

Protocol

Hematopoietic Stem Cell Transplantation for Epithelial Ovarian Cancer

(80123)

Medical Benefit		Effective Date: 04/01/13	Next Review Date: 01/18
Preauthorization	Yes	Review Dates: 04/07, 05/08, 05/09, 03/10, 01/11, 01/12, 01/13, 01/14, 01/15, 01/16, 01/17	

Preauthorization is required and must be obtained through Case Management.

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.

Populations	Interventions	Comparators	Outcomes
Individuals: <ul style="list-style-type: none">• With advanced-stage epithelial ovarian cancer	Interventions of interest are: <ul style="list-style-type: none">• Hematopoietic stem cell transplantation	Comparators of interest are: <ul style="list-style-type: none">• Standard chemotherapy regimen	Relevant outcomes include: <ul style="list-style-type: none">• Overall survival• Disease specific survival• Change in disease status• Treatment-related morbidity• Treatment-related mortality

Description

Use of hematopoietic stem cell transplantation (HSCT) has been investigated for treatment of patients with epithelial ovarian cancer. Hematopoietic stem cells are infused to restore bone marrow function after cytotoxic doses of chemotherapeutic agents with or without whole body radiotherapy.

Summary of Evidence

The evidence for HSCT in individuals who have advanced-stage epithelial ovarian cancer includes three randomized trials and data from case series and registries. Relevant outcomes are overall survival, disease-specific survival, change in disease status, and treatment related morbidity and mortality. The evidence has not shown that HSCT improves health outcomes in treating epithelial ovarian cancer, including survival, compared with conventional standard doses of chemotherapy.

Policy

Autologous and allogeneic hematopoietic stem-cell transplantations are considered **investigational** to treat epithelial ovarian cancer.

Policy Guidelines

Stem cell transplantation to treat germ cell tumors of the ovary is considered separately in the Hematopoietic Stem Cell Transplantation in the Treatment of Germ Cell Tumors Protocol.

Medicare Advantage

If a transplant is needed, we arrange to have the transplant center review and decide whether the patient is an appropriate candidate for the transplant.

Background

Hematopoietic Stem Cell Transplantation

HSCT refers to a procedure in which hematopoietic stem cells are infused to restore bone marrow function in cancer patients who receive bone-marrow-toxic doses of cytotoxic drugs with or without whole body radiotherapy. Bone marrow stem cells may be obtained from the transplant recipient (autologous HSCT) or from a donor (allogeneic HSCT). They can be harvested from bone marrow, peripheral blood, or umbilical cord blood and placenta shortly after delivery of neonates. Although cord blood is an allogeneic source, the stem cells in it are antigenically “naive” and thus are associated with a lower incidence of rejection or graft-versus-host disease. Cord blood is discussed in greater detail in the Placental and Umbilical Cord Blood as a Source of Stem Cells Protocol.

HSCT is an established treatment for certain hematologic malignancies; however, its use in solid tumors in adults is largely experimental. Initial enthusiasm for the use of autologous transplantation with high-dose chemotherapy (HDC) for solid tumors has waned with the realization that dose intensification often fails to improve survival, even in tumors with a linear-dose response to chemotherapy. With the advent of reduced-intensity conditioning (RIC) allogeneic transplant, interest has shifted to determinants of alloreactivity to metastatic solid tumors via a graft-versus-tumor effect of donor-derived T cells.

Epithelial Ovarian Cancer

Several different types of malignancies can arise in the ovary; epithelial carcinoma is the most common type. Epithelial ovarian cancer is the fifth most common cause of cancer death in women. New cases and deaths from ovarian cancer in the United States for 2016 are estimated at 22,280 and 14,240, respectively.¹ Most ovarian cancer patients present with widespread disease, and annual mortality is approximately 65% of the incidence rate.

Current management of advanced epithelial ovarian cancer is cytoreductive surgery in addition to combination chemotherapy.² Approximately 75% of patients present with International Federation of Gynecology and Obstetrics stage three to four ovarian cancer and are treated with paclitaxel plus a platinum analog, the preferred regimen for newly diagnosed advanced disease.^{3,4} Use of platinum and taxanes has improved progression-free survival and overall survival in advanced disease to between 16 and 21 months and 32 and 57 months, respectively.³ However, cancer recurs in most women and they die of the disease, because chemotherapy drug resistance leads to uncontrolled cancer growth.⁴

HDC has been investigated as a therapy to overcome drug resistance. However, limited data exist on this treatment approach; the ideal patient population and best treatment regimen remain to be established.⁴ HSCT has been tested in various patient groups with ovarian cancer:

- to consolidate remission after induction therapy

- to treat relapse after a durable response to platinum-based chemotherapy
- to treat tumors that relapsed after less than six months
- to treat refractory tumors.

Regulatory Status

The U.S. Food and Drug Administration (FDA) regulates human cells and tissues intended for implantation, transplantation, or infusion through the Center for Biologics Evaluation and Research, under Code of Federal Regulation (CFR) title 21, parts 1270 and 1271. Hematopoietic stem cells are included in these regulations. Cytotoxic drugs used in high-dose chemotherapy (HDC) require, and generally have received, FDA approval. HDC is an off-label use of approved drugs.

Related Protocols

Hematopoietic Stem Cell Transplantation for Miscellaneous Solid Tumors in Adults

Hematopoietic Stem Cell Transplantation in the Treatment of Germ Cell Tumors

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

References

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

1. American Cancer Society. Cancer Facts & Figures 2016. Atlanta, Ga: American Cancer Society; 2016. <http://www.cancer.org/research/cancerfactsstatistics/>. Accessed February 28, 2016.
2. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology: ovarian cancer, version 2.2015. http://www.nccn.org/professionals/physician_gls/PDF/ovarian.pdf. Accessed January 5, 2016.
3. Mobus V, Wandt H, Frickhofen N, et al. Phase III trial of high-dose sequential chemotherapy with peripheral blood stem cell support compared with standard dose chemotherapy for first-line treatment of advanced ovarian cancer: intergroup trial of the AGO-Ovar/AIO and EBMT. *J Clin Oncol*. Sep 20 2007; 25(27):4187-4193. PMID 17698804
4. Papadimitriou C, Dafni U, Anagnostopoulos A, et al. High-dose melphalan and autologous stem cell transplantation as consolidation treatment in patients with chemosensitive ovarian cancer: results of a single institution randomized trial. *Bone Marrow Transplant*. 2008; 41(6):547-554.

5. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). High-dose chemotherapy with autologous stem-cell support for epithelial ovarian cancer. TEC Assessments. 1998; Volume 13, Tab 6.
6. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Salvage high-dose chemotherapy with allogeneic stem cell support for relapse following high-dose chemotherapy with autologous stem cell support for non-lymphoid solid tumors. TEC Assessments. 1999; Volume 14, Tab 11.
7. Donato ML, Aleman A, Champlin RE, et al. Analysis of 96 patients with advanced ovarian carcinoma treated with high-dose chemotherapy and autologous stem cell transplantation. Bone Marrow Transplant. Jun 2004; 33(12):1219-1224. PMID 15122311
8. Ledermann JA, Herd R, Maraninchi D, et al. High-dose chemotherapy for ovarian carcinoma: long-term results from the Solid Tumour Registry of the European Group for Blood and Marrow Transplantation (EBMT). Ann Oncol. May 2001; 12(5):693-699. PMID 11432630
9. Stiff PJ, Bayer R, Kerger C, et al. High-dose chemotherapy with autologous transplantation for persistent/relapsed ovarian cancer: a multivariate analysis of survival for 100 consecutively treated patients. J Clin Oncol. Apr 1997; 15(4):1309-1317. PMID 9193322
10. Stiff PJ, Veum-Stone J, Lazarus HM, et al. High-dose chemotherapy and autologous stem-cell transplantation for ovarian cancer: an autologous blood and marrow transplant registry report. Ann Intern Med. Oct 3 2000; 133(7):504-515. PMID 11015163
11. Sabatier R, Goncalves A, Bertucci F, et al. Are there candidates for high-dose chemotherapy in ovarian carcinoma? J Exp Clin Cancer Res. 2012; 31:87. PMID 23072336