Supplementary Online Content

Bandera EV, Lee VS, Rodriguez-Rodriguez L, Powell CB, Kushi LH. Impact of chemotherapy dosing on ovarian cancer survival according to body mass index. *JAMA Oncol*. Published online July 2, 2015. doi:10.1001/jamaoncol.2015.1796

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

eTable 1. Chemotherapy variables

Variable	Calculation or Definition
Actual Dose	Dose received
Expected Dose	Based on 2013 NCCN Guidelines: For paclitaxel: 175 mg/m^2, every 3 weeks for 6 cycles. For carboplatin*: target AUC** x (CrCl + 25), every 3 weeks for 6 cycles)
Creatinine Clearance (CrCl)	Cockcroft-Gault Formula: CrCl = (140 - age in yrs) x (weight in kg) x (0.85 if female) / (72 x serum creatinine)
Actual Duration	Days from first cycle to 21 days after the date of last cycle. Divide by 7 to express in weeks.
Number of Cycles	Number of cycles received
Relative Dose Intensity (RDI)	RDI = Actual Dose Intensity/Expected Dose Intensity.
Actual Dose Intensity	Amount of drug administered (actual dose) per week.
Expected Dose Intensity	Amount of drug expected to be administered (expected dose) per week based NCCN Guidelines (see expected dose above)
Early discontinuation	<6 cycles or <4 cycles
Treatment delay	>7 days delay

***** Calvert equation
**Target AUC as assigned for first cycle in electronic medical records

eTable 2. Chemotherapy dosing, dose reduction, dose delay, and treatment parameters, by BMI at diagnosis.

	Underweight (n=20)	Normal (n=297)	Overweight (n=248)	Obese Class I (n=134)	Obese Class II (n=70)	Obese Class III (n=37)	
	Mean (SD)	*Mean (SD)*	*Mean (SD)*	*Mean (SD)*	*Mean (SD)*	*Mean (SD)*	p value*
BSA (calculated)	1.44(0.09)	1.61 (0.14)	1.75 (0.14)	1.89 (0.14)	2.08 (0.17)	2.22 (0.21)	<0.001
PACLITAXEL							
RDI first cycle (%)†	97.93 (10.55)	97.86 (12.17)	96.55 (11.78)	95.31 (10.67)	91.55 (17.27)	83.98 (22.39)	<0.001
RDI all cycles (%)	90.41 (14.61)	91.16 (11.99)	91.00 (11.31)	90.44 (11.87)	88.56 (14.00)	82.43 (14.33)	<0.01
Actual total dose in mg/kg	29.10 (11.83)	25.68 (8.04)	22.24 (7.56)	20.50 (7.11)	18.74 (5.99)	15.93 (6.03)	<0.001
Number of cycles	5.45 (2.04)	5.38 (1.59)	5.17 (1.73)	5.18 (1.68)	5.30 (1.53)	5.16 (1.61)	0.70
Treatment duration (weeks)	17.99 (7.06)	17.49 (5.65)	16.53 (5.83)	16.42 (5.49)	16.96 (5.56)	16.38 (6.17)	0.30
CARBOPLATIN							
RDI first cycle (%)	100.00 (11.58)	93.01 (13.66)	87.99 (13.54)	80.64 (13.44)	73.17 (15.52)	66.28 (16.16)	<0.001
RDI all cycles (%)	91.90 (14,25)	85.32 (15.64)	82.83 (17.68)	77.24 (15.46)	68.85 (16.42)	65.06 (*19.49)*	<0.001
Actual total dose in mg/kg	58.70 (30.26)	50.43 (19.03)	42.02 (17.32)	38.54 (15.52)	33.21 (13.79)	27.72 (*13.12)*	<0.001
Number of cycles	5.40 (2.11)	5.36 (1.61)	5.12 (1.76)	5.16 (1.68)	5.28 (1.76)	5.13 (*1.62)*	0.62
Treatment duration (weeks)	17.85 (7.28)	17.49 (5.76)	16.52 (5.95)	16.38 (5.44)	16.73 (5.69)	16.30 (*6.21)*	0.29
PACLITAXEL+CARBOPLATIN							
ARDI first cycle (%)	98.97 (6.82)	95.44 (9.62)	92.27 (9.08)	87.98 (0.09)	82.36 (13.16)	75.13 (15.00)	<0.001
ARDI all cycles (%)	91.16 (12.09)	88.24 (12.32)	86.92 (12.49)	83.84 (12.03)	78.71 (12.79)	73.74 (12.17)	<0.001
(All cycles)	*n (%)*	*n (%)*	*n (%)*	*n (%)*	*n (%)*	*n (%)*	p value**
PACLITAXEL							
Dose reduction (RDI<85%)†	6 (30.00)	77 (25.93)	64 (25.81)	35 (26.12)	20 (28.57)	20 (54.05)	0.01
Dose delay (>7 days)	8 (40.00)	103 (34.68)	65 (26.21)	34 (25.37)	17 (24.29)	8 (21.62)	0.10
Early discontinuation (<6 cycles)	7 (35.00)	89 (29.97)	87 (35.08)	42 (31.34)	26 (37.14)	14 (37.84)	0.72
Early discontinuation (<4 cycles)	3 (15.00)	43 (14.48)	48 (19.35)	24 (17.91)	8 (11.43)	8 (21.62)	0.47
CARBOPLATIN							
Dose reduction (RDI<85%)	6 (30.00)	139 (46.80)	136 (54.84)	95 (70.90)	59 (84.29)	32 (86.49)	<0.001
Dose delay (>7 days)	8 (40.00)	105 (35.35)	68 (27.42)	33 (24.63)	16 (22.86)	8 (21.62)	0.06
Early discontinuation (<6 cycles)	7 (35.00)	89 (29.97)	87 (35.08)	41 (30.60)	27 (38.57)	14 (37.84)	0.62
Early discontinuation (<4 cycles)	3 (15.00)	43 (14.48)	52 (20.97)	24 (17.91)	10 (14.29)	8 (21.62)	0.41
PACLITAXEL+CARBOPLATIN							
Dose reduction (RDI<85%)	6 (30.00)	92 (30.98)	97 (39.11)	69 (51.49)	46 (65.71)	31 (83.78)	<0.001
Dose delay (>7 days)	8 (40.00)	105 (35.35)	69 (27.82)	34 (25.37)	18 (25.71)	8 (21.62)	0.12
Early discontinuation (<6 cycles)	7 (35.00)	92 (30.98)	90 (36.29)	42 (31.34)	27 (38.57)	14 (37.84)	0.68
Early discontinuation (<4 cycles)	3 (15.00)	43 (14.48)	52 (20.97)	24 (17.91)	10 (14.29)	8 (21.62)	0.41

* Based on ANOVA; ** Based on Chi-Square

† RDI: Relative Dose Intensity. ARDI: Average RDI.

eTable 3. Comorbidities and toxicities before and during treatment by BMI at diagnosis.

	Total (n=806) n (%)	Underweight (n-20) n (%)	Normal (n=297) n (%)	Overweight (n=248) n (%)	Obese I (n=134) n (%)	Obese II (n=70) n (%)	Obese III (n=37) n (%)	p value*
Comorbidities								
Diabetes mellitus[a]	94 (11.66)	1 (5.00)	16 (5.39)	28 (11.29)	14 (10.45)	18 (25.71)	17 (49.95)	<0.001
Hypertension[a]	377 (46.77)	7 (35.00)	105 (35.35)	116 (46.77)	71 (52.99)	48 (68.57)	30 (81.08)	<0.001
Cardiovascular disease[b]	163 (20.22)	4 (20.00)	64 (21.55)	45 (18.15)	28 (20.90)	15 (21.43)	7 (18.92)	0.95
Renal disease[b]	106 (13.15)	2 (10.00)	25 (8.42)	39 (15.73)	15 (11.19)	13 (18.57)	12 (32.43)	<0.001
Toxicities (grade III/IV)								
Neutropenia								
Before chemotherapy[c]	12 (1.49)	0 (0)	4 (1.35)	2 (0.81)	4 (2.99)	2 (2.86)	0 (0)	0.46
During chemotherapy[d]	237 (29.40)	6 (30.00)	109 (36.70)	68 (27.42)	33 (24.63)	12 (17.14)	9 (24.32)	0.01
G-CSF use[c]	182 (22.58)	2 (10.00)	85 (28.62)	52 (20.97)	27 (20.15)	9 (12.86)	7 (18.92)	0.02
Thrombocytopenia								
Before chemotherapy[c]	2 (0.25)	0 (0)	1 (0.34)	0 (0)	1 (0.75)	0 (0)	0 (0)	0.79
During chemotherapy[d]	41 (5.09)	1 (5.00)	24 (8.08)	8 (3.23)	4 (2.99)	2 (2.86)	2 (5.41)	0.10
Neuropathy								
Before chemotherapy[e]	19 (2.36)	1 (5.00)	5 (1.68)	2 (0.81)	6 (4.48)	1 (1.43)	4 (10.81)	<0.01
During chemotherapy[d]	103 (12.78)	1 (5.00)	38 (12.79)	32 (12.90)	16 (11.94)	11 (15.71)	5 (13.51)	0.88
Neuropathy medications[d]	34 (4.22)	1 (5.00)	17 (5.72)	5 (2.02)	4 (2.99)	5 (7.14)	2 (5.41)	0.24

* p value based on Chi-square test

[a] Having a diagnosis any time before ovarian cancer diagnosis or during chemotherapy; [b] having these conditions diagnosed one year before ovarian cancer diagnosis or during treatment; [c] within one month from first cycle; [d] from first to last cycle; [e] one month before ovarian cancer diagnosis to first cycle

eTable 4. Predictors of dose reduction (RDI<85%).

	PACLITAXEL			CARBOPLATIN			AVERAGE		
	Yes n	No n	OR (95% CI)	Yes n	No n	OR (95% CI)	Yes n	No n	OR (95% CI)
BMI at diagnosis									
Underweight (<18.5)	6	14	1.54 (0.54-4.40)	6	14	0.49 (0.18-1.35)	6	14	1.08 (0.38-3.04)
Normal (18.5-24.99)	77	220	1.00	139	158	1.00	92	205	1.00
Overweight (25-29.99)	64	184	1.05 (0.69-1.60)	136	112	1.62 (1.12-2.33)	97	151	1.60 (1.09-2.35)
Obese I (30-34.99)	35	99	1.14 (0.68-1.91)	95	39	3.45 (2.13-5.58)	69	65	2.85 (1.79-4.55)
Obese II (35-39.99)	20	50	1.22 (0.62-2.38)	59	11	8.84 (4.18-18.72)	46	24	5.65 (3.01-10.62)
Obese III (≥40)	20	17	4.03 (1.77-9.17)	32	5	13.41 (4.62-38.87)	31	6	19.85 (7.21-54.65)
Age at diagnosis (yrs)									
21-39	8	31	1.00	26	13	1.00	16	23	1.00
40-49	30	87	0.85 (0.31-2.36)	74	43	0.85 (0.34-2.12)	57	60	1.33 (0.55-3.25)
50-69	138	365	0.87 (0.34-2.26)	288	215	0.65 (0.28-1.53)	210	293	0.97 (0.42-2.24)
≥70	46	101	0.88 (0.31-2.50)	79	68	0.65 (0.25-1.67)	58	89	0.83 (0.32-2.12)
Race									
White	173	478	1.00	392	259	1.00	278	373	1.00
African American	14	28	1.11 (0.53-2.31)	21	29	0.40 (0.19-0.81)	20	22	0.79 (0.39-1.61)
Asian	29	66	1.43 (0.84-2.42)	41	54	0.67 (0.41-1.09)	34	61	1.10 (0.66-1.81)
Other	6	12	1.25 (0.41-3.88)	13	5	1.49 (0.46-4.79)	9	9	1.20 (0.40-3.60)
Ethnicity									
Not Hispanic	197	517	1.00	408	306	1.00	295	419	1.00
Hispanic	21	61	1.01 (0.56-1.82)	53	29	0.98 (0.57-1.69)	41	41	1.16 (0.68-1.97)
AJCC Stage									
I/II	74	243	1.00	169	148	1.00	114	203	1.00
III	99	243	1.33 (0.85-2.08)	209	133	1.36 (0.92-2.02)	156	186	1.39 (0.93-2.07)
IV	47	93	1.86 (1.09-3.16)	86	54	1.40 (0.86-2.30)	69	71	1.68 (1.02-2.76)
Grade (SEER Definition)									
Well differentiated	12	38	1.00	28	22	1.00	21	29	1.00
Moderately differentiated	33	100	1.06 (0.45-2.51)	85	48	1.76 (0.81-3.80)	61	72	1.33 (0.61-2.89)
Poorly differentiated	96	222	1.07 (0.47-2.44)	179	139	1.15 (0.55-2.39)	134	184	0.92 (0.43-1.94)
Undifferentiated	31	102	0.80 (0.33-1.97)	77	56	1.40 (0.63-3.10)	52	81	0.88 (0.39-1.99)
Unknown	50	122	0.99 (0.41-2.39)	98	74	1.42 (0.65-3.12)	73	99	1.02 (0.46-2.27)

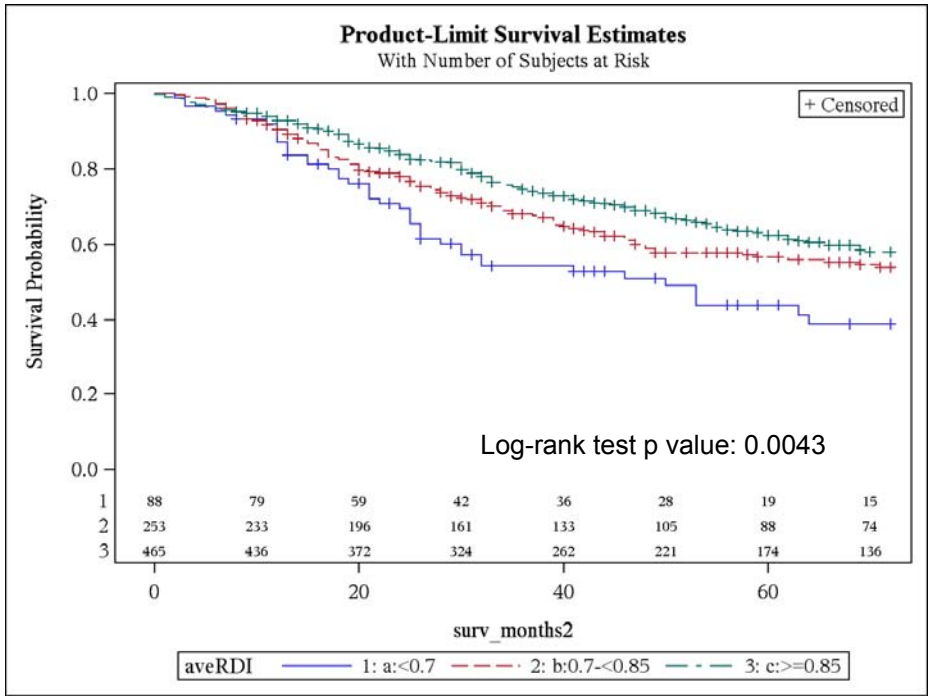
eTable 4. Predictors of dose reduction (RDI<85%), Continued.

	PACLITAXEL			CARBOPLATIN			AVERAGE		
	Yes n	No n	OR (95% CI)	Yes n	No n	OR (95% CI)	Yes n	No n	OR (95% CI)
Histology									
Serous	125	307	1.00	256	176	1.00	198	234	1.00
Mucinous	6	33	0.50 (0.18-1.37)	24	15	0.95 (0.41-2.21)	18	21	0.97 (0.43-2.19)
Endometrioid	25	82	0.84 (0.46-1.54)	63	44	0.99 (0.58-1.70)	38	69	0.57 (0.33-0.99)
Clear cell	28	48	1.90 (1.00-3.64)	37	39	0.62 (0.34-1.16)	30	46	0.83 (0.44-1.57)
Other	38	114	0.93 (0.59-1.48)	87	65	1.11 (0.73-1.70)	57	95	0.85 (0.55-1.30)
Toxicities[a]									
No	101	396	1.00	260	237	1.00	173	324	1.00
Yes	121	188	2.33 (1.65-3.30)	207	102	2.34 (1.67-3.28)	168	141	2.71 (1.94-3.78)
G-CSF use[b]									
No	151	473	1.00	354	270	1.00	254	370	1.00
Yes	71	111	1.78 (1.18-2.67)	113	69	1.09 (0.73-1.63)	87	95	1.13 (0.76-1.68)
Comorbidities[c]									
Diabetes									
No	186	526	1.00	409	303	1.00	291	421	1.00
Yes	36	58	1.32 (0.76-2.29)	58	36	0.90 (0.51-1.57)	50	44	1.05 (0.61-1.81)
Hypertension									
No	107	322	1.00	250	179	1.00	173	256	1.00
Yes	115	262	1.15 (0.78-1.69)	217	160	0.83 (0.58-1.17)	168	209	0.94 (0.66-1.34)
Cardiovascular Disease									
No	159	484	1.00	369	274	1.00	261	382	1.00
Yes	63	100	1.76 (1.16-2.65)	98	65	1.30 (0.86-1.96)	80	83	1.55 (1.03-2.33)
Renal Disease									
No	179	521	1.00	409	291	1.00	288	412	1.00
Yes	43	63	1.53 (0.94-2.48)	58	48	0.66 (0.41-1.08)	53	53	1.05 (0.65-1.70)

[a] Neutropenia, thrombocytopenia, or neuropathy one month before first cycle or during chemotherapy.
[b] During chemotherapy
[c] One year before or during chemotherapy treatment.
OR and 95% confidence intervals: multivariable model adjusted for all the other variables in the table.

eFigure 1 Kaplan-Meier Curves for Average RDI levels and overall survival and ovarian cancer-specific survival through 72 months of follow-up.

Overall Survival



Ovarian Cancer-Specific Survival