

Supplementary information

Intratumoural administration and tumour tissue targeting of cancer immunotherapies

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Supplementary Table 1 | Ongoing trials of intratumoural PRR agonist therapies

Target	Agent	Trial name	ClinicalTrials.gov identifier
TLR3	Poly I:C	In Situ Vaccine for Low-Grade Lymphoma: Combination of Intratumoral Flt3L and Poly-ICLC With Low-Dose Radiotherapy	NCT01976585
TLR3	Poly I:C	In Situ, Autologous Therapeutic Vaccination Against Solid Cancers With Intratumoral Hiltonol®	NCT02423863
TLR3	Poly I:C	Neoadjuvant Hiltonol® (PolyICLC) for Prostate Cancer	NCT03262103
TLR3	Poly I:C	Vaccination With Flt3L, Radiation, and Poly-ICLC	NCT03789097
TLR-3	Hiltonol	Poly-ICLC (Hiltonol®) Vaccine In Malignant Pleural Mesothelioma	NCT04525859
TLR4	G100	Atezolizumab Combined With Intratumoral G100 AnD Immunogenic Radiotherapy in Patients With Advanced Solid Tumors	NCT03915678
TLR7	LHC165	Study of the Safety and Efficacy of LHC165 Single Agent and in Combination With PDR001 in Patients With Advanced Malignancies	NCT03301896
TLR7/8	NKTR-262	A Study of NKTR-262 in Combination With Bempegaldesleukin (NKTR-214) and With Bempegaldesleukin Plus Nivolumab in Patients With Locally Advanced or Metastatic Solid Tumor Malignancies	NCT03435640
TLR8	VTX-2337	A Study to Evaluate Immune Biomarker Modulation in Response to VTX-2337 in Combination With an Anti- PD-1 Inhibitor in Head and Neck Cancer	NCT03906526
TLR8	Motolimod	Intratumoral Microdosing of Motolimod in HNSCC	NCT04272333
TLR9	Tilsotolimod (IMO-2125)	Intratumoral Tilsotolimod, a TLR-9 Agonist, Together With Intratumoral Ipilimumab and Intravenous Nivolumab in Patients With Advanced Cancers	NCT04270864
TLR9	Tilsotolimod (IMO-2125)	A Randomized Controlled Phase II Trial With Intradermal IMO-2125 in Pathological Tumor Stage (p) T3-4 cN0M0 Melanoma (INTRIM)	NCT04126876
TLR9	Tilsotolimod (IMO-2125)	A Study of IMO-2125 in Combination With Ipilimumab Versus Ipilimumab Alone in Subjects With Anti-PD-1 Refractory Melanoma (ILLUMINATE-301)	NCT03445533
TLR9	Tilsotolimod (IMO-2125)	Study of Tilsotolimod in Combination With Nivolumab and Ipilimumab for the Treatment of Solid Tumors (ILLUMINATE-206)	NCT03865082
TLR9	ABBV-368	A Study to Determine the Safety, Tolerability, Pharmacokinetics, and Preliminary Efficacy of ABBV-368 Plus Tilsotolimod and Other Therapy Combinations in Participants With Recurrent/Metastatic Head and Neck Squamous Cell Carcinoma	NCT04196283
TLR9	MGN1703	Ipilimumab (Immunotherapy) and MGN1703 (TLR Agonist) in Patients With Advanced Solid Malignancies	NCT02668770
TLR9	CMP-001	Clinical Study of CMP-001 in Combination With Pembrolizumab or as a Monotherapy	NCT02680184
TLR9	CMP-001	Phase 1B Study Evaluating Alternative Routes of Administration of CMP-001 in Combination With Pembrolizumab in Participants With Advanced Melanoma	NCT03084640
TLR9	CMP-001	CMP-001 for Relapsed and Refractory Lymphoma	NCT03983668
TLR9	CMP-001	Combined Immunotherapy and Radiosurgery for Metastatic Colorectal Cancer	NCT03507699
TLR9	CMP-001	CMP-001 in Combo With Nivolumab in Stage IIIB/C/D Melanoma Patients With Clinically Apparent Lymph Node Disease	NCT03618641
TLR9	CMP-001	CMP-001 and INCAGN01949 for Patients With Stage IV Pancreatic Cancer and Other Cancers Except Melanoma	NCT04387071
TLR9	SD-101	SD-101, Nivolumab, and Radiation Therapy in Treating Patients With Chemotherapy-Refractory Metastatic Pancreatic Cancer	NCT04050085
TLR9	SD-101	TLR9 Agonist SD-101, Ibrutinib, and Radiation Therapy in Treating Patients With Relapsed or Refractory Grade 1-3A Follicular Lymphoma	NCT02927964
TLR9	SD-101	Pembrolizumab +/- SD-101 in Hormone-Naïve Oligometastatic Prostate Cancer With RT and iADT	NCT03007732
TLR9	SD-101	UCDCC#271: Phase I/II Trial of Epcadostat, Intralesional SD101, Radiotherapy in Patients With Lymphoma	NCT03322384
TLR9	SD-101	TLR9 Agonist SD-101, Anti-OX40 Antibody BMS 986178, and Radiation Therapy in Treating Patients With Low-Grade B-Cell Non-Hodgkin Lymphomas	NCT03410901
TLR9	Cavrotolimod	Intratumoral Cavrotolimod Combined With Pembrolizumab or Cemiplimab in Patients With Advanced Solid Tumors	NCT03684785

TLR3, MDA5 and RIG-I	BO-112	Nivolumab and BO-112 Before Surgery for the Treatment of Resectable Soft Tissue Sarcoma	NCT04420975
TLR3, MDA5 and RIG-I	BO-112	Study of BO-112 With Pembrolizumab for Colorectal or Gastric/GEJ Cancer With Liver Metastasis	NCT04508140
TLR7/8 and RIG-I	CV8102	Study of Intratumoral CV8102 in cMEL, cSCC, hnSCC, and ACC	NCT03291002
RIG-I	MK-4621	Intratumoral/Intralesional Administration of MK-4621/JetPEI™ With or Without Pembrolizumab in Participants With Advanced/Metastatic or Recurrent Solid Tumors (MK-4621-002)	NCT03739138
STING	MIW815	Safety and Efficacy of MIW815 (ADU-S100) +/- Ipilimumab in Patients With Advanced/Metastatic Solid Tumors or Lymphomas	NCT02675439
STING	MK-1454	Study of MK-1454 Alone or in Combination With Pembrolizumab (MK-3475) in Participants With Advanced/Metastatic Solid Tumors or Lymphomas (MK-1454-001)	NCT03010176
STING	MK-1454	Study of Intratumoral (IT) MK-1454 in Combination With Intravenous (IV) Pembrolizumab (MK-3475) Compared to IV Pembrolizumab Alone as the First Line Treatment of Metastatic or Unresectable, Recurrent Head and Neck Squamous Cell Carcinoma (HNSCC) (MK-1454-002)	NCT04220866
STING	MIW815	Study of the Safety and Efficacy of MIW815 With PDR001 to Patients With Advanced/Metastatic Solid Tumors or Lymphomas	NCT03172936
STING	MK-2118	Study of MK-2118 Administered as Intratumoral Injection as Monotherapy and in Combination With Pembrolizumab (MK-3475) or by Subcutaneous Injection in Combination With Pembrolizumab in the Treatment of Adults With Advanced/Metastatic Solid Tumors or Lymphomas (MK-2118-001)	NCT03249792
STING	ADU-S100	Efficacy and Safety Trial of ADU-S100 and Pembrolizumab in Head and Neck Cancer	NCT03937141
STING	BMS-986301	An Investigational Immunotherapy Study of BMS-986301 Alone or in Combination With Nivolumab, and Ipilimumab in Participants With Advanced Solid Cancers	NCT03956680
STING	IMSA101	Safety and Efficacy Study of IMSA101 in Refractory Malignancies	NCT04020185
STING	E7766	Study of Intratumorally Administered Stimulator of Interferon Genes (STING) Agonist E7766 in Participants With Advanced Solid Tumors or Lymphomas - INSTAL-101	NCT04144140
STING	BI 1387446	A Study to Find the Best Dose of BI 1387446 Alone or in Combination With BI 754091 in Patients With Different Types of Advanced or Metastatic Cancer (Solid Tumors)	NCT04147234
STING or NLRP3	TAK-676 or BMS-986299	Phase 0 Master Protocol for CIVO Intratumoral Microdosing of Anti-Cancer Therapies	NCT04541108

MDA-5, melanoma differentiation-associated protein 5; poly I:C, polyinosinic-polycytidylic acid; PRR, pattern recognition receptor; RIG-1, retinoic acid-inducible gene; STING, stimulator of interferon genes; TLR, Toll-like receptor.

Supplementary Table 2 | Ongoing trials of intratumoural viral therapies

Type of virus	Agent	Trial name	ClinicalTrials.gov identifier
Adenovirus	VCN-01	Safety, Tolerability, and Efficacy of VCN-01 With Durvalumab in R/M Head and Neck Squamous Cell Carcinoma	NCT03799744
Adenovirus	Ad-RTS-hIL-12	A Study of Ad-RTS-hIL-12 With Veledimex in Subjects With Glioblastoma or Malignant Glioma	NCT02026271
Adenovirus	DNX-2401	Combination Adenovirus + Pembrolizumab to Trigger Immune Virus Effects (CAPTIVE)	NCT02798406
Adenovirus	DNX-2401	Oncolytic Adenovirus, DNX-2401, for Naive Diffuse Intrinsic Pontine Gliomas	NCT03178032
Adenovirus	DNX-2440	DNX-2440 Oncolytic Adenovirus for Recurrent Glioblastoma	NCT03714334
Adenovirus	LOAd703	LOAd703 Oncolytic Virus Therapy for Pancreatic Cancer	NCT02705196
Adenovirus	CAdVEC	Binary Oncolytic Adenovirus in Combination With HER2-Specific Autologous CAR VST, Advanced HER2 Positive Solid Tumors	NCT03740256
Adenovirus	OBP-301	Evaluate Efficacy, Immunological Response of Intratumoral/Intralesional Oncolytic Virus (OBP-301) in Metastatic Melanoma	NCT03190824
Adenovirus	MTG201	MTG201 Plus Nivolumab in Patients With Relapsed Pleural Mesothelioma	NCT04013334
Adenovirus	OBP-301	Phase I Study to Evaluate the Safety and Efficacy of Telomelysin (OBP-301) in Patients With Hepatocellular Carcinoma	NCT02293850
Adenovirus	ORCA-010	First in Man Clinical Study to Evaluate Safety and Tolerability of an Oncolytic Adenovirus in Prostate Cancer Patients.	NCT04097002
Adenovirus	LOAd703	Trial Investigating an Immunostimulatory Oncolytic Adenovirus for Cancer	NCT03225989
Adenovirus	DNX-2401	Combination Adenovirus + Pembrolizumab to Trigger Immune Virus Effects	NCT02798406
Adenovirus	ONCOS-102	A Pilot Study of Sequential ONCOS-102, an Engineered Oncolytic Adenovirus Expressing GMCSF, and Pembrolizumab in Patients With Advanced or Unresectable Melanoma Progressing After Programmed Cell Death Protein 1 (PD1) Blockade	NCT03003676
Adenovirus	ASN-002	Safety and Efficacy of ASN-002 Combined With a Hedgehog Pathway Inhibitor	NCT04416516
Adenovirus	Ad5-yCD/mutTKSR39rep-hIL12	Phase 1 Trial of Interleukin 12 Gene Therapy for Metastatic Pancreatic Cancer	NCT03281382
Adenovirus	GMCI	Neoadjuvant GMCI Plus Chemoradiation for Advanced Non-Metastatic Pancreatic Adenocarcinoma	NCT02446093
Adenovirus	OBP-301	Special Combination of OBP-301 and Pembrolizumab	NCT03172819
Adenovirus	OBP-301	Evaluate Efficacy, Immunological Response of Intratumoral/Intralesional Oncolytic Virus (OBP-301) in Metastatic Melanoma	NCT03190824
Vaccinia Virus	Pexa-Vec	Immunization Strategy With Intra-tumoral Injections of Pexa-Vec With Ipilimumab in Metastatic / Advanced Solid Tumors.	NCT02977156
Vaccinia Virus	ASP9801	A Study of an Intratumoral Oncolytic Virus in Patients With Advanced Metastatic Solid Tumors	NCT03954067
Vaccinia Virus	Pexa-Vec	A Trial to Evaluate the Safety and Efficacy of the Combination of the Oncolytic Immunotherapy Pexa-Vec With the PD-1 Receptor Blocking Antibody Nivolumab in the First-line Treatment of Advanced Hepatocellular Carcinoma (HCC)	NCT03071094
Vaccinia Virus	Pexa-Vec	A Study of Recombinant Vaccinia Virus in Combination With REGN2810 for Renal Cell Carcinoma	NCT03294083
Vaccinia Virus	Pexa-Vec	Hepatocellular Carcinoma Study Comparing Vaccinia Virus Based Immunotherapy Plus Sorafenib vs Sorafenib Alone	NCT02562755
Vaccinia Virus	TBio-6517	Study of TBio-6517, Given Intratumorally, Alone or in Combination With Pembrolizumab, in Solid Tumors	NCT04301011

Modified Vaccinia Ankara–Bavarian Nordic	MVA-BN-Brachyury	Perioperative Atezolizumab With MVA-BN-Brachyury and PROSTVAC For Intermediate-Risk And High-Risk Localized Prostate Cancer	NCT04020094
Dengue Virus	PV-001-DV	Arm 2: Intratumoral Injection of Dengue Virus-1 #45AZ5 (PV-001-DV) in Patients With Advanced Melanoma	NCT03989895
Dengue Virus	PV-001-DV	Arm 3: Intratumoral Injection of PV-001-DV in Combination With Infusion of PV-001-DC in Patients With Advanced Melanoma	NCT03990493
Newcastle disease virus	V938	A Study of Intratumoral/Intralesional Administration of V938 in Combination With Pembrolizumab (MK-3475) in Participants With Advanced/Metastatic or Recurrent Malignancies (V938-001)	NCT04135352
Measles virus	TMV-018	A Safety Study of TMV-018 in Patients With Tumors of the Gastrointestinal Tract	NCT04195373
Measles Virus	MV-s-NAP	A Vaccine (MV-s-NAP) for the Treatment of Patients With Invasive Metastatic Breast Cancer	NCT04521764
Measles Virus	MV-NIS	Viral Therapy In Treating Patients With Recurrent or Metastatic Squamous Cell Carcinoma of the Head and Neck Cancer or Metastatic Breast Cancer	NCT01846091
Coxsackie Virus	V937	A Study of V937 in Combination With Pembrolizumab (MK-3475) in Participants With Advanced/Metastatic Solid Tumors (V937-013)	NCT04521621
Coxsackie Virus	V937	Efficacy, Safety, and Tolerability of V937 Administered Intravenously or Intratumorally With Pembrolizumab (MK-3475) Versus Pembrolizumab Alone in Participants With Advanced/Metastatic Melanoma (V937-011)	NCT04152863
Vesicular Stomatitis Virus	VSV-IFN β -TYRP1	Modified Virus VSV-IFN β TYRP1 in Treating Patients With Stage III-IV Melanoma	NCT03865212
Vesicular Stomatitis Virus	VSV-IFN β	Viral Therapy in Treating Patient With Refractory Liver Cancer or Advanced Solid Tumors	NCT01628640
Vesicular Stomatitis Virus	VSV-IFN β -NIS	Administration of VSV-IFN β -NIS Monotherapy and in Combination With Avelumab in Patients With Refractory Solid Tumors	NCT02923466
Vesicular Stomatitis Virus	Voyager V1	Phase 2 Trial of Voyager V1 in Combination With Cemiplimab in Cancer Patients	NCT04291105
Fowlpox Virus	falimarev	Vaccine Therapy and Sargramostim in Treating Patients With Pancreas Cancer That Cannot Be Removed By Surgery	NCT00669734
Maraba Virus	MG1-MAGEA3	MG1-MAGEA3 With Ad-MAGEA3 and Pembrolizumab in Patients With Previously Treated Metastatic Melanoma or Cutaneous Squamous Cell Carcinoma	NCT03773744
Maraba Virus	MG1-E6E7	This is a Trial of MG1-E6E7 With Ad-E6E7 and Atezolizumab in Patients With HPV Associated Cancers	NCT03618953
Poliovirus	PVSRIPO	PVSRIPO for Recurrent Glioblastoma (GBM)	NCT01491893
Poliovirus	PVSRIPO	PVSRIPO and Pembrolizumab in Patients With Recurrent Glioblastoma	NCT04479241
Polio Virus	PVSRIPO	Examining Bioactivity of PVSRIPO in Invasive Breast Cancer	NCT03564782
Poliovirus	PVSRIPO	PVSRIPO for Patients With Unresectable Melanoma	NCT03712358
Arenavirus	HB-201	A Study of TheraT $\text{\textcircled{R}}$ Vector(s) Expressing HPV 16+ in Patients With HPV 16+ Confirmed Cancers	NCT04180215
Herpes Simplex Virus-1	ONCR-177	Study of ONCR-177 Alone and in Combination With PD-1 Blockade in Adult Subjects With Advanced and/or Refractory Cutaneous, Subcutaneous or Metastatic Nodal Solid Tumors	NCT04348916
Herpes Simplex Virus-	RP1	A Phase 1B Study of RP1 in Transplant Patients With Advanced Cutaneous Squamous Cell Carcinoma	NCT04349436
Herpes Simplex Virus-1	RP1	Study of RP1 Monotherapy and RP1 in Combination With Nivolumab	NCT03767348
Herpes Simplex Virus-1	RP1	Study Evaluating Cemiplimab Alone and Combined With RP1 in Treating Advanced Squamous Skin Cancer	NCT04050436
Herpes Simplex Virus-1	HSV G207	HSV G207 With a Single Radiation Dose in Children With Recurrent High-Grade Glioma	NCT04482933
Herpes Simplex Virus-1	T3011	A Clinical Study of T3011 in Patients With Advanced Cutaneous or Subcutaneous Malignancies	NCT04370587

Herpes Simplex Virus-1	OrienX010	Study to Evaluate OrienX010 in Combination With JS001 in the Treatment of Stage IV (M1c) Liver Metastasis From Melanoma	NCT04206358
Herpes Simplex Virus-1	OrienX010	Clinical Study to Evaluate OrienX010 in Combination With Treprizumab Injection as Neoadjuvant Treatment in Melanoma	NCT04197882
Herpes Simplex Virus-1	OrienX010	A Clinical Study to Evaluate the Safety and Efficacy of OrienX010 in Unresectable Malignant Melanoma Patients	NCT04200040
Herpes Simplex Virus	GEN2	GEN2 Directed Cancer Immunotherapy Trial	NCT04313868
Herpes Simplex Virus-1	rQNestin34.5v.2	A Study of the Treatment of Recurrent Malignant Glioma With rQNestin34.5v.2	NCT03152318
Herpes Simplex Virus-1	T-VEC	Single-arm Trial to Evaluate the Role of the Immune Response to Talimogene Laherparepvec in Unresected Melanoma	NCT02366195
Herpes Simplex Virus-1	T-VEC	Combining Talimogene Laherparepvec With BRAF and MEK Inhibitors in BRAF Mutated Advanced Melanoma	NCT03088176
Herpes Simplex Virus-1	T-VEC	Combination of Talimogene Laherparepvec With Atezolizumab in Early Breast Cancer	NCT03802604
Herpes Simplex Virus-1	T-VEC	Neoadjuvant T-VEC in High Risk Early Melanoma	NCT04427306
Herpes Simplex Virus-1	T-VEC	Study of Talimogene Laherparepvec (T-VEC) in Pancreatic Cancer	NCT03086642
Herpes Simplex Virus-1	T-VEC	Ipilimumab With or Without Talimogene Laherparepvec in Unresected Melanoma	NCT01740297
Herpes Simplex Virus-1	T-VEC	Neoadjuvant T-VEC in High Risk Early Melanoma	NCT04427306
Herpes Simplex Virus-1	T-VEC	A Study of T-VEC (Talimogene Laherparepvec) With or Without Radiotherapy for Melanoma, Merkel Cell Carcinoma, or Other Solid Tumors	NCT02819843
Herpes Simplex Virus-1	T-VEC	Study of T-VEC in Locally Advanced Cutaneous Angiosarcoma	NCT03921073
Herpes Simplex Virus-1	T-VEC	TVEC and Preop Radiation for Sarcoma	NCT02453191
Herpes Simplex Virus-1	T-VEC	Study of Talimogene Laherparepvec In Children With Advanced Non CNS Tumors	NCT02756845
Herpes Simplex Virus-1	T-VEC	Neo-adjuvant T-VEC + Nivolumab Combination Therapy for Resectable Early Metastatic (Stage IIIB/C/D-IV M1a) Melanoma With Injectable Disease	NCT04330430
Herpes Simplex Virus-1	T-VEC	Neoadjuvant Combination Immunotherapy for Stage III Melanoma	NCT03842943
Herpes Simplex Virus-1	T-VEC	Trial to Evaluate the Safety of Talimogene Laherparepvec Injected Into Tumors Alone and in Combination With Systemic Pembrolizumab MK-3475-611/Keynote-611	NCT02509507
Herpes Simplex Virus-1	T-VEC	T-VEC in Non-melanoma Skin Cancer	NCT03458117
Herpes Simplex Virus-1	T-VEC	Phase II Multicenter Study of Talimogene Laherparepvec in Classic or Endemic Kaposi Sarcoma	NCT04065152
Herpes Simplex Virus-1	T-VEC	Study of Talimogene Laherparepvec With Atezolizumab for Triple Negative Breast Cancer and Colorectal Cancer With Liver Metastases	NCT03256344
Herpes Simplex Virus-1	T-VEC	Single-arm Trial to Evaluate the Role of the Immune Response to Talimogene Laherparepvec in Unresected Melanoma	NCT02366195
Herpes Simplex Virus-1	T-VEC	Study to Evaluate the Safety/ Efficacy of T-VEC in Japanese Subjects With Unresectable Stage IIIB-IV Malignant Melanoma	NCT03064763
Herpes Simplex Virus-1	T-VEC	Efficacy and Safety of Talimogene Laherparepvec Neoadjuvant Treatment Plus Surgery Versus Surgery Alone for Melanoma	NCT02211131
Herpes Simplex Virus-1	T-VEC	Pembrolizumab With or Without Talimogene Laherparepvec or Talimogene Laherparepvec Placebo in Unresected Melanoma (KEYNOTE-034)	NCT02263508
Herpes Simplex Virus-1	T-VEC	Talimogene Laherparepvec With Pembrolizumab in Melanoma Following Progression on Prior Anti-PD-1 Based Therapy (MASTERKEY-115)	NCT04068181

Herpes Simplex Virus-1	T-VEC	Trial to Evaluate the Safety of Talimogene Laherparepvec Injected Into Tumors Alone and in Combination With Systemic Pembrolizumab MK-3475-611/Keynote-611	NCT02509507
Herpes Simplex Virus-1	T-VEC	Single-arm Trial to Evaluate the Role of the Immune Response to Talimogene Laherparepvec in Unresected Melanoma (TVEC-325)	NCT02366195
Herpes Simplex Virus-1	T-VEC	Talimogene Laherparepvec With Chemotherapy or Endocrine Therapy in Treating Participants With Metastatic, Unresectable, or Recurrent HER2- Negative Breast Cancer	NCT03554044
Herpes Simplex Virus-1	T-VEC	A Study of Talimogene Laherparepvec (T-VEC) in Combination With Pembrolizumab in Patients With Metastatic and/or Locally Advanced Sarcoma	NCT03069378
Herpes Simplex Virus-1	T-VEC	Talimogene Laherparepvec and Pembrolizumab in Treating Patients With Stage III-IV Melanoma	NCT02965716
Herpes Simplex Virus-1	TBI-1401 (HF10)	Phase I Study of TBI-1401(HF10) Plus Chemotherapy in Patients With Unresectable Pancreatic Cancer.	NCT03252808
Herpes Simplex Virus-1	TBI-1401 (HF10)	Neoadjuvant Trial of Nivolumab in Combination With HF10 Oncolytic Viral Therapy in Resectable Stage IIIB, IIIC, IVM1a Melanoma	NCT03259425

Supplementary Table 3 | Ongoing trials of intratumoural ICD-inducer therapies

Type of ICD inducer	Trial Name	ClinicalTrials.gov identifier
Rose bengal	A Study to Assess PV-10 Chemoablation of Cancer of the Liver	NCT00986661
Rose bengal	PV-10 in Combination With Pembrolizumab for Treatment of Metastatic Melanoma	NCT02557321
Rose bengal	A Phase 1 Study of PV-10 Chemoablation of Neuroendocrine Tumours (NET) Metastatic to the Liver	NCT02693067
Cisplatin and vinblastine	A Phase 1/2 Safety Study of Intratumorally Dosed INT230-6	NCT03058289
Nucleotide analogues (produced via adenoviral delivery of herpes simplex virus thymidine kinase)	Intratumoral Gene Mediated Cytotoxic Immunotherapy in Patients With Resectable Non-Small Cell Lung Cancer	NCT03131037
p53	Safety and Efficacy of p53 Gene Therapy Combined With Immune Checkpoint Inhibitors in Solid Tumors.	NCT03544723
Polidocanol (macrogol)	Intralesional Sclerosant for in Transit and Cutaneous Melanoma Metastases	NCT03754140
N-dihydrogalactochitosan	Intratumoral Injection of IP-001 Following Thermal Ablation in Patients With Advanced Solid Tumors.	NCT03993678
CyPep-1	CyPep-1 Injections in Cancer Inducing Lymphocyte Infiltrate Accumulations	NCT04260529
Tigilanol tiglate	Exploratory Phase Ib/IIa Study of Intratumourally Administered Tigilanol Tiglate to Assess Safety, Tolerability and Tumour Response in Patients with Head and Neck Squamous Cell Carcinoma	ACTRN12619001407189
Tigilanol tiglate	Phase I Dose-Escalation Extension Study to Determine the Safety and Tolerability of Intratumoural Injection(s) of EBC-46	ACTRN12614001207606
LTX-315 (Ruxotemitide)	Phase 1 Dose-escalation Study of LTX-315 in Patients With a Transdermally Accessible Tumour	NCT01058616
LTX-315 (Ruxotemitide)	A Phase I, Open-label, Multi-arm, Multi-centre, Multi-dose, Dose Escalation Study of LTX-315 as Monotherapy or in Combination With Either Ipilimumab or Pembrolizumab in Patients With Transdermally Accessible Tumours	NCT01986426
LTX-315 (Ruxotemitide)	An Open Label Phase II Single Centre Study Investigating the Safety and Efficacy of LTX-315 and Adoptive T-cell Therapy in Patients With Advanced/Metastatic Soft Tissue Sarcoma	NCT03725605

ICD, immunogenic cell death.

Supplementary Table 4 | Ongoing trials of intratumoural cytokine therapies

Cytokine	Trial name	ClinicalTrials.gov identifier
IL-2	Pre-Treatment of Highly Suspicious Pigmented Skin Lesions With Interleukin-2	NCT03233828
IL-2	UCDCC#272: IL-2, Radiotherapy, and Pembrolizumab in Patients Refractory to Checkpoint Blockade	NCT03474497
IL-2	The Response to Intralesional IL-2 and/or BCG Treatment for Cutaneous Metastatic Melanoma	NCT03928275
IL-2	IT-hu14.18-IL2 With Radiation, Nivolumab and Ipilimumab for Melanoma	NCT03958383
IL-2 and TNF	Efficacy of Daromun Neoadjuvant Intratumoral Treatment in Clinical Stage IIIB/C Melanoma Patients	NCT03567889
IL-2 and TNF	Intratumoral Administration of Daromun in Non-melanoma Skin Cancer Patients (DUNCAN)	NCT04362722
IL-12	A Study of Ad-RTS-hIL-12 With Veledimex in Subjects With Glioblastoma or Malignant Glioma	NCT02026271
IL-12	Tavo and Pembrolizumab in Patients With Stage III/IV Melanoma Progressing on Pembrolizumab or Nivolumab Treatment	NCT03132675
IL-12	A Study of Ad-RTS-hIL-12 + Veledimex in Pediatric Subjects With Brain Tumors Including DIPG	NCT03330197
IL-12	Tavo and Pembrolizumab With or Without Chemotherapy in Patients With Inoperable Locally Advanced or Metastatic TNBC	NCT03567720
IL-12	A Study of Ad-RTS-hIL-12 With Veledimex in Combination With Nivolumab in Subjects With Glioblastoma; a Substudy to ATI001-102	NCT03636477
IL-12	Evaluation of Ad-RTS-hIL-12 + Veledimex in Subjects With Recurrent or Progressive Glioblastoma, a Substudy to ATI001-102	NCT03679754
IL-12	Tavo With Electroporation, Pembrolizumab, and Epacadostat in Patients With Unresectable Head and Neck Cancer	NCT03823131
IL-12	A Study of MEDI1191 in Sequential and Concurrent Combination With Durvalumab in Subjects With Advanced Solid Tumors	NCT03946800
IL-12	Study of Ad-RTS-hIL-12 + Veledimex in Combination With Cemiplimab in Subjects With Recurrent or Progressive Glioblastoma	NCT04006119
IL-12	Neoadjuvant Immunotherapy With Tavo + Electroporation in Combination With Nivo. in Melanoma Patients	NCT04526730
IL-23, IL-36γ and OX40L	Dose Escalation Study of mRNA-2752 for Intratumoral Injection to Patients With Advanced Malignancies	NCT03739931
sclL-12, IFNα-2b, GM-CSF and IL-15-sushi	A First-in-Human Dose Escalation and Expansion Study to Evaluate Intratumoral Administration of SAR441000 as Monotherapy and in Combination With Cemiplimab in Patients With Advanced Solid Tumors	NCT03871348
TGFβ1 siRNA	Open Label, Dose Escalation Study for the Safety and Efficacy of STP705 in Adult Patients With isSCC	NCT04293679

GM-CSF, granulocyte-macrophage colony-stimulating factor; OX40L, OX40 ligand; sclL-12, single-chain IL-12; siRNA, small interfering RNA; TGFβ1, transforming growth factor β1; TNF, tumour necrosis factor.

Supplementary Table 5 | Ongoing trials of intratumoural immune checkpoint-targeted therapies

Target	Agent Name	Trial name	ClinicalTrials.gov identifier
CTLA4	Ipilimumab	Ipilimumab for Head and Neck Cancer Patients	NCT02812524
CTLA4	Ipilimumab	A Trial Evaluating the Safety & Efficacy of Intra-Tumoral Ipilimumab in Combination With Intra-venous Nivolumab in Patients With Metastatic Melanoma	NCT02857569
CTLA4	Ipilimumab	Intra-tumoral Ipilimumab Plus Intravenous Nivolumab Following the Resection of Recurrent Glioblastoma	NCT03233152
CTLA4	Ipilimumab	Intratumoral Tilsotolimod, a TLR-9 Agonist, Together With Intratumoral Ipilimumab and Intravenous Nivolumab in Patients With Advanced Cancers (PRIMO)	NCT04270864
PD-1	Pembrolizumab	Pembrolizumab in High-risk Ductal Carcinoma in Situ (DCIS)	NCT02872025
PD-1	Nivolumab	Intra-lesional Nivolumab Therapy for Limited Cutaneous Kaposi Sarcoma	NCT03316274
PD-1	Cemiplimab	Pre-Operative Cemiplimab Administered Intralesionally for Patients With Recurrent Cutaneous Squamous Cell Carcinoma	NCT03889912
PD-1 and CTLA4	Nivolumab Ipilimumab	A Phase 2 Trial for Men With Metastatic Prostatic Adenocarcinoma	NCT04090775
CD40	APX005M	APX005M in Combination With Systemic Pembrolizumab in Patients With Metastatic Melanoma	NCT02706353
CD40	ABBV-927	A Study of ABBV-927 and ABBV-181, an Immunotherapy, in Participants With Advanced Solid Tumors	NCT02988960
CD40	ABBV-927	A Study to Assess the Effects of Multiple Study Drug Regimens in Subjects With Newly Diagnosed Locally Advanced Head and Neck Squamous Cell Carcinoma	NCT03818542
CD40	Selicrelumab	Study of Intratumoral Selicrelumab With Atezolizumab in Patients With Refractory or Relapsed B Cell Lymphoma	NCT03892525
CD40	2141 V-11	A Study Investigating the Safety and Tolerability of an Immune Treatment in Cancer Patients With Lesions to the Skin	NCT04059588
CD40	SL-172154	Ph1 Study of SL-172154 Administered Intratumorally in Subjects With Squamous Cell Carcinoma of the Head and Neck or Skin	NCT04502888
CD40	2141-V11	Phase 1 Trial of D2C7-IT in Combination With 2141-V11 for Recurrent Malignant Glioma	NCT04547777
CD40 and CD27	TriMix	Intratumoral TriMix Injections in Early Breast Cancer Patients	NCT03788083
OX40	mRNA 2416	Dose Escalation and Efficacy Study of mRNA 2416 for Intratumoral Injection Alone and in Combination With Durvalumab for Patients With Advanced Malignancies	NCT03323398
OX40	BMS 986178	TLR9 Agonist SD-101, Anti-OX40 Antibody BMS 986178, and Radiation Therapy in Treating Patients With Low-Grade B-Cell Non-Hodgkin Lymphomas	NCT03410901
CD137	Urelumab	Phase I-II Study of Intratumoral Urelumab Combined With Nivolumab in Patients With Solid Tumors	NCT03792724

Supplementary Table 6 | Ongoing trials of intratumoural adoptive cell therapies

Type of cell therapy	Trial name	ClinicalTrials.gov identifier
CAR T cell	Phase I Trial: T4 Immunotherapy of Head and Neck Cancer	NCT01818323
CAR T cell	Genetically Modified T-cells in Treating Patients With Recurrent or Refractory Malignant Glioma	NCT02208362
CAR T cell	Memory-Enriched T Cells in Treating Patients With Recurrent or Refractory Grade III-IV Glioma	NCT03389230
CAR T cell	Interventional Therapy Sequential With the Fourth-generation CAR-T Targeting Nectin4/FAP for Malignant Solid Tumors	NCT03932565
CAR T cell	B7-H3 CAR-T for Recurrent or Refractory Glioblastoma	NCT04077866
CAR T cell	Pilot Study of B7-H3 CAR-T in Treating Patients With Recurrent and Refractory Glioblastoma	NCT04385173
DC	Sequential Intranodal Immunotherapy (SIIT) Combined With Anti-PD1 (Pembrolizumab) in Follicular Lymphoma	NCT02677155
DC	Feasibility and Safety of IMP321 for Advanced Stage Solid Tumors	NCT03252938
DC	Dendritic Cell Therapy After Cryosurgery in Combination With Pembrolizumab in Treating Patients With Stage III-IV Melanoma That Cannot Be Remove by Surgery	NCT03325101
DC	A Phase I/II, Safety Clinical Trial of DCVAC/PCa and ONCOS-102 in Men With Metastatic Castration-resistant Prostate Cancer	NCT03514836
DC	Intratumoral Administration of CCL21-gene Modified Dendritic Cell With Intravenous Pembrolizumab for Advanced NSCLC	NCT03546361
DC	Dendritic Cell Therapy for Brain Metastases From Breast- or Lung Cancer	NCT03638765
DC	Intratumoral Injection of Autologous CD1c (BDCA-1)+ myDC, Avelumab, and Ipilimumab Plus Systemic Nivolumab	NCT03707808
DC	A Study to Evaluate the Safety and Effectiveness of ILixadencel Administered Into Tumors in Combination With Checkpoint Inhibitor (CPI) in Patients With Advanced Cancer	NCT03735290
DC	Arm 1: Infusion of Autologous Monocyte-derived Lysate Pulsed Dendritic Cells (PV-001-DC) in Patients With Advanced Melanoma	NCT03803397
DC	Modified Immune Cells (Autologous Dendritic Cells) and a Vaccine (Prevnar) After High-Dose External Beam Radiation Therapy in Treating Patients With Unresectable Liver Cancer	NCT03942328
NK cell	Intra-tumoral Injection of Natural Killer Cells in High-Grade Gliomas	NCT04254419
NK cell	Natural Killer Cell (CYNK-001) IV Infusion or IT Administration in Adults With Recurrent GBM	NCT04489420
TILs	Engineered Immune Effectors Against Cervical Cancer	NCT03362619

CAR, chimeric antigen receptor; DC, dendritic cell; NK, natural killer; TILs, tumour-infiltrating lymphocytes.

Supplementary Table 7 | Trials of miscellaneous intratumoural immunotherapies

Type	Trial name	ClinicalTrials.gov identifier
Bacteria	Pembrolizumab With Intratumoral Injection of Clostridium Novyi-NT	NCT03435952
Bacteria	Safety and Tolerability of SYN1891 Injection Alone or in Combination With Atezolizumab in Adult Subjects	NCT04167137
TAA	D2C7 for Adult Patients With Recurrent Malignant Glioma	NCT02303678
TAA	pDNA Intralesional Cancer Vaccine for Cutaneous Melanoma	NCT03655756
TAA	IT-hu14.18-IL2 With Radiation, Nivolumab and Ipilimumab for Melanoma	NCT03958383
TAA	Immunotherapy With IFx-Hu2.0 Vaccine for Advanced MCC or cSCC	NCT04160065
Cathelicidin antimicrobial peptide	Intratumoral Injections of LL37 for Melanoma	NCT02225366

TAA, tumour-associated antigen.