2023 Oncology Fellows Program:
New Horizons in Quality Cancer Care™

How to Optimize Systemic Therapy Outside of the Cancer Center:

Best Practices for Managing Anticancer Therapies

B. Douglas Smith, MD

The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

Acknowledgements

- **Carmen Janes, PharmD, BCOP**
- **Lizeth Garcia-Jennings, PharmD**
- **Kelli Rourke, PharmD**

Oral Anticancer Medicines – Promises and Pitfalls

- **Promises:**
  - **Precision and Personalized Medicine – started with CML**
  - **Perceived benefits**
    - **Safety (?) Less burdensome administration (?) Compliance (?)**

- **Pitfalls:**
  - **Safety and Monitoring, Handling of Medications, Drug Interactions**
  - **Adherence**
  - **Cost, Specialty Pharmacies, Medicare**

Early Growth of Oral Anticancer Medicines 1953-2013

Figure: Timeline of the Introduction of Oral Oncolytics—Between 1953 and 2003, 27 oral chemotherapy agents were introduced, yet the same number of new oral chemotherapy agents (27) have been introduced between 2004 and the present.

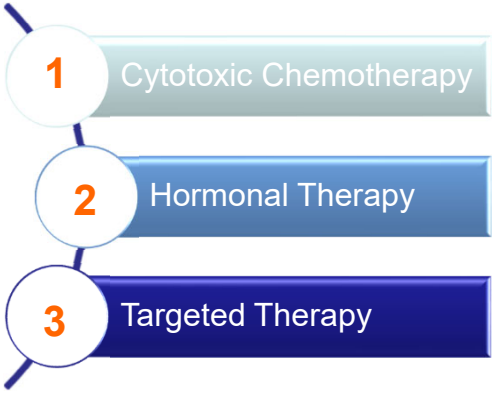

Image from: http://www.cancernetwork.com/practice-policy/oral-oncolytics-part-1-financial-adherence-and-management-challenges

Escalation of Oral Anticancer Medicines: 2014-2021

2015	2016	2017	2018	2019	2020	2021
•Palbociclib (Ibrance) •Lenvatinib (Lenvima) •Panobinostat (Farydak) •Gefitinib (Iressa) •Sonidegib (Odomzo) •Trifluridine/tipiracil (Lonsurf) •Cobimetinib (Cotellic) •Osimertinib (Tagrisso) •Ixazomib (Ninlaro) •Alectinib (Alecensa)	•Cabozantinib (Cabometyx) •Venetoclax (Venclexta) •Rucaparib (Rubraca)	•Ribociclib (Kisqali) •Niraparib (Zejula) •Brigatinib (Alunbrig) •Midostaurin (Rydapt) •Neratinib (Nerlynx) •Abemaciclib (Verzenio) •Acalabrutinib (Calquence)	•Apalutamide (Erleada) •Encorafenib (Braftovi) •Binimetinib (Mektovi) •Ivosidenib (Tibsovo) •Dulvelisib (Copiktra) •Dacomitinib (Vizimpro) •Talazoparib (Talzenna) •Lorlatinib (Lorbrena) •Glasdegib (Daurismo) •Larotrectinib (Vitrakvi) •Gilteritinib (Xospata)	•Erdafitinib (Balversa) •Enasidenib (Idhifa) •Alpelisib (Piqray) •Selinexor (Xpovio) •Darolutamide (Nubeqa) •Pexidartinib (Turalio) •Entrectinib (Rozlytrek) •Fedratinib (Inrebic) •Zanubrutinib (Brukinsa)	•Avapritinib (Ayvakit) •Tazemetostat (Tazverik) •Selumetinib (Koselugo) •Pemigatinib (Pemazyre) •Tucatinib (Tukysa) •Capmatinib (Tabrecta) •Selpercatinib (Retevmo) •Ripretinib (Qinlock) •Decitabine-Cedazuridine (Inqovi) •Pralsetinib (Gavreto) •Relugolix (Orgovyx)	•Tepotinib (Tepmetko) •Umbralisib (Ukoniq) •Tivozanib (Fotivda) •Sotorasib (Lumakras) •Infigratinib (Truseltiq)

https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm279174.htm

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* 2001: Imatinib

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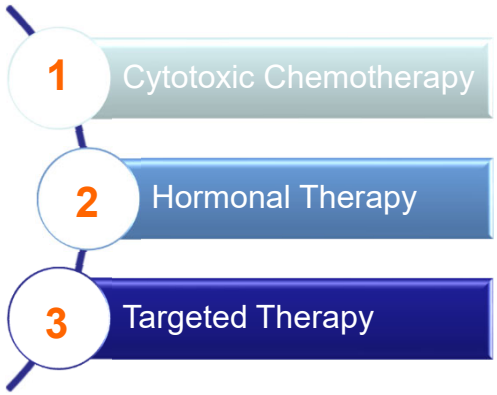

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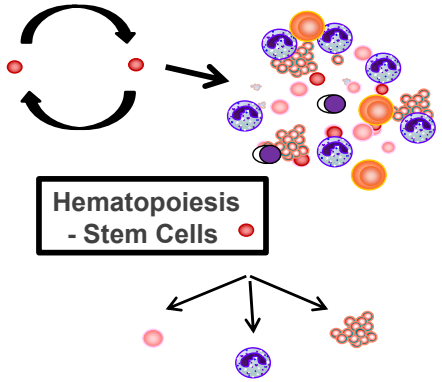
Basic Hematopoiesis Model:

Pathophysiology Marrow Failure and Myeloid Malignancies



Adapted from: Rosenfeld, List *Leukemia* 2000;14(1):2-8

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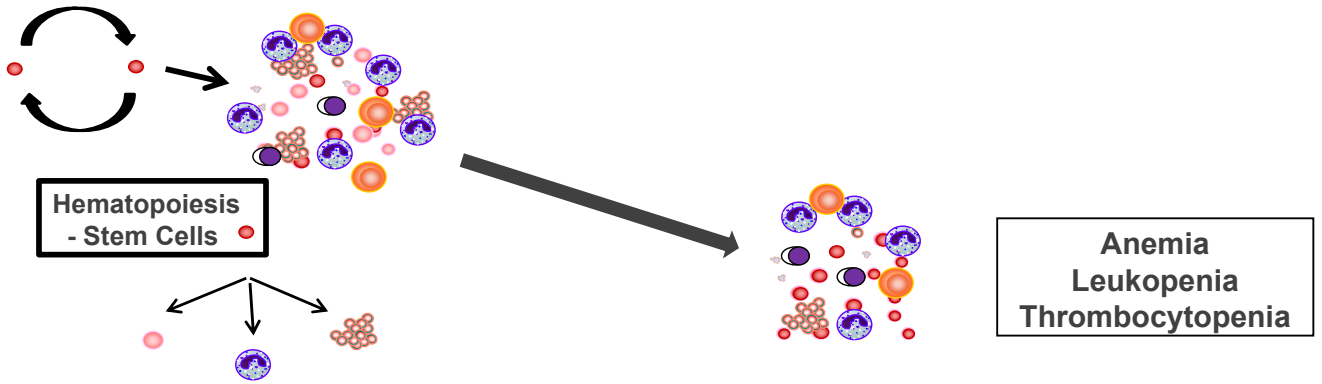

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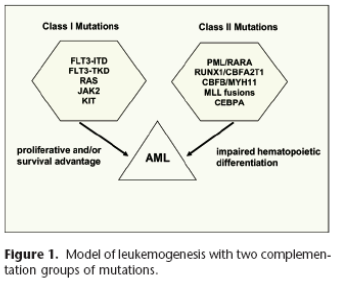
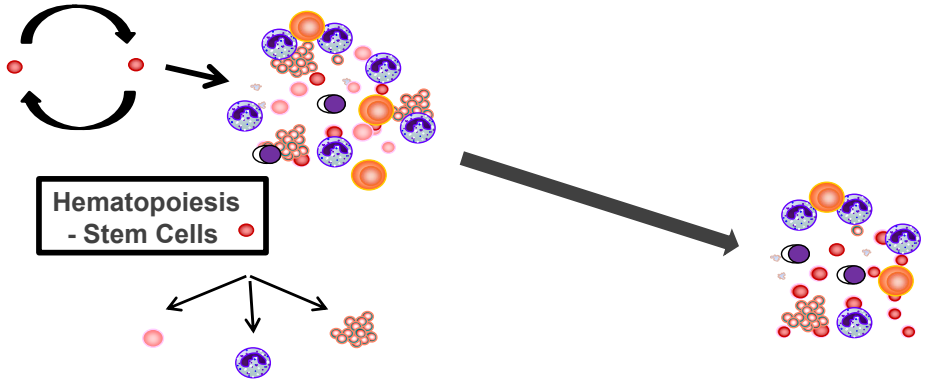


Figure 1. Model of leukemogenesis with two complementation groups of mutations.

Gaidzik et al, Semin Oncol 35:346



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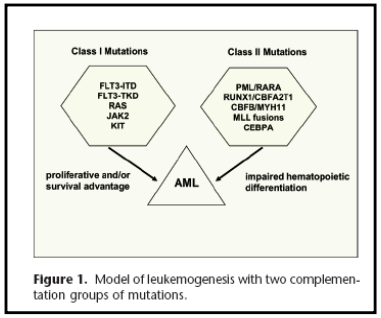

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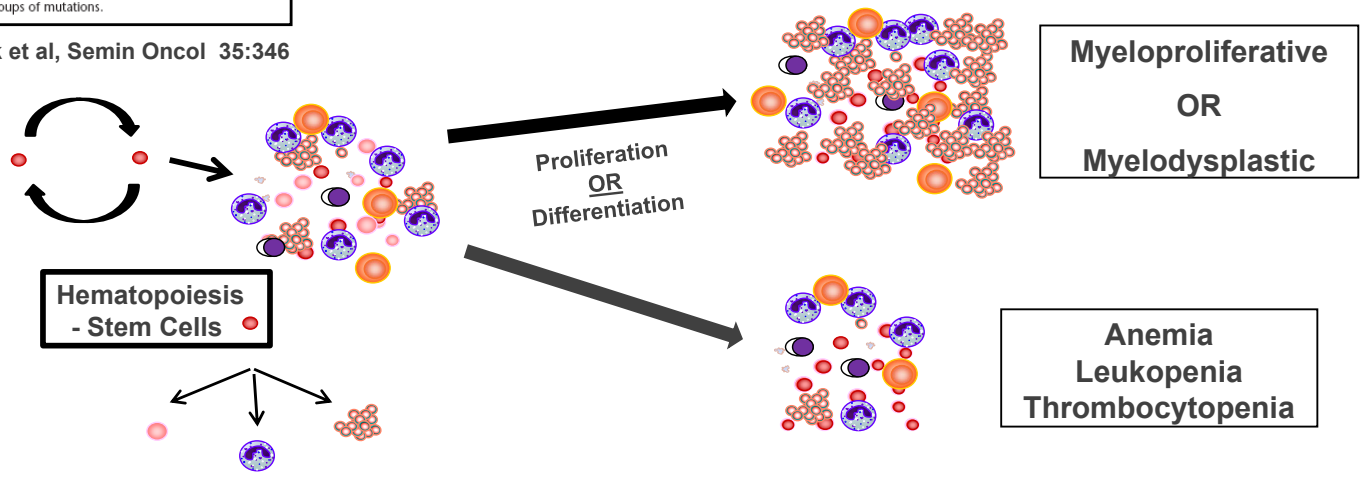

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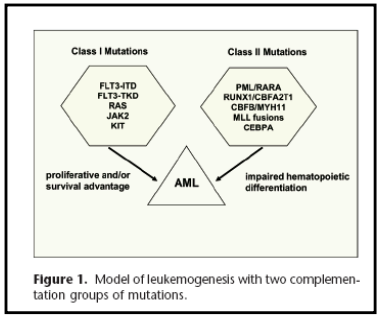

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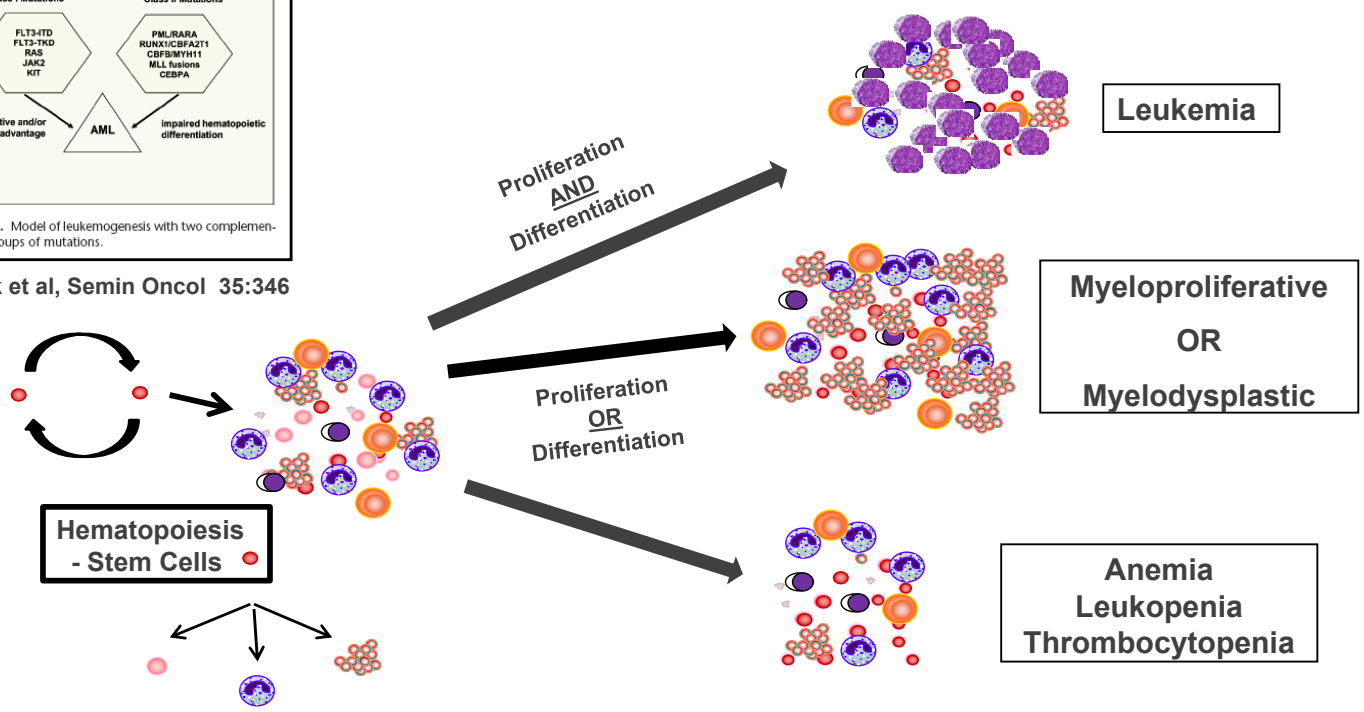

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Chronic Myeloid Leukemia:

One of the family of Myeloproliferative Neoplasms (MPN):

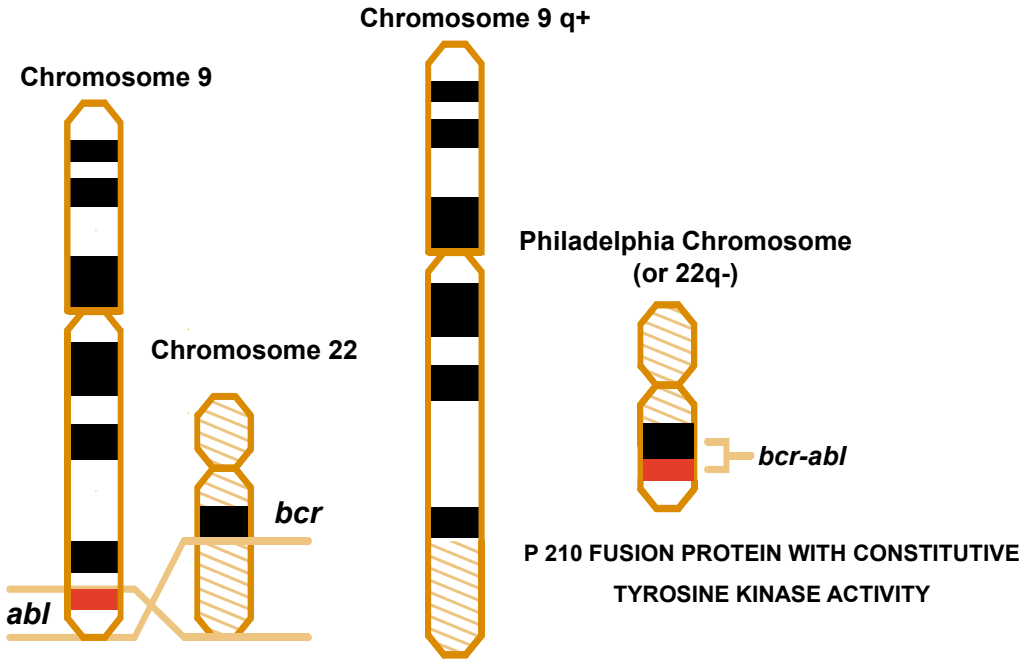
- **CML – chronic myeloid leukemia**
- **PV – polycythemia vera**
- **ET – essential thrombocythemia**
- **IMF – idiopathic myelofibrosis**

- **CMML – chronic myelomonocytic leukemia (overlap with MDS)**

Mutations impact growth, apoptosis and cells accumulate

- **Studies show cells with "normal function"**

Ph Chromosome → *BCR::ABL1* gene



Melo. *Blood*. 1996;88:2375.
Pasternak et al. *J Cancer Res Clin Oncol*. 1998;124:643.

Chronic Myeloid Leukemia: "Model" Oncologic Model

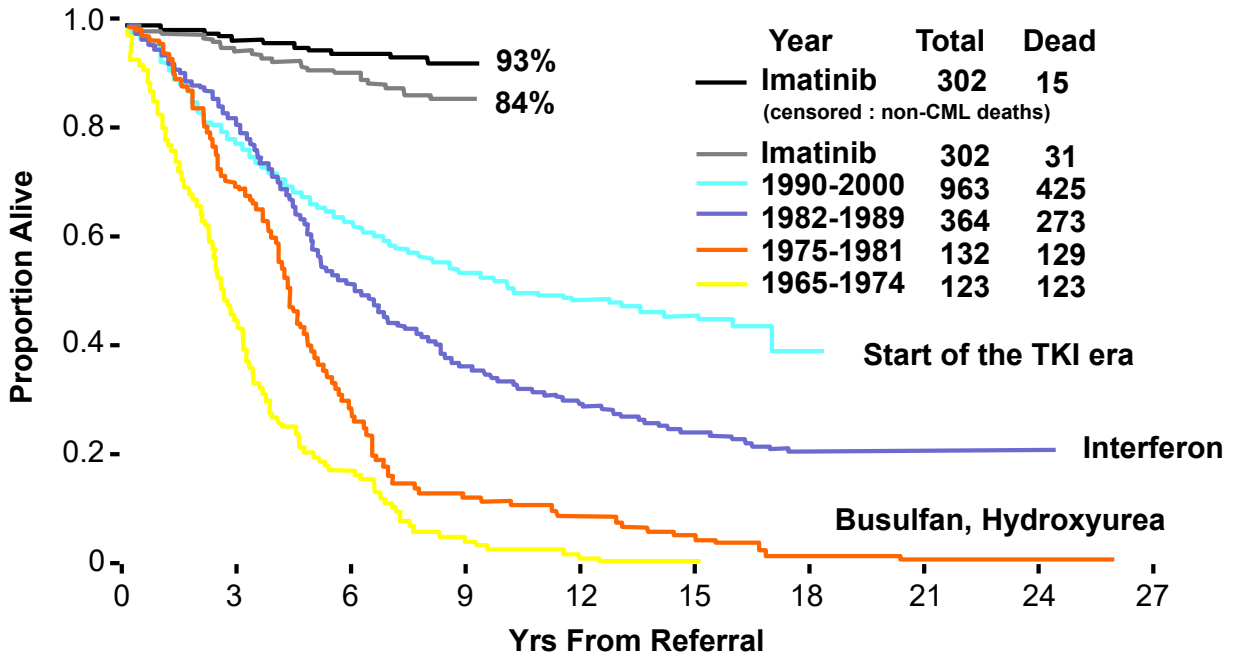
Oncogenesis – proliferation, blocked apoptosis

Stem Cell Disorder – clonal evolution

Immunologic Therapy – allogeneic hematopoietic cell transplant (HCT), donor lymphocyte infusion (DLI)

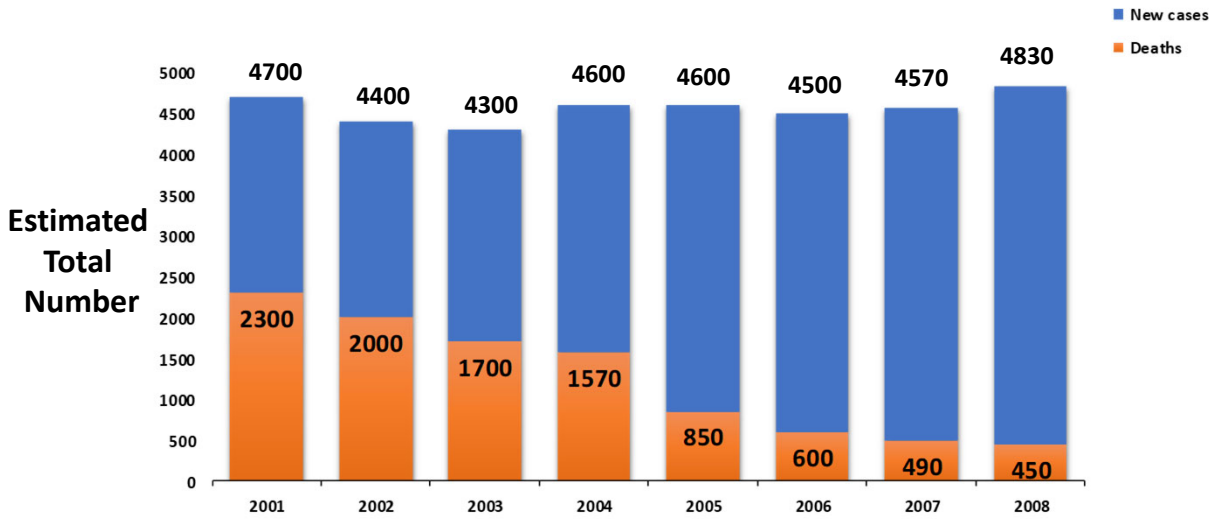
Oral, Targeted Therapy – imatinib mesylate + TKIs

Survival in Early CP-CML



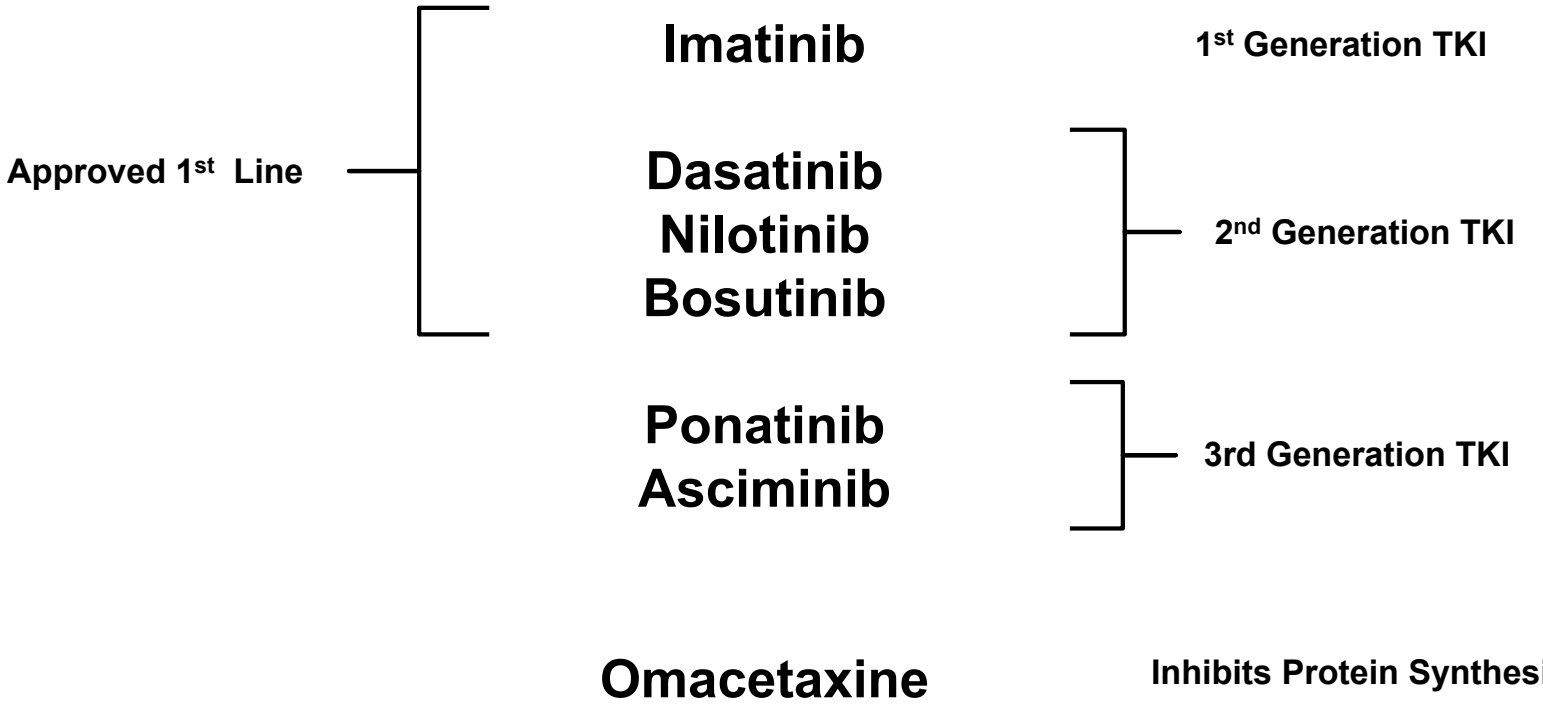
The University of Texas M. D. Anderson Cancer Center database

Decline in Deaths Related to Ph+ CML With Improvements in Therapy



American Cancer Society (ACS). *Cancer Facts & Figures 2001.* Atlanta, GA: ACS, Inc., 2001:5; ACS. *Cancer Facts & Figures 2002.* Atlanta, GA: ACS, Inc., 2002:4; ACS. *Cancer Facts & Figures 2003.* Atlanta, GA: ACS, Inc., 2003:4; ACS. *Cancer Facts & Figures 2004.* Atlanta, GA: ACS, Inc., 2004:4; ACS. *Cancer Facts & Figures 2005.* Atlanta, GA: ACS, Inc., 2005:4; ACS. *Cancer Facts & Figures 2006.* Atlanta, GA: ACS, Inc., 2006:4; ACS. *Cancer Facts & Figures 2007.* Atlanta, GA: ACS, Inc., 2007:4; ACS. *Cancer Facts & Figures 2008.* Atlanta, GA: ACS Inc., 2008:4.

Treatment Options for CML 2022



Why do Patients Prefer Oral Anticancer Medicines?

- **Convenience**
  - **Decreases office visits**
  - **Alleviates transportation and parking concerns**
- **Empowerment**

NCCN Task Force Report: Oral chemotherapy. Weingart SN et al. J Natl Compr Canc Netw. (2008)

Added Challenges with Oral Anticancer Medicines

- **Shifting of responsibility of monitoring and administration to patient**
  - **Adherence is important to maintaining response**
  - **Relies on pts willingness to follow-up on blood work, testing**
  - **Accidental hazardous exposure risk at home**
- **With oral treatments - decreased contact with the cancer care team**
  - **Traditional practices are not often set up for managing oral anticancer medicines**
- **Often more than one drug available – each with different side effects**

Common Misconceptions with Oral Anticancer Medicines

- **Fewer side effects**
  - **“Simpler” and “Safer”…“like taking a multivitamin”**
  - **Drug Interactions**
- **Less burdensome administration vs adherence**
  - **Patient may equate it to taking an antibiotic or their BP meds**
  - **Might be ok to miss doses periodically**
- **Cost – out of pocket pharmacy cost**
  - **Specialty pharmacy involvement, Medicare**
  - **Ongoing prior authorization often required**

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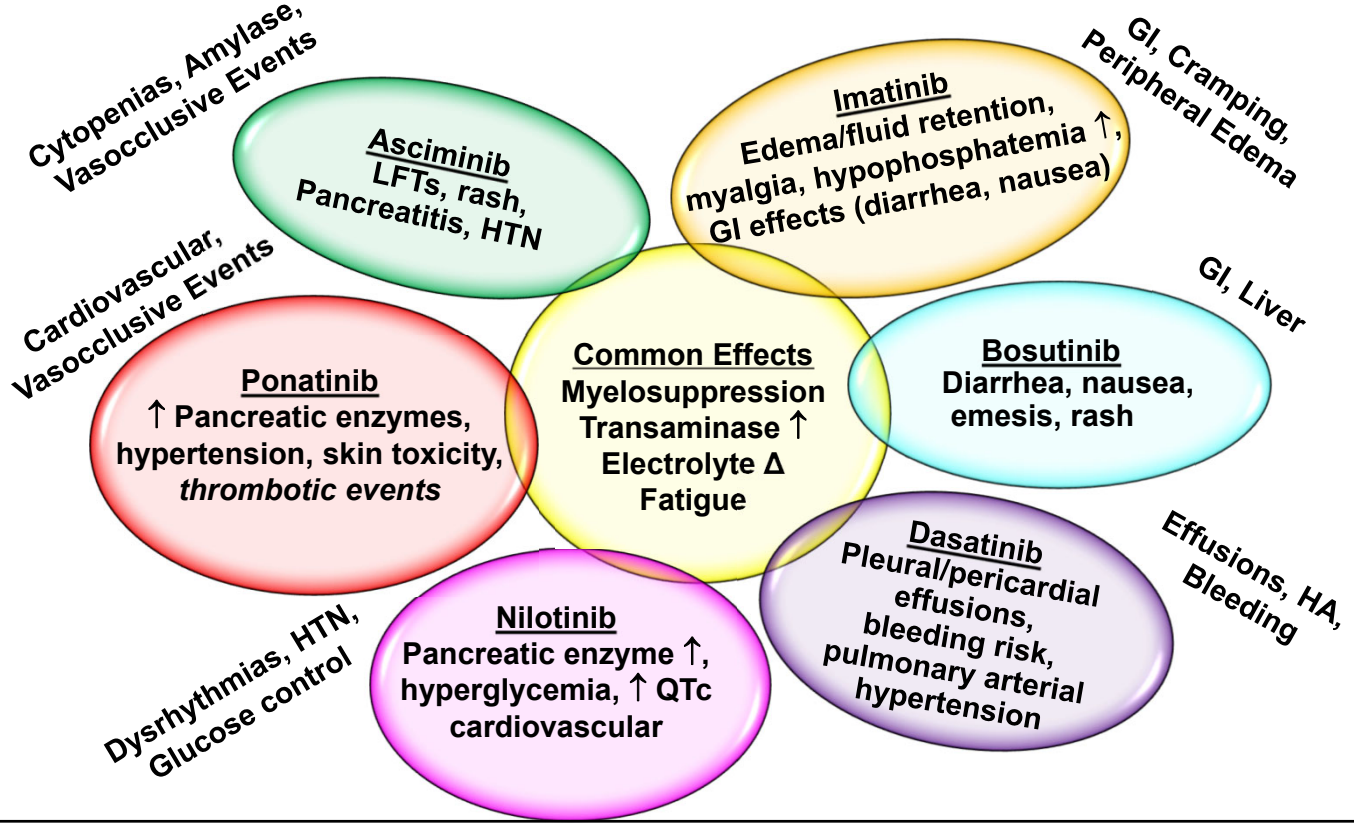
Treatment Options Based on Adverse Event Spectrum of TKIs in CML



Early Monitoring of Patients on Oral Anticancer Medicines

- **Bone marrow and peripheral counts:**
  - **Early cytopenias - can be significant**
  - **Late cytopenias – must determine etiology**
- **Liver and renal function vital – metabolism and clearance**
- **TKIs and Cardiovascular impact:**
  - **Early impact on ECG, fluid retention**
  - **Late impact on cardiac risk factors (HTN, peripheral vasculature)**

ELN and NCCN Response Guidelines for CP-CML

ELN Response Milestones			
Month	Optimal	Warnings	Failure
3	*BCR-ABL* ≤10% and/or Ph+ ≤35%	*BCR-ABL* >10% and/or Ph+ 36%-95%	<CHR and/or Ph+ >95%
6	*BCR-ABL* <1% and/or Ph+ 0	*BCR-ABL* 1%-10% and/or Ph+ 1%-35%	*BCR-ABL* > 10%, and/or Ph+ > 35%
12	*BCR-ABL*1 ≤0.1%	*BCR-ABL*1 0.1%-1%	*BCR-ABL*1 >1% and/or Ph + >0
18	*BCR-ABL*1 ≤0.1%	CCA/Ph- (-7, or 7q)	Loss of CHR, CCyR, or MMR*, Mutations
Any time	Stable or improving MMR	↑ transcript levels CCA/Ph-	Loss of CHR or CCyR, IM insensitive mutants

Cortes JE, et al. *J Natl Compr Canc Netw.* 2012;10:S1-S13; Baccarani M, et al. *Blood.* 2013;122:872-884.

EARLY TREATMENT RESPONSE MILESTONES[k,l]

BCR::ABL1 (IS)	3 months	6 months	12 months[m]
>10%[n]	YELLOW	RED	
>1%–10%	GREEN		YELLOW
>0.1%–1%	GREEN		LIGHT GREEN
≤0.1%	GREEN		

RED	TKI Resistant Disease
YELLOW	Possible TKI Resistance
GREEN	TKI-sensitive disease
LIGHT GREEN	

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Chronic Myeloid Leukemia (Version 1.2023).
© 2023 National Comprehensive Cancer Network, Inc. Available at: NCCN.org.

Safe Handling of Oral Anticancer Medicines

- **Storage**
  - **Preferred: original container or blister-pack it came in**
  - **Alternative: separate pill box for oral anticancer medicines**
- **Patient precautions: wash hands before & after**
- **Caregivers: never touch oral anticancer medicines with bare hands**
  - ***Pregnant women, breast-feeding women, men who are trying to get their partner pregnant, and children should never handle oral anticancer medicines***
- **Unless otherwise instructed, important not to crush, open, chew, break, dissolve, or cut oral anticancer medicines**

Safe Disposal of Oral Anticancer Medicines

- **Recommended not to throw it in the trash or flush down toilet**
- **Look for receptacles outside of the retail pharmacies for safe disposal**
- **National and Local Take Back Programs**
- **Drug Repositories:**
  - **Some pharmacies are allowed to collect unused, sealed medications donated by patients and re-dispense to patients in need for a very small fee**

Drug Interactions: Herbals, Vitamins, Supplements

Resources:

Memorial Sloan-Kettering Cancer Center's Guide
https://www.mskcc.org/cancer-care/diagnosis-treatment/symptom-management/integrative-medicine/herbs/search

Natural Medicine trc | natural medicines
https://naturalmedicines.therapeuticresearch.com/

Opportunity to learn more:

https://www.mskcc.org/videos/herb-drug-interactions-care

Educate patients to talk with their provider or pharmacist before taking new medications, including OTC supplements, or receiving any vaccines

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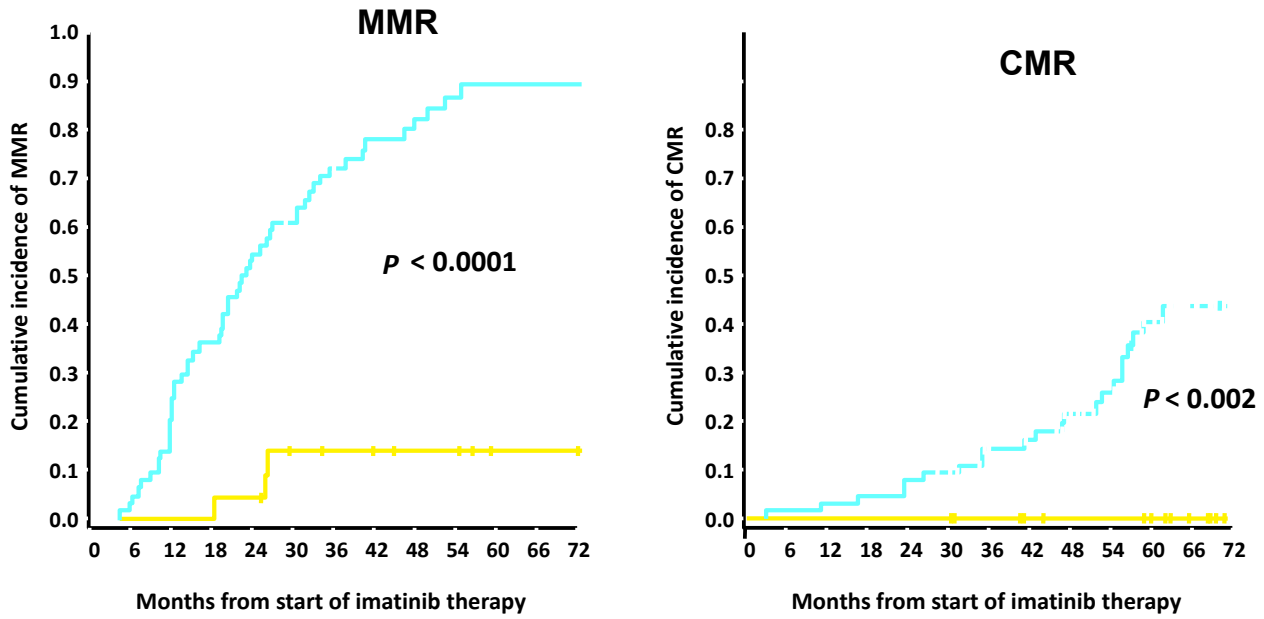
NCCN Task Force Report: Oral chemotherapy. Weingart SN et al. J Natl Compr Canc Netw. (2008)

Adherence and Molecular Response



Bazeos A, et al. *Blood.* 2009;114:abstract 3290; Ibrahim AR, et al. *Blood.* 2011;117:3733-3736.

Factors Associated with Non-Adherence

- **Complex regimens**
- **Need for substantial behavior change**
- ***Inconvenient/insufficient clinics and supervision***
- ***Poor communication with healthcare providers***
- **Patient dissatisfaction with care**
- **Patient health beliefs**
- ***Inadequate social support***
- **History of non-adherence**
- **History of mental illness**

Partridge, et al. *J Natl Cancer Inst*. 2002;94:652-661.

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Image from: http://www.martybucella.com/M111.gif

Medicare Part B

- **Historically covers outpatient provider and infusion clinic visits**
- **Covers limited (“older”) oral anticancer medications:**
  - **Busulfan, capecitabine, cyclophosphamide, etoposide, fludarabine, melphalan, methotrexate, temozolomide, and topotecan**
  - **Also covers anti-emetics (e.g., ondansetron) if patient is also receiving any of the above oral anticancer medications and they are filled on the same day**

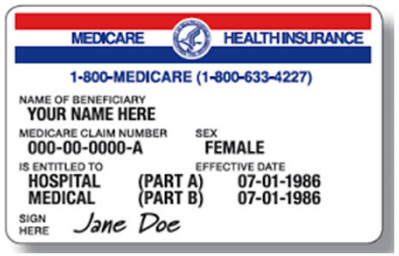

Image from: http://www.shorelineareanews.com/2017/04/dont-become-medicare-card-fraud-victim.html

Medicare Part B: Co-pay Breakdown

- **Medicare Part B only covers 80% of drug, patient with a 20% copay**
  - **E.g., $2000 cost = $1600 covered and $400 copay**
  - **Supplemental insurance (e.g., MediGap Plan, Medicare Plan F, H) to cover rest**
    - **These plans may have a deductible Medicaid functions as a supplemental plan**
  - **Medicare Part D CANNOT be used as a supplemental plan**

- **Medicare has strict requirements for Rx coverage:**
  - **Rx must have ICD-10 code Rx must be signed and dated by hand**

Specialty Pharmacies

- **Insurance plans typically require that high-cost medications be filled by a specialty pharmacy**
  - **Typically restrict to a specific specialty pharmacy that contracts with their prescription coverage**
  - **Override can be permitted so pts can fill locally before having to switch to a specialty pharmacy**

- **Out of pocket cost can still be very expensive**

High Copay: Financial Assistance

Copay Cards *(Provide Copay Assistance)*	Foundation Grants *(Provide Copay Assistance)*	Manufacturer Programs *(Provide Free Medication)*
• Brand medications • Exclude patients w/ Medicaid/Medicare (i.e., govt. funded) prescription coverage • Have monthly and/or yearly maximums	• Brand or generic medications • Funds available by disease state • Any patient that meets income requirements • Limited funding → grants get exhausted	• Brand medications only • Any patient that meets income requirements • Primarily intended for uninsured or low-income patients

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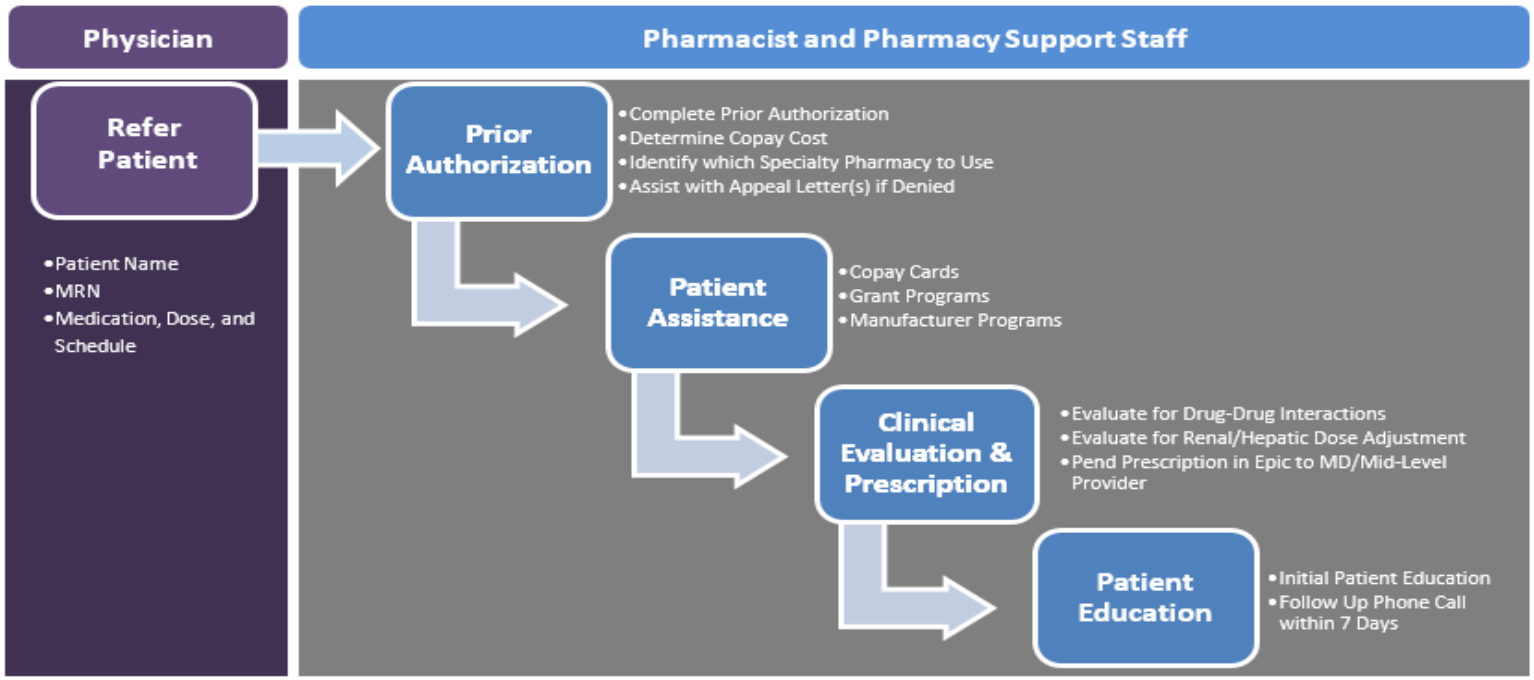
Develop an Outpatient Oral Anticancer Medicine Team + Process



Medication Specific Educational Materials

Oncology Specific Resources

ChemoCare®

https://chemocare.com/

Available in English and Spanish

HOPA Oral Chemotherapy Education

https://www.oralchemoedsheets.com/

Only available in English

General Resources

Krames®:

https://www.kramesondemand.com/Browse.aspx

Integrated into Epic via the "References" Section

Available in English and Spanish

LexiComp®

http://www.crlonline.com/lco/action/pcm

Available in ~20 languages

Micromedex

https://www.micromedexsolutions.com/carenotes/librarian?navitem=topCareNotes

Available in English and Spanish

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- **Promises:**
  - **Precision and Personalized Medicine – started with CML**
  - **Perceived benefits**

    Safety (?) **Less burdensome administration (?)** **Compliance (?)**

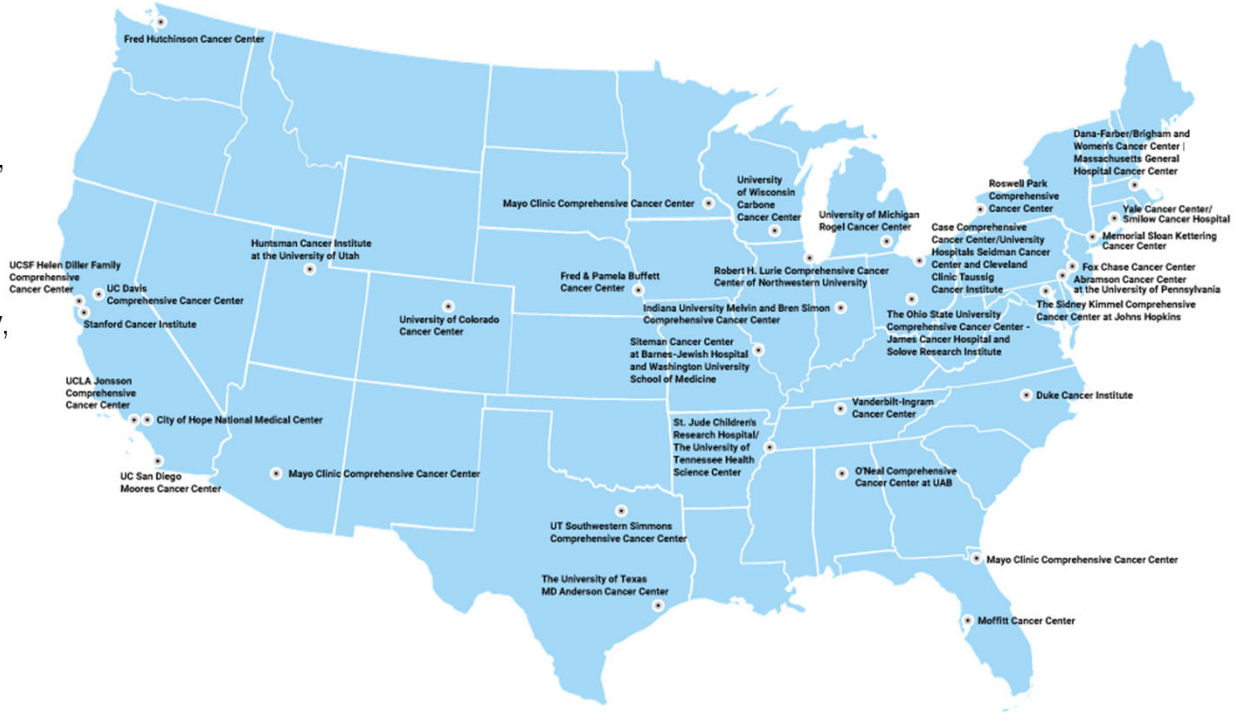
- **Pitfalls:**
  - **Safety and Monitoring, Handling of meds, Drug Interactions**
  - **Adherence**
  - **Cost, Specialty Pharmacies, Medicare**

- ***A multidisciplinary team with expertise helps to improve outcomes***

National Comprehensive Cancer Network®

NCCN Member Institutions

- **Who We Are**
  An alliance of leading cancer centers devoted to patient care, research, and education
- **Our Mission**
  To improve and facilitate quality, effective, equitable, and accessible cancer care so all patients can live better lives
- **Our Vision**
  To define and advance high-quality, high-value, patient-centered cancer care globally



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