Protocol

Hematopoietic Cell Transplantation for Miscellaneous Solid Tumors in Adults

(80124)

(Formerly Hematopoietic Stem Cell Transplantation for Miscellaneous Solid Tumors in Adults)

Medical Benefit		**Effective Date**: 04/01/13	**Next Review Date**: 01/19
Preauthorization	Yes	**Review Dates**: 04/07, 05/08, 01/10, 01/11, 01/12, 01/13, 01/14, 01/15, 01/16, 01/17, 01/18	

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: • With adult soft tissue sarcomas	Interventions of interest are: • Hematopoietic cell transplantation	Comparators of interest are: • Standard care	Relevant outcomes include: • Overall survival • Disease-specific survival • Treatment-related mortality • Treatment-related morbidity
Individuals: • With small cell lung cancer	Interventions of interest are: • Hematopoietic cell transplantation	Comparators of interest are: • Standard care	Relevant outcomes include: • Overall survival • Disease-specific survival • Treatment-related mortality • Treatment-related morbidity
Individuals: • With renal cell carcinoma	Interventions of interest are: • Hematopoietic cell transplantation	Comparators of interest are: • Standard care	Relevant outcomes include: • Overall survival • Disease-specific survival • Treatment-related mortality • Treatment-related morbidity
Individuals: • With colorectal cancer	Interventions of interest are: • Hematopoietic cell transplantation	Comparators of interest are: • Standard care	Relevant outcomes include: • Overall survival • Disease-specific survival • Treatment-related mortality • Treatment-related morbidity
Individuals: • With pancreatic cancer	Interventions of interest are: • Hematopoietic cell transplantation	Comparators of interest are: • Standard care	Relevant outcomes include: • Overall survival • Disease-specific survival • Treatment-related mortality • Treatment-related morbidity

Populations	Interventions	Comparators	Outcomes
Individuals: • With nasopharyngeal cancer	Interventions of interest are: • Hematopoietic cell transplantation	Comparators of interest are: • Standard care	Relevant outcomes include: • Overall survival • Disease-specific survival • Treatment-related mortality • Treatment-related morbidity

Description

Hematopoietic cell transplantation (HCT) is an established treatment for certain hematologic malignancies and has been investigated for a variety of adult solid tumors. Interest continues in exploring nonmyeloablative allogeneic HCT for a graft-versus-tumor effect of donor-derived T cells in metastatic solid tumors.

Summary of Evidence

For individuals who have adult soft tissue sarcomas who receive HCT, the evidence includes two TEC Assessments, one randomized controlled trial (RCT), and a number of phase 2 single-arm studies, some of which have been summarized in a systematic review. Relevant outcomes are overall survival, disease-specific survival, and treatment-related morbidity and mortality. The 1995 and 1999 TEC Assessments, focusing on HCT as primary and salvage therapy for a variety of solid tumors, found that the available evidence did not permit conclusions about the effect of HCT on patient survival. Although one small phase 2 study reported longer survival for patients treated with HCT than with standard chemotherapy, this RCT did not show a survival benefit with HCT. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have small cell lung cancer (SCLC) who receive HCT, the evidence includes two TEC Assessments, several RCTs, and systematic reviews of these studies. Relevant outcomes are overall survival, disease-specific survival, and treatment-related morbidity and mortality. The 1995 and 1999 TEC Assessments, focusing on HCT as primary and salvage therapy for a variety of solid tumors, found that the available evidence did not permit conclusions about the effect of HCT on patient survival. Studies published since the TEC Assessments have not reported increased overall survival for patients with SCLC treated with HCT. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have renal cell carcinoma, colorectal cancer, pancreatic cancer, or nasopharyngeal cancer who receive HCT, the evidence includes a TEC Assessment and small single-arm series. Relevant outcomes are overall survival, disease-specific survival, and treatment-related morbidity and mortality. The 1995 and 1999 TEC Assessments, focusing on HCT as primary and salvage therapy for a variety of solid tumors, found that the available evidence did not permit conclusions about the effect of HCT on patient survival. Since publication of the TEC Assessments, the evidence for HCT to treat adult soft tissue sarcomas, renal cell carcinoma, colorectal cancer, pancreatic cancer, and nasopharyngeal cancer has been limited to small case series. The evidence is insufficient to determine the effects of the technology on health outcomes.

Policy

Autologous or allogeneic hematopoietic cell transplant is considered **investigational** for the following malignancies in adults:

- Lung cancer, any histology
- Colon cancer
- Rectal cancer
- Pancreatic cancer
- Stomach cancer
- Esophageal cancer

- Gall bladder cancer
- Cancer of the bile duct
- Renal cell cancer
- Cervical cancer
- Uterine cancer
- Cancer of the fallopian tubes
- Prostate cancer
- Nasopharyngeal cancer
- Paranasal sinus cancer
- Neuroendocrine tumors
- Soft tissue sarcomas
- Thyroid tumors
- Tumors of the thymus
- Tumors of unknown primary origin
- Malignant melanoma

Medicare Advantage

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

Background

Hematopoietic Cell Transplantation

HCT is 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. Hematopoietic stem cells may be obtained from the transplant recipient (autologous HCT) or from a donor (allogeneic HCT [allo-HCT]). They can be harvested from bone marrow, peripheral blood, or from umbilical cord blood 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 (GVHD). Cord blood is discussed in detail in the Placental and Umbilical Cord Blood as a Source of Stem Cells Protocol.

Immunologic compatibility between infused hematopoietic stem cells and the recipient is not an issue in autologous HCT. However, immunologic compatibility between donor and patient is critical for achieving a good outcome of allo-HCT. Compatibility is established by typing of human leukocyte antigens (HLAs) using cellular, serologic, or molecular techniques. HLA refers to the tissue type expressed at the HLA-A, -B, and -DR (antigen-D related) loci on each arm of chromosome 6. Depending on the disease being treated, an acceptable donor will match the patient at all or most of the HLA loci (with the exception of umbilical cord blood).

Conditioning for HCT

CONVENTIONAL CONDITIONING

The conventional ("classical") practice of allo-HCT involves administration of cytotoxic agents (e.g., cyclophosphamide, busulfan) with or without total body irradiation at doses sufficient to destroy endogenous hematopoietic capability in the recipient. The beneficial treatment effect in this procedure is a result of a combination of initial eradication of malignant cells and subsequent graft-versus-malignancy (GVM) effect mediated by non-self-immunologic effector cells that develop after engraftment of allogeneic stem cells within the patient's bone marrow space. While the slower GVM effect is considered to be the potentially curative component, it may be overwhelmed by extant disease without the use of pretransplant conditioning. However, intense conditioning regimens are limited to patients who are sufficiently fit medically to tolerate substantial adverse effects that include preengraftment opportunistic infections secondary to loss of endogenous bone marrow function and organ damage and failure caused by the cytotoxic drugs. Furthermore, in any allo-HCT, immunosuppressant drugs are required to minimize graft rejection and GVHD, which also increases susceptibility to opportunistic

infections. The immune reactivity between donor T cells and malignant cells that is responsible for the GVM effect also leads to acute and chronic GVHD.

The success of autologous HCT is predicated on the ability of cytotoxic chemotherapy with or without radiation to eradicate cancerous cells from the blood and bone marrow. This permits subsequent engraftment and repopulation of bone marrow space with presumably normal hematopoietic stem cells obtained from the patient before undergoing bone marrow ablation. As a consequence, autologous HCT is typically performed as consolidation therapy when the patient's disease is in complete remission. Patients who undergo autologous HCT are susceptible to chemotherapy-related toxicities and opportunistic infections before engraftment, but not GVHD.

REDUCED-INTENSITY CONDITIONING FOR ALLO-HCT

Reduced-intensity conditioning (RIC) refers to the pretransplant use of lower doses or less intense regimens of cytotoxic drugs or radiation than are used in conventional full-dose myeloablative conditioning treatments. The goal of RIC is to reduce disease burden but also to minimize as much as possible associated treatment-related morbidity and nonrelapse mortality (NRM) in the period during which the beneficial GVM effect of allogeneic transplantation develops. Although the definition of RIC remains arbitrary, with numerous versions employed, all seek to balance the competing effects of NRM and relapse due to residual disease. RIC regimens can be viewed as a continuum in effects, from nearly totally myeloablative, to minimally myeloablative with lymphoablation, with intensity tailored to specific diseases and patient condition. Patients who undergo RIC with allo-HCT initially demonstrate donor cell engraftment and bone marrow mixed chimerism. Most will subsequently convert to full-donor chimerism, which may be supplemented with donor lymphocyte infusions to eradicate residual malignant cells. For this protocol, RIC will refer to all conditioning regimens intended to be nonmyeloablative, as opposed to fully myeloablative (conventional) regimens.

HCT In Solid Tumors In Adults

HCT is an established treatment for certain hematologic malignancies. Its use in solid tumors is less well established, although it has been investigated for a variety of solid tumors. With the advent of nonmyeloablative allogeneic transplant, interest has shifted to exploring the generation of alloreactivity to metastatic solid tumors via a graft-versus-tumor effect of donor-derived T cells.[1]

HCT as a treatment for ovarian cancer, germ cell tumors, ependymoma, or malignant glioma is addressed separately (the Hematopoietic Cell Transplantation for Epithelial Ovarian Cancer Protocol, Hematopoietic Cell Transplantation in the Treatment of Germ Cell Tumors protocol and the Hematopoietic Cell Transplantation for Central Nervous System Embryonal Tumors and Ependymoma Protocol, respectively). HCT as a treatment for breast cancer is not addressed. This protocol collectively addresses other solid tumors of adults for which HCT has been investigated, including lung cancer, malignant melanoma, tumors of the gastrointestinal tract (affecting the colon, rectum, pancreas, stomach, esophagus, gallbladder, or bile duct), male and female genitourinary systems (e.g., renal cell carcinoma, prostate cancer, cervical cancer, uterine cancer, fallopian tube cancer), tumors of the head and neck, soft tissue sarcoma, thyroid tumors, tumors of the thymus, and tumors of unknown primary origin.

Regulatory Status

The U.S. Food and Drug Administration 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.

Related Protocols

Hematopoietic Cell Transplantation for Central Nervous System Embryonal Tumors and Ependymoma

Hematopoietic Cell Transplantation for Epithelial Ovarian Cancer

Hematopoietic Cell Transplantation in the Treatment of Germ Cell Tumors

Hematopoietic Stem Cell Transplantation for Solid Tumors of Childhood

Placental and Umbilical Cord Blood as a Source of Stem Cells

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.

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