Toward precision medicine in AML

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With the new sequencing technologies enormous progress has been made in deciphering the genetic landscape of acute myeloid leukemia (AML), thereby unraveling the enormous molecular heterogeneity of the disease and identifying new therapeutic targets. The development of precision medicine in AML is currently best illustrated by the successful development of FLT3-, IDH1/IDH2- and Bcl-2 inhibitors. When applied as single agents, most of these novel drugs only have modest clinical activity, but combining these drugs with current standard of care, such as intensive induction chemotherapy with daunorubicin/cytarabine (‘3+7’) or with the hyomethylating agents (HMA) azacitidine and decitabine, has demonstrated marked synergistic efficacy. However, despite significant improvements in outcome, the increment in response rates and in particular in survival remains modest. Numerous other new agents, including immunotherapies with bi-specific antibodies and antibody-drug conjugates, are in clinical development that hold promise to enlarge our portfolio of anti-leukemic drugs.

There remain quite a few challenges for the further successful development of precision medicine in AML, such as how to best and safely combine new agents (e.g. the development of less intensive triple therapies in older, unfit patients), or to circumvent primary and secondary resistance mechanisms. Finally, AML is a rare disease and conducting randomized phase 2/3 trials in particular in molecular subsets of the disease increasingly requires international collaborative efforts. The presentation will provide an update on the current status and promising new avenues for precision medicine in AML.