LCML - Chronic Myelogenous Leukemia

Subtype	Biology & Expression	Genomic Alterations	Clinical Features
Proliferative CMML (pCMML)	• High WBC count (>13,000/μL) • Proliferative myeloid/monocyte signatures • Increased MAPK signaling	• **RAS-pathway mutations** (e.g., **NRAS**, **KRAS**, **CBL**, **PTPN11**) in ~50% of cases	• Poorer prognosis • Higher risk of AML transformation • May respond to MEK inhibitors
Dysplastic CMML (dCMML)	• Cytopenic phenotype • Dysplasia-related genes expressed • Fewer inflammatory/proliferative signatures	• **TET2**, **SRSF2**, **ASXL1** mutations dominant • Lower frequency of RAS-pathway mutations	• Better prognosis (than pCMML) • Lower blast % • Commonly indolent course
Epigenetically driven subtype	• DNA methylation alterations • Chromatin modifier gene expression patterns	• Mutations in **TET2**, **ASXL1**, **EZH2**, **DNMT3A**, **IDH1/2**	• Associated with CMML progression • Therapeutic vulnerability to hypomethylating agents
Spliceosome-mutant subtype	• Abnormal RNA splicing pathways	• Mutations in **SRSF2**, **SF3B1**, **U2AF1**, often co-occurring with **TET2** or **ASXL1**	• Enriched in older adults • Variable prognosis; some overlap with dysplastic subtype