

Supplementary Table 1: Clinical trials of armored CAR T-cells in hematological malignancies and solid tumors

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| National clinical trial (NCT) number | Title | Disease | Target antigen | Modification to overcome the limitations | Number enrolled | Location | Phase | Status |
| NCT03635632 | C7R-GD2.CART Cells for Patients With Relapsed or Refractory Neuroblastoma and Other GD2 Positive Cancers | Relapsed or Refractory Neuroblastoma, Relapsed Osteosarcoma, Relapsed Ewing Sarcoma, Relapsed Rhabdomyosarcoma, Uveal Melanoma, Breast Tumor | Disialoganglioside (GD2) | Constitutively active IL-7 receptor | 64 | Houston, Texas, USA | Phase I | Recruiting |
| NCT04684563 | huCART19-IL18 in CD19+ Cancers | Chronic Lymphocytic Leukemia, Non-hodgkin Lymphoma, Acute Lymphoblastic Leukemia | CD19 | Co-secretion of IL-18 | 72 | Philadelphia, Pennsylvania, United States | Phase I | Recruiting |
| NCT03542799 | EGFR-IL12-CART Cells for Patients With Metastatic Colorectal Cancer (EGFRCART) | Metastatic Colorectal Cancer | Epidermal Growth Factor (EGFR) | Co-secretion of IL-12 | 20 | ShenZhen, GuangGong, China | Phase I | Unknown |

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| NCT05103631 | Interleukin-15 Armored Glypican 3-specific Chimeric Antigen Receptor Expressed in Autologous T Cells for Solid Tumors | Liver Cell Carcinoma, Wilms Tumor, Malignant Rhabdoid Tumor, Yolk Sac Tumor, Rhabdomyosarcoma, Liposarcoma, Embryonal Sarcoma of the Liver | Glypican 3 (GPC-3) | Co-secretion of IL-15 | 27 | Houston, Texas, United States | Phase I | Recruiting |
| NCT04377932 | Interleukin-15 Armored Glypican 3-specific Chimeric Antigen Receptor Expressed in T Cells for Pediatric Solid Tumors | Liver Cancer, Rhabdomyosarcoma, Malignant Rhabdoid Tumor, Liposarcoma, Wilms Tumor, Yolk Sac Tumor | GPC-3 | Co-secretion of IL-15 | 24 | Houston, Texas, United States | Phase I | Recruiting |
| NCT03721068 | Study of CAR T-Cells Targeting the GD2 With IL-15+iCaspase9 for Relapsed/Refractory Neuroblastoma or Relapsed/Refractory Osteosarcoma | Relapsed/Refractory Neuroblastoma or Relapsed/Refractory Osteosarcoma | GD2 | Co-secretion of IL-15 | 18 | Chapel Hill, North Carolina, USA | Phase I | Recruiting |

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| NCT02498912 | Cyclophosphamide Followed by Intravenous and Intraperitoneal Infusion of Autologous T Cells Genetically Engineered to Secrete IL-12 and to Target the MUC16ecto Antigen in Patients With Recurrent MUC16ecto+ Solid Tumors | Advanced Solid Tumors | Mucin 16 (MUC16) | Co-secretion of IL-12 | 18 | New York, United States | Phase I | Active, not recruiting |
| NCT04093648 | T Cells co- Expressing a Second Generation Glypican 3-specific Chimeric Antigen Receptor With Cytokines Interleukin-21 and 15 as Immunotherapy for Patients With Liver Cancer | Hepatocellular Carcinoma Hepatoblastoma | GPC-3 | Co-secretion of IL-21 and IL-15 | 0 | United States | Phase I | Not yet recruiting |
| Cytokine-modulating CARs | | | | | | | | |

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| NCT03089203 | CART-PSMA-TGFβRDN Cells for Castrate-Resistant Prostate Cancer | Prostate Cancer | Prostate-Specific Membrane Antigen (PSMA) | Co-expression of TGFβRDN | 19 | Philadelphia, Pennsylvania, United States | Phase I | Recruiting |
| NCT05693844 | CD40 Ligand Expressing MSLN-CAR T Cell Therapy in MSLN Positive Advanced/Metastatic Solid Tumors | Advanced or Metastatic Solid Tumors | Mesothelin (MSLN) | Co-secretion of CD40L | 30 | Beijing, China | Phase I/II | Recruiting |
| CARs coupled with IC blockade | | | | | | | | |
| NCT03258047 | Novel Autologous CAR-T Therapy for Relapsed/Refractory B Cell Lymphoma | Relapsed or Refractory B-cell Lymphoma | CD19 | Co-expression of the PD-1/CD28 switch receptor | 60 | Hangzhou, Zhejiang, China | Phase II | Unknown |
| NCT03932955 | MC-19PD1 CAR-T in Relapsed or Refractory B Cell Lymphoma | Relapsed or Refractory B-cell Lymphoma | CD19 | Co-expression of the PD-1/CD28 switch receptor | 15 | Beijing, China | Phase I | Unknown |
| NCT03208556 | Safety and Efficacy of iPD1 CD19 eCAR T Cells in Relapsed or Refractory B-cell Lymphoma | Relapsed or Refractory B-cell Lymphoma | CD19 | PD-1 shRNA-expressing cassette | 20 | Beijing, China | Phase I | Unknown |

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| NCT04213469 | PD1-CD19-CART in Patients With r/r B-cell Lymphoma | Relapsed or Refractory B-cell Lymphoma | CD19 | PD-1 Knockout | 20 | Hangzhou, Zhejiang, China | Not applicable | Active, not recruiting |
| NCT05812326 | PD-1 Knockout Anti-MUC1 CAR-T Cells in the Treatment of Advanced Breast Cancer | Advanced Breast Cancer | Mucin 1 (MUC1) | PD-1 Knockout | 15 | Guangzhou, Guangdong, China | Phase I/II | Completed |
| NCT03706326 | CAR T and PD-1 Knockout Engineered T Cells for Esophageal Cancer | Advanced Esophageal Cancer | MUC1 | PD-1 Knockout | 20 | Guangzhou, Guangdong, China | Phase I/II | Unknown |
| NCT03525782 | Anti-MUC1 CAR T Cells and PD-1 Knockout Engineered T Cells for NSCLC | Non-Small Cell Lung Cancer | MUC1 | PD-1 Knockout | 60 | Guangzhou, Guangdong, China | Phase I/II | Unknown |
| NCT03545815 | Study of CRISPR-Cas9 Mediated PD-1 and TCR Gene-knocked Out Mesothelin-directed CAR-T Cells in Patients With Mesothelin Positive Multiple Solid Tumors | Advanced Solid Tumors | MSLN | PD-1 Knockout | 10 | Beijing, China | Phase I | Unknown |

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| NCT03298828 | CD19 CAR and PD-1 Knockout Engineered T Cells for CD19 Positive Malignant B-cell Derived Leukemia and Lymphoma | B-ALL and Burkitt lymphoma | CD19 | PD-1 Knockout | 30 | Chongqing, China | Phase I | Unknown |
| NCT04162119 | Safety and Efficiency Study of BCMA-PD1-CART Cells in Relapsed/Refractory Multiple Myeloma | Multiple Myeloma | B-cell maturation antigen (BCMA) | PD-1-Fc protein | 30 | Sanya, Hainan, China | Phase II | Unknown |
| NCT04163302 | Safety and Efficiency Study of CD19-PD1-CART Cell in Relapsed/Refractory B Cell Lymphoma | B cell lymphoma | CD19 | PD-1-Fc protein | 30 | Sanya, Hainan, China | Phase II | Unknown |
| NCT02862028 | PD-1 Antibody Expressing CAR-T Cells for EGFR Family Member Positive Advanced Solid Tumor (Lung, Liver and Stomach) | Advanced Solid Tumors | EGFR family | PD-1 antibody | 20 | Shanghai, China | Phase I/II | Unknown |
| NCT02873390 | PD-1 Antibody Expressing CAR-T Cells for EGFR Family Member Positive Advanced Solid Tumor | Advanced Solid Tumors | EGFR family | PD-1 antibody | 20 | Ningbo, Zhejiang, China | Phase I/II | Unknown |

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| NCT03030001 | PD-1 Antibody Expressing CAR T Cells for Mesothelin Positive Advanced Malignancies | Advanced Solid Tumors | MSLN | PD-1 antibody | 40 | Ningbo, Zhejiang, China | Phase I/II | Unknown |
| NCT03615313 | PD-1 Antibody Expressing mesoCAR-T Cells for Mesothelin Positive Advanced Solid Tumor | Advanced Solid Tumors | MSLN | PD-1 antibody | 50 | Shanghai, China | Phase I/II | Unknown |
| NCT03085173 | A Trial of "Armored" CAR T Cells Targeting CD19 For Patients With Relapsed CD19+ Hematologic Malignancies | Relapsed or Refractory Chronic Lymphocytic Leukemia | CD19 | Co-secretion of 4-1BBL | 39 | New York, United States | Phase I | Active, not recruiting |
| NCT03182816 | CTLA-4 and PD-1 Antibodies Expressing EGFR-CAR-T Cells for EGFR Positive Advanced Solid Tumor | Advanced Solid Tumors | EGFR | Co-secretion of CTLA-4 and PD-1 antibodies | 40 | Ningbo, Zhejiang, China | Phase I/II | Unknown |
| NCT03182803 | CTLA-4 and PD-1 Antibodies Expressing Mesothelin-CAR-T Cells for Mesothelin Positive Advanced Solid Tumor | Advanced Solid Tumors | MSLN | Co-secretion of CTLA-4 and PD-1 antibodies | 40 | Ningbo, Zhejiang, China | Phase I/II | Unknown |

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| NCT03179007 | CTLA-4 and PD-1 Antibodies Expressing MUC1-CAR-T Cells for MUC1 Positive Advanced Solid Tumor | Advanced Solid Tumors | MUC1 | Co-secretion of CTLA-4 and PD-1 antibodies | 40 | Ningbo, Zhejiang, China | Phase I/II | Unknown |
| Self-driving CARs | | | | | | | | |
| NCT04153799 | Study of CXCR5 Modified EGFR Chimeric Antigen Receptor Autologous T Cells in EGFR- Positive Patients With Advanced Non-small Cell Lung Cancer | Non Small Cell Lung Cancer | EGFR | Co-expression of CXCR5 | 11 | Guangzhou, Guangdong, China | Phase I | Unknown |
| NCT05060796 | Study of CXCR5 Modified EGFR Targeted CAR-T Cells for Advanced NSCLC | Non Small Cell Lung Cancer | EGFR | Co-expression of CXCR5 | 11 | Guangzhou, Guangdong, China | Early Phase I | Recruiting |
| NCT05353530 | Phase I Study of IL-8 Receptor-modified CD70 CAR T Cell Therapy in CD70+ and MGMT-unmethylated Adult Glioblastoma | Glioblastoma Multiforme, Glioblastoma | CD70 | Co-expression of CXCR2 | 18 | Gainesville, Florida, United States | Phase I | Recruiting |

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| NCT01740557 | Genetically Modified Therapeutic Autologous Lymphocytes Followed by Aldesleukin in Treating Patients With Stage III or Metastatic Melanoma | Metastatic Melanoma | Nerve growth factor receptor (NGFR) | Co-expression of CXCR2 | 10 | Houston, Texas, United States | Phase I/II | Completed |
| NCT03602157 | Study of CAR-T Cells Expressing CD30 and CCR4 for r/r CD30+ HL and CTCL | Hodgkin Lymphoma, Cutaneous T Cell Lymphoma | CD30 | Co-expression of CCR4 | 59 | Chapel Hill, North Carolina, United States | Phase I | Recruiting |
| NCT04727008 | CXCR4 Modified Anti-BCMA CAR T Cells for Multiple Myeloma | Multiple Myeloma | BCMA | Co-expression of CXCR4 | 12 | Chengdu, China | Phase I | Active, not recruiting |
| ECM-targeted CARs | | | | | | | | |
| NCT01722149 | Re-directed T Cells for the Treatment (FAP)-Positive Malignant Pleural Mesothelioma | Malignant Pleural Mesothelioma | Fibroblast Activation Protein (FAP) | Targeting the extracellular matrix (ECM) | 4 | Zurich, Switzerland | Early Phase I | Recruiting |
| Combinatorial strategies | | | | | | | | |

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| NCT03932565 | Interventional Therapy Sequential With the Fourth-generation CAR-T Targeting Nectin4/FAP for Malignant Solid Tumors | Non Small Cell Lung Cancer, Breast Cancer, Ovarian Cancer, Bladder Cancer, Pancreatic cancer | Nectin Cell Adhesion Molecule-4 (Nectin4)/FAP | Co-secretion of IL-7 and CCL19, or IL-12 | 30 | Zhejiang, China | Phase I | Unknown |
| NCT04381741 | CD19 CAR-T Expressing IL7 and CCL19 Combined With PD1 mAb for Relapsed or Refractory Diffuse Large B Cell Lymphoma | Relapsed or Refractory Diffuse Large B Cell Lymphoma | CD19 | Co-secretion of IL-7, CCL19 and PD-1 antibody | 24 | Zhejiang, China | Phase I | Enrolling by invitation |
| NCT03929107 | Interleukin-7 and Chemokine (C-C Motif) Ligand 19-expressing CD19-CAR-T for Refractory/Relapsed B Cell Lymphoma | Relapsed or Refractory Diffuse Large B Cell Lymphoma | CD19 | Co-secretion of IL-7 and CCL19 | 80 | Hangzhou, Zhejiang, China | Phase II | Unknown |
| NCT04833504 | Clinical Follow-up Study of CD19 CAR-T Expressing IL7 and CCL19 for Relapsed or Refractory B Cell Lymphoma | Relapsed or Refractory Diffuse Large B Cell Lymphoma | CD19 | Co-secretion of IL-7 and CCL19 | 39 | Hangzhou, Zhejiang, China | Not applicable | Completed |

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| NCT03778346 | Integrin β 7, BCMA, CS1, CD38 and CD138 as the Single or Compound Targets for the Fourth Generation of CAR-T Cells | Recurrent or Refractory Multiple Myeloma | CD138, integrin β 7, CS1, CD38, and BCMA | Co-secretion of IL-7 and CCL19 | 30 | Lishui, Zhejiang, China | Phase I | Unknown |
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