Table 1. ACT clinical trial tumor responses and toxicities.[a]

Target antigen	Cancer(s)	Receptor type	Tumor responses (patients responding/ patients treated)	Immune-mediated toxicities (patients experiencing toxicity/ patients treated)
gp100	Melanoma	TCR	3/16[1]	Skin rash (15/16) Uveitis (4/16) Hearing impairment (5/16)
MART1	Melanoma	TCR	6/20[1]	Skin rash (14/20) Uveitis (11/20) Hearing impairment (10/20)
CEA	Colon cancer	TCR	1/3[2]	Colitis (3/3)
CAIX	Renal cell carcinoma	CAR	0/8[3,4]	Hepatotoxicity (4/8)[b]
HER2/Neu	Colon cancer	CAR	0/1[5]	Cytokine release syndrome (1/1)
MAGE-A3/A9/A12[c]	Melanoma, synovial cell sarcoma, esophageal cancer	TCR	5/9[6]	Central nervous system toxicities (4/9)
MAGE-A3/titin[d]	Multiple myeloma, melanoma	TCR	0/2[7]	Cardiac toxicity (2/2)
CD19	B-cell malignancies	CAR	6/8[8]	Prolonged B cell deficiency (4/8) Cytokine release syndrome (4/8)
			3/3[9,10]	Prolonged B cell deficiency (3/3)
			2/2[11]	Prolonged B cell deficiency (2/2) Cytokine release syndrome (2/2)
			2/2[12]	Cytokine release syndrome (2/2)
GD2	Neuroblastoma	CAR	1/7[13]	None
NY-ESO-1	Synovial cell sarcoma, melanoma	TCR	9/17[14]	None

[a] Antigen receptor gene therapy trials in which regression of bulky tumors or autoimmune toxicities occurred.
[b] All patients had at least grade 1 and four patients had grade 3 or 4 liver enzyme elevations.
[c] The MAGE-A3-specific TCR targeted an epitope shared by MAGE-A3 and MAGE-A9 and had cross-reactivity against an epitope of MAGE-A12.
[d] The MAGE-A3-specific TCR was cross-reactive against an epitope of titin.

Table 2. Rationally selected candidate target antigens for ACT.					
Antigen	Tumor type	Expression frequency (%)	Healthy tissue expression	Advantages	Disadvantages
Cancer testis antigens (testis-restricted or tissue-restricted)[a]					
CTAG1B	Myeloma	7-36	Germ cells[15]	Multiple tumor types, many potential epitopes	MHC restricted, tissue restriction uncertain, frequency and intensity of positive cells varies
	Adult T-cell leukemia	61			
	Transitional cell	35-45			
	Medulloblastoma	20			
	Esophageal squamous cell	41			
	Oral squamous cell	28			
	Hepatocellular	1-44			
	Non-small cell lung	2-33			
	Melanoma	0-71			
	Ovarian	10-30			
MAGEA1	Myeloma	20-52			
	Transitional cell	57			
	Glioblastoma	0-40			
	Head and neck	10-30			
	Hepatocellular	46-80			
	Non-small cell lung	10-70			
	Melanoma	16-90			
	Neuroblastoma	36			
	Serous ovarian	42			
MAGE-C1	Myeloma	30-77			
	Medulloblastoma	28			
	Hepatocellular	48			
	Non-small cell lung	16-37			
	Melanoma	52			
SSX2	Myeloma	12-23			
	Glioblastoma	29			
	Hepatocellular	9-47			
	Non-small cell lung	12-17			
	Melanoma	0-35			
	Sarcoma	50			
MAGE-A2B	Ependymoma	57			
	Medulloblastoma	18-60			
	Hepatocellular	35			
	Non-small cell lung	0-33			
	Melanoma	41-70			
	Serous ovarian	21			
	Osteosarcoma	82			
Brachyury	Lung	41 [16]	Thyroid, B-cells, testis[16,17]	Functionally important, many potential epitopes	MHC restricted, tissue restriction uncertain, frequency and intensity of positive cells varies
NY-BR-1	Breast	84 [18]	Breast, testis[18]	Many potential epitopes, cell surface	Tissue restriction uncertain

				expression	
Other tissue restricted antigens					
CD19	B-cell malignancies	100	B cells	No MHC restriction	Normal tissue targeted, escape variants [11]
BCMA	Multiple myeloma	100	B cells, plasma cells[19]	No MHC restriction	Normal tissue targeted
Mutated proteins[b]					
KRAS G13D	Colon	5	None	Functionally important	MHC restricted, few epitopes, generally low frequency of mutation
KRAS G12V	Colon	7			
	Pancreas	18			
KRAS G12R	Pancreas	7			
KRAS G12D	Colon	11			
	Pancreas	29			
KRAS G12C	Lung	7			
EGFRviii	Glioblastoma	24-67[20,21]	None	No MHC restriction, functionally important	Frequency and intensity of positive cells varies
	Head and neck	42[22]			
Viral antigens					
HPV 16 E6 HPV 16 E7	Oropharynx	61[23]	None	Functionally important, constitutively expressed, many potential epitopes	MHC restricted
	Cervix	53[24]			
	Vagina	50[25]			
	Vulva	30[25]			
	Anus	70[25]			
	Penis	28[26]			
HPV18 E6 HPV18 E7	Cervix	13[24]			

[a] Expression frequencies were extracted from the CTpedia database [27]. All studies had ≥ 10 specimens tested. Tissues with ≥ 20% positive samples in at least one study are included.
[b] Mutation frequencies are as reported by Warren and Holt [28].

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