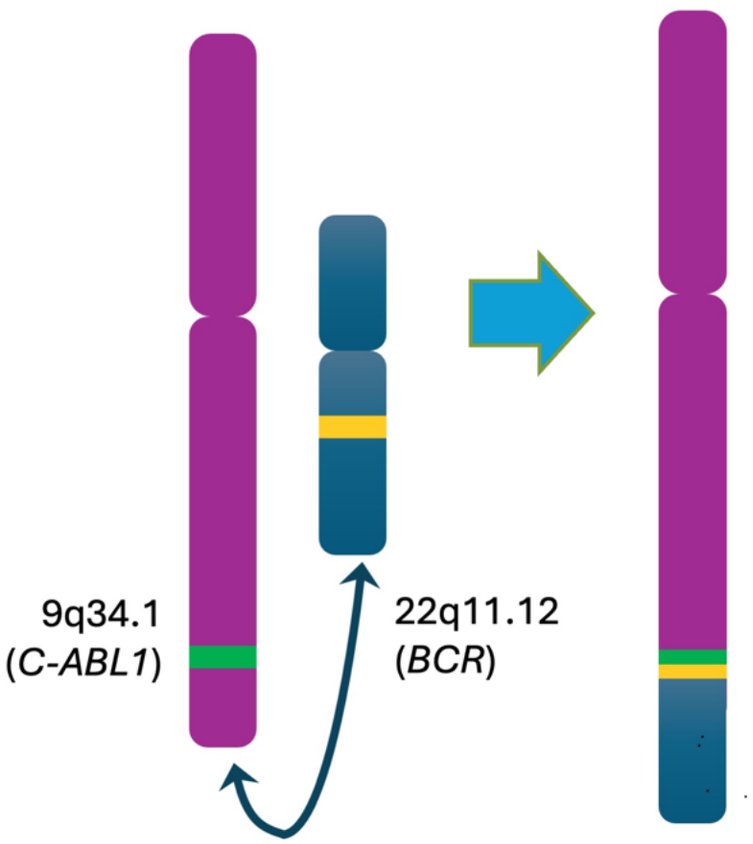
Pathogenesis of Chronic Myeloid Leukaemia



The 9, 22 Reciprocal Translocation

Reciprocal translocation between chromosomes 9 and 22 [**Philedelphia chromosome** t(9;22)(q34;q11)] results in the formation of the fusion gene BCR-ABL1 that is the driver mutation in CML and Ph+ ALL.

BCR-ABL1 Fusion Gene

CML Phenotype

- Marked Leucocytosis
- Basophilia/Eosinophilia Anemia/Thrombocytosis
- Splenomegaly
- Blast Crisis

X

ATP Binding Site Inhibitors	STAMP Inhibitor
• Imatinib • Dasatinib, Nilotinib, Bosutinib • Ponatinib	Asciminib

Protein Isoform	Transcript	% in CML	% in Ph+ ALL	Clinical Features & Associations
p210	Major (M-bcr)	> 95%	~ 25–30%	The classic "CML transcript.
p190	Minor (m-bcr)	1%	~ 70–75%	Common in ALL rare in CML. p190+ CML is aggressive with monocytosis
p230	Micro (μ-bcr)	< 1%	Virtually Absent	Associated with Neutrophilic-

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