613. Acute Myeloid Leukemia: Clinical Studies: Risk Factors and Response-Adapted Personalized Medicine

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Minimal-Residual Disease Guided Treatment with Azacitidine in MDS/AML Patients at Imminent Risk of Relapse: Results of the Prospective RELAZA2 Trial

Uwe Platzbecker, MD[1], Jan Moritz Middeke, MD[1*], Katja Sockel, MD[2*], Anke Mütherig, MD[1*], et al.

The authors of the study conclude that:

Pre-emptive MRD-guided therapy with AZA can prevent or substantially delay hematologic relapse in patients with MDS and AML at high-risk of relapse. Success of AZA-based MRD therapy seems to be context-dependent emphasizing the potential immunomodulatory effect of hypomethylating agents.

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Low Relapse Rate in Younger Patients ≤ 60 Years Old with Newly Diagnosed FLT3-Mutated Acute Myeloid Leukemia (AML) Treated with Crenolanib and Cytarabine/Anthracycline Chemotherapy

Eunice S. Wang, MD[1], Martin S. Tallman, MD[2], Richard M. Stone, MD[3*], Roland B. Walter, MD, PhD[4], et al.

The authors of the study conclude that:

In patients aged ≤ 60 yrs with FLT3 mutated AML, induction treatment with cytarabine/anthracycline/crenolanib resulted in a CR in 24/29 (83%) patients. With a median follow up of 14 months, only one systemic and one isolated CNS relapse have occurred in these 24 patients who achieved a CR. These data suggest that adding crenolanib, a potent FLT3 inhibitor, to standard induction chemotherapy

in younger patients with FLT3-mutated AML may be associated with a low relapse rate, especially if HSCT is routinely used. A phase 3 trial of crenolanib in combination with 7+3 vs midostaurin in combination with 7+3 is being initiated.

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Therapy for Acute Myeloid Leukemia (AML) Adjusted to Genetic Data and Minimal Residual Disease: Results of the AML12 Trial of the Spanish Cetlam Group in Adults up to the Age of 70 Years

Jorge Sierra[1], Ana Garrido, MD[2*], Susana Vives, MD[3*], Maria Paz Queipo De Llano[4*], et al.

The authors of the study conclude that:

Risk adapted therapy for primary AML based on genetics and MRD is feasible in a cooperative group setting. The proportion of patients in whom the risk of an alloSCT in first CR may be avoided is 38% when considering cytogenetics, molecular findings and MRD information after the end of consolidation phase. MRD assessment at the end of consolidation moved 4% of patients from FR and IR to AR. AlloSCT in AR patients was feasible in most instances, even in the AR group. Despite this, relapses remain above 40% in the intermediate and adverse AML categories and further approaches after transplant such as novel agents and immune therapy deserve investigation.

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IDH1/2-Mutated Acute Myeloid Leukemia Has Impaired DNA Damage Response and Is Sensitive to Monotherapy with the PARP Inhibitior Olaparib

Remco J Molenaar[1*], Tomas Radivoyevitch, PhD[2*], Yasunobu Nagata, MD, PhD[3*], Bartlomiej P. Przychodzen, MSc[4*], et al.

The authors of the study conclude that:

IDH1/2^{MUT} AML cells have an impaired DNA damage response via repression of ATM, which is associated with sensitization of IDH1/2^{MUT} AML cells to the PARP inhibitor olaparib. Furthermore, the sensitization of IDH1/2^{MUT} AML cells to olaparib is reversed when olaparib is combined with an IDH1/2^{MUT} inhibitor. Olaparib, either as monotherapy but preferably combined with a DNA-damaging agent, is thus effective in exploiting ineffective DNA damage repair in IDH1/2^{MUT} AML cells and may represent a possible effective future therapy for IDH1/2^{MUT} AML.

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Mature Analysis of the Prospective Oxford Down Syndrome (DS) Cohort Study: Timing and Clinical Impact of Preleukemic *GATA1* Mutations and Lessons for Management of Newborns with DS

Irene Roberts, MD[1,2], Neha Bhatnagar, ND[3*], Amelie Chaussade, MD[4*], Laure Nizery, MD[4*], et al.

The authors of the study conclude that:

Acquired N-terminal mutations in GATA1 are very frequent in neonates with DS and most probably occur or expand in the 3rd trimester; in the majority of cases mutant GATA1 clones are very small, clinically silent, resolve spontaneously and confer an extremely low risk of ML-DS.

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Molecular Epidemiology of Acute Myeloid Leukemia (AML): Novel Association of Clinical Epidemiologic Exposures with Unique Mutation Groups on Exome Sequencing of Leukemia DNA in the Mayo Clinic AML Epidemiology Cohort

James M. Foran, MD[1], Michael Heckman, MS[2*], Rhett P. Ketterling, MD[3*], Lisa Sproat, MD, MSW[4], et al.

The authors of the study conclude that:

For the first time (apart from sAML) we have identified a unique leukemia genotype associated with some common clinical and epidemiologic exposures. Some mutations groups (Cohesin, TP53) were not associated with any clinical exposures, suggesting alternate mechanisms of leukemogenesis. ExSeq was for the first time successfully performed on archived diagnostic cytogenetic cell pellets, we believe a novel source of leukemia DNA. These results will guide a planned prospective study to determine frequency and mechanism of leukemogenesis after exposures, and development of strategies for prediction of leukemia risk and ultimately prevention.