The appearance of *UBE2A* variants in chronic myeloid leukemia cells could contribute to blast crisis progression through the impairment of myeloid progression

- Matched chronic myeloid leukemia (CML) chronic phase/blast crisis (CP/BC)
- Whole Exome Sequencing (WES)
  - Mutations in *RUNX1, IKZF1, NRAS, ASXL1, ABL1*
  - 41 non synonymous single nucleotide variants (SNVs) and small indels (Mean: 4 mutations/patient)

**Analysis of SNVs data**
- Mutation in *ABL1* on F486S, E255V and T315I 30%, C.I. 95% 0.574, 0.026
- Mutation in *UBE2A* (Xq24) on D114V and I33M 20%, C.I. 95% 0.447, 0.000

**Additional analysis**
- CML CP
  - 31
- Accelerated phase/blast crisis (AP/BC)
  - 14
- Acute myeloid leukemia (AML)
  - 40
- Atypical CML
  - 38

- Somatic *UBE2A* variants on D114Y and M34fs were detected only in 2 AP/BC samples
- *UBE2A* mutations are acquired during CML progression with a frequency of 16.7% in advanced phase (95% C.I. 1.78-31.62)

**UBE2A loss of function is a driver of disease progression in chronic myeloid leukemia**

Magistroni et al. Haematologica, 2019