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General AML, FLT3

ASCO 2018 | Disease monitoring in acute myeloid leukemia

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Sami N. Malek from the University of Michigan, US, gave a talk at a poster discussion session at the 2018 American Society of Oncology (ASCO) Annual Meeting. The speaker focused on disease monitoring in acute myeloid leukemia (AML) and discussed the topic by using three abstracts.[1]

Prof. Malek began his talk by discussing the relationship between AML at diagnosis and relapse. At relapse, AML is either very similar or clonally evolved from presentation AML. It has been previously shown that AML therapy creates a permissive environment for preexisting subclones to emerge at relapse.[2] Perhaps, AML relapse is due to simple regrowth of cells, similar to presentation disease. Nevertheless, all relapse disease is clonally related to the presentation of disease, and at times a result of divergent evolution.

The speaker then asked several questions as to why relapse occur in AML: “Is AML re-growth stochastic or deterministic? How many subclones are there at diagnosis and
why do some of them dominate only at relapse and not already at diagnosis? Is it important to define subclones at diagnosis?”

An abstract titled “Clonal evolution in acute myeloid leukemia (AML): Relapse after a long remission period” by Musa Yilmaz and colleagues from the MD Anderson Cancer Center (MDACC) was discussed next. The MDACC researchers aimed to determine the clonal events resulting in a late relapse of AML. Using whole exome sequencing (WES), the researchers analyzed 10 paired AML samples (diagnosis and late relapse). The study confirmed, “that AML relapse is genomically and likely in many other ways related to presentation disease”. In an interview with the AGP, Musa Yilmaz highlighted that founding leukemic clones persists after chemotherapy and establishes the basis of relapse years later in AML. However, it was observed that two cases were genomically unrelated suggesting the emergence of a second new AML. Prof. Malek suggested that “there are very rare cases out there in which, in fact, very late relapse follows a different biological scenario than the majority of AML”.[3]

The next abstract discussed was titled: “Is there a benefit of re-induction therapy in adult patients with AML with < 20% blasts?” by Kavya Kannamma Kannan from John Hopkins University. This was a retrospective study that aimed to the determine the value of re-induction (RI) in newly diagnosed AML patients with < 20% blast on day 14 nadir bone marrow biopsy (NBMB). There was no statistically significant difference in complete remission rates and overall survival, between NBMB patients that received RI and those that did not.

The final abstract discussed at this session was titled: “Impact of numerical variation, allele burden and mutation length on outcomes in acute myeloid leukemia with fms-like tyrosine kinase receptor-3 internal tandem duplication (*FLT3-ITD*) mutation” by Ahmad Ghorab from MDACC. The MDACC researchers investigated the impact of numerical variation and insert size on clinical outcomes of *FLT3-ITD* AML patients. They analyzed 330 newly diagnosed AML patients with *FLT3-ITD* mutation and found that numerical variation and insert length had no significant impact on outcomes while lower allelic burden, FLT3 inhibitor therapy trended towards better RFS.

Prof. Malek concluded that disease monitoring in AML, as well as clonal hematopoiesis in the absence of MDS in AML, has gained substantial traction.

References

1. Malek S. N. Impact of Disease Burden in Acute Myeloid Leukemia. 2018 American Society of Oncology (ASCO) Annual Meeting., Chicago, US.
2. Ding L. *et al.* Clonal evolution in relapsed acute myeloid leukaemia revealed by whole-genome sequencing Nature. 2012 Jan 26; 481(7382): 506–510. DOI: 10.1038/nature10738.
3. Yilmaz M. *et al.* Clonal evolution in acute myeloid leukemia (AML): Relapse after a long remission period. J Clin Oncol 36, 2018 (suppl; abstr 7022)
4. Kannan K. K. *et al.* Is there a benefit of re-induction therapy in adult patients with AML with <20% blasts? J Clin Oncol 36, 2018 (suppl; abstr 7021)
5. Ghorab A. *et al.* Impact of numerical variation, allele burden and mutation length on outcomes in acute myeloid leukemia with fms-like tyrosine kinase receptor-3 internal tandem duplication (FLT3-ITD) mutation. J Clin Oncol 36, 2018 (suppl; abstr 7023).