

the DNAM/TIGIT immunoreceptor axis (see, Liang et al., Journal of Clinical Oncology 2017 35:15_suppl, 3074-3074).

[0011] Anti-PVRIG antibodies (including antigen-binding fragments) that both bind to PVRIG and prevent activation by PVRL2 (*e.g.* most commonly by blocking the interaction of PVRIG and PVLR2), are used to enhance T cell and/or NK cell activation and be used in treating diseases such as cancer and pathogen infection. As such, formulations for administering such antibodies are needed.

[0012] Accordingly, it is an object of the invention to provide stable liquid pharmaceutical formulations comprising anti-PVRIG antibodies or use in disease treatment (*e.g.*, anti-PVRIG antibodies including those with CDRs identical to those shown in Figure 3).

~~BRIEF SUMMARY OF THE INVENTION~~

[0013] Accordingly, it is an object of the ~~invention~~disclosure to provide stable liquid pharmaceutical formulations of anti-PVRIG antibodies as described herein.

[0014] ~~The In one aspect, the~~ present ~~invention~~disclosure provides a stable liquid pharmaceutical formulation of an anti-PVRIG antibody comprising:

- (a) an anti-PVRIG antibody, wherein said anti-PVRIG antibody comprises:
 - i) a heavy chain variable domain comprising the vhCDR1, vhCDR2, and vhCDR3 from the heavy chain of CHA.7.518.1.H4(S241P) (SEQ ID NO:4), and
 - ii) a light chain variable domain comprising the vlCDR1, vlCDR2, and vlCDR3 from the light chain of CHA.7.518.1.H4(S241P) (SEQ ID NO:9);
 - (b) from 10 mM to 100 mM histidine;
 - (c) from 30 mM to 100 mM NaCl;
 - (d) from 20 mM to 150 mM L-Arginine; and
 - (e) from 0.005% to 0.1% w/v polysorbate 80,
- wherein the composition has a pH from 5.5 to 7.0.

[0014a] In another aspect, the present disclosure refers to the stable liquid pharmaceutical formulation disclosed herein, for use in therapy.

[0014b] In another aspect, the present disclosure refers to the use of the stable liquid pharmaceutical formulation disclosed herein in the manufacture of a medicament for treating cancer, wherein said cancer selected from the group consisting of prostate cancer, liver cancer (HCC), colorectal cancer (CRC), colorectal cancer MSS (MSS-CRC; including refractory MSS colorectal), CRC (MSS unknown), ovarian cancer (including ovarian carcinoma), endometrial cancer (including endometrial carcinoma), breast cancer, pancreatic cancer, stomach cancer, cervical cancer, head and neck cancer, thyroid cancer, testis cancer, urothelial cancer, lung cancer, melanoma, non-melanoma skin cancer (squamous and basal cell carcinoma), malignant melanoma, glioma, renal cell cancer (RCC), renal cell carcinoma (RCC), lymphoma (non-Hodgkins' lymphoma (NHL) and Hodgkin's lymphoma (HD)), Acute myeloid leukemia (AML), T cell Acute Lymphoblastic Leukemia (T-ALL), Diffuse Large B cell lymphoma, multiple myeloma, testicular germ cell tumors, mesothelioma, esophageal cancer, triple negative breast cancer, Merkel Cells cancer, MSI-high cancer, KRAS mutant tumors, adult T-cell leukemia/lymphoma, pleural mesothelioma, anal SCC, small-cell lung cancer, neuroendocrine lung cancer (including neuroendocrine lung carcinoma), NSCLC, NSCL (large cell), NSCLC large cell, NSCLC, squamous cell cancer, adenocarcinoma of the lung, cervical SCC, malignant melanoma, pancreatic cancer, pancreatic adenocarcinoma, adenoid cystic cancer (including adenoid cystic carcinoma), primary peritoneal cancer, microsatellite stable primary peritoneal cancer, platinum resistant microsatellite stable primary peritoneal cancer, and/or Myelodysplastic syndromes (MDS).

[0015] In some ~~embodiment~~examples of the stable liquid pharmaceutical formulation said anti-PVRIG antibody comprises a CH1-hinge-CH2-CH3 sequence of IgG4 (SEQ ID NO:17 or SEQ ID NO:50), wherein said hinge region optionally comprises mutations.

[0016] In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation said anti-PVRIG antibody comprises the CH1-hinge-CH2-CH3 region from IgG1, IgG2, IgG3, or IgG4, wherein said hinge region optionally comprises mutations.

[0017] In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation said heavy chain variable domain is from the heavy chain of CHA.7.518.1.H4(S241P) (SEQ ID NO:4) and said light chain variable domain is from the light chain of CHA.7.518.1.H4(S241P) (SEQ ID NO:9).

[0018] In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation said anti-PVRIG antibody comprises a CL region of human kappa 2 light chain.

[0019] In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation, said pharmaceutical formulation comprises from 10 mM to 80 mM histidine, from 15 mM to 70 mM histidine, from 20 mM to 60 mM histidine, from 20 mM to 50 mM histidine, or from 20 mM to 30 mM histidine.

[0020] In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation, said pharmaceutical formulation comprises about 25 mM histidine.

[0021] In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation, said pharmaceutical formulation comprises from 30 mM to 100 mM NaCl, from 30 mM to 90 mM NaCl, from 40 mM to 80 mM NaCl, from 30 mM to 70 mM histidine, or from 45 mM to 70 mM NaCl.

[0022] In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation, said pharmaceutical formulation comprises about 60 mM NaCl.

[0023] In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation, said pharmaceutical formulation comprises from 20 mM to 140 mM L-arginine, from 30 mM to 140 mM L-arginine, from 40 mM to 130 mM L-arginine, from 50 mM to 120 mM L-arginine, from 60 mM to 110 mM L-arginine, from 70 mM to 110 mM L-arginine, from 80 mM to 110 mM L-arginine, or from 90 mM to 110 mM L-arginine.

[0024] In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation, said pharmaceutical formulation comprises about 100 mM L-arginine.

[0025] In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation, said pharmaceutical formulation comprises from 0.006% to 0.1% w/v polysorbate 80, from 0.007% to 0.09% w/v polysorbate 80, from 0.008% to 0.08% w/v polysorbate 80, from

0.009% to 0.09% w/v polysorbate 80, from 0.01% to 0.08% w/v polysorbate 80, from 0.01% to 0.07% w/v polysorbate 80, from 0.01% to 0.07% w/v polysorbate 80, or from 0.01% to 0.06% w/v polysorbate 80, or from 0.009% to 0.05% w/v polysorbate 80.

[0026] In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation, said pharmaceutical formulation comprises about 0.01% polysorbate 80.

[0027] In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation, said pH is from 6 to 7.0.

[0028] In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation, said pH is from 6.3 to 6.8.

[0029] In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation, said pH is 6.5 +/- 0.2.

[0030] In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation, said anti-PVRIG antibody is at a concentration of from 10 mg/mL to 40 mg/mL, 15 mg/mL to 40 mg/mL, 15 mg/mL to 30 mg/mL, 10 mg/mL to 25 mg/mL, or 15 mg/mL to 25 mg/mL.

[0031] In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation, said formulation is stable at 2°C to 8°C for at least 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, 9 weeks, or 10 weeks.

[0032] In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation, said formulation is stable at about 20°C to 25 °C for at least 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, or 6 weeks.

[0033] In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation, said formulation is stable at 35°C to 40°C for at least 1 week, 2 weeks, 3 weeks, 4 weeks, or 5 weeks.

[0034] In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation, said anti-PVRIG antibody is at a concentration of about 20 mg/mL.

[0035] In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation, said anti-PVRIG antibody formulation comprises:

- a) a heavy chain comprising:

- i) a VH-CH1-hinge-CH2-CH3, wherein the VH is from CHA.7.518.1.H4(S241P) (SEQ ID NO:4) and wherein the CH1-hinge-CH2-CH3 region is from IgG4; and
- b) a light chain comprising:
 - i) a VL-CL, wherein the VL from CHA.7.518.1.H4(S241P) (SEQ ID NO:9) and wherein the CL region is from human kappa 2 light chain.

[0036] In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation, said hinge region optionally comprises mutations.

[0037] In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation, said hinge region optionally comprises mutations.

[0038] In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation, said anti-PVRIG antibody formulation comprises:

- i) a heavy chain comprising the heavy chain from CHA.7.518.1.H4(S241P) (SEQ ID NO:8); and
- ii) a light chain comprising the light chain from CHA.7.518.1.H4(S241P) (SEQ ID NO:13).

[0039] In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation, said anti-PVRIG antibody formulation comprises:

- (a) an anti-PVRIG antibody, wherein said anti-PVRIG antibody comprises:
 - i) a heavy chain variable domain comprising the vhCDR1, vhCDR2, and vhCDR3 from the heavy chain of CHA.7.518.1.H4(S241P) (SEQ ID NO:4), and
 - ii) a light chain variable domain comprising the vlCDR1, vlCDR2, and vlCDR3 from the light chain of CHA.7.518.1.H4(S241P) (SEQ ID NO:9);
- (b) about 25 mM histidine;
- (c) about 60 mM NaCl;
- (d) about 100 mM L-Arginine; and

- (e) about 0.01% w/v polysorbate 80,
wherein the composition has a pH from 6.5 +/- 0.2.

[0040] In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation, said anti-PVRIG antibody formulation comprises:

- (a) an anti-PVRIG antibody, wherein said anti-PVRIG antibody comprises:
 - i) a heavy chain comprising the heavy chain from CHA.7.518.1.H4(S241P) (SEQ ID NO:8); and
 - ii) a light chain comprising the light chain from CHA.7.518.1.H4(S241P) (SEQ ID NO:13);
- (b) about 25 mM histidine;
- (c) about 60 mM NaCl;
- (d) about 100 mM L-Arginine; and
- (e) about 0.01% w/v polysorbate 80,
wherein the composition has a pH from 6.5 +/- 0.2.

[0041] In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation, said formulation is administered at a dosage of about 0.01 mg/kg to about 20 mg/kg of the anti-PVRIG antibody. In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation, said formulation is administered at a dosage of about 0.01 mg/kg to about 10 mg/kg of the anti-PVRIG antibody.

[0042] In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation, said formulation is administered at a dosage of about 0.01 mg/kg, 0.03 mg/kg, 0.1 mg/kg, 0.3 mg/kg, 1 mg/kg, 3 mg/kg, 10 mg/kg, or 20 mg/kg of the anti-PVRIG antibody.

[0043] In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation said anti-PVRIG antibody is administered 20 mg/kg every 4 weeks. In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation said anti-PVRIG antibody is administered 20 mg/kg IV every 4 weeks.

[0044] In some [embodimentexamples](#) of the method of treatment, said formulation is administered 20 mg/kg IV every for 4 weeks for up to 24 months until disease progression,

unacceptable toxicity, initiation of a new anticancer therapy, withdrawal of subject consent or death. In some [embodimentexamples](#), administration is up to 6 months, 12, months, 18 months or 24 months, until disease progression, unacceptable toxicity, initiation of a new anticancer therapy, withdrawal of subject consent and/or death.

[0045] In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation, said stable liquid pharmaceutical formulation is administered for the treatment of cancer.

[0046] In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation, said stable liquid pharmaceutical formulation is for use in a method of treating cancer.

[0047] In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation, said cancer selected from the group consisting of prostate cancer, liver cancer (HCC), colorectal cancer (CRC), colorectal cancer MSS (MSS-CRC; including refractory MSS colorectal), CRC (MSS unknown), ovarian cancer (including ovarian carcinoma), endometrial cancer (including endometrial carcinoma), breast cancer, pancreatic cancer, stomach cancer, cervical cancer, head and neck cancer, thyroid cancer, testis cancer, urothelial cancer, lung cancer, melanoma, non-melanoma skin cancer (squamous and basal cell carcinoma), glioma, renal cell cancer (RCC), renal cell carcinoma (RCC), lymphoma (non-Hodgkins' lymphoma (NHL) and Hodgkin's lymphoma (HD)), Acute myeloid leukemia (AML), T cell Acute Lymphoblastic Leukemia (T-ALL), Diffuse Large B cell lymphoma, testicular germ cell tumors, mesothelioma, esophageal cancer, triple negative breast cancer, Merkel Cells cancer, MSI-high cancer, KRAS mutant tumors, adult T-cell leukemia/lymphoma, pleural mesothelioma, anal SCC, neuroendocrine lung cancer (including neuroendocrine lung carcinoma), NSCLC, NSCL (large cell), NSCLC large cell, NSCLC squamous cell, cervical SCC, malignant melanoma, pancreatic cancer, pancreatic adenocarcinoma, adenoid cystic cancer (including adenoid cystic carcinoma), primary peritoneal cancer, microsatellite stable primary peritoneal cancer, platinum resistant microsatellite stable primary peritoneal cancer, and/or Myelodysplastic syndromes (MDS).

[0048] The present [inventiondisclosure](#) provides for the use of a stable liquid pharmaceutical formulation of an anti-PVRIG antibody in a method of treating cancer, wherein the anti-PVRIG antibody comprises:

- (a) an anti-PVRIG antibody, wherein said anti-PVRIG antibody comprises:

i) a heavy chain variable domain comprising the vhCDR1, vhCDR2, and vhCDR3 from the heavy chain of CHA.7.518.1.H4(S241P) (SEQ ID NO:4), and

ii) a light chain variable domain comprising the vlCDR1, vlCDR2, and vlCDR3 from the light chain of CHA.7.518.1.H4(S241P) (SEQ ID NO:9);

(b) from 10 mM to 100 mM histidine;

(c) from 30 mM to 100 mM NaCl;

(d) from 20 mM to 150 mM L-Arginine; and

(e) from 0.005% to 0.1% w/v polysorbate 80,

wherein the composition has a pH from 5.5 to 7.0.

[0049] In some [embodimentexamples](#) of the use of a stable liquid pharmaceutical formulation of an anti-PVRIG antibody in a method of treating cancer according to paragraph [0048], said anti-PVRIG antibody comprises a CH1-hinge-CH2-CH3 sequence of IgG4 (SEQ ID NO:17 or SEQ ID NO:50), wherein said hinge region optionally comprises mutations.

[0050] In some [embodimentexamples](#) of the use of a stable liquid pharmaceutical formulation of an anti-PVRIG antibody in a method of treating cancer according to paragraphs [0048]-[0049], said anti-PVRIG antibody comprises the CH1-hinge-CH2-CH3 region from IgG1, IgG2, IgG3, or IgG4, wherein said hinge region optionally comprises mutations.

[0051] In some [embodimentexamples](#) of the use of a stable liquid pharmaceutical formulation of an anti-PVRIG antibody in a method of treating cancer according to paragraphs [0048]-[0050], said heavy chain variable domain is from the heavy chain of CHA.7.518.1.H4(S241P) (SEQ ID NO:4) and said light chain variable domain is from the light chain of CHA.7.518.1.H4(S241P) (SEQ ID NO:9).

[0052] In some [embodimentexamples](#) of the use of a stable liquid pharmaceutical formulation of an anti-PVRIG antibody in a method of treating cancer according to paragraphs [0048]-[0051], said anti-PVRIG antibody comprises a CL region of human kappa 2 light chain.

[0053] In some [embodimentexamples](#) of the use of a stable liquid pharmaceutical formulation of an anti-PVRIG antibody in a method of treating cancer according to paragraphs [0048]-[0052], said pharmaceutical formulation comprises from 10 mM to 80 mM histidine, from 15 mM to

70 mM histidine, from 20 mM to 60 mM histidine, from 20 mM to 50 mM histidine, or from 20 mM to 30 mM histidine.

[0054] In some [embodimentexamples](#) of the use of a stable liquid pharmaceutical formulation of an anti-PVRIG antibody in a method of treating cancer according to paragraphs [0048]-[0053], said pharmaceutical formulation comprises about 25 mM histidine.

[0055] In some [embodimentexamples](#) of the use of a stable liquid pharmaceutical formulation of an anti-PVRIG antibody in a method of treating cancer according to paragraphs [0048]-[0054], said pharmaceutical formulation comprises from 30 mM to 100 mM NaCl, from 30 mM to 90 mM NaCl, from 40 mM to 80 mM NaCl, from 30 mM to 70 mM histidine, or from 45 mM to 70 mM NaCl.

[0056] In some [embodimentexamples](#) of the use of a stable liquid pharmaceutical formulation of an anti-PVRIG antibody in a method of treating cancer according to paragraphs [0048]-[0055], said pharmaceutical formulation comprises about 60 mM NaCl.

[0057] In some [embodimentexamples](#) of the use of a stable liquid pharmaceutical formulation of an anti-PVRIG antibody in a method of treating cancer according to paragraphs [0048]-[0056], said pharmaceutical formulation comprises from 20 mM to 140 mM L-arginine, from 30 mM to 140 mM L-arginine, from 40 mM to 130 mM L-arginine, from 50 mM to 120 mM L-arginine, from 60 mM to 110 mM L-arginine, from 70 mM to 110 mM L-arginine, from 80 mM to 110 mM L-arginine, or from 90 mM to 110 mM L-arginine.

[0058] In some [embodimentexamples](#) of the use of a stable liquid pharmaceutical formulation of an anti-PVRIG antibody in a method of treating cancer according to paragraphs [0048]-[0057], said pharmaceutical formulation comprises about 100 mM L-arginine.

[0059] In some [embodimentexamples](#) of the use of a stable liquid pharmaceutical formulation of an anti-PVRIG antibody in a method of treating cancer according to paragraphs [0048]-[0058], said pharmaceutical formulation comprises from 0.006% to 0.1% w/v polysorbate 80, from 0.007% to 0.09% w/v polysorbate 80, from 0.008% to 0.08% w/v polysorbate 80, from 0.009% to 0.09% w/v polysorbate 80, from 0.01% to 0.08% w/v polysorbate 80, from 0.01% to 0.07% w/v polysorbate 80, from 0.01% to 0.07% w/v polysorbate 80, or from 0.01% to 0.06% w/v polysorbate 80, or from 0.009% to 0.05% w/v polysorbate 80.

[0060] In some [embodimentexamples](#) of the use of a stable liquid pharmaceutical formulation of an anti-PVRIG antibody in a method of treating cancer according to paragraphs [0048]-[0059], said pharmaceutical formulation comprises about 0.01% polysorbate 80.

[0061] In some [embodimentexamples](#) of the use of a stable liquid pharmaceutical formulation of an anti-PVRIG antibody in a method of treating cancer according to paragraphs [0048]-[0060], said pH is from 6 to 7.0.

[0062] In some [embodimentexamples](#) of the use of a stable liquid pharmaceutical formulation of an anti-PVRIG antibody in a method of treating cancer according to paragraphs [0048]-[0061], said pH is from 6.3 to 6.8.

[0063] In some [embodimentexamples](#) of the use of a stable liquid pharmaceutical formulation of an anti-PVRIG antibody in a method of treating cancer according to paragraphs [0048]-[0062], said pH is 6.5 +/- 0.2.

[0064] In some [embodimentexamples](#) of the use of a stable liquid pharmaceutical formulation of an anti-PVRIG antibody in a method of treating cancer according to paragraphs [0048]-[0063], said anti-PVRIG antibody is at a concentration of from 10 mg/mL to 40 mg/mL, 15 mg/mL to 40 mg/mL, 15 mg/mL to 30 mg/mL, 10 mg/mL to 25 mg/mL, or 15 mg/mL to 25 mg/mL.

[0065] In some [embodimentexamples](#) of the use of a stable liquid pharmaceutical formulation of an anti-PVRIG antibody in a method of treating cancer according to paragraphs [0048]-[0064], said formulation is stable at 2°C to 8°C for at least 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, 9 weeks, or 10 weeks.

[0066] In some [embodimentexamples](#) of the use of a stable liquid pharmaceutical formulation of an anti-PVRIG antibody in a method of treating cancer according to paragraphs [0048]-[0065], said formulation is stable at about 20°C to 25 °C for at least 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, or 6 weeks.

[0067] In some [embodimentexamples](#) of the use of a stable liquid pharmaceutical formulation of an anti-PVRIG antibody in a method of treating cancer according to paragraphs [0048]-[0066], said formulation is stable at 35°C to 40°C for at least 1 week, 2 weeks, 3 weeks, 4 weeks, or 5 weeks.

[0068] In some [embodimentexamples](#) of the use of a stable liquid pharmaceutical formulation of an anti-PVRIG antibody in a method of treating cancer according to paragraphs [0048]-[0067], said anti-PVRIG antibody is at a concentration of about 20 mg/mL.

[0069] In some [embodimentexamples](#) of the use of a stable liquid pharmaceutical formulation of an anti-PVRIG antibody in a method of treating cancer according to paragraphs [0048]-[0068], said anti-PVRIG antibody formulation comprises:

- a) a heavy chain comprising:
 - i) a VH-CH1-hinge-CH2-CH3, wherein the VH is from CHA.7.518.1.H4(S241P) (SEQ ID NO:4) and wherein the CH1-hinge-CH2-CH3 region is from IgG4; and
- b) a light chain comprising:
 - i) a VL-CL, wherein the VL from CHA.7.518.1.H4(S241P) (SEQ ID NO:9) and wherein the CL region is from human kappa 2 light chain.

[0070] In some [embodimentexamples](#) of the use of a stable liquid pharmaceutical formulation of an anti-PVRIG antibody in a method of treating cancer according to paragraphs [0048]-[0069], said hinge region optionally comprises mutations.

[0071] In some [embodimentexamples](#) of the use of a stable liquid pharmaceutical formulation of an anti-PVRIG antibody in a method of treating cancer according to paragraphs [0048]-[0070], said hinge region optionally comprises mutations.

[0072] In some [embodimentexamples](#) of the use of a stable liquid pharmaceutical formulation of an anti-PVRIG antibody in a method of treating cancer according to paragraphs [0048]-[0071], said anti-PVRIG antibody formulation comprises:

- i) a heavy chain comprising the heavy chain from CHA.7.518.1.H4(S241P) (SEQ ID NO:8); and
- ii) a light chain comprising the light chain from CHA.7.518.1.H4(S241P) (SEQ ID NO:13).

[0073] In some [embodimentexamples](#) of the use of a stable liquid pharmaceutical formulation of an anti-PVRIG antibody in a method of treating cancer according to paragraphs [0048]-[0072], said anti-PVRIG antibody formulation comprises:

- (a) an anti-PVRIG antibody, wherein said anti-PVRIG antibody comprises:
 - i) a heavy chain variable domain comprising the vhCDR1, vhCDR2, and vhCDR3 from the heavy chain of CHA.7.518.1.H4(S241P) (SEQ ID NO:4), and
 - ii) a light chain variable domain comprising the vlCDR1, vlCDR2, and vlCDR3 from the light chain of CHA.7.518.1.H4(S241P) (SEQ ID NO:9);
- (b) about 25 mM histidine;
- (c) about 60 mM NaCl;
- (d) about 100 mM L-Arginine; and
- (e) about 0.01% % w/v polysorbate 80,
wherein the composition has a pH from 6.5 +/- 0.2.

[0074] In some [embodimentexamples](#) of the use of a stable liquid pharmaceutical formulation of an anti-PVRIG antibody in a method of treating cancer according to paragraphs [0048]-[0073], said anti-PVRIG antibody formulation comprises:

- (a) an anti-PVRIG antibody, wherein said anti-PVRIG antibody comprises:
 - i) a heavy chain comprising the heavy chain from CHA.7.518.1.H4(S241P) (SEQ ID NO:8); and
 - ii) a light chain comprising the light chain from CHA.7.518.1.H4(S241P) (SEQ ID NO:13);
- (b) about 25 mM histidine;
- (c) about 60 mM NaCl;
- (d) about 100 mM L-Arginine; and
- (e) about 0.01% % w/v polysorbate 80,
wherein the composition has a pH from 6.5 +/- 0.2.

[0075] In some [embodimentexamples](#) of the use of a stable liquid pharmaceutical formulation of an anti-PVRIG antibody in a method of treating cancer according to paragraphs [0048]-[0074], said formulation is administered at a dosage of about 0.01 mg/kg to about 20 mg/kg of the anti-PVRIG antibody. In some [embodimentexamples](#) of the stable liquid pharmaceutical formulation, said formulation is administered at a dosage of about 0.01 mg/kg to about 10 mg/kg of the anti-PVRIG antibody.

[0076] In some [embodimentexamples](#) of the use of a stable liquid pharmaceutical formulation of an anti-PVRIG antibody in a method of treating cancer according to paragraphs [0048]-[0075], said formulation is administered at a dosage of about 0.01 mg/kg, 0.03 mg/kg, 0.1 mg/kg, 0.3 mg/kg, 1 mg/kg, 3 mg/kg, 10 mg/kg, or 20 mg/kg of the anti-PVRIG antibody.

[0077] In some [embodimentexamples](#) of the use of a stable liquid pharmaceutical formulation of an anti-PVRIG antibody in a method of treating cancer, said anti-PVRIG antibody is administered 20 mg/kg every 4 weeks. In some [embodimentexamples](#) of the use in a method for treatment according to paragraphs [0048]-[0076], said formulation is administered 20 mg/kg IV every 4 weeks.

[0078] In some [embodimentexamples](#) of the method of treatment according to paragraphs [0048]-[0077], said formulation is administered 20 mg/kg IV every for 4 weeks for for up to 24 months until disease progression, unacceptable toxicity, initiation of a new anticancer therapy, withdrawal of subject consent or death. In some [embodimentexamples](#), administration is up to 6 months, 12, months, 18 months or 24 months, until disease progression, unacceptable toxicity, initiation of a new anticancer therapy, withdrawal of subject consent and/or death.

[0079] In some [embodimentexamples](#) of the use of a stable liquid pharmaceutical formulation of an anti-PVRIG antibody in a method of treating cancer according to paragraphs [0048]-[0078], said cancer selected from the group consisting of prostate cancer, liver cancer (HCC), colorectal cancer (CRC), colorectal cancer MSS (MSS-CRC; including refractory MSS colorectal), CRC (MSS unknown), ovarian cancer (including ovarian carcinoma), endometrial cancer (including endometrial carcinoma), breast cancer, pancreatic cancer, stomach cancer, cervical cancer, head and neck cancer, thyroid cancer, testis cancer, urothelial cancer, lung cancer, melanoma, non-melanoma skin cancer (squamous and basal cell carcinoma), glioma, renal cell cancer (RCC), renal cell carcinoma (RCC), lymphoma (non-Hodgkins' lymphoma (NHL) and Hodgkin's lymphoma (HD)), Acute myeloid leukemia (AML), T cell Acute Lymphoblastic Leukemia (T-ALL), Diffuse Large B cell lymphoma,

WHAT IS CLAIMED:

1. A stable liquid pharmaceutical formulation of an anti-PVRIG antibody comprising:
 - (a) an anti-PVRIG antibody, wherein said anti-PVRIG antibody comprises:
 - i) a heavy chain variable domain comprising the vhCDR1, vhCDR2, and vhCDR3 from the heavy chain of CHA.7.518.1.H4(S241P) (SEQ ID NO:4), and
 - ii) a light chain variable domain comprising the vlCDR1, vlCDR2, and vlCDR3 from the light chain of CHA.7.518.1.H4(S241P) (SEQ ID NO:9);
 - (b) from 10 mM to 100 mM histidine;
 - (c) from 30 mM to 100 mM NaCl;
 - (d) from 20 mM to 150 mM L-Arginine; and
 - (e) from 0.005% to 0.1% w/v polysorbate 80,wherein the composition has a pH from 5.5 to 7.0.
2. The stable liquid pharmaceutical formulation according to any one of claim 1, wherein said anti-PVRIG antibody comprises a CH1-hinge-CH2-CH3 sequence of IgG4 (SEQ ID NO:17 or SEQ ID NO:50), wherein said hinge region optionally comprises mutations.
3. The stable liquid pharmaceutical formulation according to any one of claims 1 or 2, wherein said anti-PVRIG antibody comprises the CH1-hinge-CH2-CH3 region from IgG1, IgG2, IgG3, or IgG4, wherein said hinge region optionally comprises mutations.
4. The stable liquid pharmaceutical formulation according to any one of claims 1-3, wherein said heavy chain variable domain is from the heavy chain of CHA.7.518.1.H4(S241P) (SEQ ID NO:4) and said light chain variable domain is from the light chain of CHA.7.518.1.H4(S241P) (SEQ ID NO:9).
5. The stable liquid pharmaceutical formulation according to any one of claims 1-4, wherein said anti-PVRIG antibody comprises a CL region of human kappa 2 light chain.
6. The stable liquid pharmaceutical formulation according to any one of claims 1-5, wherein said pharmaceutical formulation comprises from 10 mM to 80 mM histidine, from 15 mM to 70 mM histidine, from 20 mM to 60 mM histidine, from 20 mM to 50 mM histidine, or from 20 mM to 30 mM histidine.

7. The stable liquid pharmaceutical formulation according to any one of claims 1-6, wherein said pharmaceutical formulation comprises about 25 mM histidine.
8. The stable liquid pharmaceutical formulation according to any one of claims 1-7, wherein said pharmaceutical formulation comprises from 30 mM to 100 mM NaCl, from 30 mM to 90 mM NaCl, from 40 mM to 80 mM NaCl, from 30 mM to 70 mM histidine, or from 45 mM to 70 mM NaCl.
9. The stable liquid pharmaceutical formulation according to any one of claims 1-8, wherein said pharmaceutical formulation comprises about 60 mM NaCl.
10. The stable liquid pharmaceutical formulation according to any one of claims 1-9, wherein said pharmaceutical formulation comprises from 20 mM to 140 mM L-arginine, from 30 mM to 140 mM L-arginine, from 40 mM to 130 mM L-arginine, from 50 mM to 120 mM L-arginine, from 60 mM to 110 mM L-arginine, from 70 mM to 110 mM L-arginine, from 80 mM to 110 mM L-arginine, or from 90 mM to 110 mM L-arginine.
11. The stable liquid pharmaceutical formulation according to any one of claims 1-10, wherein said pharmaceutical formulation comprises about 100 mM L-arginine.
12. The stable liquid pharmaceutical formulation according to any one of claims 1-11, wherein said pharmaceutical formulation comprises from 0.006% to 0.1% w/v polysorbate 80, from 0.007% to 0.09% w/v polysorbate 80, from 0.008% to 0.08% w/v polysorbate 80, from 0.009% to 0.09% w/v polysorbate 80, from 0.01% to 0.08% w/v polysorbate 80, from 0.01% to 0.07% w/v polysorbate 80, from 0.01% to 0.07% w/v polysorbate 80, or from 0.01% to 0.06% w/v polysorbate 80, or from 0.009% to 0.05% w/v polysorbate 80.
13. The stable liquid pharmaceutical formulation according to any one of claims 1-12, wherein said pharmaceutical formulation comprises about 0.01% polysorbate 80.
14. The stable liquid pharmaceutical formulation according to any one of claims 1-13, wherein said pH is from 6 to 7.0.
15. The stable liquid pharmaceutical formulation according to any one of claims 1-14, wherein said pH is from 6.3 to 6.8.

16. The stable liquid pharmaceutical formulation according to any one of claims 1-15, wherein said pH is 6.5 +/- 0.2.
17. The stable liquid pharmaceutical formulation according to any one of claims 1-16, wherein said anti-PVRIG antibody is at a concentration of from 10 mg/mL to 40 mg/mL, 15 mg/mL to 40 mg/mL, 15 mg/mL to 30 mg/mL, 10 mg/mL to 25 mg/mL, or 15 mg/mL to 25 mg/mL.
18. The stable liquid pharmaceutical formulation according to any one of claims 1-17, wherein said formulation is stable at 2°C to 8°C for at least 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, 9 weeks, or 10 weeks.
19. The stable liquid pharmaceutical formulation according to any one of claims 1-18, wherein said formulation is stable at about 20°C to 25 °C for at least 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, or 6 weeks.
20. The stable liquid pharmaceutical formulation according to any one of claims 1-19, wherein said formulation is stable at 35°C to 40°C for at least 1 week, 2 weeks, 3 weeks, 4 weeks, or 5 weeks.
21. The stable liquid pharmaceutical formulation according to any one of claims 1-20, wherein said anti-PVRIG antibody is at a concentration of about 20 mg/mL.
22. The stable liquid pharmaceutical formulation according to any one of claims 1-21, wherein said anti-PVRIG antibody formulation comprises:
- a) a heavy chain comprising:
 - i) a VH-CH1-hinge-CH2-CH3, wherein the VH is from CHA.7.518.1.H4(S241P) (SEQ ID NO:4) and wherein the CH1-hinge-CH2-CH3 region is from IgG4; and
 - b) a light chain comprising:
 - i) a VL-CL, wherein the VL from CHA.7.518.1.H4(S241P) (SEQ ID NO:9) and wherein the CL region is from human kappa 2 light chain.

23. The stable liquid pharmaceutical formulation according to claim 24, wherein said hinge region optionally comprises mutations.

24. The stable liquid pharmaceutical formulation of claim 23, wherein said hinge region optionally comprises mutations.

25. The stable liquid pharmaceutical formulation according to any one of claims 1-24, wherein said anti-PVRIG antibody formulation comprises:

- i) a heavy chain comprising the heavy chain from CHA.7.518.1.H4(S241P) (SEQ ID NO:8); and
- ii) a light chain comprising the light chain from CHA.7.518.1.H4(S241P) (SEQ ID NO:13).

26. The stable liquid pharmaceutical formulation according to any one of claims 1-25, said anti-PVRIG antibody formulation comprising:

- (a) an anti-PVRIG antibody, wherein said anti-PVRIG antibody comprises:
 - i) a heavy chain variable domain comprising the vhCDR1, vhCDR2, and vhCDR3 from the heavy chain of CHA.7.518.1.H4(S241P) (SEQ ID NO:4), and
 - ii) a light chain variable domain comprising the vlCDR1, vlCDR2, and vlCDR3 from the light chain of CHA.7.518.1.H4(S241P) (SEQ ID NO:9);
- (b) about 25 mM histidine;
- (c) about 60 mM NaCl;
- (d) about 100 mM L-Arginine; and
- (e) about 0.01% w/v polysorbate 80,

wherein the composition has a pH from 6.5 +/- 0.2.

27. The stable liquid pharmaceutical formulation according to any one of claims 1-26, said anti-PVRIG antibody formulation comprising:

- (a) an anti-PVRIG antibody, wherein said anti-PVRIG antibody comprises:

i) a heavy chain comprising the heavy chain from CHA.7.518.1.H4(S241P) (SEQ ID NO:8); and

ii) a light chain comprising the light chain from CHA.7.518.1.H4(S241P) (SEQ ID NO:13);

(b) about 25 mM histidine;

(c) about 60 mM NaCl;

(d) about 100 mM L-Arginine; and

(e) about 0.01% w/v polysorbate 80,

wherein the composition has a pH from 6.5 +/- 0.2.

~~28. The stable liquid pharmaceutical formulation according to any one of claims 1-27, wherein said anti-PVRIG antibody is administered at a dosage of about 0.01 mg/kg to about 20 mg/kg of the anti-PVRIG antibody or about 0.01 mg/kg to about 10 mg/kg of the anti-PVRIG antibody.~~

~~29. The stable liquid pharmaceutical formulation according to any one of claims 1-27, wherein said anti-PVRIG antibody is administered at a dosage of about 0.01 mg/kg, 0.03 mg/kg, 0.1 mg/kg, 0.3 mg/kg, 1 mg/kg, 3 mg/kg, 10 mg/kg, or 20 mg/kg of the anti-PVRIG antibody.~~

~~30. The stable liquid pharmaceutical formulation according to any one of claims 1-29, wherein said anti-PVRIG antibody is administered 20 mg/kg every 4 weeks.~~

~~31. The stable liquid pharmaceutical formulation according to any one of claims 1-30, wherein said stable liquid pharmaceutical formulation is administered for the treatment of cancer.~~

~~32~~28. The stable liquid pharmaceutical formulation according to any one of claims 1-~~31~~27, for use in ~~a method of treating cancer~~therapy.

~~33~~29. Use of ~~The stable liquid pharmaceutical formulation according to any one of claims 1-27~~ claim 31 or 32 in the manufacture of a medicament for treating cancer, wherein said cancer selected from the group consisting of prostate cancer, liver cancer (HCC), colorectal cancer

(CRC), colorectal cancer MSS (MSS-CRC; including refractory MSS colorectal), CRC (MSS unknown), ovarian cancer (including ovarian carcinoma), endometrial cancer (including endometrial carcinoma), breast cancer, pancreatic cancer, stomach cancer, cervical cancer, head and neck cancer, thyroid cancer, testis cancer, urothelial cancer, lung cancer, melanoma, non-melanoma skin cancer (squamous and basal cell carcinoma), [malignant melanoma](#), glioma, renal cell cancer (RCC), renal cell carcinoma (RCC), lymphoma (non-Hodgkins' lymphoma (NHL) and Hodgkin's lymphoma (HD)), Acute myeloid leukemia (AML), T cell Acute Lymphoblastic Leukemia (T-ALL), Diffuse Large B cell lymphoma, [multiple myeloma](#), testicular germ cell tumors, mesothelioma, esophageal cancer, triple negative breast cancer, Merkel Cells cancer, MSI-high cancer, KRAS mutant tumors, adult T-cell leukemia/lymphoma, pleural mesothelioma, anal SCC, [small-cell lung cancer](#), neuroendocrine lung cancer (including neuroendocrine lung carcinoma), NSCLC, NSCL (large cell), NSCLC large cell, NSCLC, squamous cell [cancer](#), [adenocarcinoma of the lung](#), cervical SCC, malignant melanoma, pancreatic cancer, pancreatic adenocarcinoma, adenoid cystic cancer (including adenoid cystic carcinoma), primary peritoneal cancer, microsatellite stable primary peritoneal cancer, platinum resistant microsatellite stable primary peritoneal cancer, and/or Myelodysplastic syndromes (MDS).

[30. The stable liquid pharmaceutical formulation for use according to claim 28, or the use of claim 29, wherein said anti-PVRIG antibody is to be administered at a dosage of 0.01 mg/kg to 20 mg/kg of the anti-PVRIG antibody or 0.01 mg/kg to 10 mg/kg of the anti-PVRIG antibody.](#)

[31. The stable liquid pharmaceutical formulation for use according to claim 28, or the use of claim 29, wherein said anti-PVRIG antibody is to be administered at a dosage of about 0.01 mg/kg, 0.03 mg/kg, 0.1 mg/kg, 0.3 mg/kg, 1 mg/kg, 3 mg/kg, 10 mg/kg, or 20 mg/kg of the anti-PVRIG antibody.](#)

[32. The stable liquid pharmaceutical formulation for use according to claim 28, or the use of claim 29, wherein said anti-PVRIG antibody is to be administered 20 mg/kg every 4 weeks.](#)