Supplemental Table 1. Demographic and disease characteristics of patients receiving ipilimumab therapy

Characteristic	Ipilimumab (n = 60)
Median age (range)	65 (35-88)
Male sex (%)	32 (53.3)
Primary site (%)	
Cutaneous	34 (53.7)
Mucosal*	12 (20.0)
Uveal	2 (3.3)
Unknown**	12 (20.0)
Elevated LDH level over ULN (%)	9 (15.0)
***BRAF V600* mutation (%)**	
Positive	15 (25.0)
Negative	41 (68.3)
Unknown	4 (6.7)
Active brain metastases (%)	9 (15.0)
Prior radiotherapy (%)	16 (26.7)
Prior surgery for tumor lesions (%)	51 (85.0)
Number of cycles with ipilimumab therapy (%)†	
2	5 (8.3)
3	5 (8.3)
4	50 (83.3)
Line of previous systemic therapy (%)	
0	40 (66.7)
1	18 (60.0)
2	2 (3.3)
Type of previous systemic therapy‡	
Chemotherapy	16
BRAF or MEK inhibitors or both	3
Others	1

LDH, lactate dehydrogenase; ULN, upper limit of the normal range

*Vagina 5, Maxillary sinus 2, Oral mucosa 1, GI tract 1, Esophagus 1, Cervix 1, Anus 1

**Most cases were presumed as cutaneous primary.

†All cases with 2 or 3 cycles withdrew due to severe immune-related adverse events.

‡Only therapy administered for advanced or metastatic disease is listed.

Supplemental Table 2. Results of univariate and multivariate analyses

	HR	95% CI	P value
Univariate analysis			
Age			
≥ 75 years	1.433	0.723-2.841	0.302
< 75 years	1.000 (ref)		
Sex			
Man	0.953	0.507-1.790	0.881
Woman	1.000 (ref)		
Line of previous chemotherapy status			
≥ 1	1.894	1.180-3.041	0.008
0	1.000 (ref)		
Primary site of melanoma			
Others and unknown	1.060	0.558-2.011	0.859
Cutaneous	1.000 (ref)		
Prior radiotherapy			
Yes	2.227	1.123-4.418	0.022
No	1.000 (ref)		
Prior surgery			
Yes	0.603	0.252-1.445	0.256
No	1.000 (ref)		
Elevated LDH level over ULN			
Yes	2.037	0.879-4.724	0.097
No	1.000 (ref)		
Active brain metastases			
Present	2.600	1.129-5.987	0.025
Absent	1.000 (ref)		
Receiving ipilimumab cycles			
< 4	1.017	0.433-2.484	0.936
4	1.000 (ref)		
PERCIST5			
Non-responder	1.530	1.031-2.269	0.035
Responder	1.000 (ref)		
imPERCIST1			
Non-responder	2.543	1.202-5.379	0.015
Responder	1.000 (ref)		
imPERCIST5			
Non-responder	3.853	1.498-9.911	0.005
Responder	1.000 (ref)		
BRAF V600 mutate			
Present	1.061	0.510-2.205	0.875
Absent	1.000 (ref)		
Multivariate analysis			
imPERCIST5			
Non-responder	3.853	1.498-9.911	0.005
Responder	1.000 (ref)		

Supplemental Table 3. Summary of comparison of imPERCIST and PERCIST

Characteristic	Immunotherapy-modified PERCIST (imPERCIST, draft definition)	PERCIST1.0
Measurability of lesions at baseline	Same as PERCIST1.0.	1. Measurable target lesion is hottest single tumor lesion SUL of "maximal 1.2-cm diameter volume ROI in tumor" (SUL peak). SUL peak is at least 1.5-fold greater than liver SUL mean + 2 SDs (in 3-cm spherical ROI in normal right lobe of liver). If liver is abnormal, primary tumor should have uptake > 2.0 × SUL mean of blood pool in 1-cm-diameter ROI in descending thoracic aorta extended over 2-cm z-axis. 2. Tumor with maximal SUL peak is assessed after treatment. Although typically this is in same region of tumor as that with highest SUL peak at baseline, it need not be. 3. Uptake measurements should be made for peak and maximal single-voxel tumor SUL. Other SUV metrics, including SUL mean at 50% or 70% of SUV peak, can be collected as exploratory data; TLG can be collected ideally on basis of voxels more intense than 2 SDs above liver mean SUL. 4. These parameters can be recorded as exploratory data on up to 5 measurable target lesions, typically the 5 hottest lesions, which are typically the largest, and no more than 2 per organ. Tumor size of these lesions can be determined per RECIST 1.1.
Normalization of uptake	Same as PERCIST1.0	Normal liver SUL must be within 20% (and <0.3 SUL mean units) for baseline and follow-up study to be assessable. If liver is abnormal, blood-pool SUL must be within 20% (and <0.3 SUL mean units) for baseline and follow-up study to be assessable. Uptake time of baseline study and follow-up study 2 must be within 15 min of each other to be assessable. Typically, these are at mean of 60 min after injection but no less than 50 min after injection. Same scanner, or same scanner model at same site, injected dose, acquisition protocol (2- vs. 3-dimensional), and software for reconstruction, should be used. Scanners should provide reproducible data and be properly calibrated.

Selection of target lesions at follow-up scan	Up to 5 measurable target lesions, typically the 5 hottest lesions among ALL lesions including NEW lesions, and no more than 2 per organ. Tumor size of these lesions can be determined per RECIST 1.1. The threshold of SUL is not defined in this version.	If 5 lesions are used as exploratory approach, it is suggested that sum of SULs of baseline 5 lesions serve as baseline for study. After treatment, sum of same 5 lesions should be used. Percentage change in SUL is based on change in these sums from study 1 to study 2. Exploratory analysis can include calculating percentage change in SUL in individual lesions and averaging them. This may produce different result. We believe summed SUL approach will be less prone to minor errors in measurements. Same to baseline target lesions or, highest 5 lesions (SULpeak) among baseline lesions.
Evaluation for non-target lesion	Not defined in this version	Nontarget lesions: CMR, disappearance of all 18F-FDG–avid lesions: PMD, unequivocal progression of 18F-FDG–avid nontarget lesions or appearance of new 18F-FDG–avid lesions typical of cancer; non-PMD: persistence of one or more nontarget lesions or tumor markers above normal limits.
Approach for appearance of new lesions	Measure the FDG uptake (SULpeak) of ALL NEW suspicious sites as well as the original sites, then select the 'hottest' (up to 5) lesions from this pool of lesions and compare their summed SULpeak to the summed SULpeak of baseline lesions. PMD is only called when the summed SULpeak on follow-up scan is > 30% higher than the summed SULpeak at baseline. Again, no more than 2 lesions/organ will be picked. Presence of new lesions, per se, does NOT constitute PMD.	Categorized as PMD
Objective response		

Complete metabolic response (CMR)	Same as PERCIST	Complete resolution of 18F-FDG uptake within measurable target lesion so that it is less than mean liver activity and indistinguishable from surrounding background blood-pool levels. Disappearance of all other lesions to background blood-pool levels. Percentage decline in SUL should be recorded from measurable region. No new 18F-FDG–avid lesions in pattern typical of cancer. If progression by RECIST, must verify with follow-up.
Partial metabolic response (PMR)	Reduction of SULpeak in target lesions by a at least 30%, and absolute drop in SUL by at least 0.8 SUL units.	Reduction of minimum of 30% in target measurable tumor 18F-FDG SUL peak. Absolute drop in SUL must be at least 0.8 SUL units, as well. Measurement is commonly in same lesion as baseline but can be another lesion if that lesion was previously present and is the most active lesion after treatment. ROI does not have to be in precisely same area as baseline scan, though typically it is. No increase, >30% in SUL. Reduction in extent of tumor 18F-FDG uptake is not requirement for PMR. Percentage decline in SUL should be recorded. No new lesions.
Stable metabolic disease (SMD)	SMD: not CMR, PMR, or PMD.	SMD: not CMR, PMR, or PMD. SUL peak in metabolic target lesion should be recorded.
Progressive metabolic disease (PMD)	>30% increase in SUL peak, with >0.8 SUL unit increase in tumor SUVpeak, from baseline scan in a pattern typical of tumor and not of infection/treatment effect.	>30% increase in 18F-FDG SUL peak, with >0.8 SUL unit increase in tumor SUV peak from baseline scan in pattern typical of tumor and not of infection/treatment effect. OR: New 18F-FDG–avid lesions that are typical of cancer and not related to treatment effect or infection. PMD other than new visceral lesions should be confirmed on follow-up study within 1 mo unless PMD also is clearly associated with progressive disease by RECIST 1.1.
Overall response	Same as PERCIST1.0	1. Best response recorded in measurable disease from treatment start to disease progression or recurrence. 2. Non-PMD in measurable or non-measurable nontarget lesions will reduce CR in target lesion to overall PMR. 3. Non-PMD in nontarget lesions will not reduce PR in target lesions.

Duration of response	Same as PERCIST1.0	1. Overall CMR: from date CMR criteria are first met; to date recurrent disease is first noted. 2. Overall response: from date CMR or PMR criteria are first met (whichever status came first); to date recurrent disease is first noted. 3. SMD: from date of treatment start to date PMD is first noted.

CMR = complete metabolic response; PMR = partial metabolic response; PD = progressive disease; SMD = stable metabolic disease; PMD = progressive metabolic disease; CR = complete remission; PR = partial remission; NC = no change.