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Medical Policy Manual Transplant, Policy No. 45.34

Autologous Hematopoietic Cell Transplantation for Malignant Astrocytomas and Gliomas

Effective: April 1, 2019

Next Review: January 2020
Last Review: March 2019

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Hematopoietic cell transplantation is performed to restore normal function following chemotherapy treatment.

MEDICAL POLICY CRITERIA

Note: See Appendix I for glossary of terms.

Autologous HCT is considered **investigational** as a treatment of malignant astrocytomas and malignant gliomas, including both glioblastoma multiforme and oligodendroglioma.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

CROSS REFERENCES

1. Donor Lymphocyte Infusion for Malignancies Treated with an Allogeneic Hematopoietic Cell Transplant, Transplant, Policy No. 45.03
2. Placental and Umbilical Cord Blood as a Source of Stem Cells, Transplant, Policy No. 45.16
3. Hematopoietic Cell Transplantation for Miscellaneous Solid Tumors in Adults, Transplant, Policy No. 45.27

4. Hematopoietic Cell Transplantation for CNS Embryonal Tumors and Ependymoma, Transplant, Policy No. 45.33
5. Hematopoietic Cell Transplantation for Solid Tumors of Childhood, Transplant, Policy No. 45.37

BACKGROUND

Hematopoietic cell transplantation (HCT, previously referred to in this policy as a hematopoietic stem cell transplant [HSCT]) refers to a procedure in which hematopoietic cells are infused to restore bone marrow function in cancer patients who receive myeloablative doses of cytotoxic drugs with or without whole body radiation therapy. Although broadly speaking there are two types of HSCTs, autologous and allogeneic, only autologous HCT is relevant to this discussion. In autologous HCT, hematopoietic cells are obtained from the transplant recipient.

PREPARATIVE CONDITIONING FOR HCT

Autologous HCT necessitates myeloablative chemotherapy to eradicate cancerous cells from the blood and bone marrow, thus permitting subsequent engraftment and repopulation of bone marrow space with presumably normal hematopoietic progenitor cells. 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 prior to engraftment, but not graft-versus-host disease.

ASTROCYTOMAS AND GLIOMAS

Diffuse fibrillary astrocytomas are the most common type of brain tumor in adults. These tumors are classified histologically into three grades of malignancy: grade II astrocytoma, grade III anaplastic astrocytoma, and grade IV glioblastoma multiforme. Oligodendrogliomas are diffuse neoplasms that are clinically and biologically most closely related to diffuse fibrillary astrocytomas. However, these tumors generally have better prognoses than diffuse astrocytomas, with mean survival times of ten years versus two to three years. In addition, oligodendrogliomas appear to be more chemosensitive than other types of astrocytomas. Glioblastoma multiforme is the most malignant stage of astrocytoma, with survival times of less than two years for most patients.

Treatment of primary brain tumors focuses on surgery, either with curative intent or optimal tumor debulking. Surgery may be followed by radiation therapy and/or chemotherapy. Survival after chemoradiotherapy is largely dependent on the extent of residual tumor after surgical debulking. Therefore, tumors arising in the midline, basal ganglia, or corpus callosum or those arising in the eloquent speech or motor areas of the cortex, which typically cannot be extensively resected, have a particularly poor outcome. Treatment of children younger than three years is complicated by the long-term effects of radiation therapy on physical and intellectual function. Therefore, in young children, radiation of the central nervous system (CNS) is avoided whenever possible.

Note: Astrocytomas and gliomas arise from the glial cells. Tumors arising from the neuroepithelium constitute a separate category of malignancies that include CNS neuroblastoma, medulloblastoma, ependymoblastomas, and pinealblastomas. Collectively these tumors may be referred to as primitive neuroectodermal tumors (PNETs).

Ependymomas also arise from the neuroepithelium but, because of their more mature histologic appearance, are not considered a member of the PNET family.

EVIDENCE SUMMARY

LITERATURE REVIEWS AND SUMMARY OF THE EVIDENCE TO SUPPORT OUR POSITION.

Systematic Reviews

The 1994 BlueCross BlueShield Association Technology Evaluation Center (TEC) Assessment[1] concluded that the evidence did not demonstrate that autologous hematopoietic cell transplantation (HCT) improved health outcomes of adult patients with high-grade glial tumors of the brain. The 1999 update of this TEC assessment confirmed these conclusions and noted that although there was much research interest in use of autologous HCT for glioblastoma multiforme due to its uniformly poor prognosis, the published literature was relatively scant, consisting primarily of single-institution case series.

Randomized Controlled Trials

No randomized controlled trials of autologous HCT for astrocytoma or glioma were identified.

Nonrandomized Studies

In 2006, Abrey published a phase II study of hematopoietic cell transplantation in 39 patients with newly diagnosed oligodendroglioma.[2] The authors reported the median follow-up of surviving patients was 80.5 months, with 78 months progression-free survival. The overall survival median had not been reached, and 18 patients (46%) had relapsed.

A 2008 study by Finlay compared survival outcomes of 27 children (0.4–22 years) with recurrent malignant astrocytomas who underwent myeloablative chemotherapy and autologous HSCT with outcomes in a matched historical cohort (n=56) that received standard chemotherapy regimens following tumor recurrence.[3] Among the 27 children who received myeloablative chemotherapy and autologous HSCT, five (18%) succumbed to treatment-related toxicities within about two months of transplantation, 17 (63%) had disease progression, while five survived and were alive a median of 11 years (range: 8–13 years) after transplantation. Overall survival rates at four years were 40 +/- 14% for transplant patients versus 7 +/- 4% with conventional chemotherapy (p=0.018, HR=1.9, 95% CI: 1.1–3.2). These results suggest myeloablative chemotherapy with autologous HSCT can improve long-term survival among children with recurrent malignant astrocytoma. However, lack of a contemporaneous treatment comparison group precludes conclusions as to the relative efficacy of this approach.

A 2016 phase I study evaluated the use of high-dose chemotherapy in combination with autologous HCT in patients with recurrent malignant brain tumors.[4] This study included 27 patients, 12 of whom had high-grade glioma. The authors noted prolonged survival with this treatment regimen, but there was no control group for comparison.

Additional reports on small, uncontrolled series of patients with pontine gliomas,[5] recurrent oligodendrogliomas,[6] or those undergoing radiation therapy for high-grade gliomas[7,8] also did not suggest that this treatment improves survival.

PRACTICE GUIDELINE SUMMARY

The National Comprehensive Cancer Network (NCCN) Guidelines on Central Nervous System cancers (v.2.2018) do not list HCT as a treatment option for patients with astrocytomas or gliomas.[9]

SUMMARY

There is not enough research to show that autologous hematopoietic cell transplantation (HCT) improves health outcomes for patients with malignant astrocytomas and gliomas. No clinical guidelines based on research recommend HCT for people with malignant astrocytomas and gliomas. Therefore, autologous HCT is considered investigational for patients with malignant astrocytomas and gliomas.

REFERENCES

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2. Abrey, LE, Childs, BH, Paleologos, N, et al. High-dose chemotherapy with stem cell rescue as initial therapy for anaplastic oligodendroglioma: long-term follow-up. *Neuro Oncol*. 2006 Apr;8(2):183-8. PMID: 16524945
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7. Jakacki, RI, Siffert, J, Jamison, C, Velasquez, L, Allen, JC. Dose-intensive, time-compressed procarbazine, CCNU, vincristine (PCV) with peripheral blood stem cell support and concurrent radiation in patients with newly diagnosed high-grade gliomas. *J Neurooncol*. 1999 Aug;44(1):77-83. PMID: 10582673
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9. National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology™. Central Nervous System Cancers. v.2.2018. [cited 3/11/2019]; Available from: http://www.nccn.org/professionals/physician_gls/pdf/cns.pdf

10. BlueCross BlueShield Association Medical Policy Reference Manual "Autologous Hematopoietic Stem-Cell Transplantation for Malignant Astrocytomas and Gliomas." Policy No. 8.01.31

CODES

Codes	Number	Description
CPT	38204	Management of recipient hematopoietic cell donor search and cell acquisition
	38205	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection, allogeneic
	38206	;autologous
	38207	Transplant preparation of hematopoietic progenitor cells; cryopreservation and storage
	38208	;thawing of previously frozen harvest, without washing, per donor
	38209	;thawing of previously frozen harvest with washing, per donor
	38210	;specific cell depletion with harvest, T cell depletion
	38211	;tumor cell depletion
	38212	;red blood cell removal
	38213	;platelet depletion
	38214	;plasma (volume) depletion
	38215	;cell concentration in plasma, mononuclear, or buffy coat layer
	38220	Diagnostic bone marrow; aspiration(s)
	38221	Diagnostic bone marrow; biopsy(ies)
	38222	Diagnostic bone marrow; biopsy(ies) and aspiration(s)
	38230	Bone marrow harvesting for transplantation; allogeneic
	38232	Bone marrow harvesting for transplantation; autologous
	38240	Bone marrow or blood-derived peripheral stem-cell transplantation; allogeneic
	38241	;autologous
	38242	Allogeneic donor lymphocyte infusions
	38243	Hematopoietic progenitor cell (HPC); allogeneic transplantation per donor, HPC boost
HCPCS	J9000–J9999	Chemotherapy drugs code range
	Q0083–Q0085	Chemotherapy administration code range
	S2140	Cord blood harvesting for transplantation; allogeneic
	S2142	Cord blood derived stem-cell transplantation, allogeneic
	S2150	Bone marrow or blood-derived peripheral stem-cell harvesting and transplantation, allogeneic or autologous, including pheresis, high-dose chemotherapy, and the number of days of post-transplant care in the global definition (including drugs; hospitalization; medical surgical, diagnostic and emergency services)

APPENDIX I: Glossary of Terms Used in this Policy

consolidation therapy[1] - Treatment that is given after cancer has disappeared following the initial therapy. Consolidation therapy is used to kill any cancer cells that may be left in the body. It may include radiation therapy, a stem cell transplant, or treatment with drugs that kill cancer cells. Also called intensification therapy and postremission therapy.

relapse[2] - The return of a disease or the signs and symptoms of a disease after a period of improvement.
salvage therapy[3] - Treatment that is given after the cancer has not responded to other treatments.
tandem transplant[4] – Refers to a planned second course of high-dose therapy and HCT within six months of the first course.

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2. NCI Dictionary of Cancer Terms | https://www.cancer.gov/publications/dictionaries/cancer-terms?CdrID=45866 | Accessed Sept 25 2018
3. NCI Dictionary of Cancer Terms | https://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=44176 | Accessed Sept 25 2018
4. NCCN Guidelines Version 1.2019 Multiple Myeloma | https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf | Accessed Sept 25 2018

Date of Origin: *May 2010*