Investigation of the associations between somatic variants in epigenetic modifiers and response to imatinib and 2G-TKIs given from diagnosis of chronic myeloid leukemia in chronic phase

Ion Torrent Personal-Genome-Machine next-generation sequencing of 71 candidate genes

124 untreated subjects with chronic phase chronic myeloid leukaemia (CML-CP)

Treatments

	Imatinib	Second-generation tyrosine kinase-inhibitors (2G-TKIs)
	62	62
On the basis of the *BCRABL1* transcript levels within the first year		
Responders	33	36
Non responders	29	26

Incidence of somatic variants in CML-CP

• 43 somatic variants were observed 49 times in	18; **29%**, [20, 43%]	19; **31%** [21, 45%]	
• Incidence of subjects with ≥ 1 somatic variant	Responders 15/69; **22%** [14, 33%]	Non responders 22/55; **40%** [28, 53%]	p=0.031
• Most of the 49 somatic variants identified in **21/71 genes**			
• The most frequently altered genes: *ASXL1*, *IKZF1*, *DNMT3A*, *CREBBP*, *KMT2D*, *KMT2E* and *EP300*			

Somatic variants and outcomes in subjects treated with imatinib

	Variant subjects	Non-variant subjects	
5-year MR3	**47%** [11, 68%]	**94%** [67, 99%]	p=0.048
8-year EFS	**28%** [13, 59%]	**68%** [55, 85%]	p=0.003
8-year PFS	**61%** [42, 88%]	**85%** [74, 97%]	p=0.025
8-year CML-related survival	**58%** [37, 92%]	**84%** [73, 97%]	p=0.039

Nteliopoulos *et al.*, Haematologica, 2019