

Claims:

[Claim 1]. A combination of (i) an oncolytic adenovirus (OncAd), (ii) a helper-dependent adenovirus (HDA) comprising nucleic acid encoding IL-12 and an antagonist anti-PD-L1 antibody, and (iii) at least one T cell comprising a chimeric antigen receptor (CAR) wherein the CAR comprises an antigen binding domain capable of specific binding to HER2, for use in a method of treating a cancer comprising cells expressing HER2.

[Claim 2]. The combination for use according to claim 1, wherein the virus comprising nucleic acid encoding IL-12 and an antagonist anti-PD-L1 antibody further comprises nucleic acid encoding a thymidine kinase.

[Claim 3]. The combination for use according to claim 1 or claim 2, wherein the oncolytic adenovirus (OncAd) is derived from adenovirus 5 (Ad5).

[Claim 4]. The combination for use according to any one of claims 1 to 3, wherein the oncolytic adenovirus (OncAd) encodes an E1A protein which displays reduced binding to Rb protein as compared to E1A protein encoded by Ad5.

[Claim 5]. The combination for use according to any one of claims 1 to 4, wherein the oncolytic adenovirus (OncAd) encodes an E1A protein lacking the amino acid sequence LTCHEACF (SEQ ID NO:52).

[Claim 6]. The combination for use according to any one of claims 1 to 5, wherein the oncolytic adenovirus (OncAd) encodes an E1A protein comprising, or consisting of, the amino acid sequence SEQ ID NO:34.

[Claim 7]. The combination for use according to any one of claims 4 to 6, wherein the oncolytic adenovirus (OncAd) comprises a nucleic acid sequence having at least 90% sequence identity to SEQ ID NO:55.

[Claim 8]. The combination for use according to any one of claims 1 to 7, wherein the CAR comprises an antigen-binding domain comprising:

a VL domain comprising:

LC-CDR1: SEQ ID NO:10;

LC-CDR2: SEQ ID NO:11;

LC-CDR3: SEQ ID NO:12;

and a VH domain comprising:

HC-CDR1: SEQ ID NO:13;

HC-CDR2: SEQ ID NO:14;

HC-CDR3: SEQ ID NO:15;

or

a VL domain comprising:

LC-CDR1: SEQ ID NO:18;

LC-CDR2: SEQ ID NO:19;

LC-CDR3: SEQ ID NO:20;

and a VH domain comprising:

HC-CDR1: SEQ ID NO:21;

HC-CDR2: SEQ ID NO:22;

HC-CDR3: SEQ ID NO:23;

or

a VL domain comprising:

LC-CDR1: SEQ ID NO:26;

LC-CDR2: SEQ ID NO:27;

LC-CDR3: SEQ ID NO:28;

and a VH domain comprising:

HC-CDR1: SEQ ID NO:29;

HC-CDR2: SEQ ID NO:30;

HC-CDR3: SEQ ID NO:31;

or

a VL domain comprising:

LC-CDR1: SEQ ID NO:57;

LC-CDR2: SEQ ID NO:58;

LC-CDR3: SEQ ID NO:59;

and a VH domain comprising:

HC-CDR1: SEQ ID NO:60;

HC-CDR2: SEQ ID NO:61;

HC-CDR3: SEQ ID NO:62.

[Claim 9]. The combination for use according to claim 8, wherein the CAR comprises an antigen binding domain comprising:

a VL comprising, or consisting of, an amino acid sequence having at least 75% sequence identity to SEQ ID NO:16 and a VH comprising, or consisting of, an amino acid sequence having at least 75% sequence identity to SEQ ID NO:17;

or

a VL comprising, or consisting of, an amino acid sequence having at least 75% sequence identity to SEQ ID NO:24 and a VH comprising, or consisting of, an amino acid sequence having at least 75% sequence identity to SEQ ID NO:25;

or

a VL comprising, or consisting of, an amino acid sequence having at least 75% sequence identity to SEQ ID NO:32 and a VH comprising, or consisting of, an amino acid sequence having at least 75% sequence identity to SEQ ID NO:33;

or

a VL comprising, or consisting of, an amino acid sequence having at least 75% sequence identity to SEQ ID NO:63 and a VH comprising, or consisting of, an amino acid sequence having at least 75% sequence identity to SEQ ID NO:64.

[Claim 10]. The combination for use according to any one of claims 2 to 9, wherein the thymidine kinase is HSV-1 thymidine kinase.

[Claim 11]. The combination for use according to any one of claims 1 to 10, wherein the method of treating a cancer comprises:

(a) isolating at least one cell from a subject;

(b) modifying the at least one cell to express or comprise a CAR specific for a cancer cell antigen, or a nucleic acid encoding a CAR specific for a cancer cell antigen,

(c) optionally expanding the modified at least one cell, and;

(d) administering the modified at least one cell to a subject.

[Claim 12]. The combination for use according to any one of claims 1 to 11, wherein the cancer is selected from head and neck cancer, nasopharyngeal carcinoma (NPC), cervical

carcinoma (CC), oropharyngeal carcinoma (OPC), gastric carcinoma (GC), hepatocellular carcinoma (HCC) and lung cancer.