Supplementary Online Content

Schoenfeld JD, Hanna GJ, Jo VY, et al. Neoadjuvant nivolumab or nivolumab plus ipilimumab in untreated oral cavity squamous cell carcinoma: a phase 2 open-label randomized clinical trial. *JAMA Oncol*. Published online August 27, 2020. doi:10.1001/jamaoncol.2020.2955

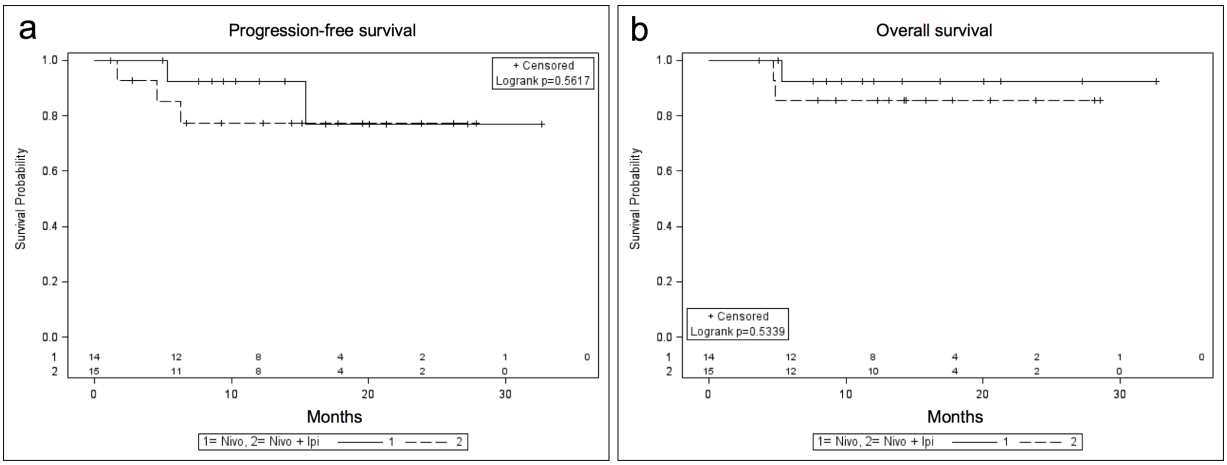
This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1: Agreement between the different response metrics used in the trial. As reference Cohen's kappa indicate: 0.01-0.2, slight agreement; 0.21-0.4, fair agreement, 0.41-0.6, moderate agreement; 0.61-0.8 substantial agreement; >0.8, near perfect agreement.[1]

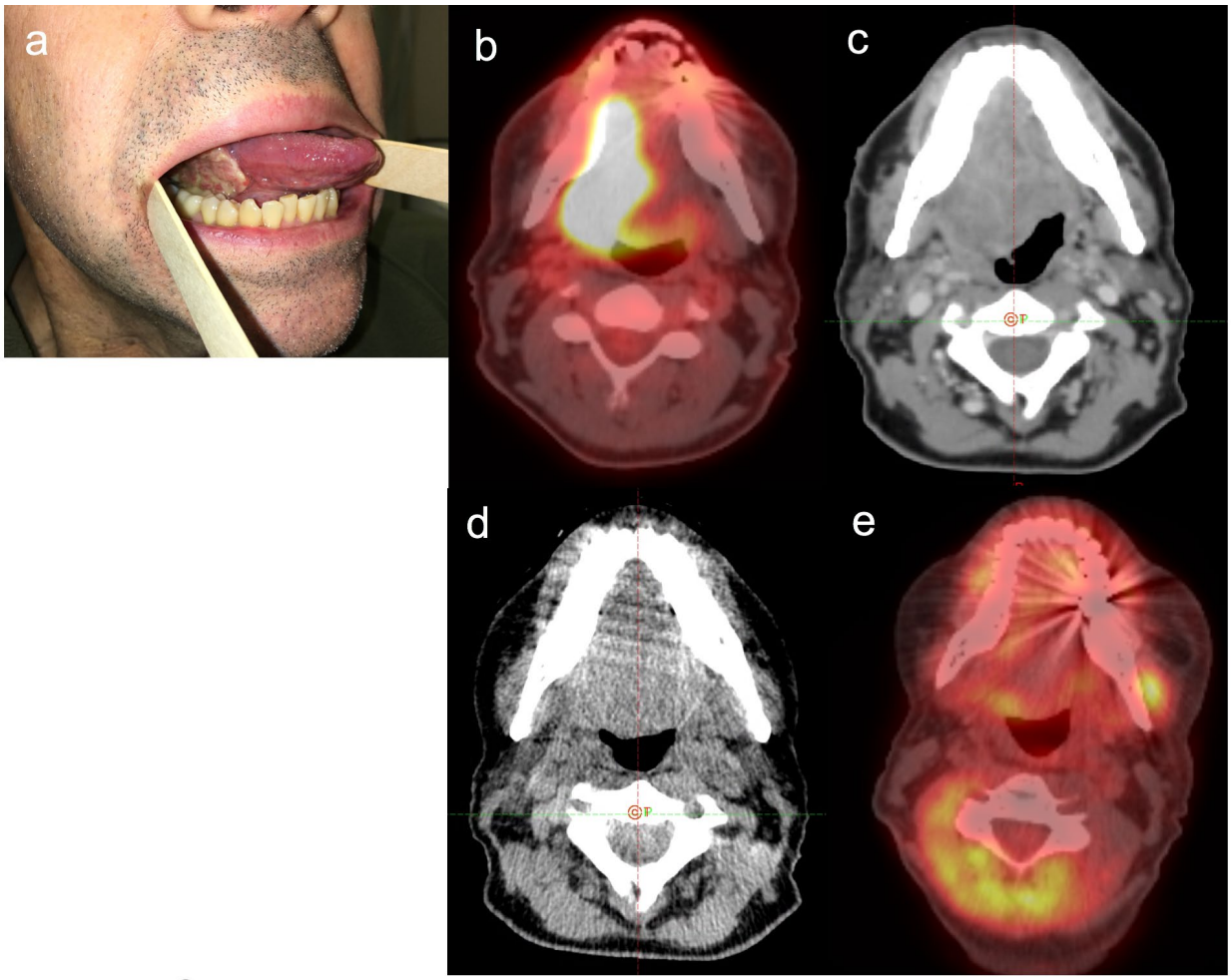
Parameter 1	Parameter 2	% Agreement	Cohen's k
Volumetric response	Clinical to pathologic downstaging	68%	0.36
Volumetric response	RECIST response	75%	0.50
Volumetric response	<90% viable tumor on pathology	65%	0.29
Volumetric response	<10% viable tumor on pathology	64%	0.29
Clinical to pathologic downstaging	RECIST response	53%	0.15
Clinical to pathologic downstaging	<90% viable tumor on pathology	75%	0.47
Clinical to pathologic downstaging	<10% viable tumor on pathology	53%	0.19
RECIST response	<90% viable tumor on pathology	67%	0.39
RECIST response	<10% viable tumor on pathology	87%	0.59

[1] Landis, JR & Koch, GG (1977). The measurement of observer agreement for categorical data. Biometrics, 33, 159-174.

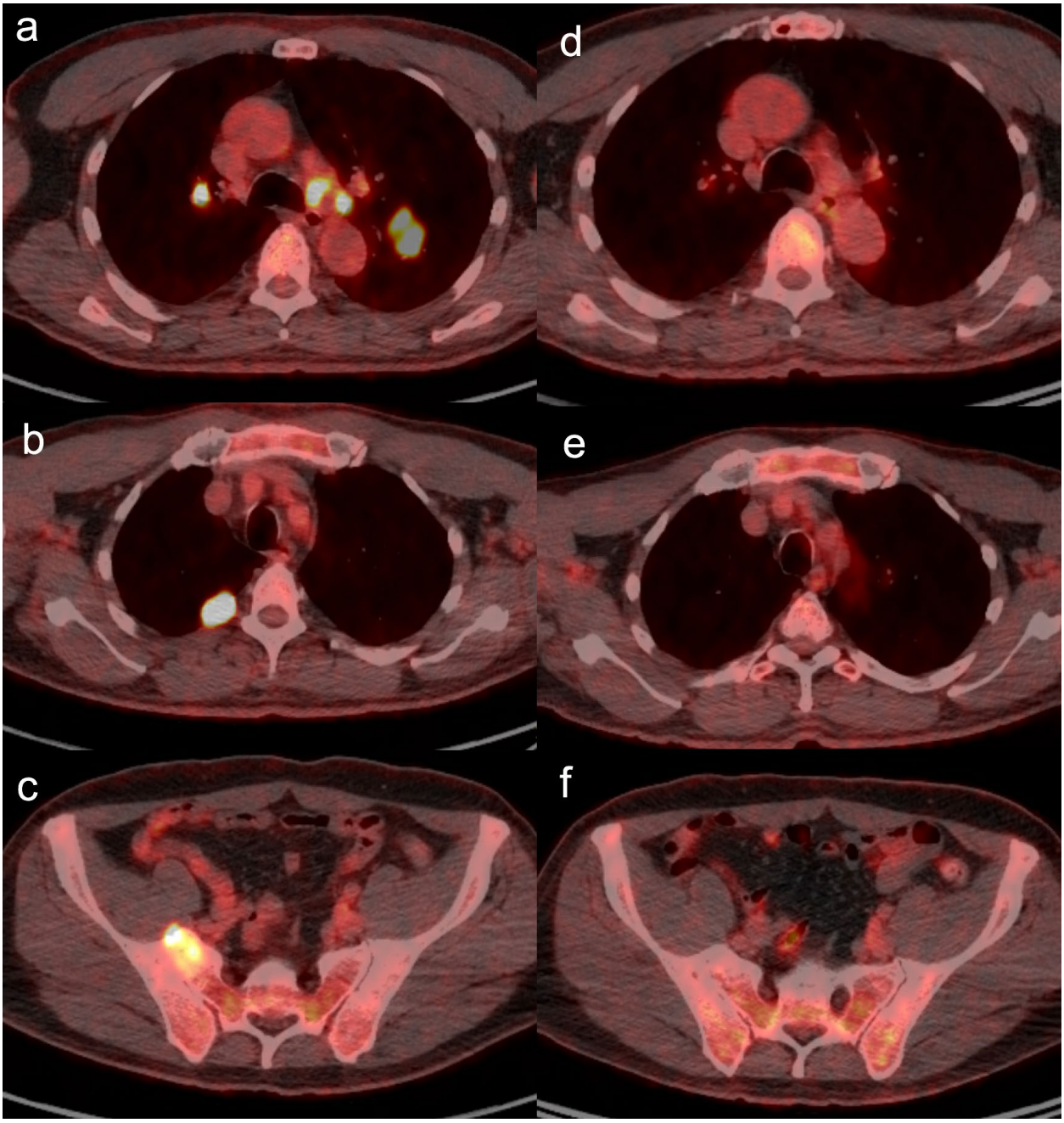
eFigure 1: Progression-free (A) and overall-survival (B).



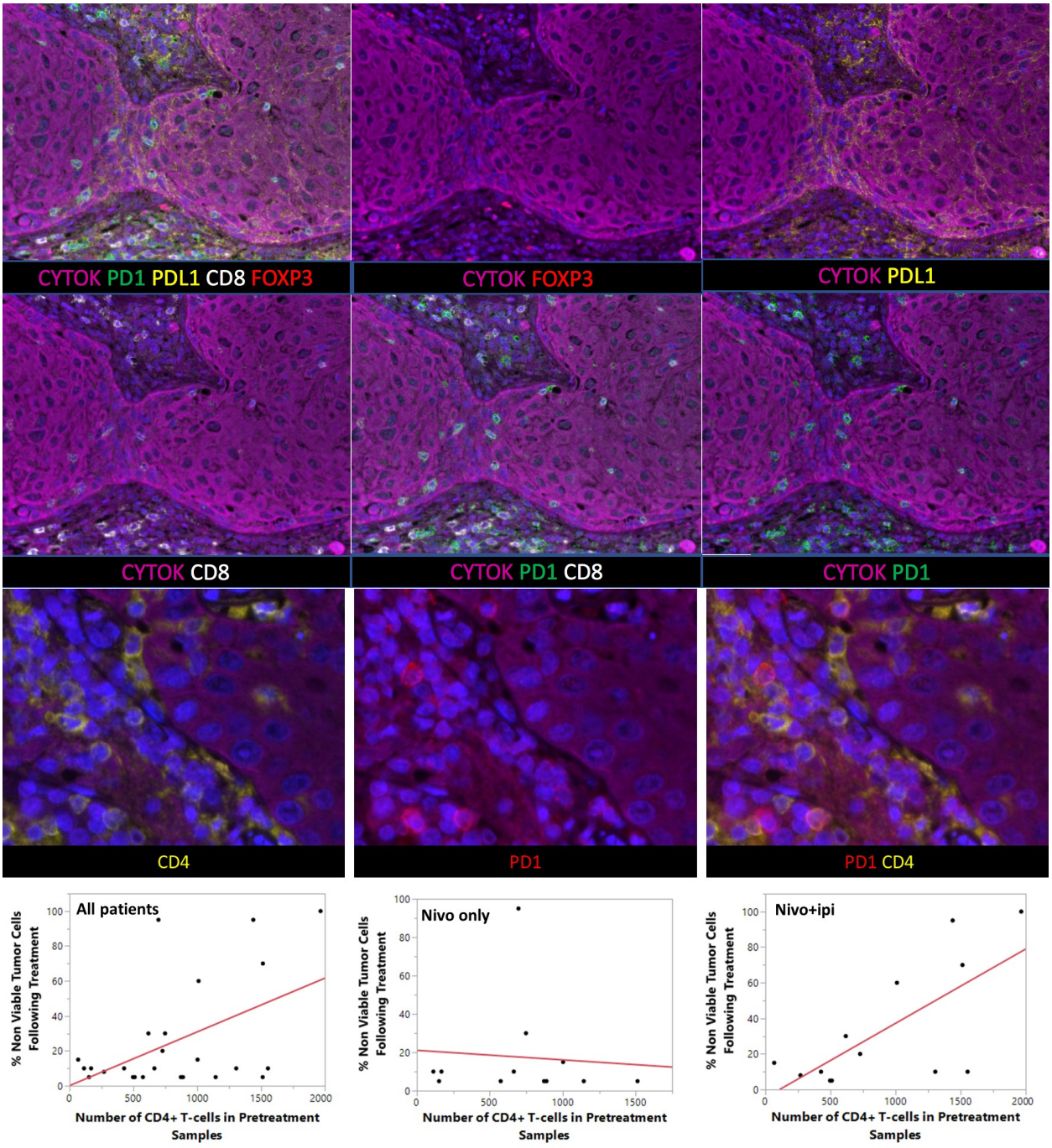
eFigure 2: Patient with cT4aN2c disease on clinical exam (A) and preoperative PET (B)-CT (C). He was treated with neoadjuvant nivolumab (1 cycle) with restaging scans suggesting slight decrease in tumor size (15%). Extent of disease identified in the operating room prompted change in management to definitive chemoradiation. Restaging scans after 1 week of chemoradiation demonstrated ongoing response (D) and then complete metabolic response at the time of the first restaging 3 months following the completion of all treatment (E).



eFigure 3: Patient with 70% pathologic response at the time of surgery developed metastatic disease to lung (A, B), bone (C). He was subsequently treated with nivolumab monotherapy and had complete metabolic response (D, E, F).



eFigure 4: Multiplex immunofluorescent staining performed to identify specific immune populations and positive association identified between CD4+ populations and pathologic response (bottom).



eFigure 5: Example of patient who demonstrated increased avidity within draining cervical lymph nodes after (B) neoadjuvant immunotherapy, as compared to before (A). The right level 2 and 3 lymph nodes that were FDG-avid were found to demonstrate reactive follicular and interfollicular hyperplasia with histiocytes, and immunoblastic and dendritic cell hyperplasia in the follicles, without any evidence of squamous cell carcinoma.