

AperTO - Archivio Istituzionale Open Access dell'Università di Torino

Antiemetic prophylaxis in patients undergoing hematopoietic stem cell transplantation: a multicenter survey of the Gruppo Italiano Trapianto Midollo Osseo (GITMO) transplant programs

This is a pre print version of the following article:

Original Citation:

Availability:

This version is available <http://hdl.handle.net/2318/1732792> since 2020-03-05T22:35:34Z

Published version:

DOI:10.1007/s00277-020-03945-3

Terms of use:

Open Access

Anyone can freely access the full text of works made available as "Open Access". Works made available under a Creative Commons license can be used according to the terms and conditions of said license. Use of all other works requires consent of the right holder (author or publisher) if not exempted from copyright protection by the applicable law.

(Article begins on next page)

Antiemetic prophylaxis in patients undergoing hematopoietic stem cell transplantation: a multicentre survey of the Gruppo Italiano Trapianto Midollo Osseo (GITMO) transplant programmes

Pastore D¹, Bruno B², De Candia MS¹, Mammoliti S³, Borghero C⁴, Chierichini A⁵, Pavan F⁶, Casini M⁷, Pini M⁸, Nassi L⁹, Greco R¹⁰, Tambaro FP¹¹, Stefanoni P¹², Console G¹³, Marchesi F¹⁴, Facchini L¹⁵, Mussetti A¹⁶, Cimminiello M¹⁷, Saglio F¹⁸, Vincenti D¹⁹, Falcioni S²⁰, Chiusolo P²¹, Olivieri J²², Natale A²³, Faraci M²⁴, Cesaro S²⁵, Marotta S²⁶, Proia A²⁷, Donnini I²⁸, Caravelli D²⁹, Zuffa E³⁰, Iori AP³¹, Soncini E³², Bozzoli V³³, Pisapia G³⁴, Scalone R³⁵, Villani O³⁶, Prete A³⁷, Ferrari A³⁸, Menconi M³⁹, Mancini M⁴⁰, Gigli F⁴¹, Pini M⁴², Gargiulo G⁴³, Bruno B³, Patriarca F⁴⁴, Bonifazi F⁴⁵

Author information

1 Hematology, Brindisi, Italy

2 S.S.C.V.D Trapianto di Cellule Staminali, A.O.U. Città della Salute e della Scienza di Torino, Italy

3 National Registry GITMO& Data Managing, Ospedale San Martino, Genova, Italy

4 Department of Cellular Therapy and Hematology, San Bortolo Hospital, Vicenza, Italy

5 Department of Hematology, S. Giovanni Addolorata Hospital, Rome, Italy

6 Clinica Pediatrica Ospedale S. Gerardo, Fondazione MBBM, University of Milano-Bicocca, Monza, Italy

7 Hematology Department, San Maurizio Regional Hospital, South Tyrol, Italy

8 Ematologia, AON SS Antonio e Biagio e Cesare Arrigo, Alessandria, Italy

9 Department of Translational Medicine, University of Eastern Piedmont, Novara, Italy

10 Hematology and Bone Marrow Transplantation Unit, IRCCS San Raffaele Hospital, Milan, Italy

11 S.S.D. TMO - AORN Santobono-Pausilipon, Napoli, Italy

12 Hematology Unit, Ospedale Papa Giovanni XXIII, Bergamo, Italy

13 Hematology and Bone Marrow Transplant Unit, AO BMM, Reggio Calabria

14 Hematology and Stem Cell Transplant Unit, Experimental and Clinical Oncology Department, IRCCS Regina Elena National Cancer Institute, Rome, Italy

15 Hematology Unit, Arcispedale S Maria Nuova-IRCCS, Reggio Emilia, Italy

16 Dipartimento di Ematologia e Onco-Ematologia Pediatrica, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

17 UOC di Ematologia con TMO, Ospedale San Carlo, Potenza, Italy

18 Pediatric Onco-Hematology, Stem Cell Transplantation and Cellular Therapy Division, Regina Margherita Children's Hospital, Torino, Italy

19 U.O.C. Oncoematologia, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Università degli

- Studi di Milano, Milano, Italy
- 20U.O.C. Ematologia e Trapianto di Cellule Staminali Emopoietiche, Ospedale Mazzoni, Ascoli Piceno, Italy
- 21Istituto di Ematologia, Policlinico Universitario A Gemelli, Università Cattolica, Roma, Italy
- 22UOC Medicina Interna ed Ematologia, ASUR-AV3, Civitanova Marche, Italy
- 23Bone Marrow Transplant Center, Department of Hematology, Transfusion Center and Biotechnology, Ospedale Civile, Pescara, Italy
- 24Hematopoetic Stem Cell Transplant Unit, Hematology-Oncology, G. Gaslini Institute, Genoa, Italy
- 25Department of Pediatric Hematology Oncology, Azienda Ospedaliera Universitaria Integrata, Policlinico G.B. Rossi, Verona, Italy
- 26Hematology, Department of Clinical Medicine and Surgery, Federico II University, Naples, Italy
- 27Unit of Hematology and Stem Cell Transplant, Azienda Ospedaliera S. Camillo-Forlanini, Roma, Italy
- 28SODc Terapie Cellulari e Medicina Trasfusionale, AOU Careggi, Firenze
- 29Medical Oncology, Hematopoietic Stem Cells Unit, Turin Metropolitan Transplant Center, Candiolo Cancer Institute-FPO, IRCCS, Candiolo, Italy
- 30Unità Operativa di Ematologia, Ravenna, Italy
- 31Department of Hematology, Azienda Policlinico Umberto I, Sapienza University of Roma, Roma, Italy
- 32Pediatric Hematology-Oncology, BMT Unit, Spedali Civili, Brescia, Italy
- 33Divisione di Ematologia, Ospedale di Lecce, Lecce, Italy
- 34Hematology Unit and BMT, Department of Oncology, San Giuseppe Moscati Hospital, Taranto, Italy
- 35Dipartimento Oncologico "La Maddalena", UOC di Oncoematologia e TMO, Palermo, Italy
- 36Department of Onco-Hematology, IRCCS-CROB, Referral Cancer Centre of Basilicata, Rionero in Vulture (Pz), Italy
- 37Oncology, Hematology and Hematopoietic Stem Cell Transplant Program, U.O. Pediatrics- S. Orsola-Malpighi University of Bologna, Bologna, Italy
- 38Haematology unit, AOU Sant'Andrea, Rome, Italy
- 39Division of Hematology, Department of Clinical and Experimental Medicine, University of Pisa
- 40Division of Hematology, Azienda Ospedaliera Universitaria Ospedali Riuniti, Ancona, Italy
- 41Hematology, Istituto Europeo di Oncologia, Milan, Italy
- 42Ematologia, AON SS Antonio e Biagio e Cesare Arrigo, Alessandria, Italy
- 43UOC Hematology and TCSE, AOU Federico II, Napoli, Italy
- 44 Clinica Ematologica, Azienda sanitaria Universitaria Integrata, DAME, Università di Udine, Udine, Italy
- 45 Unit of Hematology and Medical Oncology, " L. and A. Seragnoli", St. Orsola-Malpighi Polyclinic, Bologna, Italy

ABSTRACT

A survey within hematopoietic stem cell transplant (HSCT) centres of the Gruppo Italiano Trapianto Midollo Osseo (GITMO) was performed in order to describe current antiemetic prophylaxis in patients undergoing HSCT. The multicentre survey was performed by questionnaire, covering the main areas on chemotherapy induced nausea and vomiting (CINV): antiemetic prophylaxis guidelines used, antiemetic prophylaxis in different conditioning regimens, methods of CINV evaluation. The survey was carried out in November 2015 [before the publication of the Multinational Association of Supportive Care in Cancer (MASCC)/ European Society for Medical Oncology (ESMO) specific guidelines on antiemetic prophylaxis in HSCT] and its was repeated six months later. The results show a remarkable heterogeneity of prophylaxis among the various centers and a significant difference between the guidelines and the clinical practice. In the main conditioning regimens, the combination of a serotonin₃ receptor antagonist (5-HT₃-RA) with dexamethasone and neurokin₁ receptor antagonist (NK1-RA), as recommended by MASCC/ESMO guidelines, increased from 0-14% (before the publication of the guidelines) to 10-25% (after the publication of the guidelines). This study shows a lack of compliance with specific antiemetic guidelines, resulting mainly in under-prophylaxis. Concerted strategies are required to improve the current CINV prophylaxis, to draft shared common guidelines and to increase the knowledge and the adherence to the current recommendations for CINV prophylaxis in the specific field of HSCT.

INTRODUCTION

Over the past years, the attention on antiemetic prophylaxis in patients undergoing hematopoietic stem cell transplantation (HSCT) has considerably increased due a series of factors, including the following: recent research on chemotherapy-induced nausea and vomiting (CINV) physiopathology, distinguishing between acute and delayed physiopathology [1-7]; the possibility to use new phase-specific molecules for antiemetic prophylaxis [8-10]; and the ever growing concern about the “quality of life” of transplanted, and overall onco-hematological patients [11]. As a matter of fact, CINV cases after HSCT are among the most distressing side effects, in addition to the negative impact they create on patients’ quality of life. Finally, such concern was also determined by the lack of specific guidelines for transplanted patients until 2017, when MASCC/ESMO published, for the first time, specific guidelines for the patients undergoing HSCT [12,13].

These guidelines recommend a combination of a triple association serotonin₃-receptor antagonist (5HT₃-RA)RA with dexamethasone and a neurokin₁ receptor antagonist (NK1-RA). Previous guidelines did not provide a specific CINV prophylaxis for patients receiving HSCT. The 2015 National Comprehensive Cancer Network (NCCN) guidelines[14] recommended either a combination of a 5HT₃-RA with dexamethasone and a NK1-RA, the combination of netupitant/palonosetron (NEPA) and dexamethasone, or the combination of olanzapine with dexamethasone and a NK1-RA for patients receiving high emetic risk chemotherapy. Also, the latest 2017 ASCO guidelines[15] did not state a specific CINV prophylaxis for patients undergoing HSCT .

In order to investigate current clinical practice within Gruppo Italiano Trapianto Midollo Osseo (GITMO) transplant centres regarding the antiemetic prophylaxis in the principal condition regimens and the adherence to the international literature pertaining to antiemetic prophylaxis, a questionnaire-based survey was created and completed before and after the publication of the MASCC/ESMO specific guidelines for HSCT. This paper presents the results of this survey and also a discussion on the implications of this practice.

METHODS

Invitation to participate in the survey was emailed to the transplant directors of 50 centres that are part of the GITMO; the response rate was 86% of the interviewed centers. The questionnaire was placed on a web platform, and a database was created to facilitate data collection. The questionnaire was anonymous. The first survey was sent during the period from November to December 2015 before the publication of MASCC guidelines. A second survey was sent in the period March-May 2016 after the publication of MASCC guidelines. The questions covered the following topics: antiemetic prophylaxis guidelines used, antiemetic prophylaxis in the principal conditioning regimen, methods of CINV evaluation, medical perception of impacts on patients' quality of life and the extent of the CINV problem.

RESULTS

Tab. 1 shows the characteristics of the transplant centres responding to the survey. The majority (72%) are transplant centres for adult patients and perform both autologous and allogeneic transplants (82%), with just 18% performing exclusively autologous transplantation. After the publication of the MASCC/ESMO guidelines, 42% of the centers reported adherence to these guidelines, 40% of centers reported that they had internal CINV prophylaxis guidelines and only 18% reported that they followed other international guidelines (NCCN and ASCO), which are not specific for HSCT (**Tab. 2**). Fifty-five per cent of transplant centres use the “Common Terminology Criteria for adverse events”(CTCAE) for the evaluation of vomiting and 47% for nausea. However, only 4% and 25% of transplant centers use Functional Living-Index Emesis Score and visual analogue scale to evaluate nausea, respectively. As for the use of dexamethasone, only 18% of transplant centers use dexamethasone in all patients, while 16% do not use dexamethasone in any patient; the most administered dose (in 38% of transplantation centers) was 16 mg per day. The NK1-RA were used in all patients in 15% of transplant centers (10% before the publication of the MASCC/ESMO guidelines), but 30% of transplant centers do not use NK1-RA in any patient (56% before the publication of the guidelines). As for the second generation 5HT₃-RA (palonosetron), 18% use the palonosetron in all patients, while 48% of centres do not use palonosetron (**Tab.3**).

Analysing the main conditioning regimens of autologous transplantation (**Tab. 3**), figures show that the most used antiemetic prophylaxis, in the Melphalan 200 mg/m² regimen, after the publication of guidelines, is 5HT₃-RA plus dexamethasone (45% of patients), while the triple combination of 5HT₃-RA, dexamethasone and NK1-RA is only administered in 30% of patients (15% before the publication of the MASCC/ESMO guidelines). For the BEAM/FEAM/TEAM/BeEAM conditioning regimen, the most used antiemetic prophylaxis is 5HT₃-RA plus dexamethasone (50 % of patients), while only 30% of patients are given the triple combination of 5HT₃-RA, dexamethasone and NK1-RA (10% before the publication of the guidelines). The survey performed after the publication of the MASCC/ESMO guidelines regarding the antiemetic prophylaxis during the conditioning regimens of allogeneic transplantation showed that 5HT₃-RA given alone is the most used prophylaxis in the regimens of tiothepa, fludarabine and cyclophosphamide (42% of patients), busulphan and cyclophosphamide (42% of patients), busulphan and fludarabine (51% of patients), total body irradiation and cyclophosphamide (41%), TBI(48% of patients) and cyclophosphamide (43% of patients)(**Tab. 4**). The use of dexamethasone in allogeneic transplantation ranges from 41% (tiothepa, busulphan and fludarabine conditioning regimen) to 60% (in the TBI plus cyclophosphamide conditioning regimen) and the most used dose of dexamethasone (in 38% of centers) is 16 mg die. The triple

combination of 5HT₃-RA, dexamethasone and NK1-RA was reported in 15% of cases treated with thiotepa, fludarabine, cyclophosphamide, 25% with busulphan and cyclophosphamide, 20 % with busulfan and fludarabine, 19% with TBI and cyclophosphamide, 10% with TBF and 12% with cyclophosphamide. Overall, in all conditioning regimens (autologous and allogeneic), the combination of a 5-HT₃ receptor antagonist with dexamethasone and NK1-RA, as recommended by MASCC/ESMO, increased from 0-14% (before the publication of the guidelines) to 10-30% (after the publication of the guidelines).

A significant number of centres (66%) reported that CINV had a deleterious impact on quality of life and 65% reported an optimal response to CINV prophylaxis.

DISCUSSION

Our study, in which every effort was made to reflect the reality of clinical practice, shows that the problem of CINV in stem cell transplant recipients is far from being solved. Our survey describes CINV prophylaxis practices in 50 hematopoietic stem cell transplant centers, all of which are members of the GITMO. This analysis suggests that in Italy, the proportion of patients that, in routine practice, received MASCC/ESMO guidelines-consistent antiemetic prophylaxis is only a minority. In fact, only a percentage of patients between 10% and 25%, depending on the different conditioning regimen, received the triple prophylaxis with dexamethasone, NK1RA, and 5HT₃RA. Moreover, about half of the centers use the "Common Terminology Criteria for adverse events" to assess nausea and vomiting, a very low percentage (25%) uses a visual analogue scale for nausea and similarly only 4% use the Functional Living-Index emesis score. This indicates the healthcare workers' poor perception of the CINV problem from the patients' perspective. In recent years, phase III studies have been published regarding the use of modern three-drug antiemetic prophylaxis for patients undergoing HSCT. A double-blind phase III [16] study randomized 181 patients to ondansetron and dexamethasone with or without aprepitant given on each day of the high-dose preparative regimen. The study showed a significant reduction in emesis without increasing toxicity or use of rescue medication in patients receiving aprepitant. The CR rate was 82% with the aprepitant arm versus 66%, however, there was no effect in the overall visual analog scale (VAS). The efficacy of aprepitant in patients with multiple myeloma undergoing high-dose chemotherapy with autologous SCT was investigated in phase II [17] and phase III clinical studies [18]. In the phase III study, patients with multiple myeloma were randomized to receive

either aprepitant administered at a dose of 125 mg orally on day 1 and 80 mg orally on days 2 to 4, granisetron and dexamethasone or matching placebo, granisetron and dexamethasone. The CR rate was significantly higher in the aprepitant arm compared to the control group (58 vs 41%); absence of major nausea (94 vs 88%) and vomiting (78 vs 65%) within 120 hours was significantly improved by aprepitant. Svanberg et al[17] randomized 96 patients to the 5-HT₃ receptor antagonist and dexamethasone with or without aprepitant for 7 days following HDCT and autologous SCT. Thirty-eight patients in the triple therapy regimen had no vomiting compared to 16 patients in the control group, and this difference was statistically significant. On the basis of these three studies the MASCC/ESMO[13] for the first time recommended a combination of 5-HT₃receptor antagonist with dexamethasone and aprepitant (NK1-RA) before chemotherapy for HSCT. Moreover, numerous studies have been published on the triple prophylaxis (dexamethasone, 5HT₃-RA and NK1-RA) for CINV in both autologous and allogeneic transplantation [19-25], showing a greater effectiveness compared to the combination of dexamethasone and 5HT₃-RA.

This survey demonstrates that in “real life” the adherence to antiemetic MASCC guidelines is very low for the main conditioning regimens; in fact, in the autologous setting the proportion of patients who received the triple prophylaxis with dexamethasone, NK1-RA, 5HT₃-RA, is only 30% for melphalan (200 mg/m²), 30 % for BEAM/TEAM/BeEAM/FEAM; in allogeneic setting 25% for busulphan and cyclophosphamide, 19% for TBI and cyclophosphamide, 10% for TBF and 15% for thiotepa, cyclophosphamide and fludarabine. Various factors may have contributed to the low percentage (15%) of centers using NK1-RA in all patients. First of all, the registered schedule of aprepitant (125 mg on the first day and 80 mg on the second and third day) may not be considered suitable for multiday therapy like most conditioning regimens. Furthermore, there may be concerns for pharmacological interference during the conditioning regimen as aprepitant is an inhibitor of CYP3A4 which may increase the AUC of dexamethasone [26] and, in the survey, in 38% of transplant centers a dose of dexamethasone of 16 mg per day was used, a high dose that could create problems especially in the setting of allogeneic transplantation. The same plasma concentration of aprepitant may also increase with the use of CYP3A4 inhibitor drugs, such as, voriconazole, posaconazole. Moreover, since the addition of NK1-RA has been highly recommended for HSCT in the last updating on the antiemetic guidelines and it was optional in the previous versions, it will take more time to change the clinical practice of the HSCT centres. Finally, there may be difficulties in the prescription of NK1-RA (aprepitant or NEPA) in HSCT setting, which have to be registered with the Italian Medicin Agency (AIFA) for the CINV prophylaxis in high emetogenic chemotherapy with cisplatin or in moderately emetogenic

chemotherapy. These aspects are likely to have a negative influence on the adherence to guidelines. The Pan European Emesis Registry (PEER) study demonstrated that the use of guidelines-consistent CINV prophylaxis resulted in a greater proportion of patients achieving complete response to CINV, as compared to guideline-inconsistent CINV prophylaxis[27]. Moreover, the ISPIRE study [28] showed that the increased adherence to antiemetic guidelines could significantly reduce the incidence of CINV after high and moderately emetogenic chemotherapy. The implementation of specific guideline recommendations for CINV prophylaxis could be considered as a means to reduce the burden of CINV. The results of this survey are particularly useful for two reasons. First, this is not an interventional study, and, therefore, the results are a picture of the real world, and reproduce the wide variations of CINV prophylaxis. Second, the research highlights how the majority of the transplant centres (66%) are aware of the CINV negative effects on patients' quality of life, yet only 42% of them stick to international specific guidelines to deal with such an important matter. In conclusion this survey shows that there is a lack of compliance with antiemetic guidelines; the main observation is that there is an underprophylaxis. This gap between guidelines and current practice should be urgently filled up either sensitizing transplant physicians and nurses to advances in CINV prophylaxis or promoting specific clinical research for HSCT patients.

REFERENCES

1. Janelins MC, Tejani MA, Kamen C, Peoples AR, Mustian KM, Morrow GR (2013) Current pharmacotherapy for chemotherapy-induced nausea and vomiting in cancer patients. *Expert Opin Pharmacother* 14(6):757-66
2. Navari RM (2013) Management of chemotherapy-induced nausea and vomiting: focus on newer agents and new uses for older agents. *Drugs* 73(3):249-62
3. Grunberg SM, Slusher B, Rugo HS (2013) Emerging treatments in chemotherapy-induced nausea and vomiting. *Clin Adv Hematol Oncol* 11(2 Suppl 1):1-18
4. Hesketh PG (2008) Chemotherapy-induced nausea and vomiting. *N Engl J Med* 358(23):2482-94
5. Jordan K, Jahn F, Aapro M (2015) Recent developments in the prevention of chemotherapy-induced nausea and vomiting (CINV) : a comprehensive review. *Annals of Oncology* 26:1081-1090

6. Rojas C, Raje M, Tsukamoto T, Slusher BS (2014) Molecular mechanism of 5-HT₃ and NK₁ receptor antagonist in prevention of emesis. *Eur J Pharmacol* 722:26-37
7. Ettinger DS, Armstrong DK, Barbour S, Berger MJ, Bierman PJ, Bradbury B et al (2012) Antiemesis. *J Natl Compr Can Netw* 10(4):456-85
8. Grunberg SM, Warr D, Gralla RJ, Rapoport BL, Hesketh PJ, Jordan K et al (2011) Evaluation of new antiemetic agents and definition of antineoplastic agent emetogenicity-state of art. *Support Care Cancer* 19 Suppl 1:S43-47
9. Lorusso V (2016) Management of chemotherapy-induced nausea and vomiting by risk profile: role of netupitant/palonosetron. *Therapeutics and Clinical Risk Management* 12:917-925
10. Navari RM (2013) Management of chemotherapy-induced nausea and vomiting: focus on newer agents and new uses for older agents. *Drugs* 73(3):249-62
11. Grulke N, Albani C, Bailer H (2012) Quality of life in patients before and after haematopoietic stem cell transplantation measured with the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Core Questionnaire QLQ-C30. *Bone Marrow Transplant* 47(4):473-82
12. Kris MG, Hesketh PJ, Somerfield MR, Feyer P, Clark-Snow R, Koeller JM et al (2006) American Society of Clinical Oncology guideline for antiemetics in oncology: update 2006. *J Clin Oncol* 24(18):2932-2947
13. Einhorn LH, Rapoport B, Navari RM, Herrstedt J, Brames JM (2017) 2016 updated MASCC/ESMO consensus recommendations: prevention of nausea and vomiting following multiple-day chemotherapy, and breakthrough nausea and vomiting. *Support Care Cancer* 25:303-308
14. NCCN 2015. Antiemesis
15. Hesketh PJ, Kris MG, Basch E, Bohlke K, Barbour SY, Clark-Snow RA et al (2017) Antiemetics: American Society of Clinical Oncology Practice Guideline Update *J Clin Oncol* 35:3240-3261
16. Stiff PJ, Fox-Geiman MP, Kiley K, Rychlik K, Parthasarathy M, Fletcher-Gonzales D et al (2013) Prevention of nausea and vomiting associated with stem cell transplantation: results of a prospective, randomized trial of aprepitant used with highly emetogenic preparative regimen. *Biol Blood Marrow Transplant* 19:49-55
17. Svanberg A, Biregard G (2015) Addition of aprepitant (Emend) to standard antiemetic regimen continued for 7 days after chemotherapy for stem cell transplantation provides significant reduction of vomiting. *Oncology* 89:31-36
18. Schmitt T, Goldschmidt H, Neben K, Freiberger A, Husing J, Gronkowski M et al (2014) Aprepitant, granisetron, and dexamethasone for prevention of

- chemotherapy-induced nausea and vomiting after high-dose melphalan in autologous transplantation for multiple myeloma: results of a randomized, placebo-controlled phase III trial. *J Clin Oncol* 32:3413-3420
19. Pielichowski W, Barzal J, Gawronski K, Mlot B, Oborska S, Wasko-Grabowska A et al (2011) A triple-drug combination to prevent nausea and vomiting following BEAM chemotherapy before autologous hematopoietic stem cell transplantation. *Transplant Proc* 43:3107-3110
 20. Heskett PJ, Bohlke K, Lyman GH, Basch E, Chesney M, Clark-Snow RA et al (2015) Antiemetics: American Society of Clinical Oncology focused Guideline update. *J Clin Oncol* 34:381-386
 21. Pielichowski W, Barzal J, Gawronski K, Mlot B, Wasko-Grabowska A, Rzepecki P et al (2011) A triple-drug combination to prevent nausea and vomiting following BEAM chemotherapy before autologous hematopoietic stem cell transplantation. *Transplantation Proceedings* 43:3107-3110
 22. Pielichowski W, Gawronski K, Mlot B, Oborska S, Wasko-Grabowska A, Rzepecki P (2011) Triple drug combination in the prevention of nausea and vomiting following busulfan plus cyclophosphamide chemotherapy before allogeneic hematopoietic stem cell transplantation. *Journal of BUON* 16:541-546
 23. Bechtel T, McBride A, Crawford B, Bullington S, Hofmeister CC, Benson DM et al (2014) Aprepitant for the control of delayed nausea and vomiting associated with the use of high-dose melphalan for autologous peripheral blood stem cell transplants in patients with multiple myeloma: a phase II study. *Support Care Cancer* 22:2911
 24. Uchida M, Ikesue H, Miyamoto T, Kato K, Suetsugu K, Ikinose K et al (2013) Effectiveness and safety of antiemetic aprepitant in Japanese patients receiving high-dose chemotherapy prior to autologous hematopoietic stem cell transplantation. *Biol Pharm Bull* 36:819-824
 25. Sakurai M, Mori T, Kato J, Koda Y, Kikuchi T, Kohashi S et al (2014) et al Efficacy of aprepitant in preventing nausea and vomiting due to high-dose melphalan-based conditioning for allogeneic hematopoietic stem cell transplantation. *Int J Hematol* 99:457-462
 26. Rapaport B, Smit T (2017) Clinical pharmacology of neurokinin-1 receptor antagonists for the treatment of nausea and vomiting associated with chemotherapy. *Expert Opin Drug Saf* 16:697-710
 27. Pastorelli D, Locatelli MA, Melotti B, Pisano G, Turano S, Mellino U et al (2013) The Pan European Emesis Registry (PEER): a critical appraisal of the Italian experience. *Journal of chemotherapy* 25:309-317
 28. Gilmore JW, Peacock NW, Gu A, Szabo S, Rammage M, Sharpe J et al (2013) Antiemetic guideline consistency and incidence of chemotherapy-induced

nausea and vomiting in US community oncology practice: INSPIRE Study.
Journal of Oncology Practice 10:68-74

Tab.1 Characteristics of the 43 transplant centres responding to the survey

Patient group	
Adult only	72%
Pediatric only	18%
Both adult and pediatric	10%
Transplant type performed	
Autologous	18%
Autologous and allogeneic	82%

Tab.2

Questions	
Which CINV prophylaxis guideline does your institution follow?	<ul style="list-style-type: none"> ○ MASCC/ESMO guidelines 42% ○ Internal guidelines 40% ○ NCCN/ASCO guidelines 18%
In your Center, do you use the “Common Terminology Criteria for adverse events” to evaluate vomiting?	<ul style="list-style-type: none"> ○ Yes 55% ○ No 45%
In your Center, do you use the “Common Terminology Criteria for adverse events” to evaluate nausea?	<ul style="list-style-type: none"> ○ No 53% ○ Yes 47%
In your Center, do you use the Functional Living-Index emesis score?	<ul style="list-style-type: none"> ○ No 96% ○ Yes 4%
In your Center, do you use the visual analogue scale to evaluate nausea?	<ul style="list-style-type: none"> ○ No 75% ○ Yes 25%
In your Center, do you use dexamethasone?	<ul style="list-style-type: none"> ○ In 0% of patients 16% ○ In 25% of patients 34% ○ In 50% of patients 14% ○ In 75% of patients 18% ○ In all patients 18%

What dexamethasone daily dose is recommended in your institution's CINV prophylaxis?	<input type="radio"/> 16 mg 38% <input type="radio"/> 8 mg 30% <input type="radio"/> 12 mg 20% <input type="radio"/> 20 mg 12%
In your Center, do you use NK1-RA?	<input type="radio"/> In 0% of patients 30% <input type="radio"/> In 25% of patients 20% <input type="radio"/> In 50% of patients 20% <input type="radio"/> In 75% of patients 15% <input type="radio"/> In all patients 15%
In your Center, do you use Palonosetron?	<input type="radio"/> In 0% of patients 48% <input type="radio"/> In 25% of patients 22% <input type="radio"/> In 50% of patients 8% <input type="radio"/> In 75% of patients 4% <input type="radio"/> In all patients 18%

Tab. 3 CINV prophylaxis in autologous conditioning regimens

Questions	Before MASCC/ESMO 2016	After MASCC/ESMO 2016
Which CINV prophylaxis do you use in melphalan conditioning regimen (200 mg/m ²)?	5HT₃RA+Dexa 45% 5HT ₃ RA+Dexa+NK1RA 15% 5HT ₃ RA 30% 5HT ₃ RA+NK1RA 10%	5HT₃RA+Dexa 45% 5HT ₃ RA+Dexa+NK1RA 30% 5HT ₃ RA 22% 5HT ₃ RA+NK1RA 3%
Which CINV prophylaxis do you use in BEAM/FEAM/BeEAM/TEAM conditioning regimen?	5HT₃RA+Dexa 45% 5HT ₃ RA+Dexa+NK1RA 10% 5HT ₃ RA 30% 5HT ₃ RA+NK1RA 15%	5HT₃RA+Dexa 50% 5HT ₃ RA+Dexa+NK1RA 30% 5HT ₃ RA 15% 5HT ₃ RA+NK1RA 5%

Tab.4 CINV prophylaxis in allogeneic conditioning regimens

	Before MASCC/ESMO 2016	After MASCC/ESMO 2016
Which CINV prophylaxis do you use in thiotepa, fludarabine, cyclophosphamide reduced intensity conditioning regimen?	5HT₃ RA 42% 5HT ₃ RA +Dexa 35% 5HT ₃ RA + NK1RA 23%	5HT₃ RA 42% 5HT ₃ RA +Dexa 31% 5HT ₃ RA + NK1RA 10% 5HT ₃ RA+Dexa+NK1RA 15%
Which CINV prophylaxis do you use in busulphan plus cyclophosphamide conditioning regimen?	5HT₃RA+ Dexa 48% 5HT ₃ RA 42% 5HT ₃ RA+NK1RA 10%	5HT₃RA 42% 5HT ₃ RA + Dexa 24% 5HT ₃ RA+Dexa+NK1RA 25% 5HT ₃ RA+NK1RA 9%
Which CINV prophylaxis do you use in busulphan plus fludarabine regimen?	5HT₃RA 42% 5HT ₃ RA+Dexa 30% 5HT ₃ RA+NK1RA 28%	5HT₃RA 51% 5HT ₃ RA+Dexa 25% 5HT ₃ RA+Dexa+NK1RA 20% 5HT ₃ RA+NK1RA 4%
Which CINV prophylaxis do you use in TBI plus cyclophosphamide conditioning regimen?	5HT₃RA+Dexa 49% 5HT ₃ RA 21% 5HT ₃ RA+NK1RA 16% 5HT ₃ RA+Dexa+NK1RA 14%	5HT₃RA+Dexa 51% 5HT ₃ RA+Dexa+NK1RA 19% 5HT ₃ RA 16% 5HT ₃ RA+NK1RA 14%
Which CINV prophylaxis do you use in TBF conditioning regimen?	5HT₃RA+Dexa 33% 5HT ₃ RA 32% 5HT ₃ +NK1RA 27% 5HT ₃ +Dexa+NK1RA 8%	5HT₃RA 48% 5HT ₃ RA+Dexa 31% 5HT ₃ RA+Dexa+NK1RA 10% 5HT ₃ RA+NK1RA 11%
Which CINV prophylaxis do you use in CTX (200 mg/m²)?	5HT₃RA+Dexa 45% 5HT ₃ RA 36% 5HT ₃ +Anti NK1 19%	5HT₃RA 43% 5HT ₃ RA +Dexa 31% 5HT ₃ RA+Dexa+NK1RA 12% 5HT ₃ RA+NK1RA 14%

--	--	--

Tab.5

Conditioning regimen	Compliance with 2016 MASCC/ESMO guidelines
Melphalan (200 mg/m²)	30 %
BEAM/FEAM/BeEAM/TEAM	30 %
Thiotepa, Fludarabine, cyclophosphamide(RIC)	10%
Busulphan plus cyclophosphamide	25%
Busulphan plus fludarabine	20%
TBI plus cyclophosphamide	19%
TBF	10%
CTX (200 mg/m²)	12%