SUMMARY

[0008] The present disclosure relates to methods for increasing cell-mediated immunity against varicella zoster virus (VZV) in a human subject in need thereof by administration of an immunogenic composition comprising effective amounts of a VZV glycoprotein E antigen and an oligonucleotide comprising an unmethylated cytidine-phospho-guanosine (CpG) motif. The immunogenic compositions are suitable for prevention of herpes zoster and/or postherpetic neuralgia.

[0008a] In one aspect, the present disclosure refers to an immunogenic composition for use in increasing cell-mediated immunity against varicella zoster virus (VZV) in a human subject in need thereof, the immunogenic composition comprising: i) an unmethylated cytidine-phospho-guanosine (CpG)-containing oligonucleotide comprising the sequence of 5'-TGACTGTGAA CGTTCGAGAT GA-3'(SEQ ID NO:1); and ii) a truncated VZV glycoprotein E (gE) antigen, which are present in the immunogenic composition in amounts effective to increase cell-mediated immunity against VZV relative to cell-mediated immunity against VZV in the subject prior to administration of the immunogenic composition, wherein a first dose and a second dose of the immunogenic composition is to be administered to the human subject, with the second dose to be administered from 2 months to 6 months after the first dose.

[0008b] In one aspect, the present disclosure refers to use of an immunogenic composition in the manufacture of a medicament for increasing cell-mediated immunity against varicella zoster virus (VZV) in a human subject in need thereof, wherein: the immunogenic composition comprises: i) an unmethylated cytidine-phospho-guanosine (CpG)-containing oligonucleotide comprising the sequence of 5'-TGACTGTGAA CGTTCGAGAT GA-3'(SEQ ID NO:1); and ii) a truncated VZV glycoprotein E (gE) antigen, which are present in the immunogenic composition in amounts effective to increase cell-mediated immunity against VZV relative to cell-mediated immunity against VZV in the subject prior to administration of the immunogenic composition, and wherein a first dose and a second dose of the immunogenic composition is to be administered to the human subject, with the second dose to be administered from 2 months to 6 months after the first dose.

[0008c] In one aspect, the present disclosure refers to an immunogenic composition for use in increasing an immune response against varicella zoster virus (VZV) in a human subject in need thereof, the immunogenic composition comprising: i) an unmethylated cytidine-phospho-guanosine (CpG)-containing oligonucleotide comprising the sequence of 5'-TGACTGTGAA CGTTCGAGAT GA-3'(SEQ ID NO:1); and ii) a truncated VZV glycoprotein E (gE) antigen, wherein the immunogenic composition comprises about 100 µg of the gE antigen and about 3000 µg or about 6000 µg of the oligonucleotide.

[0008d] In one aspect, the present disclosure refers to use of an immunogenic composition in the manufacture of a medicament for increasing an immune response against varicella zoster virus (VZV) in a human subject in need thereof, wherein: the immunogenic composition comprises: i) an unmethylated cytidine-phospho-guanosine (CpG)-containing oligonucleotide comprising the sequence of 5'-TGACTGTGAA CGTTCGAGAT GA-3'(SEQ ID NO:1); and ii) a truncated VZV glycoprotein E (gE) antigen, wherein the immunogenic composition comprises about 100 µg of the gE antigen and about 3000 µg or about 6000 µg of the oligonucleotide.

[0008e] In one aspect, the present disclosure refers to an immunogenic composition comprising: i) an unmethylated cytidine-phospho-guanosine (CpG)-containing oligonucleotide comprising the sequence of 5'-TGACTGTGAA CGTTCGAGAT GA-3'(SEQ ID NO:1); ii) a truncated VZV glycoprotein E (gE) antigen; and iii) at least one excipient, wherein the gE antigen is a recombinant protein produced in mammalian cells and is present in the immunogenic composition in an amount of from about 25 µg to about 150 µg, the oligonucleotide is present in the immunogenic composition in an amount of from about 750 µg to about 6000 µg, and the at least one excipient comprises a pharmaceutically acceptable buffer.

[0008f] In one aspect, the present disclosure refers to an immunogenic composition comprising i) an unmethylated cytidine-phospho-guanosine (CpG)-containing oligonucleotide comprising the sequence of 5'-TGACTGTGAA CGTTCGAGAT GA-3'(SEQ ID NO:1); ii) a truncated VZV glycoprotein E (gE) antigen; and iii) at least one excipient, wherein the gE antigen is a recombinant protein produced in mammalian cells and is present in the immunogenic composition in an amount of about 100 µg, the oligonucleotide is present in the immunogenic composition in an amount of about 3000 µg or about 6000 µg, and the at least one excipient comprises a pharmaceutically acceptable buffer.

BRIEF DESCRIPTION OF THE DRAWINGS

[0009] **FIG. 1** shows the frequency of VZV gE-reactive CD4+ T cells expressing 2, 3 and 4 markers of activation after incubation of PBMCs in the presence of a series of overlapping peptides spanning VZV gE, with non-stimulated (background) response subtracted. PBMCs were isolated from blood samples obtained from study subjects at Week 0 (baseline).

[0010] **FIG. 2** shows the frequency of VZV gE-reactive CD4+ T cells expressing 2, 3 and 4 markers of activation after incubation of PBMCs in the presence of a series of overlapping peptides spanning VZV gE, with non-stimulated (background) response subtracted. PBMCs were isolated from blood samples obtained from study subjects at Week 8 (~4 weeks after first injection).

[0011] **FIG. 3** shows the frequency of VZV gE-reactive CD4+ T cells expressing 2, 3 and 4 markers of activation after incubation of PBMCs in the presence of a series of overlapping peptides spanning VZV gE, with non-stimulated (background) response subtracted. PBMCs were isolated from blood samples obtained from study subjects at Week 12 (~4 weeks after second injection).

DETAILED DESCRIPTION

[0012] The present disclosure relates to methods for increasing cell-mediated immunity against varicella zoster virus (VZV) in a human subject in need thereof by administration of an immunogenic composition comprising effective amounts of a VZV glycoprotein E antigen and an oligonucleotide comprising an unmethylated cytidine-phospho-guanosine (CpG) motif. The immunogenic compositions are suitable for prevention of herpes zoster (HZ) and/or postherpetic neuralgia (PHN).