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# CONSENSUS ON INDICATIONS FOR HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PEDIATRICS. UPDATE 2020: GERM CELL TUMORS AND WILMS TUMORS

V Meeting of Brazilian Guidelines on Hematopoietic Stem Cell Transplantation of the Brazilian Society of Bone Marrow Transplantation – SBTMO

Patricia Shimoda Ikeuti[1], Simone de Castro Resende Franco[2], Cláudio Galvão de Castro Junior[3,4]

*1- Instituto de Oncologia Pediátrica IOP/GRAACC/Unifesp – São Paulo, Brasil*
*2- Hospital da Criança de Brasilia José de Alencar – Brasília – DF- Brasil*
*3- Hemomed Instituto de Oncologia e Hematologia – São Paulo – SP - Brasil*
*4- Hospital São Camilo – São Paulo – SP – Brasil*

Correspondence to: claudio.junior1967@gmail.com

## SUMMARY

The indications for hematopoietic stem cell transplantation in solid tumors in children do not change a lot since our first Brazilian consensus publication in 2009. In this article, we are going to review indications to hematopoietic stem cell transplantation in pediatric germ cell tumors and wilms tumor.
For the consensus, a review was made using the most relevant articles, and a series of meetings was done to discuss the recommendations.

**Keywords:** Germ cell tumor; Wilms tumor; Hematopoietic Stem Cell Transplantation; Pediatrics

## INTRODUCTION

Most studies of extracranial germ cell tumors are in adult patients. Transplantation appears to be beneficial in patients after the first or second relapse, with response to chemotherapy and with the least amount of residual disease.[1-2]

There is a tendency to use tandem transplantation[3]. Currently, an international prospective randomized study is in progress with HSCT as a rescue therapy for patients with first-line treatment failure.[4]

## IN FIRST REMISSION

It may also be an option, as a first line, for some patients with unfavorable prognostic factors, especially for those with slow drop in markers after the first two cycles of chemotherapy.[5,6]

## RELAPSED OR REFRACTORY PATIENTS

The standard rescue treatment for relapsed/refractory GCTs includes either conventional chemotherapy or high dose chemotherapy with autologous hematopoietic stem cell transplantation (HSCT).[3]

The use of high-dose chemotherapy with autologous HSCT seems to show better results in relation to progression-free survival.[3,7]

There is an international prospective randomized study is in progress with HSCT as a rescue therapy for patients with first-line treatment failure.[4]

## SEQUENTIAL HSCT (TANDEM)

Randomized studies comparing a single transplantation with sequential HSCT do not show significant differences in relation to overall survival, progression-free survival and event-free survival.[8-9] However, they show a significant difference in terms of mortality related to transplantation.[8]

Thus, there is a tendency to increasingly use sequential HSCT with a preference for intervals between

transplants less than 28 days that show better results in relation to relapse and progression-free survival.[3]

## PEDIATRIC PATIENTS

Studies in the pediatric population are scarce and mostly retrospective. They demonstrate beneficial results in the rescue treatments in children with extragonadal GCT, but there is a need for prospective studies[10], in addition to the importance of resection of the primary tumor for the results.[11]

## WILMS TUMORS

Most patients with Wilms tumors WT have good overall survival outcomes. Despite the relatively small number of patients with relapsed Wilms' tumor, limiting the randomization of subgroups, there is relevant information extracted from literature reports favoring the use of HSCT. A meta-analysis study suggests that patients with initial stage III or IV and isolated pulmonary relapse within one year of diagnosis are the most benefited by HSCT [12,13].

A review of 234 transplanted children found similar findings, suggesting that HSCT has a positive impact on survival in patients with advanced early stage, unfavorable histology, previous exposure to more than 4 chemotherapeutic agents, in second relapse, or with disease progressing after first relapse[14].

Very high-risk patients can be transplanted in the first line, preferably within clinical trials[15]. There are no robust studies on better conditioning, but melphalan used alone seems to be an adequate regimen[15,16]. In all publications, only autologous transplantation is mentioned, with the allogeneic transplant out of context.

In the table 1 all indications are summarized.

**TABLE 1-** Indications for Hematopoietic Stem cell Transplantation in Pediatric Solid Tumors

| TUMOR | AUTOLOGOUS | ALLOGENEIC |
|---|---|---|
| Germ Cell Tumor – First Line High Risk Features | CI | NR |
| Germ Cell Tumor – Relapse | CI | NR |
| Wilms Tumor – First Line - Very High Risk | CI | NR |
| Wilms Tumor Relapsed | CI | NR |

## REFERENCES


1. Lorch A, Bascoul-Mollevi C, Kramar A, Einhorn L, Necchi A, Massard C, et al. Conventional-Dose Versus High-Dose Chemotherapy As First Salvage Treatment in Male Patients With Metastatic Germ Cell Tumors: Evidence From a Large International Database. J Clin Oncol. 2011; 29:2178-2184.

2. Simonelli M, Rosti G, Banna GL, Pedrazzoli P. Intensified chemotherapy with stem-cell rescue in germ-cell tumors. Annals of Oncology. 2012; 23:815–822.

3. Kilari D, D'Souza A, Fraser R, Qayed M, Davila O, Agrawal V, et al. Autologous Hematopoietic Stem Cell Transplantation for Male Germ Cell Tumors: Improved Outcomes Over 3 Decades. Biol Blood Marrow Transplant. 2019;25(6):1099-110.

4. Feldman DR, Huddart R, Hall E, Jörg B, Powles T.Is High Dose Therapy Superior to Conventional Dose Therapy as Initial Treatment for Relapsed Germ Cell Tumors? The TIGER Trial. Journal of Cancer. 2011;2:374-377.

5. Rosti G, De Giorgi U, Wandt H, Lioure B, Leyvraz S, Kolbe K, et al. Solid Tumours Working Party. First-line High-Dose Chemotherapy for Patients With Poor Prognosis Extragonadal Germ Cell Tumors: The Experience of the European Bone Marrow Transplantation (EBMT) Solid Tumors Working Party. Bone Marrow Transplant. 2004;34(12):1033-7.

6. Motzer RJ, Nichols CJ, Margolin KA, Bacik J, Richardson PG, Vogelzang NJ, et al. Phase III Randomized Trial of Conventional-Dose Che-

motherapy With or Without High-Dose Chemotherapy and Autologous Hematopoietic Stem-Cell Rescue As First-Line Treatment for Patients With Poor-Prognosis Metastatic Germ Cell. J Clin Oncol. 2007;25:247-256.

7.Feldman DR, Sheinfeld J, Bajorin DF, Fischer P, Turkula S, Ishill N, et al. J. TI-CE High-Dose Chemotherapy for Patients With Previously Treated Germ Cell Tumors: Results and Prognostic Factor Analysis. J Clin Oncol. 2010;28(10):1706-13.

8. Lorch A, Kollmannsberger C, Hartmann JT, Metzner B, Schmidt-Wolf IG, Berdel WE, et al. German Testicular Cancer Study Group. Single Versus Sequential High-Dose Chemotherapy in Patients With Relapsed or Refractory Germ Cell Tumors: A Prospective Randomized Multicenter Trial of the German Testicular Cancer Study Group. J Clin Oncol. 2007;25(19):2778-84.

9. Lorch A, Kleinhans A, Kramar A, Kollmannsberger CK, Hartmann JT, Bokemeyer C, et al. Sequential Versus Single High-Dose Chemotherapy in Patients With Relapsed or Refractory Germ Cell Tumors: Long-Term Results of a Prospective Ra domized Trial. J Clin Oncol. 2012;30(8):800-5.

10. De Giorgi U, Rosti G, Slavin S, Yaniv I, Harousseau JL, Ladenstein R, et al. European Group for Blood and Marrow Transplantation Solid Tumours and Paediatric Disease Working Parties. Salvage High-Dose Chemotherapy for Children With Extragonadal Germ-Cell Tumours. Br J Cancer. 2005;93(4):412-7.

11. Faure-Conter C, Orbach D, Cropet C, Baranzelli MC, Martelli H, Thebaud E, et al. Salvage Therapy for Refractory or Recurrent Pediatric Germ Cell Tumors: The French SFCE Experience. Pediatr Blood Cancer. 2014;61(2):253-9.

12. Presson A, Moore TB, Kempert P. Efficacy of high-dose chemotherapy and autologous stem cell transplant for recurrent Wilms' tumor: a meta-analysis. J Pediatr Hematol Oncol. 2010;32(6):454-61.

13. Malogolowkin MH, Hemmer MT, Le-Rademacher J, Hale GA, Mehta PA, Smith AR, et al. Outcomes following autologous hematopoietic stem cell transplant for patients with relapsed Wilms' tumor: a CIBMTR retrospective analysis. Bone Marrow Transplant. 2017;52(11):1549-1555.

14. Ha TC, Spreafico F, Graf N, Dallorso S, Dome JS, Malogolowkin M, et al. An international strategy to determine the role of high dose therapy in recurrent Wilms' tumour. Eur J Cancer. 2013;49(1):194-210.

15. Spreafico F, Dalissier A, Pötschger U, Locatelli F, Michon JM, Peters C, et al. High dose chemotherapy and autologous hematopoietic cell transplantation for Wilms tumor: a study of the European Society for Blood and Marrow Transplantation. Bone Marrow Transplant. 2020;55(2):376-383.

16. Kobayashi R, Inoue M, Takahashi Y, Kikuta A, Ogawa A, Koga Y, Koh K, et al. Autologous Stem Cell Transplantation for Children With Renal Tumors, and Adults With Wilms Tumor: Retrospective Analysis of the Japanese Transplant Registry Unified Management Program. J Pediatr Hematol Oncol. 2020;42(4):251-255.