ELN Guidelines for CML 2020 vs 2013

The 2020 guidelines include some significant changes since the previous version, published in 2013. Use this quick reference guide to help identify updates and key differences from the 2013 guidelines.

Baseline diagnostics

Prognostic system to predict probability of dying from CML at diagnosis

2013

Sokal, Euro, and EUTOs prognostic systems[1]

2020

ELTS prognostic system[2]
ELTS score apportions fewer patients into high- and intermediate-risk groups than the Sokal score[2]

Risk strata proportions and outcome[2]

	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

Detailed diagnostic work-up

Not included[1]

A diagnostic work-up completed by a physical examination performed at baseline to measure spleen and liver size, standard biochemical profile including hepatitis B serology, cholesterol, lipase and HbA1c values, and an electrocardiogram[2]

Cost effectiveness

2013

Not included[1]

2020

Now includes a section for cost effectiveness to address concerns regarding TKI and costs[2]

Early treatment milestones

Definition of treatment failure mandating a change in treatment

2013

>10% *BCR-ABL1* transcript levels at 6 months[1]

2020

>10% *BCR-ABL1* transcript levels at 3 months if confirmed within 1-3 months[2]

BCR-ABL1 resistance mutations

Not included[1]

Recommendations for TKIs in case of *BCR-ABL1* resistance mutations are included[2]

Treatment-free remission (TFR)

2013

Not included[1]

2020

TFR is included as a new significant goal of CML management. The guidelines recommend consideration of TFR in appropriate patients after careful discussion employing the concept of shared decision making. The panel's recommendations for TKI discontinuation are summarized below[2]:

Requirements for TKI discontinuations[2]

Mandatory	• CML in first CP only (data are lacking outside this setting) • Motivated patient with structured communication • Access to high-quality quantitative PCR using the IS with rapid turnaround of PCR test results • Patient's agreement to more frequent monitoring after stopping treatment. This means monthly for the first 6 months, every 2 months for months 6–12, and every 3 months thereafter
Minimal (stop allowed)	• First-line therapy or second-line if intolerance was the only reason for changing TKI • Typical e13a2 or e14a2 *BCR-ABL1* transcripts • Duration of TKI therapy >5 years (>4 years for second-generation TKI) • Duration of DMR (MR^4 or better) >2 years • No prior treatment failure
Optimal (stop recommended for consideration)	• Duration of TKI therapy >5 years • Duration of DMR >3 years if MR^4 • Duration of DMR >2 years if MR$^{4.5}$

BCR-ABL=breakpoint cluster region-Abelson; CML=chronic myelogenous leukemia; CP=chronic phase; DMR=deep molecular response; ELN=European LeukemiaNet; ELTS=EUTOS Long-Term Survival; EUTOS=European Treatment and Outcome Study; LRD=leukemia-related death; MR=molecular response; OS=overall survival; PCR=polymerase chain reaction; TKI=tyrosine kinase inhibitor.

ELN Guidelines for CML 2020 vs 2013

Treatment recommendations

2013	2020
First line	
• Imatinib[1] • Dasatinib[1] • Nilotinib[1]	• Imatinib[2] • Dasatinib[2] • Nilotinib[2] • Generic imatinib[2] UPDATED • Bosutinib[2] UPDATED
Generics	
Not included[1]	Now includes a dedicated section on generics. Generic imatinib, now available worldwide, has been included as a first-line recommendation. Monitoring the response to generics must be the same as with branded drugs. If a patient is changed from a branded to a generic product, then enhanced vigilance for the first 6 months in terms of sustaining response and observing for new adverse events is advisable[2]
Second line and subsequent lines	
• Imatinib[1] • Dasatinib[1] • Nilotinib[1] • Bosutinib: recommended for patients intolerant of imatinib or in whom imatinib treatment failed[1] • Ponatinib: only recommended for second line in patients who had failed previous TKI therapy or carry the *T315I* mutation[1]	The criteria for the choice of the second-line TKI are almost entirely patient related and depend on factors such as age, comorbidities, and toxicity of first TKI • Imatinib[2] • Dasatinib[2] • Nilotinib[2] • Bosutinib: now included as a second-line recommendation independent of prior resistance of intolerance[2] UPDATED Note: Ponatinib is no longer a second-line recommendation, and has been moved to the "treatment beyond second line" section[2]

Guidance for first-line agents based on comorbidities and contraindications

The 2020 ELN Guidelines also included recommendations on appropriate TKI considerations based on patient comorbidities and TKI contraindications. Click on the links to learn about recommendations for each of the specific TKIs:

Imatinib | Nilotinib | Dasatinib | Bosutinib | Ponatinib

2013	2020
Not included[1]	The following pages outline considerations around contraindications and comorbidities for TKIs approved for use in CML.[2]

TKI=tyrosine kinase inhibitor.

References: 1. Baccarani M, Deininger MW, Rosti G, et al. European LeukemiaNet recommendations for the management of chronic myeloid leukemia: 2013. *Blood.* 2013;122(6):872-884. **2.** Hochhaus A, Baccarani M, Silver RT, et al. European LeukemiaNet 2020 recommendations for treating chronic myeloid leukemia. *Leukemia.* 2020;34(4):966-984.

Imatinib

Summary of ELN recommendations based on TKI contraindications		
2020		
TKI	**ELN recommendations[1]**	**Contraindications**
Imatinib	• No absolute contraindications and no life-threatening complications reported • Patients with low cardiac ejection fraction and a low GFR should be monitored for related organ toxicity	• SmPC: Hypersensitivity to the active substance or to any of the excipients[2] • PI: None[3]

Summary of ELN recommendations on appropriate TKI considerations based on patient comorbidities	
2020	
Previous or concomitant diseases	**Imatinib**
Cardiovascular risk factors	No relevant restriction
Peripheral arterial disease	No relevant restriction
Arterial hypertension	No relevant restriction
Arteriosclerosis	No relevant restriction
Lung disease (eg, pleural effusion, respiratory failure)	No relevant restriction
Pulmonary arterial hypertension	No relevant restriction
Pericarditis	No relevant restriction
Autoimmune diseases	No relevant restriction
Hypercholesterolemia	No relevant restriction
Diabetes mellitus	No relevant restriction
Pancreatitis	No relevant restriction
Liver disease	No relevant restriction
Diarrhea / inflammatory bowel disease	No relevant restriction
Renal failure	With limitation

GFR=glomerular filtration rate.

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References: 1. Hochhaus A, Baccarani M, Silver RT, et al. European LeukemiaNet 2020 recommendations for treating chronic myeloid leukemia. *Leukemia*. 2020;34(4):966-984. **2.** Glivec [summary of product characteristics]. Novartis; 2020. **3.** Gleevec [prescribing information]. Novartis; 2020.

Nilotinib

Summary of ELN recommendations based on TKI contraindications

2020

TKI	ELN recommendations[1]	Contraindications
Nilotinib	**Strong contraindications** • History of coronary heart disease • History of cerebrovascular accidents • History of peripheral AOD **Contraindications** Pancreatitis history **Other high-risk conditions** • Hypertension • Hypercholesterolemia • Diabetes mellitus	• SmPC: Hypersensitivity to the active substance or to any of the excipients[2] • PI: Hypokalemia, hypomagnesemia, long QT syndrome[3]

Summary of ELN recommendations on appropriate TKI considerations based on patient comorbidities

2020

Previous or concomitant diseases	Nilotinib
Cardiovascular risk factors	With limitation
Peripheral arterial disease	Strong contraindication
Arterial hypertension	With limitation
Arteriosclerosis	Strong contraindication
Lung disease (eg, pleural effusion, respiratory failure)	No relevant restriction
Pulmonary arterial hypertension	No relevant restriction
Pericarditis	No relevant restriction
Autoimmune diseases	No relevant restriction
Hypercholesterolemia	With limitation
Diabetes mellitus	With limitation
Pancreatitis	Strong contraindication
Liver disease	With limitation
Diarrhea / inflammatory bowel disease	No relevant restriction
Renal failure	No relevant restriction

AOD=arterial occlusive disease.

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References: 1. Hochhaus A, Baccarani M, Silver RT, et al. European LeukemiaNet 2020 recommendations for treating chronic myeloid leukemia. *Leukemia*. 2020;34(4):966-984. **2.** Tasigna [summary of product characteristics]. Novartis; 2020. **3.** Tasigna [prescribing information]. Novartis; 2020.

Dasatinib

Summary of ELN recommendations based on TKI contraindications

2020

TKI	ELN recommendations[1]	Contraindications
Dasatinib	**Strong contraindications** • Respiratory failure • Previous or concomitant pleuropulmonary disease • Previous or concomitant pericardial disease	• SmPC: Hypersensitivity to the active substance or to any of the excipients[2] • PI: None[3]

Summary of ELN recommendations on appropriate TKI considerations based on patient comorbidities

2020

Previous or concomitant diseases	Dasatinib
Cardiovascular risk factors	No relevant restriction
Peripheral arterial disease	No relevant restriction
Arterial hypertension	With limitation (risk of pleural effusion)
Arteriosclerosis	With limitation (risk of pleural effusion)
Lung disease (eg, pleural effusion, respiratory failure)	Strong contraindication
Pulmonary arterial hypertension	With limitation
Pericarditis	Strong contraindication
Autoimmune diseases	With limitation (risk of pleural effusion)
Hypercholesterolemia	With limitation (risk of pleural effusion)
Diabetes mellitus	No relevant restriction
Pancreatitis	No relevant restriction
Liver disease	No relevant restriction
Diarrhea / inflammatory bowel disease	No relevant restriction
Renal failure	No relevant restriction

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References: 1. Hochhaus A, Baccarani M, Silver RT, et al. European LeukemiaNet 2020 recommendations for treating chronic myeloid leukemia. *Leukemia*. 2020;34(4):966-984. **2.** Sprycel [summary of product characteristics]. Bristol-Myers Squibb; 2020. **3.** Sprycel [prescribing information]. Bristol-Myers Squibb; 2018.

Bosutinib

Summary of ELN recommendations based on TKI contraindications

2020

TKI	ELN recommendations[1]	Contraindications
Bosutinib	• No relevant comorbidities or strong contraindications	• SmPC: Hypersensitivity to the active substance or to any of the excipients, hepatic impairment[2] • PI: Hypersensitivity to bosutinib[3]

Summary of ELN recommendations on appropriate TKI considerations based on patient comorbidities

2020

Previous or concomitant diseases	Bosutinib
Cardiovascular risk factors	No relevant restriction
Peripheral arterial disease	No relevant restriction
Arterial hypertension	No relevant restriction
Arteriosclerosis	No relevant restriction
Lung disease (eg, pleural effusion, respiratory failure)	No relevant restriction
Pulmonary arterial hypertension	No relevant restriction
Pericarditis	No relevant restriction
Autoimmune diseases	No relevant restriction
Hypercholesterolemia	No relevant restriction
Diabetes mellitus	No relevant restriction
Pancreatitis	With limitation
Liver disease	With limitation
Diarrhea / inflammatory bowel disease	With limitation
Renal failure	No relevant restriction

Click here for the BOSULIF SmPC

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References: 1. Hochhaus A, Baccarani M, Silver RT, et al. European LeukemiaNet 2020 recommendations for treating chronic myeloid leukemia. *Leukemia.* 2020;34(4):966-984. **2.** Bosulif [summary of product characteristics]. Pfizer Inc.; 2021. **3.** Bosulif [prescribing information]. Pfizer Inc.; 2020.

Ponatinib

Only recommended for second line in patients who had failed previous TKI therapy or carry the *T315I* mutation.[1]

ELN recommendations on TKI contraindications only covered TKI agents approved for 1L, and therefore excluded ponatinib.

Summary of ELN recommendations on appropriate TKI considerations based on patient comorbidities	
2020	
Previous or concomitant diseases	**Ponatinib**
Cardiovascular risk factors	With limitation
Peripheral arterial disease	Strong contraindication
Arterial hypertension	With limitation
Arteriosclerosis	Strong contraindication
Lung disease (eg, pleural effusion, respiratory failure)	No relevant restriction
Pulmonary arterial hypertension	No relevant restriction
Pericarditis	No relevant restriction
Autoimmune diseases	No relevant restriction
Hypercholesterolemia	No relevant restriction
Diabetes mellitus	With limitation
Pancreatitis	No relevant restriction
Liver disease	No relevant restriction
Diarrhea / inflammatory bowel disease	No relevant restriction
Renal failure	No relevant restriction

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Reference: 1. Baccarani M, Deininger MW, Rosti G, et al. European LeukemiaNet recommendations for the management of chronic myeloid leukemia: 2013. *Blood*. 2013;122(6):872-884.