Medical Coverage Policy | Adoptive Immunotherapy

EFFECTIVE DATE: 03/16/2010
POLICY LAST UPDATED: 12/06/2016

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 Products

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

MEDICAL CRITERIA

Not pplicable

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 have yielded select populations of cytotoxic T 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. Recently, 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 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 (ie, 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 *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.

Clinical studies using adoptive immunotherapy are primarily small, early-stage investigations of novel immunologic treatments for a variety of cancers. Although there is some evidence of benefit with cytokine-induced killer cells for end points such as recurrence rate, improvement in overall survival has not been demonstrated. Additionally, available studies are from non-U.S. centers in heterogeneous patient populations, and have methodological shortcomings that limit conclusions. Studies of cytotoxic T lymphocytes, lymphokine-activated killer cells, tumor-infiltrating lymphocytes, autologous dendritic cells, and genetically engineered T cells suggest that some adoptive immunotherapies (e.g., autologous dendritic cells) may improve outcomes in some cancer types (e.g., glioblastoma multiforme). However, impact of adoptive immunotherapy on patient outcomes (e.g., increased survival, improved quality of life) has yet to be clarified in large, randomized, controlled trials. Specifically, high-quality trials with adequate follow up are needed to show that there is an advantage for adoptive immunotherapy strategies in important end points for a significant cohort of cancer patients compared with standard treatments.
Therefore, adoptive immunotherapy is considered not medically necessary as there is insufficient medical literature to support the efficacy of this treatment.

COVERAGE

Benefits may vary between groups/contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage, or Subscriber Agreement for limitations of benefits/coverage when services are not medically necessary.

CODING

Blue CHiP for Medicare and Commercial Products

The following code is considered not medically necessary:

S2107

RELATED POLICIES

None

PUBLISHED

Provider Update	January 2016
Provider Update	April 2015
Provider Update	Auguset 2014
Provider Update	May 2013
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