

Davda et al. SUPPLEMENTARY INFORMATION

Supplementary Table S1 Immunomodulatory agents

Agent	Target	Target cell types	Structure	ROA	Patient population from which ADA data are listed	Immunogenicity (% treated patients)		Reference
						ADA	NAb	
Oncology Agents								
Alemtuzumab	CD52	Lymphocytes, monocytes, DCs	IgG1, humanized	IV	B-cell chronic lymphocytic leukemia	8.3	2	Package insert
Atezolizumab	PDL-1	Monocytes/macrophages, DCs, activated T cells, keratinocytes, placental trophoblasts, myocardial endothelium, cortical thymic epithelial cells	IgG1, aglycosylated, humanized	IV	Lung and bladder cancer	30-48	NR	Package insert
Avelumab	PD-L1	Monocytes/macrophages, DCs, activated T cells, keratinocytes, placental trophoblasts, myocardial endothelium, cortical thymic epithelial cells	IgG1, human	IV	Merkel cell carcinoma	4.1	NR	Package insert
Blinatumomab	CD19 / CD3	B cells, follicular DCs	BiTE	IV	Acute lymphoblastic leukemia	1	<1	Package insert
Brentuximab vedotin	CD30	Surface of sALCL cells and Hodgkin Reed-Sternberg (HRS) cells in classical HL. Limited expression on healthy tissue	IgG1, chimeric; ADC with MMAE payload	IV	Hodgkin lymphoma, systemic anaplastic large-cell lymphoma	7	4.2	Package insert
Cantuzumab mertansine	CanAg epitope on MUC1	Activated T cells, B cells, epithelial cells	IgG1, humanized; ADC with DM1 payload	IV	Colorectal cancer	0	NR	Tolcher et al. J. Clin. Oncol. 2003; 21:211–22
Gemtuzumab ozogamicin	CD33	Monocytes, granulocytes, myeloblasts, promyelocytes, myelocytes, metamyelocytes	IgG4, humanized, ADC with calicheamicin payload	IV	Acute myeloid leukemia	1.1	NR	Hock et al. AAPS J. 2015; 17:35–43

Ipilimumab	CTLA-4	T cells, activated B cells	IgG1, human	IV	Metastatic melanoma	4.9-5.4	0	Package insert
Nivolumab	PD-1	Subsets of thymocytes, activated T cells, B cells, myeloid cells	IgG4, human	IV	Melanoma, non-small cell lung cancer	8.5	0.6	Package insert
Obinutuzumab	CD20	Pre-B-cells, resting and activated B cells, follicular DCs, a small subset of circulating T lymphocytes	IgG1, humanized; afucosylated	IV	Chronic lymphocytic leukemia	0.2-7	NR	Package insert
Ofatumumab	CD20	Pre-B-cells, resting and activated B cells, follicular DCs, a small subset of circulating T lymphocytes	IgG1, human	IV	Chronic lymphocytic leukemia	<1	NR	Package insert
Pembrolizumab	PD-1	Subsets of thymocytes, activated T cells, B cells, myeloid cells	IgG4, humanized	IV	Melanoma	2.1	0	Package insert
Tremelimumab	CTLA-4	T cells, activated B cells, DCs	IgG2, human	IV	Melanoma, solid tumors	0	NR	Millward et al. Br J Cancer. 2013; 108:1998–2004

Non-oncology Agents

Adalimumab	TNF	T cells, monocytes, macrophages, neutrophils, endothelial cells, hepatocytes, chondrocytes, fibroblasts	IgG1, human	SC	Rheumatoid arthritis	53	76	Cohen et al. Annals Rheum. Dis. 2018; 77:914-921
Alemtuzumab	CD52	Lymphocytes, monocytes, DCs	IgG1, humanized	IV	Multiple sclerosis	29-83	78	Package insert
Basiliximab	IL-2R α	Subsets of thymocytes and peripheral blood lymphocytes including CD4+CD25+ regulatory T cells and memory T cells, activated B cells, macrophages	IgG1, chimeric	IV	Renal transplant	1.2-1.5	NR	Package insert
Belimumab	BLyS (BAFF)	B cells, some populations of myeloid cells, DCs, bone marrow stromal cells	IgG1, human	IV/SC	Systemic lupus erythematosus	4.8	0.5	Package insert
Brodalumab	IL-17R α	Fibroblasts, epithelial and endothelial cells, monocytes/macrophages, mast cells (broad expression)	IgG2, human	SC	Psoriasis	3	0	Package insert

Canakinumab	IL-1 β	B cells, neutrophils, monocytes, bone marrow progenitor cells	IgG1, human	SC	CAPS, SJIA	1.5-3.1	0	Package insert
Certolizumab pegol	TNF	T cells, monocytes, macrophages, neutrophils, endothelial cells, hepatocytes, chondrocytes, fibroblasts	Humanized Fab, PEGylated	SC	Crohn's disease	7-8	6	Package insert
Daclizumab	IL-2R	Subsets of thymocytes and peripheral blood lymphocytes including CD4+CD25+ regulatory T cells and memory T cells	IgG1, humanized	SC	Multiple sclerosis	19	8	Package insert
Denosumab	RANK-L	T- and B-cells, osteoclasts	IgG2, human	SC	Bone loss	<1	0	Package insert
Dupilumab	IL-4R α	B and T cells, and a variety of other hematopoietic/non-hematopoietic cells	IgG4, human	SC	Atopic dermatitis	7	1	Package insert
Eculizumab	C5	DCs, mast cells, macrophages, B cells, T cells	IgG2/4, humanized	IV	Paroxysmal nocturnal hemoglobinuria	3-5	0	Package insert
Efalizumab	CD11a	Leukocytes	IgG1, humanized	SC	Psoriasis	6.3	N.R.	Package insert
Golimumab	TNF	T cells, monocytes, macrophages, neutrophils, endothelial cells, hepatocytes, chondrocytes, fibroblasts	IgG1, human	SC	Rheumatoid arthritis, PsA	16-28	4	Package insert
Infliximab	TNF	T cells, monocytes, macrophages, neutrophils, endothelial cells, hepatocytes, chondrocytes, fibroblasts	IgG1, chimeric	IV	Crohn's disease	10-51	NR	Package insert
Ixekizumab	IL-17 α	Fibroblasts, epithelial and endothelial cells, monocytes/macrophages, mast cells (broad expression)	IgG4, humanized	SC	Psoriasis	9-22	2	Package insert
Mepolizumab	IL-5	B1 B cells, eosinophils, basophils, mast cells	IgG1, humanized	SC	Severe eosinophilic asthma	6	0	Package insert
Natalizumab	α 4 integrin	Lymphocytes, monocytes, thymocytes, NK cells, some B and T cells	IgG4, humanized	IV	Multiple sclerosis	6-10	6	Package insert
Ocrelizumab	CD20	Pre-B cells, resting and activated B cells, follicular DCs, a small subset of	IgG1, humanized	IV	Multiple sclerosis	1	0.2	Package insert

		circulating T lymphocytes						
Omalizumab	IgE	B cells, monocytes, macrophages, eosinophils, platelets, DCs, Langerhans cells	IgG1, humanized	SC	Asthma	<0.1	0	Package insert
Reslizumab	IL-5	B1 B cells, eosinophils, basophils, mast cells	IgG4, humanized	IV	Severe asthma	4.8-5.4	NR	Package insert
Rituximab	CD20	Pre-B-cells, resting and activated B cells, follicular DCs, a small subset of circulating T lymphocytes	IgG1, chimeric	IV	Rheumatoid arthritis	11	NR	Package insert
Sarilumab	IL-6R	Activated plasma cells, most leucocytes, epithelial cells, fibroblasts, hepatocytes, skeletal muscle and neural cells	IgG1, human	SC	Rheumatoid arthritis	9.2	6.7	Package insert
Secukinumab	IL-17 α	Fibroblasts, epithelial and endothelial cells, monocytes/macrophages and mast cells (broad expression)	IgG1, human	SC	Psoriasis	<1	0.2	Package insert
Siltuximab	IL-6	Activated plasma cells, most leucocytes, epithelial cells, fibroblasts, hepatocytes, skeletal muscle and neural cells	IgG1, chimeric	IV	Castleman disease	0.2	0	Package insert
Tocilizumab	IL-6R	Activated plasma cells, most leucocytes, epithelial cells, fibroblasts, hepatocytes, skeletal muscle and neural cells	IgG1, humanized	IV	Rheumatoid arthritis	2	1.1	Package insert
Ustekinumab	P40 subunit of IL-12 and 23	Macrophages, DCs, monocytes, Langerhans cells, neutrophils, keratinocytes	IgG1, human	IV/SC	Psoriasis, Crohn's disease	6-12.4	6	Package insert
Vedolizumab	α 4 β 7 integrin	Most mature lymphocytes, small subsets of thymic and bone marrow cells	IgG1, humanized	IV	Ulcerative colitis, Crohn's disease	4-13	0.6	Package insert

ADA anti-drug antibody, ADC antibody-drug conjugate, BiTE bi-specific T-cell engager, CAPS cryopyrin-associated periodic syndromes, CD Crohn's disease, CTLA-4 cytotoxic T-lymphocyte-associated antigen 4, DC dendritic cell, DM1 emtansine, IL interleukin, IV intravenous, MMAE monomethyl auristatin E, NAb neutralizing antibody, NR not reported, PD-1 programmed death 1, PD-L1 PD-ligand 1, PsA psoriatic arthritis, R receptor, ROA route of administration, SC subcutaneous, SJIA Still's juvenile idiopathic arthritis, TNF tumor necrosis factor

Supplementary Table S2 Non-immunomodulatory agents

Agent	Target	Structure	Immunogenicity (% treated patients)	Reference
			ADA	
Abciximab	GPIIb/IIIa	Fab, chimeric	6-27	Package insert
Dinutuximab	GD2	IgG1, chimeric	13-18	Package insert
Alirocumab	PCSK9	IgG1, human	4.8	Package insert
Guselkumab	IL-23	IgG1, human	6.0	Package insert
Ramucirumab	VEGF-R2	IgG1, human	3.0	Package insert
Ado-trastuzumab emtansine	HER2	IgG1, humanized, ADC	5.3	Package insert
Cetuximab	EGFR	IgG1, chimeric	5.0	Package insert
Ranibizumab	VEGF	Fab, humanized	1-9	Package insert
Panitumumab	EGFR	IgG2, human	4.6	Package insert
Necitumumab	EGFR	IgG1, human	4.1	Package insert
Idarucizumab	Dabigatran	Fab, humanized	4.0	Package insert
Olaratumab	PDGFR α	IgG1, human	3.5	Package insert
Pertuzumab	HER2	IgG1, humanized	2.8	Package insert
Palivizumab	RSV	IgG1, humanized	1.1-1.5	Package insert
Bevacizumab	VEGF	IgG1, humanized	0.6	Package insert
Evolocumab	PCSK9	IgG2, human	0.1	Package insert
Trastuzumab	HER2	IgG1, humanized	0.1	Package insert
Bezlotoxumab	<i>C. difficile</i> toxin B	IgG, human	0	Package insert
Raxibacumab	Anthrax	IgG1, human	0	Package insert

ADA anti-drug antibody, *ADC* antibody-drug conjugate, *EGFR* epithelial growth factor receptor, *GD2* disialoganglioside 2, *IL-23* interleukin 23, *PDGFR α* platelet-derived growth factor receptor α , *PCSK9*, proprotein convertase subtilisin/kexin type 9, *RSV* respiratory syncytial virus, *VEGF* vascular endothelial growth factor, *VEGF-R2* VEGF-receptor 2