

## 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							
2013		2020					
Prognostic system to predict probability of dying from CML at diagnosis							
Sokal, Euro, and EUTOs prognostic systems <sup>1</sup>	ELTS prognostic system <sup>2</sup> ELTS score apportions fewer patients into high- and intermediate-risk groups than the Sokal score <sup>2</sup>						
	Risk strata proportions and outcome <sup>2</sup>						
		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 <sup>1</sup>	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 <sup>2</sup>						
Cost effectiveness							
2013		2020					
Not included <sup>1</sup>	Now includes a section for cost effectiveness to address concerns regarding TKI and costs <sup>2</sup>						
Early treatment milestones							
2013		2020					
Definition of treatment failure mandating a change in treatment							
>10% <i>BCR-ABL1</i> transcript levels at 6 months <sup>1</sup>	>10% <i>BCR-ABL1</i> transcript levels at 3 months if confirmed within 1-3 months <sup>2</sup>						
<i>BCR-ABL1</i> resistance mutations							
Not included <sup>1</sup>	Recommendations for TKIs in case of <i>BCR-ABL1</i> resistance mutations are included <sup>2</sup>						
Treatment-free remission (TFR)							
2013		2020					
Not included <sup>1</sup>	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 <sup>2</sup> :						
	Requirements for TKI discontinuations <sup>2</sup>						
	Mandatory	<ul style="list-style-type: none"> <li>CML in first CP only (data are lacking outside this setting)</li> <li>Motivated patient with structured communication</li> <li>Access to high-quality quantitative PCR using the IS with rapid turnaround of PCR test results</li> <li>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</li> </ul>					
	Minimal (stop allowed)	<ul style="list-style-type: none"> <li>First-line therapy or second-line if intolerance was the only reason for changing TKI</li> <li>Typical e13a2 or e14a2 <i>BCR-ABL1</i> transcripts</li> <li>Duration of TKI therapy &gt;5 years (&gt;4 years for second-generation TKI)</li> <li>Duration of DMR (MR<sup>4</sup> or better) &gt;2 years</li> <li>No prior treatment failure</li> </ul>					
Optimal (stop recommended for consideration)	<ul style="list-style-type: none"> <li>Duration of TKI therapy &gt;5 years</li> <li>Duration of DMR &gt;3 years if MR<sup>4</sup></li> <li>Duration of DMR &gt;2 years if MR<sup>4-5</sup></li> </ul>						

## ELN Guidelines for CML 2020 vs 2013

Treatment recommendations	
2013	2020
<b>First line</b>	
<ul style="list-style-type: none"> <li>• Imatinib<sup>1</sup></li> <li>• Dasatinib<sup>1</sup></li> <li>• Nilotinib<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Imatinib<sup>2</sup></li> <li>• Dasatinib<sup>2</sup></li> <li>• Nilotinib<sup>2</sup></li> <li>• Generic imatinib<sup>2</sup> <b>UPDATED</b></li> <li>• Bosutinib<sup>2</sup> <b>UPDATED</b></li> </ul>
<b>Generics</b>	
Not included <sup>1</sup>	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 <sup>2</sup>
<b>Second line and subsequent lines</b>	
<ul style="list-style-type: none"> <li>• Imatinib<sup>1</sup></li> <li>• Dasatinib<sup>1</sup></li> <li>• Nilotinib<sup>1</sup></li> <li>• Bosutinib: recommended for patients intolerant of imatinib or in whom imatinib treatment failed<sup>1</sup></li> <li>• Ponatinib: only recommended for second line in patients who had failed previous TKI therapy or carry the <i>T315I</i> mutation<sup>1</sup></li> </ul>	<p>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</p> <ul style="list-style-type: none"> <li>• Imatinib<sup>2</sup></li> <li>• Dasatinib<sup>2</sup></li> <li>• Nilotinib<sup>2</sup></li> <li>• Bosutinib: now included as a second-line recommendation independent of prior resistance of intolerance<sup>2</sup> <b>UPDATED</b></li> </ul> <p>Note: Ponatinib is no longer a second-line recommendation, and has been moved to the “treatment beyond second line” section<sup>2</sup></p>
<b>Guidance for first-line agents based on comorbidities and contraindications</b>	
<p>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:</p>	
<div style="display: flex; justify-content: space-around; align-items: center;"> <div style="border: 1px solid black; border-radius: 10px; padding: 5px 20px; background-color: #e67e22; color: white; text-align: center; width: 15%;">Imatinib</div> <div style="border: 1px solid black; border-radius: 10px; padding: 5px 20px; background-color: #e67e22; color: white; text-align: center; width: 15%;">Nilotinib</div> <div style="border: 1px solid black; border-radius: 10px; padding: 5px 20px; background-color: #e67e22; color: white; text-align: center; width: 15%;">Dasatinib</div> <div style="border: 1px solid black; border-radius: 10px; padding: 5px 20px; background-color: #e67e22; color: white; text-align: center; width: 15%;">Bosutinib</div> <div style="border: 1px solid black; border-radius: 10px; padding: 5px 20px; background-color: #e67e22; color: white; text-align: center; width: 15%;">Ponatinib</div> </div>	
2013	2020
Not included <sup>1</sup>	The following pages outline considerations around contraindications and comorbidities for TKIs approved for use in CML. <sup>2</sup>

TKI=tyrosine kinase inhibitor.

# Imatinib

Summary of ELN recommendations based on TKI contraindications		
2020		
TKI	ELN recommendations <sup>1</sup>	Contraindications
<b>Imatinib</b>	<ul style="list-style-type: none"> <li>No absolute contraindications and no life-threatening complications reported</li> <li>Patients with low cardiac ejection fraction and a low GFR should be monitored for related organ toxicity</li> </ul>	<ul style="list-style-type: none"> <li>SmPC: Hypersensitivity to the active substance or to any of the excipients<sup>2</sup></li> <li>PI: None<sup>3</sup></li> </ul>

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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# Nilotinib

## Summary of ELN recommendations based on TKI contraindications

2020

TKI	ELN recommendations <sup>1</sup>	Contraindications
<b>Nilotinib</b>	<p><b>Strong contraindications</b></p> <ul style="list-style-type: none"> <li>• History of coronary heart disease</li> <li>• History of cerebrovascular accidents</li> <li>• History of peripheral AOD</li> </ul> <p><b>Contraindications</b></p> <p>Pancreatitis history</p> <p><b>Other high-risk conditions</b></p> <ul style="list-style-type: none"> <li>• Hypertension</li> <li>• Hypercholesterolemia</li> <li>• Diabetes mellitus</li> </ul>	<ul style="list-style-type: none"> <li>• SmPC: Hypersensitivity to the active substance or to any of the excipients<sup>2</sup></li> <li>• PI: Hypokalemia, hypomagnesemia, long QT syndrome<sup>3</sup></li> </ul>

## 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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# Dasatinib

## Summary of ELN recommendations based on TKI contraindications

2020

TKI	ELN recommendations <sup>1</sup>	Contraindications
Dasatinib	<b>Strong contraindications</b> <ul style="list-style-type: none"> <li>• Respiratory failure</li> <li>• Previous or concomitant pleuropulmonary disease</li> <li>• Previous or concomitant pericardial disease</li> </ul>	<ul style="list-style-type: none"> <li>• SmPC: Hypersensitivity to the active substance or to any of the excipients<sup>2</sup></li> <li>• PI: None<sup>3</sup></li> </ul>

## 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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# Bosutinib

Summary of ELN recommendations based on TKI contraindications		
2020		
TKI	ELN recommendations <sup>1</sup>	Contraindications
<b>Bosutinib</b>	<ul style="list-style-type: none"> <li>No relevant comorbidities or strong contraindications</li> </ul>	<ul style="list-style-type: none"> <li>SmPC: Hypersensitivity to the active substance or to any of the excipients, hepatic impairment<sup>2</sup></li> <li>PI: Hypersensitivity to bosutinib<sup>3</sup></li> </ul>

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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## Ponatinib

Only recommended for second line in patients who had failed previous TKI therapy or carry the *T315I* mutation.<sup>1</sup>

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.

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