HEMATOLOGY, TRANSFUSION AND CELL THERAPY

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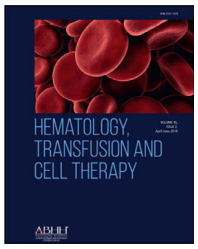

PEDIATRIC PRESENTATIONS

Sp01

INFLAMMATION AND CANCER

Jean-François Rossi

Normal inflammatory response represents the initial phase of the immune response. This normal or "good" inflammatory response is transient, followed by a return to the normal status. Dysregulated or "bad" inflammatory responses are observed in inflammatory, infectious diseases and cancers, and can be characterized by inappropriate levels of inflammatory markers, speed of generation, and major site of production, such as a vital organ. Chronic or smoldering inflammation is associated to cancer initiation as observed in lung, gut, or cervical cancers and with obesity, which is associated to multiple factors such as dysmetabolism, gut dysbiosis, immune dysfunction and immune exhaustion. Inflammation is also associated with cancer promotion, proliferation, metastasis, and thrombosis risks. Due to the persistent and high inflammatory response, immune tolerance is also amplified and leads to immune resistance. Thus, to amplify cancer cell control, the dynamics of the inflammatory response must be evaluated to determine its negative impact and to open a more personalized therapy including the return to a normal inflammatory/immune response. To optimize anti-IL6 therapies, we developed an algorithm to mathematically model inhibition of IL-6 activity in the presence of either siltuximab (anti-IL-6), tocilizumab (anti-IL-6R), or both. By analyzing data in COVID-19 cytokine storm, biological efficiency was not reached showing that there is a need to optimize anti-IL6/antiIL6R therapies which were not correctly used. We also retrospectively analyzed data from the randomized study with siltuximab in Castleman disease, and open new possibilities in cancer, particularly for immune therapies.

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Sp02

NEW ADVANCES IN PEDIATRIC ACUTE MYELOID LEUKEMIA

Özlem Tüfekçi

Pediatric acute myeloid leukemia (AML) accounts for ~20% of childhood leukemias and has been a clinical challenge due to its heterogeneity, high relapse rate and therapy-related toxicity. As compared to 90% overall survival in childhood acute lymphoblastic leukemia, event-free survival and overall survival remain suboptimal at 45% and 65%, respectively at three years and nearly half of children will relapse. Treatment protocols for pediatric AML have converged to a standard that includes four or five cycles of intensified myelosuppressive chemotherapy with cytarabine and anthracyclines followed by hematopoietic stem cell transplantation (HSCT) for a subgroup of patients. It is clear that the ceiling to further intensification of standard chemotherapy has been reached in AML, urgently necessitating novel therapeutic strategies. Recent developments in comprehensive mutation testing and integration of data from adult clinical trials led physicians try novel agents in pediatric AML patients especially in the relapse/refractory setting. In this context major treatment modalities and novel drugs in childhood AML include immunotherapy including drug-antibody conjugates and chimeric antigen receptor T-cell (CAR-T cell) therapy, epigenetic modifiers, tyrosine kinase inhibitors,and other novel agents. The addition of gemtuzumab ozogamicin and FLT3 inhibitors to some standard chemotherapy protocols has been becoming a standard of care in treatment of pediactric AML. Besides, major advances have also been achieved in acute promyelocytic leukemia (APL). The combination of ATO and ATRA without chemotherapy is now the standard chemotherapy for adults that are in the standard risk. Based on these findings; recent trials on pediatric APL patients aim to use ATRA plus ATO while minimizing the use of chemotherapy.

Recently, considerable progresses have been achieved in defining the molecular landscape of AML that lead scientists to discovery of novel drugs. There have been numereous ongoing studies on new therapeutic agents for AML, and