2022 ASCO ANNUAL MEETING

Les « Scoops » en Oncologie Gynécologique

Dr Coriolan LEBRETON

Oncologie médicale - Institut Bergonié Bordeaux

Liens d'intérêts

- Orateur pour un laboratoire pharmaceutique :
  - Clovis, Eisai
- Prise en charge par un laboratoire pharmaceutique de la participation à un congrès national ou international :
  - Amgen, Chugai, Eisai, Pfizer, GSK
- Consultant : Non
- Investigateur principal d'un essai de l'industrie pharmaceutique: Non
- Parts sociales ou action dans un laboratoire pharmaceutique : Non

2022 ASCO ANNUAL MEETING

ATHENA–MONO (GOG-3020/ENGOT-ov45): A Randomized, Double-blind, Phase 3 Trial Evaluating Rucaparib Monotherapy Vs Placebo As Maintenance Treatment Following Response To First-line Platinum-based Chemotherapy In Ovarian Cancer

Bradley J. Monk,[1] Christine Parkinson,[2] Myong Cheol Lim,[3] David M. O'Malley,[4] Ana Oaknin,[5] Michelle K. Wilson,[6] Robert L. Coleman,[7] Domenica Lorusso,[8] Amit Oza,[9] Sharad Ghamande,[10] Athina Christopoulou,[11] Emily Prendergast,[12] Fuat Demirkiran,[13] Ramey D. Littell,[14] Anita Chudecka-Głaz,[15] Mark A. Morgan,[16] Sandra Goble,[17] Stephanie Hume,[17] Keiichi Fujiwara,[18] Rebecca S. Kristeleit[19]

[1]GOG Foundation, HonorHealth Research Institute, University of Arizona College of Medicine, Creighton University School of Medicine, Phoenix, AZ, USA; [2]Addenbrooke's Hospital, Cambridge, UK; [3]National Cancer Center Korea, Goyang-si, Gyeonggi-do, Republic of Korea; [4]The Ohio State University, James Cancer Center, Columbus, OH, USA; [5]Vall d'Hebron Institute of Oncology (VHIO), Hospital Universitari Vall d'Hebron, Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain; [6]Auckland City Hospital, Auckland, New Zealand; [7]US Oncology Research, The Woodlands, TX, USA; [8]MITO and Fondazione Universitario A. Policlinico Gemelli IRCCS and Catholic University of Sacred Heart, Rome, Italy; [9]Princess Margaret Hospital Cancer Centre, Toronto, Ontario, Canada; [10]Augusta University, Augusta, GA, USA; [11]St. Andrews General Hospital, Patras, Greece; [12]Minnesota Oncology and Metro-Minnesota Community Oncology Research Consortium, Minneapolis, MN, USA; [13]Istanbul University, Cerrahpaşa, Istanbul, Turkey; [14]Kaiser Permanente Northern California Gynecologic Cancer Program, San Francisco, CA, USA; [15]Pomeranian Medical University, Szczecin, Poland; [16]University of Pennsylvania Health System, Philadelphia, PA, USA; [17]Clovis Oncology, Inc., Boulder, CO, USA; [18]Saitama Medical University International Medical Center, Hidaka, Saitama, Japan; [19]Guy's and St Thomas' NHS Foundation Trust, London, UK

PRESENTED BY:
Bradley J. Monk, MD, FACS, FACOG (LBA5500)

Background

Rucaparib

- bénéfice en SSP en maintenance de rechute platine sensible quelque soit le statut BRCA/HRD-LOH (1)

Inhibiteurs de PARP augmentent la SSP en primo-maintenance

- avec un bénéfice variable en fonction du statut BRCA/HRD (2-5)

Schéma de maintenance encore imparfait

- en fonction du statut HRD
- place du bevacizumab?
- place des anti-PD-(L)1?

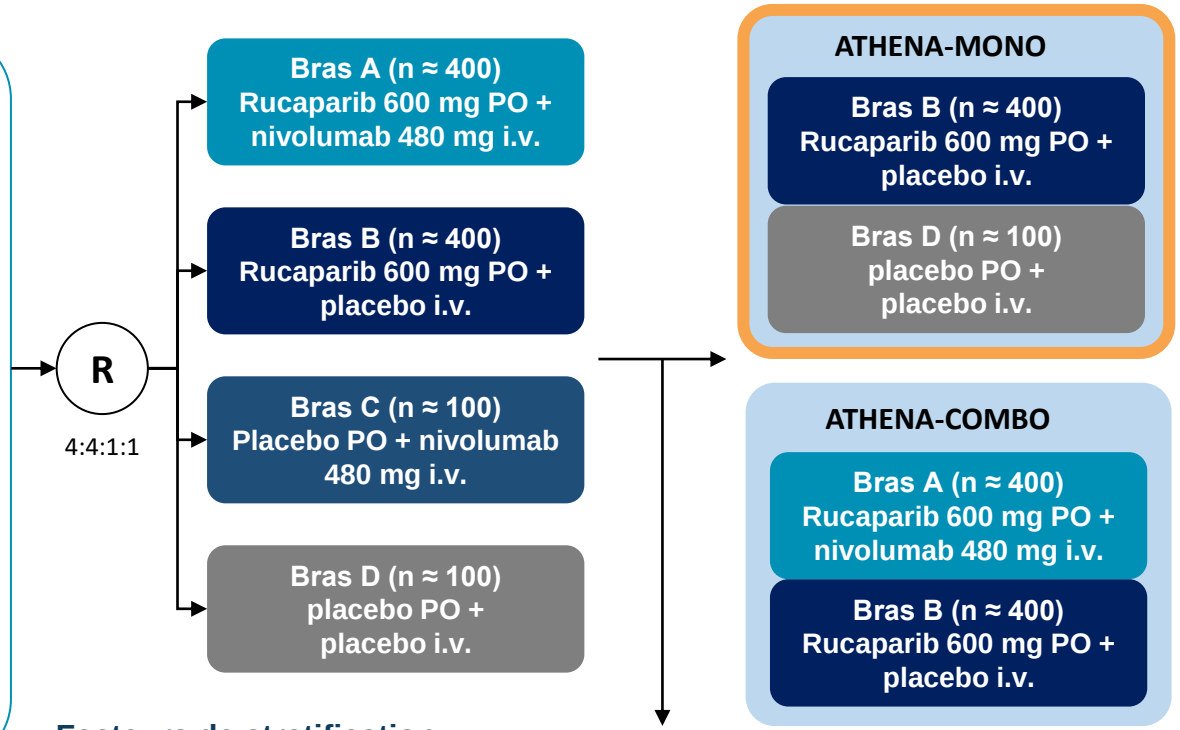
Essai ATHENA : international, randomisé, contre placebo, en double-aveugle, évaluant le Rucaparib en primo-maintenance

(1) Coleman et al. Lancet 2017
(2) Moore et al. N Engl J Med 2018
(3) Gonzalez-Martin et al. N Engl J Med 2019
(4) Ray-Coquard et al. N Engl J Med 2019
(5) Banerjee et al. Lancet Oncol 2021

schéma de l'étude

Critères d'éligibilité

- Cancer de l'ovaire épithélial avancé (stade FIGO III-IV) nouvellement diagnostiqué, trompe de Fallope ou cancer primitif du péritoine
- Chimiothérapie de première ligne à base de doublets de platine et une intervention chirurgicale
  - Obtention d'une RC ou RP évaluée par l'investigateur
  - Chirurgie cytoréductrice (primaire ou d'intervalle; R0/résection complète autorisée)
- Statut ECOG 0 ou 1
- Aucun traitement antérieur pour le cancer de l'ovaire, y compris tout traitement d'entretien autre que le régime de platine de première ligne



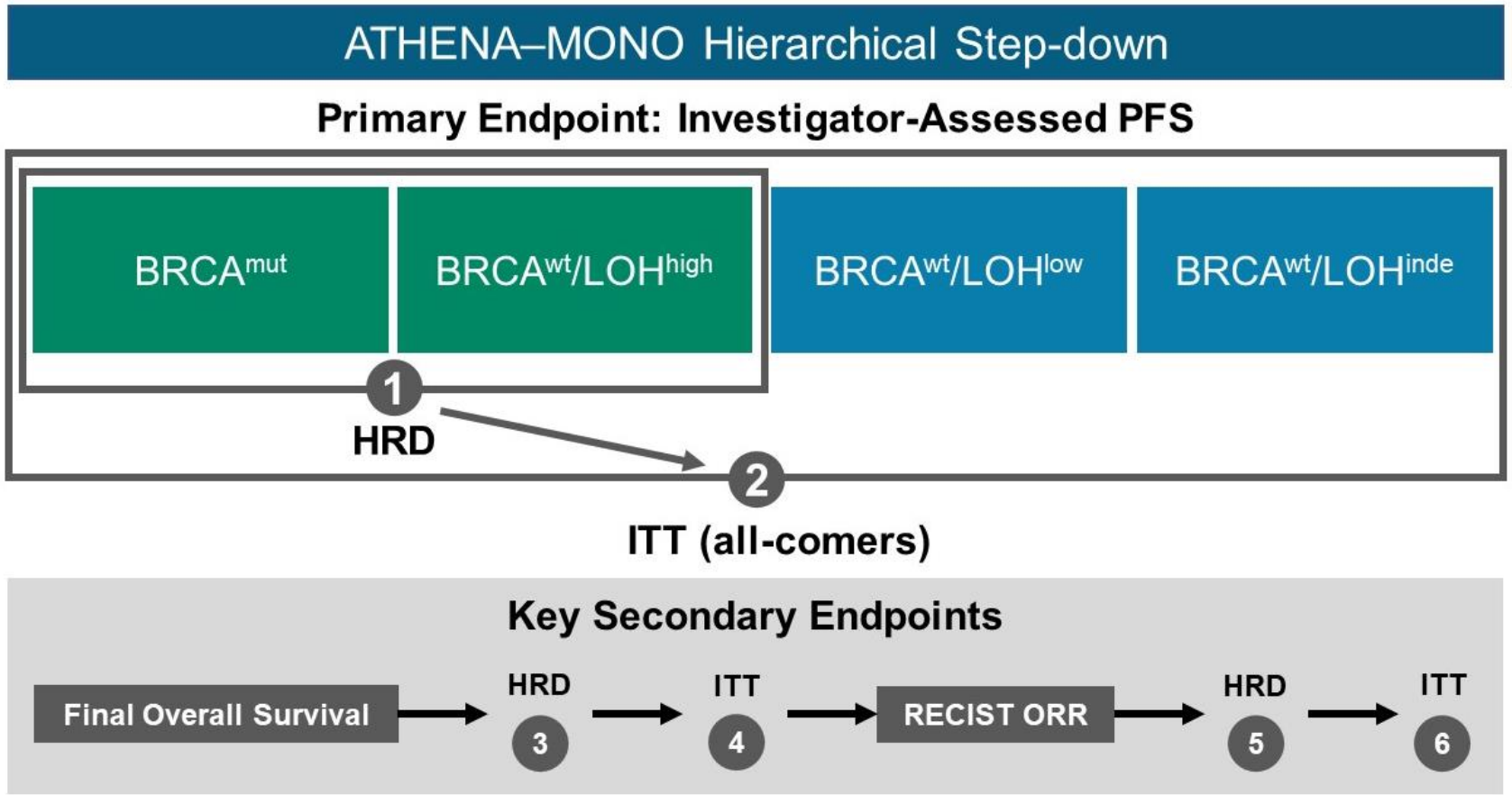
Facteurs de stratification

- Statut HRD
- Réponse après chimiothérapie
- Moment de la chirurgie

Traitement pendant 24 mois, ou jusqu'à progression radiographique, toxicité inacceptable, ou autre raison d'arrêt

Monk et al. J Clin Oncol 2022 (abstr LBA5500)

Statistiques



- 90% power at a two-sided significance level of 0.025
- Sample size assumptions for primary endpoint:

	HR	Median PFS, mo (Rucaparib vs Placebo)
HRD	0.45	26.7 vs 12.0
ITT	0.60	20.0 vs 12.0

- BICR-assessed PFS is a stand-alone secondary efficacy endpoint outside of the step-down analysis

BICR, blinded independent central radiology review; BRCA, *BRCA1* or *BRCA2*; HR, hazard ratio; HRD, homologous recombination deficiency; inde, indeterminate; ITT, intent-to-treat; LOH, loss of heterozygosity; mut; mutant; ORR, objective response rate; PFS, progression-free survival; RECIST, Response Evaluation Criteria In Solid Tumors, version 1.1; wt, wild type

Monk et al. J Clin Oncol 2022 (abstr LBA5500)

Résultats – Population à l'étude

Characteristic	HRD Population		ITT Population	
	Rucaparib n=185	Placebo n=49	Rucaparib n=427	Placebo n=111
Randomization stratification factors, n (%)[a]				
Timing of surgery				
Primary surgery	104 (56.2)	27 (55.1)	209 (48.9)	54 (48.6)
Interval debulking	81 (43.8)	22 (44.9)	218 (51.1)	57 (51.4)
Disease status post-chemotherapy				
No residual disease	137 (74.1)	35 (71.4)	322 (75.4)	82 (73.9)
Residual disease	48 (25.9)	14 (28.6)	105 (24.6)	29 (26.1)
HRD test status				
HRD positive				
$BRCA^{mut}$	91 (49.2)	24 (49.0)	91 (21.3)	24 (21.6)
$BRCA^{wt}/LOH^{high}$	94 (50.8)	25 (51.0)	94 (22.0)	25 (22.5)
HRD negative				
$BRCA^{wt}/LOH^{low}$	0	0	189 (44.3)	49 (44.1)
HRD unknown				
$BRCA^{wt}/LOH^{indeterminate}$	0	0	53 (12.4)	13 (11.7)
Measurable disease at baseline, n (%)	17 (9.2)	5 (10.2)	41 (9.6)	11 (9.9)

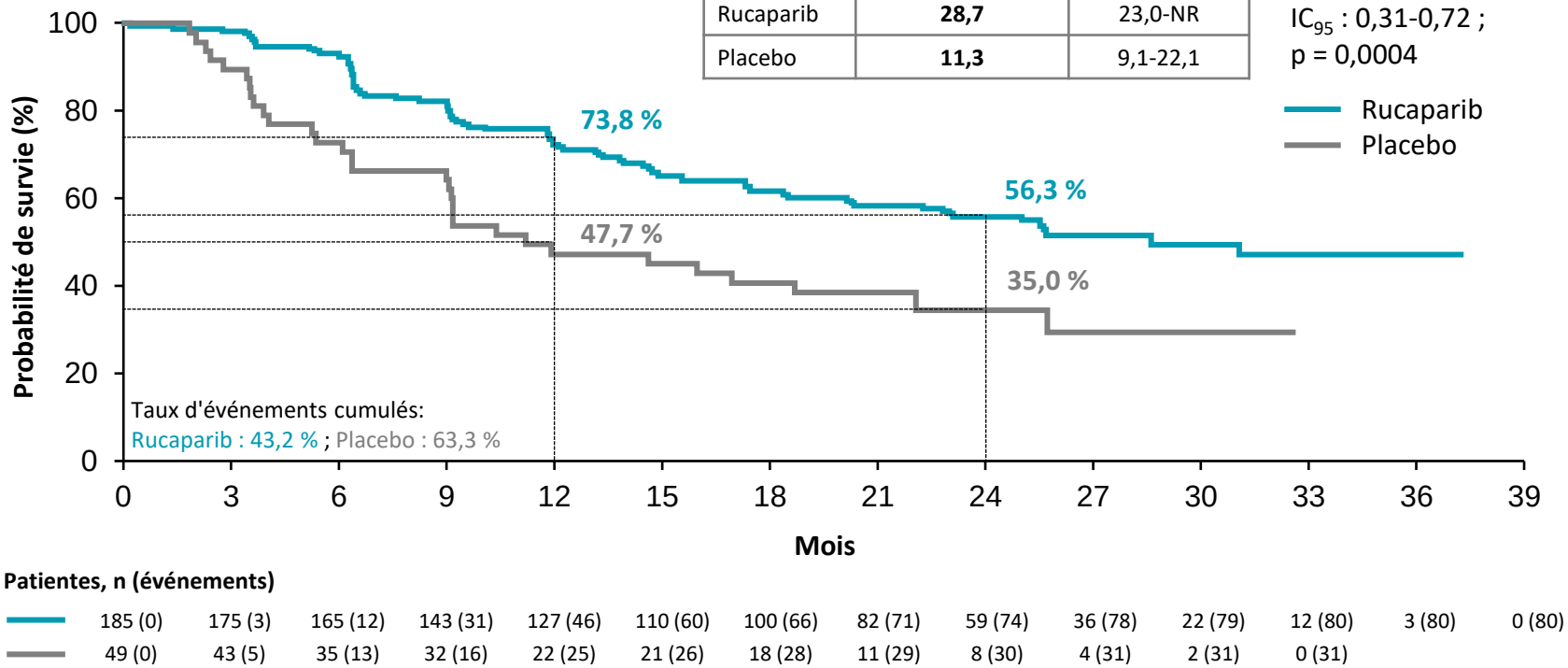
Data cutoff date: March 23, 2022. [a]As entered by investigators at the time of randomization.
BRCA, *BRCA1* or *BRCA2*; HRD, homologous recombination deficiency; ITT, intent-to-treat; LOH, loss of heterozygosity; mut, mutant; wt, wild type.

Monk et al. J Clin Oncol 2022 (abstr LBA5500)

Critère de jugement principal SSP dans la population HRD

	SSP médiane	IC_{95}
Rucaparib	**28,7**	23,0-NR
Placebo	**11,3**	9,1-22,1

HR = 0,47 ;
IC_{95} : 0,31-0,72 ;
p = 0,0004



Patientes, n (événements)

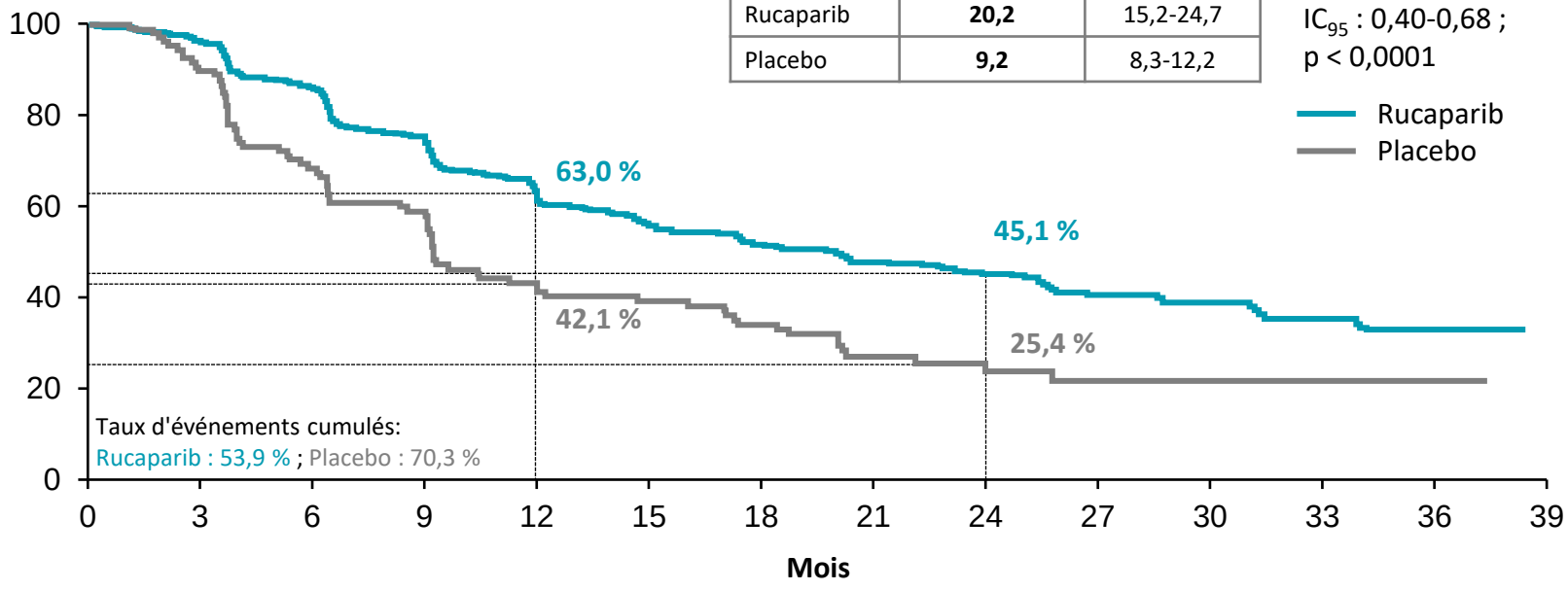
Rucaparib	185 (0)	175 (3)	165 (12)	143 (31)	127 (46)	110 (60)	100 (66)	82 (71)	59 (74)	36 (78)	22 (79)	12 (80)	3 (80)	0 (80)
Placebo	49 (0)	43 (5)	35 (13)	32 (16)	22 (25)	21 (26)	18 (28)	11 (29)	8 (30)	4 (31)	2 (31)	0 (31)		

Monk et al. J Clin Oncol 2022 (abstr LBA5500)

Critère de jugement principal SSP dans la population ITT

	SSP médiane	IC_{95}
Rucaparib	**20,2**	15,2-24,7
Placebo	**9,2**	8,3-12,2

HR = 0,52 ;
IC_{95} : 0,40-0,68 ;
p < 0,0001



Rucaparib	427 (0)	398 (15)	351 (57)	298 (101)	245 (149)	213 (176)	190 (193)	151 (207)	114 (214)	67 (224)	42 (226)	23 (229)	7 (230)	0 (230)
Placebo	111 (0)	97 (11)	72 (34)	60 (44)	42 (61)	39 (64)	31 (69)	18 (75)	14 (76)	8 (78)	5 (78)	3 (78)	1 (78)	0 (78)

Monk et al. J Clin Oncol 2022 (abstr LBA5500)

Analyses en sous groupes de SSP

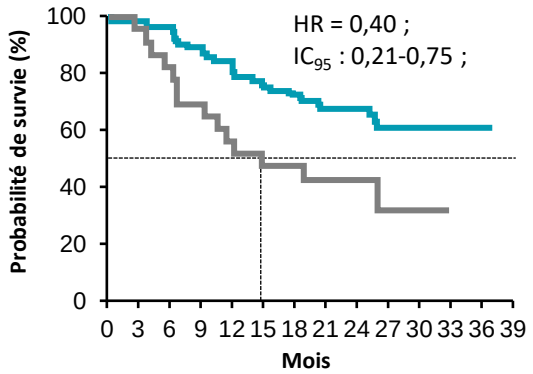
HRD positif

HRD négatif

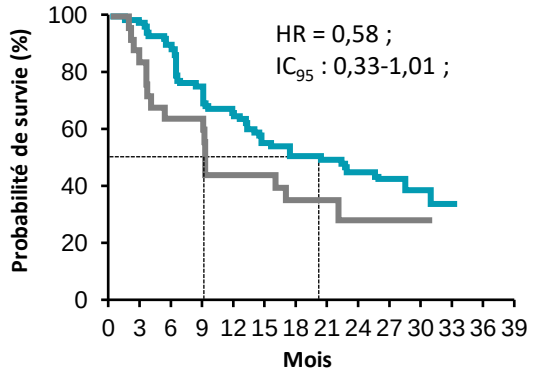
BRCA^{mut}

BRCA^{wt}/LOH^{high}

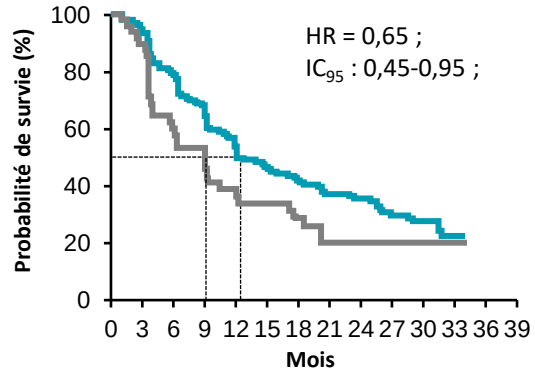
BRCA^{wt}/LOH^{low}



	Médiane	IC_{95}
Rucaparib	NR	25,8-NR
Placebo	14,7	6,4-NR



	Médiane	IC_{95}
Rucaparib	20,3	13,4-31,1
Placebo	9,2	4,0-22,1



	Médiane	IC_{95}
Rucaparib	12,1	11,1-17,7
Placebo	9,1	4,0-12,2

Le rucaparib a démontré un avantage thérapeutique par rapport au placebo, indépendamment du statut BRCA et du statut HRD

Monk et al. J Clin Oncol 2022 (abstr LBA5500)

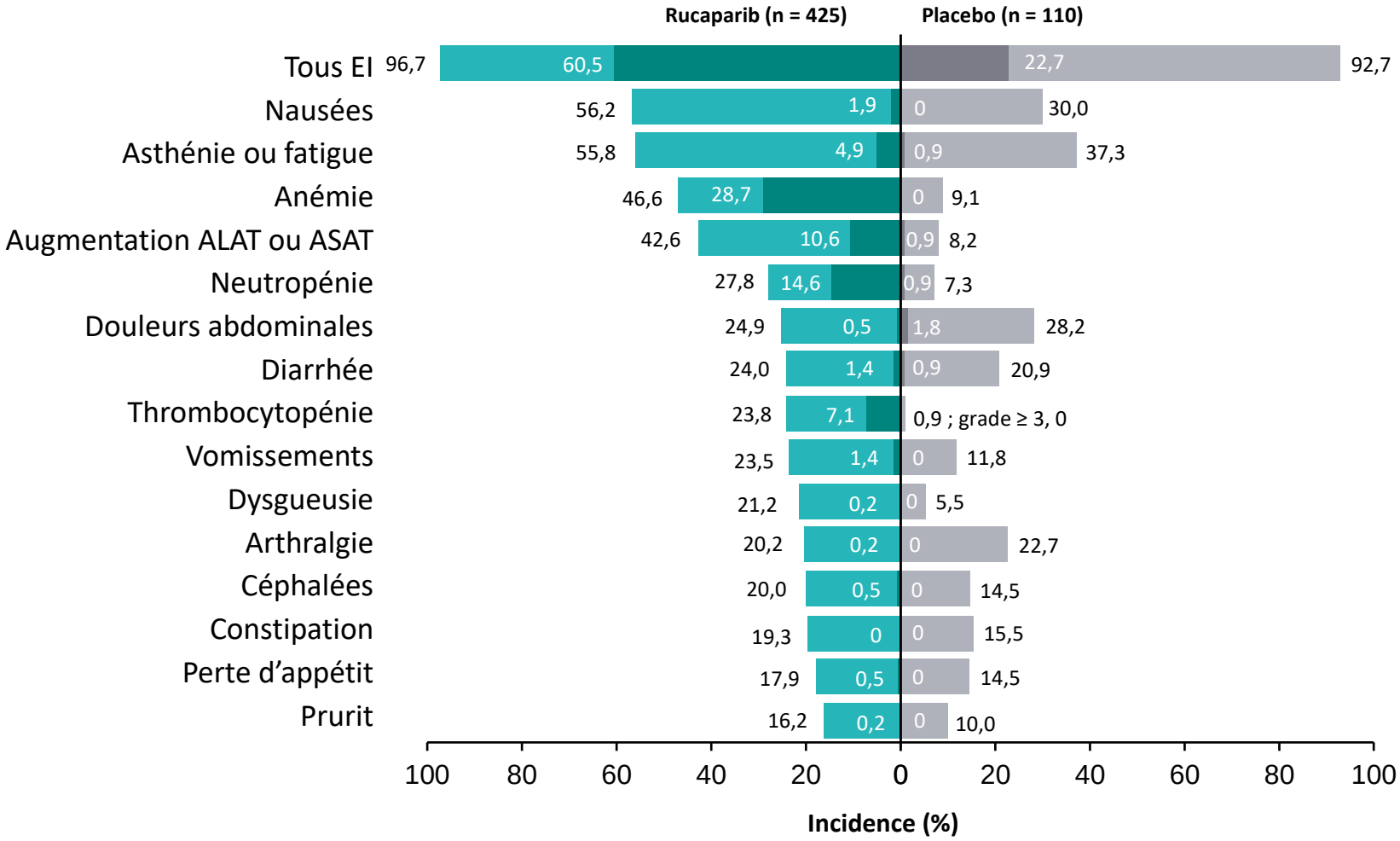
Taux de réponse sur maladie résiduelle

	HRD Population		ITT Population	
	Rucaparib	Placebo	Rucaparib	Placebo
Measurable disease at baseline, n/N (%)	**17/185 (9.2)**	**5/49 (10.2)**	**41/427 (9.6)**	**11/111 (9.9)**
Confirmed ORR per RECIST, n/N (% [95% CI])	**10/17 (58.8 [32.9–81.6])**	**1/5 (20.0 [0.5–71.6])**	**20/41 (48.8 [32.9–64.9])**	**1/11 (9.1 [0.2–41.3])**
Complete response, n (%)	0	0	1 (2.4)	0
Partial response, n (%)	10 (58.8)	1 (20.0)	19 (46.3)	1 (9.1)
Stable disease, n (%)	6 (35.3)	2 (40.0)	10 (24.4)	4 (36.4)
Progressive disease, n (%)	1 (5.9)	2 (40.0)	10 (24.4)	6 (54.5)
Not evaluable, n (%)	0	0	1 (2.4)	0
Duration of response				
Median, months (95% CI)	16.7 (5.7–NR)	5.5 (NA)	22.1 (8.4–NR)	5.5 (NA)

Data cutoff date: March 23, 2022.
HRD, homologous recombination deficiency; ITT, intent-to-treat; NA, not applicable (only 1 responder); NR, not reached; ORR, objective response rate; RECIST, Response Evaluation Criteria In Solid Tumors, version 1.1.

Monk et al. J Clin Oncol 2022 (abstr LBA5500)

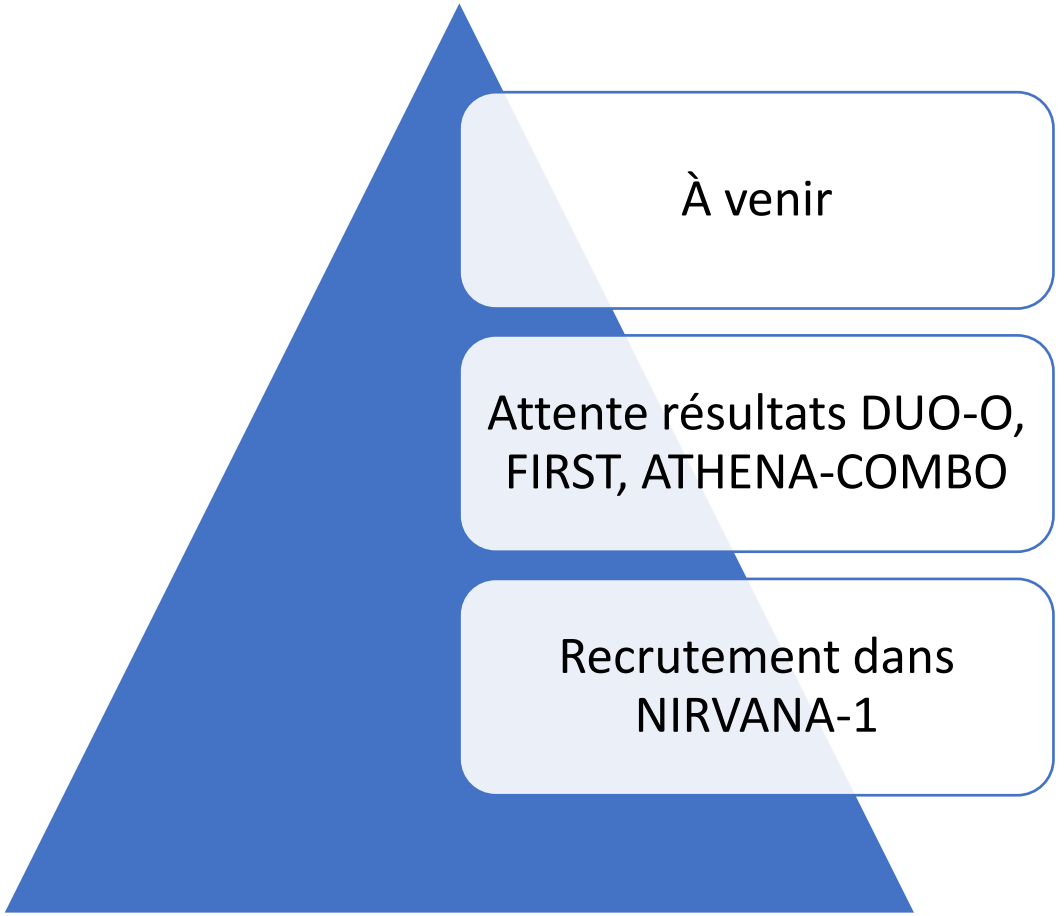
Effets indésirables ≥ 15%



Monk et al. J Clin Oncol 2022 (abstr LBA5500)

Conclusion

- Efficacité du Rucaparib quelque soit le statut HRD/LOH
- Bénéfice sur maladie résiduelle
- Un nouveau dans la galaxie des PARP inhibiteurs?
- Attente des résultats de combo avec anti-PD-1
- Place du Bevacizumab?



2022 ASCO ANNUAL MEETING

Conclusion

ONCO NOUVELLE-AQUITAINE Réseau Régional de Cancérologie

BRIO BORDEAUX | Recherche Intégrée Oncologie

Primo-Maintenance après réponse aux Platines

Etude	SOLO1[1, 2]	PRIMA[3]			ATHENA-MONO[4]			PAOLA-1[5]		
PARP inhibiteur	Olaparib	Niraparib			Rucaparib			Olaparib/Bevacizumab		
Inclusion	Chirurgie	Chirurgie CC1 ou inopérable			Chirurgie			Chirurgie		
Testing	g-sBRCAm	sBRCAm	HRD/BRCAwt	HRp	g/sBRCAm	LOHhigh/BRCAwt	LOHlow	g/sBRCAm	HRD/BRCAwt	HRp
Difference PFS, months	42.2	11.2	11.4	2.7	mPFS NR	11.1	3	19.5	11.5	no
PFS HR	0.33	0.40	0.50	0.68	0.40	0.58	0.65	0.33	0.43	-
Dose reduction (%)	28	71			49.4			41		
%AE $\geq$ 3 (65%)	39	65			61			57		

(1) Moore N Engl J Med 2018

(2) Banerjee Lancet Oncol 2021

(3) Gonzalez Martin N Engl J Med 2019

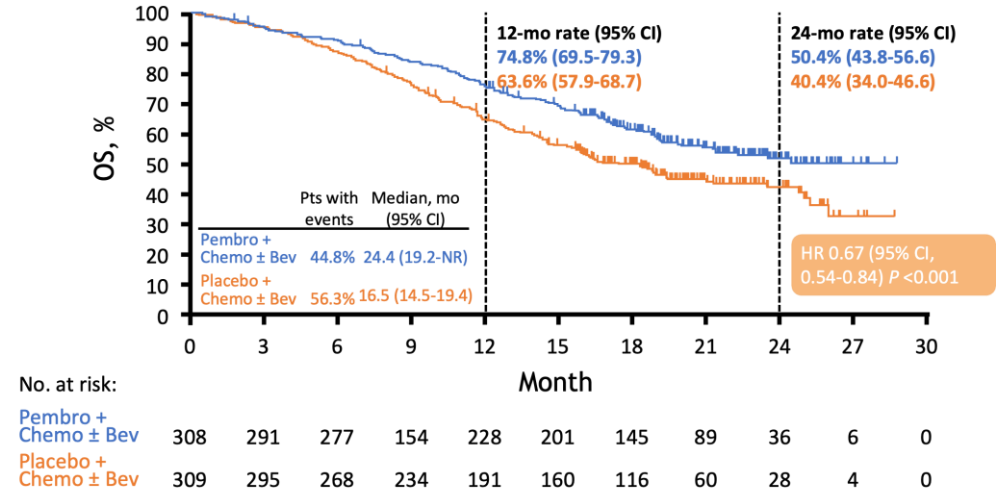
(4) Monk J Clin Oncol 2022

(5) Ray-Coquard N Engl J Med 2019

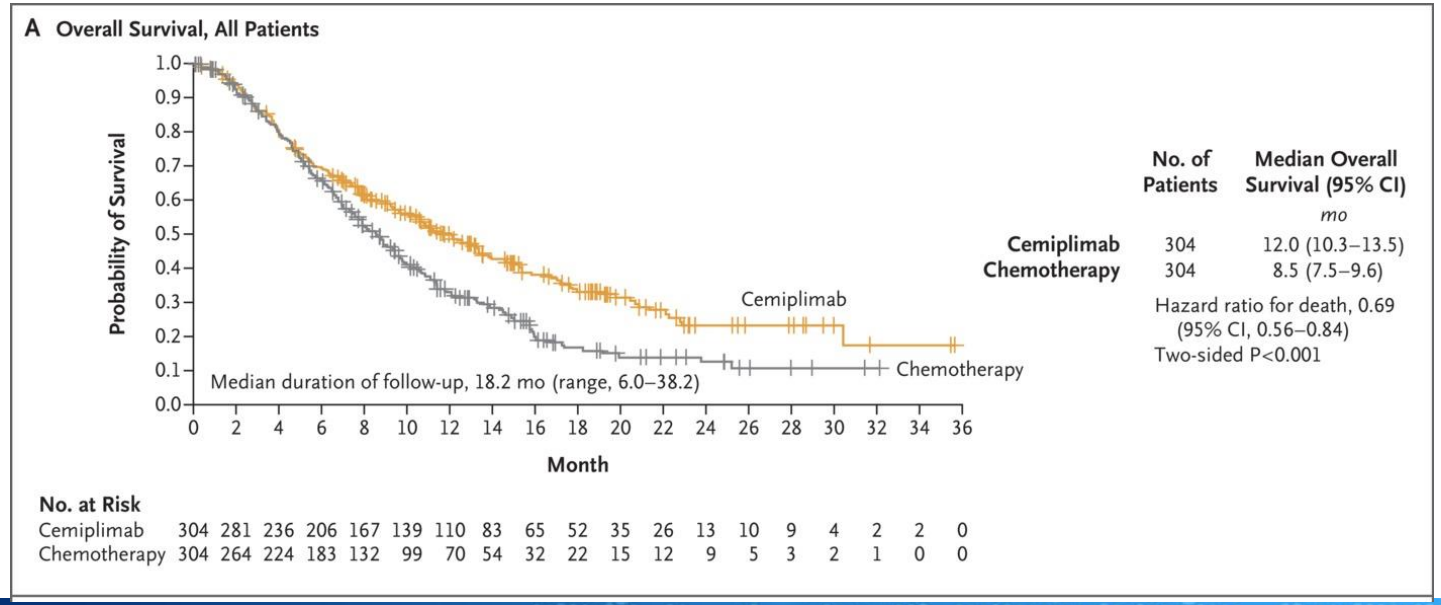
2021… Cancer du col avancé et anti-PD-(L)1 Bénéfices en SG

KN 826

OS: All-comer population



EMPOWER Cervical -1



Colombo et al. N Eng J Med 2021
Tewari et al. N Engl J Med 2022

2022 ASCO ANNUAL MEETING

…2022? L'année des ADC? Tisotumab vedotin

ONCO NOUVELLE-AQUITAINE Réseau Régional de Cancérologie

BRIO BORDEAUX | Recherche Intégrée Oncologie

Anticorps drogue conjugué

- cible le facteur tissulaire
- délivre une chimiothérapie ciblant les microtubules
- effet immunomodulateur

Efficacité dans l'essai Innova TV 204 (2)

- ORR 24%
- mDOR 8.3 mois

Données précoces suggérant une synergie anti-tumorale avec pembrolizumab, carboplatine et bevacizumab (2)

(1) Coleman et al. Lancet Oncol 2021
(2) Gray et al. J Immunotherapy for Cancer 2020

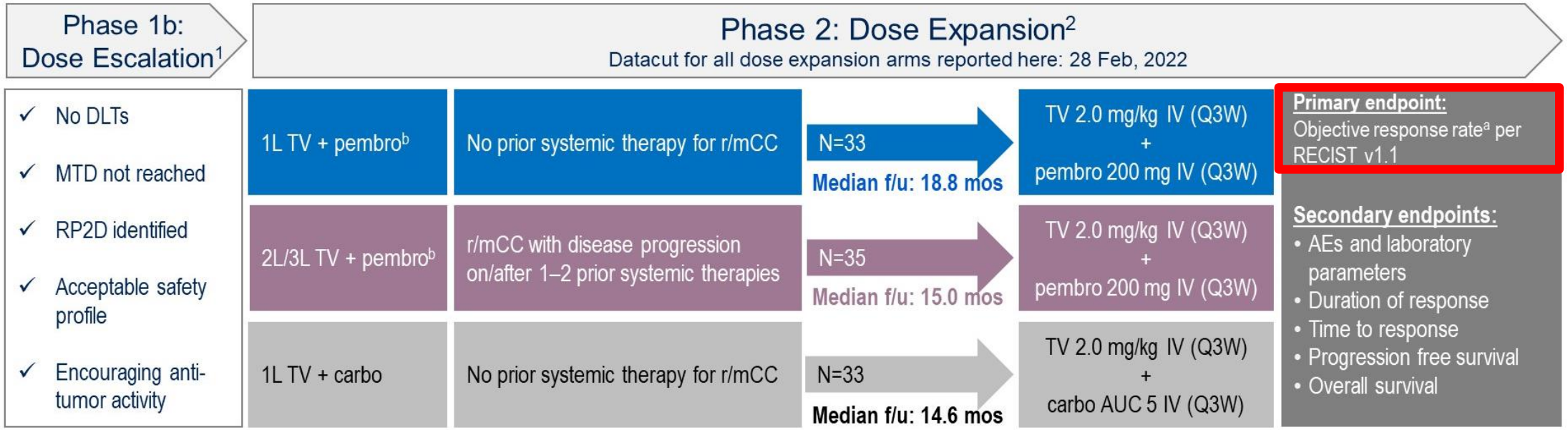
2022 ASCO ANNUAL MEETING

Tisotumab vedotin + pembrolizumab in first-line recurrent or metastatic cervical cancer: Interim results of ENGOT Cx8/GOG 3024/innovaTV 205

Domenica Lorusso[1], **Ignace Vergote[2]**, Roisin E. O'Cearbhaill[3], Anne M. Westermann[4], Susana Banerjee[5], Els Van Nieuwenhuysen[2], David A. Iglesias[6], Dearbhaile Collins[7], David Cibula[8], Kristine Madsen[9], Krishnansu S. Tewari[10], Sandro Pignata[11], Jean-Francois Baurain[12], Ingrid A. Boere[13], Hannelore Denys[14], Camilla Mondrup Andreassen[15], Ibrahima Soumaoro[16], Shweta Jain[17], Christine Gennigens[18], and Bradley J. Monk[19]

[1]Fondazione Policlinico Gemelli IRCCS, Rome, Italy; [2]Belgium and Luxembourg Gynaecological Oncology Group (BGOG), and Leuven Cancer Institute University Hospital Leuven, Leuven, Belgium; [3]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [4]Dutch Gynaecological Oncology Group (DGOG) and Amsterdam University Medical Centers, Amsterdam, Netherlands; [5]The Royal Marsden NHS Foundation Trust and Institute of Cancer Research, National Cancer Research Institute (NCRI), London, United Kingdom; [2]BGOG and Leuven Cancer Institute University Hospital Leuven, Leuven, Belgium; [6]Virginia Tech Carilion School of Medicine and Carilion Clinic, Roanoke, VA, USA; [7]Cork University Hospital, Wilton, Cork, Ireland; [8]Department of Obstetrics and Gynecology, General University Hospital in Prague, 1st Medical Faculty of the Charles University, Prague, Czech Republic; [9]Rigshospitalet, University Hospital of Copenhagen, Copenhagen, Denmark; [10]Division of Gynecologic Oncology, Department of Obstetrics & Gynecology, University of California, Irvine, CA, USA; [11]Department of Urology and Gynecology, Istituto Nazionale Tumori di Napoli IRCCS Fondazione G Pascale, Naples, Italy; [12]BGOG, Cliniques Universitaires Saint-Luc and Université Catholique de Louvain, Brussels, Belgium; [13]Department of Medical Oncology, Erasmus MC Cancer Institute, Rotterdam, Netherlands; [14]BGOG and University Hospital, Ghent, Belgium; [15]Genmab A/S, Copenhagen, Denmark; [16]Genmab US, Inc., Princeton, NJ, USA; [17]Seagen Inc., Bothell, WA, USA; [18]BGOG and CHU of Liege, Liege, Belgium; [19]GOG Foundation, Creighton University, University of Arizona, Phoenix, AZ, USA.

Design de l'étude



1L TV + pembro in patients with r/mCC: First disclosure

2L/3L TV + pembro & 1L TV + carbo: Updated with longer follow-up

[a]Tumor response assessed every 6 weeks; [b]Pembro will be administered up to 35 cycles, approximately 2 years.
f/u, follow-up; r/mCC, recurrent or metastatic cervical cancer; TV, tisotumab vedotin.
1. Monk B, et al. International Gynecologic Cancer Society: 2021; 2. Vergote I, et al. European Society for Medical Oncology 2021. (initial disclosure of 1L TV + carbo and 2L/3L TV + pembro)

LoRusso et al. ASCO meeting 2022; abstr 5507

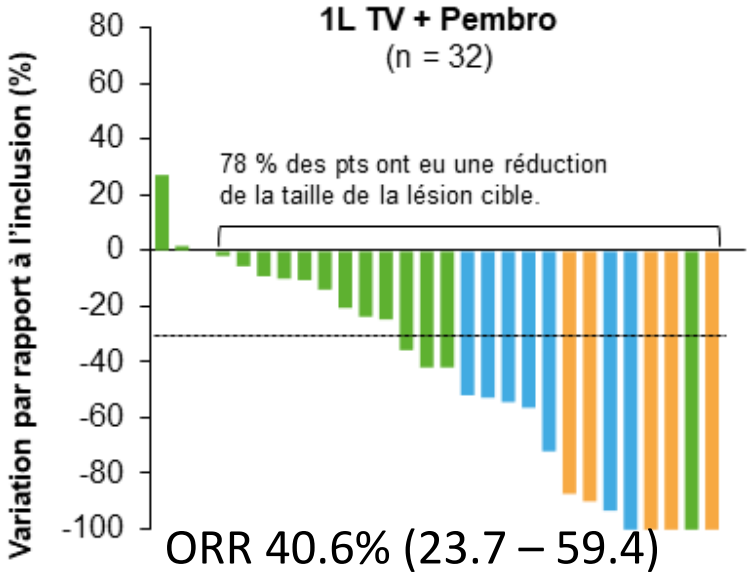
Populations à l'étude

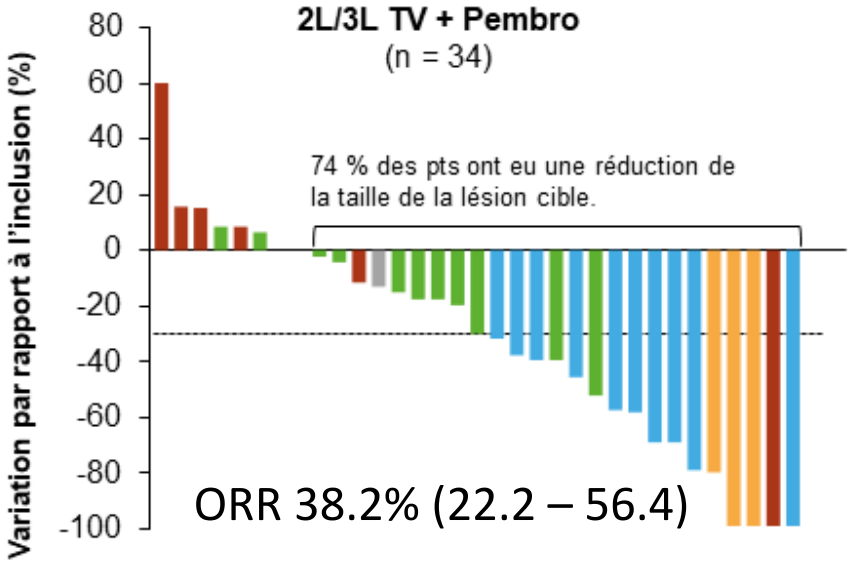
Demographics and characteristics	1L TV + Pembro (N = 33)	2L/3L TV + Pembro (N = 35)	1L TV + Carbo (N = 33)
Age, median (range), years	47 (29 - 76)	47 (31 - 73)	51 (25 - 78)
Race (White), n (%)	31 (93.9)	27 (77.1)	28 (84.8)
Ethnicity (Not Hispanic/Latino), n (%)	32 (97.0)	29 (82.9)	29 (87.9)
ECOG performance status, n (%)			
0	25 (75.8)	22 (62.9)	21 (63.6)
1	8 (24.2)	13 (37.1)	12 (36.4)
Cancer recurrence at the time of screening, n (%)	26 (78.8)	31 (88.6)	30 (90.9)
Histology, n (%)			
Squamous	22 (66.7)	19 (54.3)	24 (72.7)
Adenocarcinoma	11 (33.3)	15 (42.9)	8 (24.2)
Adenosquamous	0	0	1 (3.0)
Other	0	1 (2.9)	0
PD-L1 positive,[a] n (%)	28 (96.6)[b]	22 (81.5)[b]	NA
Prior radiotherapy, n (%)	25 (75.8)	30 (85.7)	27 (81.8)
Prior chemoradiation, n (%)	24 (72.7)	19 (54.3)	23 (69.7)
Prior lines of systemic regimen,[c] n (%)			
0	33 (100)	0	33 (100)
1	0	25 (71.4)	0
2	0	10 (28.6)[d,e]	0
Prior bevacizumab,[f] n (%)	NA	19 (54.3)	NA

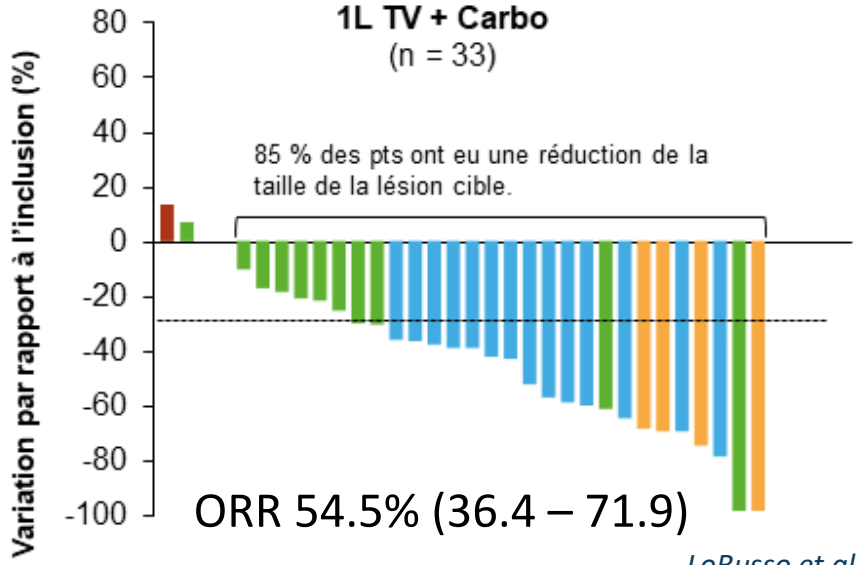
[a]Prevalence of CPS PD-L1 ≥ 1. [b]Based on evaluable biopsies, n=29 and 27 for 1L and 2L/3L TV + pembro respectively. [c]Systemic regimen administered in the metastatic or recurrent setting, excludes chemoradiation. [d]Includes 1 patient receiving prior 1L treatment with nivolumab + ipilimumab. [e]Includes 1 patient receiving prior 2L treatment with pembro. [f]Adjuvant and neoadjuvant settings are excluded.
There were 2 Asian patients each in the 1L and 2L TV+pembro arms, and 1 in the 1L TV + carbo arm. The number of Hispanic/Latino patients was 1, 0, and 0, respectively; ethnicity is missing for 0, 6, and 4 patients; respectively.
TV, tisotumab vedotin.

LoRusso et al. ASCO meeting 2022; abstr 5507

Taux de réponse





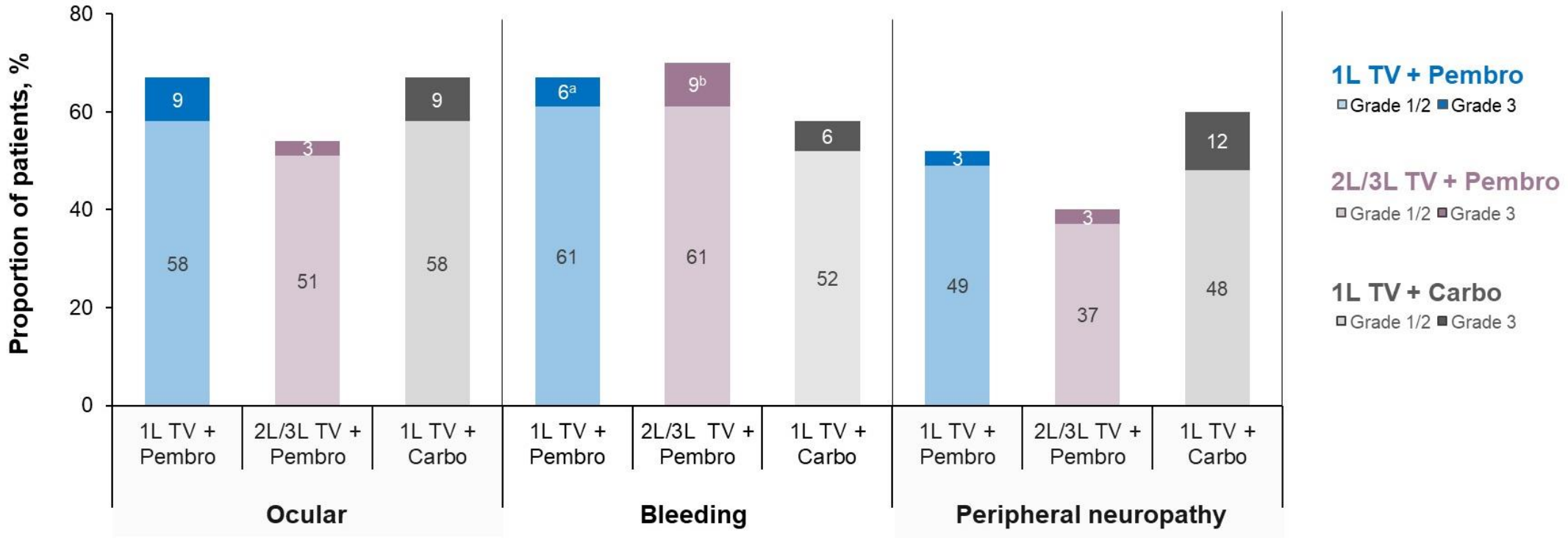


- Réponse complète
- Réponse partielle
- Maladie stable
- Progression
- Non évaluable

→ **Réduction constante des lésions cibles dans tous les bras de traitement.**

LoRusso et al. ASCO meeting 2022; abstr 5507

Effets indésirables d'intérêt particulier liés au TV



[a]Includes one patient with grade 5 disseminated intravascular coagulation; [b]Includes one patient with grade 4 hematuria

AEs of special interest with TV were generally consistent across cohorts and were mostly grade 1-2

TV, tisotumab vedotin.

LoRusso et al. ASCO meeting 2022; abstr 5507

2022 ASCO ANNUAL MEETING

Conclusion

ONCO NOUVELLE-AQUITAINE Réseau Régional de Cancérologie

BRIO BORDEAUX | Recherche Intégrée Oncologie

Signaux d'efficacité

- notamment en situation de 2ème et 3ème ligne

Une toxicité nouvelle à bien cerner

- propre aux ADC, notamment oculaire

Un nouveau combo en 1ère ligne ?

- essai NCT03786081 en cours

Un intérêt à venir en association au pembrolizumab en 2ème ligne?

- bénéfice pembrolizumab/CT en première ligne

à venir essai SGNTV-003-ENGOT cx12

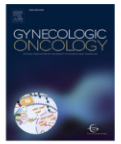
- TV vs monochimiothérapie en L2 et L3

Gynecologic Oncology 165 (2022) 385–392

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno



Mitigation and management strategies for ocular events associated with tisotumab vedotin

Stella K. Kim [a,*], Paul Ursell [b], Robert L. Coleman [c], Bradley J. Monk [d], Ignace Vergote [e]

Key Resources and Materials for Required Eye Care

An eye care plan based on clinical trial experience was developed to help reduce the risk of ocular adverse events with tisotumab vedotin. With these measures, ocular adverse events may be detected early on, and symptoms can be alleviated prior to impacting vision.

Access to eye care providers

- Conduct ophthalmic exam including visual acuity and slit lamp exam at baseline, prior to each dose and as clinically indicated
- Promptly refer patient to an eye care provider if new or worsening ocular symptoms occur

Eye drops ready for use

1. Topical steroid (Rx): e.g. dexamethasone 0.1%
2. Topical ocular vasoconstrictor (Rx): e.g. brimonidine tartrate 0.2%
3. Topical lubricating (OTC)

Cold packs during infusion

- E.g., standard chemical cold packs which reach approximately 35F
- Apply cold pack fully over eyes following administration of vasoconstrictor eye drops and leave on during the infusion
- Change cold packs as needed throughout infusion to ensure eye area remains cold

2022 ASCO ANNUAL MEETING

ONCO NOUVELLE-AQUITAINE Réseau Régional de Cancérologie

BRIO BORDEAUX | Recherche Intégrée Oncologie

Des questions?

c.lebreton@bordeaux.unicancer.fr

Merci de votre attention

Place aux questions !