Treatment strategies for diffuse large B-cell lymphoma: the GELA experience

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Supporting the way towards a cure in multiple myeloma

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Innovative approaches in the treatment and support of acute myeloid leukemia

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A breakthrough in the treatment of ITP

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Acute myeloid leukemia (AML) is a genetically heterogeneous disease characterized by an accumulation of acquired mutations in hematopoietic progenitor cells. At present, well-established chemotherapy regimens, such as the 7+3 induction regimen of cytarabine plus an anthracycline, are the standard of care for all AML subtypes. New induction and consolidation regimens are, however, being investigated. Supportive care with growth factors can be important to aid recovery from treatment-related aplasia. Filgrastim has been used in this setting, and data now show that pegfilgrastim is also effective. Perhaps the greatest benefit from growth factor support is observed following consolidation therapy. For example, use of pegfilgrastim after high-dose cytarabine consolidation therapy reduced time to neutrophil recovery, incidence of neutropenic fever and time in hospital compared with controls.

Looking to the future, our improving knowledge of leukemogenesis will increasingly translate into more accurate prognostic assessment and genotype-specific treatment strategies. In a recent metaanalysis we attributed induction success in AML patients exhibiting a normal karyotype to those having mutations either in NPM1 in the absence of FLT3-ITD or in CEBPA. These favorable genotypes emerged as highly significant prognostic markers for relapse-free and overall survival; they also acted as predictive markers with the beneficial effects of an allogeneic stem cell transplant in first complete remission being evident only in patients without a favorable genotype. The utility of genotyping has been further demonstrated in core binding factor (CBF) leukemias, which exhibit a higher expression of KIT compared to other AML subtypes. Here, KIT mutations have been associated with an unfavorable prognosis.

New drugs are being developed to specifically inhibit molecularly-defined targets. The efficacy of tyrosine kinase inhibitors is being investigated in FLT3mut and CBF AML, while other examples include the use of all-trans retinoic acid in NPM1mut AML. It is of note, however, that nearly all new targeted treatments combine innovative agents with a backbone of chemotherapy such as the 7+3 induction regimen and consolidation therapy with high-dose cytarabine.

In conclusion, the future of AML treatment lies in genotype-specific strategies. Since most new agents will be combined with conventional chemotherapy appropriate supportive care, including growth factors, will remain a consideration in management of AML.

**ROMIPLOSTIM: A BREAKTHROUGH IN THE TREATMENT OF IMMUNE THROMBOCYTOPENIC PURPURA**

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Immune thrombocytopenic purpura (ITP) is an immune-mediated, haematologic disorder of increased platelet destruction and concomitant sub-optimal platelet production. Patients typically have abnormally low platelet counts (<30 x 10^9/L). Clinical signs and symptoms include bleeding, purpura, petechiae, and at very low platelet counts, there is a risk of major non-fatal and fatal bleed events. ITP affects patients of all ages and ethnic groups, and there are approximately 390 new cases of ITP per million people per year. (1) Current approved treatment options include corticosteroids whose long-term use can be associated with various side effects, including hypertension, diabetes, and osteoporosis. Splenectomy is an option for patients with severe ITP refractory to corticosteroids, but the trend is now for more conservative management of patients.

Romiplostim is a thrombopoiesis-stimulating Fc-peptide fusion protein (peptibody) that binds to and activates the thrombopoietin receptor on megakaryocytes in the bone marrow, thereby increasing platelet production. The efficacy and safety of romiplostim as a new treatment option for ITP was investigated in two parallel, multicentre, double-blind, randomised, placebo-controlled, phase III studies conducted in the US and Europe. (2) Romiplostim was administered as a weekly subcutaneous injection (starting dose 1µg/kg/week, adjusted to maintain platelet counts between 50-200 x 10^9/L) for 24 weeks to 83 adults with ITP (splenectomised N=42; non-splenectomised N=41). Altogether 88% of the non-splenectomised patients and 79% of the splenectomised patients receiving romiplostim achieved either a durable or transient platelet response during the study period compared with placebo-treated patients (p<0.0001). Patients receiving romiplostim required fewer ITP rescue medications and were able to discontinue or reduce the use of concurrent ITP drugs such as corticosteroids.

Headache was the most frequently reported adverse event in the romiplostim-treated group (22% vs 16% placebo). Significant bleeding events occurred in 12% and 7% of the patients receiving placebo and romiplostim, respectively; there was a 42% reduction in ≥ grade 3 bleeding events in favour of the romiplostim-treated patients. (3) These phase III data indicate that romiplostim offers a promising breakthrough in the treatment of ITP in splenectomised and non-splenectomised adults.

3. Lyons et al. The American Society of Hematology Annual Meeting 2007; Abstract 1300