Supplementary Online Content

Tolaney SM, Barroso-Sousa R, Keenan T, et al. Effect of eribulin with or without pembrolizumab on progression-free survival for patients with hormone receptor–positive, *ERBB2*-negative metastatic breast cancer: a randomized clinical trial. *JAMA Oncol*. Published online September 3, 2020. doi:10.1001/jamaoncol.2020.3524

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

eTable 1. Patient characteristics at baseline, continued.

Characteristic	Eribulin + Pembrolizumab (N=44)	Eribulin (N=44)
PD-L1		
Positive	13 (29.5%)	11 (25.0%)
Negative	21 (47.7%)	20 (45.4%)
Unknown	10 (22.7%)	13 (29.5%)
Tumor-infiltrating lymphocytes		
Median (range)	5 (<5-30)	5 (<5-30)
0-10%	25 (57)	22 (50)
>10%	6 (14)	5 (11)
Unknown	13 (29)	17 (39)
Tumor Mutational Burden (TMB)		
Median (range)	7.0 (2.4-21.3)	5.3 (1.5-14.5)
TMB≤6	11 (25.0%)	13 (29.5%)
6<TMB<10	12 (27.3%)	9 (20.5%)
TMB≥10	5 (11.4%)	2 (4.5%)
Unknown	16 (36.4%)	20 (45.4%)

eTable 2. Most common adverse events* during the study.

Adverse Event	Eribulin + pembrolizumab (n=44)		Eribulin (n=44)	
	All Grades	Grade 3-4	All Grades	Grade 3-4
Any event	44 (100%)	30 (68%)	44 (100%)	27 (61%)
Fatigue	36 (82%)	2 (5%)	31 (70%)	3 (7%)
Alopecia	24 (55%)	0 (0%)	18 (41%)	0 (0%)
Neuropathy (peripheral)	23 (52%)	4 (9%)	24 (55%)	3 (7%)
Nausea	22 (50%)	1 (2%)	24 (55%)	0 (0%)
Neutropenia	21 (48%)	16 (36%)	29 (66%)	16 (36%)
AST elevation	17 (39%)	6 (14%)	12 (27%)	2 (5%)
Diarrhea	16 (36%)	0 (0%)	9 (21%)	0 (0%)
Dyspnea	13 (30%)	2 (5%)	3 (7%)	0 (0%)
ALT elevation	13 (30%)	1 (2%)	9(20%)	3 (7%)
Anorexia	13 (30%)	0 (0%)	13 (30%)	0 (0%)
Anemia	11 (25%)	1 (2%)	12 (27%)	2 (5%)
Constipation	12 (27%)	0 (0%)	8 (18%)	0 (0%)
Cough	11 (25%)	0 (0%)	0 (0%)	0 (0%)
Headache	10 (23%)	0 (0%)	8 (18%)	0 (0%)
Mucositis oral	10 (23%)	2 (5%)	10 (23%)	3 (7%)
Vomiting	11 (25%)	1 (2%)	5 (12%)	0 (0%)
Fever	8 (18%)	0 (0%)	9 (21%)	0 (0%)

***All relatedness**

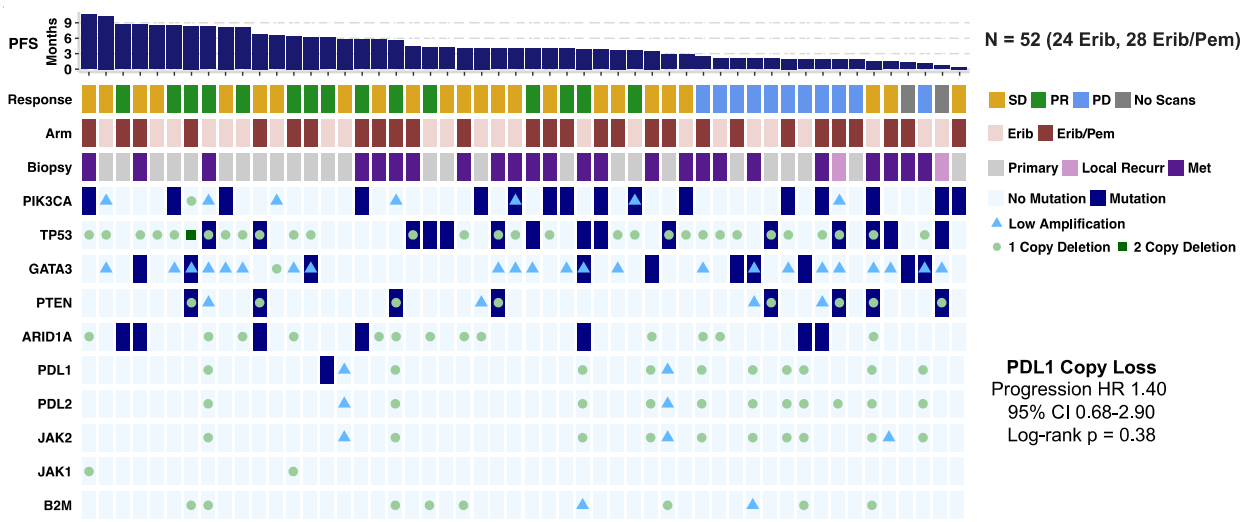
Abbreviations: ALT, alanine transaminase; AST, aspartate aminotransferase; only includes events occurring in $\geq$ 20% of patients

eTable 3. Adverse events suggestive of potential immune-related etiology.

Adverse Event	Eribulin + pembrolizumab (n=44)	
	All Grades	Grade ≥ 3
Liver enzyme/bilirubin elevation	17 (39%)	6 (14%)
Rash	13 (30%)	0(0%)
Hypothyroidism	6 (14%)	0 (0%)
Hyperthyroidism	6 (14%)	0 (0%)
Flu-like symptoms	5 (11%)	0 (0%)
Arthralgias	5 (11%)	0 (0%)
Pneumonitis	3 (7%)	1 (2%)
Myocarditis	1 (2%)	1 (2%)
Colitis*	2 (5%)	2 (5%)

*2 patients experienced treatment related grade 5 events; both patients experienced colitis, neutropenia and sepsis

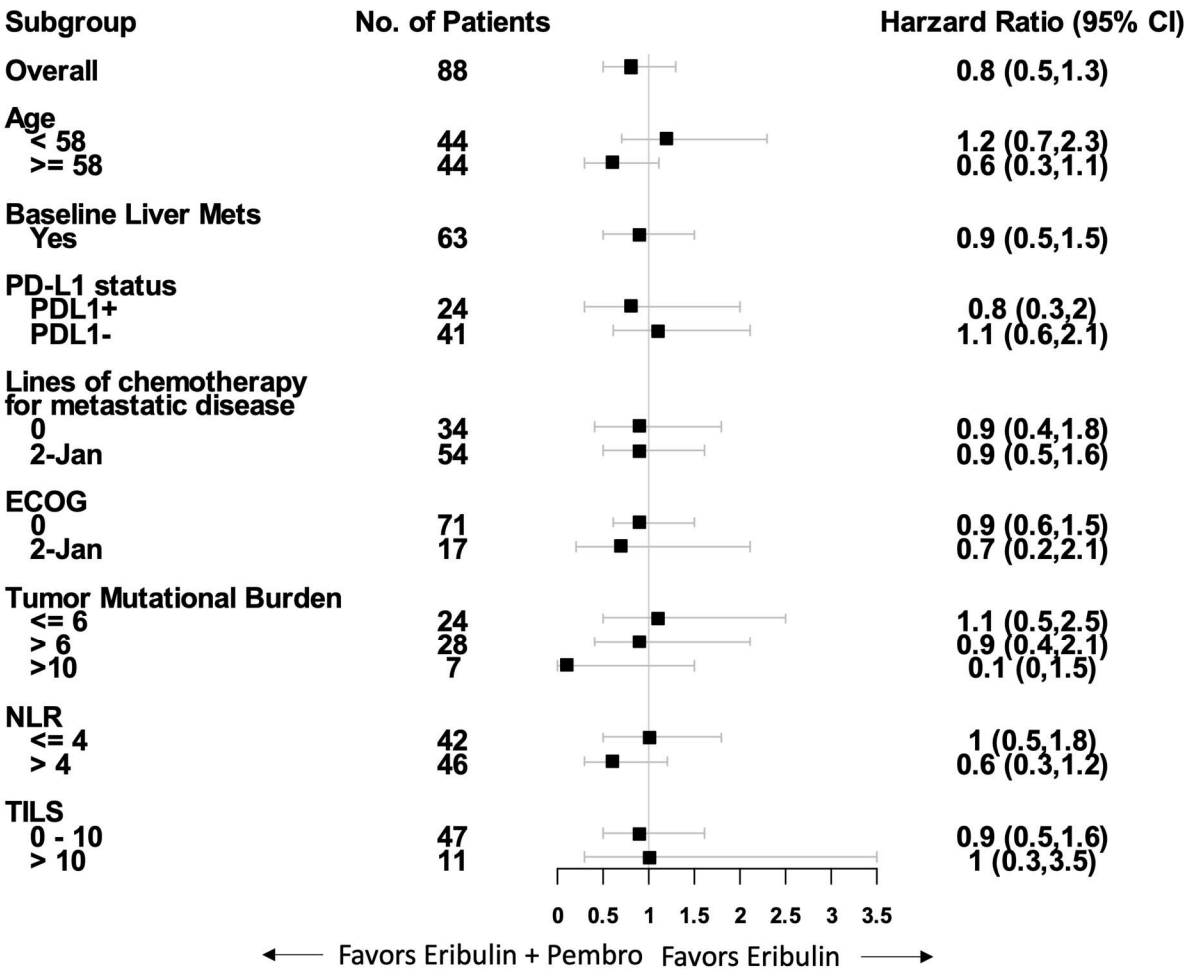
eFigure 1. Tumor genomic alterations ordered by progression-free survival (PFS).



Each column represents a tumor unique to a patient. Shown are the five most commonly mutated genes in this cohort (*PIK3CA*, *TP53*, *GATA3*, *PTEN*, *ARID1A*) and five immunotherapy-related genes (*PDL1* also called *CD274*, *PDL2* also called *PDCD1LG2*, *JAK2*, *JAK1*, *B2M*).

Abbreviations: CI, confidence interval; Erib, eribulin; Erib/Pem, eribulin/pembrolizumab; HR, hazard ratio; Local Recurr, local recurrence; Met, metastasis; PD, progressive disease; PR, partial response; SD, stable disease.

eFigure 2. Forest-plot analyses of progression-free survival (PFS) in key subgroups.



Abbreviations: Pembro: Pembrolizumab; NRL: neutrophil-lymphocyte ratio, which is defined as absolute neutrophil count divided by absolute lymphocyte count; TIL, tumor-infiltrating lymphocyte.

eFigure 3. Kaplan–Meier analysis of progression-free survival (PFS) in patients of Arm B who received pembrolizumab following progression to eribulin.