Supplemental Online Content

Oudard S, Ratta R, Voog E, et al. Biweekly vs triweekly cabazitaxel schedule in men 65 years or older with metastatic castration-resistant prostate cancer: the CABASTY phase 3 randomized clinical trial. *JAMA Oncol*. Published online October 19, 2023. doi:10.1001/jamaoncol.2023.4255

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

eAppendix 1. List of Investigators

Centre N°	Centres	mail	PI
250-001	HEGP	stephane.oudard@aphp.fr	Stéphane Oudard
250-019	Foch Hospital	r.ratta@hopital-foch.com	Rafaele Ratta
250-023	Victor Hugo Clinics	e.voog@ilcgroupe.fr	Eric Voog
250-015	Strasbourg Hospital	p.barthelemy@icans.eu	Philippe Barthélémy
250-002	Minjoz University Hospital	a.thieryvuillemin@mac.com	Antoine Thierry-Vuillemin
250-004	IMM	Mostefa.Bennamoun@imm.fr	Mostefa Bennamoun
250-020	Pasteur Clinics	alihasbini@oncologie-brest.fr	Ali Hasbini
250-012	Polyclinique Saint Côme	kais.aldabbagh@stcome.com	Kais Aldabbagh
250-017	Henri Mondor Hospital	carolina.saldana@aphp.fr	Carolina Saldana
250-016	Maurice Tubiana Centre, Caen	e.sevin@i-l-c.fr	Emmanuel Sevin
250-022	Cancerology Center Les Dentellières, Valenciennes	ericamela@yahoo.fr	Eric Amela
276-008	Hamburg-Eppendorf Universitätsklinikum	g.von-amsberg@uke.de	Gunhild von Amsberg
250-014	Caremeau University Hospital	nadine.HOUEDE@chu-nimes.fr	Nadine Houédé
250-008	Armorican centre of Radiotherapy	d.besson@cario-sante.fr	Dominique Besson
276-006	Nürtingen Studienpraxis Urologie	feyerabend@studienurologie.de	Susan Feyerabend
276-009	Münster University Hospital	martin.boegemann@ukmuenster.de	Martin Bögemann
276-007	Köln Uniklinik	david.pfister@uk-koeln.de	David Pfister
276-001	Magdeburg University Hospital	martin.schostak@med.ovgu.de	Martin Schostak
250-003	Hôpital Cochin, Paris	olivier.huillard@aphp.fr	Olivier Huillard
250-006	Rouen University Hospital	Frederic.difiore@chu-rouen.fr	Frederic Di Fiori
250-010	Bordeaux University Hospital	amandine.quivy@chu-bordeaux.fr	Amandine Quivy
276-004	Bernburg Oncology Health Centre	Carsten.Lange2@gmx.net	Carsten Lange
250-013	Bégin Military Teaching Hospital	carole.helissey@gmail.com	Carole Helissey

eTable 1. Cabazitaxel Exposure (Safety Patient Population)

Characteristic	CBZ25 q3w[a] (n = 96)	CBZ16 q2w [a] (n = 98)	Overall (n = 194)	p-value[b]
Number of cycles received				.03
Mean (SD)	6.5 (3.0)	5.6 (2.6)	6.0 (2.8)	
Median (IQR)	6.0 (4.0-10.0)	5.0 (4.0-7.0)	6.0 (4.0-9.0)	
Range	(1.0-10.0)	(1.0-10.0)	(1.0-10.0)	
Treatment duration (weeks)				.21
Mean (SD)	19.8 (9.2)	22.1 (10.8)	20.9 (10.1)	
Median (IQR)	19.0 (12.0-30.0)	20.0 (13.9-30.8)	19.4 (12.1-30.0)	
Range	(3.0-33.7)	(4.0-42.0)	(3.0-42.0)	
Cumulative dose, No[c] (mg/m²)				.20
Mean (SD)	146.6 (69.1)	165.9 (83.0)	156.2 (76.8)	
Median (IQR)	142.5 (87.2-205.0)	142.7 [101.7-225.3)	142.7 (96.4-209.5)	
Range	(11.8-253.8)	(27.6-326.2)	(11.8-326.2)	
Dose intensity, No. [c] (mg/m²/cycle)				< .001
Mean (SD)	22.4 (2.6)	30.1 (2.2)	26.2 (4.6)	
Median (IQR)	22.8 (20.5-24.5)	30.7 (29.0-31.7)	25.2 (22.7-30.7)	
Range	(11.8-25.9)	(22.6-32.8)	(11.8-32.8)	
Relative dose intensity, No. [c] (%)				.75
Mean (SD)	91.1 (9.6)	92.0 (7.8)	91.5 (8.7)	
Median (IQR)	92.7 (83.7-98.9)	92.8 (87.0-98.9)	92.7 (86.3-98.9)	
Range	(47.1-103.5)	(69.6-103.1)	(47.1-103.5)	
Patients with ≥ 1 dose reduction, No. (%)				< .001
Yes	45.0 (46.9)	10.0 (10.2)	55.0 (28.4)	

Abbreviations: CBZ16 q2w, biweekly cabazitaxel 16mg/m²; CBZ25 q3w, triweekly cabazitaxel 25mg/m²; IQR, interquartile range; SD, standard deviation;

[a] Duration of each cycle is 3 weeks in CBZ25q3w arm and 4 weeks in CBZ16 q2w.

[b]Quantitative variable: Student t test (normal distribution) or Wilcoxon-Mann-Whitney (non-normal distribution) / Qualitative variable: Chi-squared test or Fisher's exact test.

** * Missing values < 5%.

eTable 2. Baseline Characteristics of Patients Who Developed or Not Grade ≥3 Neutropenia During Treatment, Regardless of Treatment Arm

Characteristic	No Grade ≥3 neutropenia (n = 131)	Grade ≥3 Neutropenia (n = 65)	Overall (n = 196)	p-value[a]
Arms, No. (%)				< .001
CBZ25 q3w	37 (28)	60 (92)	97 (49)	
CBZ16 q2w	94 (72)	5 (8)	99 (51)	
Age, years				< .001
median (q1; q3) [range]	74.4 (6.1) 73.53 [69.7;78.2] (65;95.8)	77.4 (5.8) 77.2 [72.8;81.5] (65.6;92.1)	74.6 [70.4;79.3] (65;95.8)	
Age class, years, No. (%)				.01
< 75 years	76 (58)	24 (37)	100 (51)	
75-80 years	33 (25)	21 (32)	54 (28)	
⩾ 80 years	22 (17)	20 (31)	42 (21)	
ECOG performance status, No. (%)				.25
0-1	123 (94)	58 (89)	181 (92)	
2	8 (6)	7 (11)	15 (8)	
Gleason score, No. (%)				.92
⩽ 7	63 (52)	33 (52)	96 (52)	
8 to 10	59 (48)	30 (48)	89 (48)	
Baseline PSA values[b], (ng/ml)				.84
Mean (SD)	229.6 (351.9)	126.4 (147.3)	194.3 (301.6)	
Median (IQR)	69.7 [22.3;255.5]	67.1 [35.1;178.9]	68.4 [23.5;217]	
Range	(2.7;2073.0)	(4.31;718.0)	(2.7;2073.0)	
Lactate dehydrogenase (LDH), No.[b] (%)				.92
⩾ ULN	67 (55)	33 (54)	100 (55)	
Alkaline phosphatase, No.[b] (%)				.43
⩾ ULN	52 (42)	30 (48)	82 (44)	
Hemoglobin, No.[b] (%)				.69
< LLN	79 (62)	37 (59)	116 (61)	
Neutrophils, No./Total No.[b] (%)				.04
⩾ median (= 4.10)	71 (55)	25 (40)	96 (50)	
NLR, No./Total No.[b] (%)				.15
⩾ 3	75 (59)	30 (48)	105 (55)	
M1 disease at cancer diagnostic, No. (%)				.96
Yes	63 (50)	31 (49)	94 (49)	

Characteristic	No Grade ≥3 neutropenia (n = 131)	Grade ≥3 Neutropenia (n = 65)	Overall (n = 196)	p-value[a]
No	64 (50)	32 (51)	96 (51)	
Metastases, No. (%)				
Bone	101 (81)	54 (87)	155 (83)	.28
Lymph	56 (45)	23 (37)	79 (42)	.32
Lung	14 (11)	6 (10)	20 (11)	.75
Liver	12 (10)	6 (10)	18 (10)	.99
G8 score, No. (%)				.43
< 14	24 (18)	15 (23)	39 (20)	
⩾ 14	107 (82)	50 (77)	157 (80)	
SIOG health status, No. (%)				.97
Fit	91 (69)	46 (71)	137 (70)	
Vulnerable	16 (12)	8 (12)	24 (12)	
Frail	24 (18)	11 (17)	35 (18)	
Comorbidities, No. (%)				
HTA	49 (37)	20 (31)	69 (35)	.36
Hypercholesterolaemia	15 (11)	5 (8)	20 (10)	.41
Diabetes	18 (14)	7 (11)	25 (13)	.85
Pain visual analog score, No.[b] (%)				.77
0-3	105 (81)	52 (83)	157 (81)	
4-10	25 (19)	11 (17)	36 (19)	
Prior AR-targeted agent lines, No.[b] (%)				.96
1 line	31 (25)	16 (25)	47 (25)	
2 lines	34 (27)	17 (28)	51 (27)	
⩾ 3 lines	62 (49)	29 (46)	91 (48)	
Prior chemotherapy lines, No.[b] (%)				.61
1 line	111 (85)	55 (85)	166 (85)	
2 lines	13 (10)	5 (8)	18 (9)	
⩾ 3 lines	6 (5)	5 (8)	11 (6)	
Prior docetaxel, No. (%)				---
Yes	97 (100)	99 (100)	196 (100)	
Cumulative docetaxel dose[b], mg/m²				1
Median (IQR)	450.0 [300.0;596.5]	450.0 [300.0;556.0]	450.0 [300.0;593.0]	
Type of prior AR-targeted agent, No[b] (%)				

Characteristic	No Grade ≥3 neutropenia (n = 131)	Grade ≥3 Neutropenia (n = 65)	Overall (n = 196)	p-value[a]
Abiraterone	82 (63)	40 (62)	122 (62)	.89
Enzalutamide	75 (57)	36 (55)	111 (57)	.80
Abiraterone/enzalutamide	43 (33)	23 (35)	66 (34)	.72
Apalutamide	2 (2)	2 (3)	4 (2)	.60
Darolutamide	4 (3)	1 (2)	5 (3)	1

Abbreviations: AR, androgen receptor; ECOG, Eastern Cooperative Oncology Group; HTA, hypertension; IQR, interquartile range; LLN, lower limit of normal; NLR, neutrophil to lymphocyte ratio; PSA, Prostate Specific Antigen; SIOG, International Society of Geriatric Oncology; SD, standard deviation; ULN, upper limit of normal
[a]Quantitative variable: Student t test (normal distribution) or Wilcoxon-Mann-Whitney (non-normal distribution) / Qualitative variable: Chi-squared test or Fisher's exact test.

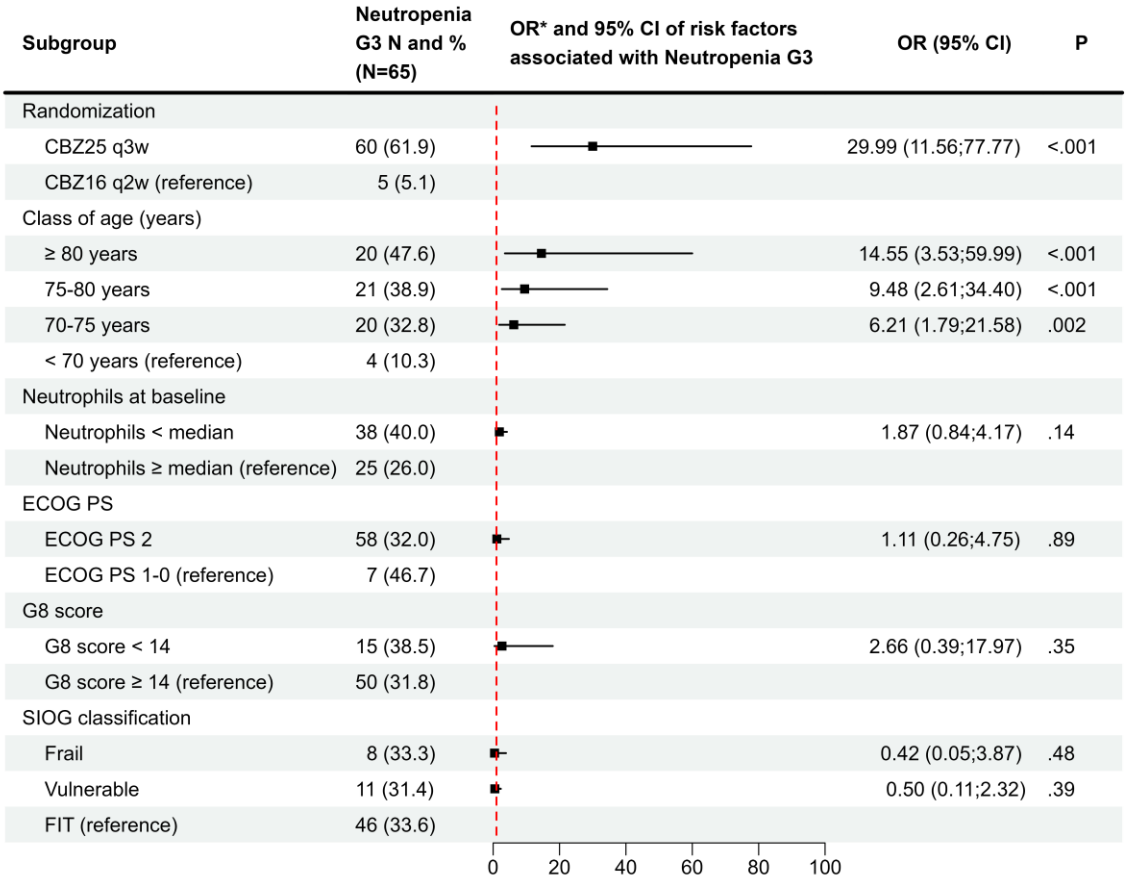
[b] Missing values < 5%.

eTable 3. First Occurrence of Grade ≥3 Neutropenia per Treatment Cycle (Safety Population)

Characteristic	CBZ25 q3w (n = 96)	CBZ16 q2w (n = 98)	Overall (n=194)
Patients with grade ≥ 3 neutropenia	60	5	65
Time to Nadir (days)	8	12	NA
Distribution per cycle of the 1st neutropenia episode			
Cycle 1	41	1	42
Cycle 2	9	2	11
Cycle 3	3	0	3
Cycle 4	2	0	2
Cycle 5	2	1	3
Cycle 6	0	0	0
Cycle 7	1	0	1
Cycle 8	1	0	1
Cycle 9	0	0	0
Cycle 10	1	1	1

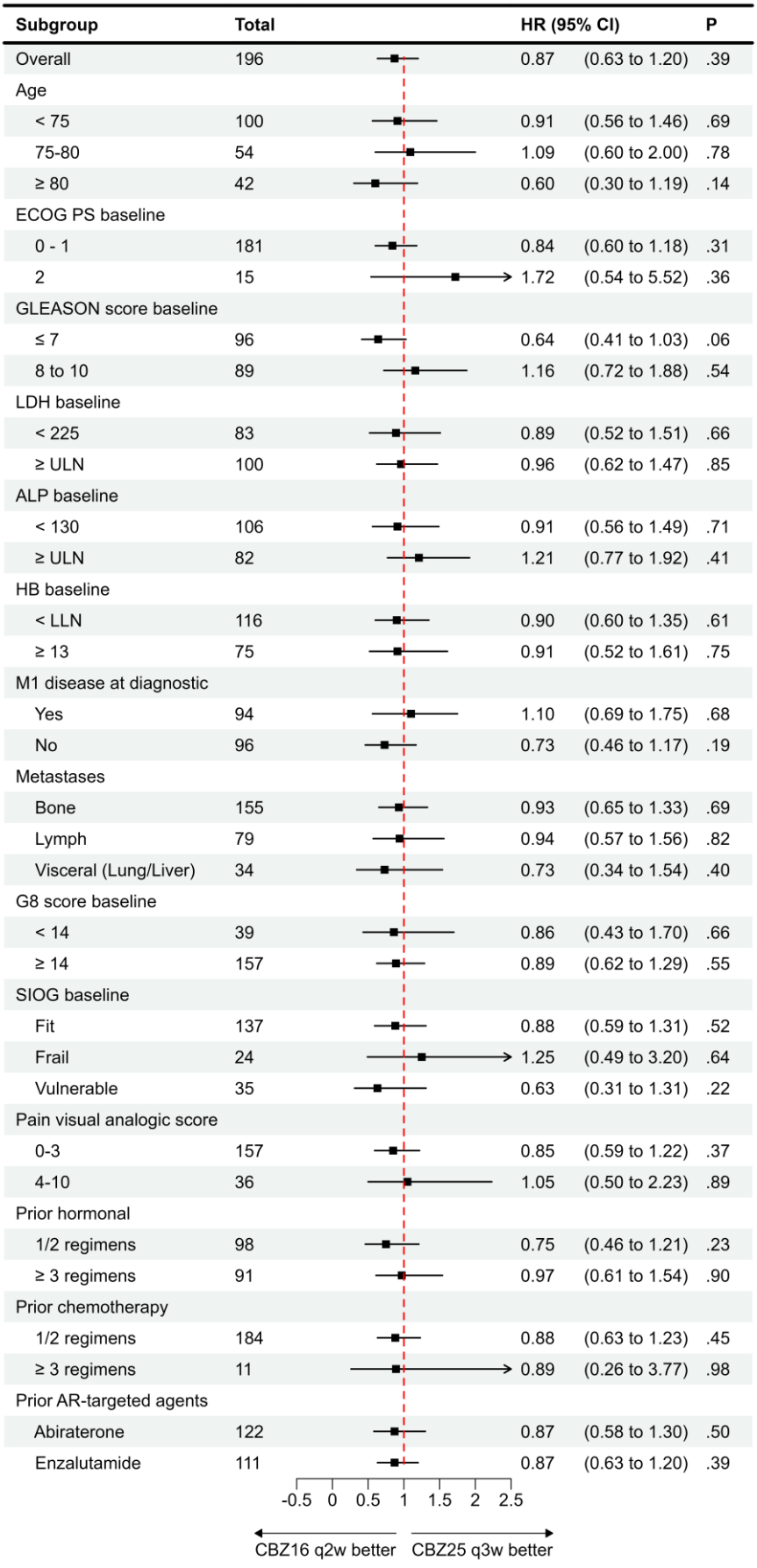
Abbreviations: CBZ25 q3w, triweekly cabazitaxel 25mg/m^2 ;CBZ16 q2w, biweekly cabazitaxel 16mg/m^2

eFigure 1. Forest Plot of Logistic Regression on Incidence of Grade ≥3 Neutropenia and/or Neutropenic Complications (Safety Population)



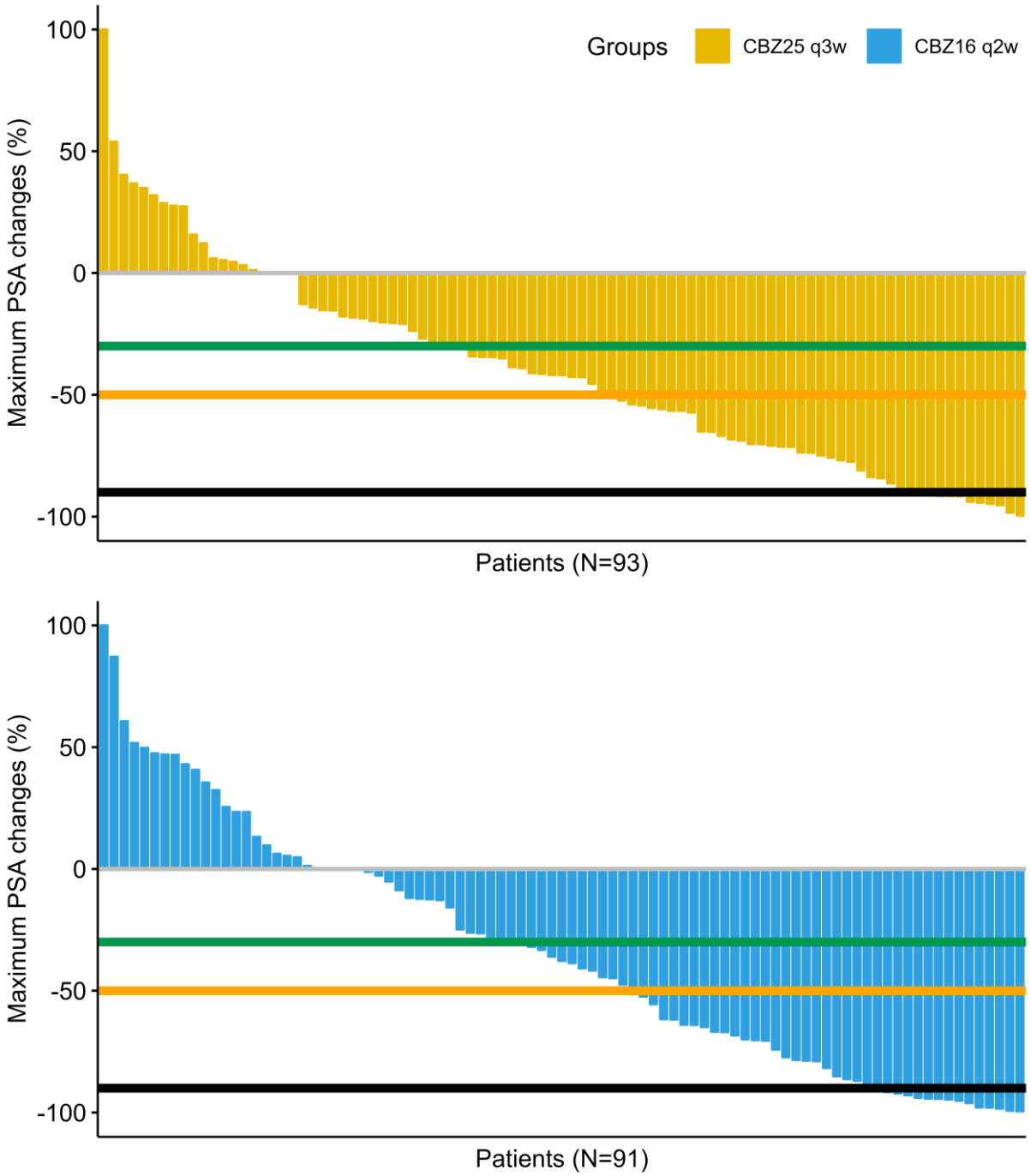
The probability to have a grade 3 neutropenia versus not was calculated using a Firth's Penalized Likelihood logistic regression, adjusted on randomization arm, neutrophils at baseline, SIOG classification, G8 score and class of age. [a]Each class of age was compared to the <70 years class. Abbreviations : CI: confidence interval; G3 : Grade 3 ; G8: geriatric-8; OR: Odds Ratio; ECOG PS : Eastern Cooperative Oncology Group Performance Status; SIOG: International Society of Geriatric Oncology.

eFigure 2. Forest Plot of Treatment Effect on Overall Survival (Intent-to-Treat Population)



Abbreviations: ALP, alkaline phosphatase; AR, androgen receptor; CBZ16 q2w, biweekly cabazitaxel 16mg/m^2; CBZ25 q3w, triweekly cabazitaxel 25mg/m^2; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; HB, hemoglobin; HR, hazard ratio; LDH, lactate dehydrogenase; LLN, lower limit of normal; SIOG, International Society of Geriatric Oncology;

eFigure 3. Waterfall Plot of the PSA Response



PSA response was evaluable in 184 patients (93 patients in the CBZ25 q3w arm and 91 in the CBZ16 q2w group). Patients with PSA level < 2ng/mL at baseline were excluded from this analysis.

eTable 4. Adverse Events (AEs) (Safety Population)

Event	CBZ25 q3w (n = 96)		CBZ16 q2w (n = 98)	
	Any grade	Grade ⩾ 3	**Any grade**	Grade ⩾ 3
Any AE – No. (%)	95 (99.0)	---	98 (100)	---
Any grade ⩾ 3 AE – No. (%)	---	70 (72.9)	---	55 (56.1)
Any serious AE – No. (%)	42 (43.8)	---	45 (45.9)	---
Any AE leading to permanent treatment discontinuation – no (%)	32 (33.3)	25 (26)	31 (31.6)	18 (18.4)
TEAEs leading to death within 30 days of CBZ – No. (%)	5 (5.2)	5 (5.2)	10 (10.2)	10 (10.2)
Common AE – No. (%)				
Fatigue	65 (67.7)	13 (13.5)	67 (68.4)	8 (8.2)
Diarrhea	57 (59.4)	4 (4.2)	54 (55.1)	6 (6.1)
Nausea or vomiting	28 (29.2)	0 (0.0)	41 (41.8)	1 (1.0)
Infection	28 (29.2)	7 (7.3)	37 (37.7)	11 (11.2)
Decreased appetite	29 (10.4)	2 (2.1)	28 (28.6)	1 (1.0)
Musculoskeletal pain or discomfort	22 (22.9)	1 (1.0)	34 (34.7)	0
Hematuria	19 (19.8)	0 (0.0)	32 (32.7)	2 (2.0)
Peripheral neuropathy	18 (18.7)	1 (1.0)	24 (24.4)	0 (0.0)
Constipation	19 (19.8)	0 (0.0)	22 (22.4)	0 (0.0)
Bladder and urethral symptoms	12 (12.5)	2 (2.0)	21 (21.4)	0 (0.0)
Abdominal pain	10 (10.4)	1 (1.0)	11 (10.2)	1 (1.0)
Stomatitis	9 (9.4)	0 (0.0)	10 (10.2)	0 (0.0)
Peripheral edema	10 (10.4)	1 (1.0)	8 (8.1)	0 (0.0)
Arthralgia	10 (10.4)	1 (1.0)	7 (7.1)	0 (0.0)
Dyspnea	10 (10.4)	2 (2.1)	4 (4.1)	1 (1.0)
Renal disorder	7 (7.3)	1 (1.0)	8 (8.1)	2 (2.0)
Alopecia	8 (8.3)	0 (0.0)	5 (5.1)	0 (0.0)
Cardiac and vascular disorder	6 (6.3)	2 (2.0)	6 (6.1)	4 (4.0)
Hypertensive disorder	3 (3.1)	0 (0.0)	6 (6.1)	0 (0.0)
Bone fracture	4 (4.2)	2 (2.0)	2 (2.0)	1 (1.0)
Nail disorder	5 (5.2)	1 (1.0)	1 (1.0)	0 (0.0)

Event	CBZ25 q3w (n = 96)		CBZ16 q2w (n = 98)	
	Any grade	Grade ⩾ 3	**Any grade**	Grade ⩾ 3
Hematologic TEAEs based on laboratory abnormalities, No./total (%)				
Anemia	95 (99.0)	15 (15.6)	97 (99.0)	14 (14.3)
Leukopenia	70 (72.9)	54 (56.2)	12 (12.2)	4 (4.1)
Neutropenia	93 (96.9)	60 (62.5)	78 (79.6)	5 (5.1)
Thrombocytopenia	96 (100.0)	4 (4.1)	96 (98.0)	1 (1.0)

Abbreviations: CBZ, cabazitaxel; CBZ16 q2w, biweekly cabazitaxel 16mg/m^2; CBZ25 q3w, triweekly cabazitaxel 25mg/m^2; TEAE, treatment emergent adverse event