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

10 Matched chronic myeoloid 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

31 CML CP

14 Accelerated phase/blast crisis (AP/BC)

40 Acute myeloid leukemia (AML)

38 Atypical CML

- 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