

Table SI. Gastroids of SPEM induced by different approaches for IL research.

IL	Cell source	Isolation region	Growth model	Method of addition	Cytokine	Formation, h	Observation, days	Photomicrograph device	(Ref.)
IL-13	C57BL/6 mice	Corpus region	Matrigel medium	Direct	5 ng/ml recombinant mouse IL13 (cat. no. 413-ML; R&D Systems, Inc.)	48-72	7	Cytation 5 Cell Imaging Multi-Mode Reader (Agilent Technologies, Inc.)	(125)
IL-13	Human organ donation	Corpus region	Matrigel medium	Direct	5 ng/ml recombinant human IL13 (cat. no. 213-ILL-005; R&D Systems, Inc.)	48-72	7	Cytation 5 Cell Imaging Multi-Mode Reader (Agilent Technologies, Inc.)	(125)
IL-13	Mist1-KRAS mice	Corpus mucosa	Matrigel (ECM; Sigma-Aldrich; Merck KGaA)	Co-culture and direct	IL-13-positive ILC2s; cellular source, 1 ng/ml rIL13	48	7	Real-Time Cell History Recorder (NanoEntek, Inc.); EVOS M7000 inverted microscope (Thermo Fisher Scientific, Inc.).	(39)
IL-13	Patient-sourced	Corpus mucosa	Matrigel medium	Co-culture and direct	IL-13-positive ILC2s; cellular source, 1 ng/ml rIL13	48	7	Real-Time Cell History Recorder (NanoEntek, Inc.)	(39)
IL-13	gp130 ^{F/F} mice	Gastric tissue	Matrigel medium	Direct	IL13 (cat. no. MAB413; R&D Systems, Inc.); IL13 (cat. no. 413-ML; R&D Systems, Inc.)	48	7	Inverted microscope	(121)
IL-17A	BALB/c mice	Corpus region	Matrigel (cat. no. 356234; Corning, Inc.)	Direct	3 ng/ml recombinant murine IL-17A (cat. no. 576002; Biolegend, Inc.)	48	3	Photomicroscopy and ImageJ software (version 1.49; National Institutes of Health,).	(34)
IL-25	gp130 ^{F/F} mice	Gastric tissue	Matrigel medium	Direct	IL25 (cat. no. 1399-IL; R&D Systems, Inc.); α -IL25 (cat. no. MAB13992; R&D Systems, Inc.)	48	7	Inverted microscope	(121)

IL, interleukin; SPEM, spasmodic polypeptide-expressing metaplasia; gp130, glycoprotein 130.

Table SII. Clinical trials harnessing ILs for gastric cancer therapy.

A, Clinical trials involving IL-1 and its engineered variants						
Drug	NCT number	Phase	Status	Intervention/Treatment	Institute, country of residence	Patients, n
CA-4948	NCT05187182	I	Recruiting	Drug: CA-4948 Biological: Nivolumab Biological: Pembrolizumab Drug: Trastuzumab Drug: mFOLFOX7	Washington University School of Medicine, United States	42
B, Clinical trials involving IL-2 and its engineered variants						
Drug	NCT number	Phase	Status	Intervention/Treatment	Institute, country of residence	Patients, n
Aldesleukin	NCT02662348	I	Unknown status	Drug: Recombinant human IL-2 Drug: HER2Bi-armed T cells	The First Affiliated Hospital with Nanjing Medical University, China	6
Aldesleukin	NCT05483491	I	Recruiting	Biological: KK-LC-1 TCR-T cells Drug: Aldesleukin	The State University of New Jersey, United States	30
Aldesleukin	NCT05802056	I	Recruiting	Biological: Aldesleukin Drug: Fluorouracil Drug: Leucovorin calcium Biological: Nivolumab Drug: Oxaliplatin	Mayo Clinic, United States	15
Aldesleukin	NCT03745326	I/II	Recruiting	Drug: Cyclophosphamide Drug: Fludarabine Drug: Aldesleukin Biological: Anti-KRAS G12D mTCR PBL	National Institutes of Health Clinical Center, United States	70
Aldesleukin	NCT03190941	I/II	Recruiting	Drug: Cyclophosphamide Drug: Fludarabine Biological: Anti-KRAS G12V mTCR PBL Drug: Aldesleukin	National Institutes of Health Clinical Center, United States	110
Aldesleukin	NCT04426669	I/II	Active, not recruiting	Drug: Cyclophosphamide Drug: Fludarabine Biological: TIL Drug: Aldesleukin	Intima Bioscience, United States	20
Aldesleukin	NCT01212887	I	Terminated	Biological: MFE23 scFv-expressing autologous	Cancer Research UK, United	14

				anti-CEA MFEz T lymphocytes Biological: Aldesleukin Drug: Cyclophosphamide Drug: Fludarabine phosphate	Kingdom	
Aldesleukin	NCT00003125	II	Completed	Biological: ALVAC-CEA vaccine Biological: Aldesleukin Biological: Sargramostim Biological: Vaccinia-CEA vaccine	Georgetown University, United Kingdom	24
Aldesleukin	NCT00003125	I/II	Terminated	Biological: ALVAC-CEA vaccine Biological: Aldesleukin Biological: Sargramostim Biological: Vaccinia-CEA vaccine	Cellularity Incorporated, United Kingdom	1
Aldesleukin	NCT05400122	I	Recruiting	Drug: Vactosertib Drug: Fludarabine Phosphate Drug: Cyclophosphamide Drug: IL-2 Drug: Natural Killer Cells	Case Comprehensive Cancer Center, United Kingdom	12
Aldesleukin	NCT03935893	II	Recruiting	Biological: TIL Drug: Fludarabine + cyclophosphamide combination	University of Pittsburgh, United Kingdom	240
ALKS 4230 (Nemvaleukin alfa)	NCT03861793	I/II	Completed	Biological: ALKS 4230 Biological: Pembrolizumab	Mural Oncology, Inc, United States	116
NKTR-214	NCT02983045	I/II	Completed	Drug: NKTR-214, nivolumab and ipilimumab	Nektar Therapeutics, United States	557
THOR-707 (SAR 444245)	NCT05104567	II	Completed	Drug: THOR-707 Drug: Pembrolizumab Drug: Cetuximab	Sanofi, United States	138
C, Clinical trials involving IL-15						
Drug	NCT number	Phase	Status	Intervention/Treatment	Institute, country of residence	Patients, n
N-803	NCT04847466	II	Active, not recruiting	Drug: N-803 Drug: Pembrolizumab Biological: PD-L1 t-haNK	National Institutes of Health Clinical Center, United States	18
N-803	NCT03228667	II	Recruiting	Drug: N-803, pembrolizumab, nivolumab, atezolizumab, avelumab, durvalumab, PD-L1 t-	ImmunityBio, United States	40

				haNK and docetaxel		
SO-C101 (SCT101)	NCT04234113	I	Terminated	Drug: Nanrilkefusp alfa Drug: Pembrolizumab	Sotio Biotech, Inc., United States	115
D, Clinical trials involving IL-7						
Drug	NCT number	Phase	Status	Intervention/Treatment	Institute, country of residence	Patients, n
NT-I7	NCT04594811	I	Terminated	Drug: NT-I7 Drug: Nivolumab	NeoImmuneTech, United States and Poland	10
E, Clinical trials involving IL-12						
Drug	NCT number	Phase	Status	Intervention/Treatment	Institute, country of residence	Patients, n
Edodekin alfa	NCT00003046	I	Completed	Biological: Recombinant IL-12	M.D. Anderson Cancer Center, United States	29
Edodekin alfa	NCT00003439	I	Completed	Biological: Recombinant IL-12	National Cancer Institute, United States	36
Edodekin alfa	NCT00028535	I	Completed	Biological: Trastuzumab Drug: Paclitaxel Biological: Recombinant IL-12	National Cancer Institute (NCI), United States	18
Edodekin alfa	NCT00004074	I	Completed	Biological: Recombinant IL-12 Biological: ABI-007/carboplatin/trastuzumab	National Cancer Institute (NCI), United States	15
IL-12	NCT02960594	I	Completed	Biological: INO-1400 Biological: INO-9012 Biological: INO-1401	Novio Pharmaceuticals, United States	93
VG161	NCT06008925	I/II	Recruiting	Drug: Recombinant human IL12/15-PDL1B Oncolytic HSV-1 injection (Vero cell) Drug: Nivolumab injection	NBG-Virogin Biotech, China	43
BioTTT001	NCT06283121	II	Not yet recruiting	Biological: BioTTT001 intraperitoneal infusion Drug: SOX regimen Drug: Toripalimab	China Medical University, China	30

IL, interleukin; WBC, white blood cells; NK, natural killer; FOLFOX, folinic acid, fluorouracil and oxaliplatin; PD-1, programmed death-1; TIL, tumor-infiltrating lymphocytes ; HER2, human epidermal growth factor receptor 2; HER2Bi, HER2 bispecific antibody; TCR, T-cell receptor; LC, lung cancer; PD-L1, programmed death ligand 1; mTCR, modified TCR; PBL, peripheral blood lymphocytes; CEA, carcinoembryonic antigen; ALVAC, canarypox virus vector; scFv, single-chain variable fragment; G12D, glycine to aspartic acid mutation at position 12; G12V, glycine to valine mutation at position 12; HSV-1, herpes simplex virus type 1; SOX, S-1, oxaliplatin.