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HIGHLIGHTS IN THERAPY: CHRONIC MYELOID LEUKEMIA (CML)

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**World
CML Day**
22 SEPTEMBER

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WELCOMING REMARKS

HIGHLIGHTS IN THERAPY: CHRONIC MYELOID LEUKEMIA



Lizette Figueroa-Rivera, MA
Sr. Director, Education & Support
The Leukemia & Lymphoma Society



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FACULTY

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DISCLOSURES

HIGHLIGHTS IN THERAPY: CHRONIC MYELOID LEUKEMIA

Dr. Gabriela Hobbs, has the following financial relationships to disclose: Abbvie, Morphosys, BMS, Pfizer, Novartis, Pharmaxis and Cogent (*Consultant*); Incyte (*Research Support*).



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Outline

- CML background
- CML treatment and monitoring
- Side-effect management
- Treatment free remission
- Quality of life
- New therapies on the horizon for CML



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Background

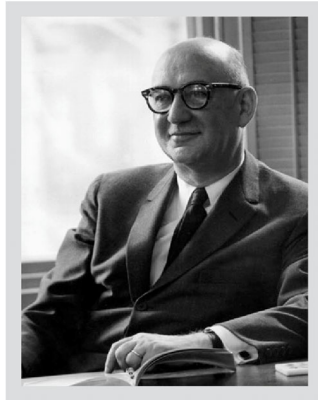
- CML occurs from the reciprocal translocation between chromosomes 9 and 22 forming the BCR-ABL1 fusion gene.
- 15-20% of leukemias in adult
- Incidence of 1-2 cases per 100,000
- Prevalence is increasing due success of current therapy
- Median age 50, slight male predominance
- Untreated CML will progress from:
 - Chronic to accelerated to blast phase (similar to acute leukemia)



Chen Leuk Lymphoma 54: 1411-1417
Siegel Cancer Statistics, 2014, CA Cancer J Clin 64:9-29

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A bit of history



1951- William Dameshek described the concept of Myeloproliferative diseases including chronic granulocytic leukemia.

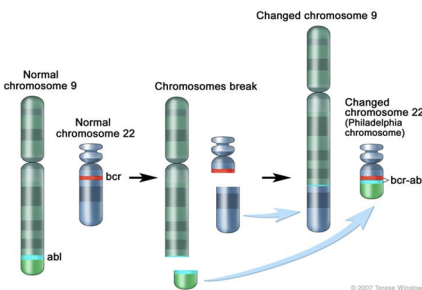
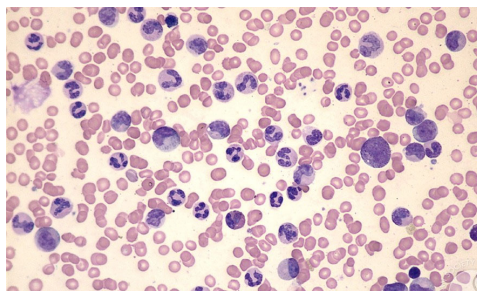


1959- David Hungerford and Peter Nowel observed abnormality in chromosomes cultured from CML patients. First cytogenetic change consistently associated with neoplasia.



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Genetics of CML: *BCR-ABL1* and the Philadelphia Chromosome



ASH Image Bank

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The Advent of Tyrosine Kinase Inhibitors (TKI) in CML Treatment: Successes and Remaining Challenges

In 2023 there are 4 TKIs available for first-line therapy:

- Imatinib
- Dasatinib
- Nilotinib
- Bosutinib

There are 2 TKIs for 3-line therapy:

- Ponatinib
- Asciminib

Challenges:

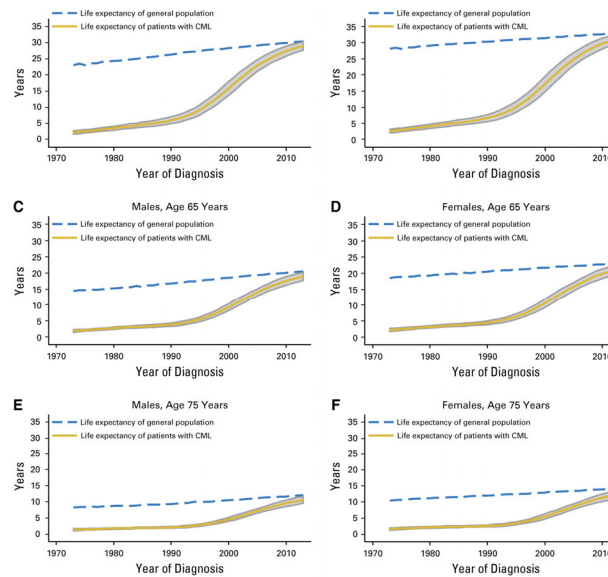
- Chronic side effects
- Resistance
- Cost



O'Brien SG, et al. *New Engl J Med.* 2003;348(11):994-1004. Radich JP, et al. *J Natl Compr Canc Netw.* 2018;16(9):1108-1135.

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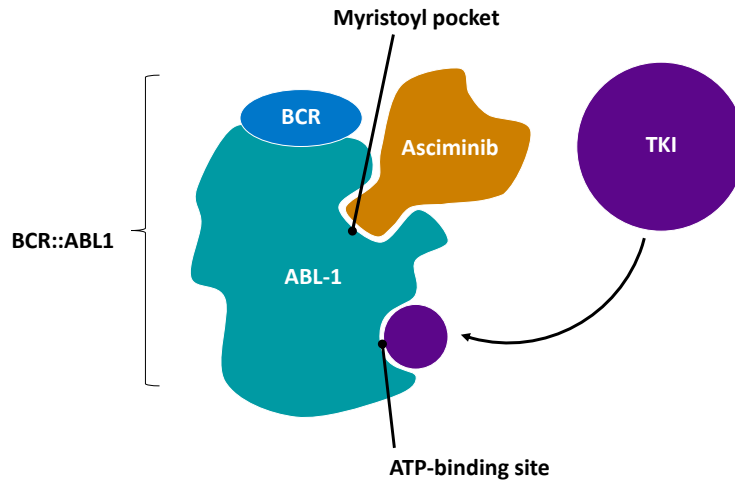
Life expectancy in CML is now near normal



Bower JCO 2016

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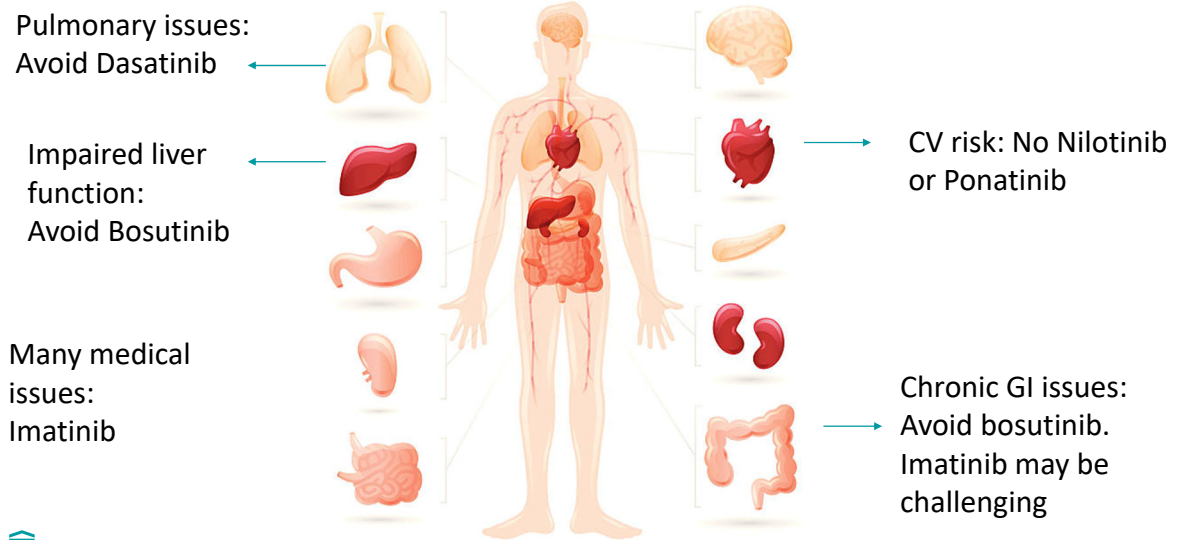
How do the TKIs work?



Hughes. NEJM. 2019;381:2315.

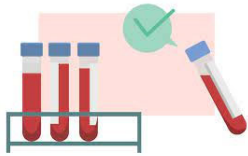
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Choosing therapy that's right for each patient



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What to expect in the first three months?



Frequent lab draws



New pills



Frequent clinic visits

Feeling scared

Anxiety

Side effects
From treatment



The good news is...



Monitoring

First three months	First year	After MMR (PCR <0.1)	Side effects? Questions?
Weekly to monthly visits	Every 3 months	Every 6 months	Visits can occur more frequently
Blood counts, check liver/kidney function	PCR- for BCR-ABL every 3 months	PCR- for BCR-ABL every 3 months	



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CML Milestones

<i>BCR::ABL1</i> (IS)	3 Mo	6 Mo	12 Mo
>10%	Possible TKI resistance (CAUTION)	TKI resistance (STOP)	
>1% to 10%	TKI sensitive (GO)		Possible TKI resistance (CAUTION)
>0.1% to 1%	TKI sensitive (GO)		TKI sensitive (TENTATIVE)
≤0.1%	TKI sensitive (GO)		



NCCN. Clinical practice guidelines in oncology: chronic myeloid leukemia. v.1.2023. nccn.org.

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What does success look like?



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The goal of therapy is living well with CML- Supportive care is critical!

Seek care if you don't feel well

TKI	Side effects
Imatinib	Fluid retention, fatigue, rash, myalgias, GI
Dasatinib	Pleural effusion (30% at 5 years), PAH
Nilotinib	Vascular events, PVD, hyperglycemia, QTc, rash
Bosutinib	Diarrhea, LFT elevation
Ponatinib	Thrombotic events, vascular occlusion, CHF, hepatotoxicity, headache, rash, pancreatitis, HTN
Asciminib	LFT elevation, increased blood pressure

LFT= Liver function test CHF= Congestive heart failure PVD= peripheral vascular disease



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Drug-Drug interactions- why it matters

Ensure that there aren't drug interactions with your CML medication

- Interactions can change efficacy
- Interactions can increase side effects

Common medications may have interactions (for example- acid blocking medications)

Effects can be impactful- muscle pain, swelling, impact on blood counts, vomiting, diarrhea, rash, liver function abnormalities, renal insufficiency

Patients on more medications are at increased risk

Theoretically can affect TKI response, but this has not been clinically documented



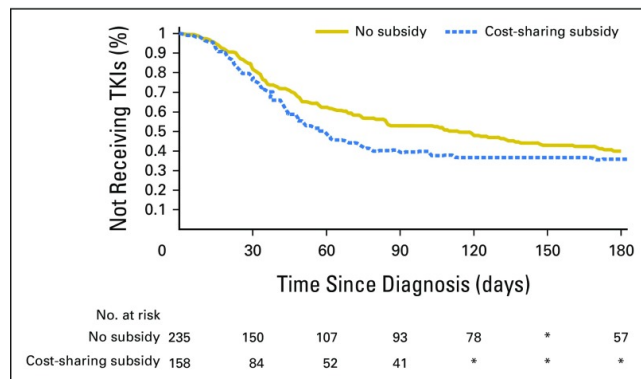
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Cost is a side effect

Ask about patient assistance programs or alternative TKI

Patients delay initiation of therapy due to upfront costs

Patients with high co-payment costs are more likely to discontinue or be nonadherent to therapy



68% of Medicare recipients start therapy within the first 6 months of diagnosis

Winn JCO 2016 Dec 20; 34(36):4323-4328.
 Dusetzina JCO 2014 Feb 1;32(4):306-11).
 Winn JCO 2016 Dec 20;34(36): 4323-4328



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Treatment success- empowering YOU!

Discuss side effects/questions with providers

Ensure side effects well managed

Is cost an issue?
Delivery of medication?

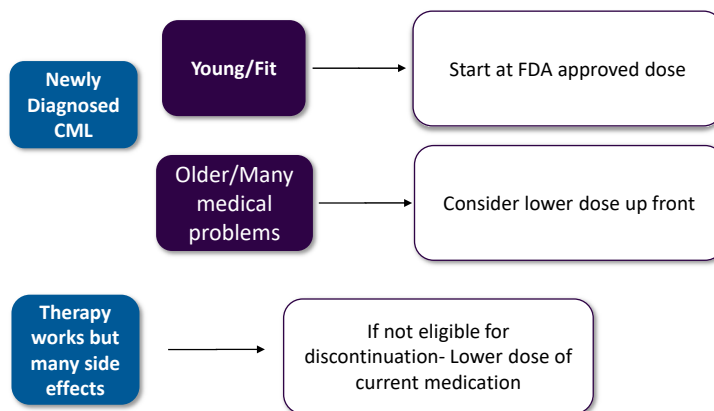
Are there medications that can be stopped?

Know what to expect from treatments and tests



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What about different doses? Lowering the dose can help



Cancer. 2020;126(1):67-75 and Gener-Ricos G, et al. ASH conference 2022. Abstract 619
Lancet Haematol. 2021;8(12):e902-e911
Rea D, et al. Blood. 2017 Dec;130(Supplemental 1): 318



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Treatment free remission

Also known as- stopping your therapy!



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Treatment free remission- who can stop therapy?

Criteria for TKI Discontinuation

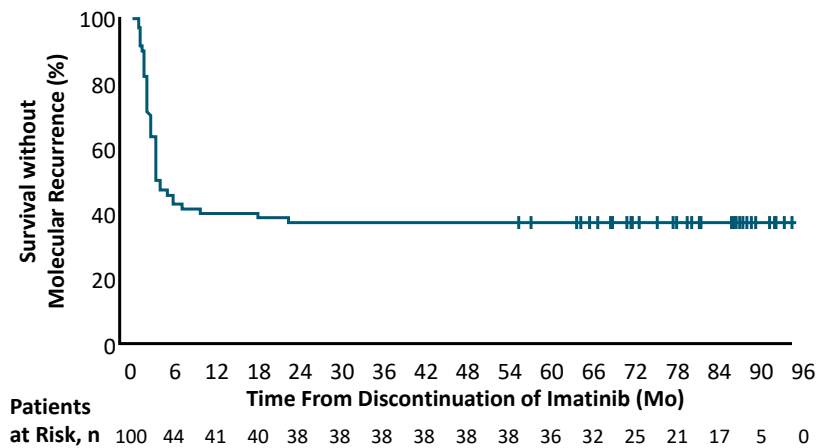
- Age ≥ 18 yr
- CP-CML with no history of AP-CML or BP-CML
- On approved TKI ≥ 3 yr
- Prior evidence of quantifiable *BCR::ABL1* transcript
- Stable molecular response (MR⁴; *BCR::ABL1* $\leq 0.01\%$ IS) for ≥ 2 yr on ≥ 4 tests performed ≥ 3 mo apart



NCCN. Clinical practice guidelines in oncology: chronic myeloid leukemia. v.1.2023. nccn.org.

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Long-term Follow-up From STIM1 Trial in CP-CML: OS Without Recurrence



Similar data have been obtained from numerous studies with other TKIs

Etienne. JCO. 2017;35:298.

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How to monitor after discontinuation?

- Monthly molecular monitoring for months 1-6
- Bimonthly for months 7-12,
- Quarterly thereafter
- If loss of MMR (PCR>0.1%), resume TKI within 4 weeks
 - Molecular monitoring monthly until MMR regained, then quarterly thereafter
 - Consider mutation testing in those who fail to regain MMR after 3 mo of TKI resumption



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Are there downsides to discontinuing therapy?

- Frequent monitoring initially
- Some patients experience a syndrome of withdrawal
- Anxiety about being off therapy



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Therapeutic strategies in development

New TKIs

- BCR-ABL TKI- Radotinib

Efforts to combine therapies:

- Asciminib + other TKIs
- Interferon + TKI
- Nilotinib + ruxolitinib (JAK inhibitor)
- Aurora Kinase inhibitors- Lonafarnib, tipifarnib
- Farnesyl transferase inhibitors- Danusertib, Tozasertib



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Areas of unmet need

- Cost of therapy (and of monitoring)
- Better therapies for advanced CML (accelerated phase and blast phase)
- Better strategies to help patients discontinue therapy and to remain off therapy
- Wide spread availability of testing and therapy across the US and globally




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Thank you



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ASK A QUESTION HIGHLIGHTS IN THERAPY: CHRONIC MYELOID LEUKEMIA

Ask a question by **phone**:
Press star (*) then the number 1 on your keypad.


Ask a question by **web**:
Click "Ask a question"
Type your question
Click "Submit"

Due to time constraints, we can only take one question per person. Once you've asked your question, the operator will transfer you back into the audience line.



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LLS EDUCATION & SUPPORT RESOURCES

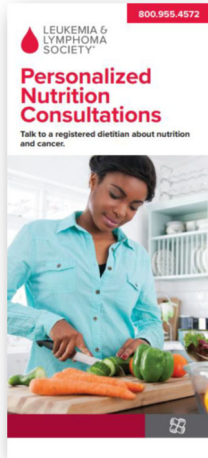


HOW TO CONTACT US:


To contact an **Information Specialist** about disease, treatment and support information, resources and clinical trials:
www.LLS.org/InformationSpecialists

Call: (800) 955-4572
Monday to Friday, 9 a.m. to 9 p.m. ET
Chat live online: www.LLS.org/InformationSpecialists
Monday to Friday, 10 a.m. to 7 p.m. ET
Email: www.LLS.org/ContactUs
All email messages are answered within one business day.

CLINICAL TRIAL SUPPORT CENTER
Work one-on-one with an LLS Clinical Trial Nurse Navigator who will help you find clinical trials and personally assist you throughout the entire clinical-trial process.
www.LLS.org/Navigation

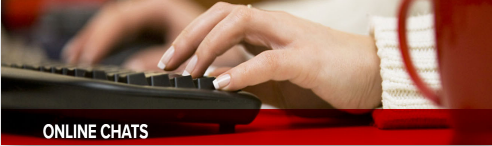


PERSONALIZED NUTRITION CONSULTATIONS
Our registered dietitian has expertise in oncology nutrition and provides free one-on-one consultations by phone or email.
www.LLS.org/Consult



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LLS EDUCATION & SUPPORT RESOURCES



ONLINE CHATS

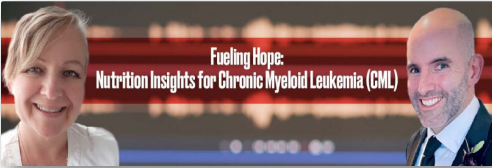
Online Chats

Online Chats are free, live sessions, moderated by oncology social workers. To register for one of the chats below, or for more information, please visit www.LLS.org/Chat




Education Videos

View our free education videos on disease, treatment, and survivorship. To view all patient videos, please visit www.LLS.org/EducationVideos

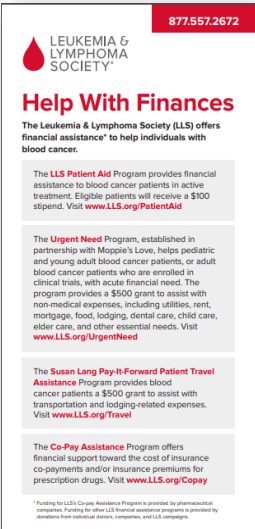


Patient Podcast

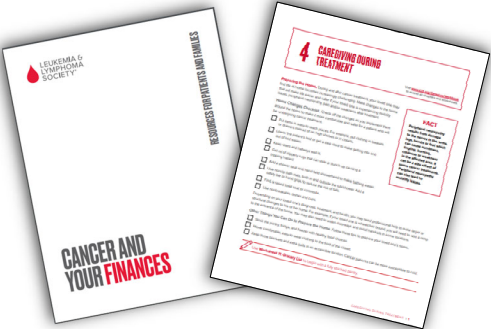
The Bloodline with LLS is here to remind you that after a diagnosis comes hope. To listen to an episode, please visit www.TheBloodline.org




LLS EDUCATION & SUPPORT RESOURCES



The Leukemia & Lymphoma Society (LLS) offers the following financial assistance programs to help individuals with blood cancers:
www.LLS.org/Finances



To order free materials: www.LLS.org/Booklets





THANK YOU

We have one goal: A world without cancer.



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