Table 1: Immune checkpoint inhibitors in phases III and IV clinical trials.

Sl No	Drug	Cancer type	Clinical trial ID
1	Pembrolizumab (Anti-PD-1)	NSCLC	NCT03134456, NCT02220894, NCT02142738, NCT02864394, NCT03302234, NCT01905657, NCT02504372, NCT02775435, NCT02578680
2		Small cell lung cancer	NCT03066778
3		Head and neck squamous cell carcinoma	NCT02252042, NCT03040999, NCT02358031
4		Renal cell carcinoma	NCT03142334, NCT02853331
5		Gastric adenocarcinoma	NCT02370498
6		Nasopharyngeal neoplasms	NCT02611960
7		Urothelial carcinoma	NCT02853305, NCT03244384, NCT02256436, NCT03374488, NCT03361865
8		Colorectal cancer	NCT02563002
9		Pleural mesothelioma	NCT02991482
10		TNBC	NCT02819518, NCT03036488, NCT02555657
11		Esophageal neoplasms	NCT03189719, NCT02564263
12		Multiple myeloma	NCT02579863, NCT02576977
13		Gastric and gastroesophageal junction cancer	NCT03019588, NCT03221426
14		Gastric adenocarcinoma	NCT02494583
15		Melanoma	NCT02362594, NCT01866319
16		Hodgkin lymphoma	NCT02684292
17		Hepatocellular carcinoma	NCT02702401, NCT03062358

18		Lung cancer	NCT03322540
19		Head and neck cancer	NCT03358472
20	Nivolumab (A+C15+B22:B2+B22:B28	NSCLC	NCT02041533, NCT01642004, NCT01673867
21		Mesothelioma	NCT03063450
22		Non-Hodgkin lymphoma	NCT03366272
23		Metastatic clear cell renal carcinoma	NCT01668784
24		Head and neck cancer	NCT02741570, NCT03342352
25		Lung cancer	NCT03348904
26		Melanoma	NCT03068455, NCT01844505
27	Ipilimumab (Anti-CTLA-4)	NSCLC	NCT03469960, NCT03351361, NCT02785952, NCT03302234
28		Squamous cell lung carcinoma	NCT02785952
29		Mesothelioma	NCT02899299
30		Gastric cancer	NCT02872116
		Gastroesophageal junction cancer	
31		Metastatic melanoma	NCT03445533, NCT00636168, NCT01274338, NCT02339571, NCT02506153, NCT02224781, NCT00094653
32		Metastatic non-cutaneous melanoma	NCT02506153
33	Avelumab (Anti-PD-L1)	NSCLC	NCT02576574, NCT02395172
35		Urothelial cancer	NCT02603432
35		Diffuse Large B-cell lymphoma	NCT02951156

36		Renal cell cancer	NCT02684006
37		Gastric and gastroesophageal junction cancer	NCT02625623, NCT02625610
40	Atezolizumab (Anti-PD-L1)	Ovarian cancer, fallopian tube cancer	NCT03038100, NCT02839707, NCT02891824
		Peritoneal neoplasms	
41		NSCLC	NCT02813785, NCT02008227, NCT02367781, NCT02366143, NCT02409342, NCT02486718, NCT02367794, NCT03191786, NCT02409355, NCT02657434, NCT03456063
42		Extensive stage small cell lung cancer	NCT02763579
43		TNBC	NCT03197935, NCT02425891, NCT03125902, NCT03281954
44		Renal cell carcinoma	NCT02420821, NCT03024996
45		Bladder cancer	NCT02302807
46		Squamous cell carcinoma of the head and neck	NCT03452137
47		Urothelial carcinoma	NCT02807636
48		Transitional cell carcinoma	NCT02450331
49		Prostatic neoplasms	NCT03016312
50	Durvalumab (Anti-PD-L1)	NSCLC	NCT02352948, NCT03003962, NCT02453282, NCT02273375, NCT02542293,

			NCT03164616, NCT02125461,
51		Squamous cell lung carcinoma	NCT02154490, NCT02551159
52		Recurrent or metastatic PD-L1 positive or negative SCCHN	NCT02369874
53		Recurrent squamous cell lung caner	NCT02766335, NCT02154490
54		Urothelial cancer	NCT02516241
55		Advanced solid malignancies	NCT03084471
56		SCCHN, hypopharyngeal squamous cell carcinoma, laryngeal squamous cell carcinoma	NCT02551159, NCT03258554
57	REGN2810 (Anti-PD-1)	NSCLC	NCT03409614, NCT03088540
58	BMS-936558 (Anti-PD-1)	Unresectable or metastatic melanoma	NCT01721746, NCT01721772
59	SHR1210 (Anti-PD-1)	NSCLC	NCT03134872
60		Nasopharyngeal neoplasms	NCT03427827
61	KN035 (Anti-PD-L1)	Biliary tract neoplasms	NCT03478488
62	IBI308 (Anti-PD-1)	Squamous cell lung carcinoma	NCT03150875
63	PDR001 (Anti-PD-1)	Melanoma	NCT02967692
64	Anti-PD-1	Metastatic melanoma	NCT02821013
65	BGB-A317 (Anti-PD-1)	NSCLC	NCT03358875
66		Esophageal squamous cell carcinoma	NCT03430843
67		Hepatocellular carcinoma	NCT03412773

68	BCD-100 (Anti-PD-1)	NSCLC	NCT03288870
70	JS001 (Anti-PD-1)	Metastatic melanoma	NCT03430297

Anti-PD-1, anti-programme death-1; anti-PD-L1, anti-programme death ligand-1; NSCLC, Non-small cell lung cancer; SCCHN, squamous cell carcinomas of the head and neck. Table adapted and modified from [71].

Table 2: A range of currently available immunotherapies

Strategy	Basic mechanism and major advantages	Major disadvantages
Cytokines		
IL-2	-Stimulates the host's immune system	-Low response rates -Significant risk of serious systemic inflammation
IFN-α	-Stimulates the host's immune system -Durable responses (from a small subset of melanoma patients)	-Low response rates -High-dose toxicity
Cell-based therapies		
Vaccines	-Stimulates the host's immune system -Minimal toxicity (e.g., sipuleucel-T) -Administered in the outpatient clinic	-Lack of universal antigens and ideal immunization protocols lead to poor efficacy and response
Adoptive cellular therapy	-Omits the task of breaking tolerance to tumour antigens -Produces a high avidity in effector T-cells -Lymphodepleting conditioning regimen prior to TIL infusion enhances efficacy -Genetic T-cell engineering broadens TIL to malignancies other than melanoma	-Restricted to melanoma -Safety issues, serious adverse effects, and lack of long lasting responses in many patients -Requires time to develop the desired cell populations -Expensive
Immune checkpoint blockade		
Anti-CTLA-4 monoclonal antibodies	-Unleashes pre-existing anticancer T-cell responses and possibly triggers new -Exhibits potent antitumor properties -Prolongation of overall survival	-Only a relatively small fraction of patients obtain clinical benefit -Severe immune-related adverse events have been observed in up to 35 % of patients

Anti-PD1 and anti-PD-L1 antibodies	-Sufficient clinical responses which are often long-lasting -Therapeutic responses in patients within a broad range of human cancers -Reduced toxicity compared to anti-CTLA-4 antibodies	-Only a relatively small fraction of patients obtain clinical benefit
Combination immunotherapy	-Improvement of anti-tumour responses/immunity	-May lead to increases in the magnitude, frequency, and onset of side effects

IL-2, Interleukin 2; IFN-α, Interferon-alpha; PD1, Programmed cell death protein 1; TIL, Tumour infiltrating lymphocytes, CTLA-4, Cytotoxic T lymphocyte-associated protein 4. Table adapted and modified from [70].