xviii) incidence or severity of one or more immune-related Adverse Events may be reduced as compared to one or more immune-related Adverse Events following a therapeutically equivalent amount of the anti-PD-1 therapeutic agent or the anti-PD-L1 therapeutic agent administered by an intravenous delivery route.

The present disclosure also provides a use of an anti-PD-1 therapeutic agent or an anti-PD-L1 therapeutic agent in the manufacture of a medicament for treating cancer in a patient, wherein the anti-PD-1 therapeutic agent or anti-PD-L1 therapeutic agent is to be administered with a device comprising a plurality of microneedles to be placed 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; 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 anti-PD-1 therapeutic agent or anti-PD-L1 therapeutic agent is to be administered via the plurality of microneedles to the first position.

The present disclosure also provides a use of an anti-PD-1 therapeutic agent or an anti-PD-L1 therapeutic agent in the manufacture of a medicament for preventing or reducing cancer metastasis in a patient, wherein the anti-PD-1 therapeutic agent or anti-PD-L1 therapeutic agent is to be administered with a device comprising a plurality of microneedles to be placed on the skin of the patient proximate to a first position under the skin of the patient located between an intervening lymph node and a solid cancer tumor, wherein said intervening lymph node is at least one lymph node located in the patient that intervenes in the lymphatic system between a solid cancer tumor and a draining duct, 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; and wherein the anti-PD-1 therapeutic agent or anti-PD-L1 therapeutic agent is to be administered via the plurality of microneedles to the first position.

The present disclosure also provides a use of an anti-PD-1 therapeutic agent or an anti-PD-L1 therapeutic agent in the manufacture of a medicament for preventing or reducing cancer metastasis in a patient, wherein the anti-PD-1 therapeutic agent or anti-PD-L1 therapeutic agent is to be administered with a device comprising a plurality of microneedles to be placed 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 the intervening lymph node, wherein said intervening lymph node is at least one lymph node located in the patient that intervenes in the lymphatic system between a solid cancer tumor located in the patient and a draining duct, 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 wherein the anti-PD-1 therapeutic agent or anti-PD-L1 therapeutic agent is to be administered via the plurality of microneedles to the lymph capillaries and/or lymph vessels that flow into the intervening lymph node.

BRIEF DESCRIPTION OF THE DRAWINGS

For a more complete understanding of the present disclosure and the associated features and advantages, reference is now made to the following description, taken in conjunction with the accompanying drawings, which are not to scale, and in which:

FIG. 1 is a schematic of (i) an example SOFUSA® (Sorrento Therapeutics, Inc. Corporation Delaware) Nanotopographical Device for infusing anti-PD-1 or anti-PD-L1 into the sub-epidermal space, which includes a (ii) microfluidic fluid block with a microfluidic distributor (green) and silicon microneedle array (gray). As an exemplary embodiment, each microneedle is 350 μm long, 110 μm wide with a 30 μm hole located off center through which the therapeutic agent flows out. (iii) SOFUSA® infuses therapeutic agent into the sub-epidermal space where the initial lymphatics provide uptake, whereas deeper subcutaneous injections deposit drug below the initial lymphatics, reducing uptake.

FIG. 2 is a schematic of an example SOFUSA® Nanotopographical Device, showing (i) the Microfluidic Fluid Block with a perforated attachment adhesive (tan), microfluidic distributor (green), perforated attachment adhesive (yellow), and silicon microneedle array (gray). Each microneedle is 350 μm long, 110 μm wide with a 30 μm hole located off center through which the drug flows out. Also shown is (ii) Scanning Electron Microscopy (SEM) image of nanotopographic film heat formed over the silicon microneedles (scale bar represents 300 μm) and (iii) SEM of individual microneedle, and (iv) SEM image of the nanostructures on each microneedle (scale bar = 3 μm).

FIG. 3 is (i) a schematic showing example placement of SOFUSA® on dorsal back of mice and Near-Infrared Fluorescence (NIRF) (ii) dorsal and (iii) lateral images of SOFUSA® delivery of indocyanine green (ICG) to brachial lymph nodes (LN).

FIG. 4A and FIG. 4B include a set of example images showing in FIG. 4A, left: Applied SOFUSA® device infusing ICG and FIG. 4A, right: NIRF imaging of lymphatic vessels

propelling ICG-laden lymph during infusion (right) and intradermal (i.d.) injection (left) of ICG in the medial ankle and lateral calf with arrows showing i.d. injection and SOFUSA® infusion placement. FIG. 4B. is example near-infrared fluorescence images of SOFUSA®