EFFECTIVE DATE: 03/16/2010
POLICY LAST UPDATED: 06/03/2014

OVERVIEW

This policy documents the coverage determination for Adoptive Immunotherapy. The spontaneous regression of certain cancers, such as renal cell cancer or melanoma, supports the idea that a patient's immune system can delay tumor progression and, on rare occasions, can eliminate the tumor altogether. These observations have led to research interest in a variety of immunologic therapies designed to stimulate a patient's own immune system. Adoptive immunotherapy is a method of activating lymphocytes for the treatment of cancer and other diseases.

PRIOR AUTHORIZATION

Not Applicable

POLICY STATEMENT

BlueCHiP for Medicare and Commercial

Adoptive immunotherapy is not medically necessary as there is insufficient medical literature to support the efficacy of this treatment.

MEDICAL CRITERIA

Not Applicable

BACKGROUND

Adoptive immunotherapy uses "activated" lymphocytes as a treatment modality. Both nonspecific and specific lymphocyte activation are used therapeutically. Nonspecific, polyclonal proliferation of lymphocytes by cytokines (immune system growth factors), also called autolymphocyte therapy, increases the number of activated lymphocytes. Initially, this was done by harvesting peripheral lymphokine-activated killer cells and activating them *in vitro* with the T cell growth factor interleukin-2 (IL-2) and other cytokines. More recent techniques yield select populations of lymphocytes with specific reactivity to tumor antigens. Peripheral lymphocytes are propagated *in vitro* with antigen-presenting dendritic cells that have been pulsed with tumor antigens. Alternatively, tumor-infiltrating lymphocytes (TIL) from the tumor biopsy are propagated in vitro with IL-2 and anti-CD3 antibody, a T cell activator. Expansion of TIL for clinical use is labor intensive and requires laboratory expertise. Only a few cancers are infiltrated by T cells in significant numbers; of these, TIL can be expanded in only approximately 50% of cases. These factors limit the widespread applicability of TIL treatment. Cytokine-induced killer cells have recently been recognized as a new type of antitumor effector cells, which can proliferate rapidly in vitro, with stronger antitumor activity and broader spectrum of targeted tumor than other reported antitumor effector cells.

The spontaneous regression of certain cancers, such as renal cell cancer or melanoma, supports the idea that a patient's immune system can delay tumor progression and, on rare occasions, can eliminate the tumor altogether. These observations led to research interest in a variety of immunologic therapies designed to stimulate a patient's own immune system. The major research challenge in adoptive immunotherapy is to develop immune cells with antitumor reactivity in quantities sufficient for transfer to tumor-bearing patients. In current trials, 2 methods are studied: adoptive cellular therapy (ACT) and antigen-loaded dendritic cell infusions.

ACT is "the administration of a patient's own (autologous) or donor (allogeneic) anti-tumor lymphocytes following a lymphodepleting preparative regimen." Protocols vary, but include these common steps:

1. lymphocyte harvesting (either from peripheral blood or from tumor biopsy)
2. propagation of tumor-specific lymphocytes in vitro using various immune modulators
3. selection of lymphocytes with reactivity to tumor antigens with ELISA
4. lymphodepletion of the host with immunosuppressive agents
5. adoptive transfer (i.e., transfusion) of lymphocytes back into the tumor-bearing host

Dendritic cell-based immunotherapy uses autologous dendritic cells (ADC) to activate a lymphocyte-mediated cytotoxic response against specific antigen s*in vivo*. ADCs harvested from the patient are either pulsed with antigen or transfected with a viral vector bearing a common cancer antigen. The activated ADCs are then transfused back into the patient, where they present antigen to effector lymphocytes (CD4+ T cells, CD8+ T cells, and in some cases, B cells). This initiates a cytotoxic response against the antigen and against any cell expressing the antigen. In cancer immunotherapy, ADCs are pulsed with tumor antigens; effector lymphocytes then mount a cytotoxic response against tumor cells expressing these antigens.

In an attempt to further regulate the host immune system, recent protocols use various cytokines (e.g., IL-7 and IL-15 instead of IL-2) to propagate lymphocytes. Protocols also differ in the extent of host lymphodepletion induced prior to transfusing the lymphocytes to the tumor-bearing host.

COVERAGE

Benefits may vary between groups/contracts. Please refer to the appropriate Evidence of Coverage, Subscriber Agreement for applicable not medically necessary benefits/coverage.

CODING

Blue CHiP for Medicare and Commercial

The following code is considered not medically necessary:

S2107

RELATED POLICIES

None

PUBLISHED

Provider Update	Aug 2014
Provider Update	May 2013
Provider Update	Apr 2012
Provider Update	Apr 2011
Provider Update	May 2010

REFERENCES

Amedei A, Niccolai E, D'Elios MD. T Cells and Adoptive Immunotherapy: Recent Developments and Future Prospects in Gastrointestinal Oncology. 2011(2011); 320571:17.

American Cancer Society: Accessed on 1/7/10:

http://www.cancer.org/Treatment/TreatmentsandSideEffects/TreatmentTypes/Immunotherapy/index?siteareа=ETO.

Besser MJ, Shapira-Frommer R, Treves AJ, Zippel D, Itzhaki O, Hershkovitz L, et al. *Clinical responses in a phase II study using adoptive transfer of short-term cultured tumor infiltration lymphocytes in metastatic melanoma patients.*Clinical Cancer Research; 2010May1;16(9):2646-2655.

National Cancer Institute. Accessed on 1/22/10: http://www.cancer.gov/.

Stift A, Friedl J, Dubsky P, et al. *Dendritic cell-based vaccination in solid cancer.*Journal of Clinical Oncology;2003;21(1):135-42.

Wolfe J. *Adoptive Cell Transfer Continues to Show Promise for Melanoma.* Practical Dermatology (Oncology Watch); June 2010:21-22.

Tang X, Liu T, Zang X et al. Adoptive cellular immunotherapy in metastatic renal cell carcinoma: a systematic review and meta-analysis. PLoS One 2013; 8(5):e62847.

Xie F, Zhang X, Li H et al. Adoptive immunotherapy in postoperative hepatocellular carcinoma: a systemic review. PLoS One 2012; 7(8):e42879

Yang L, Ren B, Li H et al. Enhanced antitumor effects of DC-activated CIKs to chemotherapy treatment in a single cohort of advanced non-small-cell lung cancer patients. Cancer Immunol Immunother 2013; 62(1):65-73.

National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Available online at: www.nccn.org/professionals/physician_gls/f_guidelines.asp#site. Last accessed November, 2011.

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