Core binding factor (CBF) AML is cytogenetically defined by the presence of t(8;21)(q22;q22) or inv(16)(p13q22)/t(16;16)(p13;q22). According to the World Health Organization (WHO) 2008 classification of myeloid neoplasms, CBF AML is categorized as one type of AML with recurrent genetic abnormalities. CBF AML usually has a good prognosis and mainly affect elderly patients, with an incidence growing consensually with patients’ age.

Prior studies have defined clinical and laboratory prognostic markers. These are actually being used to stratify patients by risk, and to decide the therapy. Some hematological institutions, including “Istituto L. A. Seragnoli”, are also able to use minimal residual disease (MRD) as predictor of relapse but that has no role in the choice of front-line treatment. In most recent years molecular markers like FLT3, NPM1, and KIT have been related with the prognosis and the KIT mutation alone is considered sufficient to define “intermediate risk” by the ongoing cooperative Gruppo Italiano Malattie EMatologiche dell’Adulto (GIMEMA) AML1310 trial and other studies. To have more than 3 cytogenetic abnormalities at karyotyping is shown to be an independent predictor of adverse prognosis by Martinelli, Mosna et al. in a submitted retrospective study.

Considering the rising importance of molecular alterations as prognostic markers and the well known evidence that genomic macroscopic alterations could impact the prognosis we would use Next Generation Sequencing (NGS) to deeply and widely search for alterations in the coding portion of DNA of patients with CBF AML. Is our opinion that some of CBF leukemias, those with worst prognosis and highest relapse rate, are due to a state of “genetic instability” overlying some unknown molecular abnormalities. With the powerful NGS tool we also aim to search for epigenetic alterations or gene mutations that could be implicated in the genesis of this instability.

Our primary goal is to find new genetic abnormalities. We will verify if they could be linked with a specific subgroup of CBF AML, with clinical or laboratory alterations or with some macroscopic (ie cytogenetic or shown by FISH) abnormalities. Then we would check if any of these alterations will significantly affect the prognosis or will show some non-statistical trend to define their prognostic value. Finally these hypothetical alterations will be cross-checked to show if some of those are more common in patients with specific, already known characteristics (eg clinical or laboratory findings at diagnosis, response to therapy, aggressive course of the disease, age).

Identifying new molecular markers will improve our knowledge of CBF AML. In the future those hypothetical markers could be helpful in therapeutic choices defining groups of patients at higher or lower risk. They also could be targets for new and less toxic therapies.
Identifying specific groups of patients in which an alteration is most likely to be found can also improve therapies and daily clinical practice.

Our work could be particularly useful in upgrading stratification algorithm for elderly patients (more than 60 y), for whom to define the prognosis could address the physician’s decision between a conservative and a curative therapeutic approach. In this group could be relevant, more than in younger patients, to assess if some of the found alterations make the patient like or unlike to largely benefit of traditional therapies. More than every other patients the elderly ones could benefit of new targeted therapies.

References