HEMATOLOGY, TRANSFUSION AND CELL THERAPY

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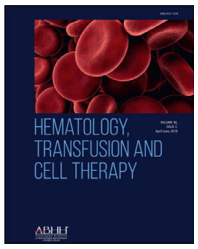


# PEDIATRIC PRESENTATIONS

**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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2531-1379/

**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

some of them have already been included in the standard treatment protocols, but further studies on other new agents are needed to determine their efficacy in children.

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Sp03

## MEDICAL TREATMENT IN HODGKIN LYMPHOMA

Nilgun Kurucu

The treatment of HL has been designed according to risk stratification. Risk stratification is based on presenting features at diagnosis. Stage of disease, presence of bulky disease, presence of B symptoms, and number of involved nodes are the parameters of risk determination. Low risk group includes stage IA and IIA disease with no tumor bulk and no extranodal involvement. Stage IA and IIA with bulky disease or extranodal involvement, and stage IB and stage IIIA are defined as intermediate risk. Stage IIB with with bulky disease or extranodal involvement, IIIB and IV diseases are in high risk group. Treatment of HL in children consists of combined modality treatment including multiagent chemotherapy and low dose involved field radiotherapy. Modern therapy of HL can be based on both risk group and response (Table I, II, III). Standard chemotherapy in Hodgkin disease is ABVD or MOPP derivatives. Adriamycine, Dacarbazine, Bleomisin and Vinblastin are the major drugs of ABVD derivative protocols. MOPP derivatives include generally cylophospamide, vincristine, procarbazine, prednisolone. Hodgkin lymphoma is a radiosensitive disease. In general, doses of 15 to 25 Gy are used with modification based on patient and disease characteristics. In combined modality era, the extended treatment volumes are no longer needed. The Involved fields reduce the exposure of normal tissue and the late side effects by not reducing local control rate. The implementation of more tailored fields is a progress toward this goal, treating only the individual lymph nodes with a margin for microscopic disease. This, in conjunction with modern imaging, will continue to reduce exposure of normal tissue to radiation while maintaining equivalent local disease control rates. In some recent trials, radiotherapy was omitted in localized low risk disease and early responder patients.

Combined modality treatment will result in very high cure rates (Table I, II, III). The treatment results in children with early stage disease are perfect. Disease-free survival and overall survival reach up to 95% and 100%, respectively. About ten to twenty percent of advance stage patients may relapse. Since the prognostic outlook and life expectancy of HL have shown significant progress over the last decades, the quality of life and prevention of late side effects have gained considerable importance. Balance ensuring the best opportunity for long-term disease-free survival and the lowest risk of severe treatment toxicity should be achieved.

Table I. Treatment of Low Risk Group

| Low Risk Studies | Treatment | | EFS |
|---|---|---|---|
| POG 8625 | 6 MOPP/ABVD | +None | 83% |
| (1986-92, 247 pts) | 4 MOPP/ABVD | +LD-IFRT | 91% |
| CCG 5942 | 4COPP/ABV | + None | 89% |
| (1995-98, 826 pts) | 4COPP/ABV | + LD-IFRT | 100% |
| COG 9426 | 2 DBVE | CR ⇨ +LDIFRT | 87% |
| (1996-2000, 294 pts) | | <CR ⇨ +2DBVE+ LDIFRT | 85% |
| COG AHOD0431 | AVPC | CR ⇨ +None | 78% |
| (2006-2009, 278 pts) | | <CR ⇨ +LDIFRT | 83% |
| MDH90 | 4 VBVP | CR ⇨ +IFRT | 90% |
| (1990-2008,202 pts) | 4 VBVP | <CR ⇨ +2-4 OPPA +IFRT | 78% |
| GPOH-HD 2002 | 2 OEPA(M)/OPPA(F) | CR ⇨ +None | 93% |
| (2002-2005,573 pts) | | <CR ⇨ +LD-IFRT | 92% |

Table II. Treatment of Intermediate Risk Group

| İntermediate Risk Studies | Treatment | | EFS |
|---|---|---|---|
| CCG 5942 | 6 COPP/ABV | ⇨ + None | 78% |
| (1995-98,834 pts) | | ⇨ + LD-IFRT | 84% |
| POG 9425 | 3 ABVE-PC | RER ⇨ +LDIFRT | 86% |
| (1997-2001, 219 pts) | | SER ⇨ +2ABVE-PC+ LDIFRT | 88% |
| AHOD0031 | 2 ABVE–PC | RER ⇨ CR +2ABVE-PC + None | 84% |
| (2002-2009, 1734) | | RER ⇨ CR + 2ABVE-PC+ LDIFRT | 88% |
| | | RER ⇨ <CR +2ABVE-PC+LDIFRT | 87% |
| | | SER ⇨ +2DECA+2ABVE- | 79% |
| | | PC+LDIFRT | 75% |
| | | SER ⇨ +2ABVE-PC+LDIFRT | |
| GPOH-HD2002 | 2 OEPA/OPPA+4COPP/COPADC +SDIFRT | | 88% |
| (1997-2001, 219 pts) | | | |