High-dose chemotherapy in germ cell tumors: an old story still young.

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Editorial

Germ cell tumours represent a model of curable solid tumours. In stage 1 and 2 more than 90% the patients can achieve cure, while in advanced cases such a goal is achieved in 70-80%.

For metastatic cases the standard treatment has been for more than three decades the combination of cisplatin, etoposide and bleomycin (PEB) for three or four courses depending on the prognostic category (good or intermediate/poor).

Surgery on the residuum is a fundamental part of the whole program, especially in non seminoma and all efforts have to be undertaken to remove residual disease.

But despite these good results, a not negligible minority of patients do relapse usually in the first one or two years. Cure can still be achieved with second line chemotherapy in 25-40% of the patients, depending on type of relapse.

In the last decades high-dose chemotherapy supported initially by autologous bone marrow an in the last twenty years by peripheral blood progenitors, has emerged as a possible option for relapsing or refractory patients, with nearly 500 patients treated each year in Europe.

The reasons for embarking in such a treatment option is due to early impressive results in the early phase two trials, but also to the unique end peculiar chemo sensitivity of germ cell cancers, and also to the fact that the majority of patients are younger compared to other major cancers.

Treatment related mortality was high in the early years, but nowadays it has been reduced to 1-2% due to better knowledge of the procedure, to more skilled staff in dedicated high-volume centers and moreover to early treatment in the course of the disease and the introduction of granulocyte stimulating factors.

A recent report by the European society for Blood and Marrow Transplantation (EBMT) has shown that even in patients over 40 years the procedure is safe.

From mono-institutional dataset, nearly 40% of germ cell tumor patients, in third or subsequent relapse do achieve long results with the curve plateauing after one year, while in second line cure rate is close to 70%.

An International database with more than 1,500 patients treated in second line has shown that those who undergoing high-dose chemotherapy did significantly better than those receiving standard second line programs in all subsets, except those with a very good prognosis.

Many International Guidelines do recommend high-dose chemotherapy as an option in second or third relapse, possibly with a tandem procedure based on carboplatin and etoposide high doses. Peripheral progenitor cells are mobilized with a paclitaxel/ifosfamide combination.

An ongoing study on behalf of EORTC is comparing high-dose chemotherapy versus standard treatment in second line (TIGER STUDY) and the results are awaited in three years from now.

At the present time anyway, and in the absence of new effective drugs including immunotherapeutic agents (check point inhibitors) which, even if in the infancy of their use in germ cell tumors, did not mirror so far the same good results in other malignant diseases, high-dose chemotherapy with peripheral blood progenitor cells transplantation is and will remain a good option for patients not cured in first or second line.

But these procedures have to be performed only in high-volume dedicate centers with expertise in germ cell tumors treatment and autologous transplantation. This is a must.

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