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Apoptosis: a *Janus bifrons* in T-cell immunotherapy

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ABSTRACT

Immunotherapy has revolutionized the treatment of cancer. In particular, immune checkpoint blockade, bispecific antibodies, and adoptive T-cell transfer have yielded unprecedented clinical results in hematological malignancies and solid cancers. While T cell-based immunotherapies have multiple mechanisms of action, their ultimate goal is achieving apoptosis of cancer cells. Unsurprisingly, apoptosis evasion is a key feature of cancer biology. Therefore, enhancing cancer cells' sensitivity to apoptosis represents a key strategy to improve clinical outcomes in cancer immunotherapy. Indeed, cancer cells are characterized by several intrinsic mechanisms to resist apoptosis, in addition to features to promote apoptosis in T cells and evade therapy. However, apoptosis is double-faced: when it occurs in T cells, it represents a critical mechanism of failure for immunotherapies. This review will summarize the recent efforts to enhance T cell-based immunotherapies by increasing apoptosis susceptibility in cancer cells and discuss the role of apoptosis in modulating the survival of cytotoxic T lymphocytes in the tumor microenvironment and potential strategies to overcome this issue.

THE DUAL ROLE OF APOPTOSIS IN CANCER IMMUNOTHERAPY

Cancer immunotherapies exploit the immune system to combat cancers and thus have revolutionized the field of immuno-oncology, leading to unprecedented outcomes in relapsed and refractory patients.[1] Especially, modulation of T cell's anticancer activity through immune checkpoint blockade (ICB) (eg, anti-programmed cell death protein-1 (PD-1)/programmed death ligand-1 or anti-cytotoxic T-lymphocytes-associated protein 4 (CTLA-4) antibodies, online supplemental box 1) showed a significant clinical response in a subset of solid and hematologic malignancies. Bispecific antibodies (online supplemental box 1) represent another strategy triggering cancer recognition by T cells.[2] The anti-CD19/CD3 bispecific T-cell engager blinatumomab was approved in 2014 for B-acute lymphoblastic leukemia (B-ALL) and several anti-CD20/CD3, and anti-BCMA/CD3 antibodies are in advanced clinical development (online supplemental box 1).[3–6] Although checkpoint inhibitors are currently the treatment backbone for several cancer types, many patients eventually develop secondary resistance and progressive disease in the end.[7] Chimeric antigen receptor T-cell (CAR-T) therapy, a form of adoptive cell transfer (ACT),[8] has also demonstrated substantial anticancer efficacy in treating relapsed or refractory B-cell leukemias, lymphomas, and multiple myeloma, which resulted in the approval of multiple CAR-T products by the US Food and Drug Administration (FDA) (online supplemental box 1).[9–14] Nevertheless, approximately 50% of pediatric B-ALL and up to 70% of patients with B-cell lymphoma still do not respond or eventually relapse to the CAR-T therapy.[10 12 13 15] Therefore, improving the potency of T cell-based immunotherapies is critical for improving the clinical outcomes of patients with cancer.

The ultimate goal of anticancer therapy, including T cell-based immunotherapies, is to eliminate cancer cells, mainly by efficiently inducing apoptosis in cancer cells. Apoptosis, a programmed cellular mechanism leading to cell death, is a complex biological process involving a vast array of tightly controlled cellular components.[16] The acquisition of resistance to programmed cellular death (eg, apoptosis) is a key feature of cancer progression.[17] For instance, genetic alteration of the anti-apoptotic regulator (eg, translocation and/or gain of B-cell lymphoma 2 (BCL-2)) has been well characterized as a key biological marker in multiple lymphomas, including follicular B-cell non-Hodgkin's lymphoma, diffuse large B-cell lymphoma, and B-cell chronic lymphocytic leukemia (CLL).[18] High levels of BCL-2 expression protect these fast-growing lymphomas against apoptosis, allowing malignant B cells to survive under various stress factors, such as cytokine deprivation. The critical role of

apoptosis in cancer development has been further identified during the transformation of premalignant cells into malignant cells. While MYC expression in premalignant cells increases sensitivity to apoptosis, a similar expression of MYC in malignant cells provides a strong proliferative advantage without inducing apoptosis. This proliferative advantage of MYC expression can be attributed to the co-expression of anti-apoptotic regulators (ie, BCL-2) in malignant cells, indicating that acquiring resistance to apoptosis by increasing expression of anti-apoptotic regulator (ie, BCL-2) during malignant transformation is an important checkpoint in cancer development.[18 19] Considering the critical role of apoptotic resistance in cancer development, this resistance may also provide a strong protective mechanism against T cell-based immunotherapies. Therefore, it is essential to understand not only the general molecular mechanisms of apoptosis but also the evasion mechanism of cancer cells to enhance the anticancer activity of T cell-based immunotherapies.

Multiple cellular insults and external stimuli, broadly categorized as intrinsic or extrinsic, can promote apoptosis. Intrinsic apoptosis is triggered by DNA damage, excessive reactive oxygen species (ROS), hypoxia, or cellular/metabolic stress.[20] In contrast, extrinsic apoptosis is initiated by the so-called 'death ligands,' such as Fas ligand (FasL or CD95L), TRAIL (TNF-related apoptosis-inducing ligand), and tumor necrosis factors (TNFs).[21] Immune cells, particularly T cells, use both pathways to activate apoptosis in cancer cells (figure 1). On T-cell receptor (TCR) engagement, T cells release cytolytic granules containing granzymes and perforin in the immune synaptic space to initiate the intrinsic apoptotic pathway. Perforins are pore-forming proteins that diffuse across immunological synapses and oligomerize

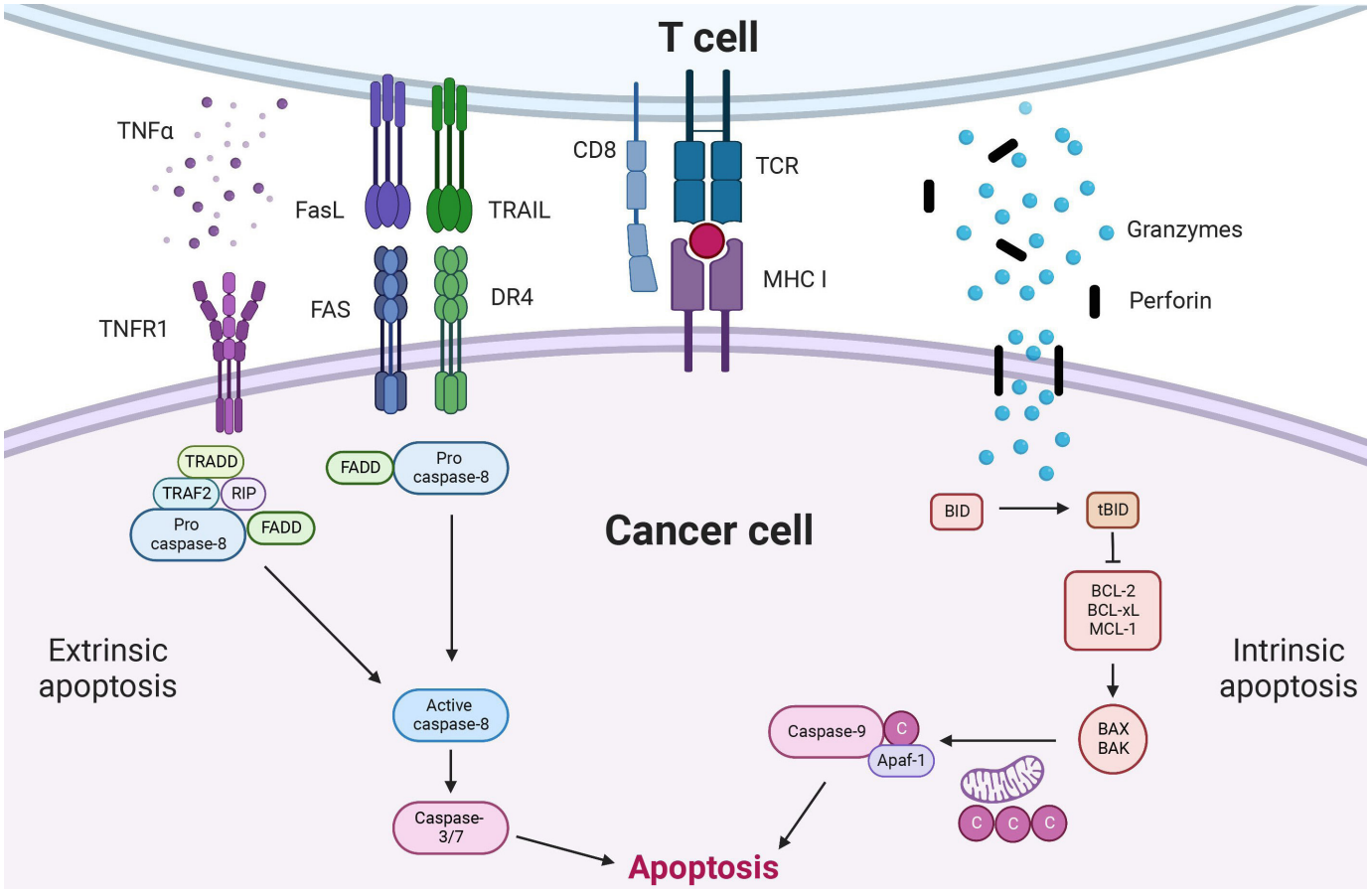

Figure 1 Apoptosis induced by T cells. T cells can induce apoptosis in cancer by both extrinsic and intrinsic pathways. To promote intrinsic apoptosis in cancer, granzymes is first transported into cancer cell via perforin, and granzymes cleave BID to generate truncated BID (tBID). tBID inhibits anti-apoptotic regulators (eg, BCL-2, BCL-xL, MCL-1), leading to the formation of homodimer or heterodimer of BAX and BAK on the membrane of mitochondria. These BAK/BAX dimerization releases cytochrome C and Apaf-1 from mitochondria to the cytoplasm. Together with Caspase-9, cytochrome C and Apaf-1 form apoptosomes that can cause apoptosis in cancer cells. FasL, TRAIL, and TNF-α expressed by T cells engage with their corresponding receptor in cancer cells to initiate extrinsic apoptosis. On engagement, death receptor complexes are formed and activate Caspase-8. Finally, activated Caspase-8 stimulates the activity of Caspase-3/7, resulting in the induction of apoptosis in the cancer cell. C: cytochrome C, BCL-2, B-cell lymphoma 2; FADD, Fas-associated death domains; FasL, Fas ligand; MHC, major histocompatibility complex; TCR, T-cell receptor; TNF, tumor necrosis factor; TRADD, TNF receptor type 1-associated death protein; TRAIL, TNF-related apoptosis-inducing ligand.

to form pores on the target cell membrane, facilitating the entry of granzymes into the target cell.[22] Granzymes generally enter target cells through pores formed by perforin; it has also been described that granzymes can pass the cell membrane of target cells without requiring perforin, via pinocytosis.[23] Four subsets of granzymes (granzyme A, B, K, and M) have been identified in human T cells; particularly granzyme B plays an essential role in promoting T cell-induced apoptosis in target cells.[24] On entry into the target cell, granzyme B cleaves BH3 Interacting Domain Death Agonist (BID), a BCL-2 homology (BH3)-only pro-apoptotic protein that plays an essential role in promoting apoptosis. Cleavage of BID results in the generation of the active form of BID (truncated BID/tBID). Subsequently, tBID activates pro-apoptotic effector proteins, such as BAX and BAK, by interfering with their interaction with BCL-2. This activation of effector proteins leads to the induction of instability of the mitochondrial membrane potential and the release of cytochrome c from the mitochondria to the cytoplasm. Cytochrome c leads to the formation of apoptosome complexes (cytochrome c:APAF-1:Caspase-9), which activate effectors, Caspase-3 and Caspase-7, promoting downstream apoptotic signaling cascades.[25] However, to trigger the extrinsic apoptotic pathway, the engagement of T cell-derived death ligands and their associated receptors in target cells is necessary. When T cells are activated, it leads to an increase in the expression of death ligands, such as FasL, TNF-α, and TRAIL. These death ligands bind to their respective death receptors (eg, FasL-Fas (CD95), TNF-α-TNFRSF1A (TNFR1), and TRAIL-TNFRSF10A (DR4)) on target cells, triggering the formation of death-inducing signaling complexes (DISCs), comprizing adaptor proteins (eg, Fas-associated death domains (FADD) or TNF receptor type 1-associated death protein (TRADD)) and initiator Caspase-8. DISCs eventually initiate downstream apoptotic signaling cascades to induce cellular apoptosis.[25]

Cancers have developed several strategies to evade immune cell-mediated apoptosis. For instance, mutation of TP53, a key tumor suppressor gene that confers resistance to apoptosis is strongly associated with decreased immune function genes (eg, granzymes and perforin) in patients with gastric cancer.[26 27] This observation suggests that aberrant TP53 activity could affect the anticancer immune response. Modulation of anti-apoptotic (eg, BCL-2, CFLAR, and BIRC2) and pro-apoptotic proteins (FAS, FADD, TNFRSF10B (death receptor 5—DR5), BID, and Caspase-8) is another important mechanism used by cancer cells to blunt cancer immunotherapy's anticancer efficacy.[28–33] Maruyama *et al* reported that >40% of patients with metastatic renal cell cancer with no response or progressive disease were positive for immunohistochemical staining of BCL-2, while patients with complete or partial responses were negative for BCL-2 during the treatment course of immune-stimulatory treatments (eg, interferon (IFN)-α, IFN-γ, and interleukin-2).[28] Furthermore, we performed a retrospective analysis of the clinical response of patients with lymphoma treated with anti-CD19 CAR-T therapy and showed that patients with genetic alterations in BCL-2 (ie, gain or translocation of BCL-2) show significantly lower response and overall survival to CAR-T treatments than patients without genetic alterations of BCL-2,[33] implicating that genetic alteration of BCL-2 plays a crucial role in the anticancer efficacy of CAR-T therapy. In addition to the effect of altered intrinsic regulators of apoptosis on cancer immunotherapy, our group also demonstrated that CAR-T cells' anticancer efficacy is significantly reduced when leukemic cells display decreased expression of positive regulators of apoptosis, especially in the death receptor pathway (FasL, TRAIL, and TNF-α).[34] By using unbiased genome-wide CRISPR knock-out (KO) screening, we identified that the deletion of anti-apoptotic regulators (eg, BIRC2, CFLAR, and TRAF2) in the B-ALL cell line NALM-6 led to significant enhancement of the anticancer activity of CAR-T cells, while KO of pro-apoptotic regulators (eg, FADD, Caspase-8, BID, and TNFRSF10B) resulted in a decrease of anticancer activity of CAR-T cells. Further validation with clinical data revealed that the downregulation of pro-apoptotic regulators was significantly associated with a poor clinical response in patients with B-ALL treated with anti-CD19 CAR-T cells. Likewise, Upadhyay *et al* showed that Fas-FasL-mediated cancer killing plays a crucial role in T cell-based immunotherapy, and the expression of Fas in cancer strongly correlates with the clinical outcome of CAR-T therapy.[29] Importantly, these studies suggest that mechanisms conferring resistance to apoptosis in some cancer cells can also drive T-cell dysfunction, leading to poor clinical outcomes of T cell-based immunotherapy.

Given that resistance to apoptosis in cancers could be a critical factor associated with poor clinical outcomes of T-cell mediated immunotherapy by causing dysfunction of T cells, this review will highlight several novel therapeutic strategies designed to augment T cell-mediated cancer apoptosis. Furthermore, it discusses tumor-derived or tumor microenvironment (TME)-derived factors that govern T-cell apoptosis and rational strategies to prevent it.

STRATEGIES TO ENHANCE T-CELL MEDIATED CANCER APOPTOSIS

Despite remarkable clinical outcomes of T cell-based immunotherapies, a substantial number of patients do not benefit from these approaches.[9–15] Considering the importance of cancer apoptosis susceptibility in the cytolytic activity of T-cell therapy, several interesting therapeutic approaches have been investigated to overcome apoptosis resistance in cancer cells (figure 2 and table 1).

First, researchers have tested whether conventional anticancer therapeutics, such as chemotherapy or radiotherapy, can enhance cancer apoptosis during immunotherapy. Both, chemotherapeutic agents (eg, alkylating agents, anthracyclines, vinca alkaloids, and antimetabolites) and radiation (eg, X-ray), potently promote intrinsic

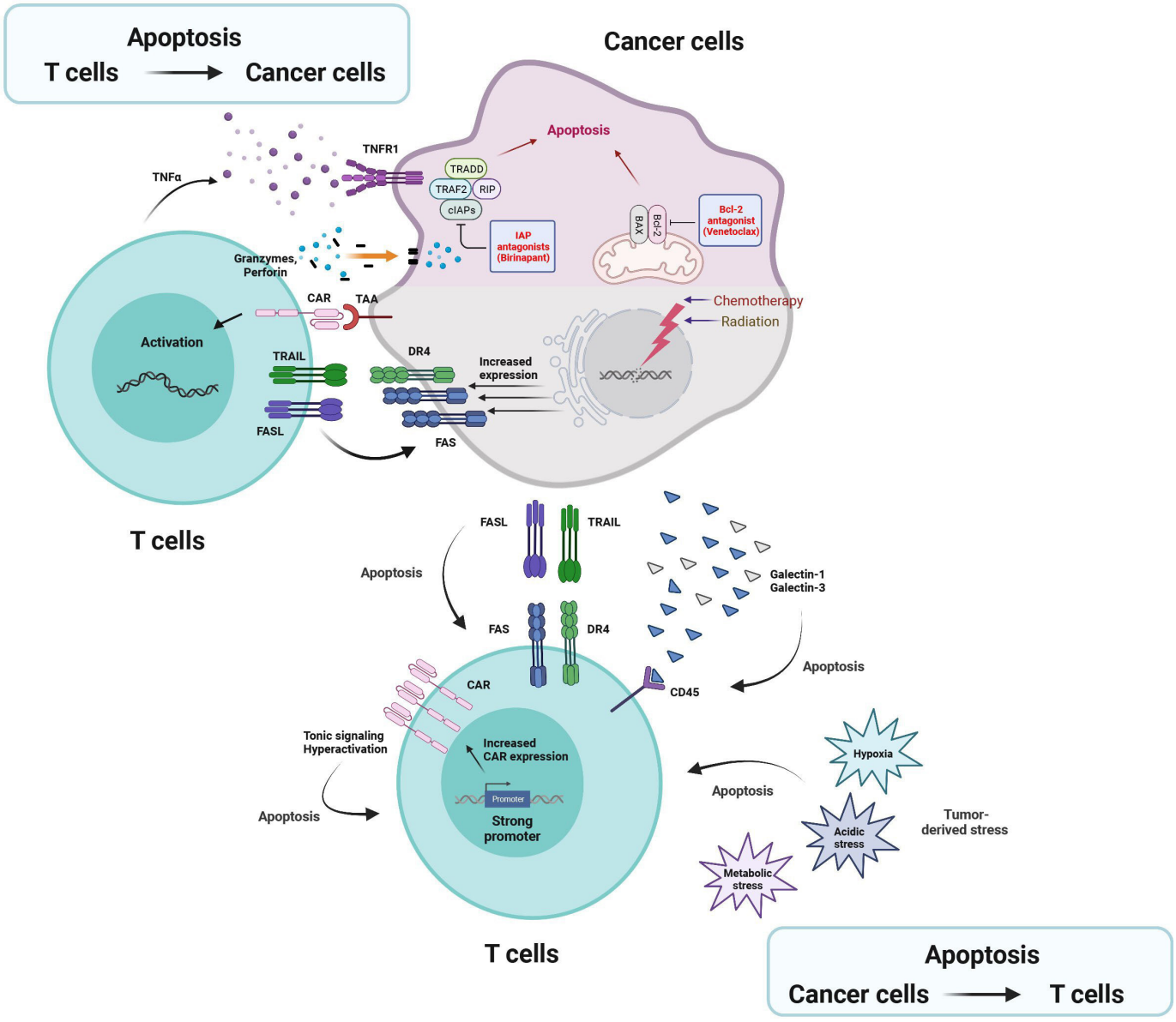

Figure 2 Dual effects of apoptosis in T cell-based immunotherapy. On the cancer cells side, chemotherapy and radiation therapy induces the expression of DR4 and Fas in cancer cells, sensitizing cancer cell to TRAIL-mediated and FasL-mediated apoptosis. In addition, treatment of small molecules that can specifically inhibit anti-apoptotic regulators (eg, IAP and BCL-2) leads to the enhancement of cancer apoptosis mediated by TNF-α or granzymes/perforin. On the T-cell side, multiple factors (eg, FasL, TRAIL, and galectin) and stress (eg, hypoxia, metabolic alteration, and acidification) derived from cancer cell and tumor microenvironment promote apoptosis in T cells. Hyperactivation and tonic signaling of CAR-T cells by increased CAR expression on the surface induce apoptosis in T cell. BCL-2, B-cell lymphoma 2; CAR, chimeric antigen receptor; cIAP, cellular IAP; DR4, death receptor 4; FasL, Fas ligand; IAP, inhibitor of apoptosis proteins; TAA, Tumor associated antigen; TNF, tumor necrosis factor; TRADD, TNF receptor type 1-associated death protein; TRAIL, TNF-related apoptosis-inducing ligand.

apoptosis in cancer cells by inducing DNA damage and/or inhibiting cell cycle.[35 36] Moreover, treatment with selected chemotherapies (eg, etoposide, doxorubicin, and 5-fluorouracil) and radiation can also modulate death receptor-mediated extrinsic apoptosis in cancer cells by affecting the transcriptional activity of death receptors (eg, Fas and TNFRSF10 families).[37–41] On exposure to etoposide, DR5 and Fas expression increased in human lung, colorectal, prostate, bladder, and breast cancer cell lines, leading to improved immune cell (natural killer T cell-mediated killing).[37] Similarly, sublethal doses of doxorubicin upregulate TRAIL receptors on cancer cells (eg, MAR and JOHW colorectal carcinoma cell lines), promoting natural killer and tumor-infiltrating lymphocyte (TIL) cytotoxicity.[39]

Interestingly, the authors also observed that doxorubicin treatment reduced the expression of intracellular FLICE inhibitory protein (c-FLIP), a key anti-apoptotic inhibitor of death receptor-mediated apoptosis. This finding suggests that doxorubicin can sensitize cancer cells to immune cell-mediated extrinsic apoptosis by modulating both pro-apoptotic and anti-apoptotic regulators.

Table 1 Summary of the preclinical combinations of pro-apoptotic drugs and T cell-based immunotherapies

Class	Drug	Target	Combination	Cancer type	Effect	Ref
Chemo therapy	Cisplatin, etoposide	DNA damage	NKT cells	NSCLC cell lines CRC cell lines PC cell lines BC cell lines	Sensitization to TRAIL-mediated and FasL-mediated apoptosis	37
Chemo therapy	Doxorubicin, 5-fluorouracyl	DNA damage	Vγ9Vδ2 T cells	CRC cell lines	Sensitization to TRAIL-mediated apoptosis	38
Chemo therapy	Doxorubicin	DNA damage	NK or T cells	Melanoma and bladder cancer cell lines	Sensitization to TRAIL-mediated apoptosis	39
Radiation	Sublethal irradiation	–	antitumor CTLs and NK cells	CRC cell lines	Sensitization to TRAIL-mediated and FasL-mediated apoptosis	40
Radiation	Sublethal irradiation	–	CEA-specific HLA-A2-restricted CD8(+) CTLs	23 human carcinoma cell lines (12 colons, 7 lungs, and 4 prostate)	Sensitization to FasL-mediated apoptosis	41
SMAC mimetic	Birinapant	Inhibition of XIAP and cIAP1/2	anti-CD19 CAR T cells	B-ALL	Increase of CAR T cell-mediated apoptosis	34
SMAC mimetic	Birinapant	Inhibition of IAPs	anti-HER2 CAR T cells	HER2+patient-derived colorectal tumoroids	Sensitization to TNF-α-mediated apoptosis	56
SMAC mimetic	Birinapant	Inhibition of IAPs	anti-CD19 CAR T cells	B-ALL	Sensitization to TNF-α-mediated apoptosis	32
SMAC mimetic	ASTX660	Inhibition of IAPs	cytotoxic TIL	HNSCC	Enhanced immunogenic cell death	59
BH3 mimetic	ABT737	Bcl-2 family anti-apoptotic proteins	anti-CD19 CAR T cells	Patients with childhood precursor-B ALL	Increase of CAR T cell-mediated apoptosis	65
BH3 mimetic	Venetoclax	Bcl-2 family anti-apoptotic proteins	anti-CD19 CAR T cells	B-ALL and B-lymphoma cell lines	Increase of CAR T cell-mediated apoptosis	67

B-ALL, B-cell acute lymphoblastic leukemia; BC, breast cancer; BCL-2, B-cell lymphoma 2 ; CAR, chimeric antigen receptor; CRC, colorectal cancer; CTL, cytotoxic T cell; FasL, Fas ligand; HER2, human epidermal growth factor receptor-2; HNSCC, head and neck cancer; IAP, inhibitor of apoptosis proteins; NK, natural killer; NKT, natural killer T; NSCLC, non-small cell lung cancer; PC, prostate cancer; SMAC, second mitochondria-derived activator of caspase; TIL, tumor-infiltrating lymphocyte; TNF, tumor necrosis factor; TRAIL, TNF-related apoptosis-inducing ligand .

Another evidence of chemotherapy-induced immune killing reported that 5-fluorouracil treatment upregulates the expression of DR5 in colon cancer-initiating cells in vitro, leading to enhancement of T cell-mediated cytotoxicity.[38] In addition to chemotherapeutic agents, irradiation, which causes DNA damage and intracellular stress, can also lead to the induction of death receptor-mediated cancer cell apoptosis. For instance, a sublethal dose of irradiation can upregulate the expression of Fas and DR5 in colorectal carcinoma cell lines, making them susceptible to TRAIL-induced and Fas-induced apoptosis.[40] Further investigation identified that a sublethal dose of irradiation can increase Fas expression in over 40% of the cancer cell lines, including colon, lung, and prostate cancers.[41] This suggests that radiation may be an effective strategy in combination with T cell-based immunotherapy to enhance the sensitivity of extrinsic apoptosis in cancer cells. In addition to the modulation of cytolytic activity of endogenous T cells in radiation therapy and chemotherapy, the use of recombinant anti-Fas and anti-DR4/5 agonists along with radiation and chemotherapeutic agents has been investigated. Treatment with recombinant TRAIL combined with bortezomib, vorinostat (SAHA), and valproic acid significantly induced cancer cell apoptosis by sensitizing cancer cells to extrinsic apoptosis signal.[42–45]

Finally, with ample preclinical evidence that chemotherapy and radiation therapy can increase the sensitivity of cancer cells to T cell-mediated apoptosis, various clinical trials exploiting the combination of immunotherapy and chemo/radiation have been registered and conducted (see online supplemental table 1). First, the combination of pembrolizumab (online supplemental box 1) and chemotherapy (ie, carboplatin and either paclitaxel or nanoparticle albumin-bound-paclitaxel) significantly improved overall survival and progression-free survival in patients with metastatic squamous non-small cell lung cancer (NSCLC) as compared with chemotherapy only treated patients.[46] Another clinical investigation using an immunotherapeutic combination (nivolumab and ipilimumab, online supplemental box 1) with chemotherapy (carboplatin, paclitaxel, pemetrexed, and cisplatin) showed similar results.[47] These two independent clinical trials eventually led to FDA approval of chemotherapy in combination with checkpoint blockade for first-line metastatic squamous NSCLC treatment. Despite the substantial

synergy between immune checkpoint inhibitors and chemo/radiation therapy, one caveat remains: apoptosis of T cells can also be increased by chemotherapy and radiation due to the lack of ability of chemotherapy and radiation to distinguish target cells (ie, cancer cells) and effector cells (ie, T cells). The resistance mechanisms of T cells to chemotherapy-induced and radiation-induced apoptosis remain largely unknown. Several studies have highlighted that memory T cells can escape apoptosis triggered by chemotherapy and irradiation, implicating the potential role of memory T cells in synergy strategies.[48 49] Considering the resistance of memory T cells to apoptosis, one possible explanation is that a high level of BCL-2[50] and low level of Bcl-2-like 11 (BIM)[51] expression in memory T cells may increase the threshold of apoptotic sensitivity, allowing them to evade chemotherapy-induced and radiation-induced apoptosis. However, further investigations are required to fully understand survival mechanisms of T cells during chemotherapy and radiation.

While chemotherapy and/or radiation increase the sensitivity of cancer cells to apoptosis, direct inhibition of apoptotic regulators has also been observed in combination with T cell-based immunotherapy. One example is the inhibitor of apoptosis proteins (IAPs) that are overexpressed in many cancers[52] and include several members, such as cellular IAP1 (cIAP1), cIAP2, X-linked IAP (xIAP), neuronal apoptosis inhibitory protein (NAIP), livin, and survivin.[53] cIAP1 plays a critical role in inhibiting TNF-α-mediated apoptosis by preventing the formation of the apoptotic complex (FADD/RIPK1/Caspase-8). Moreover, xIAP inhibits apoptosis by blocking Caspase-3 and Caspase-7 by directly binding to them.[54] Given the importance of IAPs in inhibiting apoptosis in cancer, multiple agents have been investigated to promote IAP degradation, thereby sensitizing cancer cells to apoptosis. Second mitochondria-derived activator of caspase (SMAC) mimetics are small synthetic molecules whose structural and functional features are similar to SMAC, which are endogenous antagonists of IAPs. Several SMAC mimetics (eg, birinapant, LCL-161, ASTX660, Debio1143, BV-6, GDC-0152, CUCD-427, HGS1029, and AT-406) have been developed (online supplemental box 2).[55] Particularly, birinapant has been extensively evaluated for its anticancer properties, including in combination with T cell-based immunotherapies such as immune checkpoint inhibitors, such as anti-PD-1 and anti-CTLA-4 antibodies, driving significantly enhanced TNF-α-mediated cancer cell apoptosis and increase in survival in a murine glioblastoma (GBM) model.[32 34 56 57] Birinapant also improved the anticancer efficacy of CAR-T therapy in murine models. Treatment with birinapant enhanced anti-human epidermal growth factor receptor-2 CAR-T cells-mediated cancer killing by sensitizing cancer cells to TNF-mediated apoptosis.[56] Likewise, Song *et al* also found that treatment of birinapant enhances CAR-T cell-mediated tumor killing in GBM model.[58] Using a CRISPR Cas9 KO library, key mediators of synergy between CAR-T cells and birinapant such as RIPK1, FADD, and TNFRSF10B in cancer cells are identified.[32] Our group also demonstrated that birinapant treatment improved CAR-T cells ability to eliminate B-ALL, which otherwise lacks sensitivity to extrinsic apoptosis[34]; however, these results were obtained in vitro and in vivo validation is required to exclude toxicity on CAR T cells. In addition to birinapant, Ye *et al* studied the combinatorial efficacy of cytotoxic TILs and ASTX660, another antagonist of cIAP1/2 and xIAP, in a preclinical model with head and neck squamous cell carcinoma (HNSCC).[59] The authors found that ASTX660 treatment induced—in the presence of TNF-α—calreticulin (CRT) expression, heat shock proteins 70/90, and high mobility group protein on the surface of human HNSCC cell lines (eg, UMSCC-46 and UMSCC-47). These are key molecular signatures for immunogenic cell death (ICD), suggesting that ASTX660 and TNF-α promoted ICD in HNSCC cell lines. ASTX660-mediated induction of ICD was further confirmed in syngeneic murine cancer models (HNSCC) when combined with radiation. Interestingly, the authors identified that ASTX660 treatment plus TNF-α led to clonal expansion of antigen-specific T-cell clones. This might be due to the enhancement of the antigen-processing machinery in cancer cells, as evidenced by the upregulation of critical components of the antigen-processing machinery (eg, human leukocyte antigen (HLA)-A, HLA-B, HLA-C, ERp57, CRT (intracellular), Transporter associated with antigen processing 1 (TAP1), and TAP2) in human HNSCC cell lines after exposure to ASTX660 and TNF-α.

Members of the BCL-2 family, such as BCL-2, BCL-XL, MCL-1, BAX, and BAK, play a critical role in regulating intrinsic apoptosis by modulating the permeabilization of the mitochondrial membrane.[60] As previously discussed, upregulation of BCL-2 activity via overexpression or translocation is one of the key features of various cancers.[61] Several BCL-2 inhibitors have been developed, including obatoclax, AT101, ABT737, S-055746, S65487, PNT-2258, navitoclax, and venetoclax (online supplemental box 2).[62] In particular, venetoclax, an orally available small-molecule inhibitor with high specificity to BCL-2, has demonstrated substantial anticancer efficacy in treating CLL, other lymphomas, and acute myeloid leukemia, leading to its FDA approval in these settings.[63] Recently, Kohlhapp *et al* reported that venetoclax could enhance the anticancer efficacy of anti-PD-1 antibody (MDX-1106) treatment.[64] Interestingly, the authors found that venetoclax treatment increased tumor infiltrating effector memory T cells, which could also explain the potential role of memory T cells in synergy with pro-apoptotic drugs. The beneficial effects of venetoclax in T cell-based immunotherapy were further identified by our group. Using a combination of venetoclax and CAR-T therapy, we demonstrated a significant improvement in CAR-T cells' anticancer activity against various lymphoma and leukemia xenograft models (eg, OCI-Ly18, MINO, NALM6, KG-1, and MOLM-14).[33] In addition to venetoclax, the combinatory effect of different BCL-2 inhibitors (ie, ABT737) with CAR-T therapy was tested, and it was

found that adding ABT737 to CART19 resulted in an increase in Caspase 3/7 activity in cancer cells, leading to cancer killing enhancement.[65]

While, increasing cancer cell sensitivity to apoptosis using aforementioned pro-apoptotic molecules results in the enhancement of the anticancer response of T cell-based immunotherapies in some models, one potential concern of this approach is the unintended toxicity of these agents on effector immune cells such as T cells, which could be critical for the long-term efficacy of combination immunotherapy. A study showed that SMAC mimetic (ie, LBW242) treatment significantly inhibited virus-specific $CD8^+$ T-cell expansion in vivo by inducing T-cell apoptosis, ultimately leading to the failure of virus replication.[66] Moreover, although Lee *et al* and Kohlhapp *et al* demonstrated that venetoclax augmented the anticancer response of CAR-T therapy and anti-PD-1 treatment, they also found that co-culture of venetoclax with genetically non-modified T cells and CAR-T cells potently reduced their viability.[33 64] These observations strongly suggest that careful design of combination therapies and the sequence of administration are required to avoid T-cell toxicity and ensure long-term therapeutic efficacy. One possible administration strategy to avoid bystander effects on T cells is to pretreat the cancer cells with cytotoxic drugs. Recently we reported that patients with lymphoma receiving venetoclax during bridging therapy prior CAR-T cell infusion achieved significant improvement in clinical response compared with patients treated with no venetoclax-included bridging therapy.[33] In line with our clinical observations, pretreatment of cancer cells with venetoclax enhanced CAR-T cell-mediated anticancer activity in vitro.[67] These preclinical and clinical data strongly suggest that pre-sensitizing cancer cells with anti-apoptotic inhibitors could enhance the anticancer effect of T cell-based immunotherapy while reducing toxicity to T cells.

T-CELL APOPTOSIS LIMITS ANTICANCER IMMUNITY IN THE TME

Apoptosis in cancer therapy could induce both cancer cells to die and result in T-cell death. T-cell apoptosis is an *indirect* result of multiple immunosuppressive mechanisms in cancer genesis. For example, T-cell dysfunction, such as exhaustion, is a physiological state in which T cells lose their effector functions while maintaining viability. Prolonged exhaustion ultimately leads to T cells undergoing cellular apoptosis.[68] Furthermore, the immunosuppressive TME, including immunosuppressive immune cells (eg, T regulatory cells, tumor-associated macrophages, and myeloid-derived suppressor cells)[69 70] and lack of key nutrients (ie, low arginine and changes in available metabolites)[71–73] also have substantial effects on the proliferation and survival of cytotoxic T cells in the TME. Because there are already extensive revisions of the literature on T-cell exhaustion[74–76] and other immunosuppressive factors,[77–79] we focused on the mechanisms of immune evasion that *directly* trigger apoptosis in T-cells.

On activation, T cells enhance the expression of pro-apoptotic proteins (eg, FasL, TRAILs, and TNF), potentially promoting the death of target cells as well as death receptors on their surface (Fas, TRAIL receptors, TNF receptor). This upregulation of death receptors increases the susceptibility of activated T cells to apoptosis.[80 81] This process is called activation-induced cell death (AICD) and plays a vital role in maintaining peripheral immune tolerance and preventing autoimmune disease development.[82] Cancer cells can take advantage of this T-cell liability by using it as a potential immunoevasion strategy. Reports in the late 1990s demonstrated that FasL expression in several malignancies (melanoma, colon, head/neck, liver, and lung) serves as a mechanism of cancer evasion.[83–86] This phenomenon, coupled with evidence that T cells increase the expression of Fas on activation, highlights that cancers can induce apoptosis in T cells via the extrinsic pathway to evade immune surveillance. There has also been evidence of upregulation of TRAIL in a few malignancies (melanoma, liver, breast, and lung), although its correlation with the clinical outcome has been controversial.[87–90] While Bron *et al* found no correlation with prognosis in patients with melanoma,[87] Cross *et al* observed a negative association between TRAIL expression in breast cancers and the clinical outcome of patients with breast cancer.[88] Moreover, heterogeneity exists in the ubiquity of FasL and TRAIL expression across cancers. Another captivating aspect of this mechanism is the observation that cancer can secrete exosomes expressing FasL and independently induce T-cell apoptosis.[91–93] Such observations amplify the potency of FasL-mediated apoptosis of T cells directed by cancer cells, which may cause peripheral T-cell dysfunction.[94]

This cancer-induced, death receptor-mediated T-cell apoptosis has been proven to directly hinder responses to immunotherapy.[95–99] Zhu *et al* used a novel autochthonous melanoma mouse model to demonstrate that FasL-mediated T-cell apoptosis facilitates cancer resistance to anti-CTLA-4 antibody, anti-PD-1 antibody, and ACT.[98] Similar to TCR-mediated activation, CAR-driven T-cell activation also increases the susceptibility of CAR-T cells to apoptosis by upregulating death receptors and associated ligands on their surface. Hyperstimulation of CAR-T cells by incorporating two co-stimulatory domains (CD28 and 4-1BB) also increases Fas and DR5 expression and promoted CAR-T cells apoptosis.[96 97] Lastly, tonic signaling of 4-1BB co-stimulation due to greater anti-CD19 CAR expression driven by a strong promoter, such as retroviral long terminal repeat, increases levels of FasL, leading to apoptosis of CAR-T cells on activation.[99] While introducing multiple co-stimulatory domains into CAR construct was intended to enhance activation,[95] these data present a potential concern of overstimulation suggesting a need of 'modulating' CAR-activation in T cells rather than just boosting it.

Cancer and TME cells also secrete factors that can directly trigger T-cell apoptosis.[100 101] Galectins are a family of proteins produced and secreted by various cells, including cancer and immune cells.[102] Galectins bind to β-galactosides on glycoproteins and glycolipids via a conserved carbohydrate recognition domain, thereby regulating miscellaneous biological events, including apoptosis.[100 101] Many studies have demonstrated that cancer-secreted galectin-3 (Gal-3) can induce T-cell apoptosis in various cancers, including melanoma, lung, and colorectal cancer, on binding to their target TCRs, such as CD7, CD29, CD45, and CD71.[103–108] Mechanistically, cancer-secreted Gal-3 binds to CD45, activating independent pathways involving protein kinase C and ROS, resulting in sustained ERK 1/2 phosphorylation, Caspase-9 activation, cytochrome c release, and Caspase-3 activation to induce apoptosis.[109] Besides the function of Gal-3, secreted Gal-1 in the TME also correlated with increased cancer progression (following ICB therapy), which could be due to T-cell apoptosis, likely mediated through a CD45-binding dependent mechanism.[110–116] However, this correlation is not consistent across cancers. While elevated Gal-1 correlates with T-cell apoptosis in pancreatic[117] and lung[110] cancer cell lines, it was not confirmed in a melanoma cell line[108] or in vitro against activated primary T cells,[118] suggesting that its effects may be heterogeneous across malignancies.

Similarly, gangliosides and sialic acid-containing glycosphingolipids found on outer plasma membranes are overexpressed in cancers and shed into the TME.[119] Although the apoptotic effects of gangliosides and their expression in different cancers have not been investigated as extensively as galectins, Finke and Tannenbaum have elucidated their general effect on T-cell apoptosis through a series of studies. Finke *et al* demonstrate in both a GBM and a renal cell carcinoma model that cancer gangliosides are responsible for inducing T-cell apoptosis.[120 121] Moreover, Bharti and Singh show the induction of bone marrow cell apoptosis through T-cell lymphoma-derived gangliosides.[122] Regarding the mechanism of ganglioside-mediated T-cell apoptosis, gangliosides have been shown to be internalized by activated T cells, resulting in ROS production, cytochrome c release, and Caspases-8 and Caspase-9 activation.[123] This implies that gangliosides may promote both intrinsic and extrinsic apoptosis. Notably, gangliosides facilitate the intrinsic pathway of apoptosis, as evidenced by the induction of ROS, cytochrome c release, Caspase-9 activation, and downregulation of anti-apoptotic BCL genes, such as BCL-XL and BCL-2.[124]

Metabolic pathways and associated enzymes may also play important roles in T-cell apoptosis. For instance, glucose deprivation can reduce the proliferation of Jurkat cells and primary human T cells in vitro.[125] This reduction might be linked to the increase in intrinsic apoptosis since the knockdown of pro-apoptotic BH-3-only protein (ie, Noxa) improves the survival of T cells when limited glucose is available. Considering that T cells encounter significant competition in the uptake of glucose by cancer cells in TME,[126] the lack of glucose in T cells may increase the susceptibility of T cells to apoptosis, leading to impairment of the anticancer activity of T cells. In addition to the glycolytic pathway, fatty acid metabolism is critical for T cell-mediated anticancer activity. While T cells use fatty acid oxidation to form and maintain the memory phenotype,[127] inhibiting fatty acid synthase potentially reduces the expression of FasLs, preventing T cells from restimulation-induced cell death.[128] In addition to the intrinsic alteration of T-cell metabolism in inducing apoptosis, metabolites from cancer cells may also promote apoptosis in T cells. For example, kynurenine, a metabolite of tryptophan by indoleamine 2,3-dioxygenase in cancer cells, can induce apoptosis in thymocytes and terminally differentiated T helper cells.[129]

The last well-documented secretion-based methods of direct cancer-induced T-cell apoptosis are the acidic and hypoxic stress found in the TME. Acidity is caused by the 'Warburg effect', whereby cancer cells preferentially engage in aerobic glycolysis rather than oxidative phosphorylation metabolism of glucose.[130] Consequently, they increase their glucose intake to meet their energy demands, producing excess lactate acid, which is secreted into the microenvironment, causing acidification of the extracellular space.[131] Long-term exposure (>3 days) to acidic pH in the TME (pH 6.5) caused permanent damage and T-cell apoptosis in C57BL-murine B16-melanoma TILs.[132] Under extreme conditions, acidic stress (pH 3.3 for 25 min at 37°C) induces intrinsic apoptosis in Jurkat T cells by increasing cell cycle arrest.[133] Although in vitro studies demonstrated that acidic stress can alter apoptosis in T cells, the effect of acidic conditions in vivo remains unknown and requires careful validation. Along with increased acidity, hypoxia in the TME can also be a critical factor affecting T-cell apoptosis. Kiang *et al* found hypoxia-induced apoptosis in the Jurkat cell line.[134] The authors attributed apoptosis to increase NO production due to the upregulation of NO synthase, subsequently increasing Caspase-9 activation, cytochrome c levels, and Caspase-3 activation. In addition, hypoxia (1% O_2) induces apoptosis in primary T cells from healthy donors, hypothesizing it to result from a buildup of endogenous adenosine in the extracellular medium. The authors found that T cells had an upregulation of the adenosine receptor A2aR. The downstream effects of these receptors in inducing apoptosis have not been characterized.[135]

STRATEGIES TO AVOID T-CELL APOPTOSIS IN THE TME

Long-term survival and functionality of T cells are critical to ensure the anticancer efficacy of cancer immunotherapies.[136] Several strategies have been developed to prevent T-cell apoptosis. Yamamoto *et al* established a novel CAR-T cell that inhibits FasL-mediated T-cell apoptosis by truncating the intracellular death domain of Fas or introducing a point mutation (I246N) in the Fas death domain.[137] These modifications allow CAR-T cells to become resistant to cancer-induced FasL-mediated

apoptosis by inhibiting the recruitment of FADD into the apoptotic complex and preventing DISC formation. The failure of DISC formation enhanced CAR-T cell persistence and anticancer activity in a murine B16 melanoma cancer model. Importantly, Fas-engineered T cells did not show uncontrolled proliferation, at least in in-vivo models, suggesting that modulation of T-cell extrinsic apoptosis may be a safe and feasible strategy.[137] Similarly, another study reported that CRISPR-mediated KO of Fas reduced the AICD of anti-CD19 CAR-T cells during chronic exposure to target cells, which led to increased T-cell expansion.[138] In addition to modifying extrinsic apoptosis in T cells, Charo *et al* generated murine T cells that overexpress BCL-2 and tested whether this modification leads to enhanced anticancer activity of cytolytic T cells by preventing apoptosis.[35] The authors identified that BCL-2 overexpressing T cells show superior anticancer activity compared with wild-type T cells by improving long-term survival in the absence of a survival signal. Recently, another study revealed that constitutive overexpression of BCL-2 in CAR-T cells improves CAR-T cells proliferation and reduces AICD in CAR-T cells.[139] Our group further demonstrates that higher levels of BCL-2 expression in CAR-T cells of patients with lymphoma significantly correlate with enhanced clinical response (ie, CAR-T persistence and overall survival) of CAR-T therapy, suggesting that modulating intrinsic apoptosis in T cells is an important strategy to enhance CAR-T therapy.[33] In addition to BCL-2, there are other critical anti-apoptotic regulators (ie, MCL-1 and BCL-xL) affecting T-cell survival and differentiation. Studies using transgenic expression of these anti-apoptotic regulators have suggested their potential implications in T cell-based immunotherapy. For instance, constitutive expression of BCL-xL rescued activation-induced cell death of $CD8^+$ T cells in a viral infectious model.[140] Enhanced expression of MCL-1 promotes long-term memory formation in the acute phase of vaccinia virus infections.[141] Despite the beneficial effect of BCL-2 family overexpression in T cells, altering the BCL-2 signal in T cells requires additional attention, as the constitutive expression of BCL-2 in murine T cells promoted T-cell lymphoma development (ie, 18 of 68 BCL-2 transgenic mice developed T-cell lymphoma).[142]

Finally, developing strategies to avoid T-cell apoptosis would be beneficial for preventing potential apoptosis of T cells when combining immunotherapies with pro-apoptotic drugs. Our group recently reported a novel strategy to overcome venetoclax-mediated CAR-T cell toxicity by developing venetoclax-resistant CAR-T cells (ven-CAR-T).[33] In ven-CAR-T, we introduced a mutant form of BCL-2 containing a point mutation at the 104 amino acid residue (Phe104Leu or F104L) located in the binding pocket of venetoclax. Accordingly, venetoclax cannot bind to BCL-2(F104L) and loses its inhibitory function.[143 144] Therefore, by overexpressing BCL-2(F104L) in ven-CAR-T, ven-CAR-T showed strong resistance to venetoclax, leading to a significant enhancement of CAR-T cells and venetoclax combination effects.

CONCLUSIONS

As immunotherapy is ready to make its next steps and advances as a line of therapy for patients, a critical factor is the development of strategies to overcome the current limitations that preclude responses in a significant subset of patients. This review discussed the dual role of apoptosis in T cell-based immunotherapy, from cancer (ie, resistance to apoptosis) as well as a T-cell side (ie, apoptotic death).

Most cancers are characterized by resistance to apoptosis through several mechanisms, including neutralizing pro-apoptotic signals by either increasing expression of anti-apoptotic molecules such as IAPs and BCL-2 or decreasing positive regulators of the death receptor-mediated apoptosis. Therefore, increasing the sensitivity of cancer cells to apoptosis should be considered a vital strategy to improve the anticancer activity of T cell-based immunotherapies. Combining pro-apoptotic drugs may be an appealing approach for sensitizing cancer cells to T cell-mediated death; for instance, inhibiting key anti-apoptotic regulators (IAPs and BCL-2) by targeted small molecules (SMAC mimetics and ABT737) enhanced CAR-T cell-mediated anticancer activities. However, because such drugs may also induce T-cell apoptosis, careful consideration of the administration timing/dose of pro-apoptotic drugs or apoptosis-sensitizing treatments must be made to determine the optimal therapeutic regimens.

Regarding T-cell apoptosis, cancer evades immunotherapy by secreting pro-apoptotic inducers against cytolytic T cells and developing a hostile TME. Thus, there is a clear need for combinations that can prevent these evasion mechanisms. CAR-T cell therapy presents a versatile option not only for combination strategies but also for the possibility of performing genetic engineering (eg, Fas KO, mutant Fas, or constitutive overexpression of BCL-2). However, as a consequence of enhancing T-cell survival/expansion by aforementioned modulations, safety concerns such as abnormal lymphoproliferation and tumorigenesis of modified T cells appear. Therefore, it is critical to include safety switches in these models to maximize safety in clinical use (eg, the anti-inducible Caspase-9 system and antibody-mediated cellular cytotoxicity using a truncated epidermal growth factor receptor/anti-epidermal growth factor receptor antibody).

In conclusion, apoptosis is a crucial player in T cell-based immunotherapy. Deep knowledge of mechanisms of apoptosis resistance in cancer and T-cell biology is necessary to promote cancer cell apoptosis and prevent T-cell death. Several novel agents being developed together with the most recent advances in bioengineering will pave the way for the success of next-generation therapeutic combinations.

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Class	Drug	Target
CAR-T therapy	Tisagenlecleucel	CD19
	Axicabtagene ciloleucel	CD19
	Brexucabtagene autoleucel	CD19
	Lisocabtagene maraleucel	CD19
	Idecabtagene vicleucel	B-cell maturation antigen (BCMA)
	Ciltacabtagene autoleucel	B-cell maturation antigen (BCMA)
Immune checkpoint blockade	Ipilimumab	CTLA-4
	Pembrolizumab	PD-1
	Nivolumab	PD-1
	Atezolizumab	PD-L1
	Avelumab	PD-L1
	Durvalumab	PD-L1
	Cemiplimab	PD-1
	Dostarlimab	PD-1
Bi-specific antibody	Blinatumomab	CD19-CD3
	Mosunetuzumab	CD20-CD3
	Glofitamab	CD20-CD3
	Epcoritamab	CD20-CD3
	Solitomab	EpCAM-CD3
	Teclistamab	BCMA-CD3
	Elranatamab	BCMA-CD3

Box 1. List of T cell-based immunotherapies

Class	Drug	Target
SMAC mimetics	Birinapant	IAPs
	LCL-161	IAPs
	ASTX660	IAPs
	Debio1143	IAPs
	BV-6	IAPs
	GDC-0152	IAPs
	CUCD-427	IAPs
	HGS1029	IAPs
	AT-406	IAPs
	Venetoclax	BCL-2
	Obatoclax	A1/Bfl-1, BCL-2, BCL-B, BCL-w, BCL-XL, MCL-1
	AT101	BCL-2, BCL-XL, MCL-1
	ABT737	BCL-2, BCL-w, BCL-XL
BCL-2 inhibitors	S-055746	BCL-2
	S65487	BCL-2
	PNT-2258	BCL-2
	Navitoclax	BCL-2, BCL-w, BCL-XL

Box 2. List of pro-apoptotic drugs associated with targets

Supplementary Table I

Therapy	Study title	Chemotherapy	Radiation therapy	Clinical trials identifier
Checkpoint inhibitor	18F-FDG PET/CT to Evaluate pD-1 Monoclonal Antibody Combined With First-line Chemotherapy in Advanced Non-small Cell Lung Cancer	Y		https://ClinicalTrials.gov/show/NCT04996927
Checkpoint inhibitor	A Clinical Study Evaluating Nivolumab-containing Treatments in Patients With Advanced Non-small Cell Lung Cancer After Failing Previous PD-1/(L)1 Therapy and Chemotherapy	Y		https://ClinicalTrials.gov/show/NCT04151563
Checkpoint inhibitor	A Clinical Study of HLX10 Combined With Chemotherapy Versus Placebo Combined With Chemotherapy for Neoadjuvant/Adjuvant Treatment of Gastric Cancer	Y		https://ClinicalTrials.gov/show/NCT04139135
Checkpoint inhibitor	A Clinical Study to Evaluate Efficacy and Safety of HLX10 Combined With Albumin-Bound Paclitaxel in Patients With Advanced Cervical Cancer Who Have Progressive Disease or Intolerable Toxicity After First-Line Standard Chemotherapy	Y		https://ClinicalTrials.gov/show/NCT04150575
Checkpoint inhibitor	A Clinical Study to Evaluate Efficacy and Safety of HLX10 Combined With HLX04 and Chemotherapy (XELOX) in Patients With Metastatic Colorectal Cancer (mCRC)	Y		https://ClinicalTrials.gov/show/NCT04547166
Checkpoint inhibitor	A Clinical Trial Comparing HLX10 With Placebo Combined With Chemotherapy (Cisplatin + 5-fu) in the First-line Treatment of Locally Advanced/Metastatic Esophageal Squamous Cell Carcinoma (ESCC)	Y		https://ClinicalTrials.gov/show/NCT03958890
Checkpoint inhibitor	A Global Study to Assess the Effects of MEDI4736 Following Concurrent Chemoradiation in Patients With Stage III Unresectable Non-Small Cell Lung Cancer	Y	Y	https://ClinicalTrials.gov/show/NCT02125461
Checkpoint inhibitor	A Multicenter Phase II Trial of Post-operative Concurrent Chemoradiotherapy Using Weekly Cisplatin With Tislelizumab for Patients With High-risk Head and Neck Squamous Cell Carcinoma the POTENTIAL Study	Y		https://ClinicalTrials.gov/show/NCT04814069
Checkpoint inhibitor	A Multicenter, Phase 3, Randomized Trial of Sequencial Chemoradiotherapy With or Without Toripalimab (PD-1 Antibody) in Newly Diagnosed Early-Stage Extranodal Natural Killer/T Cell Lymphoma, Nasal Type (ENKTL)	Y		https://ClinicalTrials.gov/show/NCT04365036
Checkpoint inhibitor	A Phase Ib/II Study of AK104 and AK117 in Combination With or Without Chemotherapy in Advanced Malignant Tumors	Y		https://ClinicalTrials.gov/show/NCT05235542
Checkpoint inhibitor	A Phase II Study of SHR-1210 vs Placebo as Consolidation Chemotherapy After Radical Concurrent Chemoradiotherapy in Locally Advanced ESCC	Y		https://ClinicalTrials.gov/show/NCT03817658
Checkpoint inhibitor	A Phase II Study to Test the Efficacy of AB928 (Dual Adenosine Receptor Antagonist) and AB122 (a PD1 Checkpoint Inhibitor) in Combination With Short Course Radiotherapy and Consolidation Chemotherapy for Rectal Cancer.	Y		https://ClinicalTrials.gov/show/NCT05024097
Checkpoint inhibitor	A Phase II Trial of Preoperative Chemoradiotherapy and MK-3475 for Esophageal Squamous Cell Carcinoma	Y		https://ClinicalTrials.gov/show/NCT02844075
Checkpoint inhibitor	A Phase III Study to Evaluate Efficacy and Safety of First-Line Treatment With HLX10 + Chemotherapy in Patients With Advanced Cervical Cancer	Y		https://ClinicalTrials.gov/show/NCT04806945
Checkpoint inhibitor	A Phase III Trial of Neoadjuvant Sintilimab and Chemotherapy for NSCLC Harboring No Driver Mutations	Y		https://ClinicalTrials.gov/show/NCT05157776
Checkpoint inhibitor	A Pilot Study to Investigate the Safety and Clinical Activity of Avelumab (MSB0010718C) in Thymoma and Thymic Carcinoma After Progression on Platinum-Based Chemotherapy	Y		https://ClinicalTrials.gov/show/NCT03076554
Checkpoint inhibitor	A Randomized, Double-blind, Placebo Controlled Phase III Study to Investigate Efficacy and Safety of First-Line Treatment With HLX10 + Chemotherapy (Carboplatin-Nanoparticle Albumin Bound (Nab) Paclitaxel) in Patients With Stage IIIB/IIIC or IV NSCLC	Y		https://ClinicalTrials.gov/show/NCT04033354
Checkpoint inhibitor	A Randomized, Double-blind, Placebo Controlled Phase III Study to Investigate Efficacy and Safety of HLX10 + Chemotherapy (Carboplatin- Etoposide) in Patients With Extensive Stage Small Cell Lung Cancer (ES-SCLC)	Y		https://ClinicalTrials.gov/show/NCT04063163
Checkpoint inhibitor	A Study Comparing Atezolizumab (Anti PD-L1 Antibody) In Combination With Adjuvant Anthracycline/Taxane-Based Chemotherapy Versus Chemotherapy Alone In Patients With Operable Triple-Negative Breast Cancer	Y		
Checkpoint inhibitor	A Study Evaluating the Association of Hypofractionated Stereotactic Radiation Therapy and Durvalumab for Patients With Recurrent Glioblastoma		Y	https://ClinicalTrials.gov/show/NCT02866747
Checkpoint inhibitor	A Study Evaluating Toripalimab Injection Combined With Standard Chemotherapy as a First-line Treatment for Locally Advanced or Metastatic Urothelial Carcinoma	Y		https://ClinicalTrials.gov/show/NCT04568304
Checkpoint inhibitor	A Study in Ovarian Cancer Patients Evaluating Rucaparib and Nivolumab as Maintenance Treatment Following Response to Front-Line Platinum-Based Chemotherapy	Y		https://ClinicalTrials.gov/show/NCT03522246
Checkpoint inhibitor	A Study of Anti-PD-L1 Antibody in Neoadjuvant Chemotherapy of Esophageal Squamous Cell Carcinoma.	Y		https://ClinicalTrials.gov/show/NCT04460066
Checkpoint inhibitor	A Study of Atezolizumab Administered in Combination With Bevacizumab and/or With Chemotherapy in Participants With Locally Advanced or Metastatic Solid Tumors	Y		https://ClinicalTrials.gov/show/NCT01633970
Checkpoint inhibitor	A Study of Atezolizumab Compared With Chemotherapy in Participants With Locally Advanced or Metastatic Urothelial Bladder Cancer [IMvigor211]	Y		https://ClinicalTrials.gov/show/NCT02302807
Checkpoint inhibitor	A Study of Atezolizumab Compared With Docetaxel in Non-Small Cell Lung Cancer (NSCLC) After Failure With Platinum-Containing Chemotherapy	Y		https://ClinicalTrials.gov/show/NCT02813785
Checkpoint inhibitor	A Study of Atezolizumab Compared With Platinum Doublet Chemotherapy for PD-L1 Highly Expressed, Chemotherapy-Naive Patients With Stage IV Non-Squamous or Squamous Non-Small Cell Lung Cancer	Y		https://ClinicalTrials.gov/show/NCT05047250
Checkpoint inhibitor	A Study of Atezolizumab in Combination With Carboplatin or Cisplatin + Pemetrexed Compared With Carboplatin or Cisplatin + Pemetrexed in Participants Who Are Chemotherapy-Naive and Have Stage IV Non-Squamous Non-Small Cell Lung Cancer (NSCLC) (IMpower 132)	Y		https://ClinicalTrials.gov/show/NCT02657434
Checkpoint inhibitor	A Study of Camrelizumab Combined With Chemotherapy as Neoadjuvant Therapy in Adcanced Esophageal Squamous Cell Carcinoma (ESCC)	Y		https://ClinicalTrials.gov/show/NCT04767295
Checkpoint inhibitor	A Study of Camrelizumab Combined With Concurrent Chemoradiation in Patients With Cervical Cancer	Y	Y	https://ClinicalTrials.gov/show/NCT04974827
Checkpoint inhibitor	A Study of Camrelizumab Plus Apatinib as Consolidation Therapy in Non-Small Cell Lung Cancer Patients Treated With Chemoradiotherapy	Y		https://ClinicalTrials.gov/show/NCT04749394
Checkpoint inhibitor	A Study of Carboplatin-Paclitaxel/Nab-Paclitaxel Chemotherapy With or Without Pembrolizumab (MK-3475) in Adults With First Line Metastatic Squamous Non-small Cell Lung Cancer (MK-3475-407/KEYNOTE-407)	Y		https://ClinicalTrials.gov/show/NCT02775435
Checkpoint inhibitor	A Study of Carboplatin-Paclitaxel/Nab-Paclitaxel Chemotherapy With or Without Pembrolizumab (MK-3475) in Adults With First Line Metastatic Squamous Non-small Cell Lung Cancer (MK-3475-407/KEYNOTE-407)-China Extension Study	Y		https://ClinicalTrials.gov/show/NCT03875092
Checkpoint inhibitor	A Study of Carilizumab Combined With Concurrent Chemoradiotherapy	Y		https://ClinicalTrials.gov/show/NCT05151549
Checkpoint inhibitor	A Study of Chemoradiation Plus Pembrolizumab for Locally Advanced Laryngeal Squamous Cell Carcinoma	Y	Y	https://ClinicalTrials.gov/show/NCT02759575
Checkpoint inhibitor	A Study of Combination of Anti-PD1 Antibody-activated TILs and Chemotherapy in Colorectal Cancer	Y		https://ClinicalTrials.gov/show/NCT03904537
Checkpoint inhibitor	A Study of Concurrent Chemoradiation in Combination With or Without PD1 Inhibitor AB122 Adenosine 2a Receptor / Adenosine 2b Receptor Inhibitor AB928 Therapies in Locally Advanced Head and Neck Cancers	Y	Y	https://ClinicalTrials.gov/show/NCT04892875
Checkpoint inhibitor	A Study of Concurrent Chemoradiation With Atezolizumab in Participants With Untreated Extensive-Stage (ES) Small Cell Lung Cancer (SCLC)	Y	Y	https://ClinicalTrials.gov/show/NCT04636762
Checkpoint inhibitor	A Study of Dato-DXd Versus Investigator's Choice Chemotherapy in Patients With Locally Recurrent Inoperable or Metastatic Triple-negative Breast Cancer, Who Are Not Candidates for PD-1/PD-L1 Inhibitor Therapy (TROPION-Breast02)	Y		https://ClinicalTrials.gov/show/NCT05374512
Checkpoint inhibitor	A Study of Durvalumab (Anti-PDL1) Plus Radiation Therapy for the Treatment of Solitary Bone Plasmacytoma		Y	https://ClinicalTrials.gov/show/NCT03196401
Checkpoint inhibitor	A Study of Epacadostat in Combination With Pembrolizumab and Chemotherapy in Participants With Advanced or Metastatic Solid Tumors (ECHO-207/KEYNOTE-723)	Y		https://ClinicalTrials.gov/show/NCT03085914
Checkpoint inhibitor	A Study of HLX07 + HLX10 With or Without Chemotherapy Versus HLX10 With Chemotherapy in First Line sqNSCLC	Y		https://ClinicalTrials.gov/show/NCT04976647
Checkpoint inhibitor	A Study of INCMGA00012 in Squamous Carcinoma of the Anal Canal Following Platinum-Based Chemotherapy (POD1UM-202)	Y		https://ClinicalTrials.gov/show/NCT03597295
Checkpoint inhibitor	A Study of Nivolumab Plus Chemotherapy in First Line Treatment of Adult Participants With Advanced or Metastatic Gastric Cancer	Y		https://ClinicalTrials.gov/show/NCT05165264
Checkpoint inhibitor	A Study of Pembrolizumab (MK-3475) in Combination With Chemotherapy or Immunotherapy in Participants With Non-small Cell Lung Cancer (MK-3475-021/KEYNOTE-021)	Y		https://ClinicalTrials.gov/show/NCT02039674
Checkpoint inhibitor	A Study of Pembrolizumab Plus Epacadostat With Platinum-based Chemotherapy Versus Pembrolizumab Plus Platinum-based Chemotherapy Plus Placebo in Metastatic Non-Small Cell Lung Cancer (KEYNOTE-715-06/ECHO-306-06)	Y		https://ClinicalTrials.gov/show/NCT03322566

Checkpoint inhibitor	A Study of Radiation Therapy With Pembrolizumab and Olaparib in Women Who Have Triple-Negative Breast Cancer		Y	https://ClinicalTrials.gov/show/NCT04683679
Checkpoint inhibitor	A Study of Sacituzumab With Chemoimmunotherapy to Treat Advanced Triple-Negative Breast Cancer After Prior Therapies	Y		https://ClinicalTrials.gov/show/NCT04927884
Checkpoint inhibitor	A Study of Sargramostim Plus Pembrolizumab With or Without Pemetrexed in Patients With Advance Non-small Cell Lung Cancer After Completion of Chemoimmunotherapy	Y		https://ClinicalTrials.gov/show/NCT04856176
Checkpoint inhibitor	A Study of SHR-1210 in Combination With Apatinib or Chemotherapy in Subjects With Advanced PLC or BTC	Y		https://ClinicalTrials.gov/show/NCT03092895
Checkpoint inhibitor	A Study of Sintilimab Plus Chemoradiation Before Surgery for Esophageal Cancer	Y	Y	https://ClinicalTrials.gov/show/NCT03940001
Checkpoint inhibitor	A Study of the Efficacy and Safety of Chemotherapy Combined With Toripalimab in Advanced Biliary Tract Cancer	Y		https://ClinicalTrials.gov/show/NCT03796429
Checkpoint inhibitor	A Study of the Efficacy and Safety of RO7198457 in Combination With Atezolizumab Versus Atezolizumab Alone Following Adjuvant Platinum-Doublet Chemotherapy in Participants Who Are ctDNA Positive After Surgical Resection of Stage II-III Non-Small Cell Lung Cancer	Y		https://ClinicalTrials.gov/show/NCT04267237
Checkpoint inhibitor	A Study of Tislelizumab (BGB-A317) Plus Chemoradiotherapy Followed by Tislelizumab Monotherapy in Newly Diagnosed, Stage III Subjects With Locally Advanced, Unresectable Non-small Cell Lung Cancer	Y		https://ClinicalTrials.gov/show/NCT03745222
Checkpoint inhibitor	A Study of Tislelizumab (BGB-A317) Versus Chemotherapy as Second Line Treatment in Participants With Advanced Esophageal Squamous Cell Carcinoma	Y		https://ClinicalTrials.gov/show/NCT03430843
Checkpoint inhibitor	A Study of Toripalimab Combined With Concurrent Chemoradiotherapy for Locally Advanced Esophageal Squamous Cell Carcinoma.	Y		https://ClinicalTrials.gov/show/NCT04084158
Checkpoint inhibitor	A Study of Zanidatamab in Combination With Chemotherapy Plus or Minus Tislelizumab in Patients With HER2-positive Advanced or Metastatic Gastric and Esophageal Cancers	Y		https://ClinicalTrials.gov/show/NCT05152147
Checkpoint inhibitor	A Study Tislelizumab in Combination With Chemotherapy Versus Chemotherapy in Advanced Lung Cancer.	Y		https://ClinicalTrials.gov/show/NCT03594747
Checkpoint inhibitor	A Study to Evaluate Enfortumab Vedotin (ASG-22CE) in Chinese Subjects With Locally Advanced or Metastatic Urothelial Cancer Who Previously Received Platinum-containing Chemotherapy and PD 1/PD-L1 Inhibitor Therapy	Y		https://ClinicalTrials.gov/show/NCT04995419
Checkpoint inhibitor	A Study to Evaluate the Efficacy and Safety of Sintilimab Plus Apatinib and Chemotherapy in Patients With HER-2 Negative Microsatellite Stability (MSS) Advanced or Metastatic Gastric (GC) or Gastroesophageal Junction (GEJ) Cancer	Y		https://ClinicalTrials.gov/show/NCT05216237
Checkpoint inhibitor	A Study to Investigate Atezolizumab and Chemotherapy Compared With Placebo and Chemotherapy in the Neoadjuvant Setting in Participants With Early Stage Triple Negative Breast Cancer	Y		https://ClinicalTrials.gov/show/NCT03197935
Checkpoint inhibitor	A Survival Observational Study in Patients With Advanced IIIB-IV Squamous Cell Lung Cancer Receiving PD-1 Combination With Chemotherapy	Y		https://ClinicalTrials.gov/show/NCT04306042
Checkpoint inhibitor	A Trial Evaluating Stereotactic Radiotherapy Plus Durvalumab Continuation for Patients With NSCLC Metachronous Oligometastatic Disease Under Durvalumab Consolidation Following Chemoradiation	Y	Y	https://ClinicalTrials.gov/show/NCT03955198
Checkpoint inhibitor	A Trial of AK112 (PD1/VEGF Bispecific) in Combination With Chemotherapy in Patients With NSCLC	Y		https://ClinicalTrials.gov/show/NCT04736823
Checkpoint inhibitor	A Trial of GFH018 in Combination With Toripalimab and Concurrent Chemoradiotherapy in Stage III NSCLC	Y		https://ClinicalTrials.gov/show/NCT05386888
Checkpoint inhibitor	A Trial of PEGPH20 in Combination With Avelumab in Chemotherapy Resistant Pancreatic Cancer	Y		https://ClinicalTrials.gov/show/NCT03481920
Checkpoint inhibitor	A Trial of Pembrolizumab in Combination With Chemotherapy and Radiotherapy in Stage III NSCLC (KEYNOTE-799, MK-3475-799).	Y		https://ClinicalTrials.gov/show/NCT03631784
Checkpoint inhibitor	A Trial of SHR-1316/Placebo in Combination With Chemotherapy in Patients With Resectable NSCLC	Y		https://ClinicalTrials.gov/show/NCT04316364
Checkpoint inhibitor	Adding Neoadjuvant and Adjuvant PD-1 Inhibitor to Neoadjuvant Chemotherapy Plus Concurrent Chemoradiotherapy in the Treatment of High-risk Nasopharyngeal Carcinoma	Y		https://ClinicalTrials.gov/show/NCT04557020
Checkpoint inhibitor	Addition of PD-L1 Antibody MEDI4736 to a Taxane-anthracycline Chemotherapy in Triple Negative Breast Cancer	Y		https://ClinicalTrials.gov/show/NCT02685059
Checkpoint inhibitor	Adjuvant Chemotherapy and Anti-PD-1 Antibody in Patients With Stage IIIC2-IVB Cervical Cancer	Y		https://ClinicalTrials.gov/show/NCT04918628
Checkpoint inhibitor	Afuresertib +Sintilimab+Chemotherapy in Patients With Selected Solid Tumors That Resistance to Prior Anti-PD-1/PD-L1	Y		https://ClinicalTrials.gov/show/NCT05383482
Checkpoint inhibitor	AK104 Combined With Chemotherapy as Neoadjuvant Treatment for Advanced Ovarian Cancer	Y		https://ClinicalTrials.gov/show/NCT05430906
Checkpoint inhibitor	AMP-224, a PD-1 Inhibitor, With Stereotactic Body Radiation Therapy in Metastatic Colorectal Cancer		Y	https://ClinicalTrials.gov/show/NCT02298946
Checkpoint inhibitor	An Open-Label, Randomized, Phase 3 Trial of Nivolumab Versus Investigator's Choice Chemotherapy as First-Line Therapy for Stage IV or Recurrent PD-L1+ Non-Small Cell Lung Cancer (CheckMate 026)	Y		https://ClinicalTrials.gov/show/NCT02041533
Checkpoint inhibitor	Anlotinib In Combination With PD-1/L1 Inhibitor As Sequential Therapy of Thoracic Radiotherapy After Induction Chemotherapy For Extensive-Stage Small Cell Lung Cancer:A Single Arm Study	Y		https://ClinicalTrials.gov/show/NCT04313660
Checkpoint inhibitor	Anlotinib Plus PD-1 Antibody in Standard Chemotherapy Failure Advanced NSCLC the ATHENA Study	Y		https://ClinicalTrials.gov/show/NCT04322617
Checkpoint inhibitor	Anti PD-1 Antibody With Radiation Therapy in Patients With HER2-negative Metastatic Breast Cancer		Y	https://ClinicalTrials.gov/show/NCT03430479
Checkpoint inhibitor	Anti-PD-1 and Chemotherapy for R/R Hodgkin Lymphoma	Y		https://ClinicalTrials.gov/show/NCT03664323
Checkpoint inhibitor	Anti-PD-1 and mDCF Followed by Chemoradiotherapy in Patients With Stage III Squamous Cell Anal Carcinoma.	Y		https://ClinicalTrials.gov/show/NCT04719988
Checkpoint inhibitor	Anti-PD-1 and VEGF Bispecific Antibody AK112 in Combination With Chemotherapy in Patients With ES-SCLC	Y		https://ClinicalTrials.gov/show/NCT05116007
Checkpoint inhibitor	Anti-PD-1 Antibody Alone or in Combination With Decitabine/Chemotherapy in Relapsed or Refractory Malignancies	Y		https://ClinicalTrials.gov/show/NCT02961101
Checkpoint inhibitor	Anti-PD-1 Antibody and P-GEMOX Chemotherapy Combined With Radiotherapy in High-risk Early-Stage ENKTL	Y		https://ClinicalTrials.gov/show/NCT05254899
Checkpoint inhibitor	Anti-PD-1 in Combination With Chemotherapy as First-Line Treatment to Lung Cancer	Y		https://ClinicalTrials.gov/show/NCT03432598
Checkpoint inhibitor	Antitumor Activity of Neoadjuvant Chemotherapy With or Without BINTRAFUSP ALFA in Patients With Metastatic Advanced Stage Ovarian Cancer	Y		https://ClinicalTrials.gov/show/NCT05145569
Checkpoint inhibitor	Apatinib Combined With Chemotherapy Versus Chemotherapy in Second-line Gastric Cancer Receiving Prior Anti-PD-1 Therapy	Y		https://ClinicalTrials.gov/show/NCT05029453
Checkpoint inhibitor	ATALANTE: Atezolizumab vs Placebo Phase III Study in Late Relapse Ovarian Cancer Treated With Chemotherapy+Bevacizumab	Y		https://ClinicalTrials.gov/show/NCT02891824
Checkpoint inhibitor	Atezolizumab After Chemo-radiotherapy for MIBC Patients Not Eligible for Radical Cystectomy	Y		https://ClinicalTrials.gov/show/NCT03697850
Checkpoint inhibitor	Atezolizumab Before and/or With Chemoradiotherapy in Immune System Activation in Patients With Node Positive Stage IB2, II, IIIB, or IVA Cervical Cancer	Y		https://ClinicalTrials.gov/show/NCT03738228
Checkpoint inhibitor	Avelumab in Chemo-resistant Gestational Trophoblastic Neoplasias	Y		https://ClinicalTrials.gov/show/NCT03135769
Checkpoint inhibitor	Avelumab Treatment in Patients With Neuroendocrine Carcinomas (NEC G3) Progressive After Chemotherapy	Y		https://ClinicalTrials.gov/show/NCT03352934
Checkpoint inhibitor	Avelumab With Chemoradiation in Locally Advanced Rectal Cancer	Y	Y	https://ClinicalTrials.gov/show/NCT03299660
Checkpoint inhibitor	Avelumab With Hypofractionated Radiation Therapy in Adults With Isocitrate Dehydrogenase (IDH) Mutant Glioblastoma		Y	https://ClinicalTrials.gov/show/NCT02968940
Checkpoint inhibitor	Balstilimab Versus Investigator Choice Chemotherapy in Patients With Recurrent Cervical Cancer (BRAVA)	Y		https://ClinicalTrials.gov/show/NCT04943627
Checkpoint inhibitor	Bempegaldesleukin (NKTR-214) With Radiation and Anti-PD-1 Immunotherapy for Head and Neck Squamous Cell Carcinoma		Y	https://ClinicalTrials.gov/show/NCT04936841
Checkpoint inhibitor	BGB A317 in Combination With Chemotherapy as First-Line Treatment in Adults With Inoperable, Locally Advanced or Metastatic Esophageal, Gastric, or Gastroesophageal Junction Carcinoma	Y		https://ClinicalTrials.gov/show/NCT03469557
Checkpoint inhibitor	Biomarker Analysis in High PD-L1 Expressing NSCLC Patients Treated With PD-1/PD-L1 Based Therapy With or Without the Addition of Platinum Based Chemotherapy	Y		https://ClinicalTrials.gov/show/NCT04676386
Checkpoint inhibitor	Biomarkers of Response to Pembrolizumab Combined With Chemotherapy in Non-Small Cell Lung Cancer (KEYNOTE-782, MK-3475-782)	Y		https://ClinicalTrials.gov/show/NCT03664024
Checkpoint inhibitor	Biomarkers of Response to Pembrolizumab Combined With Chemotherapy in Non-Small Cell Lung Cancer (KEYNOTE-782, MK-3475-782)	Y		https://ClinicalTrials.gov/show/NCT03664024
Checkpoint inhibitor	BLAST MRD AML-1: BLockade of PD-1 Added to Standard Therapy to Target Measurable Residual Disease in Acute Myeloid Leukemia 1- A Randomized Phase 2 Study of Anti-PD-1 Pembrolizumab in Combination With Intensive Chemotherapy as Frontline Therapy in Patients With Acute Myeloid Leukemia	Y		https://ClinicalTrials.gov/show/NCT04214249
Checkpoint inhibitor	Blockade of PD-1 in Conjunction With the Dendritic Cell/AML Vaccine Following Chemotherapy Induced Remission	Y		https://ClinicalTrials.gov/show/NCT01096602
Checkpoint inhibitor	Camrelizumab Combined With Chemotherapy for Recurrent or Advanced Cervical Neuroendocrine Carcinomas	Y		https://ClinicalTrials.gov/show/NCT04635956
Checkpoint inhibitor	Camrelizumab Combined With Induction Chemotherapy and Intensity Modulated Radiotherapy for the Treatment of Locally Advanced Nasopharyngeal Carcinoma	Y		https://ClinicalTrials.gov/show/NCT05097209
Checkpoint inhibitor	Camrelizumab With Chemotherapy in Adults With Medically Inoperable Early Stage NSCLC	Y		https://ClinicalTrials.gov/show/NCT04530227

Checkpoint inhibitor	Cemiplimab and ISA101b Vaccine in Adult Participants With Recurrent/Metastatic Human Papillomavirus (HPV)16 Cervical Cancer Who Have Experienced Disease Progression After First Line Chemotherapy	Y		https://ClinicalTrials.gov/show/NCT04646005
Checkpoint inhibitor	Chemoradiation vs Immunotherapy and Radiation for Head and Neck Cancer	Y	Y	https://ClinicalTrials.gov/show/NCT03383094
Checkpoint inhibitor	Chemoradiotherapy Combined With or Without PD-1 Blockade in Anal Canal Squamous Carcinoma Patients	Y		https://ClinicalTrials.gov/show/NCT05374252
Checkpoint inhibitor	Chemoradiotherapy Plus Anti-PD1 in Recurrent NPC: A Multicenter, Open-label, Randomised, Controlled, Phase III Trial	Y		https://ClinicalTrials.gov/show/NCT05340491
Checkpoint inhibitor	Chemoradiotherapy With or Without Sintilimab in Limited-stage SCLC	Y		https://ClinicalTrials.gov/show/NCT04189094
Checkpoint inhibitor	Chemotherapy Combined With Apatinib and PD-1 Antibody	Y		https://ClinicalTrials.gov/show/NCT05025033
Checkpoint inhibitor	Chemotherapy Combined With Immunotherapy in HER 2 Insertion or Amplification Advanced NSCLC	Y		https://ClinicalTrials.gov/show/NCT04324125
Checkpoint inhibitor	Chemotherapy Combines With Bevacizumab and PD-1 Inhibitor in Non-squamous NSCLC	Y		https://ClinicalTrials.gov/show/NCT05267366
Checkpoint inhibitor	Chemotherapy or Chemotherapy Plus PD-1 Antibody in RET Fusion Positive Advanced NSCLC Patitnts: the POSEIDON Trial	Y		https://ClinicalTrials.gov/show/NCT04322591
Checkpoint inhibitor	Chemotherapy Plus Subsequent Loco-regional Radiotherapy Combined With Toripalimab in the De Novo Metastatic Nasopharyngeal Carcinoma	Y		https://ClinicalTrials.gov/show/NCT04398056
Checkpoint inhibitor	Chemotherapy With Pembrolizumab Continuation After Progression to PD-1/L1 Inhibitors	Y		https://ClinicalTrials.gov/show/NCT03656094
Checkpoint inhibitor	Chidamide Plus Sintilimab for Chemotherapy-refractory Advanced High-grade Neuroendocrine Neoplasm	Y		https://ClinicalTrials.gov/show/NCT05113355
Checkpoint inhibitor	Clinical Study of Camrelizumab in Combination With Neoadjuvant Chemotherapy for Operable Locally Advanced Head and Neck Squamous Cell Carcinoma	Y		https://ClinicalTrials.gov/show/NCT04922450
Checkpoint inhibitor	Clinical Study of Neoadjuvant PD-1 Antibody (Toripalimab) Plus Chemotherapy for Locally Advanced Thymic Epithelial Tumor	Y		https://ClinicalTrials.gov/show/NCT04667793
Checkpoint inhibitor	Clinical Study of PD-1 Antibody (BGB-A317) Plus Chemotherapy (Cisplatin and Etoposide) for Limited Stage Small Cell Lung Cancer	Y		https://ClinicalTrials.gov/show/NCT04542369
Checkpoint inhibitor	Clinical Study of PD-L1 Antibody (TQB2450) Plus Chemotherapy (Cisplatin and Etoposide) for Previously Untreated Small Cell Lung Cancer	Y		https://ClinicalTrials.gov/show/NCT04539977
Checkpoint inhibitor	Clinical Study of SHR-1701 Plus Chemotherapy as Perioperative Treatment in Subjects With Gastric Cancer	Y		https://ClinicalTrials.gov/show/NCT05149807
Checkpoint inhibitor	Clinical Trial of Neoadjuvant Chemotherapy With Atezolizumab or Placebo in Patients With Triple-Negative Breast Cancer Followed After Surgery by Atezolizumab or Placebo	Y		https://ClinicalTrials.gov/show/NCT03281954
Checkpoint inhibitor	Combination of Anti-PD-1 Antibody and Chemotherapy for Unresectable Intrahepatic Cholangiocarcinoma	Y		https://ClinicalTrials.gov/show/NCT04413734
Checkpoint inhibitor	Combination of Anti-PD-1 Antibody and Chemotherapy in Metastatic Pancreatic Cancer	Y		https://ClinicalTrials.gov/show/NCT03977272
Checkpoint inhibitor	Combination of Anti-PD-1 Antibody and Chemotherapy in Pancreatic Cancer	Y		https://ClinicalTrials.gov/show/NCT03983057
Checkpoint inhibitor	Combination of Chemotherapy Plus RT and SHR-1210 to Treat Patients With ESCC	Y		https://ClinicalTrials.gov/show/NCT03671265
Checkpoint inhibitor	Combination of Radiation Therapy and Anti-PD-1 Antibody in Treating Patients With Pancreatic Cancer		Y	https://ClinicalTrials.gov/show/NCT03374293
Checkpoint inhibitor	Combination of Radiation Therapy and Anti-PD-1 Antibody SHR-1210 in Treating Patients With Esophageal Cancer		Y	https://ClinicalTrials.gov/show/NCT03187314
Checkpoint inhibitor	Combination Radiation and PD-1 Inhibition in Metastatic or Recurrent Renal Cell Carcinoma (RCC)		Y	https://ClinicalTrials.gov/show/NCT02962804
Checkpoint inhibitor	Combinations of Cemiplimab (Anti-PD-1 Antibody) and Platinum-based Doublet Chemotherapy in Patients With Lung Cancer	Y		https://ClinicalTrials.gov/show/NCT03409614
Checkpoint inhibitor	Combinatory ImmunoTherapy-1 (Com-IT-1) Irradiation and PD-1 Blockade in Locally Advanced / Advanced NSCLC		Y	https://ClinicalTrials.gov/show/NCT03644823
Checkpoint inhibitor	Combined Atezolizumab and Chemotherapy (Carboplatin Plus Etoposide) in Neoadjuvant Treating Limited-Stage Small Cell Lung Cancer Patients	Y		https://ClinicalTrials.gov/show/NCT04696939
Checkpoint inhibitor	Combined Inhibition of PD-1 and DNA Hypomethylating Agent +/- Chemotherapy in High-risk AML or Elderly Patients With AML Who Are Unfit for Intensive Chemotherapy	Y		https://ClinicalTrials.gov/show/NCT04541277
Checkpoint inhibitor	Combined Therapy Using Oxaliplatin and Gemcitabine Chemotherapy, Lenvatinib and PD1 Antibody (JS001) for Patients With Advanced and Unresectable Intrahepatic Cholangiocarcinoma	Y		https://ClinicalTrials.gov/show/NCT03951597
Checkpoint inhibitor	Combining RT With Toripalimab and Chemotherapy in Metastatic Nasopharyngeal Carcinoma	Y		https://ClinicalTrials.gov/show/NCT05385926
Checkpoint inhibitor	Comparing Chemotherapy With/Without Toripalimab For Primary Metastatic Nasopharyngeal Carcinoma	Y		https://ClinicalTrials.gov/show/NCT04517214
Checkpoint inhibitor	Comparing the New Anti-cancer Drug Eribulin With or Without Chemotherapy Against the Usual Chemotherapy Alone in Metastatic Urothelial Cancer	Y		https://ClinicalTrials.gov/show/NCT04579224
Checkpoint inhibitor	Concurrent and Adjuvant PD-1 Blockade Combined With Induction Chemotherapy Plus Radiotherapy in Nasopharyngeal Carcinoma	Y		https://ClinicalTrials.gov/show/NCT03984357
Checkpoint inhibitor	Concurrent and Adjuvant PD1 Treatment Combined With Chemo-radiotherapy for High-risk Nasopharyngeal Carcinoma	Y		https://ClinicalTrials.gov/show/NCT04453826
Checkpoint inhibitor	Consolidation Sintilimab After Concurrent Chemoradiation in Patients With Unresectable Stage III NSCLC	Y	Y	https://ClinicalTrials.gov/show/NCT03884192
Checkpoint inhibitor	CT-Guided Adaptive Radiation Therapy Combine With Anti-PD-1 Antibody Adjuvant Immunotherapy for Thoracic Cancer Patients		Y	https://ClinicalTrials.gov/show/NCT03732430
Checkpoint inhibitor	CTLA-4 /PD-L1 Blockade Following Transarterial Chemoembolization (DEB-TACE) in Patients With Intermediate Stage of HCC (Hepatocellular Carcinoma) Using Durvalumab and Tremelimumab	Y		https://ClinicalTrials.gov/show/NCT03638141
Checkpoint inhibitor	Disitamab Vedotin Combined With PD-1 and Neoadjuvant Chemotherapy for Locally Advanced Gastric Cancer	Y		https://ClinicalTrials.gov/show/NCT05113459
Checkpoint inhibitor	Durvalumab And Radiation Therapy Followed by Adjuvant Durvalumab in Patients With Urothelial Cancer (T2-4 N0-2 M0) of the Bladder		Y	https://ClinicalTrials.gov/show/NCT02891161
Checkpoint inhibitor	Durvalumab in Combination With a CSF-1R Inhibitor (SNDX-6532) Following Chemo or Radio-Embolization for Patients With Intrahepatic Cholangiocarcinoma	Y		https://ClinicalTrials.gov/show/NCT04301778
Checkpoint inhibitor	Durvalumab in Combination With a CSF-1R Inhibitor (SNDX-6532) Following Chemo or Radio-Embolization for Patients With Intrahepatic Cholangiocarcinoma	Y		https://ClinicalTrials.gov/show/NCT04301778
Checkpoint inhibitor	Durvalumab in Combination With Chemotherapy in Treating Patients With Advanced Solid Tumors, (DURVA+ Study)	Y		https://ClinicalTrials.gov/show/NCT03907475
Checkpoint inhibitor	Durvalumab Plus CV301 With Maintenance Chemotherapy in Metastatic Colorectal or Pancreatic Adenocarcinoma	Y		https://ClinicalTrials.gov/show/NCT03376659
Checkpoint inhibitor	Durvalumab vs Placebo With Stereotactic Body Radiation Therapy in Early Stage Unresected Non-small Cell Lung Cancer (NSCLC) Patients / Osimertinib Following SBRT in Patients With Early Stage Unresected NSCLC Harboring an EGFR Mutation		Y	https://ClinicalTrials.gov/show/NCT03833154
Checkpoint inhibitor	DuRvalumab With chEmotherapy as First Line treAtment in Advanced Pleural Mesothelioma	Y		https://ClinicalTrials.gov/show/NCT04334759
Checkpoint inhibitor	Durvalumab, an Anti-PDLl Antibody, and Tremelimumab, an Anti-CTLA4 Antibody, and Chemoradiation Before Surgery for Esophageal Cancer	Y	Y	https://ClinicalTrials.gov/show/NCT02962063
Checkpoint inhibitor	Durvalumab(MEDI4736) After chemoRadioTherapy(DART) for NSCLC-a Translational and Biomarker Study	Y		https://ClinicalTrials.gov/show/NCT04392505
Checkpoint inhibitor	Dynamic PET/CT Evaluated the Response of Neoadjuvant Anti-PD1 Combination With Chemotherapy for NSCLC	Y		https://ClinicalTrials.gov/show/NCT04586465
Checkpoint inhibitor	Effect of Chemotherapy on PD-L1 in NSCLC	Y		https://ClinicalTrials.gov/show/NCT03701607
Checkpoint inhibitor	Effect of Chemotherapy on TMB in NSCLC	Y		https://ClinicalTrials.gov/show/NCT03683407
Checkpoint inhibitor	Effectiveness of Neoadjuvant Chemotherapy Combined With PD-1 Monoclonal Antibody in the Treatment of Operable Esophageal Squamous Cell Carcinoma	Y		https://ClinicalTrials.gov/show/NCT05174325
Checkpoint inhibitor	Efficacy and Safety of BCD-100 (Anti-PD-1) in Combination With Platinum-Based Chemotherapy and Bevacizumab in Patients With Recurrent, Persistent or Metastatic Cervical Cancer (CAESURA)	Y		https://ClinicalTrials.gov/show/NCT03912402
Checkpoint inhibitor	Efficacy and Safety of BCD-100 (Anti-PD-1) in Combination With Platinum-Based Chemotherapy as First Line Treatment in Patients With Advanced Non-Squamous NSCLC	Y		https://ClinicalTrials.gov/show/NCT03912389
Checkpoint inhibitor	Efficacy and Safety of BCD-100 (Anti-PD-1) in Combination With Platinum-Based Chemotherapy With and Without Bevacizumab as First-Line Treatment of Subjects With Advanced Cervical Cancer (FERMATA)	Y		https://ClinicalTrials.gov/show/NCT03912415
Checkpoint inhibitor	Efficacy and Safety of First-line Anti-PD-1/PD-L1 Monoclonal Antibody in Combination With Chemotherapy and Bronchoscopy-assisted Interventional Therapy in Patients With Advanced Central Non-small Cell Lung Cancer	Y		https://ClinicalTrials.gov/show/NCT04702009
Checkpoint inhibitor	Efficacy and Safety of Lenvatinib (E7080/MK-7902) Plus Pembrolizumab (MK-3475) Plus Chemotherapy in Participants With Advanced/Metastatic Gastroesophageal Adenocarcinoma (MK-7902-015/E7080-G000-321/LEAP-015)	Y		https://ClinicalTrials.gov/show/NCT04662710
Checkpoint inhibitor	Efficacy and Safety of Pembrolizumab (MK-3475) Plus Lenvatinib (E7080/MK-7902) Plus Chemotherapy in Participants With Metastatic Esophageal Carcinoma (MK-7902-014/E7080-G000-320/LEAP-014)	Y		https://ClinicalTrials.gov/show/NCT04949256

Checkpoint inhibitor	Efficacy and Safety of Pembrolizumab (MK-3475) With Lenvatinib (E7080/MK-7902) vs. Docetaxel in Participants With Metastatic Non-Small Cell Lung Cancer (NSCLC) and Progressive Disease (PD) After Platinum Doublet Chemotherapy and Immunotherapy (MK-7902-008/E7080-G000-316/LEAP-008)	Y		https://ClinicalTrials.gov/show/NCT03976375
Checkpoint inhibitor	Efficacy and Safety of Pembrolizumab Plus Investigational Agents in Combination With Chemotherapy as First-Line Treatment in Extensive-Stage Small Cell Lung Cancer (ES-SCLC) (MK-3475-B99/ KEYNOTE-B99)	Y		https://ClinicalTrials.gov/show/NCT04924101
Checkpoint inhibitor	Efficacy and Safety of Perioperative Chemotherapy Plus PD-1 Antibody in Gastric Cancer	Y		https://ClinicalTrials.gov/show/NCT04367025
Checkpoint inhibitor	Efficacy and Safety of Platinum-based Chemotherapy + Bevacizumab + Durvalumab, and Salvage SBRT for IV Non-Small Cell Lung Cancer Patients With EGFR Mutations After Failure of First Line Osimertinib: A Multicenter, Prospective, Phase II Clinical Study	Y		https://ClinicalTrials.gov/show/NCT04517526
Checkpoint inhibitor	Efficacy and Safety Study of First-line Treatment With Pembrolizumab (MK-3475) Plus Chemotherapy Versus Placebo Plus Chemotherapy in Women With Persistent, Recurrent, or Metastatic Cervical Cancer (MK-3475-826/KEYNOTE-826)	Y		https://ClinicalTrials.gov/show/NCT03635567
Checkpoint inhibitor	Efficacy Comparison of Cobolimab + Dostarlimab + Docetaxel to Dostarlimab + Docetaxel to Docetaxel Alone in Participants With Advanced Non-Small Cell Lung Cancer Who Have Progressed on Prior Anti-Programmed Death-ligand 1 (PD-[L]1) Therapy and Chemotherapy	Y		https://ClinicalTrials.gov/show/NCT04655976
Checkpoint inhibitor	Efficacy of Neoadjuvant PD-1 Blockade Plus Chemotherapy for Esophageal Squamous Cell Carcinoma	Y		https://ClinicalTrials.gov/show/NCT04225364
Checkpoint inhibitor	Efficacy of PD-1 Blockade Plus Platinum-based Chemotherapy in Patients With EGFR Sensitive Mutated NSCLC	Y		https://ClinicalTrials.gov/show/NCT05284539
Checkpoint inhibitor	Efficacy of Perioperative Chemotherapy Plus PD-1 Antibody in the Locally Advanced Gastric Cancer	Y		https://ClinicalTrials.gov/show/NCT04250948
Checkpoint inhibitor	Envafolimab Plus Chemoradiotherapy for Locally Advanced NPC, a Prospective, Single Armed Phase II Trial.	Y		https://ClinicalTrials.gov/show/NCT05397769
Checkpoint inhibitor	Exploration of Immunodynamic Monitoring in the Population Evaluation of Neoadjuvant Chemotherapy Immunotherapy in Patients With Solid Tumors of the Chest.	Y		https://ClinicalTrials.gov/show/NCT05044728
Checkpoint inhibitor	First-line Esophageal Carcinoma Study With Chemo vs. Chemo Plus Pembrolizumab (MK-3475-590/KEYNOTE-590)	Y		https://ClinicalTrials.gov/show/NCT03189719
Checkpoint inhibitor	First-line Esophageal Carcinoma Study With Chemo vs. Chemo Plus Pembrolizumab (MK-3475-590/KEYNOTE-590)-China Extension Study	Y		https://ClinicalTrials.gov/show/NCT03881111
Checkpoint inhibitor	Fluzoparib and Camrelizumab in Treating Patients With R/M NPC That Progressed After First-line Chemotherapy	Y		https://ClinicalTrials.gov/show/NCT04978012
Checkpoint inhibitor	GP Chemotherapy in Combination With Anti-PD-1 and Anti-TIGIT in Unresectable Advanced BTC	Y		https://ClinicalTrials.gov/show/NCT05023109
Checkpoint inhibitor	GP Chemotherapy in Combination With Tislelizumab and Ociperlimab as First-line Treatment in Advanced BTC	Y		https://ClinicalTrials.gov/show/NCT05019677
Checkpoint inhibitor	GYNecological Cancers Treated With NETrin mAbs in Combination With Chemotherapy and /or Pembrolizumab	Y		https://ClinicalTrials.gov/show/NCT04652076
Checkpoint inhibitor	Hepatic Artery Infusion Chemotherapy (HAIC) Plus Durvalumab for Advanced Hepatocellular Carcinoma	Y		https://ClinicalTrials.gov/show/NCT04945720
Checkpoint inhibitor	HLX07+HLX10+Chemotherapy or HLX07 Monotherapy in Patients With Advanced Metastatic Gastric Cancer	Y		https://ClinicalTrials.gov/show/NCT05246982
Checkpoint inhibitor	HMPL-453 (FGFR Inhibitor) in Combination With Chemotherapy or Anti-PD-1 Antibody in Advanced Solid Tumors	Y		https://ClinicalTrials.gov/show/NCT05173142
Checkpoint inhibitor	HX008 Plus Chemotherapy VS Pembrolizumab Plus Chemotherapy As the First-line Treatment in Participants With Advanced or Metastatic Nonsquamous Non-small Cell Lung Cancer	Y		https://ClinicalTrials.gov/show/NCT04750083
Checkpoint inhibitor	Immune Checkpoint Inhibition (Tremelimumab and/or MEDI4736) in Combination With Radiation Therapy in Patients With Unresectable Pancreatic Cancer		Y	https://ClinicalTrials.gov/show/NCT02311361
Checkpoint inhibitor	Immune Checkpoint Inhibitor PD-1 Antibody Combined With Chemotherapy in the Perioperative Treatment of Locally Advanced Resectable Gastric or Gastroesophageal Junction Adenocarcinoma	Y		https://ClinicalTrials.gov/show/NCT04908566
Checkpoint inhibitor	Immunotherapy for Recurrent Cervical Cancer Refractory to Platinum-based Chemotherapy	Y		https://ClinicalTrials.gov/show/NCT04188860
Checkpoint inhibitor	Immunotherapy for Recurrent Cervical Cancer Refractory to Platinum-based Chemotherapy: Multi-Center Trial	Y		https://ClinicalTrials.gov/show/NCT05290935
Checkpoint inhibitor	Immunotherapy With Neo-adjuvant Chemotherapy for OVarian Cancer	Y		https://ClinicalTrials.gov/show/NCT03249142
Checkpoint inhibitor	Impact of eHealth Monitoring on Overall Survival in Patients With Metastatic NSCLC / Extensive-stage SCLC / Advanced TNBC Under First-line Treatment With Atezolizumab Plus Chemotherapy	Y		https://ClinicalTrials.gov/show/NCT03911219
Checkpoint inhibitor	INCMGA00012 in Combination With Chemoradiation in Participants With Stage III Non-Small Cell Lung Cancer (POD1UM-301)	Y	Y	https://ClinicalTrials.gov/show/NCT04203511
Checkpoint inhibitor	INCMGA00012 Plus Chemotherapy in Participants With Advanced Solid Tumors (POD1UM-105)	Y		https://ClinicalTrials.gov/show/NCT03920839
Checkpoint inhibitor	Induction Chemotherapy and Toripalimab for Larynx Preservation in Resectable Laryngeal/Hypopharyngeal Carcinoma	Y		https://ClinicalTrials.gov/show/NCT04995120
Checkpoint inhibitor	Induction of Immune-mediated aBscOpal Effect thrOugh STEreotactic Radiation Therapy in Metastatic Melanoma Patients Treated by PD-1 + CTLA-4 Inhibitors (BOOSTER MELANOMA)		Y	https://ClinicalTrials.gov/show/NCT03354962
Checkpoint inhibitor	IO102 With Pembrolizumab, With or Without Chemotherapy, as First-line Treatment of Metastatic NSCLC	Y		https://ClinicalTrials.gov/show/NCT03562871
Checkpoint inhibitor	IO102 With Pembrolizumab, With or Without Chemotherapy, as First-line Treatment of Metastatic NSCLC	Y		https://ClinicalTrials.gov/show/NCT03562871
Checkpoint inhibitor	Ipilimumab, Nivolumab, and Radiation Therapy in Treating Patients With HPV Positive Advanced Oropharyngeal Squamous Cell Carcinoma		Y	https://ClinicalTrials.gov/show/NCT03799445
Checkpoint inhibitor	KEYMAKER-U01 Substudy 1: Efficacy and Safety Study of Pembrolizumab (MK-3475) Plus Chemotherapy When Used With Investigational Agents in Treatment-naïve Participants With Advanced Non-small Cell Lung Cancer (NSCLC) (MK-3475-01A/KEYMAKER-U01A)	Y		https://ClinicalTrials.gov/show/NCT04165070
Checkpoint inhibitor	KEYMAKER-U01 Umbrella Master Study: Studies of Investigational Agents With Either Pembrolizumab (MK-3475) Alone or With Pembrolizumab PLUS Chemotherapy in Participants With Advanced Non-small Cell Lung Cancer (NSCLC) (MK-3475-U01/KEYMAKER-U01)	Y		https://ClinicalTrials.gov/show/NCT04165798
Checkpoint inhibitor	Lenvatinib (E7080/MK-7902) in Combination With Pembrolizumab (MK-3475) vs. Standard Chemotherapy and Lenvatinib Monotherapy in Participants With Recurrent/Metastatic Head and Neck Squamous Cell Carcinoma That Progressed After Platinum Therapy and Immunotherapy (MK-7902-009/E7080-G000-228/LEAP-009)	Y		https://ClinicalTrials.gov/show/NCT04428151
Checkpoint inhibitor	Local Consolidative Therapy and Durvalumab for Oligoprogressive and Polyprogressive Stage III NSCLC After Chemoradiation and Anti-PD-L1 Therapy	Y	Y	https://ClinicalTrials.gov/show/NCT04892953
Checkpoint inhibitor	Localized Radiation Therapy or Recombinant Interferon Beta and Avelumab With or Without Cellular Adoptive Immunotherapy in Treating Patients With Metastatic Merkel Cell Carcinoma		Y	https://ClinicalTrials.gov/show/NCT02584829
Checkpoint inhibitor	LYT-200 Alone and in Combination With Chemotherapy or Anti-PD-1 in Patients With Metastatic Solid Tumors	Y		https://ClinicalTrials.gov/show/NCT04666688
Checkpoint inhibitor	MPDL3280A With Chemoradiation for Lung Cancer	Y	Y	https://ClinicalTrials.gov/show/NCT02525757
Checkpoint inhibitor	Multi-agent Low Dose Chemotherapy GAX-CI Followed by Olaparib and Pembro in Metastatic Pancreatic Ductal Cancer.	Y		https://ClinicalTrials.gov/show/NCT04753879
Checkpoint inhibitor	Multi-omics Model Predicts Efficacy of Preoperative Neoadjuvant Chemoradiotherapy Combined PD-1 Antibody Therapy for Locally Advanced Rectal Cancer	Y		https://ClinicalTrials.gov/show/NCT05368051
Checkpoint inhibitor	NBTXR3, Radiation Therapy, and Pembrolizumab for the Treatment of Recurrent or Metastatic Head and Neck Squamous Cell Cancer		Y	https://ClinicalTrials.gov/show/NCT04862455
Checkpoint inhibitor	NBTXR3, Radiation Therapy, Ipilimumab, and Nivolumab for the Treatment of Lung and/or Liver Metastases From Solid Malignancy		Y	https://ClinicalTrials.gov/show/NCT05039632
Checkpoint inhibitor	Neoadjuvant Anti-PD-1 Antibody (Toripalimab) or Combined With Chemotherapy in HNSCC Patients	Y		https://ClinicalTrials.gov/show/NCT04164238
Checkpoint inhibitor	Neoadjuvant Anti-PD-1 Antibody SHR-1210 and Radiation in Resectable Esophageal Squamous Cell Carcinoma		Y	https://ClinicalTrials.gov/show/NCT03200691
Checkpoint inhibitor	Neoadjuvant Arterial Embolization Chemotherapy Combined PD-1 Inhibitor for Locally Advanced Rectal Cancer	Y		https://ClinicalTrials.gov/show/NCT05420584
Checkpoint inhibitor	Neoadjuvant Camrelizumab Plus Chemotherapy in Triple Negative Breast Cancer	Y		https://ClinicalTrials.gov/show/NCT05088057
Checkpoint inhibitor	Neoadjuvant Chemoradiation Plus PD-1 Antibody(SHR-1210) in Locally Advanced Proximal Stomach Adenocarcinoma	Y	Y	https://ClinicalTrials.gov/show/NCT03631615
Checkpoint inhibitor	Neoadjuvant Chemoradiotherapy Combined With PD-1 Antibody in Locally Advanced Esophageal Cancer	Y		https://ClinicalTrials.gov/show/NCT04177875
Checkpoint inhibitor	Neoadjuvant Chemoradiotherapy Plus Tislelizumab Followed by TME for LARC.	Y		https://ClinicalTrials.gov/show/NCT04911517
Checkpoint inhibitor	Neoadjuvant Durvalumab and Tremelimumab Plus Radiation for High Risk Soft-Tissue Sarcoma	Y		https://ClinicalTrials.gov/show/NCT03116529
Checkpoint inhibitor	Neoadjuvant Immunotherapy (PD-1 / PD-L1) Combined With Chemotherapy for Locally Advanced Thoracic Esophageal Squamous Cell Carcinoma: a Single Center, Prospective, Open, One Arm Exploratory Clinical Study	Y		https://ClinicalTrials.gov/show/NCT05028231
Checkpoint inhibitor	Neoadjuvant Immunotherapy and Chemotherapy Followed by Surgery in Unresectable Stage NSCLC	Y		https://ClinicalTrials.gov/show/NCT04943029
Checkpoint inhibitor	Neoadjuvant Immunotherapy With Durvalumab (MEDI4736) in Non-Surgical Early Stage or Locally Advanced Non-Small Cell Lung Cancer (NSCLC) Followed by Radical Radiotherapy or Chemoradiotherapy	Y		https://ClinicalTrials.gov/show/NCT05267392

Checkpoint inhibitor	Neoadjuvant PD-1 Antibody Plus Apatinib or Chemotherapy for Non-small Cell Lung Cancer	Y		https://ClinicalTrials.gov/show/NCT04379739
Checkpoint inhibitor	Neoadjuvant PD-1 Antibody Plus Chemotherapy in Resectable Stage IIIA-N2 Non-Small-Cell Lung Cancer	Y		https://ClinicalTrials.gov/show/NCT04422392
Checkpoint inhibitor	Neoadjuvant PD-1 Blockade Combined With Chemotherapy Followed by Concurrent Immunoradiotherapy for Locally Advanced Anal Canal Squamous Carcinoma Patients	Y		https://ClinicalTrials.gov/show/NCT05060471
Checkpoint inhibitor	Neoadjuvant PD-1 Inhibitor, Anlotinib Combined With Chemotherapy in Resectable Stage IIA-IIIB NSCLC	Y		https://ClinicalTrials.gov/show/NCT05400070
Checkpoint inhibitor	Neoadjuvant PD-1 Monoclonal Antibody Plus Cisplatin-based Chemotherapy in Locally Advanced Upper Tract Urothelial Carcinoma	Y		https://ClinicalTrials.gov/show/NCT04672317
Checkpoint inhibitor	Neoadjuvant Sintilimab Combined With Reduction of Cycles of Chemotherapy in Resectable Oral Cavity or Oropharyngeal Squamous Cell Carcinoma (OOC-002)	Y		https://ClinicalTrials.gov/show/NCT05098119
Checkpoint inhibitor	Neoadjuvant Study of Camrelizumab Plus Chemotherapy in Triple Negative Breast Cancer (TNBC)	Y		https://ClinicalTrials.gov/show/NCT04676997
Checkpoint inhibitor	Neoadjuvant Toripalimab Combined With Chemotherapy in the Treatment of Malignant Pleural Mesothelioma	Y		https://ClinicalTrials.gov/show/NCT04713761
Checkpoint inhibitor	Nivolumab and Epacadostat With Platinum Doublet Chemotherapy Versus Platinum Doublet Chemotherapy in Non-Small Cell Lung Cancer	Y		https://ClinicalTrials.gov/show/NCT03348904
Checkpoint inhibitor	Nivolumab and Ipilimumab in Combination With Immunogenic Chemotherapy for Patients With Advanced NSCLC	Y		https://ClinicalTrials.gov/show/NCT04043195
Checkpoint inhibitor	NIvolumab COmbination With Standard First-line Chemotherapy and Radiotherapy in Locally Advanced Stage IIIA/B Non-Small Cell Lung Carcinoma	Y		https://ClinicalTrials.gov/show/NCT02434081
Checkpoint inhibitor	Nivolumab in Combination With Chemotherapy Pre-Surgery in Treating Patients With Borderline Resectable Pancreatic Cancer	Y		https://ClinicalTrials.gov/show/NCT03970252
Checkpoint inhibitor	Nivolumab in Combination With Metronomic Chemotherapy in Paediatrics Refractory / Relapsing Solid Tumors	Y		https://ClinicalTrials.gov/show/NCT03585465
Checkpoint inhibitor	Nivolumab Plus Epacadostat in Combination With Chemotherapy Versus the EXTREME Regimen in Squamous Cell Carcinoma of the Head and Neck (CheckMate 9NA/ECHO-310)	Y		https://ClinicalTrials.gov/show/NCT03342352
Checkpoint inhibitor	Nivolumab With Radiation Therapy and Bevacizumab for Recurrent MGMT Methylated Glioblastoma		Y	https://ClinicalTrials.gov/show/NCT03743662
Checkpoint inhibitor	Ociperlimab With Tislelizumab and Chemotherapy in Patients With Untreated Metastatic Non-Small Cell Lung Cancer	Y		https://ClinicalTrials.gov/show/NCT05014815
Checkpoint inhibitor	Optimal Sequencing of Pembrolizumab (MK-3475) and Standard Platinum-based Chemotherapy in First-Line NSCLC	Y		https://ClinicalTrials.gov/show/NCT02591615
Checkpoint inhibitor	Pd-1 Antibody Combined Neoadjuvant Chemotherapy for Locally Advanced Cervical Cancer	Y		https://ClinicalTrials.gov/show/NCT04516616
Checkpoint inhibitor	PD-1 Antibody Combined Neoadjuvant Chemotherapy for Ovarian Cancer	Y		https://ClinicalTrials.gov/show/NCT04815408
Checkpoint inhibitor	PD-1 Antibody Combined With Chemoradiotherapy in Recurrent Nasopharyngeal Carcinoma Patients	Y		https://ClinicalTrials.gov/show/NCT03907826
Checkpoint inhibitor	PD-1 Antibody Following Preoperative Chemoradiotherapy for Locally Advanced pMMR/MSS Rectal Cancer	Y		https://ClinicalTrials.gov/show/NCT04833387
Checkpoint inhibitor	PD-1 Antibody Plus Chemoradiotherapy for IB2-IIIB Cervical Cancer	Y		https://ClinicalTrials.gov/show/NCT05311566
Checkpoint inhibitor	PD-1 Antibody Plus Chemotherapy for TKI Failure Driver Gene Mutation Positive Advanced NSCLC	Y		https://ClinicalTrials.gov/show/NCT04322890
Checkpoint inhibitor	PD-1 Antibody Versus Best Supportive Care After Chemoradiation in Locoregionally Advanced Nasopharyngeal Carcinoma	Y	Y	https://ClinicalTrials.gov/show/NCT03427827
Checkpoint inhibitor	PD-1 Blockade Combined With De-intensification Radical Chemoradiotherapy in Nasopharyngeal Carcinoma	Y		https://ClinicalTrials.gov/show/NCT04907370
Checkpoint inhibitor	PD-1 Blockade Combined With Definitive Chemoradiation in Locoregionally-advanced Nasopharyngeal Carcinoma	Y	Y	https://ClinicalTrials.gov/show/NCT03619824
Checkpoint inhibitor	PD-1 Blockade With JS001 Plus Neoadjuvant Chemotherapy for Gastric/Gastroesophageal Junction Cancer	Y		https://ClinicalTrials.gov/show/NCT05033392
Checkpoint inhibitor	PD-1 Combined With Pyrotinib for Chemotherapy Failure HER2 Insertion Mutation Advanced NSCLC	Y		https://ClinicalTrials.gov/show/NCT04144569
Checkpoint inhibitor	PD-1 Immune Checkpoint Inhibitor Combined With Bevacizumab for Patients With Recurrent/Metastatic Nasopharyngeal Carcinoma After Failure of First Line Chemotherapy	Y		https://ClinicalTrials.gov/show/NCT04872582
Checkpoint inhibitor	PD-1 Inhibitor and Chemotherapy With Concurrent Irradiation at Varied Tumour Sites in Advanced Non-small Cell Lung Cancer	Y	Y	https://ClinicalTrials.gov/show/NCT03774732
Checkpoint inhibitor	PD-1 Inhibitor Combined With Neoadjuvant Chemoradiotherapy Plus Surgery for Locally Advanced ESCC	Y		https://ClinicalTrials.gov/show/NCT05357846
Checkpoint inhibitor	PD-1 Inhibitor Combined With Neoadjuvant Chemotherapy in Subjects With Resectable Locally Advanced Thoracic Esophageal Squamous Cell Carcinoma	Y		https://ClinicalTrials.gov/show/NCT05007145
Checkpoint inhibitor	PD-1 Inhibitor Concurrent With Chemotherapy as Neoadjuvant Therapy for TNBC	Y		https://ClinicalTrials.gov/show/NCT04809779
Checkpoint inhibitor	PD-L1 PET Imaging During Neoadjuvant (Chemo)Radiotherapy in Esophageal and Rectal Cancer	Y		https://ClinicalTrials.gov/show/NCT04564482
Checkpoint inhibitor	Pd1 Antibody Sintilimab Chemoradiotherapy for Locally Advanced Rectal Cancer	Y		https://ClinicalTrials.gov/show/NCT04304209
Checkpoint inhibitor	PD1 Antibody Toripalimab and Chemoradiotherapy for dMMR/MSI-H Locally Advanced Colorectal Cancer	Y		https://ClinicalTrials.gov/show/NCT04301557
Checkpoint inhibitor	PD1 Combined With Chemotherapy for Adjuvant Treatment of Gastric Cancer	Y		https://ClinicalTrials.gov/show/NCT05180734
Checkpoint inhibitor	PDR001 in Combination With Platinum-doublet Chemotherapy and Other Immunology Agents in PD-L1 Unselected, Metastatic NSCLC Patients	Y		https://ClinicalTrials.gov/show/NCT03064854
Checkpoint inhibitor	Pembrolizumab (MK-3475) Plus Chemotherapy Versus Placebo Plus Chemotherapy in Participants Gastric or Gastroesophageal Junction (GEJ) Adenocarcinoma (MK-3475-859/KEYNOTE-859)	Y		https://ClinicalTrials.gov/show/NCT03675737
Checkpoint inhibitor	Pembrolizumab (MK-3475) Plus Chemotherapy Versus Placebo Plus Chemotherapy in Participants Gastric or Gastroesophageal Junction (GEJ) Adenocarcinoma (MK-3475-859/KEYNOTE-859)-China Extension	Y		https://ClinicalTrials.gov/show/NCT04859582
Checkpoint inhibitor	Pembrolizumab (MK-3475) Versus Placebo Following Surgery and Radiation in Participants With Locally Advanced Cutaneous Squamous Cell Carcinoma (MK-3475-630/KEYNOTE-630)		Y	https://ClinicalTrials.gov/show/NCT03833167
Checkpoint inhibitor	Pembrolizumab + Platinum Doublets Without Radiation for Programmed Death-ligand 1 (PD-L1) 50% Locally Advanced NSCLC		Y	https://ClinicalTrials.gov/show/NCT04153734
Checkpoint inhibitor	PEmbrolizumab Combined With Chemoradiotherapy in Squamous Cell Carcinoma of the Head and Neck	Y		https://ClinicalTrials.gov/show/NCT02819752
Checkpoint inhibitor	Pembrolizumab in Combination With Decitabine and Hypofractionated Index Lesion Radiation in Pediatrics and Young Adults		Y	https://ClinicalTrials.gov/show/NCT03445858
Checkpoint inhibitor	Pembrolizumab in Treating Patients With Hormone Receptor Positive, Localized Inflammatory Breast Cancer Who Are Receiving Hormone Therapy and Did Not Achieve a Pathological Complete Response to Chemotherapy	Y		https://ClinicalTrials.gov/show/NCT02971748
Checkpoint inhibitor	Pembrolizumab Plus Chemo in Neoadjuvant Treatment of Esophageal Squamous Cell Carcinoma	Y		https://ClinicalTrials.gov/show/NCT05281003
Checkpoint inhibitor	PEmbRolizumab verSus chEmotherapy and pEmbrolizumab in Non-small-cell Lung Cancers (NSCLC) With PDL1 50 %	Y		https://ClinicalTrials.gov/show/NCT04547504
Checkpoint inhibitor	Pembrolizumab With Chemotherapy for Poorly Chemo-responsive Thyroid and Salivary Gland Tumors	Y		https://ClinicalTrials.gov/show/NCT03360890
Checkpoint inhibitor	Pembrolizumab With Chemotherapy in Front Line Advanced Ovarian, Primary Peritoneal and Fallopian Tube Cancer	Y		https://ClinicalTrials.gov/show/NCT03410784
Checkpoint inhibitor	Pembrolizumab, Paclitaxel, Carboplatin, and Radiation Therapy in Treating Patients With Stage II-IIIB Non-Small Cell Lung Cancer		Y	https://ClinicalTrials.gov/show/NCT02621398
Checkpoint inhibitor	Pembrolizumab/Placebo Plus Trastuzumab Plus Chemotherapy in Human Epidermal Growth Factor Receptor 2 Positive (HER2+) Advanced Gastric or Gastroesophageal Junction (GEJ) Adenocarcinoma (MK-3475-811/KEYNOTE-811)	Y		https://ClinicalTrials.gov/show/NCT03615326
Checkpoint inhibitor	Pembrolizumab/Vibostolimab Coformulation (MK-7684A) or Pembrolizumab/Vibostolimab Coformulation Plus Docetaxel Versus Docetaxel for Metastatic Non Small Cell Lung Cancer (NSCLC) With Progressive Disease After Platinum Doublet Chemotherapy and Immunotherapy (MK-7684A-002, KEYVIBE-002)	Y		https://ClinicalTrials.gov/show/NCT04725188
Checkpoint inhibitor	Penpulimab Plus Chemotherapy With/Without Anlotinib for Patients With Advanced Esophageal Squamous Cell Carcinoma	Y		https://ClinicalTrials.gov/show/NCT05214222
Checkpoint inhibitor	Perioperative Chemoimmunotherapy With/Without Preoperative Chemoradiation for Locally Advanced Gastric Cancer	Y	Y	https://ClinicalTrials.gov/show/NCT05161572
Checkpoint inhibitor	Perioperative Enfortumab Vedotin (EV) Plus Pembrolizumab (MK-3475) Versus Neoadjuvant Chemotherapy for Cisplatin-eligible Muscle Invasive Bladder Cancer (MIBC) (MK-3475-B15/ KEYNOTE-B15 / EV-304)	Y		https://ClinicalTrials.gov/show/NCT04700124
Checkpoint inhibitor	Perioperative Pembrolizumab (MK-3475) Plus Neoadjuvant Chemotherapy Versus Perioperative Placebo Plus Neoadjuvant Chemotherapy for Cisplatin-eligible Muscle-invasive Bladder Cancer (MIBC) (MK-3475-866/KEYNOTE-866)	Y		https://ClinicalTrials.gov/show/NCT03924856
Checkpoint inhibitor	Phase 1 Study of Tremelimumab, Durvalumab, High-dose Chemotherapy, + Autologous Stem Cell Transplant	Y		https://ClinicalTrials.gov/show/NCT02716805
Checkpoint inhibitor	Phase 2 Study to Evaluate PVX-410 + Pembrolizumab + Chemotherapy for Metastatic, PD-L1+ Triple-Negative Breast Cancer	Y		https://ClinicalTrials.gov/show/NCT04634747
Checkpoint inhibitor	Phase 2 Trial for Chemo-Resistant Gestational Trophoblastic Neoplasias With Pembrolizumab (CR-GTP)	Y		https://ClinicalTrials.gov/show/NCT04303884

Checkpoint inhibitor	Phase II MEDI4736 in Combination With Chemotherapy for First-Line Treatment of Unresectable Mesothelioma	Y		https://ClinicalTrials.gov/show/NCT02899195
Checkpoint inhibitor	Phase II Study of the Effects of Laparoscopic Hyperthermic Intraperitoneal Chemotherapy (HIPEC) in Patients With Advanced Gastric Cancer	Y		https://ClinicalTrials.gov/show/NCT04107077
Checkpoint inhibitor	Phase II, Multi-center, Open-label, Randomized Trial on Efficacy and Safety of Neoadjuvant Long-course Chemoradiation Plus Tislelizumab in Mid-low Locally Advanced Rectal Cancer	Y	Y	https://ClinicalTrials.gov/show/NCT05245474
Checkpoint inhibitor	Phase III Study of Camrelizumab in Combination With Chemotherapy in Recurrent/Metastatic Nasopharyngeal Carcinoma	Y		https://ClinicalTrials.gov/show/NCT03707509
Checkpoint inhibitor	Phase III Study to Determine the Efficacy of Durvalumab in Combination With Chemotherapy in Completely Resected Stage II-III Non-small Cell Lung Cancer (NSCLC)	Y		https://ClinicalTrials.gov/show/NCT04385368
Checkpoint inhibitor	Phase-II Trial of Induction Chemotherapy and Chemoradiotherapy Plus/Minus Durvalumab and Consolidation Immunotherapy in Patients With Resectable Stage III NSCLC.	Y		https://ClinicalTrials.gov/show/NCT04202809
Checkpoint inhibitor	PHOENIX DDR/Anti-PD-L1 Trial: A Pre-surgical Window of Opportunity and Post-surgical Adjuvant Biomarker Study of DNA Damage Response Inhibition and/or Anti-PD-L1 Immunotherapy in Patients With Neoadjuvant Chemotherapy Resistant Residual Triple Negative Breast Cancer	Y		https://ClinicalTrials.gov/show/NCT03740893
Checkpoint inhibitor	Placebo-controlled, Study of Concurrent Chemoradiation Therapy With Pembrolizumab Followed by Pembrolizumab and Olaparib in Newly Diagnosed Treatment-Naive Limited-Stage Small Cell Lung Cancer (LS-SCLC) (MK 7339-013/KEYLYNK-013)	Y	Y	https://ClinicalTrials.gov/show/NCT04624204
Checkpoint inhibitor	Platinum-Based Chemotherapy Plus Ramucirumab in Patients With Advanced NSCLC Who Have Progressed on First Line Anti-PD-1 Immunotherapy	Y		https://ClinicalTrials.gov/show/NCT03904108
Checkpoint inhibitor	Platinum-Based Chemotherapy With/Without INCMGA00012, an Anti-PD-1 Antibody, in Non-Small Cell Lung Cancer	Y		https://ClinicalTrials.gov/show/NCT04205812
Checkpoint inhibitor	Plinabulin in Combination With Radiation/Immunotherapy in Patients With Select Advanced Cancers After Progression on PD-1 or PD-L1 Targeted Antibodies		Y	https://ClinicalTrials.gov/show/NCT04902040
Checkpoint inhibitor	Pre-Operative Pembrolizumab + Chemoradiation in Patients With Locally Advanced Esophageal Squamous Cell Carcinoma	Y	Y	https://ClinicalTrials.gov/show/NCT04435197
Checkpoint inhibitor	Precision Radiation of Immune Checkpoint Therapy Resistant Melanoma Metastases		Y	https://ClinicalTrials.gov/show/NCT04793737
Checkpoint inhibitor	Preoperative Anti-PD-1 Antibody Combined With Chemoradiotherapy for Locally Advanced Squmous Cell Carcinoma of Esophageus	Y		https://ClinicalTrials.gov/show/NCT03792347
Checkpoint inhibitor	Programmed Death Ligand (PD-L1) Combined With Chemotherapy for Patients With BTC	Y		https://ClinicalTrials.gov/show/NCT03478488
Checkpoint inhibitor	Programmed Death-1 (PD-1) Antibody Combined With Chemoradiotherapy in High-risk Recurrent Nasopharyngeal Carcinoma	Y		https://ClinicalTrials.gov/show/NCT03930498
Checkpoint inhibitor	QUILT-3.046: NANT Melanoma Vaccine: Combination Immunotherapy in Subjects With Melanoma Who Have Progressed On or After Chemotherapy and PD-1/PD-L1 Therapy	Y		https://ClinicalTrials.gov/show/NCT03167177
Checkpoint inhibitor	QUILT-3.047: NANT Head and Neck Squamous Cell Carcinoma (HNSCC) Vaccine: Combination Immunotherapy in Subjects With HNSCC Who Have Progressed on or After Chemotherapy and PD-1/PD-L1 Therapy	Y		https://ClinicalTrials.gov/show/NCT03169764
Checkpoint inhibitor	QUILT-3.048: NANT Urothelial Cancer Vaccine: Combination Immunotherapy in Subjects With Urothelial Cancer Who Have Progressed on or After Chemotherapy and PD-1/PD-L1 Therapy	Y		https://ClinicalTrials.gov/show/NCT03197571
Checkpoint inhibitor	Radiation Therapy and Durvalumab With or Without Tremelimumab in Treating Participants With Unresectable, Locally Advanced, or Metastatic Bladder Cancer		Y	https://ClinicalTrials.gov/show/NCT03601455
Checkpoint inhibitor	Radiation Therapy and Durvalumab, With or Without Tremelimumab, in Patients With Bladder Cancer		Y	https://ClinicalTrials.gov/show/NCT03150836
Checkpoint inhibitor	Radiation, Immunotherapy and PARP Inhibitor in Triple Negative Breast Cancer		Y	https://ClinicalTrials.gov/show/NCT04837209
Checkpoint inhibitor	Radiochemotherapy +/- Durvalumab for Locally-advanced Anal Carcinoma. A Multicenter, Randomized, Phase II Trial of the German Anal Cancer Study Group	Y		https://ClinicalTrials.gov/show/NCT04230759
Checkpoint inhibitor	Radiotherapy in Combo With Chemo and Immunotherapy in Patients With PD-L1 Positive Metastatic TNBC	Y		https://ClinicalTrials.gov/show/NCT05233696
Checkpoint inhibitor	RADVAX: A Trial of Combined Pembrolizumab and Hypofractionated Radiation in Patients With Advanced Urothelial Cancer Who Have Progressed on Anti-PD-1/PD-L1 Monotherapy		Y	https://ClinicalTrials.gov/show/NCT02880345
Checkpoint inhibitor	Randomized Phase II Trial of a PD-1 Inhibitor INCMGA00012 as Consolidation Therapy After Definitive Concurrent Chemoradiotherapy(RHAPSODY)	Y		https://ClinicalTrials.gov/show/NCT04494009
Checkpoint inhibitor	Real World Evidence of PD-L1, TMB Prevalence and Efficacy of 1st Line Chemotherapy in These High or Low Population for Stage IV Urothelial Cancer	Y		https://ClinicalTrials.gov/show/NCT04052113
Checkpoint inhibitor	Real-world Experience of ICIs Plus Chemotherapy for Advanced ESCC.	Y		https://ClinicalTrials.gov/show/NCT05142709
Checkpoint inhibitor	Rectal Artery Infusion Chemotherapy Combined With Anti-PD1 Antibody for MSS LARC	Y		https://ClinicalTrials.gov/show/NCT05307198
Checkpoint inhibitor	REGN2810 (Anti-PD-1 Antibody), Platinum-based Doublet Chemotherapy, and Ipilimumab (Anti-CTLA-4 Antibody) Versus Pembrolizumab Monotherapy in Patients With Lung Cancer	Y		https://ClinicalTrials.gov/show/NCT03515629
Checkpoint inhibitor	REirradiation and Programmed Cell Death Protein 1 (PD-1) Blockade On Recurrent Squamous Cell Head and Neck Tumors		Y	https://ClinicalTrials.gov/show/NCT03317327
Checkpoint inhibitor	Reirradiation With Pembrolizumab in Locoregional Inoperable Recurrence or Second Primary Squamous Cell CA of the Head and Neck	Y		https://ClinicalTrials.gov/show/NCT02289209
Checkpoint inhibitor	Safety and Efficacy of Atezolizumab Combined to Preoperative Radio-chemotherapy in Localized Rectal Cancer	Y		https://ClinicalTrials.gov/show/NCT03127007
Checkpoint inhibitor	Safety and Efficacy of Durvalumab Combined to Neoadjuvant Chemotherapy in Localized Luminal B HER2(-) and Triple Negative Breast Cancer.	Y		https://ClinicalTrials.gov/show/NCT03356860
Checkpoint inhibitor	Safety and Efficacy of Lenvatinib (E7080/MK-7902) With Pembrolizumab (MK-3475) in Combination With Transarterial Chemoembolization (TACE) in Participants With Incurable/Non-metastatic Hepatocellular Carcinoma (MK-7902-012/E7080-G000-318/LEAP-012)	Y		https://ClinicalTrials.gov/show/NCT04246177
Checkpoint inhibitor	Safety and Efficacy of Pembrolizumab (MK-3475) Plus Binimetinib Alone or Pembrolizumab Plus Chemotherapy With or Without Binimetinib in Metastatic Colorectal Cancer (mCRC) Participants (MK-3475-651)	Y		https://ClinicalTrials.gov/show/NCT03374254
Checkpoint inhibitor	Safety and Efficacy of Retifanlimab (INCMGA00012) Alone or in Combination With Other Therapies in Participants With Advanced or Metastatic Endometrial Cancer Who Have Progressed on or After Platinum-based Chemotherapy.	Y		https://ClinicalTrials.gov/show/NCT04463771
Checkpoint inhibitor	Safety And Efficacy Study Of Avelumab Plus Chemotherapy With Or Without Other Anti-Cancer Immunotherapy Agents In Patients With Advanced Malignancies	Y		https://ClinicalTrials.gov/show/NCT03317496
Checkpoint inhibitor	Safety and Efficacy Study of Pembrolizumab (MK-3475) in Combination With Chemotherapy as Neoadjuvant Treatment for Participants With Triple Negative Breast Cancer (TNBC) (MK-3475-173/KEYNOTE-173)	Y		https://ClinicalTrials.gov/show/NCT02622074
Checkpoint inhibitor	Safety and Efficacy Study of Pemetrexed + Platinum Chemotherapy + Pembrolizumab (MK-3475) With or Without Lenvatinib (MK-7902/E7080) as First-line Intervention in Adults With Metastatic Nonsquamous Non-small Cell Lung Cancer (MK-7902-006/E7080-G000-315/LEAP-006)-China Extension Study	Y		https://ClinicalTrials.gov/show/NCT04716933
Checkpoint inhibitor	Safety and Efficacy Study of Pemetrexed + Platinum Chemotherapy + Pembrolizumab (MK-3475) With or Without Lenvatinib (MK-7902/E7080) as First-line Intervention in Adults With Metastatic Nonsquamous Non-small Cell Lung Cancer (MK-7902-006/E7080-G000-315/LEAP-006)	Y		https://ClinicalTrials.gov/show/NCT03829319
Checkpoint inhibitor	Safety and Efficacy Study of Pemetrexed + Platinum Chemotherapy + Pembrolizumab (MK-3475) With or Without Lenvatinib (MK-7902/E7080) as First-line Intervention in Adults With Metastatic Nonsquamous Non-small Cell Lung Cancer (MK-7902-006/E7080-G000-315/LEAP-006)-China Extension Study	Y		https://ClinicalTrials.gov/show/NCT04716933
Checkpoint inhibitor	Safety and Tolerability Evaluation of Low-dose Radiation in Combination With CS1001 in Relapsed SCLC Patients		Y	https://ClinicalTrials.gov/show/NCT04421352
Checkpoint inhibitor	Safety and Tolerability Evaluation of Sintilimab in Combination With Radiation in Stage IV NSCLC Patients		Y	https://ClinicalTrials.gov/show/NCT03812549
Checkpoint inhibitor	Safety Testing of Adding Nivolumab to Chemotherapy in Patients With Intermediate and High-Risk Local-Regionally Advanced Head and Neck Cancer	Y		https://ClinicalTrials.gov/show/NCT02764593
Checkpoint inhibitor	SBRT/LDRT in Combination With Camrelizumab and Apatinib in Metastatic Non-small Cell Lung Cancer Patient Previously Treated With PD-1/L1 Inhibitor and Chemotherapy	Y		https://ClinicalTrials.gov/show/NCT04878107
Checkpoint inhibitor	Sequential PD-1/PD-L1 Inhibitor and LENvatinib in TLCT and Refractory Hepatoblastoma After Chemotherapy	Y		https://ClinicalTrials.gov/show/NCT05322187
Checkpoint inhibitor	Short Course Neoadjuvant Chemo-radiotherapy Plus Toripalimab for Locally Advanced Resectble Squamous Cell Carcinoma of Esophagus	Y		https://ClinicalTrials.gov/show/NCT05424432
Checkpoint inhibitor	SHR-1210 in Combination With Apatinib and Chemotherapy in Patients With Advanced Esophageal Squamous Cell Cancer	Y		https://ClinicalTrials.gov/show/NCT03603756
Checkpoint inhibitor	SHR-1210 in Recurrent/Metastatic Nasopharyngeal Carcinoma Who Have Received Previous At Least Two Lines of Chemotherapy.	Y		https://ClinicalTrials.gov/show/NCT03558191
Checkpoint inhibitor	SHR-1316 in Combination With Chemotherapy in Patients With Esophageal Squamous Cell Cancer	Y		https://ClinicalTrials.gov/show/NCT03732508
Checkpoint inhibitor	Single Agent Chemotherapy +/- Nivolumab in Patients With Advanced Squamous or Non-squamous NSCLC With Primary Resistance to Prior PD-1 or PDL-1 Inhibitor	Y		https://ClinicalTrials.gov/show/NCT03041181

Checkpoint inhibitor	Sintilimab (PD-1 Antibody) and Chemoradiotherapy in Locoregionally-advanced Nasopharyngeal Carcinoma	Y		https://ClinicalTrials.gov/show/NCT03700476
Checkpoint inhibitor	SinTilimab After Radiation (STAR Study)		Y	https://ClinicalTrials.gov/show/NCT04167657
Checkpoint inhibitor	Sintilimab in Combination With Chemotherapy in Neoadjuvant Treatment of Potentially Resectable Esophageal Cancer	Y		https://ClinicalTrials.gov/show/NCT03946969
Checkpoint inhibitor	Sintilimab or Placebo With Chemotherapy in Esophageal Squamous Cell Carcinoma	Y		https://ClinicalTrials.gov/show/NCT03748134
Checkpoint inhibitor	Stereotactic Ablative Radiation for Oligo-Progression of Urothelial Cancer	Y		https://ClinicalTrials.gov/show/NCT04131634
Checkpoint inhibitor	Stereotactic Body Radiation Therapy (SBRT) Combined With Avelumab (Anti-PD-L1) for Management of Early Stage Non-Small Cell Lung Cancer (NSCLC)		Y	https://ClinicalTrials.gov/show/NCT03050554
Checkpoint inhibitor	Stereotactic Body Radiation Therapy Combined With Anti-PD-1 Antibody in Metastatic Triple Negative Breast Cancer		Y	https://ClinicalTrials.gov/show/NCT03151447
Checkpoint inhibitor	Stereotactic Body Radiation Therapy Combined With Anti-PD-1 Antibody in Patients With Hepatocellular Carcinoma		Y	https://ClinicalTrials.gov/show/NCT03857815
Checkpoint inhibitor	Study of Adjuvant Chemotherapy With or Without PD-1 Inhibitors and Chemoradiotherapy in Resected pN3 Gastric (G) or GEJ Adenocarcinoma	Y		https://ClinicalTrials.gov/show/NCT04997837
Checkpoint inhibitor	Study of Anti-PD-L1 in Combination With Chemo(Radio)Therapy for Oesophageal Cancer	Y		https://ClinicalTrials.gov/show/NCT02735239
Checkpoint inhibitor	Study of Anti-PD-L1 in Combination With Chemo(Radio)Therapy for Resectable Esophageal Squamous Cell Carcinoma	Y		https://ClinicalTrials.gov/show/NCT04568200
Checkpoint inhibitor	Study of Atezolizumab as Monotherapy and in Combination With Platinum-Based Chemotherapy in Participants With Untreated Locally Advanced or Metastatic Urothelial Carcinoma	Y		https://ClinicalTrials.gov/show/NCT02807636
Checkpoint inhibitor	Study of Atezolizumab in Combination With Cabozantinib Versus Docetaxel in Patients With Metastatic Non-Small Cell Lung Cancer Previously Treated With an Anti-PD-L1/PD-1 Antibody and Platinum-Containing Chemotherapy	Y		https://ClinicalTrials.gov/show/NCT04471428
Checkpoint inhibitor	Study of Autologous CIK Cell Immunotherapy Combination With PD-1 Inhibitor and Chemotherapy in the Advanced NSCLC	Y		https://ClinicalTrials.gov/show/NCT03987867
Checkpoint inhibitor	Study of Camrelizumab (SHR-1210) in Combination With Concurrent Chemoradiotherapy in Locally Advanced Esophageal Cancer	Y		https://ClinicalTrials.gov/show/NCT04426955
Checkpoint inhibitor	Study of Chemoradiotherapy With or Without Pembrolizumab (MK-3475) For The Treatment of Locally Advanced Cervical Cancer (MK-3475-A18/KEYNOTE-A18/ENGOT-cx11/GOG-3047)	Y		https://ClinicalTrials.gov/show/NCT04221945
Checkpoint inhibitor	Study of Chemotherapy and PD-1 Inhibitor Combination With Anti-angiogenesis to Treat Elderly Lung Cancer	Y		https://ClinicalTrials.gov/show/NCT05273814
Checkpoint inhibitor	Study of Chemotherapy and PD-1 Inhibitor Combination With Autologous CIK Cell Immunotherapy to Treat Lung Cancer	Y		https://ClinicalTrials.gov/show/NCT04836728
Checkpoint inhibitor	Study of Chemotherapy Combination With Autologous Cell Immunotherapy in the Advanced Lung Cancer	Y		https://ClinicalTrials.gov/show/NCT03944980
Checkpoint inhibitor	Study of Chemotherapy Combination With Autologous Cell Immunotherapy in the Recurrent and Metastatic Colorectal Cancer	Y		https://ClinicalTrials.gov/show/NCT03950154
Checkpoint inhibitor	Study of Chemotherapy With Pembrolizumab (MK-3475) Followed by Maintenance With Olaparib (MK-7339) for the First-Line Treatment of Women With BRCA Non-mutated Advanced Epithelial Ovarian Cancer (EOC) (MK-7339-001/KEYLYNK-001/ENGOT-ov43/GOG-3036)	Y		https://ClinicalTrials.gov/show/NCT03740165
Checkpoint inhibitor	Study of Durvalumab (MEDI4736) After Chemo-Radiation for Microsatellite Stable Stage II-IV Rectal Cancer	Y	Y	https://ClinicalTrials.gov/show/NCT03102047
Checkpoint inhibitor	Study of Durvalumab + Tremelimumab With Chemotherapy or Durvalumab With Chemotherapy or Chemotherapy Alone for Patients With Lung Cancer (POSEIDON).	Y		https://ClinicalTrials.gov/show/NCT03164616
Checkpoint inhibitor	Study of Durvalumab Alone or Chemotherapy for Patients With Advanced Non Small-Cell Lung Cancer (PEARL)	Y		https://ClinicalTrials.gov/show/NCT03003962
Checkpoint inhibitor	Study of Durvalumab or Durvalumab Plus Chemotherapy in Kras Mutation Positive and PD-L1 High (50%) NSCLC Patients	Y		https://ClinicalTrials.gov/show/NCT04470674
Checkpoint inhibitor	Study of Durvalumab Versus Placebo in Combination With Definitive Chemoradiation Therapy in Patient With ESCC	Y	Y	https://ClinicalTrials.gov/show/NCT04550260
Checkpoint inhibitor	Study of Efficacy and Safety of NIS793 (With and Without Spartalizumab) in Combination With SOC Chemotherapy in First-line Metastatic Pancreatic Ductal Adenocarcinoma (mPDAC)	Y		https://ClinicalTrials.gov/show/NCT04390763
Checkpoint inhibitor	Study of Efficacy and Safety of Pembrolizumab Plus Platinum-based Doublet Chemotherapy With or Without Canakinumab in Previously Untreated Locally Advanced or Metastatic Non-squamous and Squamous NSCLC Subjects	Y		https://ClinicalTrials.gov/show/NCT03631199
Checkpoint inhibitor	Study of Epacadostat (INCB024360) Alone and In Combination With Pembrolizumab (MK-3475) With Chemotherapy and Pembrolizumab Without Chemotherapy in Participants With Advanced Solid Tumors (MK-3475-434)	Y		https://ClinicalTrials.gov/show/NCT02862457
Checkpoint inhibitor	Study of Favezelimab (MK-4280) as Monotherapy and in Combination With Pembrolizumab (MK-3475) With or Without Chemotherapy or Lenvatinib (MK-7902) AND Favezelimab/Pembrolizumab (MK-4280A) as Monotherapy in Adults With Advanced Solid Tumors (MK-4280-001)	Y		https://ClinicalTrials.gov/show/NCT02720068
Checkpoint inhibitor	Study of First-line Pembrolizumab (MK-3475) With Lenvatinib (MK-7902/E7080) in Urothelial Carcinoma Cisplatin-ineligible Participants Whose Tumors Express Programmed Cell Death-Ligand 1 and in Participants Ineligible for Platinum-containing Chemotherapy (MK-7902-011/E7080-G000-317/ LEAP-011)	Y		https://ClinicalTrials.gov/show/NCT03898180
Checkpoint inhibitor	Study of Immune Checkpoint Inhibition With Radiation Therapy in Unresectable, Non-metastatic Pancreatic Cancer		Y	https://ClinicalTrials.gov/show/NCT02868632
Checkpoint inhibitor	Study of Olaparib Plus Pembrolizumab Versus Chemotherapy Plus Pembrolizumab After Induction With First-Line Chemotherapy Plus Pembrolizumab in Triple Negative Breast Cancer (TNBC) (MK-7339-009/KEYLYNK-009)	Y		https://ClinicalTrials.gov/show/NCT04191135
Checkpoint inhibitor	Study of PD-1 Antibody and Bevacizumab in the Treatment of High-risk GTN After Combined Chemotherapy	Y		https://ClinicalTrials.gov/show/NCT04812002
Checkpoint inhibitor	Study of PD-1 Antibody Combined With Chemoradiotherapy in Oligometastatic Esophageal Cancer	Y		https://ClinicalTrials.gov/show/NCT04821765
Checkpoint inhibitor	Study of PD-1 Monoclonal Antibody in Combination With Chemotherapy in Patients With RR NHL	Y		https://ClinicalTrials.gov/show/NCT04134247
Checkpoint inhibitor	Study of Pembrolizumab (MK-3475) Compared to Platinum-Based Chemotherapies in Participants With Metastatic Non-Small Cell Lung Cancer (MK-3475-024/KEYNOTE-024)	Y		https://ClinicalTrials.gov/show/NCT02142738
Checkpoint inhibitor	Study of Pembrolizumab (MK-3475) in Combination With Adjuvant Chemotherapy With or Without Radiotherapy in Participants With Newly Diagnosed Endometrial Cancer After Surgery With Curative Intent (MK-3475-B21 / KEYNOTE-B21 / ENGOT-en11 / GOG-3053)	Y		https://ClinicalTrials.gov/show/NCT04634877
Checkpoint inhibitor	Study of Pembrolizumab (MK-3475) or Placebo With Chemoradiation in Participants With Locally Advanced Head and Neck Squamous Cell Carcinoma (MK-3475-412/KEYNOTE-412)	Y	Y	https://ClinicalTrials.gov/show/NCT03040999
Checkpoint inhibitor	Study of Pembrolizumab (MK-3475) Plus Chemotherapy Versus Placebo Plus Chemotherapy for HR+/HER2- Locally Recurrent Inoperable or Metastatic Breast Cancer (MK-3475-B49/KEYNOTE-B49)	Y		https://ClinicalTrials.gov/show/NCT04895358
Checkpoint inhibitor	Study of Pembrolizumab (MK-3475) Plus Chemotherapy Versus Placebo Plus Chemotherapy in Participants With Gastric or Gastroesophageal Junction (GEJ) Adenocarcinoma (MK-3475-585/KEYNOTE-585)	Y		https://ClinicalTrials.gov/show/NCT03221426
Checkpoint inhibitor	Study of Pembrolizumab (MK-3475) Plus Chemotherapy Versus Placebo Plus Chemotherapy in Participants With Gastric or Gastroesophageal Junction (GEJ) Adenocarcinoma (MK-3475-585/KEYNOTE-585)-China Extension	Y		https://ClinicalTrials.gov/show/NCT04882241
Checkpoint inhibitor	Study of Pembrolizumab (MK-3475) Plus Chemotherapy vs Placebo Plus Chemotherapy as Neoadjuvant Therapy and Pembrolizumab vs Placebo as Adjuvant Therapy in Participants With Triple Negative Breast Cancer (TNBC) (MK-3475-522/KEYNOTE-522)	Y		https://ClinicalTrials.gov/show/NCT03036488
Checkpoint inhibitor	Study of Pembrolizumab (MK-3475) Plus Chemotherapy vs. Placebo Plus Chemotherapy for Previously Untreated Locally Recurrent Inoperable or Metastatic Triple Negative Breast Cancer (MK-3475-355/KEYNOTE-355)	Y		https://ClinicalTrials.gov/show/NCT02819518
Checkpoint inhibitor	Study of Pembrolizumab (MK-3475) Plus Docetaxel Versus Placebo Plus Docetaxel in Chemotherapy-naive Metastatic Castration-resistant Prostate Cancer (mCRPC) (MK-3475-921/KEYNOTE-921)	Y		https://ClinicalTrials.gov/show/NCT03834506
Checkpoint inhibitor	Study of Pembrolizumab (MK-3475) Plus Docetaxel Versus Placebo Plus Docetaxel in Chemotherapy-naive Metastatic Castration-resistant Prostate Cancer (mCRPC) (MK-3475-921/KEYNOTE-921)-China Extension	Y		https://ClinicalTrials.gov/show/NCT04907227
Checkpoint inhibitor	Study of Pembrolizumab (MK-3475) Subcutaneous (SC) Versus Pembrolizumab Intravenous (IV) Administered With Platinum Doublet Chemotherapy in Participants With Metastatic Squamous or Nonsquamous Non-Small Cell Lung Cancer (NSCLC) (MK-3475-A86)	Y		https://ClinicalTrials.gov/show/NCT04956692
Checkpoint inhibitor	Study of Pembrolizumab (MK-3475) Versus Chemotherapy in Chinese Participants With Stage IV Colorectal Cancer (MK-3475-C66)	Y		https://ClinicalTrials.gov/show/NCT05239741

Checkpoint inhibitor	Study of Pembrolizumab (MK-3475) Versus Chemotherapy in Mismatch Repair Deficient (dMMR) Advanced or Recurrent Endometrial Carcinoma (MK-3475-C93/KEYNOTE-C93/GOG-3064/ENGOT-en15)	Y		https://ClinicalTrials.gov/show/NCT05173987
Checkpoint inhibitor	Study of Pembrolizumab (MK-3475) Versus Chemotherapy in Participants With Advanced Melanoma (MK-3475-002/P08719/KEYNOTE-002)	Y		https://ClinicalTrials.gov/show/NCT01704287
Checkpoint inhibitor	Study of Pembrolizumab (MK-3475) Versus Investigator's Choice of Chemotherapy for Participants With Advanced Esophageal/Esophagogastric Junction Carcinoma That Progressed After First-Line Therapy (MK-3475-181/KEYNOTE-181)-China Extension Study	Y		https://ClinicalTrials.gov/show/NCT03933449
Checkpoint inhibitor	Study of Pembrolizumab (MK-3475) Versus Placebo in Combination With Neoadjuvant Chemotherapy & Adjuvant Endocrine Therapy in the Treatment of Early-Stage Estrogen Receptor-Positive, Human Epidermal Growth Factor Receptor 2-Negative (ER+/HER2-) Breast Cancer (MK-3475-756/KEYNOTE-756)	Y		https://ClinicalTrials.gov/show/NCT03725059
Checkpoint inhibitor	Study of Pembrolizumab (MK-3475) Versus Placebo in Participants With Esophageal Carcinoma Who Are Receiving Chemotherapy and Radiation Therapy (MK-3475-975/KEYNOTE-975)	Y	Y	https://ClinicalTrials.gov/show/NCT04210115
Checkpoint inhibitor	Study of Pembrolizumab (MK-3475) Versus Platinum-Based Chemotherapy for Participants With Programmed Cell Death-Ligand 1 (PD-L1)-Positive Advanced or Metastatic Non-Small Cell Lung Cancer (MK-3475-042/KEYNOTE-042)	Y		https://ClinicalTrials.gov/show/NCT02220894
Checkpoint inhibitor	Study of Pembrolizumab (MK-3475) Versus Platinum-Based Chemotherapy for Participants With Programmed Cell Death-Ligand 1 (PD-L1)-Positive Advanced or Metastatic Non-Small Cell Lung Cancer (MK-3475-042/KEYNOTE-042)-China Extension Study	Y		https://ClinicalTrials.gov/show/NCT03850444
Checkpoint inhibitor	Study of Pembrolizumab and Chemotherapy With or Without Radiation in Small Cell Lung Cancer (SCLC)	Y	Y	https://ClinicalTrials.gov/show/NCT02934503
Checkpoint inhibitor	Study of Pembrolizumab With Concurrent Chemoradiation Therapy Followed by Pembrolizumab With or Without Olaparib in Stage III Non-Small Cell Lung Cancer (NSCLC) (MK-7339-012/KEYLYNK-012)	Y	Y	https://ClinicalTrials.gov/show/NCT04380636
Checkpoint inhibitor	Study of Pembrolizumab With or Without Defactinib Following Chemotherapy as a Neoadjuvant and Adjuvant Treatment for Resectable Pancreatic Ductal Adenocarcinoma	Y		https://ClinicalTrials.gov/show/NCT03727880
Checkpoint inhibitor	Study of Pembrolizumab With or Without Platinum-based Combination Chemotherapy Versus Chemotherapy Alone in Urothelial Carcinoma (MK-3475-361/KEYNOTE-361)	Y		https://ClinicalTrials.gov/show/NCT02853305
Checkpoint inhibitor	Study of Pembrolizumab With Single Agent Chemotherapy in Elderly Patients With Advanced NSCLC	Y		https://ClinicalTrials.gov/show/NCT04754815
Checkpoint inhibitor	Study of Pembrolizumab/Vibostolimab (MK-7684A) in Combination With Concurrent Chemoradiotherapy Followed by Pembrolizumab/Vibostolimab Versus Concurrent Chemoradiotherapy Followed by Durvalumab in Participants With Stage III Non-small Cell Lung Cancer (MK-7684A-006/KEYVIBE-006)	Y		https://ClinicalTrials.gov/show/NCT05298423
Checkpoint inhibitor	Study of Pemetrexed + Platinum Chemotherapy With or Without Pembrolizumab (MK-3475) in Adults With Tyrosine Kinase Inhibitor- (TKI)-Resistant Epidermal Growth Factor Receptor- (EGFR)-Mutated Metastatic Non-squamous Non-small Cell Lung Cancer (NSCLC) (MK-3475-789/KEYNOTE-789)	Y		https://ClinicalTrials.gov/show/NCT03515837
Checkpoint inhibitor	Study of Pemetrexed+Platinum Chemotherapy With or Without Cosibelimab (CK-301) in First Line Metastatic Non-squamous Non-Small Cell Lung Cancer	Y		https://ClinicalTrials.gov/show/NCT04786964
Checkpoint inhibitor	Study of Pemetrexed+Platinum Chemotherapy With or Without Pembrolizumab (MK-3475) in Participants With First Line Metastatic Nonsquamous Non-small Cell Lung Cancer (MK-3475-189/KEYNOTE-189)	Y		https://ClinicalTrials.gov/show/NCT02578680
Checkpoint inhibitor	Study of Pemetrexed+Platinum Chemotherapy With or Without Pembrolizumab (MK-3475) in Participants With First Line Metastatic Nonsquamous Non-small Cell Lung Cancer (MK-3475-189/KEYNOTE-189)-Japan Extension Study	Y		https://ClinicalTrials.gov/show/NCT03950674
Checkpoint inhibitor	Study of REGN 2810 Compared to Platinum-Based Chemotherapies in Participants With Metastatic Non-Small Cell Lung Cancer (NSCLC)	Y		https://ClinicalTrials.gov/show/NCT03088540
Checkpoint inhibitor	Study of Sacituzumab Govitecan-hziy (SG) Versus Docetaxel in Participants With Advanced or Metastatic Non-Small Cell Lung Cancer (NSCLC) With Progression on or After Platinum-Based Chemotherapy and Anti-programmed Death Protein 1 (PD-1)/Programmed Death Ligand 1 (PD-L1) Immunotherapy	Y		https://ClinicalTrials.gov/show/NCT05089734
Checkpoint inhibitor	Study of Safety and Efficacy of Pembrolizumab and Chemotherapy in Participants With Newly Diagnosed Classical Hodgkin Lymphoma (cHL) (MK-3475-C11/KEYNOTE-C11)	Y		https://ClinicalTrials.gov/show/NCT05008224
Checkpoint inhibitor	Study of SHR-1210 in Combination With Chemotherapy in Advanced Esophageal Cancer	Y		https://ClinicalTrials.gov/show/NCT03691090
Checkpoint inhibitor	Study of SHR2150 (TLR7 Agonist) in Combination With Chemotherapy Plus PD-1 or CD47 Antibody in Subjects With Unresectable/ Metastatic Solid Tumors	Y		https://ClinicalTrials.gov/show/NCT04588324
Checkpoint inhibitor	Study of Single Agent Pembrolizumab (MK-3475) Versus Single Agent Chemotherapy for Metastatic Triple Negative Breast Cancer (MK-3475-119/KEYNOTE-119)	Y		https://ClinicalTrials.gov/show/NCT02555657
Checkpoint inhibitor	Study of the PD-L1 Inhibitor Atezolizumab With or Without Low-dose, Local Radiation in Patients With Relapsed or Refractory Advanced Stage Follicular Lymphoma		Y	https://ClinicalTrials.gov/show/NCT03465891
Checkpoint inhibitor	Study of ZKAB001 for Maintenance Therapy in Patients With High-grade Osteosarcoma After Adjuvant Chemotherapy	Y		https://ClinicalTrials.gov/show/NCT04359550
Checkpoint inhibitor	Study Title: Peri-operative Immuno-Chemotherapy in Operable Oesophageal and Gastric Cancer	Y		https://ClinicalTrials.gov/show/NCT03399071
Checkpoint inhibitor	Study to Assess Safety and Efficacy of Atezolizumab (MPDL3280A) Compared to Best Supportive Care Following Chemotherapy in Patients With Lung Cancer [IMpower010]	Y		https://ClinicalTrials.gov/show/NCT02486718
Checkpoint inhibitor	Study With Atezolizumab Plus Bevacizumab in Patients With Chemotherapy Resistant, MSI-like, Colorectal Cancer	Y		https://ClinicalTrials.gov/show/NCT02982694
Checkpoint inhibitor	Systemic Chemotherapy Plus PD-1 for Metastasis ICC	Y		https://ClinicalTrials.gov/show/NCT04398927
Checkpoint inhibitor	Tapestry: Addition of TGF-b and PDL-1 Inhibition to Definitive Chemoradiation in Esophageal Squamous Cell Carcinoma	Y	Y	https://ClinicalTrials.gov/show/NCT04595149
Checkpoint inhibitor	Targeting PD-1 Therapy Resistance With Focused High or High and Low Dose Radiation in SCCHN		Y	https://ClinicalTrials.gov/show/NCT03085719
Checkpoint inhibitor	Testing Combination Erdafitinib and Enfortumab Vedotin in Metastatic Bladder Cancer After Treatment With Chemotherapy and Immunotherapy	Y		https://ClinicalTrials.gov/show/NCT04963153
Checkpoint inhibitor	Testing the Addition of Anti-Cancer Drug, ZEN003694 (ZEN-3694) and PD-1 Inhibitor (Pembrolizumab), to Standard Chemotherapy (Nab-Paclitaxel) Treatment in Patients With Advanced Triple-Negative Breast Cancer	Y		https://ClinicalTrials.gov/show/NCT05422794
Checkpoint inhibitor	Testing the Addition of Radiation Therapy to Immunotherapy for Merkel Cell Carcinoma		Y	https://ClinicalTrials.gov/show/NCT03304639
Checkpoint inhibitor	Testing the Addition of Radiation Therapy to the Usual Treatment (Immunotherapy With or Without Chemotherapy) for Stage IV Non-Small Cell Lung Cancer Patients Who Are PD-L1 Negative	Y	Y	https://ClinicalTrials.gov/show/NCT04929041
Checkpoint inhibitor	Testing the PD-1 Inhibitor Pembrolizumab as Maintenance Therapy After Initial Chemotherapy in Metastatic Bladder Cancer	Y		https://ClinicalTrials.gov/show/NCT02500121
Checkpoint inhibitor	TGF-b And PDL-1 Inhibition in Esophageal Squamous Cell Carcinoma Combined With Chemoradiation TheRapY	Y	Y	https://ClinicalTrials.gov/show/NCT04481256
Checkpoint inhibitor	The Efficacy of JS001 Combined With Chemotherapy in Patients With Locally Advanced Colon Cancer	Y		https://ClinicalTrials.gov/show/NCT03985891
Checkpoint inhibitor	The Safety and Efficacy of PD-1 Monoantrapical Chemotherapy in the Treatment of Local Advanced Stomach Cancer	Y		https://ClinicalTrials.gov/show/NCT05000554
Checkpoint inhibitor	The Safety and Efficacy of Transarterial Chemoembolization (TACE) + Lenvatinib + Programmed Cell Death Protein 1 (PD-1) Antibody of Advanced Unresectable Hepatocellular Carcinoma	Y		https://ClinicalTrials.gov/show/NCT04997850
Checkpoint inhibitor	Tisleilizumab (PD-1 Antibody) and Chemoradiotherapy in Locoregionally-advanced Nasopharyngeal Carcinoma	Y		https://ClinicalTrials.gov/show/NCT04870905
Checkpoint inhibitor	Tislelizumab Combined With Chemotherapy With or Without Bevacizumab in TKI-Resistant EGFR-Mutated Non-squamous NSCLC	Y		https://ClinicalTrials.gov/show/NCT04405674
Checkpoint inhibitor	Tislelizumab in Combination With Anlotinib With ES-SCLC as Maintenance Therapy After First Line Chemotherapy	Y		https://ClinicalTrials.gov/show/NCT04620837
Checkpoint inhibitor	to Evaluate Efficacy and Safety of HLX10 in Combination With Chemotherapy Versus Placebo in Combination With Chemotherapy as Neoadjuvant Therapy and HLX10 Versus Placebo as Adjuvant Therapy in Patients With Triple Negative Breast Cancer (TNBC)	Y		https://ClinicalTrials.gov/show/NCT04301739
Checkpoint inhibitor	Toripalimab as Monotherapy for Patients With Small Cell Carcinoma of Esophagus Who Failed Chemotherapy	Y		https://ClinicalTrials.gov/show/NCT03811379
Checkpoint inhibitor	Toripalimab Combined With Chemotherapy in Primary Tracheal Squamous Cell Carcinoma	Y		https://ClinicalTrials.gov/show/NCT04716751
Checkpoint inhibitor	Toripalimab in Combination With Platinum-based Chemotherapy for Mutation-negative Stage IV Oligometastatic NSCLC	Y		https://ClinicalTrials.gov/show/NCT05055583
Checkpoint inhibitor	Toripalimab Plus Concurrent Chemo-radiotherapy for Unresectable Locally Recurrent Nasopharyngeal Carcinoma	Y		https://ClinicalTrials.gov/show/NCT04453813
Checkpoint inhibitor	Toripalimab Plus TPF Chemotherapy and Radiotherapy for LA-HPSCC	Y		https://ClinicalTrials.gov/show/NCT04624308
Checkpoint inhibitor	Toripalimab With Preoperative Chemoradiotherapy for LA-EGJ	Y		https://ClinicalTrials.gov/show/NCT04061928
Checkpoint inhibitor	Toripalimab, Endostar Combined With Radiotherapy and Chemotherapy for Nasopharyngeal Carcinoma	Y		https://ClinicalTrials.gov/show/NCT04447326
Checkpoint inhibitor	TQB2450 (PD-L1 Inhibitor) Plus Anlotinib Combined With Chemotherapy in the Treatment of Gastric or Gastroesophageal Junction Adenocarcinoma	Y		https://ClinicalTrials.gov/show/NCT04891900
Checkpoint inhibitor	Treating Early-stage Non-Small Cell Lung Cancer With Durvalumab and Radiation Therapy		Y	https://ClinicalTrials.gov/show/NCT04716946
Checkpoint inhibitor	Trial of Anti-PD-1 Immunotherapy and Stereotactic Radiation in Patients With Recurrent Glioblastoma		Y	https://ClinicalTrials.gov/show/NCT04977375

Checkpoint inhibitor	Trial of Atezolizumab Plus Chemotherapy After Progression on PD-1 or PD-L1 in Cisplatin-ineligible Patients With Advanced Urothelial Carcinoma	Y		https://ClinicalTrials.gov/show/NCT03737123
Checkpoint inhibitor	Trial of Chemoradiation and Pembrolizumab in Patients With Rectal Cancer	Y	Y	https://ClinicalTrials.gov/show/NCT02586610
Checkpoint inhibitor	Trial of Nivolumab With FOLFOX After Chemoradiation in Rectal Cancer Patients	Y	Y	https://ClinicalTrials.gov/show/NCT03921684
Checkpoint inhibitor	TSR-042 as Maintenance Therapy for Patients With High-risk Locally Advanced Cervical Cancer After Chemo-radiation (ATOMICC)	Y	Y	https://ClinicalTrials.gov/show/NCT03833479
Checkpoint inhibitor	TSR-042 in Addition to Standard of Care Definitive Radiation for Inoperable Endometrial Cancer		Y	https://ClinicalTrials.gov/show/NCT03955978
Checkpoint inhibitor	TTX-030 in Combination With Immunotherapy and/or Chemotherapy in Subjects With Advanced Cancers	Y		https://ClinicalTrials.gov/show/NCT04306900
Checkpoint inhibitor	TTX-030 Single Agent and in Combination With Immunotherapy or Chemotherapy for Patients With Advanced Cancers	Y		https://ClinicalTrials.gov/show/NCT03884556
Checkpoint inhibitor	Two Stage Study of Combination of Chemotherapy, SHR-1210 and/or Decitabine for Relapsed/Refractory PMBCLs	Y		https://ClinicalTrials.gov/show/NCT03346642
Checkpoint inhibitor	CTLA-4 /PD-L1 Blockade Following Transarterial Chemoembolization (DEB-TACE) in Patients With Intermediate Stage of HCC (Hepatocellular Carcinoma) Using Durvalumab and Tremelimumab	Y		https://ClinicalTrials.gov/show/NCT03638141
Checkpoint inhibitor	Induction of Immune-mediated aBscOpal Effect thrOugh STEreotactic Radiation Therapy in Metastatic Melanoma Patients Treated by PD-1 + CTLA-4 Inhibitors (BOOSTER MELANOMA)		Y	https://ClinicalTrials.gov/show/NCT03354962
Checkpoint inhibitor	REGN2810 (Anti-PD-1 Antibody), Platinum-based Doublet Chemotherapy, and Ipilimumab (Anti-CTLA-4 Antibody) Versus Pembrolizumab Monotherapy in Patients With Lung Cancer	Y		https://ClinicalTrials.gov/show/NCT03515629
Checkpoint inhibitor	Anti-CTLA4-NF mAb (BMS986218), Nivolumab, and Stereotactic Body Radiation Therapy for the Treatment of Metastatic Solid Malignancies		Y	https://ClinicalTrials.gov/show/NCT04785287
Checkpoint inhibitor	Neoadjuvant Durvalumab and Tremelimumab Plus Radiation for High Risk Soft-Tissue Sarcoma		Y	https://ClinicalTrials.gov/show/NCT03116529
Checkpoint inhibitor	A Phase Ib/II Study of AK104 and AK117 in Combination With or Without Chemotherapy in Advanced Malignant Tumors	Y		https://ClinicalTrials.gov/show/NCT05235542
Checkpoint inhibitor	AK104 Combined With Chemotherapy as Neoadjuvant Treatment for Advanced Ovarian Cancer	Y		https://ClinicalTrials.gov/show/NCT05430906
Checkpoint inhibitor	NBTXR3, Radiation Therapy, Ipilimumab, and Nivolumab for the Treatment of Lung and/or Liver Metastases From Solid Malignancy		Y	https://ClinicalTrials.gov/show/NCT05039632
Checkpoint inhibitor	Immunotherapy With Neo-adjuvant Chemotherapy for OVarian Cancer	Y		https://ClinicalTrials.gov/show/NCT03249142
Checkpoint inhibitor	Radiation Therapy and Durvalumab With or Without Tremelimumab in Treating Participants With Unresectable, Locally Advanced, or Metastatic Bladder Cancer		Y	https://ClinicalTrials.gov/show/NCT03601455
Checkpoint inhibitor	Radiation Therapy and Durvalumab, With or Without Tremelimumab, in Patients With Bladder Cancer		Y	https://ClinicalTrials.gov/show/NCT03150836
Checkpoint inhibitor	Tremelimumab With Chemoembolization or Ablation for Liver Cancer	Y		https://ClinicalTrials.gov/show/NCT01853618
Checkpoint inhibitor	Durvalumab, an Anti-PDLI Antibody, and Tremelimumab, an Anti-CTLA4 Antibody, and Chemoradiation Before Surgery for Esophageal Cancer	Y		https://ClinicalTrials.gov/show/NCT02962063
Checkpoint inhibitor	Durvalumab, an Anti-PDLI Antibody, and Tremelimumab, an Anti-CTLA4 Antibody, and Chemoradiation Before Surgery for Esophageal Cancer		Y	https://ClinicalTrials.gov/show/NCT02962063
Checkpoint inhibitor	Abatacept, Ixazomib Citrate, and Dexamethasone in Treating Patients With Multiple Myeloma Resistant to Chemotherapy	Y		https://ClinicalTrials.gov/show/NCT03457142
Checkpoint inhibitor	Study of Immunotherapy Combined With Chemotherapy in Locally Advanced and Metastatic Pancreatic Cancer	Y		https://ClinicalTrials.gov/show/NCT04324307
Checkpoint inhibitor	Nivolumab and Ipilimumab in Combination With Immunogenic Chemotherapy for Patients With Advanced NSCLC	Y		https://ClinicalTrials.gov/show/NCT04043195
Checkpoint inhibitor	Study of Immune Checkpoint Inhibition With Radiation Therapy in Unresectable, Non-metastatic Pancreatic Cancer		Y	https://ClinicalTrials.gov/show/NCT02868632
Checkpoint inhibitor	Ipilimumab, Nivolumab, and Radiation Therapy in Treating Patients With HPV Positive Advanced Oropharyngeal Squamous Cell Carcinoma		Y	https://ClinicalTrials.gov/show/NCT03799445
Checkpoint inhibitor	The Addition of Ipilimumab to Carboplatin and Etoposide Chemotherapy for Extensive Stage Small Cell Lung Cancer	Y		https://ClinicalTrials.gov/show/NCT01331525
Checkpoint inhibitor	Immune Checkpoint Inhibition (Tremelimumab and/or MEDI4736) in Combination With Radiation Therapy in Patients With Unresectable Pancreatic Cancer		Y	https://ClinicalTrials.gov/show/NCT02311361
Checkpoint inhibitor	Phase 1 Study of Tremelimumab, Durvalumab, High-dose Chemotherapy, + Autologous Stem Cell Transplant	Y		https://ClinicalTrials.gov/show/NCT02716805
Checkpoint inhibitor	Study of Anti-PD-L1 in Combination With Chemo(Radio)Therapy for Oesophageal Cancer	Y		https://ClinicalTrials.gov/show/NCT02735239
Checkpoint inhibitor	Characterisation of TIM-3/Gal-9 Immune Checkpoints in Primary Central Nervous System Diffuse Large B Cell Lymphomas	Y		https://ClinicalTrials.gov/show/NCT05133505
Checkpoint inhibitor	An Investigational Study of Immunotherapy Combinations With Chemotherapy in Patients With Gastric or Gastroesophageal Junction (GEJ) Cancers	Y		https://ClinicalTrials.gov/show/NCT03662659
Checkpoint inhibitor	IMP321 (Eftilagimod Alpha) as Adjunctive to a Standard Chemotherapy Paclitaxel Metastatic Breast Carcinoma	Y		https://ClinicalTrials.gov/show/NCT02614833
Adoptive T cell	Treatment of Relapsed and/or Chemotherapy Refractory B-cell Malignancy by Tandem CAR T Cells Targeting CD19 and CD20	Y		https://ClinicalTrials.gov/show/NCT03097770
Adoptive T cell	Study of Anti-CEA CAR-T + Chemotherapy VS Chemotherapy Alone in Patients With CEA+Pancreatic Cancer & Liver Metastases	Y		https://ClinicalTrials.gov/show/NCT04037241
Adoptive T cell	alloSHRINK - Standard cHemotherapy Regimen and Immunotherapy With Allogeneic NKG2D-based CYAD-101 Chimeric Antigen Receptor T-cells	Y		https://ClinicalTrials.gov/show/NCT03692429
Adoptive T cell	Interleukin-7 and Chemokine (C-C Motif) Ligand 19-expressing CD19-CAR-T for Refractory/Relapsed B Cell Lymphoma.	Y		https://ClinicalTrials.gov/show/NCT03929107
Adoptive T cell	CS1-CAR T Therapy Following Chemotherapy in Treating Patients With Relapsed or Refractory CS1 Positive Multiple Myeloma	Y		https://ClinicalTrials.gov/show/NCT03710421
Adoptive T cell	Pilot Study of Autologous Anti-CD22 Chimeric Antigen Receptor Redirected T Cells In Patients With Chemotherapy Resistant Or Refractory Acute Lymphoblastic Leukemia	Y		https://ClinicalTrials.gov/show/NCT02588456
Adoptive T cell	Microbiome in Cancer Patients With High Dose Chemotherapy With Stem Cell Transplantation	Y		https://ClinicalTrials.gov/show/NCT04691284
Adoptive T cell	Phase I Study of CD19-CAR-T2 Cells for Patients With Chemotherapy Resistant or Refractory CD19+ Acute Leukemia	Y		https://ClinicalTrials.gov/show/NCT02822326
Adoptive T cell	Genetically Engineered Lymphocyte Therapy in Treating Patients With Lymphoma That is Resistant or Refractory to Chemotherapy	Y		https://ClinicalTrials.gov/show/NCT01735604
Adoptive T cell	Pilot Study of Anti-CD20-CAR-engineered T Cells in Patients With Chemotherapy Resistant or Refractory CD20+ Lymphoma	Y		https://ClinicalTrials.gov/show/NCT02965157
Adoptive T cell	Radiation Post-CAR T in Refractory Lymphoma		Y	https://ClinicalTrials.gov/show/NCT04473937
Adoptive T cell	Phase II Study of Salvage Radiation Treatment After B-cell Maturation Antigen Chimeric Antigen Receptor T-cell Therapy for Relapsed Refractory Multiple Myeloma		Y	https://ClinicalTrials.gov/show/NCT05336383
Adoptive T cell	Outcomes After Chimeric Antigen Receptor Therapy and Radiation Therapy for Hematologic Malignancies		Y	https://ClinicalTrials.gov/show/NCT04888338
Adoptive T cell	Modified T Cells, Chemotherapy, and Aldesleukin With or Without LV305 and CMB305 in Treating Participants With Advanced or Recurrent Sarcoma	Y		https://ClinicalTrials.gov/show/NCT03450122
Adoptive T cell	Stem Cell Transplant, Chemotherapy, and Biological Therapy in Treating Patients With High-Risk or Refractory Multiple Myeloma	Y		https://ClinicalTrials.gov/show/NCT00499577
Adoptive T cell	Chemotherapy, Total-Body Irradiation, Donor Natural Killer Cell Infusion, Aldesleukin, and UCB Transplant in Treating Patients With Relapsed or Refractory AML	Y		https://ClinicalTrials.gov/show/NCT00871689
Adoptive T cell	Chemotherapy and Peripheral Stem Cell Transplantation in Treating Patients With Metastatic Melanoma	Y		https://ClinicalTrials.gov/show/NCT00003552
Adoptive T cell	Localized Radiation Therapy or Recombinant Interferon Beta and Avelumab With or Without Cellular Adoptive Immunotherapy in Treating Patients With Metastatic Merkel Cell Carcinoma		Y	https://ClinicalTrials.gov/show/NCT02584829
Adoptive T cell	Chemotherapy, Total-Body Irradiation, Donor Natural Killer Cell Infusion, Aldesleukin, and UCB Transplant in Treating Patients With Relapsed or Refractory AML		Y	https://ClinicalTrials.gov/show/NCT00871689
Adoptive T cell	Irradiation-based Myeloablative Conditioning Followed by Treg/Tcon Immunotherapy in HSCT		Y	https://ClinicalTrials.gov/show/NCT03977103