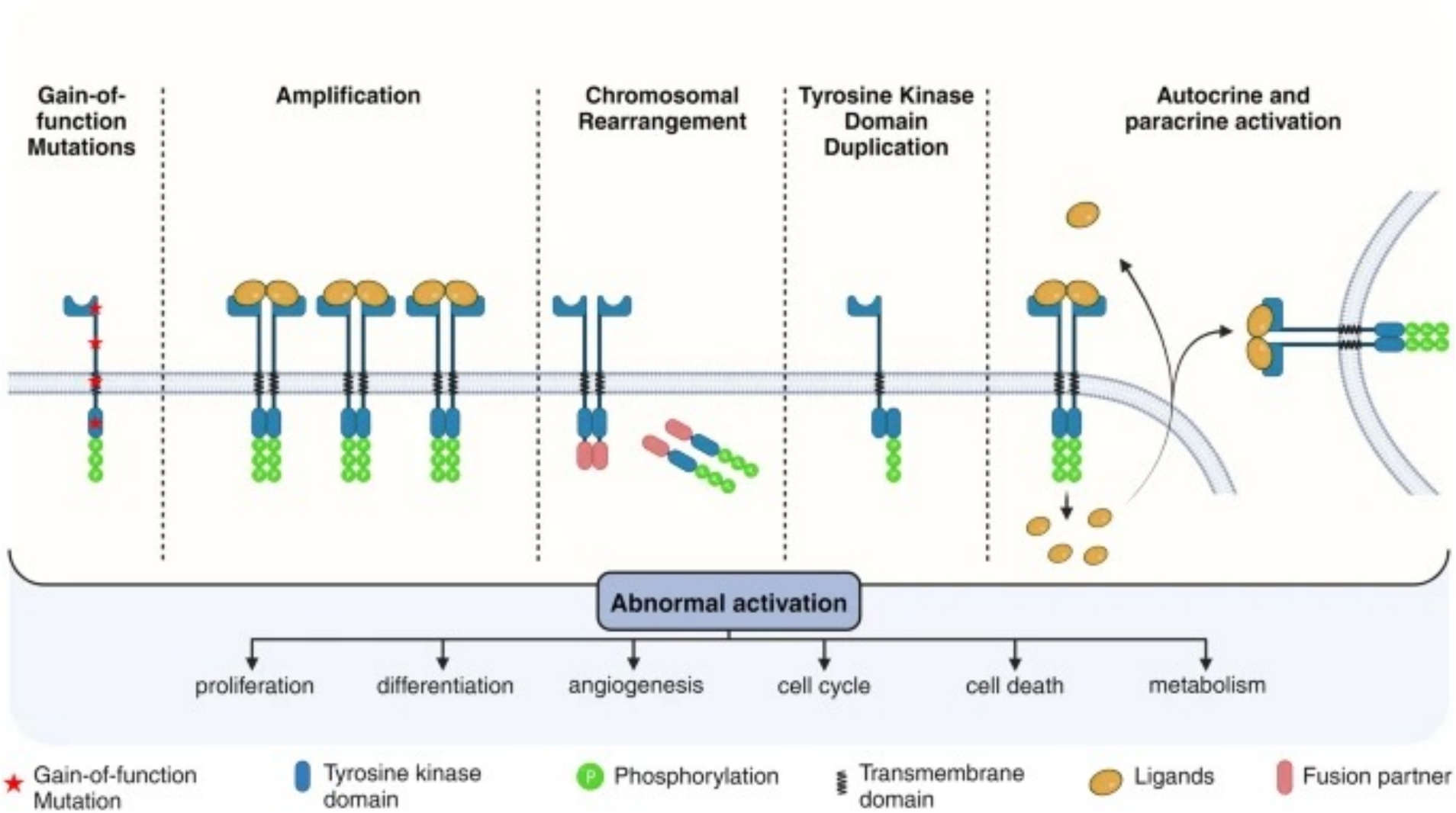
Capecitebine

- Prodrug of 5-fluorouracil
- Typical schedule: BID x14d / off x7d (21d cycle)
- Dosing is based on BSA; pills only come in 150mg and 500mg tablets
  - 1250mg/m2 x 1.5 m2 BSA = 1875mg
  - 500mg x3 tablets + 150mg x2 tablets = 1800mg
  - 5 tablets twice a day
- Major toxicities: Hand-foot syndrome, N/V/D, mucositis, myelosuppression
- DPYD deficiency
  - Dihydropyrimadine dehydrogenase breaks down 5-FU
  - Deficiency in 2-8% of people
  - Severe toxicity typically with first cycle of therapy

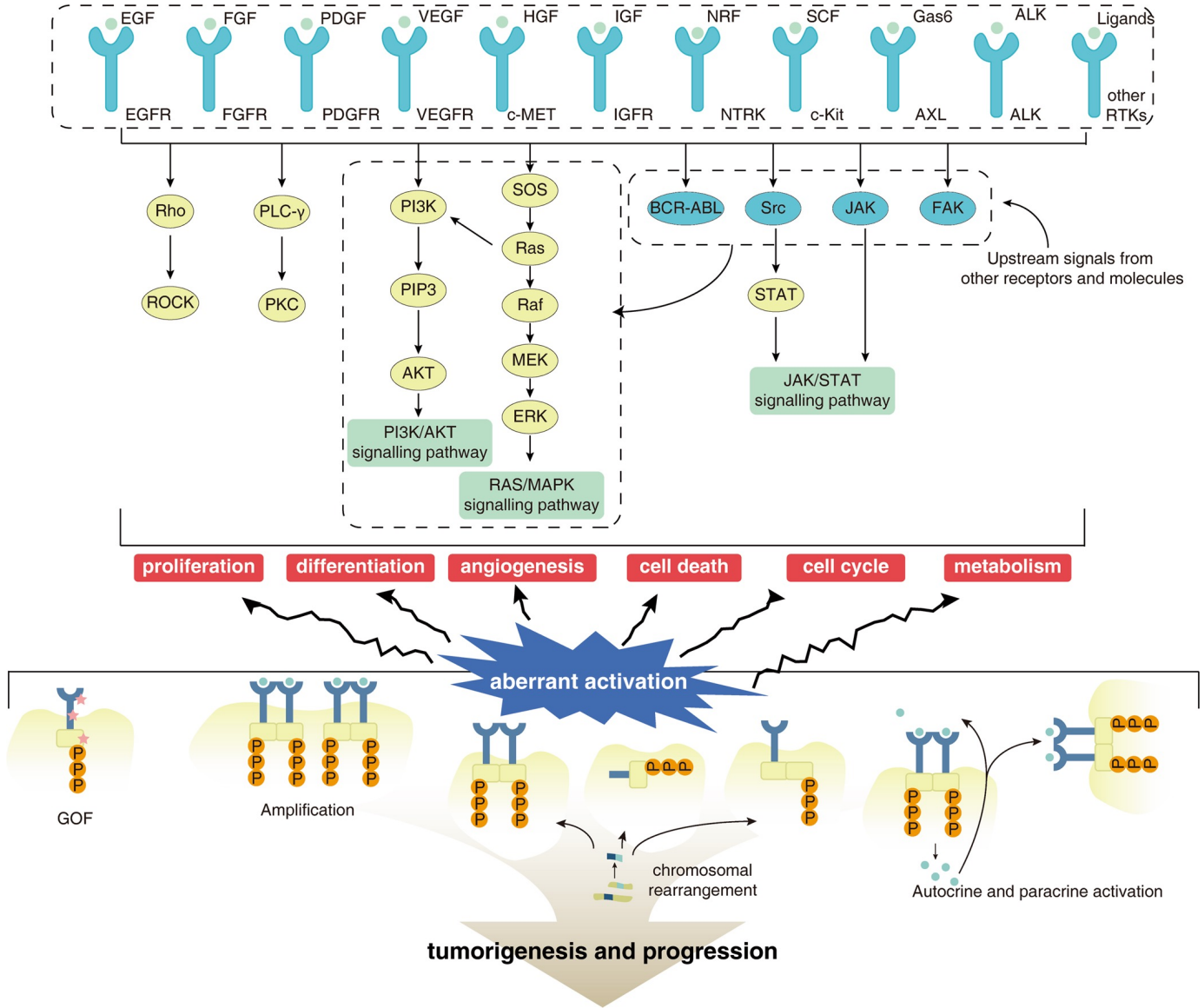
Tyrosine Kinase Inhibitors (TKIs)

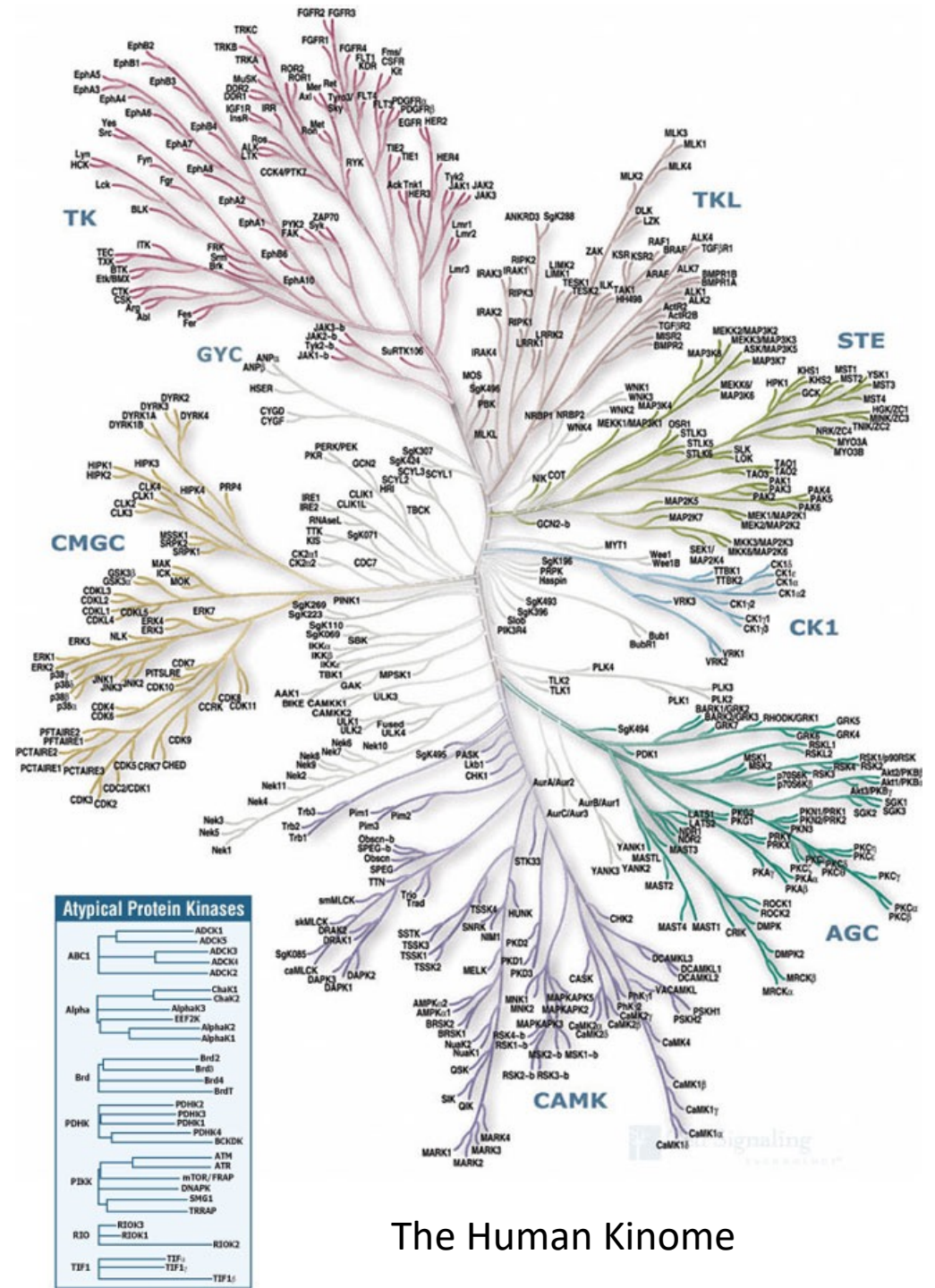
Targeting proteins (aka alphabet soup)

Tyrosine Kinases and Tumorigenesis

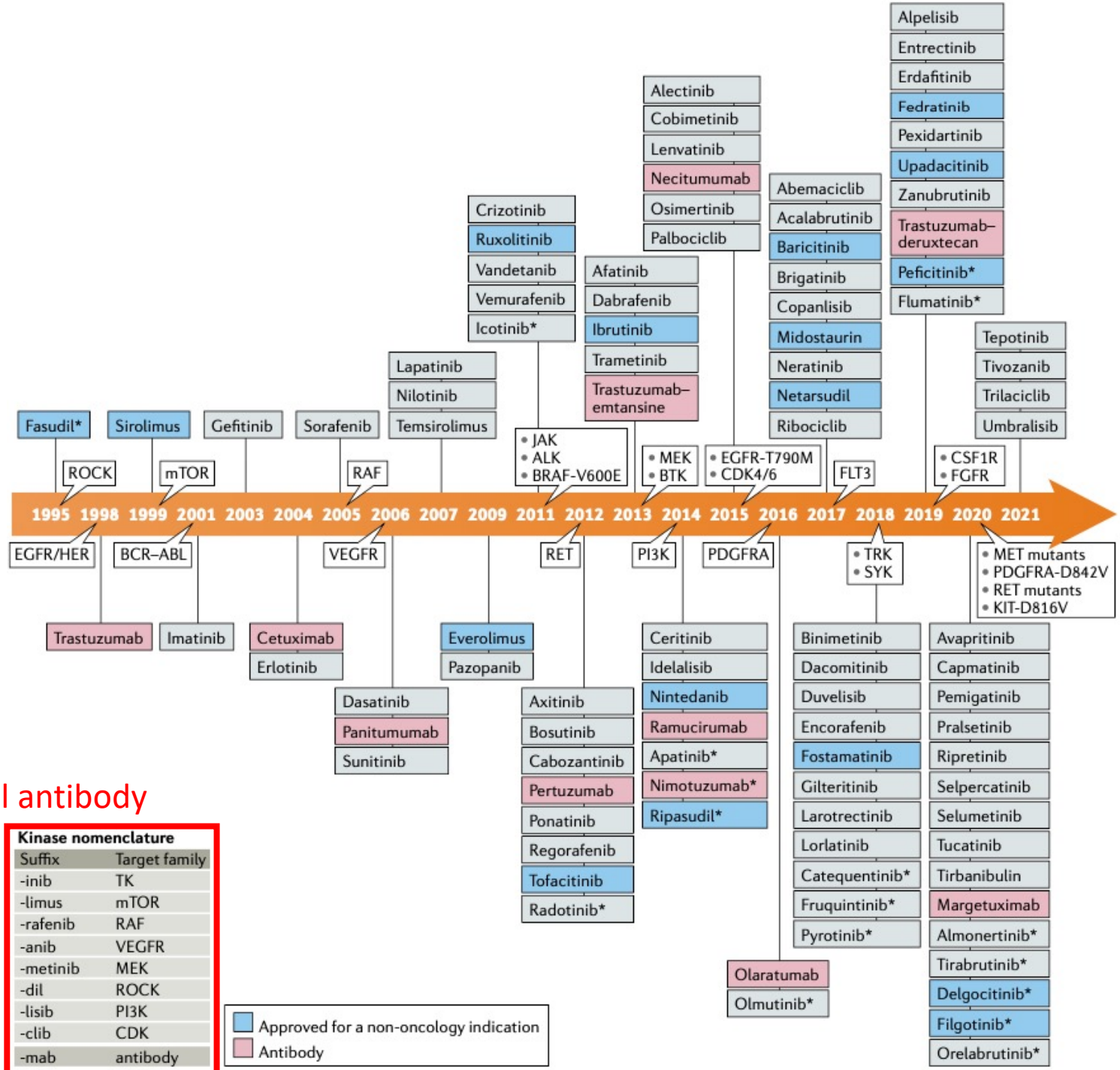


TKI Alphabet Soup





The Human Kinome



-ib = TKI

-mab = monoclonal antibody

Kinase nomenclature

Suffix	Target family
-inib	TK
-limus	mTOR
-rafenib	RAF
-anib	VEGFR
-metinib	MEK
-dil	ROCK
-lisib	PI3K
-clib	CDK
-mab	antibody

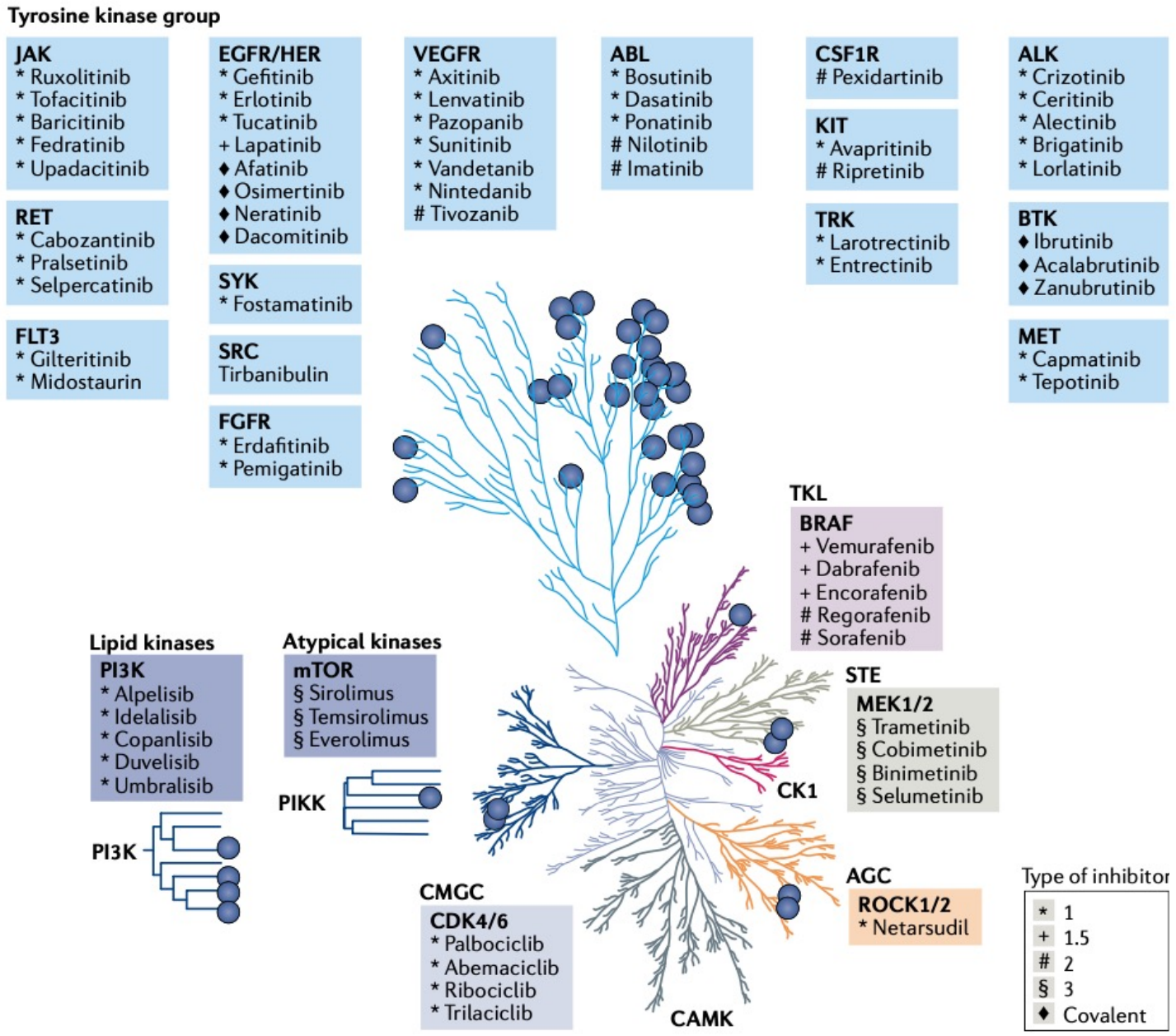
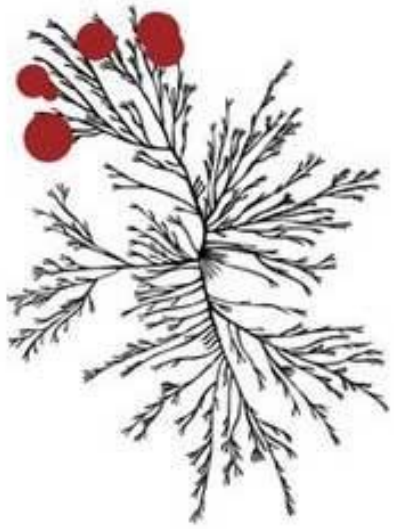


Fig. 2 | **FDA-approved kinase inhibitors mapped onto the human kinome.** The kinase targets of the 71 FDA-approved small-molecule kinase inhibitors (SMKIs) are mapped onto a phylogenetic representation of the human kinome. The primary kinase targets are identified, although many SMKIs cross-react with other kinases and in reality bind in varying degrees to other kinases. The type of kinase inhibitor is also indicated. Tirbanibulin targets the peptide substrate site of SRC.

Imatinib

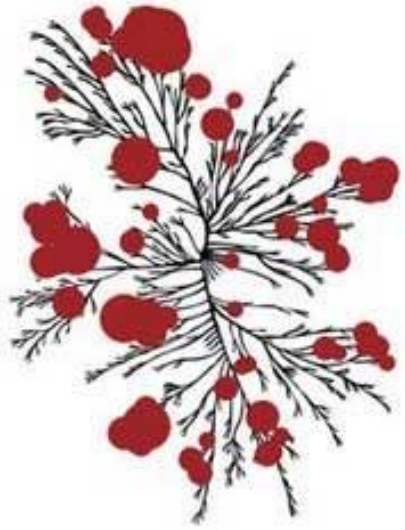


Inhibits BCR-ABL in Chronic Myeloid Leukemia

Inhibits C-KIT, PDGF, SCF

Labeled Indications:
ALL, SM, CML, Dermatofibrosarcoma, GIST, HES, MDS/MPN

Sunitinib



Multikinase inhibitor

"dirty" TKI

Broader kinase inhibition = more tumors treated = more toxicity

Rarely used now because more specific TKIs exist

TKI Takeaways

- Tyrosine Kinases are cellular proteins that regulate cell signaling
- Some cancers have mutations in Tyrosine Kinases that allow them to grow
- Tyrosine Kinases can be blocked by:
  - Monoclonal antibody drugs (large molecules given IV/IM/SC)
  - Tyrosine Kinase Inhibitors (small molecules taken PO)
- TKIs usually block more than one protein; some can be used for more than one cancer type
- The toxicity of a TKI is related to the proteins it is blocking
  - May need to be held for surgery or infections (proteins involved in wound healing and immune response)
- As of 2025 there are 85 FDA approved TKIs; only 2 are off patent (imatinib, erlotinib)

Kinase Family	Number of Approved Drugs	FDA Approved Indications	Names of Drugs
EGFR/HER2	**11**	NSCLC, HER2-positive breast cancer	Erlotinib, Gefitinib, Afatinib, Osimertinib, Dacomitinib, Lapatinib, Neratinib, Tucatinib, Mobocertinib, Amivantamab, Lazertinib
JAK	**10**	Myelofibrosis, rheumatoid arthritis, atopic dermatitis, psoriasis	Ruxolitinib, Fedratinib, Baricitinib, Tofacitinib, Upadacitinib, Abrocitinib, Deucravacitinib, Ritlecitinib, Deuruxolitinib, Itacitinib
VEGFR	**9**	Renal cell carcinoma, hepatocellular carcinoma, thyroid cancer	Sunitinib, Sorafenib, Pazopanib, Axitinib, Cabozantinib, Lenvatinib, Regorafenib, Vandetanib, Tivozanib
BCR-Abl	**6**	Chronic myeloid leukemia, acute lymphoblastic leukemia	Imatinib, Dasatinib, Nilotinib, Bosutinib, Ponatinib, Asciminib
ALK	**6**	ALK-positive NSCLC	Crizotinib, Ceritinib, Alectinib, Brigatinib, Lorlatinib, Ensartinib
FGFR	**5**	Urothelial carcinoma, cholangiocarcinoma	Erdafitinib, Pemigatinib, Infigratinib, Futibatinib, Rogaratinib
MEK1/2	**5**	BRAF-mutant melanoma, neurofibromatosis type I	Trametinib, Cobimetinib, Binimetinib, Selumetinib, Mirdametinib
B-RAF	**4**	BRAF-mutant melanoma	Vemurafenib, Dabrafenib, Encorafenib, Tovorafenib
BTK	**4**	B-cell malignancies, chronic lymphocytic leukemia	Ibrutinib, Acalabrutinib, Zanubrutinib, Tirabrutinib
CDK4/6	**4**	Hormone receptor-positive breast cancer	Palbociclib, Ribociclib, Abemaciclib, Trilaciclib
mTOR	**3**	Renal cell carcinoma, breast cancer	Everolimus, Temsirolimus, Sirolimus
Flt3	**3**	Acute myeloid leukemia	Midostaurin, Gilteritinib, Quizartinib
MET	**3**	MET exon 14 skipping mutation-positive NSCLC	Capmatinib, Tepotinib, Savolitinib
RET	**2**	RET-mutant medullary thyroid cancer, NSCLC	Selpercatinib, Pralsetinib
TRK	**2**	NTRK gene fusion-positive tumors	Larotrectinib, Entrectinib
CSF1R	**1**	Tenosynovial giant cell tumor	Pexidartinib
KIT	**3**	Gastrointestinal stromal tumor	Imatinib, Sunitinib, Regorafenib
PDGFR	**1**	Gastrointestinal stromal tumor	Imatinib
ROS1	**2**	ROS1-positive NSCLC	Crizotinib, Entrectinib
SYK	**1**	Chronic immune thrombocytopenia	Fostamatinib
TYK2	**1**	Psoriasis	Deucravacitinib

Kinase Family	FDA Approved Indications	Major/Common Toxicities	Monitoring Parameters
EGFR/HER2	NSCLC, HER2-positive breast cancer	Interstitial lung disease, hepatotoxicity, cardiotoxicity	Liver function tests, cardiac monitoring, pulmonary function tests
JAK	Myelofibrosis, rheumatoid arthritis, atopic dermatitis, psoriasis	Serious infections, thrombosis, malignancies	CBC, liver function tests, lipid profile
VEGFR	Renal cell carcinoma, hepatocellular carcinoma, thyroid cancer	Hepatotoxicity, hemorrhage, gastrointestinal perforation	Liver function tests, blood pressure monitoring, CBC
BCR-Abl	Chronic myeloid leukemia, acute lymphoblastic leukemia	QT prolongation, Ponatinib: arterial occlusion, hepatotoxicity	ECG, liver function tests, CBC
ALK	ALK-positive NSCLC	Hepatotoxicity, interstitial lung disease, QT prolongation	Liver function tests, pulmonary function tests, ECG
FGFR	Urothelial carcinoma, cholangiocarcinoma	Ocular toxicity, hyperphosphatemia	Serum phosphate levels, ophthalmologic exams
MEK1/2	BRAF-mutant melanoma, neurofibromatosis type I	Cardiomyopathy, retinal vein occlusion	Cardiac monitoring, ophthalmologic exams
B-RAF	BRAF-mutant melanoma	Cutaneous squamous cell carcinoma, QT prolongation	Dermatologic exams, ECG
BTK	B-cell malignancies, chronic lymphocytic leukemia	Hemorrhage, infections, atrial fibrillation	CBC, infection monitoring, ECG
CDK4/6	Hormone receptor-positive breast cancer	Neutropenia, hepatotoxicity, QT prolongation	CBC, liver function tests, ECG
mTOR	Renal cell carcinoma, breast cancer	Infections, pneumonitis, hyperglycemia	CBC, blood glucose levels, pulmonary function tests
Flt3	Acute myeloid leukemia	QT prolongation, differentiation syndrome	ECG, CBC
MET	MET exon 14 skipping mutation-positive NSCLC	Interstitial lung disease, hepatotoxicity	Pulmonary function tests, liver function tests
RET	RET-mutant medullary thyroid cancer, NSCLC	Hepatotoxicity, QT prolongation	Liver function tests, ECG
TRK	NTRK gene fusion-positive tumors	Neurotoxicity, hepatotoxicity	Neurologic exams, liver function tests
CSF1R	Tenosynovial giant cell tumor	Hepatotoxicity	Liver function tests
KIT	Gastrointestinal stromal tumor	Hepatotoxicity, hemorrhage	Liver function tests, CBC
PDGFR	Gastrointestinal stromal tumor	Hepatotoxicity, cardiotoxicity	Liver function tests, cardiac monitoring
ROS1	ROS1-positive NSCLC	Hepatotoxicity, QT prolongation	Liver function tests, ECG
SYK	Chronic immune thrombocytopenia	Hypertension, hepatotoxicity	Blood pressure monitoring, liver function tests
TYK2	Psoriasis	Serious infections, malignancies	CBC, liver function tests

Not a comprehensive list;
Check the FDA label

Immunomodulators (IMiDs) in Multiple Myeloma

And why the FDA created the Risk Evaluation and Mitigation Strategy (REMS) program

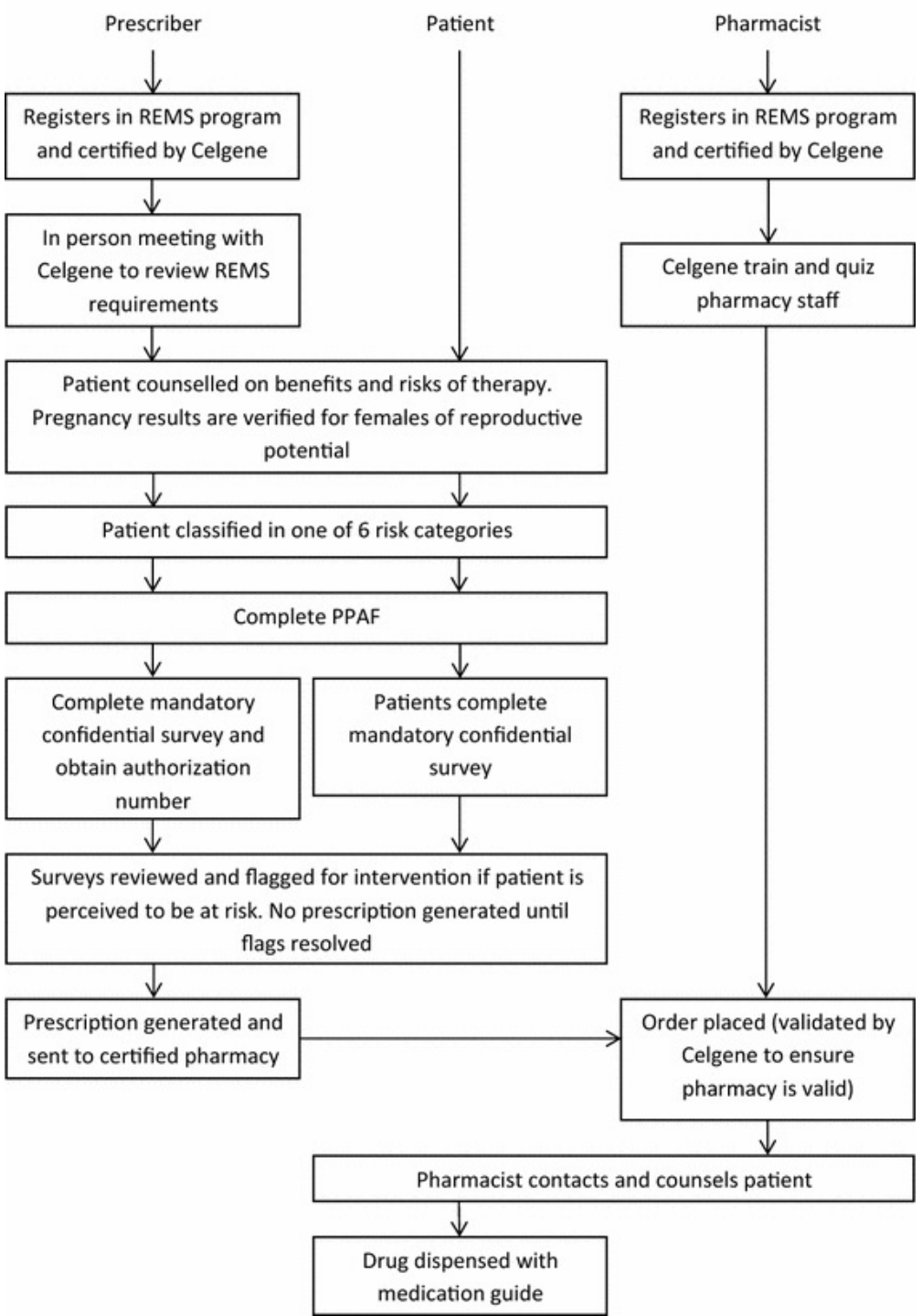
How thalidomide shaped drug regulation

- **1950s–60s**: Thalidomide was developed in West Germany and marketed as a sedative and anti-nausea drug for pregnant women.
  - Sold in over 40 countries, but not in the U.S. thanks to FDA reviewer Dr. Frances Kelsey, who resisted approval due to safety concerns.
  - Caused over 10,000 birth defects globally (limb deformities, organ malformation)
  - Catalyzed major drug regulation reforms worldwide, including the 1962 Kefauver-Harris Amendments in the U.S., which required proof of drug efficacy and safety before approval.
- **1990s**: researchers discovered that thalidomide had anti-inflammatory and anti-angiogenic properties. Found to be a potent treatment for multiple myeloma.

How thalidomide shaped drug regulation

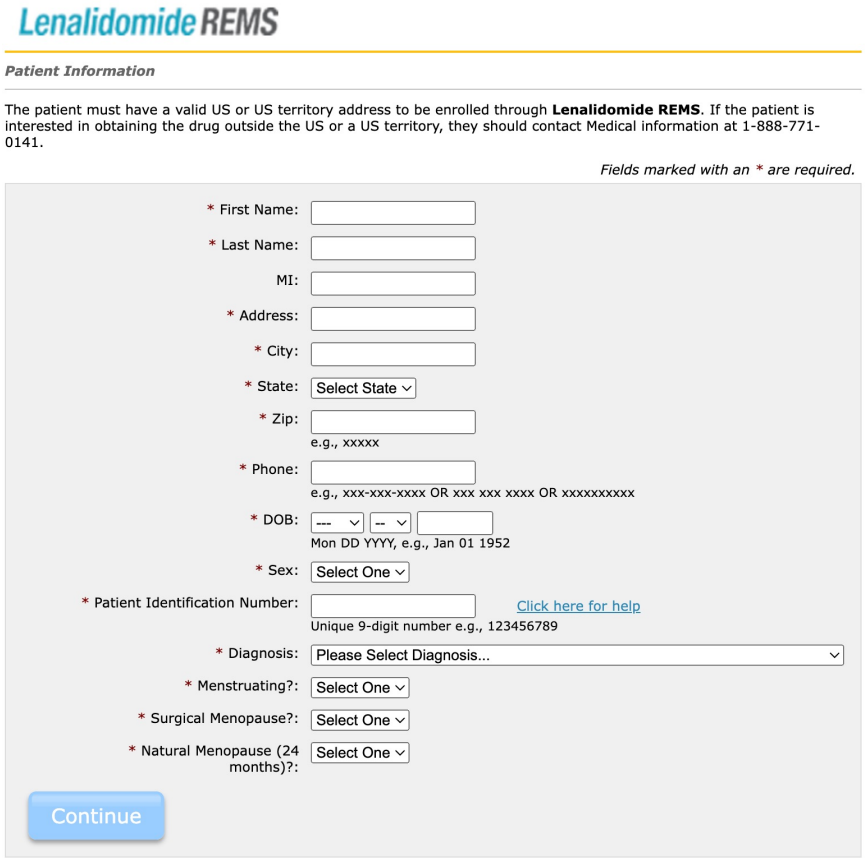
- **1998**: Celgene launched STEPS (System for Thalidomide Education and Prescribing Safety) under FDA oversight – the first major structured pharmaceutical risk management program.
    - Mandatory prescriber and pharmacy certification
    - Informed patient consent
    - Mandatory pregnancy testing before and during treatment
    - Limited distribution only through certified channels
    - Education on risks and contraception
- **2007**: REMS program formally created by the FDA Amendments Act, STEPS incorporated into REMS.
- **Thalidomide is the archetype for REMS**: a drug with clear benefit in a very specific population, but unacceptable risk without serious controls.

REMS in practice

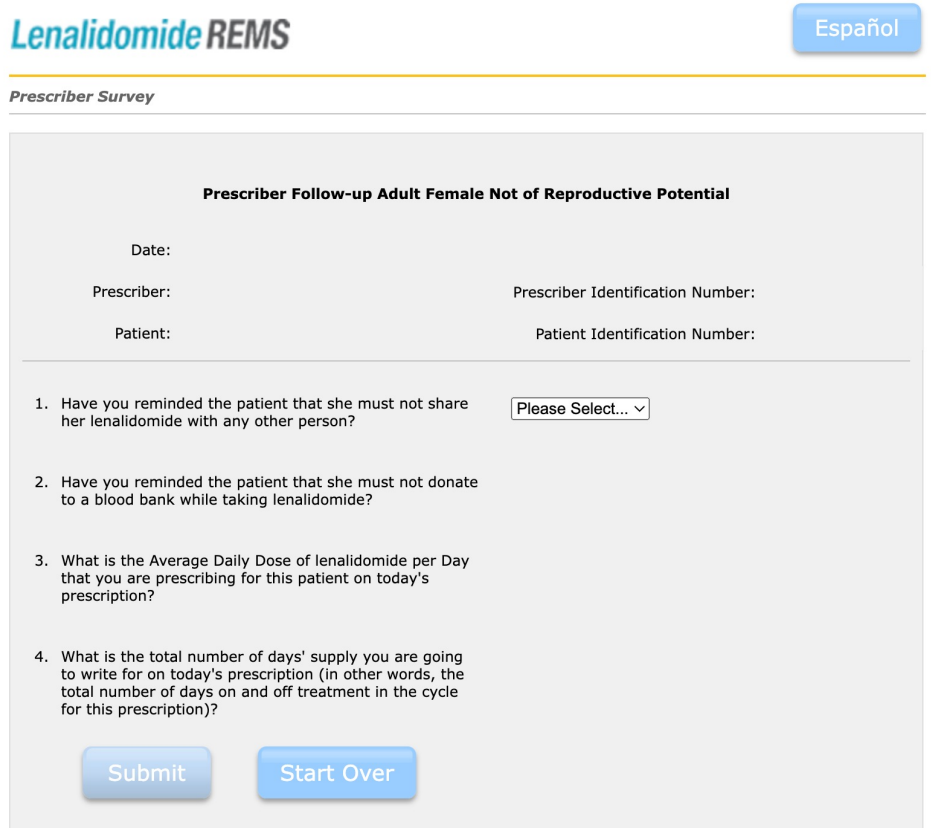


REMS in practice

https://bmsremspatientsafety.com/



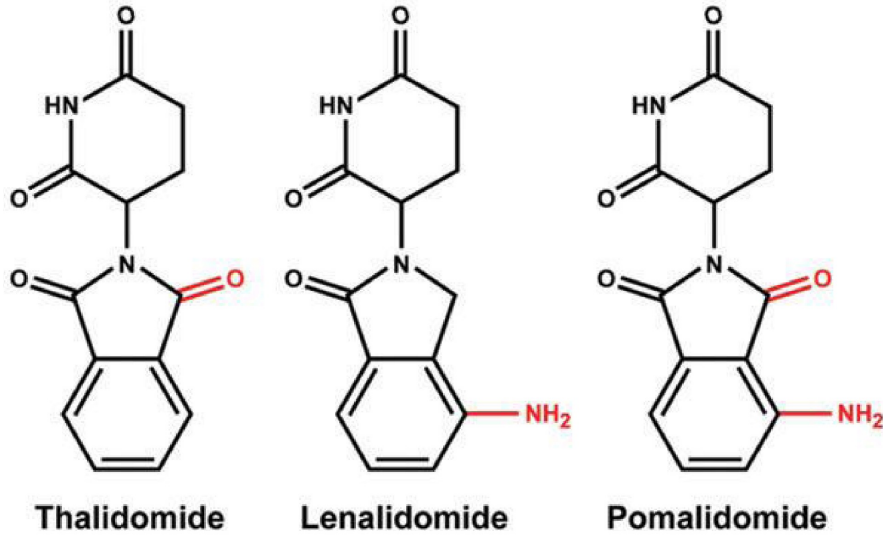
New Enrollment



Every refill
8 digit authorization number must be submitted with prescription

IMiDs

- Backbone of most frontline and second line myeloma regimens
- Dose-adjusted for renal function
  - Renal failure is a common presentation of myeloma and may prevent the safe use of IMiDs
- Risk of VTE – ASA or DVT prophylaxis indicated
- Myelosuppression
- Rash



Estimated New Cases

Males			Females		
Prostate	191,930	21%	Breast	276,480	30%
Lung & bronchus	116,300	13%	Lung & bronchus	112,520	12%
Colon & rectum	78,300	9%	Colon & rectum	69,650	8%
Urinary bladder	62,100	7%	Uterine corpus	65,620	7%
Melanoma of the skin	60,190	7%	Thyroid	40,170	4%
Kidney & renal pelvis	45,520	5%	Melanoma of the skin	40,160	4%
Non-Hodgkin lymphoma	42,380	5%	Non-Hodgkin lymphoma	34,860	4%
Oral cavity & pharynx	38,380	4%	Kidney & renal pelvis	28,230	3%
Leukemia	35,470	4%	Pancreas	27,200	3%
Pancreas	30,400	3%	Leukemia	25,060	3%
All Sites	**893,660**	**100%**	**All Sites**	**912,930**	**100%**

Hormone suppressing therapy

The most common treatment for the most common cancers

Hormone suppressing agents

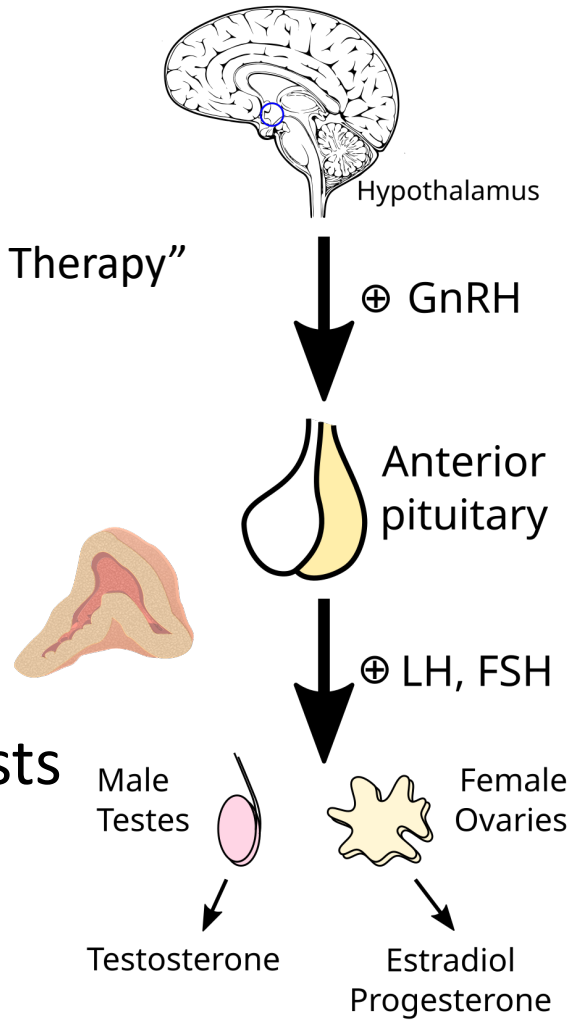
Estrogen

- GnRH agonists
  - Goserelin (SC)
- Aromatase Inhibitors (AIs)
  - Letrozole, Anastrazole, Exemestane
- Selective Estrogen Receptor Modulators (SERMs)
  - Tamoxifen, Raloxifene
- Selective Estrogen Receptor Degraders (SERDs)
  - Fulvestrant (IM), Elacestrant (PO)

Testosterone

"Androgen Deprivation Therapy"

- GnRH agonists/antagonists
  - Leuprolide (IM/SC)
  - Degarelix (SC), Relugolix (PO)
- CYP17 inhibitor
  - Abiraterone
- Androgen receptor antagonists
  - Bicalutamide
  - Enzalutamide, Apalutamide, Darolutamide



Tamoxifen vs AIs

- Tamoxifen can be used in pre and post-menopausal women
- AIs must be combined with ovarian suppression (GnRH agonist goserelin) if used in pre-menopausal women
- Common toxicities
  - Vasomotor symptoms (hot flashes)
  - Arthralgias
  - Vaginal dryness, sexual dysfunction
  - Mood changes – depression, anxiety, irritability, insomnia, fatigue
- Tamoxifen
  - Increases bone density
  - VTE
  - Uterine cancer – any new abnormal uterine bleeding should be evaluated
- AIs
  - Decrease bone density

Abiraterone & ARAs

- All of these intensify the toxicities of ADT
  - Vasomotor symptoms (hot flashes)
  - Decreased bone density
  - Loss of skeletal muscle, increased adiposity
  - Anhedonia, erectile dysfunction
  - Mood changes – depression, anxiety, irritability, insomnia, fatigue
- Abiraterone
  - Must be taken on an empty stomach
  - Must be given with prednisone 5mg to prevent mineralocorticoid excess
  - Can worsen baseline hypertension/diabetes
  - Early hepatotoxicity – monitor LFTs every 2 weeks for 3 months when starting

Conclusions

- Oral anti-cancer drugs are dispensed by specialty pharmacies
- Cytotoxic chemotherapy is rarely given in PO form; capecitebine is the most common
- Tyrosine kinase inhibitors block the proteins cancer cells use to grow
  - There's a new one every month and they all have unique toxicities and monitoring parameters – so check the FDA label!
- IMiDs in multiple myeloma require use of the FDA REMS program
- Many oral anticancer therapies need to be held briefly for surgeries or severe infections

References

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