Supplemental Table 1: Dose modifications

Reason for modification	Dose modification*			
	Chemotherapy-related		Vorinostat or placebo-related	
	Dose reduced	Discontinued	Dose reduced	Discontinued
Hematologic toxicity				
Platelets	2	2	1	2
Neutrophils	22	2	28	1
Non-hematologic toxicity				
Constipation		1		1
Diarrhea			1	
ALT-increased	2		1	
Neuropathy	6	2		3
Hypersensitivity reaction		5	1	1

*If a participant had a dose reduction prior to dose discontinuation for the same event, only the dose discontinuation is noted. If a participant had a dose reduction/discontinuation at different time points for different events, all modification reasons are noted. The modifications for chemotherapy- and vorinostat or placebo-related events are noted separately.

Supplemental Table 2: Treatment-related side effects occurring in > 3 patients across arms

Toxicity	Vorinostat Arm (N= 31)				Placebo Arm (N= 31)			
	Total Events n (%)	By Grade			Total Events n (%)	By Grade		
		≤ G2	G3	G4		≤ G2	G3	G4
Allergy/Immunology								
Allergic Reaction	1 (3%)	1	0	0	10 (32%)	8	2	0
Blood/Bone Marrow & Metabolic/Laboratory								
Anemia (hemoglobin)	20 (64.5%)	16	4	0	9 (29%)	9	0	0
Neutropenia (neutrophils)	29 (93.5%)	10	14	5	28 (90%)	14	7	7
Thrombocytopenia (platelets)	15 (48%)	15	0	0	10 (32%)	9	1	0
Elevated ALT	1 (3%)	1	0	0	4 (13%)	3	1	0
Constitutional Symptoms								
Chills	5 (16%)	5	0	0	4 (13%)	4	0	0
Fatigue	27 (87%)	26	1	0	31 (100%)	30	1	0
Insomnia	5 (16%)	5	0	0	6 (19%)	6	0	0
Dermatology/Skin								
Alopecia	29 (93.5%)	29	0	0	31 (100%)	31	0	0
Nail Changes	3 (9.5%)	3	0	0	8 (26%)	8	0	0
Pruritus	1 (3%)	1	0	0	3 (9.5%)	3	0	0
Rash	9 (29%)	9	0	0	9 (29%)	9	0	0
Gastrointestinal								
Anorexia	19 (61%)	19	0	0	17 (55%)	17	0	0
Constipation	18 (58%)	17	1	0	14 (45%)	14	0	0
Diarrhea	18 (58%)	17	1	0	18 (58%)	17	1	0
Dry Mouth	6 (19%)	6	0	0	2 (6%)	2	0	0
Flatulence	3 (9.5%)	3	0	0	7 (22.5%)	7	0	0
Heartburn /Dyspepsia	7 (22.5%)	7	0	0	9 (29%)	9	0	0
Mucositis	6 (19%)	6	0	0	10 (32%)	10	0	0
Nausea	29 (93.5%)	28	1	0	25 (80.5%)	24	1	0
Taste alteration	17 (55%)	17	0	0	13 (42%)	13	0	0
Vomiting	19 (61%)	17	2	0	10 (32%)	9	1	0
Hemorrhage/Bleeding								
Epistaxis	5 (16%)	5	0	0	14 (45%)	14	0	0
Endocrine								
Hot flashes	7 (22.5%)	7	0	0	8 (26%)	8	0	0
Infection								
Sinus Infection	4 (13%)	4	0	0	5 (16%)	5	0	0
Upper respiratory	3 (9.5%)	3	0	0	5 (16%)	5	0	0

tract infection								
Neurology								
Dizziness	1 (3%)	1	0	0	4 (13%)	4	0	0
Sensory neuropathy	20 (64.5%)	20	0	0	25 (80.5%)	25	0	0
Ocular/Visual								
Visual change	5 (16%)	5	0	0	4 (13%)	4	0	0
Pain								
Abdominal Pain	6 (19%)	5	1	0	4 (13%)	4	0	0
Arthralgia	15 (48%)	15	0	0	13 (42%)	13	0	0
Headache	5 (16%)	5	0	0	8 (26%)	8	0	0
Myalgia	13 (42%)	13	0	0	11 (35%)	11	0	0
Pulmonary/Upper Respiratory								
Cough	1 (3%)	1	0	0	3 (9.5%)	3	0	0
Dyspnea	0 (0%)	0	0	0	7 (22.5%)	7	0	0

Note: Number of worst grade adverse events possibly, probably, or definitely attributed to study drug administration. Toxicities are graded per the NCI CTCAE version 3 criteria. G1=Grade 1, G2=Grade 2, G3=Grade 3, G4=Grade 4. NOS= not otherwise specified.

Supplemental Table 3: Baseline and change in SULmax between pathological responders and non-responders (excluding patients who receiving additional pre-operative non study chemotherapy)

Variable	Responders (n = 11)	Non-responders (n = 31)	*P**
Baseline SULmax			
Mean (± SD)	8.8 (± 2.9)	5.8 (± 3.7)	
Median (range)	7.9 (5.2 – 15.1)	5.3 (1.7 – 21.0)	0.005
%Change in SULmax			
Mean (± SD)	65.0 (± 15.2)	31.4 (± 27.8)	
Median (range)	67.3 (36.3 – 85.3)	34.1 (-53.0 – 72.5)	<0.001
≥50% reduction, n[%]	9 (81.8)	10 (32.3)	0.011

*Nonparametric exact Wilcoxon rank sum test for continuous variables and Fisher's exact test for dichotomized variables.

Supplemental Table 4: Analysis of association of SULmax with pathological response

(excluding patients receiving additional pre-operative non study chemotherapy)

Variable	Univariate analysis		Multivariable analysis*	
	OR (95% CI)	*P*	Adjusted OR (95% CI)	Adjusted *P*
Baseline SULmax	1.26 (1.03–1.65)	0.048	1.08 (0.84–1.39)	0.517
%Change in SULmax	1.11 (1.05–1.21)	0.004	1.09 (1.03–1.20)	0.016
%Change in SULmax ≥ 50% vs. < 50%	9.45 (1.90–70.1)	0.010	7.09 (1.14–63.4)	0.048

OR = odds ratio; CI = confidence interval

*Multivariable logistic regression adjusting for ER and PR status.

Supplemental Table 5: Baseline and change in Ki67 and ER between pathological responders and non-responders

Variable	Responders	Non-responders	*P**
Baseline Ki67 (%)	N=15	N=44	
Mean (± SD)	61.3 (±15.5)	47.8 (±24.0)	
Median (range)	60 (39–90)	50 (1–90)	0.056
D15 Ki67 (%)	N=10	N=36	
Mean (± SD)	49.3 (±23.2)	34.2 (±17.7)	
Median (range)	45.5 (10–80)	33.5 (5–70)	0.064
Absolute change in Ki67 (%, Baseline-D15)	N=8	N=36	
Mean (± SD)	7.0 (±15.8)	12.0 (±22.7)	
Median (range)	11 (-20–31)	4.5 (-34–60)	0.988
% Change in Ki67	N=8	N=36	
Mean (± SD)	10.5 (±30.0)	-11.9 (±153.7)	
Median (range)	16.9 (-40.0–49.2)	11.0 (-850.0–90.0)	0.819
Baseline ER (%)	N=15	N=44	
Mean (± SD)	5 (±16)	44 (±43)	
Median (range)	0 (0–60)	55 (0–100)	0.001
D15 ER (%)	N=9	N=37	
Mean (± SD)	6 (±17)	46 (±43)	
Median (range)	0 (0–50)	60 (0–100)	0.008
Absolute change in ER (%, Baseline-D15)	N=8	N=37	
Mean (± SD)	4 (±7)	0.7 (±8)	
Median (range)	0 (0–20)	0 (-18–30)	0.273

*Nonparametric exact Wilcoxon rank sum test