Supplementary Materials: Harnessing Tumor Necrosis Factor Alpha to Achieve Effective Cancer Immunotherapy

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Table S1. FDA approved drugs targeting PD-1, PD-L1 and CTLA-4 (current as November 2020).

Target	Antibody	Tumor Type	Indications	Reference
PD-1	Nivolumab	Melanoma	Previously treated, PD-L1+ IHC predictive.	Weber et al., 2015 [1]
		Melanoma	Previously untreated, BRAF wild-type, PD-L1+ IHC predictive.	Robert et al., 2015 [2]
		Melanoma	Stage III and IV, adjuvant therapy after resection. PD-L1+ IHC predictive.	Weber et al., 2017 [3]
		NSCLC	Second line squamous NSCLC, PD-L1+ IHC not predictive.	Brahmer et al., 2015 [4]
		RCC	Progressive patients on or after anti-angiogenic therapies. PD-L1+ IHC not predictive.	Motzer et al., 2015 [5]
		HNSCC	Patients progressing after platinum-based chemotherapy. PD-L1+ IHC predictive.	Ferris et al., 2016 [6]
		Urothelial carcinoma	Patients progressing after chemotherapy.	Sharma et al., 2017 [7]
		Hodgkin's lymphoma	Patients progressing after autologous HSCT and brentuximab vedotin.	Ansell et al., 2015 [8]
		MSI-H and dMMR CRC	Patients progressing after or ineligible for chemotherapy.	Overman et al., 2017 [9]
		HCC	Patients progressing after sorafenib. PD-L1+ IHC not predictive.	El-Khoueiry et al., 2017 [10]
		SCLC	Patients who progressed on platinum-based therapy and at least one other line of therapy.	Antonia et al., 2016 [11]
		Esophageal squamous cell carcinoma	Unresectable advanced, recurrent or metastatic esophageal squamous cell carcinoma (ESCC) after prior fluoropyrimidine- and platinum-based chemotherapy.	Chen et al., 2020 [12]
	Pembrolizumab	Melanoma	Ipilimumab naive.	Robert et al., 2015 [13]
		Melanoma	Ipilimumab refractory.	Ribas et al., 2015 [14]
		NSCLC	PD-L1 > 50%, first line.	Reck et al., 2016 [15]
		HNSCC	Metastatic or unresectable, recurrent HNSCC either as monotherapy in patients whose tumor expresses PD-L1 or in combination with platinum and fluorouracil.	Burtness et al., 2019 [16]
		HNSCC	Recurrent or metastatic patients with progression on standard platinum-based therapy.	Seiwert et al., 2016 [17]
		NSCLC	PD-L1 > 1%, first line, combination with chemotherapy.	Langer et al., 2016 [18]
		Urothelial carcinoma	Patients progressing after chemotherapy. PD-L1+ IHC not predictive.	Bellmunt et al., 2017 [19]
		Urothelial carcinoma	Cisplatin-ineligible patients. PD-L1+ IHC predictive.	Balar et al., 2017 [20]
		Hodgkin's lymphoma	Relapsed or refractory Hodgkin's lymphoma.	Chen et al., 2017 [21]

		MSI-H and dMMR solid tumors	Patients with no satisfactory alternative treatment options.	Le et al., 2015, 2017 [22],[23]
		Gastric cancer	Disease progression after at least two prior lines of therapy.	Fuchs et al., 2017 [24]
		RCC	Combination with axitinib (Inlyta) as first-line treatment for patients with metastatic disease.	Rini et al., 2019 [25]
		Merkel cell carcinoma	First-line therapy for adult and pediatric patients with recurrent or locally advanced or metastatic disease.	Nghiem et al., 2019 [26]
		HCC	Patients who had previously been treated with sorafenib.	Zhu et al., 2018 [27]
		PMBCL	Refractory or relapsed.	Zinzani et al., 2017 [28]
		Cervical cancer	Recurrent or metastatic cervical cancer progressing on or after chemotherapy and positive for PDL-1.	Chung et al., 2019 [29]
		MSI-H and dMMR colorectal cancer	First line treatment for previously untreated unresectable or metastatic disease.	Le et al., 2020 [30]
		Triple negative breast cancer	Locally recurrent unresectable or metastatic disease, whose tumors express PD-L1.	Schmid et al., 2020 [31]
		Cutaneous squamous cell carcinoma	Recurrent or metastatic disease that is not curable by surgery or radiation.	Grob et al., 2020 [32]
		Bladder cancer	High-risk, non-muscle invasive disease in patients who are not responsive to BCG treatment and who will not undergo cystectomy.	Hsu, et al., 2019 [33]
		SCLC	Metastatic disease who experienced disease progression on or after platinum-based chemotherapy and at least one other prior line of therapy.	Rudin et al., 2020 [34]
	Cemiplimab	Cutaneous squamous cell carcinoma	Metastatic or locally advanced who are not the candidate for curative surgery or radiation.	Migden et al., 2018 [35]
	Sintilimab	Hodgkin's lymphoma	Relapsed or refractory classical Hodgkin lymphoma.	Shi et al., 2019 [36]
PD-L1	Atezolizumab	NSCLC	Previously treated. PD-L1+ IHC on tumor and IC predictive.	Fehrenbacher et al., 2016 [37]
		NSCLC	In combination with bevacizumab, paclitaxel and carboplatin for initial treatment of metastatic disease, with no EGFR or ALK.	Reck et al., 2019 [38]
		NSCLC	In combination with carboplatin and etoposide, for the initial treatment of adults with extensive-stage small-cell lung cancer.	Horn et al., 2018 [39]
		Urothelial carcinoma	Cisplatin-ineligible patients.	Balar et al., 2017 [40]
		Urothelial carcinoma	Chemotherapy refractory. PD-L1+ IHC on IC predictive.	Rosenberg et al., 2016 [41]
		Triple negative breast cancer	In combination with paclitaxel for unresectable locally advanced or metastatic cancer, in tumors that express PD-L1.	Schmid et al., 2018 [42]
		Melanoma	In combination with cobimetinib and vemurafenib for patients with BRAF V600 mutation-positive unresectable or metastatic disease.	Gutzmer et al., 2020 [43]
		HCC	In combination with bevacizumab for the treatment of patients with previously untreated disease.	Finn et al., 2020 [44]

	Durvalumab	NSCLC	Stage III, durvalumab after chemotherapy. PD-L1+ IHC not pedictive.	Antonia et al., 2017 [45]
		Urothelial carcinoma	Patients that are progressive, ineligible, or have refused platinum-based chemotherapy. PD-L1+ IHC on tumor and IC predictive.	Powles et al., 2017 [46]
		NSCLC	Unresectable stage III disease after chemoradiation therapy.	Gray et al., 2020 [47]
	Avelumab	Urothelial carcinoma	Patients failing platinum-based chemotherapy. Weak predictive value for PD-L1+ IHC.	Patel et al., 2018 [48]
		Merkel cell carcinoma	PD-L1 expression and polyomavirus status not predictive.	Kaufman et al., 2016 [49]
		RCC	In combination with axitinib (Inlyta) for the first-line treatment of patients with advanced disease.	Motzer et al., 2019 [50]
		Bladder cancer	Maintenance treatment of patients with locally advanced or metastatic disease that has not progressed with first-line platinum-containing chemotherapy.	Powles et al., 2020 [51]
CTLA-4	Ipilimumab	Melanoma	Surgically unresectable, stage 3 or 4 malignant melanoma, previously treated or untreated in adults and pediatric patients > 12 years.	McDermott et al., 2013 [52]
		Melanoma	Adjuvant treatment of cutaneous melanoma stage IIIA, IIIB, and IIIC after complete resection along with total lymphadenectomy.	Eggermont et al., 2016 [53]
PD-1 + CTLA-4	Nivolumab + Ipilimumab	Melanoma	Unresectable or metastatic melanoma across BRAF status.	Larkin et al., 2015 [54]
		RCC	Previously untreated advanced RCC, relapse and stage IV, with intermediate- or poor-risk RCC, regardless of PD-L1.	Motzer et al., 201 [55]8
		Melanoma	For unresectable or metastatic melanoma across BRAF status.	Postow et al., 2015 [56]
		RCC	For previously untreated advanced renal cell carcinoma (RCC), relapse and stage IV, with intermediate- or poor-risk RCC, regardless of PD-L1.	Hammers et al., 2017 [57]
		Colorectal cancer	For microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic disease, that has progressed following treatment with fluoropyrimidine, oxaliplatin, and irinotecan in adults and pediatric patients >12 years.	Overman et al., 2017 [9]
		NSCLC	First-line treatment for metastatic disease whose tumors express PD-L1(≥1%), with no EGFR or ALK.	Hellmann et al., 2019 [58]

Abbreviations are as follows: SCLC, small cell lung cancer; NSCLC, non small cell lung cancer; RCC, renal cell carcinoma; HNSCC, head and neck squamous cell carcinoma; MSI-H, microsatellite instability high; dMMR, mismatch repair deficient; HCC, hepatocellular carcinoma; PMBCL, primary mediastinal large B-cell lymphoma.

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