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**
  - Imatinib: 62 subjects
  - 33 responders

- **Non-responders**
  - 62 subjects
  - 29 responders

**Incidence of somatic variants in CML-CP**

- 43 somatic variants were observed 49 times in 18; 29%, [20, 43%] vs 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**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Variant subjects</th>
<th>Non-variant subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-year MR3</td>
<td>47% [11, 68%]</td>
<td>94% [67, 99%]</td>
</tr>
<tr>
<td>8-year EFS</td>
<td>28% [13, 59%]</td>
<td>68% [55, 85%]</td>
</tr>
<tr>
<td>8-year PFS</td>
<td>61% [42, 88%]</td>
<td>85% [74, 97%]</td>
</tr>
<tr>
<td>8-year CML-related survival</td>
<td>58% [37, 92%]</td>
<td>84% [73, 97%]</td>
</tr>
</tbody>
</table>

Nteliopoulos et al., Haematologica, 2019