

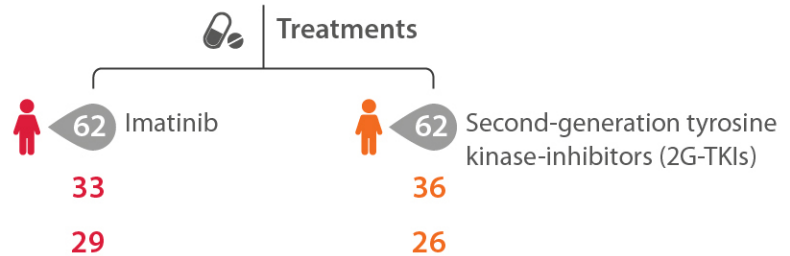
Investigation of the associations between somatic variants in epigenetic modifiers and response to imatinib and 2G-TKIs given from diagnosis of chronic myeloid leukemia in chronic phase



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



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



On the basis of the *BCRABL1* transcript levels within the first year

Responders
Non responders

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	<u>Responders</u> 15/69; 22% [14, 33%]	<u>Non responders</u> 22/55; 40% [28, 53%]	p=0.031
• Most of the 49 somatic variants identified in 21/71 genes			
• The most frequently altered genes: <i>ASXL1</i> , <i>IKZF1</i> , <i>DNMT3A</i> , <i>CREBBP</i> , <i>KMT2D</i> , <i>KMT2E</i> and <i>EP300</i>			

Somatic variants and outcomes in subjects treated with **imatinib**

	<u>Variant subjects</u>	<u>Non-variant subjects</u>	
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