

Corporation obtaining approval, the name of its representative, and the address of its main office

Name: Ehime University Hospital

Applicant: Jitsuo Higaki

Address: Shitsukawa, Touon-shi, Ehime

Approved Type 1 Use Regulation

Name of the Type of Living Modified Organism	Nonproliferative and genetically modified Moloney murine leukemia virus that expresses HLA-A*24:02-restricted WT1-specific T cell receptor alpha and beta genes, and siRNA that interfere with endogenous T cell receptor alpha and beta genes, and has env protein of Gibbon ape leukemia virus in its envelope (MS3-WT1-siTCR)
Content of the Type 1 Use of Living Modified Organism	1. Used in a clinical facility for human medical treatment, including storage, transportation, disposal, and acts incidental to them
Method of the Type 1 Use of Living Modified Organism	<p>Address: Shitsukawa, Touon-shi, Ehime Name: Ehime University Hospital</p> <p>(1). The cells transduced with MS3-WT1-siTCR is transported to the clinical facility in the frozen state with a proper nonproliferation measure of the infectious items, and stored in a freezer that is equipped with a proper nonproliferation measure of the infectious items at the facility.</p> <p>(2). When the cells transduced with MS3-WT1-siTCR is transported through an open area, it should be contained inside a sealed container, which should be put in a box etc. for transportation to avoid dropping or breaking it.</p> <p>(3). When disposing of the cells transduced with MS3-WT1-siTCR, these should be sterilized (by an autoclave, or soaking in not less 0.5% sodium hypochlorite solution , or treated with an alcohol for disinfection; the same in the followings) and then disposed of according to the waste processing rule established by Ehime University Hospital (hereinafter referred to as "waste processing rule").</p> <p>(4). The first time administration of the MS3-WT1-siTCR transduced cells to a subject has to be performed by infusion in a single room that is equipped with a proper nonproliferation measure of the infectious items to the environment (hereinafter referred to as "single room"). Additionally, devices etc. that come in direct contact with the cells transduced with MS3-WT1-siTCR at the time of administration, such as injection needles, syringes, and tubes, etc., should be disposable ones, and these should be appropriately sterilized followed by disposal in accordance with the waste processing rule. Note that when sterilization is performed in the area outside of the single room, the wastes should be contained inside a double sealed container and transported.</p>

- (5). Until the third day after the first time administration, the subject should be cared for in the single room. When the subject goes to the open area outside the single room for examinations etc., viral leakage prevention measures including the wearing of a mask and a gown must be compulsory.
- (6). Blood and body fluids of the subject during the period of being taken care of in the single room should be appropriately sterilized individually and disposed of in accordance with the waste processing rule. In addition, the excreta of the subject including urine and feces should be appropriately sterilized and disposed of in accordance with the waste processing rule until the existence of replication competent retrovirus (hereinafter referred to as "RCR") is denied by the polymerase chain reaction test using subject's blood which is performed on or after the day following administration.
Note that when sterilization is performed in the area outside of the single room, the wastes should be contained inside a double sealed container and transported. Also, note that the handling of excreta etc. from the subject that are to be used as clinical samples should be in accordance with the handling of the solution of MS3-WT1-siTCR or the cells transduced with MS3-WT1-siTCR.
- (7). During the period of being taken care of in the single room, devices etc. that have been used invasively in the subject and those that have been in contact with excreta etc. of the subject should be appropriately sterilized and be disposed of in accordance with the waste processing rule, or be sufficiently washed.
Note that when sterilization is performed in the area outside of the single room, the wastes should be contained inside a double sealed container and transported.
- (8). Before releasing the subject from being taken care of in the single room, confirm that RCR is negative in the peripheral blood mononuclear cells (hereinafter referred to as "PBMC") and the plasma of the subject. If RCR is detected, the subject should continue to be cared for in the single room.
- (9). If RCR is detected in the PBMC or the plasma of the subject after releasing the subject from being taken care of in the single room, immediately transfer the subject to be taken care of in the single room, and take the same measures as in (5) to (8) above.