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CONSENSUS UPDATE

HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR SOLID TUMORS

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INTRODUCTION

High-dose chemotherapy (HDCT) with stem-cell support is a procedure that allows the administration of high doses of chemotherapy that would otherwise be lethal. In HDCT, extra-medullary toxicity is the dose-limiting factor. Use of peripheral blood stem cells and improvement in patient management has reduced non-relapse mortality to less than 5%. Over the last decades, knowledge about HDCT in solid tumors has increased[1–3], particularly in germ cell tumors (GCT).

Testicular malignant tumors are the most frequent solid tumor of the young male, and 95% of these are germ cell tumors (GCT)[4]. They are unique tumors in which they represent a malignant transformation of a totipotent germ cell. They are divided, histologically, in seminoma and nonseminoma. Both secrete beta-human chorionic gonadotropin (beta-HCG), while only the latter produces alpha-fetoprotein (AFP). Approximately 75% of the patients are cured with conventional[5]. Follow-up includes serial image exams and of the serum markers HCG e AFP.

This is an update of the 2020 recommendations of the Sociedade Brasileira de Transplante de Medula Óssea (Brazilian Society of Bone Marrow Transplantation, SBTMO) for hematopoietic cell transplantation for solid tumors[6]. Main recommendations are summarized here, and new recommendations are marked and discussed. For the texts for the 2020 recommendations, please refer to the original paper[6].

High-dose chemotherapy (HDCT) for Germ Cell Tumor (GCT)

Recommendation: HDCT should not be offered for frontline therapy in germ cell tumors (Level of Evidence 1b, Grade of Recommendation A).

Recommendation: HDCT should be offered as second or third-line therapy of germ cell tumor, even in patients with mediastinal, platinum-refractory, or non-seminomatous GCT (Level of Evidence 2b, Grade of Recommendation B).

New recommendation: Poor-mobilizers should receive plerixafor (Level of Evidence: 4, Grade of Recommendation: C).

Recommendation: Conditioning regimen should be carboplatin and etoposide (Level of Evidence 1b, Grade of Recommendation A).

Recommendation: Two or three cycles of HDCT should be offered instead of one (Level of Evidence 1b, Grade of Recommendation B).

Recommendation: For patients with residual disease following HDCT, surgical resection should be performed (Level of Evidence 4, Grade of Recommendation C).

STEM-CELL MOBILIZATION

G-CSF-mobilized peripheral blood stem-cell graft has largely replaced bone marrow[7]after appropriate pharmacologic mobilization, have largely replaced bone marrow as the principal source of HSCs in transplants. As it is currently common practice to perform tandem or multiple sequential cycles of HDCT, it is anticipated that collection of large numbers of HSCs from the peripheral blood is a prerequisite for the success of the procedure. Moreover, the CD34+ cell dose/kg of body weight infused after HDCT has proven to be a major determinant of hematopoietic engraftment, with patients who receive $> 2 \times 106$ CD34+ cells/kg having consistent, rapid, and sustained hematopoietic recovery. However, many patients with relapsed/refractory GCTs have been exposed to multiple cycles of myelosuppres-

sive chemotherapy, which compromises the efficacy of HSC mobilization with granulocyte colony-stimulating factor with or without chemotherapy. Therefore, alternative strategies that use novel agents in combination with traditional mobilizing regimens are required. Herein, after an overview of the mechanisms of HSCs mobilization, we review the existing literature regarding studies reporting various HSC mobilization approaches in patients with relapsed/refractory GCTs, and finally report newer experimental mobilization strategies employing novel agents that have been applied in other hematologic or solid malignancies.”,”container-title”:”World Journal of Clinical Oncology”,”DOI”:”10.5306/wjco.v12.i9.746”,”ISSN”:”2218-4333”,”issue”:”9”,”-journalAbbreviation”:”World J Clin Oncol”,”language”:”eng”,”note”:”PMID: 34631440\nPMCID: PMC8479351”,”page”:”746-766”,”source”:”-PubMed”,”title”:”Hematopoietic stem cell mobilization strategies to support high-dose chemotherapy: A focus on relapsed/refractory germ cell tumors”,”title-short”:”Hematopoietic stem cell mobilization strategies to support high-dose chemotherapy”,”volume”:”12”,”author”:[{“family”:”Porfyriou”,”given”:”Eleni”},{“family”:”Letsa”,”given”:”Sylvia”},{“family”:”Kosmas”,”given”:”Christos”}],”issued”:{“date-parts”:[[“2021”,9,24]]}}}],”schema”:”https://github.com/citation-style-language/schema/raw/master/csl-citation.json”} . Peripheral blood graft collection is more convenient and associated with faster hematopoietic recovery. However, these patients usually have been exposed to platinum and other alkylating agents and therefore mobilization failure is not uncommon. Corbingi et al have demonstrated the feasibility of a “on-demand” approach using plerixafor for patients with low peripheral CD34 cells following mobilization with G-CSF (poor mobilizers) in patients with relapsed/refractory germ cell tumors[8].

HIGH-DOSE CHEMOTHERAPY FOR OTHER SOLID TUMORS

Recommendation: HDCT should be offered for ovarian germ tumor or gestational trophoblastic tumor, chemorefractory (Level of Evidence 4, Grade of Recommendation C).

Recommendation: HDCT should not be offered to any kind of breast cancer (Level of Evidence 1a, Grade of Recommendation A).

Recommendation: HDCT should not be offered for ovary or lung cancer (Level of Evidence 2b, Grade of Recommendation B).

Recommendation: HDCT should be offered to patients with high-risk localized Ewing sarcoma (Level of Evidence 1b, Grade of Recommendation A). HDCT can be offered for relapsed Ewing sarcoma (Level of Evidence 2a, Grade of Recommendation B)

Allogeneic stem cell transplantation in solid tumors

Recommendation: There is no data to recommend allogeneic stem-cell transplantation in solid tumors in any setting.

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TABLE 1. Selected conditioning regimens

INSTITUTION	CARBOPLATIN	ETOPOSIDE	CYCLOPHOSPHAMIDE	# TRANSPLANTS
MSKCC11dose-intense chemotherapy with paclitaxel and ifosfamide followed by carboplatin and etoposide (TICE	AUC=24	1,200mg/m2	x	3
Indiana12 *	2,100mg/m2	2,250mg/m2	x	2
MSKCC13	1,500mg/m2	1,200mg/m2	150mg/kg	2
Germany14	1,500mg/m2	1,500mg/m2	x	3
	Cisplatin	Etoposide	Ifosfamide	# Transplants
EORTC14etoposide, and ifosfamide (VIP	100mg/m2	1,500mg/m2	12,000mg/m2	3

*etoposide oral maintenance 50mg/day x 21 days every 4 weeks for 3 cycles