

Genomic alterations contributing to the pathogenesis of high-risk chronic lymphocytic leukemia (CLL)

Prospective clinical trials of the French/German CLL study groups (FCLLSG / GCLLSG)

146 high-risk CLL patients



Relapsed/refractory CLL patients

- 18 refractory without TP53 aberration
- 31 refractory with TP53 loss and/or mutations
- 26 relapsed with TP53 alteration



Treatment-naïve TP53-deficient primary high-risk CLL patients



- Single nucleotide polymorphism array
- Next-generation sequencing

Landscape of genomic copy number alterations (CNAs)

Median CNA numbers	38	39
Significantly enriched CNAs (GISTIC2.0 analysis)		
• gain(8)(q24.21)	< 0.0001	< 0.0001
• del(9)(p21.3)	0.0076	not significant
<i>NOTCH1</i> mutations	24%	21%
<i>SF3B1</i> mutations	24%	23%

Characterization of genomic alterations

del(9)(p21.3) covering the <i>CDKN2A/B</i> loci	11%	7%
gain(8) covering the <i>MYC</i> locus	17%	15%
Alterations associated with NOTCH1 signaling: <i>RBPJ</i> in 8.2%; <i>SPEN</i> in 3.7%; <i>SNW1</i> in 7.5%		