CCC / Cheshire and Merseyside Cancer Alliance

Guidance for TKI sequencing in chronic phase CML

Options for TKI (tyrosine kinase inhibitor) sequencing for failure of therapy in patients with CP-CML is dependent on which TKI was used in the first line (1L).

1L: Imatinib - appropriate for the majority of newly diagnosed patients with CP-CML

1L : Upfront 2GTKI (second generation) should be considered in certain circumstances:

- younger patients (especially <30 years) including females of childbearing potential
- intermediate / high by Sokal / ELTS score
- patients with additional chromosomal abnormalities (ACAs) on karyotyping

TKI sequencing following first line imatinib – see appendix for tabulated version

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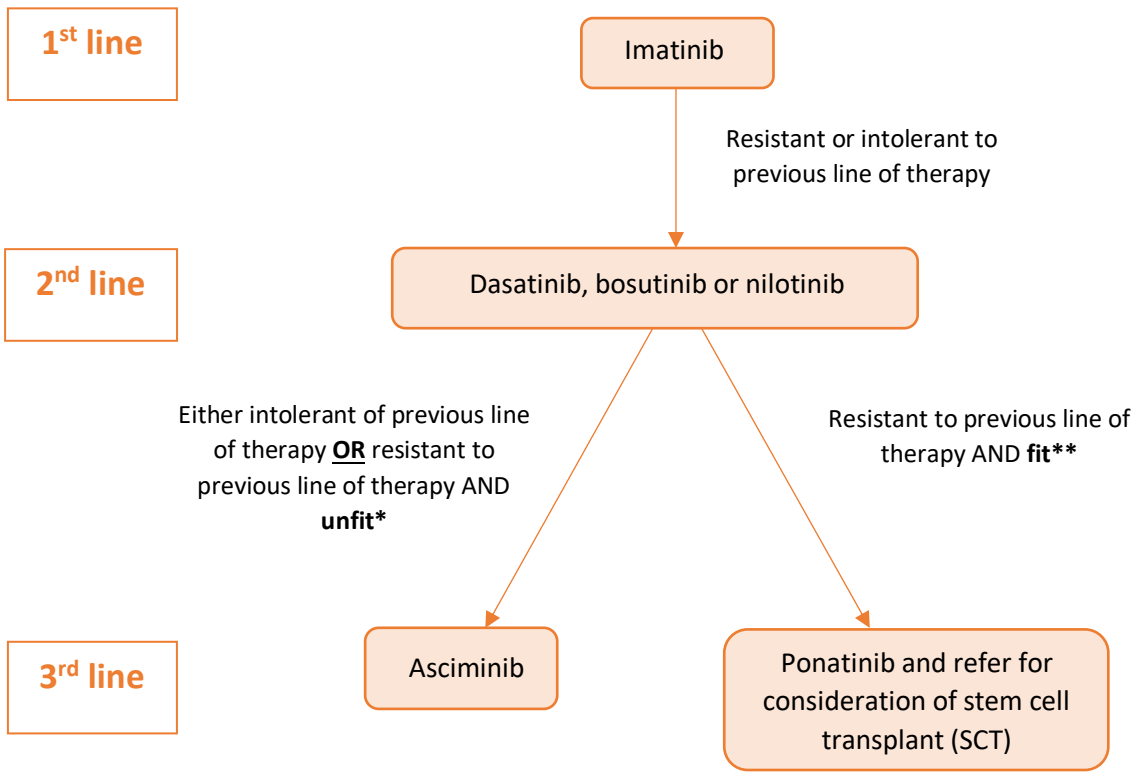

*** unfit = older, high CV risk, ** fit = younger, low CV risk**

Ref: GCLGUITKI
Review: March 2027
Version: 1.0

TKI sequencing following first line use of second generation tyrosine kinase inhibitor (2GTKI) – see appendix for tabulated version

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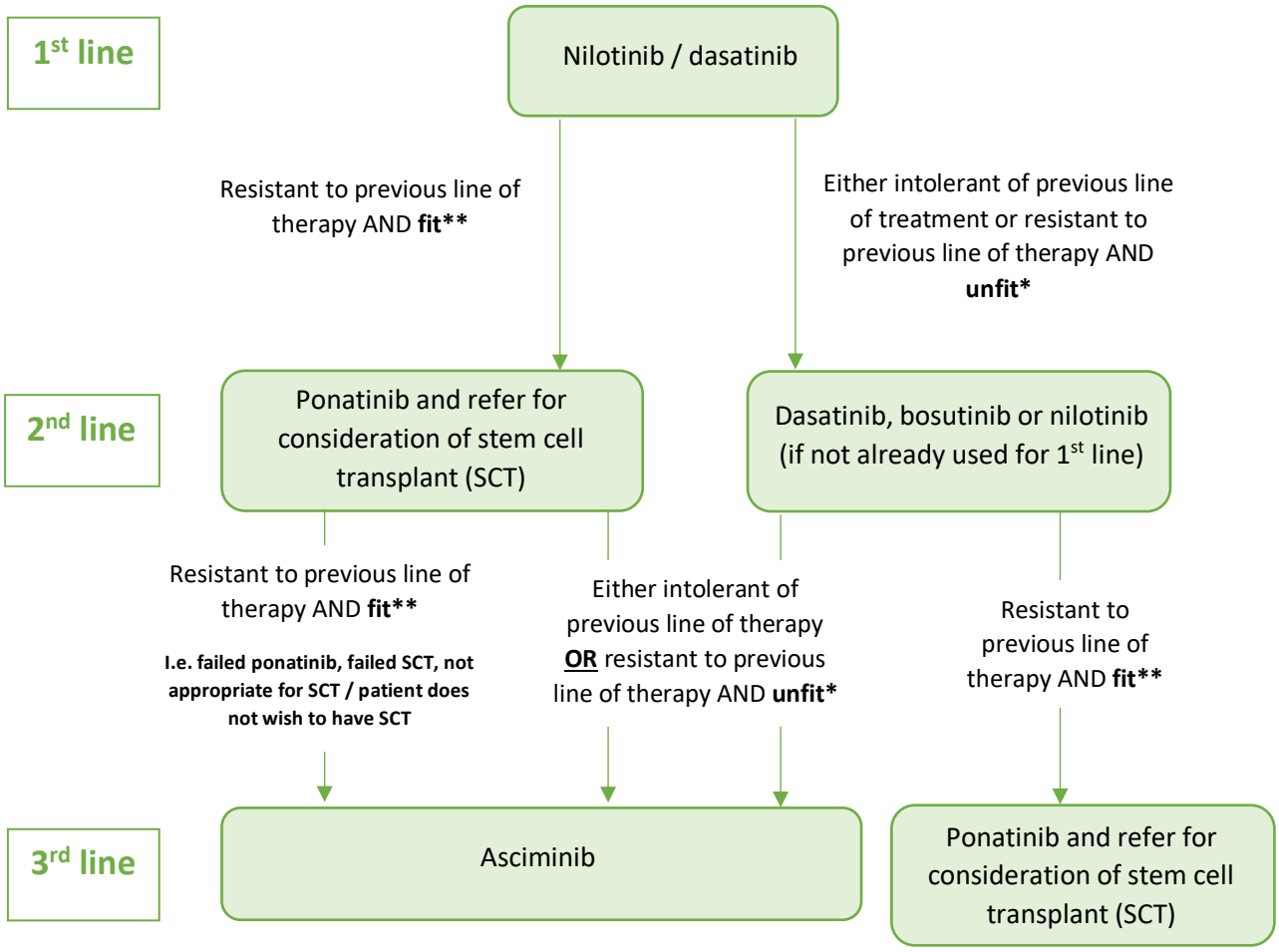

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General notes:

KD mutation screen is mandatory when switching TKI therapy for resistance and recommended in meeting the ELN 'warning' criteria.

Dose escalation of imatinib to 600–800 mg per day should no longer be considered for those failing standard dose imatinib. However a dose of 600 mg may be considered for very selected patients with a suboptimal response (meeting the ELN 'warning' criteria) with no evidence of a mutation and with good tolerance of the standard dose.

Nilotinib – rarely used as 1st choice for 2GTKI due to bd administration and cardiovascular risk

Dasatinib – risk factors for pleural effusion include - higher dose, bd dosing, advanced phase disease, cardiac disease, hypertension, hypercholesterolaemia, history of auto-immune disorders, skin rashes on imatinib, older age (>60), pulmonary disease, higher comorbidity index

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Appendix: tabulated version of the guidance

Table 1. TKI sequencing following 1L Imatinib. *

Line of therapy	Reason for failure of previous line of therapy:	Agent
1L	-	IM
2L	R or I	NIL / DAS / BOS
3L	R + fit	PON and referral for consideration of SCT
	R + unfit or I	ASC

Table 2. TKI sequencing following 1L 2GTKI. **

Line of therapy	Reason for failure of previous line of therapy:	Agent
1L	-	NIL / DAS
2L	R + fit	PON and referral for consideration of SCT
	R + unfit or I	Alternative 2GTKI including BOS
3L	R + fit	*If not previously treated with PON*, for PON and referral for consideration of SCT
	R + unfit / or I	ASC
	R + fit **I.e. failed ponatinib, failed SCT, not appropriate for SCT / patient does not wish to have SCT**	ASC

Abbreviations: R, resistance; I, intolerance; IM, imatinib; NIL, nilotinib; DAS, dasatinib; BOS, bosutinib; PON, ponatinib; SCT, stem cell transplant; ASC, asciminib; fit = younger, low CV risk; unfit = older, high CV risk