CML:Overview and Treatment Paradigms

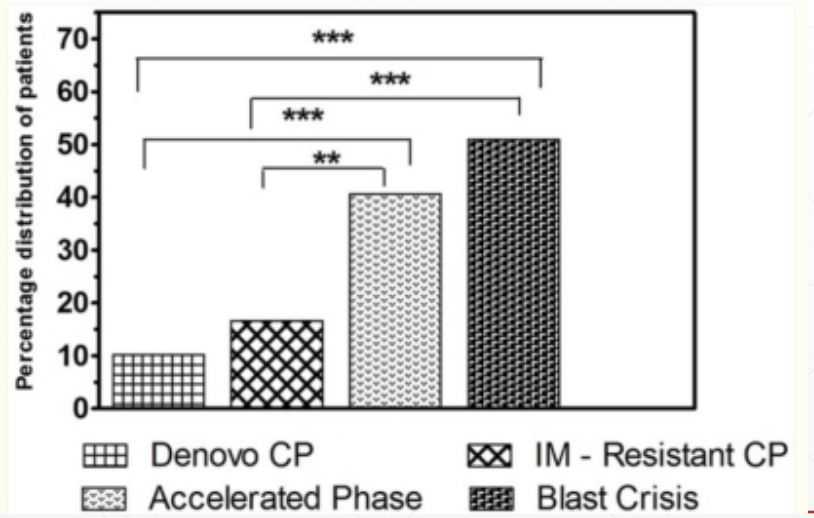
By Cristina M. Ghiuzeli
Oct 9th, 2025

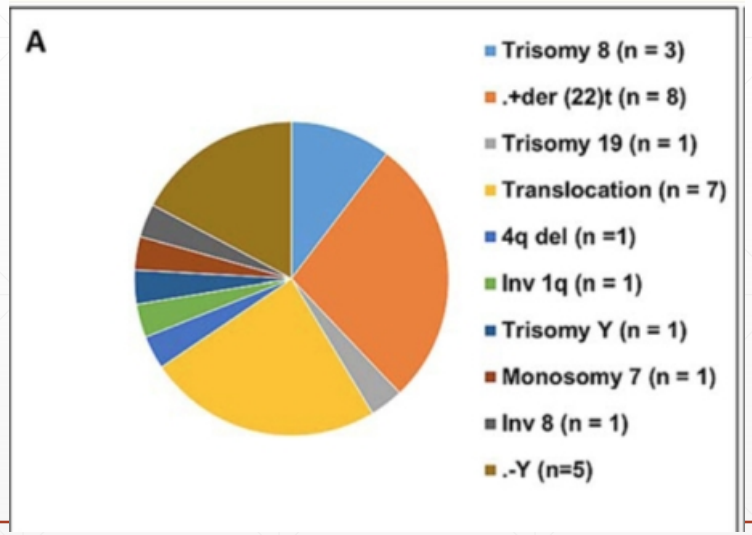
Objectives

- How to diagnose, classify, and prognosticate CML
- How to choose 1st line of treatment
- Milestones for response assessment
- Goals of CML treatment
- TKI discontinuation
- Recognizing accelerated and blast phase CML
- Indications for transplant

CML:Presentation

- PS is a 64yo F who was referred to hematology after pre-op CBC for planned knee replacement surgery showed the following:
  - wbc 283k/ul with Hb 12.1g/dl, platelets 143k/ul. Diff: 65% N, 4% Ly, 4% Mo, 1% Eo's, 2% Baso, 14% Metamyelo, 7% Myelo, 3% other immature cells (blasts)
  - On exam, spleen enlarged 2cm below costal margin -> confirmed splenomegaly on US, 17cm
    - NEXT: Bone marrow biopsy! ->cytogenetics! Philadelphia chromosome: t(9;22) (q34;q11.2)
    - Important to assess for ACA (Additional Chromosomal Abnormalities)
  - ACA:





Krishna Chandra et al Front Onc 2019; March 5;9:88
Alhuraiji Am J Hematol. 2018;93(1):84–90

CML Risk Scores

- Prognostic risk scores: Sokal, Euro and EUTOS –differences in survival, response to TKI

Age:	years
Spleen:	max. distance from costal margin cm x 10 (e.g. 6 cm = 60)
Platelet:	Plt 10^9 L (e.g 350000 µl = 350)
Blood Basophils:	% x 10 (e.g. 1.5% = 15)
Blood Eosinophils:	% x 10 (e.g 2.6% = 26)
Blood Myeloblasts:	% x 10 (e.g 0.7% = 7)

- New EUTOS Long Term Survival (ELTS) score –similar to Sokal, but takes into account that most CML patients now do NOT die of their disease

Age in completed years:	years	
Spleen size in cm below costal margin:	cm	
Blasts in peripheral blood:	%	
Platelet count in 10^9/L		

CML:Presentation (cont.)

- PS is a 64yo F with abnormal blood counts:
  - wbc 283k/ul with Hb 12.1g/dl, platelets 143k/ul. Diff: 65% N, 4% Ly, 4% Mo, 1% Eo's, 2% Baso, 14% Metamyelo, 7% Myelo, 3% other immature cells (blasts)
  - On exam, spleen enlarged 2cm below costal margin -> confirmed splenomegaly on US, 17cm
  - Bone marrow biopsy: hypercellular, neutrophilia, 2% blasts
    - Cytogenetics: 46,XX,t(9;22)(q34;q11.2),t(14;20)(q21;p12)?c[20]
    - FISH: positive for BCR-ABL in 171 out of 200 nuclei
    - PCR: BCR-ABL p210 major fusion 48.1% IS
  - Prognostic risk scores:
    - Sokal: low risk
    - ETLS: intermediate risk
      - LRD: Leukemia Related Death

(b) Risk strata proportions and outcome

	Low risk		Intermediate risk		High risk	
$n = 5154$	Sokal	ELTS	Sokal	ELTS	Sokal	ELTS
%	38	55	38	28	23	13
10-year OS	89%	88%	81%	79%	75%	68%
6-year LRD	3%	2%	4%	5%	8%	12%

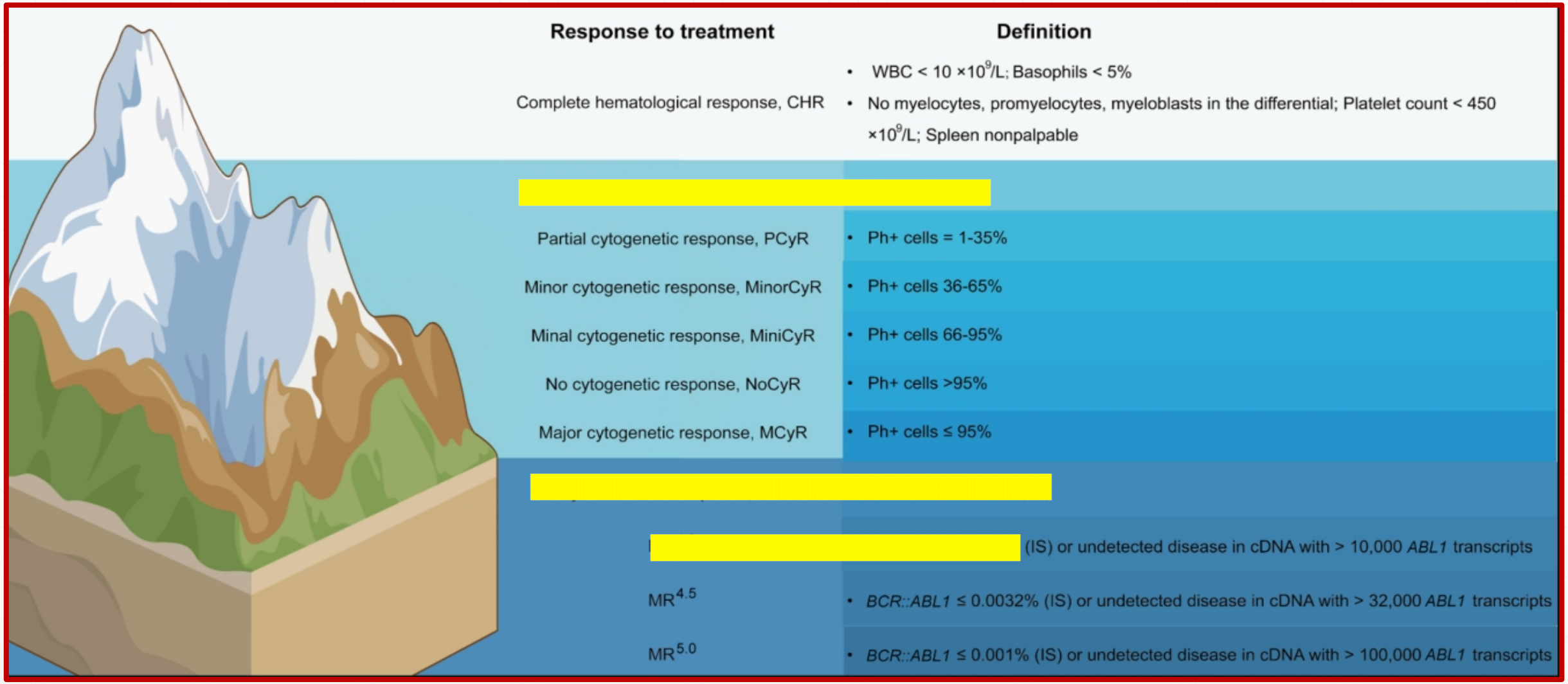
ELN2020: Hochhaus et al Leukemia (2020) 34:966–984

CML:First line treatment -considerations

- What are the goals of treatment?
  - *What are the response categories and response milestones?*
  - *Treat for a limited time or aim for TFR (treatment-free remission) in the future?*
- What is the patient's age?
  - *Young age, or older patient? Is fertility/family planning important?*
- What are the patient's comorbidities?
  - *In particular, consider cardiac history, PVD (arterial insufficiency/venous insufficiency), diabetes, hypercholesterolemia, pulmonary disease COPD*
- What is the cost of the TKI, affordability considerations?
  - *Generic options for Imatinib and Dasatinib (and available on costplusdrugs.com) vs. Asciminib (Scemblix)-$$$*
- What is the CML stage (CP, AP, BP) and CP risk score?
  - *High vs. low risk ELTS to guide 1st vs. 2nd generation or later TKI's*

ELN2020: Hochhaus et al Leukemia (2020) 34:966–984

CML Response Categories



Wang et al, Blood reviews, Volume 65, May 2024, 101196

NCCN Guidelines Version 1.2026: Early Treatment Response Milestones

Assess for mutations in ABL

BCR::ABL1 (IS)	3 months	6 months	12 months[q]
>10%[r]	YELLOW	RED	
>1%–10%[s]	GREEN		ORANGE
>0.1%–1%	GREEN		LIGHT GREEN
≤0.1%	GREEN		

COLOR	CONCERN	CLINICAL CONSIDERATIONS[u]	RECOMMENDATIONS[l,m,u]
RED	TKI-resistant disease[t]	• Evaluate patient adherence and drug interactions • Consider *BCR::ABL1* kinase domain mutational analysis[v] • Consider bone marrow cytogenetic analysis to assess additional chromosomal abnormalities (ACAs)	Switch to alternate TKI (CML-5) (other than imatinib) and evaluate for allogeneic HCT
YELLOW	Possible TKI resistance[t]	• Evaluate patient adherence and drug interactions • Consider *BCR::ABL1* kinase domain mutational analysis[v]	Switch to alternate TKI (CML-5) or Continue same TKI[r]
ORANGE	Possible TKI resistance[t]	• Evaluate patient adherence and drug interactions • Consider *BCR::ABL1* kinase domain mutational analysis[v] • Consider bone marrow cytogenetic analysis to assess for complete cytogenetic response (CCyR) at 12 mo	Consider switch to alternate TKI[s] (CML-5) or Continue the same TKI if CCyR is achieved
LIGHT GREEN	TKI-sensitive disease	• Evaluate patient adherence and drug interactions • If treatment goal is long-term survival: ≤1% optimal • If treatment goal is treatment-free remission: ≤0.1% optimal	• If optimal: continue same TKI • If not optimal: shared decision-making with patient[t,w]
GREEN	TKI-sensitive disease	• Evaluate patient adherence and drug interactions • Monitor response (CML-G)	Continue same TKI[x]

NCCN Guidelines. Chronic Myeloid Leukemia. V1.2026.

CML:First line treatment –goals and age considerations

- What is the patient's age?

  YOUNG PATIENT

  - *Is the patient's goal to eventually come off TKI?*
  - *Fertility preservation and pregnancy*
    - *Males: 1ST and 2nd generation TKI's do not appear to affect fertility or cause birth defects → DO NOT stop TKI for family planning. NOTE: Data are sparse/absent for ponatinib and asciminib, respectively.*
    - *Females: TKI's DO cause higher rates of miscarriage and fetal abnormalities → STOP TKI preferably once in deep molecular remission (PCR<=0.01%). If treatment needed during pregnancy, Peginterferon alpha-2a is safe*

  OLDER PATIENT

  - *Consider co-morbidities, adverse events of drug*
  - *If you plan to treat with TKI life long, then you only need cytogenetic complete remission ! (equivalent PCR: ≤1%!)*

Monitor PCR for BCR-ABL q3 months indefinitely

Response	Translates into
BCR::ABL1 ≤ 10% at 6 months; CCyR later	Significantly improved survival
MMR	Modest improvement in EFS; possible longer duration CCyR; no survival benefit
DMR	Possibility of therapy discontinuation

Abbreviations: CCyR, complete cytogenetic response; DMR, deep molecular response (≤4.5-log reduction to ≤4-log reduction of *BCR::ABL1* transcript levels); EFS, event-free survival; MMR, major molecular response.

Abbruzzese *Blood* (2024) 144 (Supplement 1): 2435.
Jabbour et al, Am J Hematol, 2024 Nov;99(11):2191-2212

CML: Goal to stop TKI!

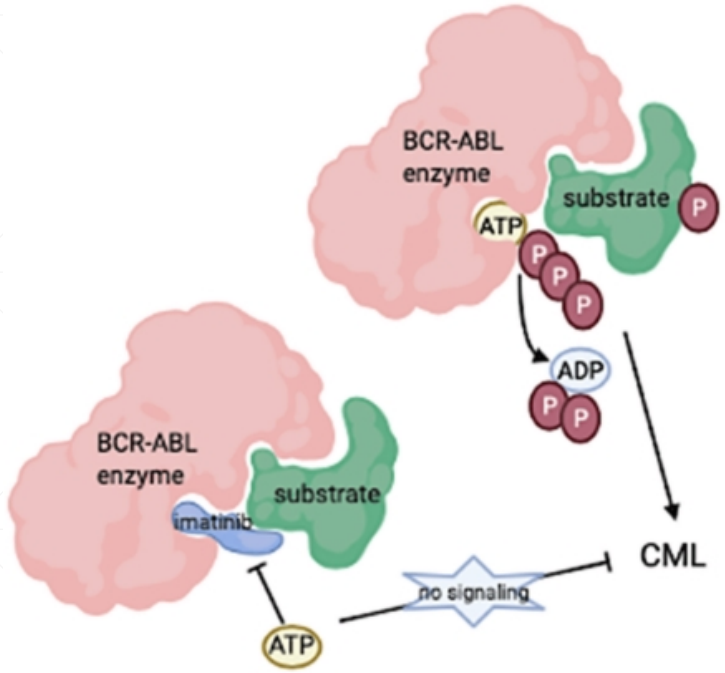
- For CP-CML (NOT AP/BP CML)
- 2 expert-opinion based recommendations (no prospective, randomized data)
  - NCCN recommends a DMR of MR^4 (0.01% PCR) or $MR^{4.5}$ (0.0032%)> **2 yrs**
  - ELN expert panel recommends TKI therapy >5 years with MR^4 > **3 years** or $MR^{4.5}$ > 2 years
- Risks of stopping:
  - Molecular recurrence → restart TKI if PCR≥0.1% within 4 weeks of MMR loss
  - TKI withdrawal syndrome → treat with NSAIDS; musculoskeletal pain, up to 30% patients

- For CP-CML (NOT AP/BP CML)
- PCR monitoring
  - Q4 weeks months 1-6
  - Q8 weeks months 7-12
  - Q3 months thereafter
- Success rates:
  - In general, about 50% long term TFR (treatment free remission)
  - May get better TRF with de-escalation?

    DESTINY trial: ½ dose TKI x12months, then stop. 72% RFS

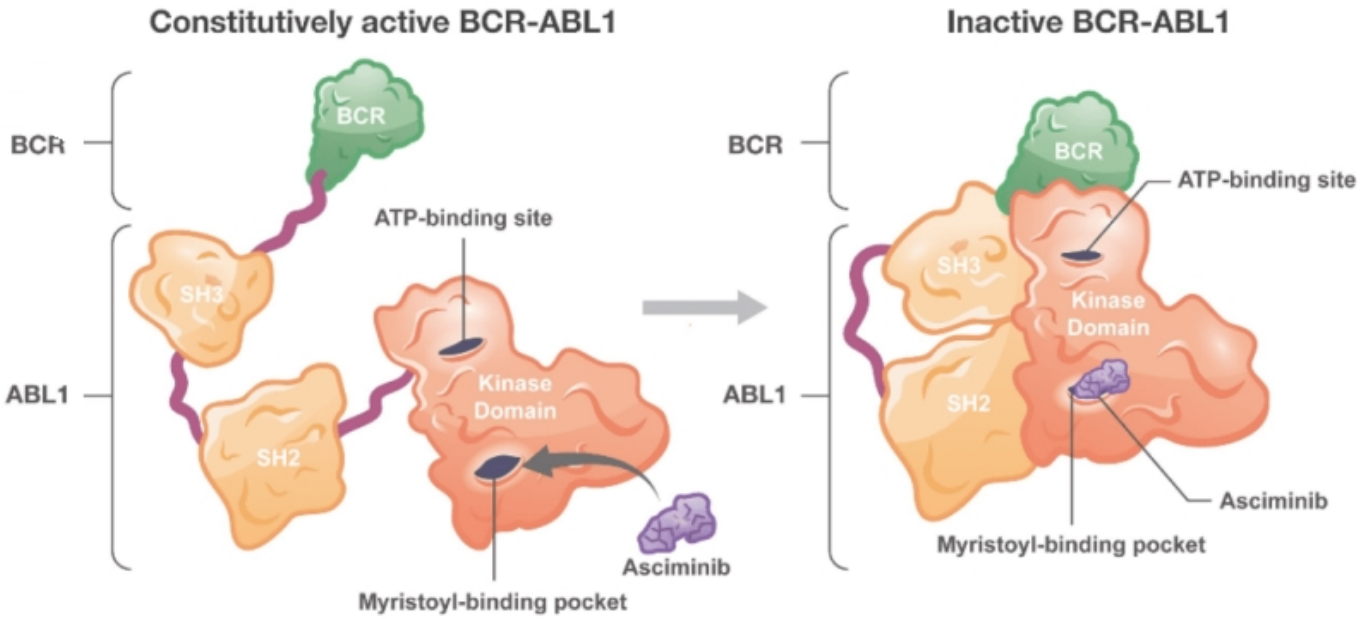
DESTINY trial: Clark et al, Lancet Haematol 2019 Jul;6(7):e375-e383

TKI's and Mechanism of Action



ATP-competitive binding site inhibitors:

- Imatinib -1st gen
- Dasatinib, Nilotinib, Bosutinib -2nd gen
- Ponatinib -3rd gen **T315I activity!**
- *In trials: Olverembatinib (HQP1351) -3rd gen* **T315I activity!**



STAMP (Specific Targets of the ATP Myristoyl-binding pocket)

- Asciminib –first one! **T315I activity!**
- *In trials: TERN-701, TGRX678*

Rea et al, Critical Reviews in Onc/Heme, vol 171, Mar 2022, 103580, Karasu et al, October 2021 Medical Oncology 38(10)

Common and Unique Toxicities of TKIs in CML

Cardiovascular, cerebrovascular and peripheral arterial vascular events

Requires close follow-up

1. Blood pressure
2. Fasting lipid panel
3. Hemoglobin A1c

Ponatinib
Arterial occulsive events, pancreatic enzymes ↑, hypertension, ocular toxicity

Imatinib
Edema/fluid retention, myalgia, hypophosphatemia, GI effects (nausea), transaminitis

Asciminib:
fatigue, headache, increased lipase, nausea, arthralgias, diarrhea, rash, and thrombocytopenia

Common Effects
Myelosuppression
Electrolyte Δ
Rash
Fatigue

Bosutinib
GI effects (diarrhea and nausea), pancreatic enzyme ↑, transaminitis

Nilotinib
Arterial occlusive events, pancreatic enzyme ↑, hyperglycemia QT prolongation, transaminitis

Dasatinib
Pleural/pericardial effusions, bleeding risk, pulmonary arterial hypertension

Medical comorbidities and older age may make it more difficult to use some 2nd generation TKIs front-line

Adapted from Dr. Michael J. Mauro, MD

Cortes JE, et al. *J Clin Oncol*. 2012;30(28):3486-3492
Kantarjian H, et al. *J Clin Oncol*. 2014;32(5 suppl):abstr 7081.
Saglio G, et al. *N Engl J Med*. 2010;362(24):2251-2259
Kantarjian H, et al. *N Engl J Med*. 2010;362(24):2260-2270

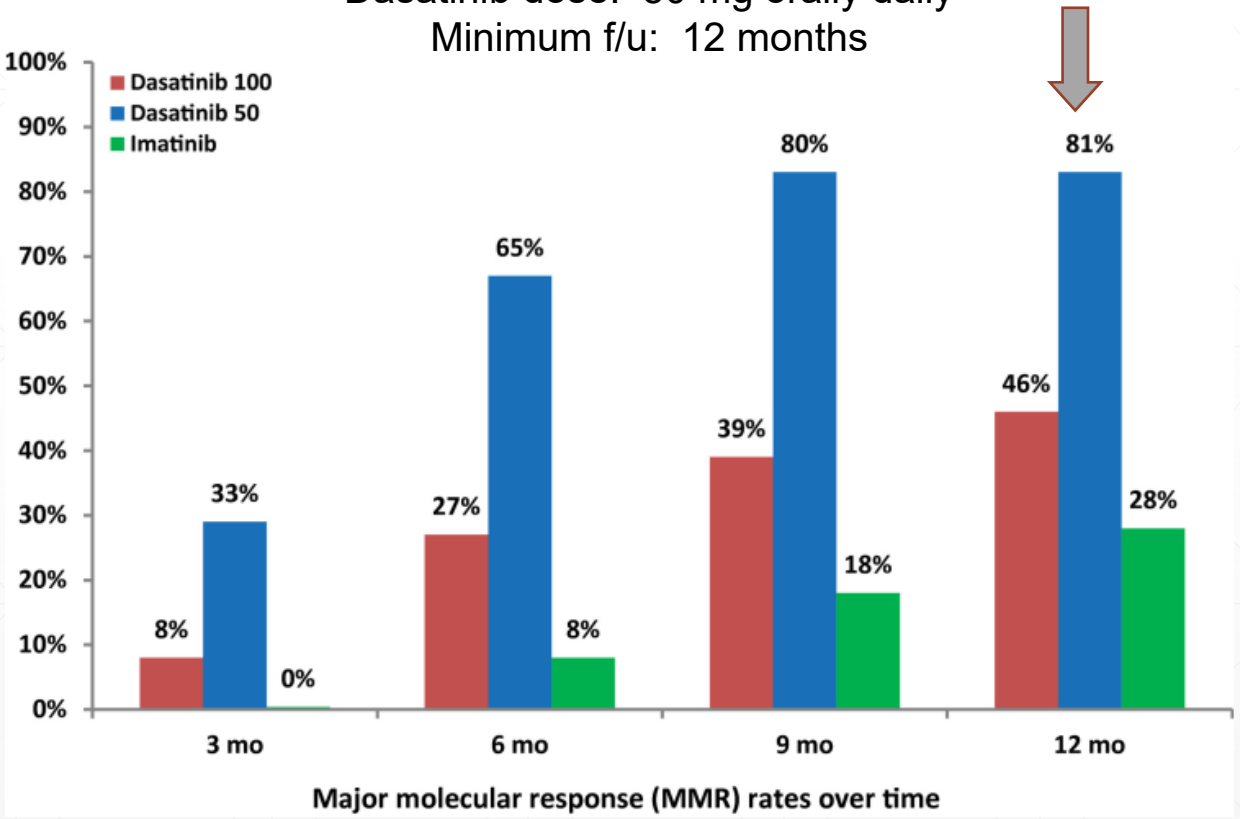
2nd GenTKI Selection Based on Co-Morbidities and Risks

History with prior TKI or co-morbidity	Preferred	Less preferred
Diabetes	Dasatinib, Bosutinib	Nilotinib
Pulmonary disease/PAH	Bosutinib, Nilotinib	Dasatinib
GI Issues	Nilotinib, Dasatinib	Bosutinib
Cardiovascular	Bosutinib	Nilotinib, Dasatinib?
Peripheral arterial	Bosutinib (*Dasatinib?*)	Nilotinib
Liver	Dasatinib (*Nilotinib?*)	Bosutinib
Renal	Nilotinib, Dasatinib	Bosutinib

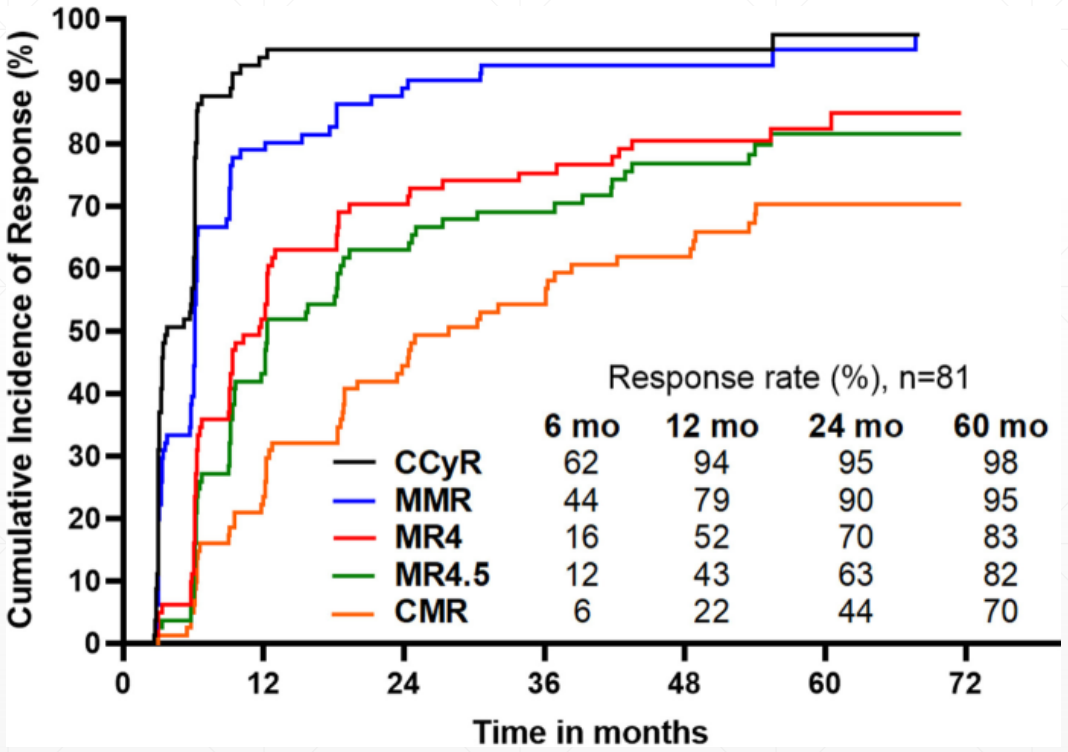
Cortes J. Blood. 2020 Nov 26;136(22):2507-2512.

Mitigating treatment related AEs: starting lower dose dasatinib first-line

N=81
Dasatinib dose: 50 mg orally daily
Minimum f/u: 12 months



5-year follow-up



Naqvi K et al. Cancer. 2020 Jan 1;126(1):67-75.
Gener-Ricos. Clin Lymphoma Myeloma Leuk. 2023 May 23:S2152-2650(23)00167-2.

11 patients (13%) developed pleural effusions
vs: up to 50% pts over age 70 develop pleural effusions with full dose Dasatinib 100mg po daily

CML: Rare TKI side effects that require TKI change!

Toxicities	TKI
Pulmonary hypertension	Dasatinib
Recurrent (more than once) pleural effusions	Dasatinib, (rare with others)
Pancreatitis	Ponatinib, nilotinib
AOEs (CVA, MI, and TIA) or VOEs or PAOEs	Ponatinib, nilotinib
Dementia-like, Lewy-body, ALS, Parkinsonism	Any TKI (rare)
Enterocolitis	Bosutinib
Immune-mediated myocarditis, hepatitis, nephritis	Any TKI

For Asciminib: Pancreatitis, grade 3 or 4 HTN, hypersensitivity reaction, grade 3 or 4 cardiac toxicity

Jabbour et al, Am J Hemat 2024; 99(11):2191-2212

CML:Cost of TKI's

- What is the cost of TKI's?

  - *Imatinib (generic): 30 day supply of 400mg tabs: $34.5 → 1 year: $414*
  - *Dasatinib (generic): 30 day supply of 100mg tabs: $363.8 → 1 year: $4366*
  - *Bosutinib (Bosulif brand name): 30 day supply of 400mg tabs: $25,800 → 1 year: $309,600*
  - *Nilotinib (Tasigna brand name): 30 day supply of 150mg tabs: $27,828 → 1 year: $333,936*
  - *Ponatinib (Inclusig brand name): 30 day supply of 30mg tabs: $27,984 → 1 year: $335,808*
  - *Asciminib (Scemblix brand name): 30 day supply of 40mg tabs: $26,838 → 1 year: $322,056*

CostPlusDrugs.com, UpToDate.com

CML:Presentation Stage

- Based on BM bx –determine presenting stage of CML: CP, AP, BP

- ICC 2022 Definitions

Accelerated phase
Bone marrow or peripheral blood blasts 10%-19%
Peripheral blood basophils ≥ 20%
Presence of additional clonal cytogenetic abnormality in Ph+ cells (ACA)*
Blast phase
Bone marrow or peripheral blood blasts ≥ 20%
Myeloid sarcoma†
Presence of morphologically apparent lymphoblasts (>5%) warrants consideration of lymphoblastic crisis‡

- ELN 2020 Definitions

Accelerated phase	**Definition**
ELN criteria	Blasts in blood or marrow 15-29%, or blasts plus promyelocytes in blood or marrow >30%, with blasts <30%
	Basophils in blood ≥20%
	Persistent thrombocytopenia (<100 × 10^9/L) unrelated to therapy
	Clonal chromosome abnormalities in Ph+ cells (CCA/Ph+), major route, on treatment
Blast phase	
ELN criteria	Blasts in blood or marrow ≥30%
	Extramedullary blast proliferation, apart from spleen

ELN 2013: Baccarani et al, Blood 2013 Jun 26;122(6):872
ICC 2022: Arber et al, Blood 2022 Sep 15;140(11):1200–1228

CML: Efficacy of TKI's Comparison

Parameter		JALSG CML212		DASISION		ENESTnd		BFORE		ASC4FIRST*		
		Dasatinib	Nilotinib	Dasatinib	Imatinib	Nilotinib 300 mg	Imatinib	Bosutinib	Imatinib	Asciminib**	Imatinib	2G-TKI
Age	Median (range)	53 (17-90)	53 (19-85)	46 (18-84)	49 (18-78)	47 (18-85)	46 (18-80)	52 (18-84)	53 (19-84)	52 (18-79)	56 (21-79)	43 (18-76)
High risk‡	%	18.5	18.9	19	19			20.7	21.2	11.4	7.8	13.7
EMR§	3 mo	73.1%	74.5%	84%	64%	91%	67%	80.6%	60.5%	89.6%	59.8%	80.4%
	12 mo	69%‖	63%‖			55%	27%	47.2%	36.9%			
	24 mo	75%‖	72%‖	64%	46%	71%	44%	66%	57.4%	NR	NR	NR
MR4	12 mo	35%‖	36%‖	NR	NR	20%	6%	20.7%	12.0%			
	24 mo	50%‖	48%‖	NR	NR	39%	18%	26.6%	34.3%	NR	NR	NR
MR4.5	12 mo	23.3%	25.1%	5%	3%	11%	1%	8.1%	3.3%	16.9%	4.9%	12.7%
	18 mo	30.8%	32.6%	13%†	7%†	21%†	6%†	NR	NR	NR	NR	NR
	24 mo	36.6%	37.4%	17%	8%	25%	9%	20.4%	15.2%	NR	NR	NR
Treatment change/discontinued	1-3 y	35.0% (3 y)	33.5% (3 y)	23% (2 y)	25% (2 y)	25.5% (2 y)	32.5% (2 y)	18.3% (1 y)	17.7% (1 y)		36.2%#	23.5%#
	5 y	NR	NR	39%	37%	40.1%	50.2%	40.3%	41.9%	NR	NR	NR

- Imatinib – lowest rate of MMR
- Asciminib – MR4 rates at least as high as 2G TKI
- Asciminib – low rate of treatment d/c due to good tolerability
- T315I: use Ponatinib or Asciminib

Veltmaat et al, *Blood Adv* (2024) 8 (20): 5339–5341

CML:Presentation (cont.)

- PS is a 64 yo F
  - Newly diagnosed chronic phase CML
  - No increase in blasts, no increase in basophils, platelet count >100 → Sokal low risk, ETLS intermediate risk
  - Cytogenetics showed t(14;20) in addition to t(9;22) → hemepath suggests that t(14;20) is germline?
- Past medical history: anxiety/depression, ovarian cyst. NO cardiac/pulmonary disease, no DM
- Treatment:
  - Dasatinib 100mg po once daily started
  - Patient quickly (within 2-3 weeks) achieved complete hematologic remission. Tolerated tx well.
  - PCR trend:
    - **PCR for BCR-ABL**
      - **@ diagnosis, pre-treatment PCR for BCR-ABL was 48.1%**
      - **@3 months, on 3/18/25 PCR for BCR-ABL was 4.1788%**
      - **@6mo, on 6/17/25 PCR for BCR-ABL** -8.9541 (**ideally <1%)**
      - **@7mo, on 7/21/25 Pcr for BCR-ABL was 21.6204 →LOSS OF RESPONSE → CHECK ABL1 MUTATIONS, BM Biopsy**

CML:Presentation (cont.)

- PS has a significant increase in the PCR for BCR-ABL checked on peripheral blood
- Patient reports good compliance with treatment
- ABL1 mutation analysis done on peripheral blood → NO mutations detected
  - T315I mutation: The BAD one!
    - Confers resistance to all TKI's except for Ponatinib, Asciminib
    - NOTE: dose for Ponatinib and Asciminib is HIGHER for T315I mutation than usual CP-CML
- BM bx done (July 2025)–showed hypercellular marrow, 2% blasts
  - FISH and Cytogenetics:

RESULT SUMMARY:	**Abnormal female karyotype (15/20)** **Abnormal FISH result: *BCR::ABL1* rearrangement with deletion of *ASS1* and *ABL1* (9q34) (64.0%) and *KMT2A* [11q23] rearrangement (59.0%)**
KARYOTYPE:	46,XX,del(8)(q22q24.1),t(9;11)(p22;q23),t(9;22)(q34;q11.2),t(14;20)(q21;p12)[15]/46,XX[5] nuc ish(ASS1x1,ABL1x2,BCRx2)(ABL1 con BCRx1)[128/200], (KMT2Ax2)(5'KMT2A sep 3'KMT2Ax1)[118/200]
INTERPRETATION:	These results suggest disease persistence. The presence of a complex karyotype suggests accelerated phase for chronic myeloid leukmia (CML). Clinicopathological correlation is recommended.

Indications for AlloSCT

High-risk features indicating the need to initiate a donor search for transplant-eligible patients
The presence of specific cytogenetic abnormalities at diagnosis or acquisition while on therapy, including ▪ Isochromosome 17q ▪ 3q26.2 ▪ Monosomy 7/7q- ▪ Complex karyotype
Failure to achieve any cytogenetic or molecular response to 2G-TKI after a minimum of 3 months of therapy
Recurrent grade IV cytopenias despite TKI dose interruptions, dose modifications, and cytokine support, especially within the first 3 months of therapy, leading to EMR failure or ELN-defined treatment failure
Recurrent grade 4 toxicity preventing consistent TKI dose intensity, resulting in EMR failure or ELN-defined treatment failure on 2 or more lines of TKI therapy
Compound kinase domain mutations involving T315I
Lymphoblasts >5% at diagnosis

Shanmuganathan et al, *Hematology Am Soc Hematol Educ Program* (2023) 2023 (1): 459–468.

Indications for AlloSCT

CP-CML patients →

- ≥ 3rd line therapy
  - Typing at failure or intolerance of 2nd-line therapy, consider in some when initiating 2nd line therapy (failure of 1st line 2nd gen TKI without mutations)

Progression to AP or BP →

- HCT using alternate TKI (+/- induction chemotherapy in BP) to bridge

PLAN for patient: Switch to Asciminib, HLA typing

***de novo* AP patients** →

- Type patient and siblings; use first-line TKI therapy with close monitoring for optimal response as some *de novo* AP patients without high-risk ACA do well. HCT in patients with high-risk ACA*; for others HCT when optimal milestones are not met.*

BP patients →

- HCT after TKI therapy +/- induction chemotherapy. I favor induction chemotherapy + TKI in most HCT candidates.

~~Median survival is ~7-12 months with TKI-based therapy~~

Ohanian et al. Clin Lymphoma Myeloma Leuk. 2014 Apr;14(2):155-162

AP Treatment Choices and Response Rates

- Goal is to revert to CP-CML or CR prior to alloSCT

Summary of hematologic and cytogenetic responses to TKI in advanced phase CML*–

	CHR		CCyR		MMR	OS	
	AP	BP	AP	BP	AP	AP	BP
Imatinib	70%- > 90%	11%-35%	16%-60%	0%-10%	19%-63%	50%-60% at 5 years	7-10 months†
Nilotinib (de novo)	>90%	—	80%-90%	—	70%	90% at 3 years	
Nilotinib (progressed)	22%-46%	21%-42%‡	0%-21%	14%-38%§	10%	60%-70% at 2 years	32% at 2 years
Dasatinib (de novo)	>90%	—	80%-90%	—	70%	90% at 3 years	
Dasatinib (progressed)	45%-52%	28%-61%‡	18%-33%	27%-35%§	10%	60%-70% at 2 years	30% at 2 years
Bosutinib (progressed)	57%‡	28%‡	40%§	50%§	11%	60% at 4 years	17% at 4 years
Ponatinib (progressed)	55%‡	32%‡	24%	18%§	34%	84% at 1 year	29% at 1 year

Asciminib in AP: Hughes et al.: 9pts w AP-CML, 7 of 8 (88%) achieved CHR, and 1 of 9 (11%) had a MMR. Response maintained >11 wks

Hughes et al, N Engl J Med 2019 381(24):2315

How et al, *Hematology Am Soc Hematol Educ Program* (2021) 2021 (1): 122–128

CML:Presentation (cont.)

- PS now has progressed to AP-CML based on complex marrow cytogenetics, including presence of KMT2A (11q23) rearrangement
- NO ABL1 mutations present
- Patient was started on Asciminib 80mg in Aug 2025
- Patient comes back in 1 month, Sept 2025
  - CBC shows wbc 18k/ul, Hb 11.2g/dl, platelet count 52k/ul, 17% peripheral blasts!
  - Flow cytometry on peripheral blood shows Abnormal myeloid blasts/blast equivalents represent approximately 17% of the white cells
  - PLAN: Admission for FLAG-Ida +Ponatinib

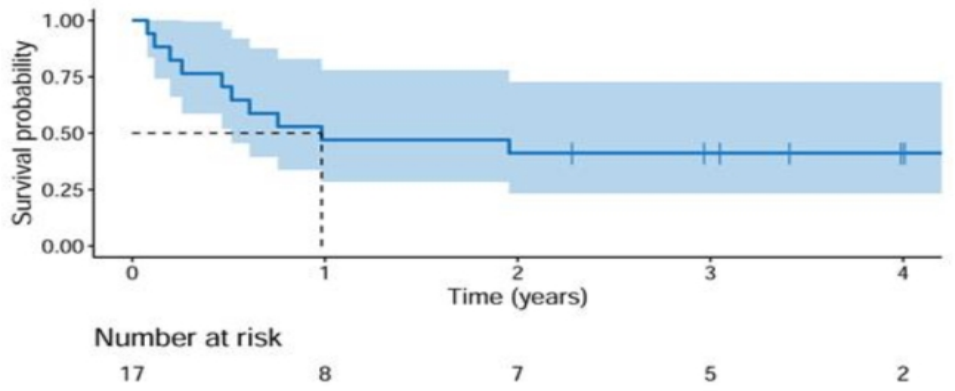
632.CHRONIC MYELOID LEUKEMIA: CLINICAL AND EPIDEMIOLOGICAL | NOVEMBER 5, 2021

Ponatinib in Combination with FLAG-IDA Chemotherapy for Blast-Phase Chronic Myeloid Leukemia: Final Results of the Seamless Phase I/II Dose-Finding UK Trials Acceleration Programme (TAP) Matchpoint Trial

Mhairi Copland, Daniel Slade, Graham McIlroy, Gillian Horne, Jennifer Byrne, Kate Rothwell, Kristian Brock, Hugues De Lavallade, Charles Craddock, Richard Clark, Matthew Smith, Rachel Fletcher, Rebecca Bishop, Dragana Milojkovic, Christina Yap

Blood (2021) 138 (Supplement 1): 312.

https://doi.org/10.1182/blood-2021-147972



CML Conclusions

- CML –characterized by Ph+ t(9;22) at diagnosis, but BM bx needed at diagnosis and progression in order to check for ACA (additional chromosomal abnormalities)
- If a CP-CML patient is losing response/not meeting milestones ->check for compliance with TKI, check for ABL1 binding site mutations
- If a T315I mutation is detected, treatment options are
  - Ponatinib –dose at 45mg once daily until PCR≤1%, then decrease to 15mg daily (CP usual starting dose is 30mg once daily)
  - Asciminib –dose at 200mg twice daily (CP usual dose is 80mg once daily)
- Be aware of clonal evolution (ACA) high risk mutations: particularly i(17)(q10)-7/del7q, and 3q26.2 rearrangements. Complex cytogenetics (≥2 mutations in Ph+ clone)

- Be aware of some TKI-specific adverse events: Arterial occlusive events (Nilotinib, Ponatinib), Pancreatitis (Asciminib), Pleural effusion, PAH (Dasatinib), GI (Bosutinib)
- Criteria for discontinuation of TKI's: >2 years DMR (≤0.01%)

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Thank you!

Questions?
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