2021 ASCO ANNUAL MEETING

Les « scoops » en oncologie gynécologique

Dr Coriolan Lebreton

Oncologie médicale – Institut Bergonié, Bordeaux

2021 ASCO ANNUAL MEETING

Optimal treatment duration of bevacizumab combined with carboplatin and paclitaxel in patients with primary epithelial ovarian, fallopian tube or peritoneal cancer

A prospective randomized Phase III ENGOT/GCIG Study of the AGO Study Group, GINECO, NSGO
AGO-OVAR 17 BOOST / GINECO OV118 / ENGOT Ov-15 / NCT01462890

Performed according to ENGOT Model A. Financial support and drug supply provided by F. Hoffmann-La Roche Ltd.

J. Pfisterer[1], F. Joly[2], G. Kristensen[3], J. Rau[4], S. Mahner[5], P. Pautier[6], A. El-Balat[7], J.-E. Kurtz[8], U. Canzler[9], J. Sehouli[10], M. L. Heubner[11], A. D. Hartkopf[12], K. Baumann[13], A. Hasenburg[14], L. Ch. Hanker[15], A. Belau[16], B. Schmalfeldt[17], D. Denschlag[18], T.-W. Park-Simon[19], P. Harter[20]

Rationnel de l'étude

BEVACIZUMAB 15 mois

- Standard traitement de première ligne des stades avancés (stades FIGO IIIB, IIIC et IV) du cancer épithélial de l'ovaire, des trompes de Fallope ou péritonéal primitif, en association avec chimiothérapie par carboplatine et paclitaxel
- Amélioration survie sans progression dans les études GOG-218 et AGO-OVAR11/ICON7 (1, 2)

Bénéfice max en survie sans progression au maximum à 12-15 mois

- Dans les 2 études

But de l'étude

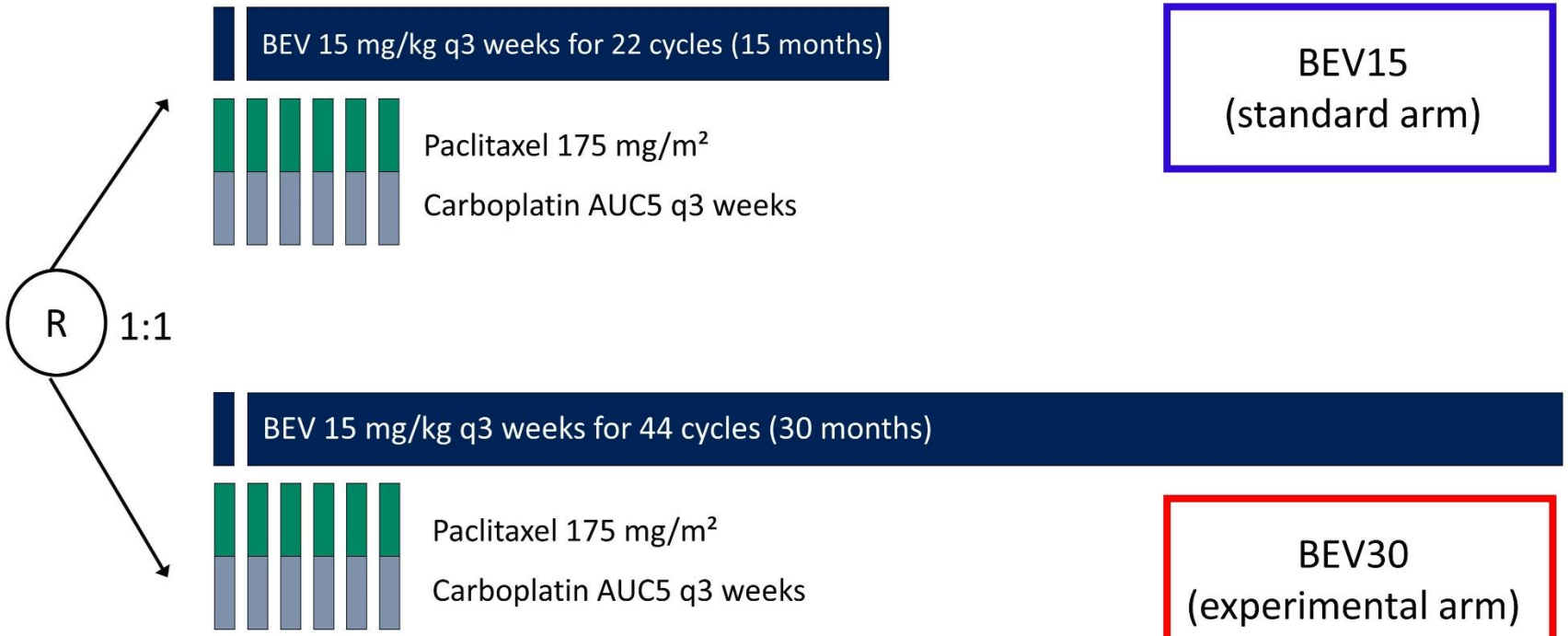
- Évaluer l'allongement du BEVACIZUMAB à 30 mois
- En terme d'efficacité

(1) Burger et al. N Engl J Med 2011
(2) Perren et al. N Engl J Med 2011

Design de l'étude

- Histologically confirmed epithelial ovarian, fallopian tube, or peritoneal cancer (excluding non-epithelial and borderline tumors)
- FIGO stage IIB–IV (any grade/ histologic subtype)
- Primary debulking surgery ≤8 weeks before treatment start, >4 weeks before first BEV dose
- Adequate coagulation parameters, bone marrow, liver, and renal function
- ECOG PS 0–2
- Standard BEV exclusion criteria

n= 927 Nov 2011 – Aug 2013



BEV15
(standard arm)

BEV30
(experimental arm)

Stratification factors

FIGO IIB–IIIC and no residual tumor
versus
FIGO IIB–IIIC with residual tumor *or* FIGO IV

Pfisterer et al. J Clin Oncol 39, 2021 (suppl 15; abstr 5501

Critères de jugement - Statistiques

Critère de jugement principal

- Survie sans progression selon RECIST 1.1 par évaluation de l'investigateur

Statistiques

- Tester la supériorité de BEV 30 à BEV 15
- Pour une puissance de 80%, nécessité d'inclure 900 patientes
- Devant un faible taux d'évènements, arrêt des inclusions après que 673 (97%) des 697 évènements ont été observés

Population à l'étude

Status: January 7th , 2021	BEV15	BEV30	Total
Intent-to-treat population, n	**464**	**463**	**927**
Withdrawn from study, n (%)			
Lost to follow-up	28 (6)	32 (7)	60 (7)
Withdrew consent	43 (9)	37 (8)	80 (9)
Died* , n (%)	257 (55)	277 (60)	534 (58)
Median follow-up, months**	84	86	85

* 2 pts in BEV30 group had missing date of death
** Reverse KM method

Pfisterer et al. J Clin Oncol 39, 2021 (suppl 15; abstr 5501

2021 ASCO ANNUAL MEETING

Population à l'étude

	BEV15 n=464	BEV30 n=463	Total n=927
Age, years			
Median (range)	61 (25–86)	60 (21–89)	61 (21–89)
ECOG performance status, n (%)			
0	236 (51)	266 (57)	502 (54)
1	205 (44)	181 (39)	386 (41)
2	23 (5)	16 (3)	39 (4)
Residual tumor, n (%)			
No	277 (60)	259 (56)	536 (58)
Yes	187 (40)	204 (44)	391 (42)
Histo-type/grading, n (%)			
High-grade serous	362 (78)	368 (79)	730 (79)
Other	102 (22)	95 (21)	197 (21)
Primary tumor type, n (%)			
Ovarian	388 (84)	388 (84)	776 (84)
Fallopian tube	35 (8)	39 (8)	74 (8)
Peritoneal	41 (9)	36 (8)	77 (8)
Stratum, n (%)			
FIGO IIB-IIIC and no residual tumor	236 (51)	230 (50)	466 (50)
FIGO IIB-IIIC with residual tumor *or* FIGO IV	228 (49)	233 (50)	461 (50)

Statut BRCA non disponible

Pfisterer et al.
J Clin Oncol 39,
2021 (suppl 15; abstr 5501)

2021 ASCO ANNUAL MEETING

Effets indésirables

	BEV15 n=448 n (%)	BEV30 n=442 n (%)	Total n=890 n (%)
Any AE	445 (99)	439 (99)	884 (99)
Serious AE	199 (44)	204 (46)	403 (45)
Grade 3-5 AE	282 (63)	300 (68)	582 (65)
AE and serious AE of special interest	145 (32)	168 (38)	313 (35)
Grade 5 AE	8 (2)	2 (1)	10 (1)

Pfisterer et al. J Clin Oncol 39, 2021 (suppl 15; abstr 5501)

2021 ASCO ANNUAL MEETING

Evènements indésirables d'intérêt particulier

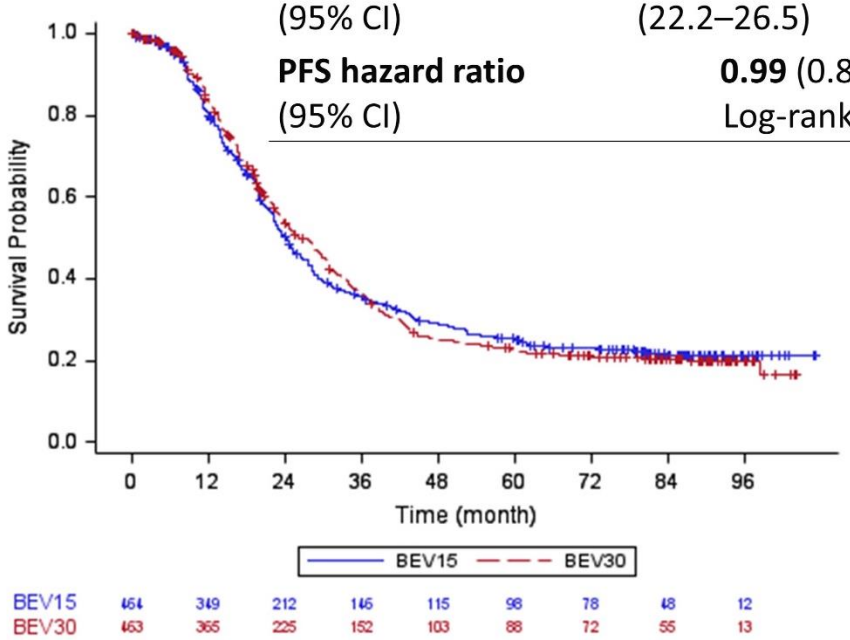
	BEV15 n=448 n (%)	BEV30 n=442 n (%)	Total n=890 n (%)
Hypertension, grade ≥ 3	88 (20)	109 (25)	197 (22)
Intestinal perforation/fistula, all grades	23 (5)	16 (4)	39 (4)
Thromboembolic events, grade ≥ 3	16 (4)	14 (3)	30 (3)
Proteinuria, grade ≥ 3	9 (2)	19 (4)	28 (3)
Myocardial infarction, grade ≥ 3	2 (0.4)	5 (1)	7 (1)
Wound dehiscence, grade ≥ 3	1 (0.2)	2 (0.5)	3 (0.3)
Posterior reversible encephalopathy syndrome, grade ≥ 3	2 (0.4)	0	2 (0.2)
Impaired wound healing, grade ≥ 3	1 (0.2)	1 (0.2)	2 (0.2)
Haemorrhage, grade ≥ 3	1 (0.2)	1 (0.2)	2 (0.2)
Stroke, grade ≥ 3	1 (0.2)	1 (0.2)	2 (0.2)
Acute coronary syndrome, grade ≥ 3	1 (0.2)	0	1 (0.1)

Pfisterer et al. J Clin Oncol 39, 2021 (suppl 15; abstr 5501)

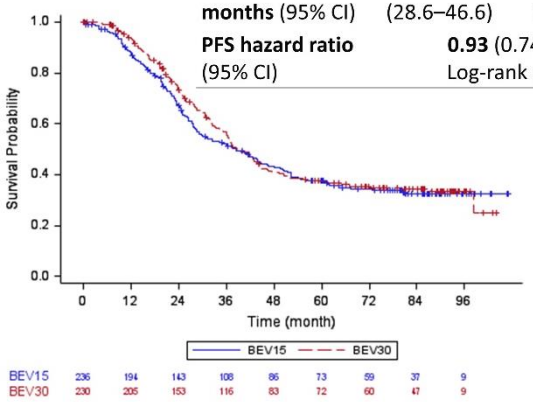
2021 ASCO ANNUAL MEETING

Critère de jugement principal : SSP

	BEV15 n=464	BEV30 n=463
PFS events, n (%)	333 (72)	340 (73)
Median PFS, months (95% CI)	**24.2** (22.2–26.5)	**26.0** (23.7–29.7)
PFS hazard ratio (95% CI)	**0.99** (0.85–1.15) Log-rank p=0.90	

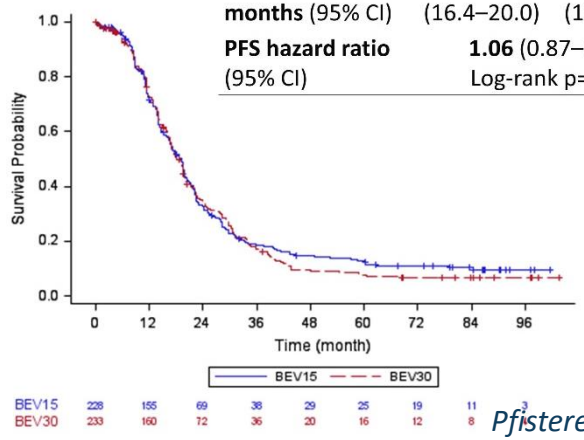


	BEV15 n=236	BEV30 n=230
PFS events, n (%)	142 (60)	139 (60)
Median PFS, months (95% CI)	**38.4** (28.6–46.6)	**38.8** (35.2–44.6)
PFS hazard ratio (95% CI)	**0.93** (0.74-1.18) Log-rank p=0.55	



Stades IIB-IIIC CC0

	BEV15 n=228	BEV30 n=233
PFS events, n (%)	191 (83)	201 (86)
Median PFS, months (95% CI)	**19.3** (16.4–20.0)	**18.2** (16.7–19.7)
PFS hazard ratio (95% CI)	**1.06** (0.87–1.29) Log-rank p=0.58	



Stades IIIC CC1-2 ou IV

Pfisterer et al. J Clin Oncol 39, 2021 (suppl 15; abstr 5501)

Conclusion essai BOOST

BEVACIZUMAB 30 mois est faisable

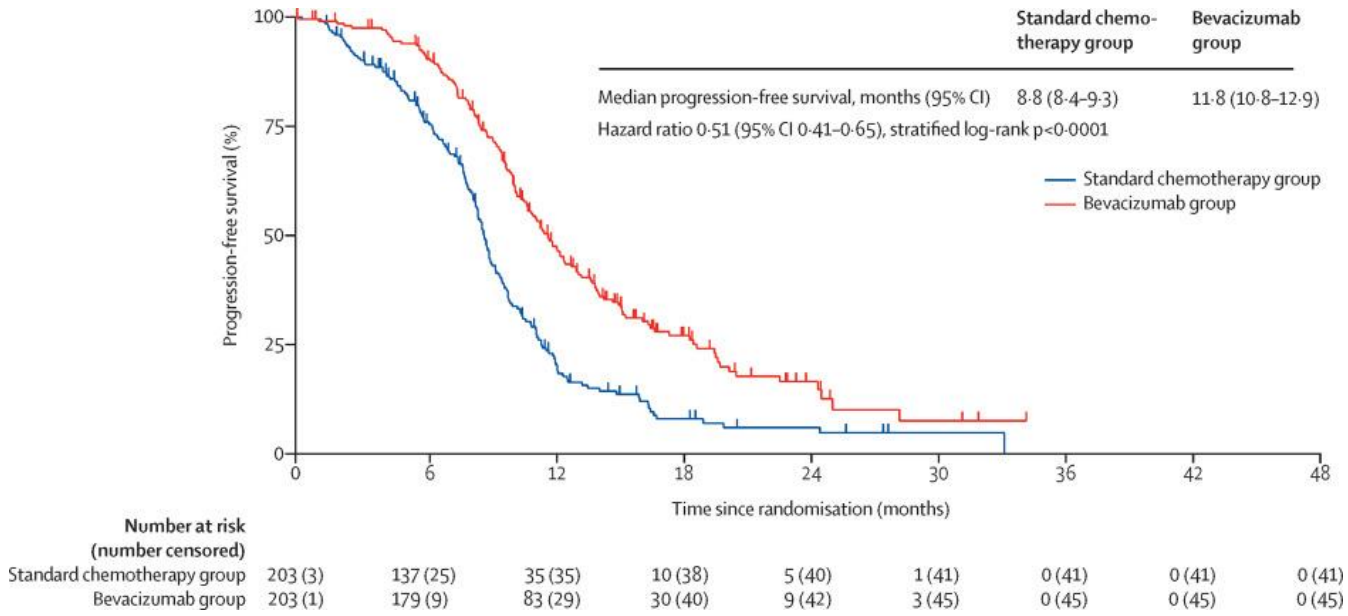
- Sans toxicité accrue
- Dans l'attente des analyses de QoL

Absence d'amélioration de la survie sans progression en prolongeant de 15 mois le bevacizumab

- SSP dans le bras standard 15 mois : environ 2 ans

Pas de changement de pratique

- Reste un traitement sur maladie tumorale macroscopique
- En primo traitement, en rechute platine sensible et résistante
- Quid du rechallenge?



Pignata et al. Lancet Oncol 2021

Pfisterer et al. J Clin Oncol 39, 2021 (suppl 15; abstr 5501)

2021 ASCO ANNUAL MEETING

VICTORIA: A MULTICENTRIC, RANDOMIZED, OPEN-LABEL, PHASE I/II OF VISTUSERTIB COMBINED WITH ANASTROZOLE IN PATIENTS WITH HORMONE RECEPTOR-POSITIVE ADVANCED OR RECURRENT ENDOMETRIAL CANCER

Heudel P, Frenel JS, Dalban C, Bazan F, Joly F, Arnaud A, Abdeddaim C, Chevalier A, Augereau P, Pautier P, Chakiba C, You B, Lancry Lecomte L, Garin G, Marcel V, Diaz JJ, Treilleux I, Pérol D, Fabbro M, Ray-Coquard I

Speaker : Dr Pierre HEUDEL, Léon Bérard cancer center, GINECO, Lyon, France

June 7, 2021

CENTRE DE LUTTE CONTRE LE CANCER LEON BERARD

ARCAGY - GINECO

Heudel et al. J Clin Oncol 39, 2021 (suppl 15; abstr 5507)

Rationnel

Dépendance aux œstrogènes des cancers de l'endomètre

- Surtout les types 1
- Avec des progressions à bas bruit, asymptomatiques

Hormonothérapie par anti-aromatase peut être considérée dans cette situation (1)

Altération moléculaire de *PTEN* et de la voie PI3K-AKT-mTOR (2)

Plusieurs études mono-bras avec inhibiteurs de PI3K/AKT/mTOR encourageantes (3)

Amélioration survie sans progression des inhibiteurs de mTOR dans les essais randomisés (4, 5)

- Mais pas de bénéfice en survie globale ou taux de réponse

VISTUSERTIB (AZD2014)

- Inhibiteur des deux complexes de mTOR (mTORC1 et mTORC2)

(1) Concin et al. Int J Gynecol Cancer 2021
(2) Slomovitz et al. Clin Cancer Res 2012
(3) Roncholato et al. Cochrane Database Syst Reviews 2019
(4) Aghajanian et al. Gyn Oncol 2018
(5) Oza et al. J Clin Oncol 2015

Design de l'étude

A multicenter, non-comparative, randomized, open label, Phase I/II

Eligibility criteria

- ER+ and/or PR+ advanced or recurrent endometrial cancer
- ≤ 1 prior CT and ≤ 2 prior endocrine therapy excluding aromatase inhibitor
- RECIST V1.1 evaluable disease
- ECOG PS 0 or 1
- Tumor lesion accessible for on-treatment biopsy (week 8)

R* 2:1

Vistusertib (125 mg BiD, 2d ON/5d OFF, po) **+ Anastrozole** (1 mg/d, po)

Anastrozole (1 mg/d, po)

Primary endpoint

Progression-free rate at 8 weeks (PFR-8W) centrally assessed

Secondary endpoints

- ORR, DoR, PFS, OS
- Safety (NCI-CTCAE V4.03)
- Translational researches

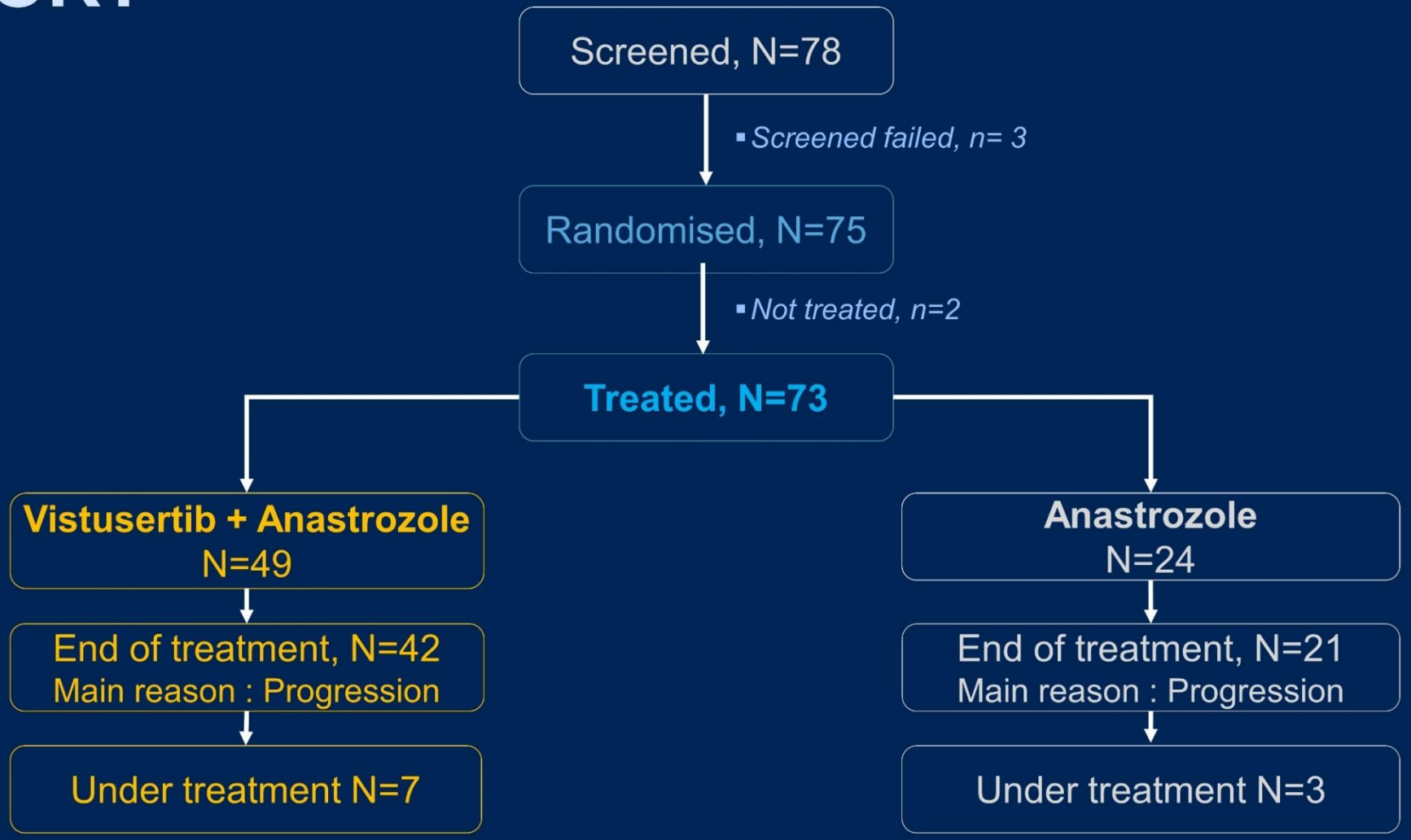
* Randomization was stratified by n° of prior CT line (0 vs. 1)

The planned sample size (n=46) in Vistusertib arm was based on a Simon's two-stage (optimal) design by using P_0: 40%; P_1: 60%, α: 0.05 and β: 0.20.

Decisions rules were the following: Stage I : PFR-8W ≥ 8/16 → Stage II ; Stage II: PFR-8W ≥ 24/46 → Further interest

Heudel et al. J Clin Oncol 39, 2021 (suppl 15; abstr 5507)

CONSORT



Heudel et al. J Clin Oncol 39, 2021 (suppl 15; abstr 5507)

2021 ASCO ANNUAL MEETING

Caractéristiques des patientes

Incidence, N (%)	Vistusertib + Anastrozole N=49		Anastrozole N=24	
Median age in years (min; max)	**70.8** (36.8; 87.0)		**68.7** (40.5; 87.8)	
BMI (kg/m²)				
BMI <25	15	(30.6%)	5	(20.8%)
BMI ≥25 et <30	15	(30.6%)	5	(20.8%)
BMI ≥30	19	(38.8%)	14	(58.3%)
ECOG				
0	26	(53.1%)	9	(37.5%)
1	23	(46.9%)	15	(62.5%)
FIGO stage				
III	10	(20.4%)	4	(16.7%)
IV	39	(79.6%)	20	(83.3%)
Endocrine receptors status				
ER+ / PR+	36	(73.5%)	19	(82.6%)
ER+ / PR-	10	(20.4%)	3	(13%)
ER- / PR+	3	(6.1%)	1	(4.3%)
Prior number of chemotherapy				
0	22	(44.9%)	10	(41.7%)
1	27	(55.1%)	14	(58.3%)
Prior number of endocrine therapy				
0	42	(85.7%)	22	(91.7%)
≥ 1	7	(14.3%)	2	(8.3%)

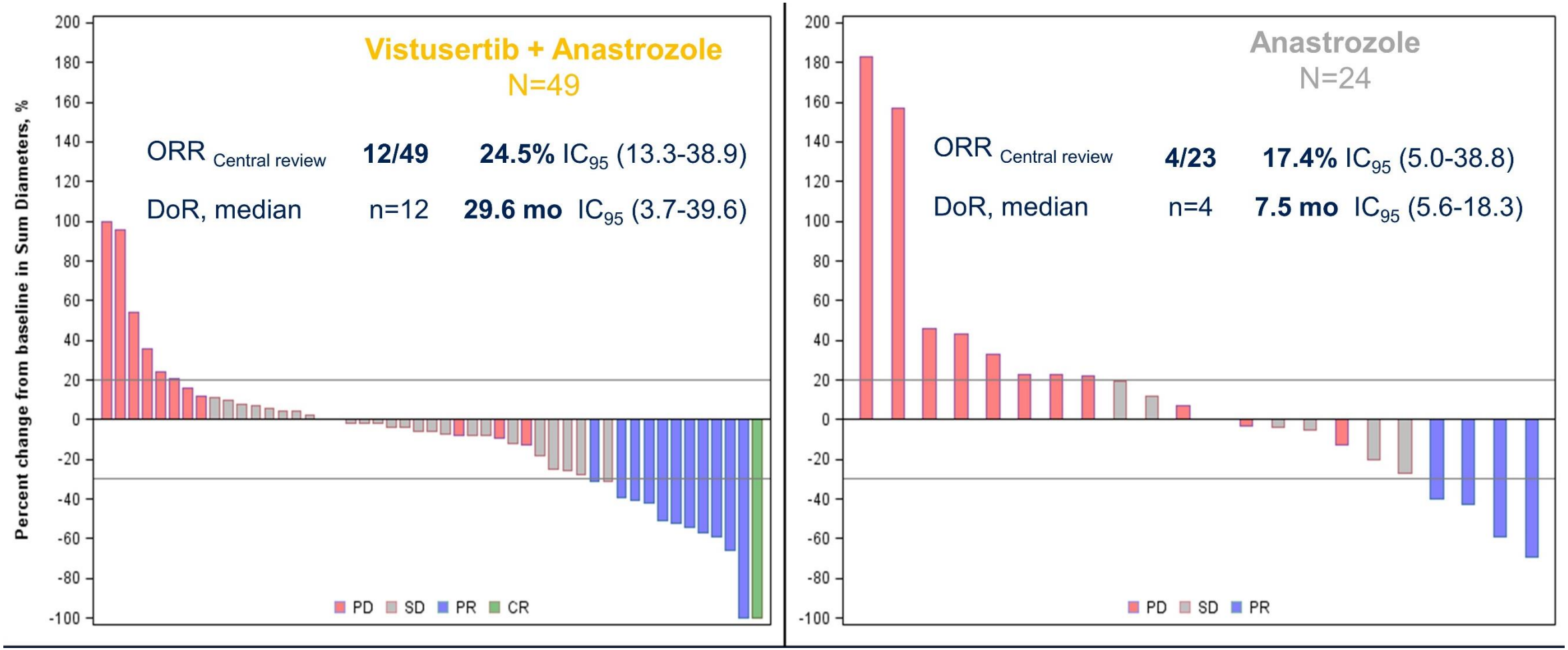
Heudel et al. J Clin Oncol 39, 2021 (suppl 15; abstr 5507)

Critère de jugement principal : taux de survie sans progression à 8 semaines

	Vistusertib + Anastrozole N=49		Anastrozole N=24	
PFR-8W central review	**33 / 49**	**(67.3%)**	**9 / 23**	**(39.1%)**
95% unilateral CI	[54.7% ; -]		[22.2% ; -]	
PFR-8W investigator	**34 / 49**	**(69.4%)**	**11 / 24**	**(45.8%)**
95% unilateral CI	[56.8% ; -]		[28.2% ; -]	

Heudel et al. J Clin Oncol 39, 2021 (suppl 15; abstr 5507)

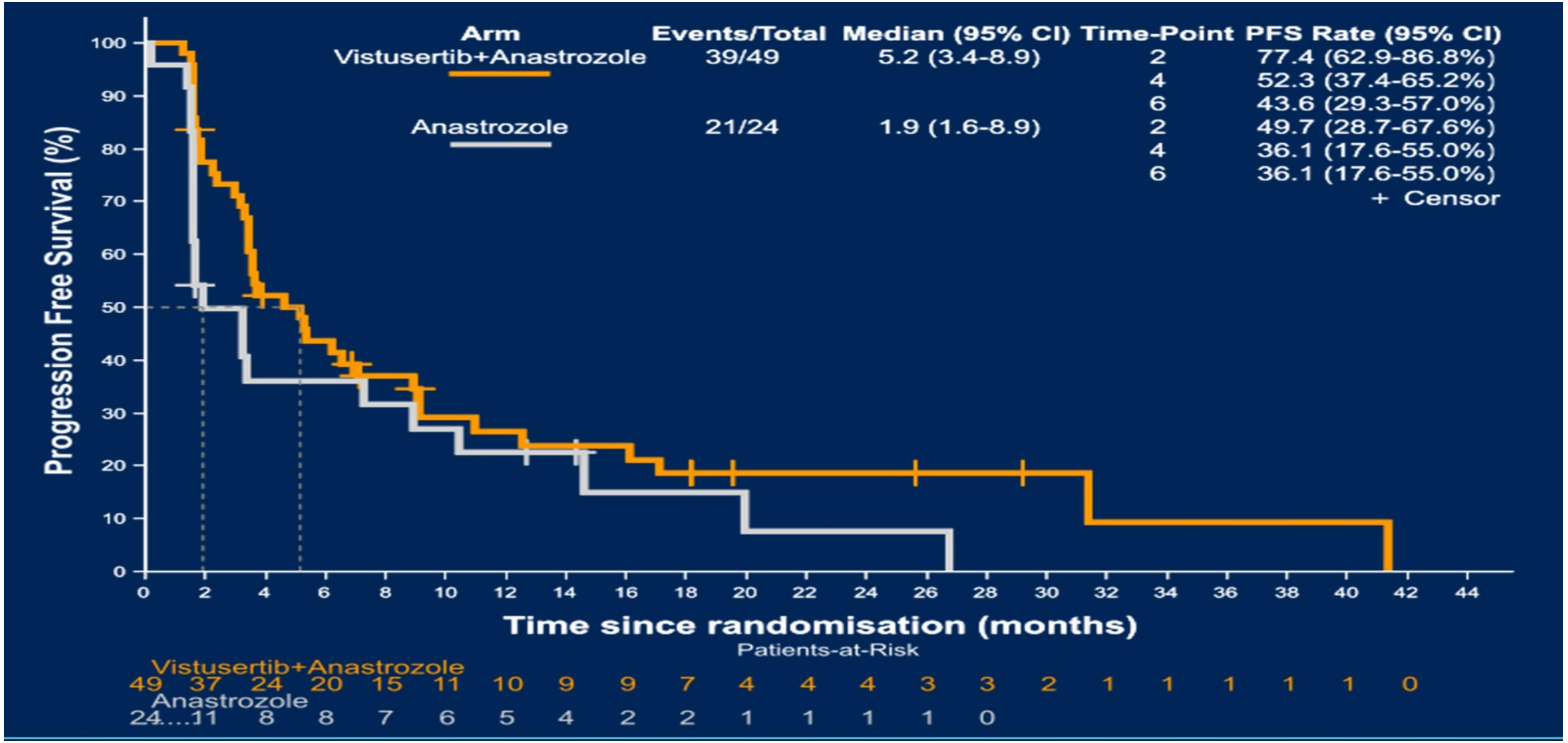
Critères de jugement secondaires : ORR et DoR



Heudel et al. J Clin Oncol 39, 2021 (suppl 15; abstr 5507)

2021 ASCO ANNUAL MEETING

Critères de jugement secondaires : PFS



Heudel et al. J Clin Oncol 39, 2021 (suppl 15; abstr 5507)

Effets indésirables

Incidence, N (%)	Vistusertib + Anastrozole N=49		Anastrozole N=24	
Grade	Any	3/4	Any	3/4
Nausea	25 (51.0%)	1 (2.0%)	2 (8.3%)	0 (0.0%)
Fatigue	34 (69.4%)	4 (8.2%)	7 (29.2%)	0 (0.0%)
Vomiting	11 (22.4%)	1 (2.0%)	1 (4.2%)	0 (0.0%)
Diarrhea	20 (40.8%)	1 (2.0%)	3 (12.5%)	0 (0.0%)
Arthralgia	11 (22.4%)	0 (0.0%)	7 (29.2%)	0 (0.0%)
Lymphocytes count decreased	17 (34.7%)	10 (20.4%)	3 (12.5%)	2 (8.3%)
Hyperglycemia	15 (30.6%)	6 (12.2%)	2 (8.3%)	0 (0.0%)
Anemia	13 (26.5%)	2 (4.1%)	1 (4.2%)	0 (0.0%)
At least one serious AE	20 (40.8%)		3 (12.5 %)	
At least one SAE related to VISTUSERTIB				
- Sponsor	10 (20,4%)		-	
- Investigator	11 (22,4%)		-	

Heudel et al. J Clin Oncol 39, 2021 (suppl 15; abstr 5507)

Conclusion

Malgré des résultats encourageants

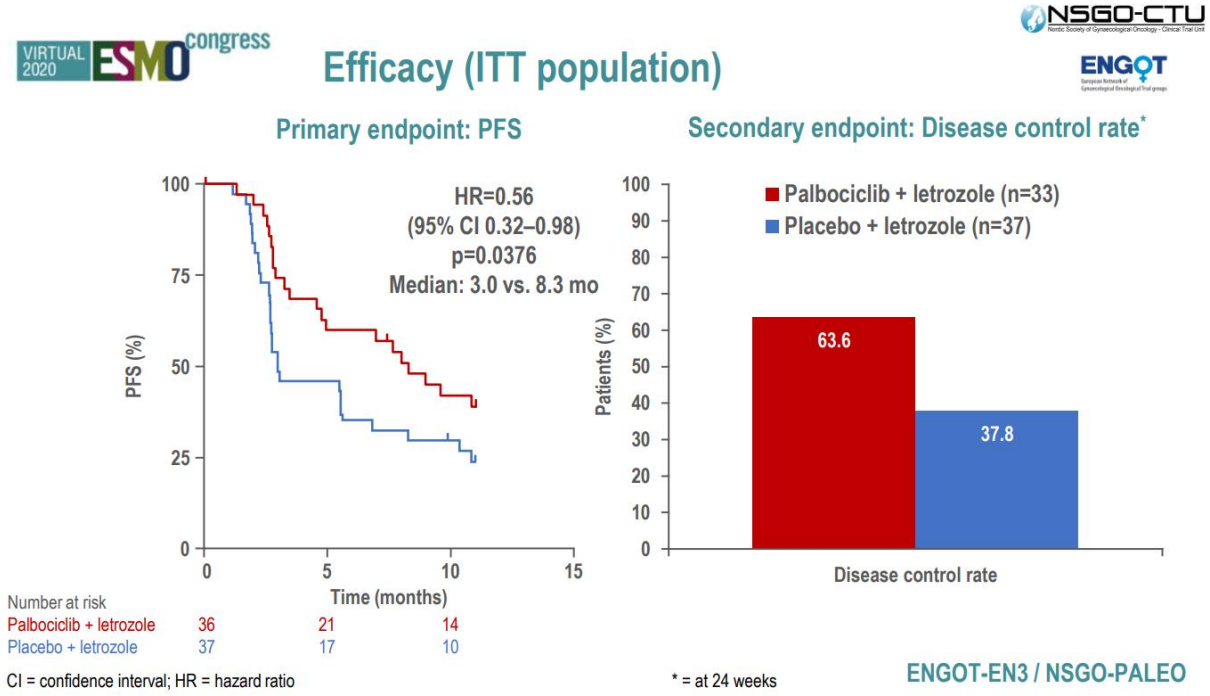
- PFR-8w 67%, mPFS 5,2 mois, ORR 24.5% et mDoR 29,6 mois
- EI manageables : hyperglycémie, lymphopénie, nausées, diarrhées

Développement du VISTUSERTIB stoppé

Analyses ancillaires en cours

- Sous groupe de population pouvant bénéficier de schémas sans chimiothérapie

Quid des associations avec des inhibiteurs de CDK4-6?



Mirza et al. ESMO 2020