Supplemental Table 1. Examples of clinical trials evaluating anti-CTLA4 antibodies

Drug Name/Company Mechanism	Combination strategy	Phase	Tumor Type	Results	Biomarker selection	Comment (Status as of May 16, 2023)	Reference/NCT Number
Ipilimumab/ Bristol-Myers Squibb/ recombinant monoclonal antibody that binds CTLA-4	Single agent	3	Melanoma	median OS of 10.1 months (95% CI, 8.0-13.8) (11)	No	Completed. FDA approved	NCT00094653
Ipilimumab	Nivolumab	3b/4	Melanoma	The objective response rate (ORR) 45.6% (95% CI, 38.1%-53.1%) (22)	No	Completed FDA approved	NCT02714218
Ipilimumab	Nivolumab (anti-PD-1)	3	NSCLC	4-year OS rate with nivolumab plus ipilimumab versus chemotherapy was 29% versus 18% (PD-L1 ≥1%); and 24% versus 10% (PD-L1 <1%) (23)	Yes/PD-L1	Completed FDA approved	CheckMate 227
Ipilimumab	Nivolumab (anti-PD-1)	3	RCC	The objective response rate was 42% versus 27% for sunitinib (P<0.001), and the complete response rate was 9% versus 1% (24).	No	Completed FDA approved	NCT02231749
Tremelimumab/ AstraZeneca/ fully human monoclonal antibody	durvalumab, and platinum-based chemotherapy	3	metastatic non-small cell lung cancer	Overall response rate was 39% (95% CI: 34,44) vs 24% (95% CI: 20, 29) in the chemotherapy arm (14,25-26)	Negative for EGFR and ALk mutations	Completed FDA approved	POSEIDON (NCT03164616
Tremelimumab	Durvalumab (anti-PD-L1)	3	Unresectable or metastatic HCC	Overall response rate was 20.1% in the tremelimumab plus durvalumab arm and 5.1% for those treated with sorafenib (27)	No	Completed FDA approved	HIMALAYA, NCT03298451
Tremelimumab	Durvalumab (anti-PD-L1) and chemoradiation	I/2	Esophageal cancer	Not reported	No	Recruiting	NCT02962063
Tremelimumab	Durvalumab (anti-PD-L1) and chemoradiation	3	Advanced or metastatic UCC	End point not met (28)	Stratified by PD-L1 status	Completed not approved	Danube NCT02516241
Quavonlimab/Merck / humanized immunoglobulin G1 monoclonal antibody that binds to CTLA-4	Co-formulated Pembrolizumab/ Quavonlimab (MK-1308A)	1/2	Advanced solid tumors	Not reported	No	Active not recruiting	NCT03179436

Quavonlimab	Co-formulated Pembrolizumab/ Quavonlimab (MK-1308A)	2	MSI-H or dMMR Metastatic Stage IV Colorectal Cancer. (29)	Not reported	dMMR/MSI-H	Recruiting	NCT04895722
Quavonlimab	Co-formulated Pembrolizumab/ Quavonlimab (MK-1308A) and Lenvatinib	3	Advanced Renal Cell Carcinoma	Not reported	No	Active, recruiting	NCT04736706
Quavonlimab	Co-formulated Pembrolizumab/ Quavonlimab (MK-1308A)	2	Microsatellite stable colorectal cancer	Not reported	Yes, GEP high Tmb low	Active, recruiting	NCT03516981
Zalifrelimab/ Agenus fully humanized IgG1 anti–CTLA-4	Balstilimab (anti-PD-1)	I/2	Advanced cervical cancer	The ORR was 25.6% (95% CI, 18.8%-33.9%), and the disease control rate (DCR) was 52% (95% CI, 43.3%-60.6% (16, 30)	No	Completed, not FDA approved	NCT03495882
Zalifrelimab	Balstilimab (anti-PD-1)	2	Advanced cervical cancer	Not reported	No	Recruiting	NCT05033132
Zalifrelimab	NLM-001 and Standard Chemotherapy	Ib/2a	Advanced pancreatic cancer	Not reported	No	Complete FDA not approved d	NCT04827953
Zalifrelimab	Doxorubicin chemotherapy	2	Advanced or Metastatic Soft Tissue Sarcomas	Not reported	No	Recruiting	NCT04028063
Zalifrelimab	monotherapy	I/2	Metastatic or Locally Advanced Solid Tumors, With Expansion to Second Line Cervical Cancer	Disease control rate (CR, PR, and SD) of 51.7%, objective response rate (ORR) of 10.3% (3/29), disease stabilization of 41.3% (12/29) (17)	No	Completed FDA not approved	NCT03104699
Botensilimab/Agenus fragment crystallizable (Fc)-engineered immunoglobulin G1 anti-cytotoxic T-lymphocyte antigen 4 (anti-CTLA-4)	Monotherapy and in combination with Balstilimab (anti-PD-1)	I	Advanced solid tumors	Not reported	No	Recruiting	NCT03860272

human monoclonal antibody							
Botensilimab	Balstilimab (anti-PD-1)	1a/1b	metastatic heavily pretreated microsatellite stable colorectal cancer (MSS CRC)	objective response rate (ORR) was 22% (95% CI, 12-35), disease control rate (DCR) was 73% (95% CI, 60-84) (31)	MSS Stable	Recruiting	NCT03860272
Botensilimab	Balstilimab and Regorafenib	1/2	Microsatellite Stable Metastatic Colorectal Cancer Who Have Progressed on Prior Chemotherapy	Not reported	MSS Stable	Not yet recruiting	NCT05672316

Abbreviations: ALK, anaplastic lymphoma kinase; CR ,complete response; CTLA-4, cytotoxic T-lymphocyte antigen 4; dMMR, deficient mismatch repair ; EGFR, epidermal growth factor receptor; FDA, food and drug administration; GEP, gene-expression profile; HCC, hepatocellular carcinoma; MSI, microsatellite instability; MSS, microsatellite stability**;** NSCLC, non-small cell lung cancer; OS, overall survival;PD-1, programmed death ligand-1; PR, partial response; RCC, renal cell carcinoma; SD, stable disease; Tmb, tumor mutational burden; UCC, urothelial cell carcinoma.

Supplemental Table 2: Patient Characteristics

All cancers	N = 514	
Median Age (range) years	61 (24-93) years	
Sex	40% male (N = 204), 60% female (N=310)	
Evaluable patients treated with immunotherapy	N=217 (42%)	
Anti-PD1/PDL-1 single agents	N=67 (31%)	
Anti-PD1-PDL-1 combination with drugs other than immunotherapies	N=132 (61%)	
Anti-CTLA-4 monotherapy	N=2 (0 %)	
Anti-CTLA-4 anti-PD1/PDL-1 combination therapy	N=16 (7%)	
Other immunotherapies	N=0 (0%)	
Diagnoses	N=514 patients	N=217 evaluable patients treated with ICI
Head and Neck Cancer	12 (2%)	5 (2%)
Lung Cancer	20 (4%)	14 (6.5%)
Liver and Bile Duct Cancer	19 (4%)	9 (4%)
Melanoma	6 (1%)	6 (3%)
Colorectal Cancer	140 (27%)	54 (25%)
Breast Cancer	49 (10%)	19 (9%)
Esophageal Cancer	17 (3%)	10 (5%)
Neuroendocrine Cancer	15 (3%)	5 (2%)
Ovarian Cancer	43 (8%)	18 (8%)
Pancreatic Cancer	55 (11%)	16 (7%)
Sarcoma	24 (5%)	9 (4%)
Small Intestine Cancer	12 (2%)	1 (0.5%)
Stomach Cancer	25 (5%)	11 (5%)
Cancer of Unknown Primary	13 (3%)	5 (2%)
Uterine Cancer	24 (5%)	12 (6%)
Cervical Cancer	5 (1%)	4 (1.8%)
All Others (< 5 samples per histology)	35 (7%)	22 (10%)

(* Database previously described (49)**)**