

Targeted Gene Delivery Therapies for Cervical Cancer

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Table S1. Gene therapy clinical trials worldwide on cervical cancer approved/initiated 1989–2018.

Therapeutic Strategy	Intervention	Clinical Trial Reference	Phase	Date Approved
Tumor suppressor gene restoration	Intratumoral administration of Gendicina® + RT in Advanced cervical cancer	CN-0010	Phase III	2008-04 Open
Oncofactor inhibition strategy	Use of CRISPR-Cas9 and TALEN to produce disruption of HPV E6/E7 knockout, in CIN	CN-0059	Phase I	2017-07 Open
Oncolytic virus	Injection of rAd type 5 (H101), an E1b-deleted adenovirus, + RT and chemotherapy, in locally advanced cervical cancer	CN-0054	Phase II	2015-03 Open
Oncolytic virus + immunopotentialion	Intravenous and intramuscular administration of Oncolytic MG1 expressing HPV E6-E7 antigen + Adenovirus vaccine expressing HPV E6-E7 proteins + Atezolizumab, in HPV Associated Cancer	US-1760	Phase I	2018-05 Open
Immunopotentialion	Vaccinia virus encoding HPV E6 and E7 antigens in Cervical cancer	UK-0001	Phase I/II	1995-06 Closed
	Intramuscular administration of a vaccinia virus encoding an IL-2, in Stage I cervical cancer	CH-0035	Phase I	1999 Closed (2002)
	Intramuscular administration of a vaccinia virus encoding an IL-2, in Advanced cervical cancer	CH-0036	Phase I	1999 Closed (2002)
	Intramuscular administration of a vaccinia virus encoding HPV antigens and IL-2, in Stage I cervical cancer	XX-0006	Phase I	1999 Closed (2002)
	Intramuscular administration of a vaccinia virus encoding HPV antigens and IL-2, in Advanced cervical cancer	XX-0007	Phase I	1999 Closed (2002)
	ZYC101a, composed by HPV E6 and E7 antigens, in Ano-genital neoplasia 3	UK-0071	Phase II	2001-01 Open
	Subcutaneous administration of RO5217790 (MVA-HPV-IL2, vaccine composed by a Modified Vaccinia Ankara (MVA) virus encoding HPV16 E6 and E7 antigens and an IL-2), in CIN 2/3	BE-0024/ ES-0010	Phase I	2009-05-05 Open
	Intramuscular administration of RO5217790 (MVA-HPV-IL2), in CIN 2/3CIN 2/3	US- 0958	Phase II	2008-12 Open
	Subcutaneous administration of TG4001 (MVA-HPV-IL2), in CIN 2/3	FR-0032	Phase II	2004 Open
Intramuscular administration of TG4001 (MVA-HPV-IL2), in CIN 3	US-0307	Phase I	1999 Closed	

Intramuscular administration of TG4001 (MVA-HPV-IL2), in Advanced cervical cancer	US-0309	Phase I	1999 Closed
MVA E2 recombinant vaccine in CIN 1/2	MX-0001	Phase II	N Open
TA-HPV, vaccine composed by HPV E6 and E7 antigens, in CIN 3	UK-0041	Phase I	1996-05 Open
TA-HPV vaccine, in CIN 3	UK-0042	Phase I	1997-08 Open
TA-HPV vaccine, in CIN 3	UK-0046	Phase I	1996-09 Closed
TA-HPV, vaccine composed by HPV E6 and E7 antigens, in CIN 3	UK-0047	Phase I	1998-01 Closed
TA-HPV vaccine, in High-grade anogenital intraepithelial neoplasia	UK-0074	Phase I	2001-01 Open
GX-188E, a DNA-based Therapeutic Vaccine composed by HPV E6 and E7 antigens, administered Intramuscularly by Electroporation, in CIN 2/3	EE-0001	Phase II	N Open
GX-188E vaccine, administered Intramuscularly by Electroporation (EP), in CIN 3	KR-0016	Phase II	2014-05 Open
Intramuscular administration of pNGVL4a-Sig/E7 (detox)/HSP70, vaccine composed by HPV16 E7 and heat shock protein 70, in CIN 2/3	US-0595	Phase I/II	2003 Open
Intramuscular administration of pNGVL4a-CRT/E7(detox), DNA vaccine composed by HPV16 E7 and CRT, in CIN 2/3	US-0984	Phase I/II	2009-06 Open
VGX-3100, a therapeutic DNA vaccine composed by HPV16 E6-E7 and HPV18 E6-E7 fusion proteins, administered intramuscularly by electroporation, in CIN 2/3	US-0916	Phase I	2008-04 Open
VGX-3100 vaccine, administered intramuscularly by electroporation, in CIN 2/3	US-1093	Phase II	2011-02 Open
VGX-3100 vaccine, administered intramuscularly by electroporation, in Cervical cancer	US-1040	Phase I	2010-04 Open
VGX-3100 vaccine, administered intramuscularly by electroporation + INO-9012, vaccine composed by IL-2, in Cervical cancer	US-1283	Phase I	2013-12 Open
VGX-3100 vaccine, administered intramuscularly by electroporation, in HSIL of cervix	US-1528	Phase IV	2016-04 Open
MEDI0457 (INO-3112), composed of HPV16 E6-E7 and HPV18 E6-E7 Fusion Protein + durvalumab (MEDI4736), anti-PD-L1, in Recurrent-Metastatic Human Papilloma Virus Associated Cancers	US-1686	Phase II	2017-10 Open
Vaccination with Listeria monocytogenes Expressing HPV16 E7, in Progressive, Recurrent and Advanced Cervical cancer	US-0592	Phase I	2003 Open
Intravenous administration of ADXS11-001, vaccine composed by HPV E7	US-1082	Phase II	2010-12 Open

antigens, in Persistent or Recurrent cervical cancer			
Intravenous administration of ADXS11-001 vaccine, in Cervical cancer	US-1361	Phase I/II	2014-11 Open
Intravenous administration of ADXS11-001 vaccine ± durvalumab (MEDI4736), anti-PD-L1, in Recurrent-Metastatic Cervical or HPV+ Head and Neck Cancer	US-1362	Phase I/II	2014-11 Open
Intravenous administration of ADXS11-001 vaccine ± Epcadostat (INCB024360), in Stage I to IIIB Cervical Cancer	US-1430	Phase II	2015-05 Open
Intravenous administration of ADXS11-001 vaccine, following CRT as adjuvant, in High risk locally advanced cervical cancer	US-1506	Phase III	2016-02 Open
Intravenous administration of ADXS11-001 vaccine, following CRT as adjuvant, in High risk locally advanced cervical cancer	XX-0042	Phase III	2017-08 Open
Intradermal administration of TTFC-E7SH vaccine, composed of the fusion protein domain1 of tetanus toxin fragment C and the shuffled version of HPV16 E7, in Stage IV squamous cell carcinoma	NL-0035	Phase I	2013-04 Open
Intradermal vaccination with naked DNA, encoding the fusion protein of a carrier sequence sig-HELP-kdel and the shuffled version of HPV16 E6 and E7 antigens, in HPV induced (pre)malignancies	NL-0039	Phase I	2015-09 Open (2025)
Replication-incompetent Semliki Forest Virus replicon particles encoding HPV16 E6 and E7 antigens, in HPV-induced premalignant cervical lesions	NL-0030	Phase I/II	2011-04-07 Open
Intramuscular administration of a HPV16-Specific Therapeutic DNA-rVaccinia Vaccination + topical imiquimod, in CIN3	US-0928	Phase I	2008-07 Open
CAR-T cells (GD2 CAR, PSMA CAR, Muc1 CAR, Mesothelin CAR) in Cervical cancer	CN-0105	Phase I/II	2017-11 Open
TCR gene therapy targeting HPV16 E6, in HPV-associated cancer	US-1331	Phase II	2014-07 Open
HPV-16/18 E6/E7- specific T-cells + Dominant Negative TGF-β Receptor II, in Relapsed HPV-Associated Cancers	US-1369	Phase I	2015-01 Open
HPV-16 E6 TCR ± - PD-1 Blockade Antibody, in HPV-Associated Cancer	US-1517	Phase I/II	2016-04 Open
HPV16 E7 TCR Engineered T Cells in Relapsed-Refractory HPV16+ Cancer	US-1793	Phase I	2018-07 Open

Abbreviations: N = no data; Note: <http://www.abedia.com/wiley/index.html>, Database of clinical trials updated in December 2018, accessed March 10, 2020.