

Humira®), Certolizumab pegol (Cimzia®), etanercept (Enbrel®), etanercept-szzs (Ereizi®, a biosimilar to Enbrel®), Golimumab (Simponi®, Simponi Aria®), Infliximab (Remicade®), and Infliximab-dyyb (Inflectra®, a biosimilar to Remicade®), while literally dozens of clinical trials are ongoing with either new therapeutic agents or expanded uses for currently approved ones. Known side effects for TNF- α inhibitors include headaches, heartburn, nausea, vomiting, allergic reactions and muscle weakness. Because TNF- α plays an important role in the immune system, altering TNF- α activity makes a patient more susceptible to secondary infections or some cancers. As such, there is need to develop a dosing regimen or method that maintains a therapeutically effective dose of the therapeutic agent in a patient while reducing the overall patient exposure to the therapeutic agent.

[0007a] In one aspect of the present disclosure, there is provided a use of an anti-CTLA-4 antibody in the manufacture of a medicament for preventing or reducing cancer metastasis in a patient, wherein the medicament is to be administered via a medical device comprising a plurality of microneedles on the skin of the patient proximate to a first position under the skin of the patient located between at least one intervening lymph node and the solid cancer tumor, wherein the first position is proximate to lymph vessels and/or lymph capillaries in the patient's lymphatic system, wherein the microneedles have a surface comprising nanotopography and the intervening lymph node is a lymph node that intervenes in the lymphatic system between a solid cancer tumor and a draining duct; wherein the plurality of microneedles are to be inserted into the patient to a depth whereby at least the epidermis is penetrated and an end of at least one of the microneedles is proximate to the first position; and wherein the medicament is to be administered via the plurality of microneedles to the first position.

[0007b] In another aspect of the present disclosure, there is provided a use of an anti-CTLA-4 antibody in the manufacture of a medicament for preventing or reducing cancer metastasis in a patient, wherein the medicament is to be administered via a medical device that comprises a plurality of microneedles on the skin of the patient at a first location on the skin of the patient that is proximate to lymph capillaries and/or lymph vessels that flow into at least one intervening lymph node, wherein the microneedles have a surface comprising nanotopography and the intervening lymph node is a lymph node which intervenes in the lymphatic system between the solid cancer tumor and a draining duct; wherein the plurality of microneedles are to be inserted into the patient to a depth whereby at least the epidermis is penetrated; and wherein the

medicament is to be administered via the plurality of microneedles to the lymph capillaries and/or lymph vessels that flow into the intervening lymph node.

[0007c] In yet another aspect, there is provided a use of an anti-CTLA-4 antibody for the manufacture of a medicament for treating cancer in a patient, wherein the medicament is to be administered via a medical device comprising a plurality of microneedles on the skin of the patient proximate to a first position under the skin of the patient, wherein the first position is proximate to lymph vessels and/or lymph capillaries in the patient's lymphatic system, and wherein the microneedles have a surface comprising nanotopography; wherein the plurality of microneedles is to be inserted into the patient to a depth whereby at least the epidermis is penetrated and an end of at least one of the microneedles is proximate to the first position.

[0008] Accordingly, the following embodiments are provided.

[0009] Embodiment 1 is a method for administering a therapeutic agent to the lymphatic system of a patient, the method comprising:

placing a first medical device comprising a plurality of microneedles on the skin of the patient at a first location proximate to a first position under the skin of the patient, wherein the first position is proximate to lymph vessels and/or lymph capillaries that drain into the right lymphatic duct, and wherein the microneedles of the first medical device have a surface comprising nanotopography;

placing a second medical device comprising a plurality of microneedles on the skin of the patient at a second location proximate to a second position under the skin of the patient, optionally wherein the first and second medical devices are the same device, wherein the second position is proximate to lymph vessels and/or lymph capillaries that drain into the thoracic duct, and wherein the microneedles of the second medical device have a surface comprising nanotopography;

inserting the plurality of microneedles of the first medical device into the patient to a depth whereby at least the epidermis is penetrated and an end of at least one of the microneedles is proximate to the first position;

inserting the plurality of microneedles of the second medical device into the patient to a depth whereby at least the epidermis is penetrated and an end of at least one of the microneedles is proximate to the second position; and

administering via the microneedles of the first medical device a first dose of the therapeutic

WHAT IS CLAIMED IS:

1. Use of an anti-CTLA-4 antibody in the manufacture of a medicament for preventing or reducing cancer metastasis in a patient, wherein the medicament is to be administered via a medical device comprising a plurality of microneedles on the skin of the patient proximate to a first position under the skin of the patient located between at least one intervening lymph node and the solid cancer tumor, wherein the first position is proximate to lymph vessels and/or lymph capillaries in the patient's lymphatic system,

wherein the microneedles have a surface comprising nanotopography and the intervening lymph node is a lymph node that intervenes in the lymphatic system between a solid cancer tumor and a draining duct;

wherein the plurality of microneedles is to be inserted into the patient to a depth whereby at least the epidermis is penetrated and an end of at least one of the microneedles is proximate to the first position; and

wherein the medicament is to be administered via the plurality of microneedles to the first position.

2. Use of an anti-CTLA-4 antibody in the manufacture of a medicament for preventing or reducing cancer metastasis in a patient, wherein the medicament is to be administered via a medical device that comprises a plurality of microneedles on the skin of the patient at a first location on the skin of the patient that is proximate to lymph capillaries and/or lymph vessels that flow into at least one intervening lymph node,

wherein the microneedles have a surface comprising nanotopography and the intervening lymph node is a lymph node which intervenes in the lymphatic system between the solid cancer tumor and a draining duct;

wherein the plurality of microneedles is to be inserted into the patient to a depth whereby at least the epidermis is penetrated; and

wherein the medicament is to be administered via the plurality of microneedles to the lymph capillaries and/or lymph vessels that flow into the intervening lymph node.

3. Use of an anti-CTLA-4 antibody for the manufacture of a medicament for treating cancer in a patient, wherein the medicament is to be administered via a medical device comprising a plurality of microneedles on the skin of the patient proximate to a first position under the skin of the patient, wherein the first position is proximate to lymph vessels and/or lymph capillaries in the patient's lymphatic system, and wherein the microneedles have a surface comprising nanotopography;
wherein the plurality of microneedles is to be inserted into the patient to a depth whereby at least the epidermis is penetrated and an end of at least one of the microneedles is proximate to the first position.
4. The use according to any one of claims 1-3, wherein the cancer comprises a tumor.
5. The use according to any one of claims 1-4, wherein the medical device is to be placed, relative to the tumor, distal to the draining duct.
6. The use according to claim 1-5, wherein at least one lymph node in the patient intervenes in the lymphatic system between the tumor and a draining duct; and the first position is located between the intervening lymph node and the tumor.
7. The use according to any one of claims 1-6, wherein the medical device is to be placed at a location on the skin of the patient having lymphatic capillaries and/or vessels that flow directly into the intervening lymph node without first passing through any prior lymph node.
8. The use according to any one of claims 1-7, wherein the cancer is a cancer of the head and neck, and the lymph nodes are selected from the group consisting of the jugular lymph nodes, the cervical lymph nodes, the supraclavicular lymph nodes, and combinations thereof.
9. The use according to any one of claims 1-7, wherein the cancer is an oral cavity cancer, and the lymph nodes are selected from the group consisting of the jugular lymph node chain, the cervical lymph nodes, the supraclavicular lymph nodes, and combinations thereof.

10. The use according to any one of claims 1-7, wherein the cancer is a cancer of the pharynx, and the lymph nodes are selected from the group consisting of the jugular lymph node chain, the cervical lymph nodes, the supraclavicular lymph nodes, and combinations thereof.
11. The use according to any one of claims 1-7, wherein the cancer is a melanoma, and the lymph nodes are selected from the group consisting of axillary lymph nodes, inguinal lymph nodes, jugular lymph nodes, cervical lymph nodes, supraclavicular lymph nodes, and combinations thereof.
12. The use according to any one of claims 1-7, wherein the cancer is breast cancer, and lymph nodes are selected from the group consisting of the axillary lymph nodes, the internal mammary lymph nodes, the supraclavicular lymph nodes and combinations thereof.
13. The use according to any one of claims 1-7, wherein the cancer is prostate cancer, and the lymph nodes are selected from the group consisting of the lumbar lymph nodes, the inguinal lymph nodes, the peritoneal lymph nodes and combinations thereof.
14. The use according to any one of claims 1-7, wherein the cancer is in the genital system of the patient with the proviso that it is not ovarian cancer, and the lymph nodes are selected from the group consisting of the lumbar lymph nodes, the inguinal lymph nodes, the peritoneal lymph nodes and combinations thereof.
15. The use according to any one of claims 1-14, wherein the anti-CTLA-4 antibody is imilimumab, a biosimilar thereof, or a bioequivalent thereof.