Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Yarchoan M, Hopkins A, Jaffee EM. Tumor mutational burden and response rate to PD-1 inhibition. N Engl J Med 2017;377:2501-2. DOI: 10.1056/NEJMc1713444

Supplemental Appendix

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Search Strategy

We aimed to identify clinical studies reporting objective response data for PD1 or PDL1 inhibitors in major solid tumor types or subtypes for which median tumor mutation burden (TMB) is known. We initially identified major solid tumor types or subtypes for which TMB has been described[1]. We subsequently conducted electronic searches of MEDLINE (from January 1, 2012 to October 23, 2017), as well as abstracts presented at the American Society of Clinical Oncology (ASCO), the European Society for Medical Oncology (ESMO), and the American Association for Cancer Research (AACR) (Annual Meetings 2012-2017) to identify clinical data for anti-PD1 or anti-PDL1 therapy in each of these cancer types or subtypes. We searched for clinical trials using the specific search terms nivolumab, BMS-936558, pembrolizumab, MK-3475, atezolizumab, MPDL3280A, durvalumab, MEDI4736, avelumab, MSB0010718C, BMS-936559, cemiplimab, and REGN2810. We also contacted experts in the field to locate additional published trials of these agents that may not have been included in our initial electronic search. We excluded studies that enrolled fewer than 10 participants, studies that investigated anti-PD1 therapies only in combination with other agents, and studies that selected patients based on PD-L1 expression or other immune-related biomarkers. Of the remaining studies, only the largest published study for each anti-PD1 therapy was included in the final assessment of pooled ORR for each cancer type or subtype. In tumor types for which phase 3 studies of any anti-PD1 therapy had been conducted, we also excluded other studies enrolling fewer than 40 patients or dose-finding studies with other anti-PD1 agents. The individual studies that comprise the pooled ORR for each cancer type or subtype are presented in Table S1 below.

Cancer Type	Nivolumab	Pembrolizumab	Atezolizumab	Durvalumab	Avelumab	Cemiplimab	BMS-936559
Adrenocortical Carcinoma					2		
Anal Cancer	3						
Breast Carcinoma			4		5		
Cervical Cancer	6	7					
Colorectal Cancer - MMRd	8	9					
Colorectal Cancer - MMRp		10					
Cutaneous Squamous Cell Carcinoma						11	
Endometrial Cancer			12				
Esophagogastric Carcinoma	13	14			15		
Germ Cell Tumor		16					
Glioblastoma	17			18			
Head and Neck	19	20					
Hepatocellular Carcinoma	21			22			
Melanoma	23	24					
Merkel Cell Carcinoma	25	26			27		
Mesothelioma	28				29		
Non-Small-Cell Lung - Nonsquamous	30	31	32		33		
Non-Small-Cell Lung - Squamous	34	31	32		33		
Other MMRd		9					
Ovarian Cancer	35				36		37
Pancreatic Cancer							37
Prostate Cancer	38	39			40		
Renal Cell Carcinoma	41		42				
Sarcoma	43	44					
Small-Cell Lung Cancer	45						
Urothelial Carcinoma	46	47	48	49	50		
Uveal Melanoma	51	51	51				

Table S1: List of citations for individual studies used in pooled analysis of objective response rate.

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