L'onco-gynécologie à l'ESMO 2024

Dr Clément Dubourd

Service d'oncologie médicale

CHU de Besançon

OVAIRE

PRIMA

BARCELONA 2024 ESMO congress

Final overall survival in patients with newly diagnosed advanced ovarian cancer treated with niraparib first-line maintenance: results from PRIMA/ENGOT-OV26/GOG-3012

Presentation LBA29

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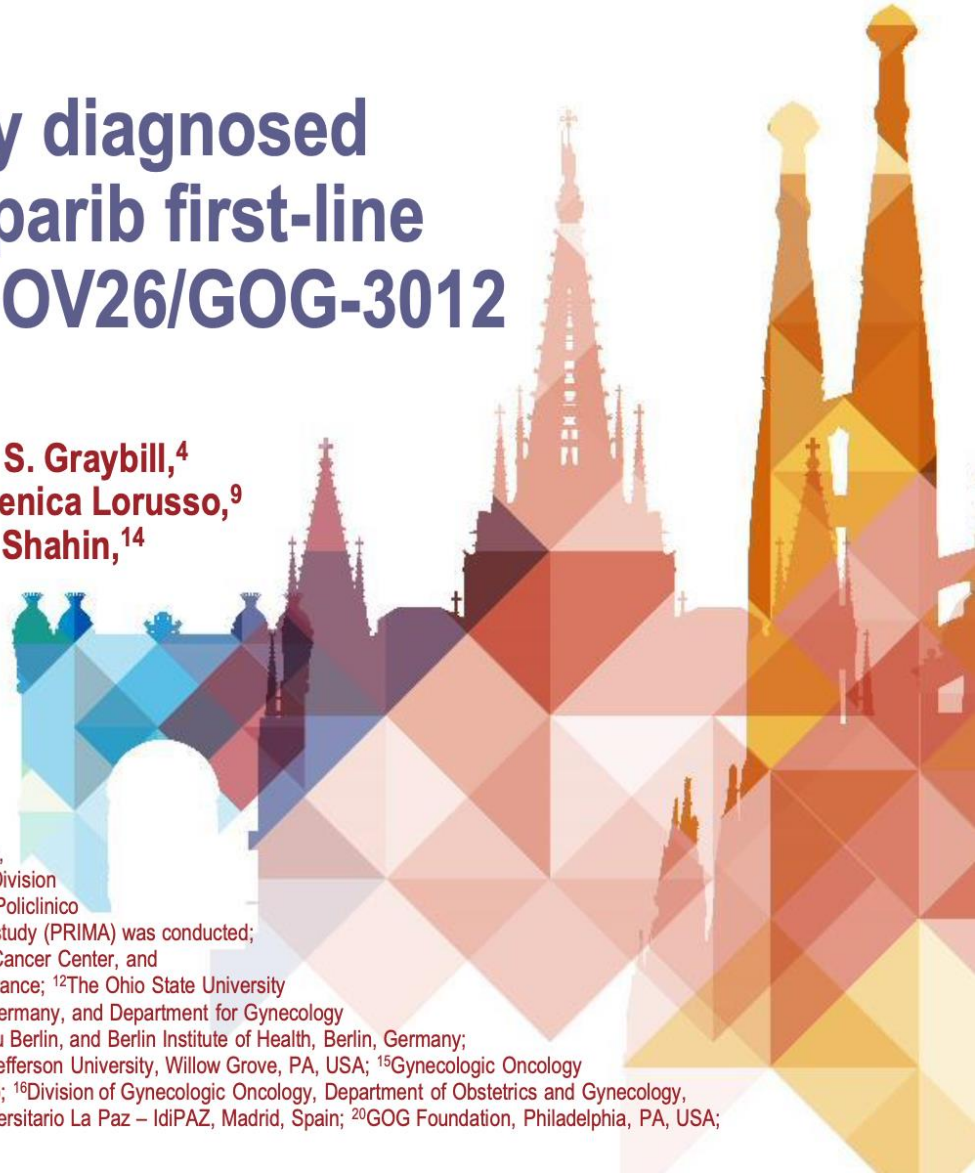


PRIMA
Design et caractéristiques de la population

Eligible patients
- Newly diagnosed HGS/HGE aOC
- CR or PR to 1L PBCT[a]
- Tumor sample for HRD testing

Stratification factors
- Neoadjuvant chemotherapy: yes or no
- Best response to 1L PBCT: CR or PR
- Tumor HRD status: HRd or HRp/HRnd

R 2:1

- Niraparib
- Placebo

Patients treated once daily[b] for 36 months or until disease progression

Endpoints

Primary endpoint:
- PFS by BICR[c]

Key secondary endpoint
- OS

Secondary endpoints:
- PFS2, TFST, PRO, safety

OS testing
- Conducted at ~60% maturity in overall population (≈440 deaths)
- Hierarchical testing: overall then HRd
- 80% power to detect a statistically significant difference if the true hazard ratio was ≤0.75 in overall population

Key risk characteristics of PRIMA population[1,2]

Disease stage
- **35.1%** stage IV disease at diagnosis

Initial treatment
- **66.7%** received neoadjuvant chemotherapy
- **30.6%** achieved partial response to 1L PBCT

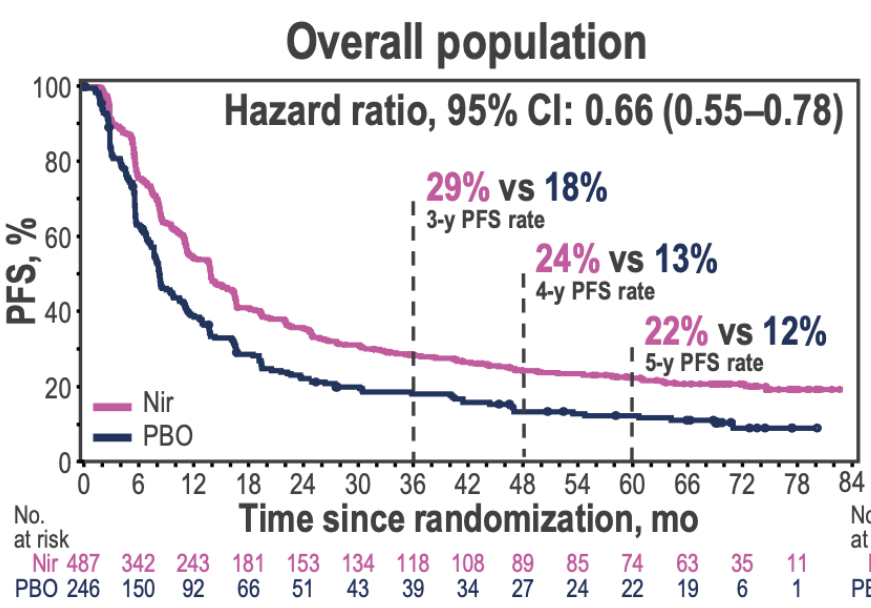
Residual disease
- **>99%** stage III disease at diagnosis with residual disease after primary debulking surgery
- **47.5%** postoperative visible residual disease or no debulking surgery

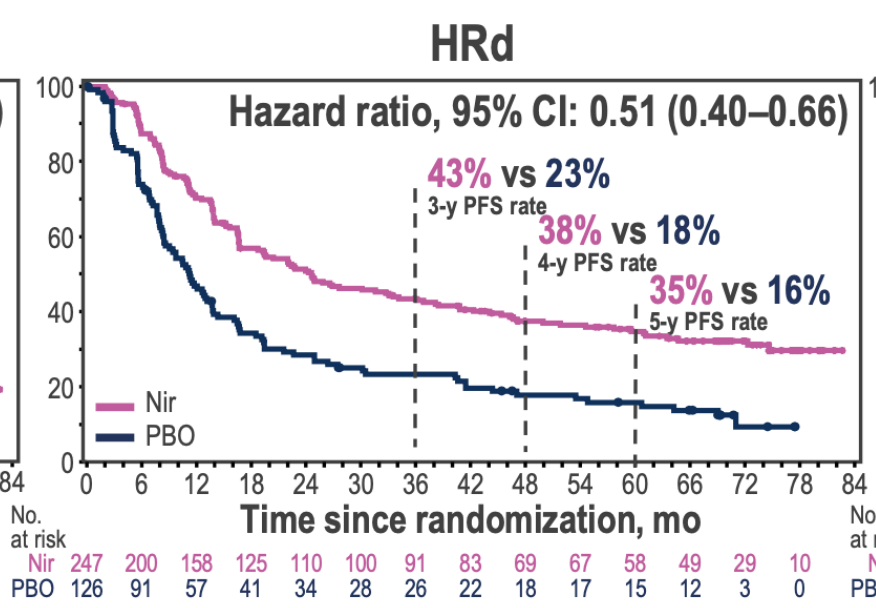
Tumor HRD/*BRCA* status
- **50.9%** HRd
- **30.4%** HRd/*BRCA*m
- **34.0%** HRp

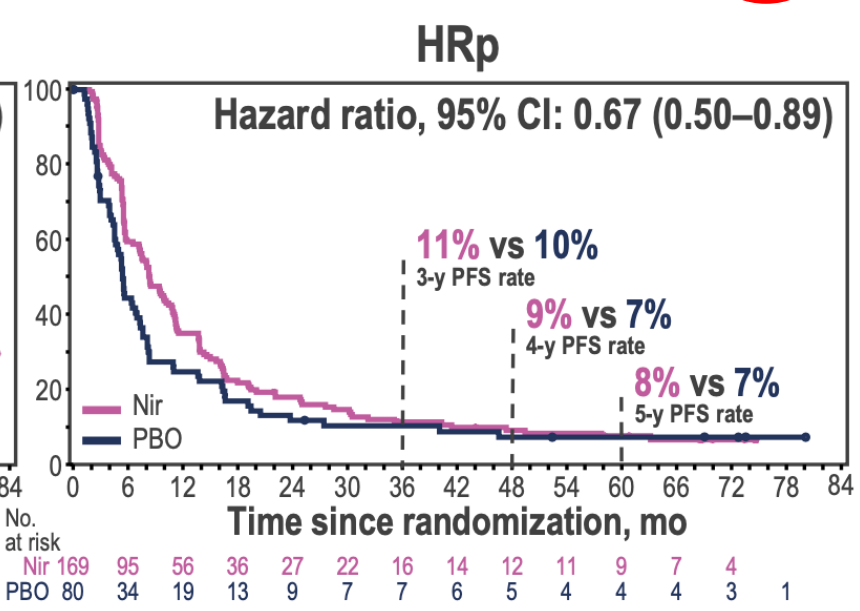
Monk BJ et al Ann Oncol. Published online Sept 14, 2024. doi:10.1016/j.annonc.2024.08.2241
Annals of Oncology (2024) 35 (suppl_2): 1-72. 10.1016/annonc/annonc1623

PRIMA

Survie sans progression à 6 ans







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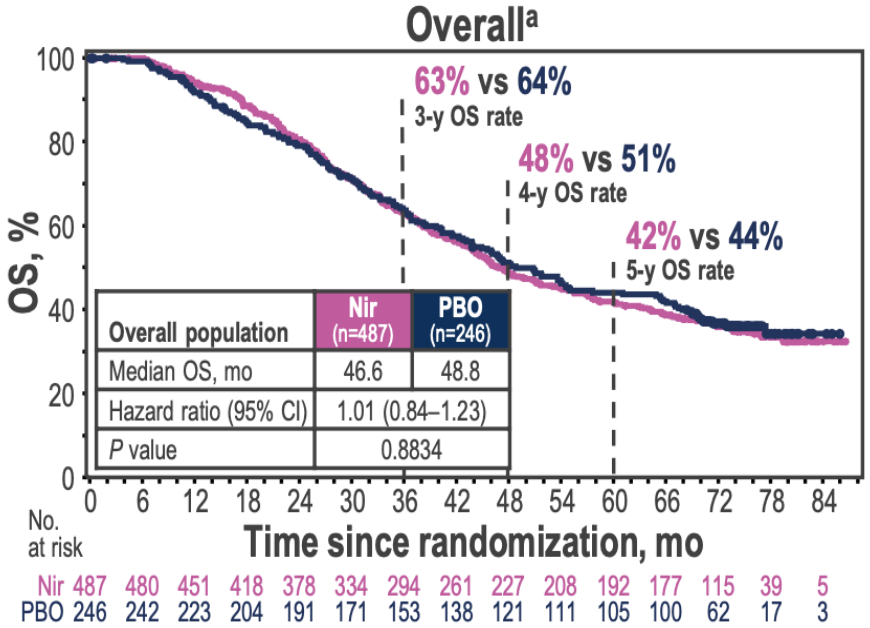
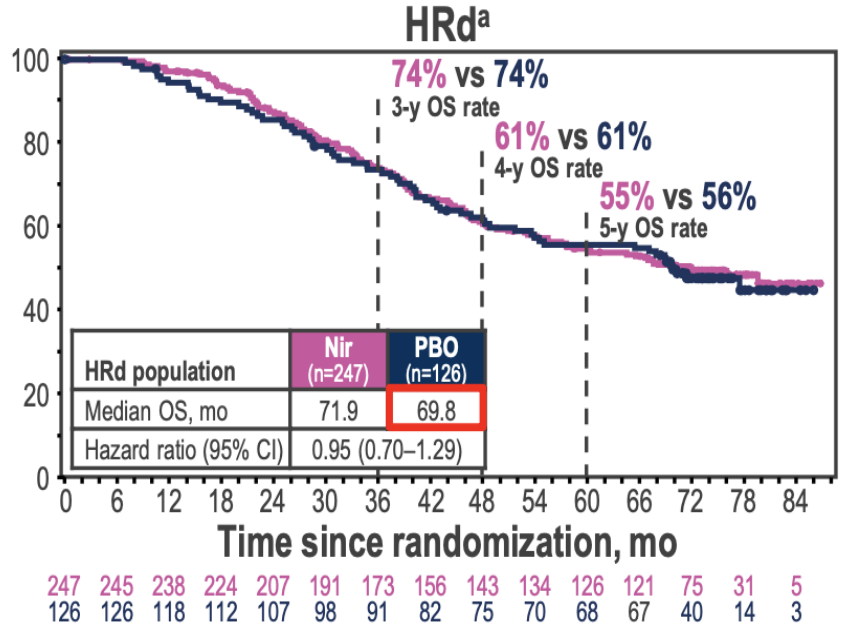
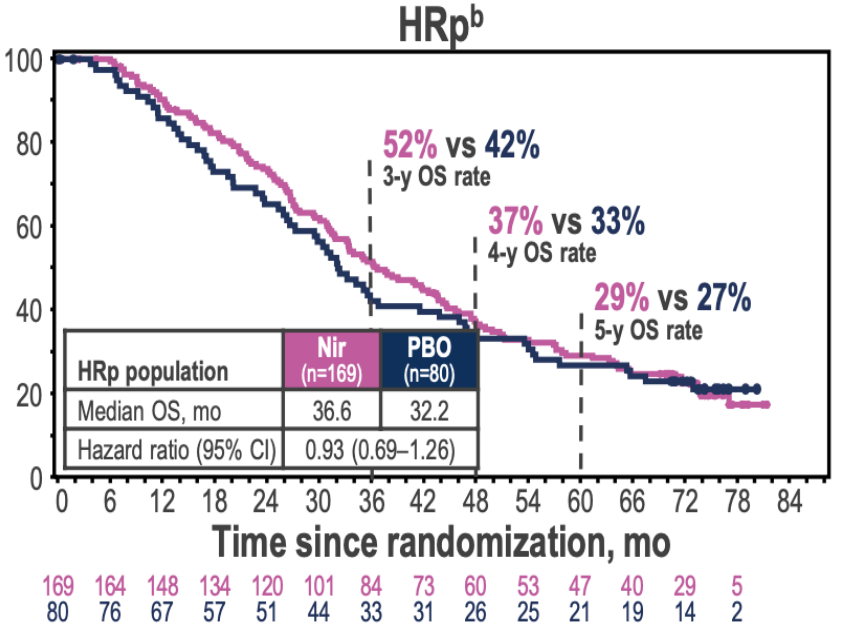
PRIMA
Survie globale (maturité 62,5%)







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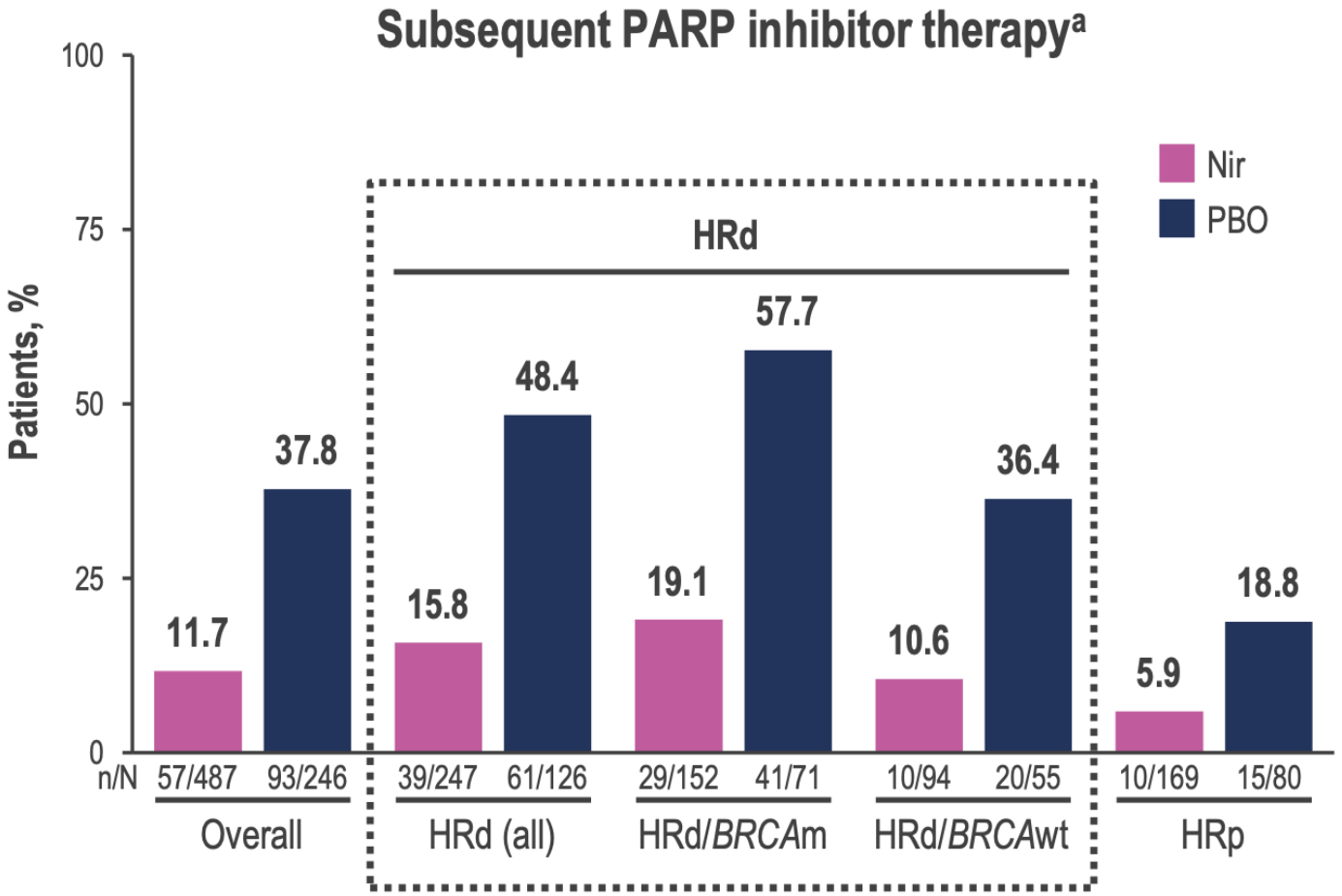
PRIMA
Discussion



- Comment expliquer l'absence de bénéfice en survie globale ?
  - La molécule ?
  - La population ? Résidu ?
  - L'usage ultérieur de iPARP ?
  - La durée de maintenance du Niraparib ?
  - Traitements de maintenance ?

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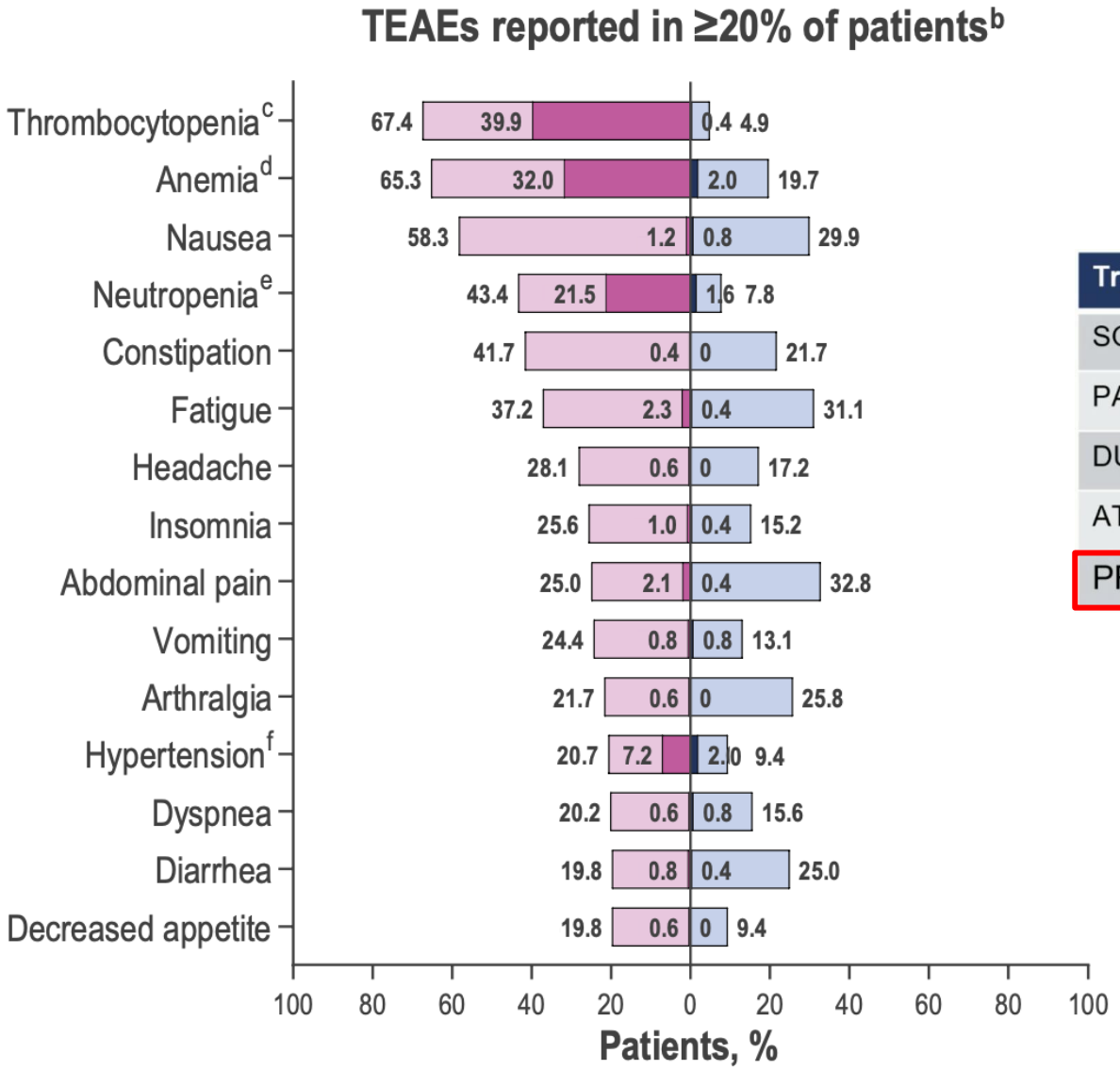
PRIMA
Tolérance



Incidence de SMD/LAM

Trial	Follow up	PARPi [%]	Placebo [%]
SOLO1 (Olaparib)	~ 7 years	1.5	0.8
PAOLA (Olaparib)	~ 5 years	1.7	2.2
DUO-O (Olaparib)	~ 2.8 years	0.8	0.1
ATHENA (Rucaparib)		0.9 [ESMO 2024]	0 [2022]
PRIMA (Niraparib)	~ 7 years	2.3	1.6

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ATHENA-COMBO

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GOG FOUNDATION

ENGOT European Network of Gynaecological Oncological Trial groups

NRG Oncology-Japan

ATHENA-COMBO (GOG-3020/ENGOT-ov45), A PHASE 3, RANDOMIZED TRIAL COMPARING RUCAPARIB + NIVOLUMAB COMBINATION THERAPY VS RUCAPARIB MONOTHERAPY AS MAINTENANCE TREATMENT IN PATIENTS WITH NEWLY DIAGNOSED OVARIAN CANCER

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[a]Affiliation at the time of the study. Current affiliation: Florida Cancer Specialists & Research Institute, West Palm Beach, FL, USA

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ATHENA-COMBO
Design

Key Patient Eligibility

- Newly diagnosed, stage III–IV, advanced, high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer
- Completed frontline platinum-doublet chemotherapy and surgery
  - Achieved investigator-assessed CR or PR
  - Received cytoreductive surgery (primary or interval; complete resection permitted)
- ECOG PS 0 or 1
- No prior frontline maintenance treatment for ovarian cancer

Randomization 4:4:1:1

Arm A (n≈400)
rucaparib 600 mg BID PO + nivolumab 480 mg IV

Arm B (n≈400)
rucaparib 600 mg BID PO + placebo IV

Arm C (n≈100)
placebo PO + nivolumab 480 mg IV

Arm D (n≈100)
placebo PO + placebo IV

Randomization Stratification Factors
- Tumor HRD test status[a]
- Disease status post-chemotherapy
- Timing of surgery

Treatment for 24 months,[b] with a 4-week lead-in of rucaparib; study drugs could be discontinued independently

Study Analyses

ATHENA-COMBO
Arm A (n≈400)
rucaparib 600 mg BID PO + nivolumab 480 mg IV

Arm B (n≈400)
rucaparib 600 mg BID PO + placebo IV

ATHENA-MONO
Arm B (n≈400)
rucaparib 600 mg BID PO + placebo IV

Arm D (n≈100)
placebo PO + placebo IV

Primary endpoint: Investigator-assessed PFS in the ITT population

- ATHENA-MONO : mPFS de 20,2 mois avec le RUCAPARIB vs 9,2 mois avec le placebo (HR = 0.52 ; 95% CI [0,40-0,68]

Monk BJ et al. J Clin Oncol. 2022;40(34):3952-3964. Annals of Oncology (2024) 35 (suppl_2): 1-72. 10.1016/annonc/annonc1623

ATHENA-COMBO
Caractéristiques de la population

Characteristic (ITT population)	Rucaparib + Nivolumab (n = 436)	Rucaparib + Placebo (n = 427)
Age, years, median (range)	61 (25–83)	61 (30–83)
Race, n (%)		
White	325 (74.5)	328 (76.8)
Asian	81 (18.6)	80 (18.7)
Black or African American	8 (1.8)	5 (1.2)
Other[a]	22 (5.0)	14 (3.3)
ECOG PS,[b] n (%)		
0	298 (68.3)	295 (69.1)
1	138 (31.7)	131 (30.7)
FIGO stage, n (%)		
III	320 (73.4)	323 (75.6)
IV	116 (26.6)	104 (24.4)
Type of cancer, n (%)		
Epithelial ovarian	340 (78.0)	336 (78.7)
Fallopian tube	63 (14.4)	50 (11.7)
Primary peritoneal	33 (7.6)	41 (9.6)
Timing of surgery, n (%)		
Primary surgery	215 (49.3)	209 (48.9)
Interval debulking	221 (50.7)	218 (51.1)

Annals of Oncology (2024) 35 (suppl_2): 1-72. 10.1016/annonc/annonc1623

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ATHENA-COMBO

Caractéristiques de la population

Characteristic (ITT population), n (%)	Rucaparib + Nivolumab (n = 436)	Rucaparib + Placebo (n = 427)
Disease status post-chemotherapy		
No residual disease	327 (75.0)	322 (75.4)
Residual disease	109 (25.0)	105 (24.6)
Best response to radiologic chemotherapy[a]		
CR	71 (16.3)	73 (17.1)
PR	78 (17.9)	76 (17.8)
No disease post-surgery	244 (56.0)	225 (52.7)
HRD status		
BRCA^{mut}	94 (21.6)	91 (21.3)
BRCA^{wt}/LOH^{high}	99 (22.7)	94 (22.0)
BRCA^{wt}/LOH^{low}	188 (43.1)	189 (44.3)
BRCA^{wt}/LOH^{indeterminate}	55 (12.6)	53 (12.4)
PD-L1 expression[b]		
≥5%	69 (15.8)	72 (16.9)
≥1%	199 (45.6)	197 (46.1)
Measurable disease at baseline	39 (8.9)	41 (9.6)

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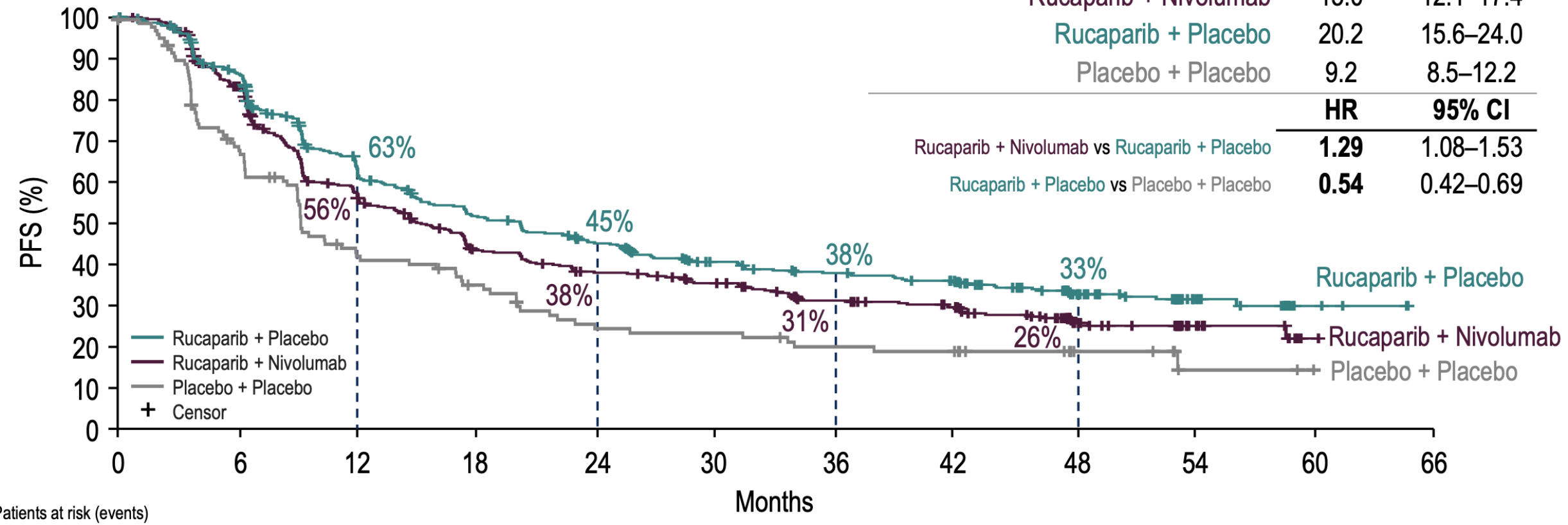
ATHENA-COMBO
Survie sans progression

	Median	95% CI
Rucaparib + Nivolumab	15.0	12.1–17.4
Rucaparib + Placebo	20.2	15.6–24.0
Placebo + Placebo	9.2	8.5–12.2
	HR	**95% CI**
Rucaparib + Nivolumab vs Rucaparib + Placebo	**1.29**	1.08–1.53
Rucaparib + Placebo vs Placebo + Placebo	**0.54**	0.42–0.69



Patients at risk (events)

Ruca+Nivo	436 (0)	333 (69)	218 (174)	159 (224)	136 (244)	122 (253)	98 (267)	87 (272)	44 (280)	14 (282)	1 (283)	0 (283)
Ruca+Plac	427 (0)	352 (57)	246 (149)	197 (193)	166 (218)	136 (234)	123 (243)	113 (249)	68 (258)	24 (260)	4 (261)	0 (261)
Plac+Plac	111 (0)	73 (34)	43 (61)	33 (69)	23 (78)	21 (80)	17 (83)	16 (84)	8 (84)	2 (85)	1 (85)	0 (85)

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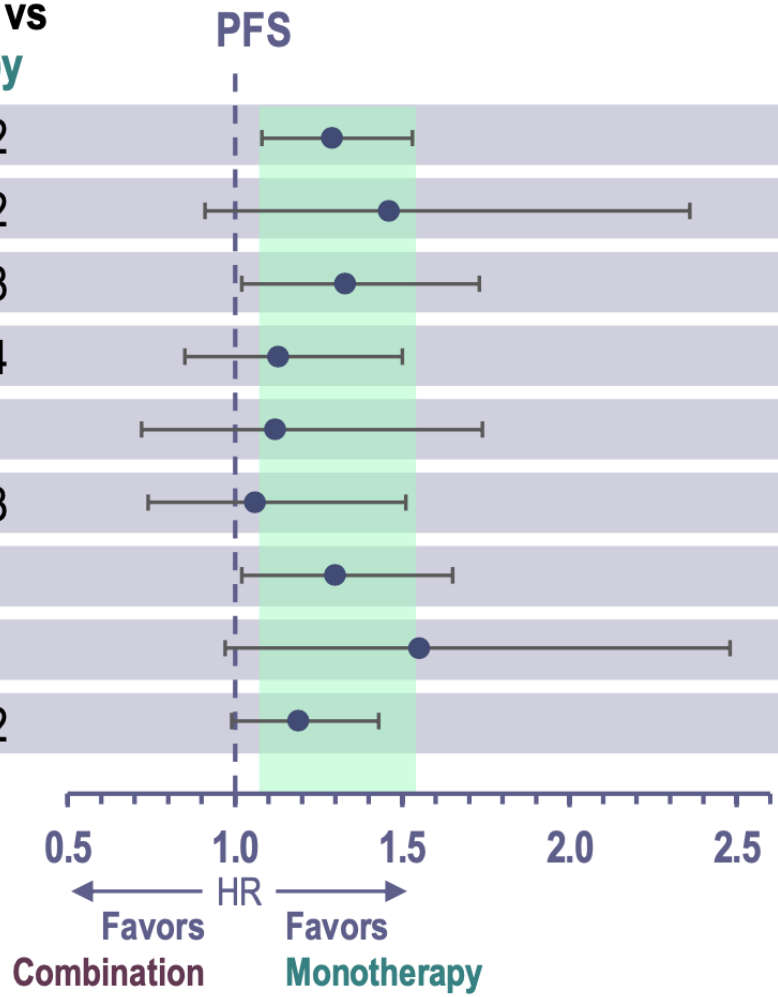
ATHENA-COMBO

Survie sans progression selon biomarqueurs

Population	Rucaparib + Nivolumab (n)	Rucaparib + Placebo (n)	Median, months Combination vs Monotherapy	HR (95% CI)
ITT	436	427	15.0 vs 20.2	1.3 (1.1–1.5)
PD-L1 ≥5%	69	72	22.8 vs 52.2	1.5 (0.9–2.4)
PD-L1 ≥1%	199	197	18.3 vs 25.8	1.3 (1.0–1.7)
HRD	193	185	28.9 vs 31.4	1.1 (0.9–1.5)
BRCA mutation	94	91	48.0 vs NR	1.1 (0.7–1.7)
BRCA wild-type/LOH^{high}	99	94	17.3 vs 22.3	1.1 (0.7–1.5)
BRCA wild-type/LOH^{low}	188	189	11.0 vs 12.1	1.3 (1.0–1.7)
BRCA wild-type/LOH^{indeterminate}	55	53	9.2 vs 17.5	1.6 (1.0–2.5)
No BRCA mutation	357	336	12.1 vs 15.2	1.2 (1.0–1.4)



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ATHENA-COMBO
Tolérance

Adverse Event, n (%)	Rucaparib + Nivolumab (n = 410)	Rucaparib + Placebo (n = 448)
Any-grade TEAE	407 (99.3)	435 (97.1)
Grade ≥3 TEAE	306 (74.6)	286 (63.8)
Oral drug treatment interruption and/or dose reduction due to TEAE	321 (78.3)	283 (63.2)
Discontinued oral study drug due to TEAE	104 (25.4)	66 (14.7)
Discontinued IV study drug due to TEAE	145 (35.4)	43 (9.6)
Discontinued oral and IV study drugs due to TEAE	63 (15.4)	19 (4.2)
Deaths[a] due to TEAE (excluding disease progression)	9 (2.2)	4 (0.9)
MDS/AML	4 (0.98)	4 (0.89)

	Rucaparib + Nivolumab (n = 436)	Rucaparib + Placebo (n = 427)
Treatment received, n (%)		
Yes	410 (94.0)	425 (99.5)
No[a]	26 (6.0)	2 (0.5)
Reason for discontinuation, n (%)[b]		
Disease progression	180 (43.9)	182 (42.8)
Adverse event	86 (21.0)	54 (12.7)
Completed protocol durations of study drug	103 (25.1)	147 (34.6)
Other[c]	41 (10.0)	42 (9.9)

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Cancers ovariens et immunothérapie…

Stade	Étude	Bras expérimental	Bras contrôle	N	PFS
Rechute platine résistante	**JAVELIN 200** *Pujade-Lauraine et al, Lancet Oncology 2021*	Caelyx + **Avelumab**	Caelyx	556	0,78 (0,59-1,24)
		Avelumab seul			1,68 (1,32-2,60)
	NINJA *Hamanishi et al, JCO 2021*	**Nivolumab**	Caelyx ou Gemcitabine	316	1,50 (1,20-1,90)
Rechute platine sensible	**ATALANTE** *Kurtz et al, JCO 2023*	Platine doublet + Bevacizumab + **Atezolizumab** et Bevacizumab et **Atezolizumab** maintenance	Platine + Bevacizumab et Bevacizumab maintenance	614	0,83 (0,69-0,93)
	ANITA *Gonzalez Martin et al, Int J Gyne Cancer 2021*	Platine doublet + **Atezolizumab** et **Atezolizumab** + Niraparib maintenance	Platine doublet et Niraparib maintenance	417	0,89 (0,71-1,10)
1e ligne	**JAVELIN 100** *Lederman et al, SGO 2020*	CT et **Avelumab** maintenance	Platine + Paclitaxel	951	1,43 (1,05-1,95)
		CT + **Avelumab** et **Avelumab** maintenance			1,14 (0,83-1,56)
	Imagyn 050 *Moore et al, JCO 2021*	Platine + Bevacizumab + **Atezolizumab** et Bevacizumab + **Atezolizumab** maintenance	Platine + Bevacizumab et Bevacizumab maintenance	1301	0,92 (0,79-1,07)
	DUO-O *Harter et al, JCO 2023*	Platine + Bevacizumab + **Durvalumab**	Platine + Bevacizumab	1130	0,87 (0,71-1,04)
		Platine + Bevacizumab + Olaparib + **Durvalumab**			0,63 (0,52-0,76)
	ATHENA-COMBO *Monk et al, ESMO 2024*	Platine et Rucaparib et **Nivolumab** entretien	Platine et Rucaparib entretien	863	1,29 (1,08-1,53)

COL DE L'UTÉRUS

KEYNOTE-A18

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Pembrolizumab Plus Chemoradiotherapy for High-Risk Locally Advanced Cervical Cancer: Overall Survival Results from the Randomized, Double-Blind, Phase 3 ENGOT-cx11/GOG-3047/KEYNOTE-A18 Study

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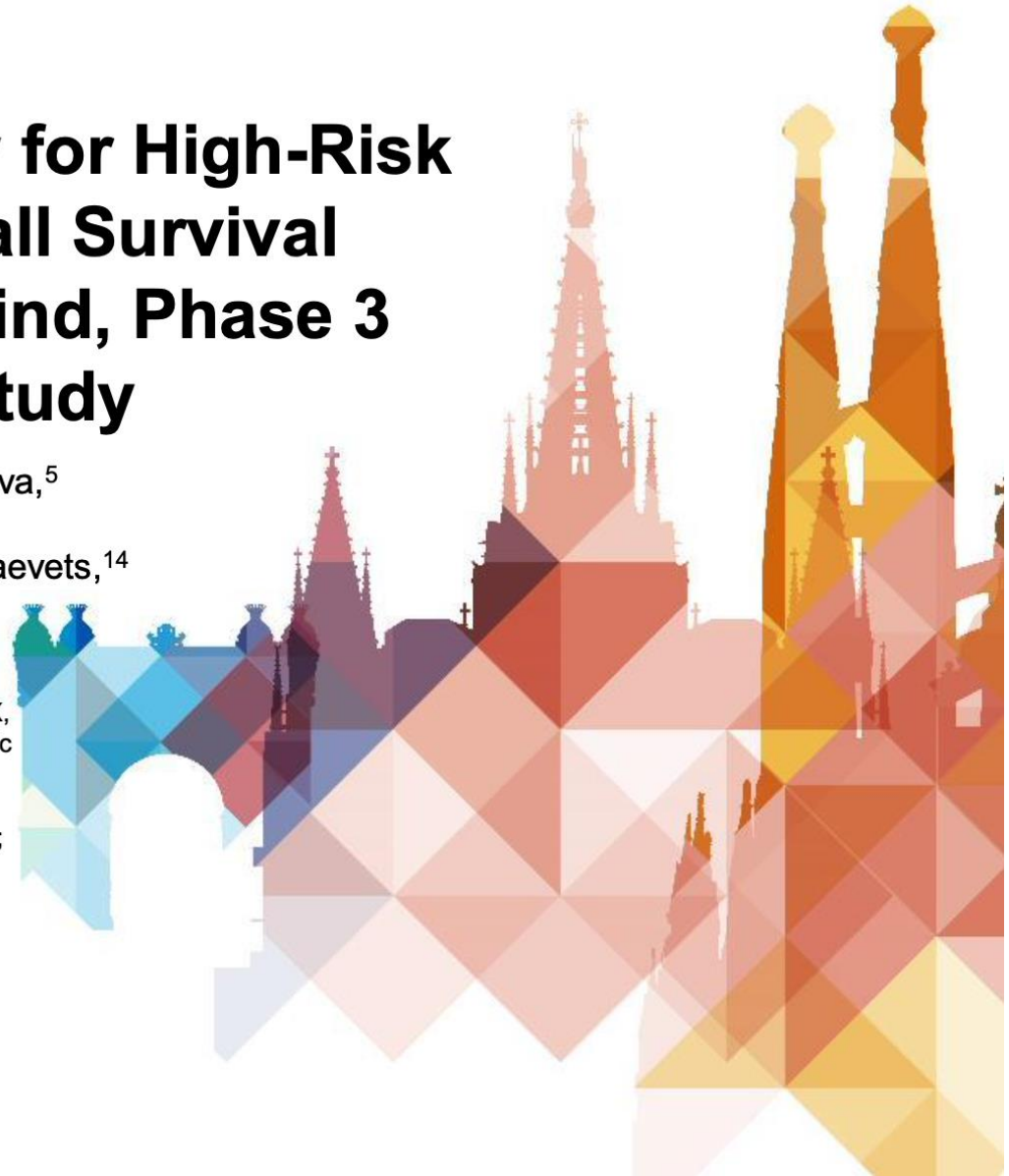
*Drs. Pignata and Duska contributed equally to this presentation.



KEYNOTE-A18
Design

Key Eligibility Criteria

- FIGO 2014 stage IB2-IIB (node-positive disease) or FIGO 2014 stage III-IVA (either node-positive or node-negative disease)
- RECIST 1.1 measurable or non-measurable disease
- Treatment naïve

Stratification Factors

- Planned EBRT type (IMRT or VMAT vs non-IMRT or non-VMAT)
- Stage at screening (stage IB2-IIB N+ vs III-IVA)
- Planned total radiotherapy dose (<70 Gy vs ≥70 Gy [EQD2])

R
1:1
N = 1060

- Cisplatin 40 mg/m^2 QW for 5 cycles[a] + EBRT followed by brachytherapy + Pembrolizumab 200 mg Q3W for 5 cycles
- Pembrolizumab 400 mg Q6W for 15 cycles
- Cisplatin 40 mg/m^2 QW for 5 cycles[a] + EBRT followed by brachytherapy + Placebo Q3W for 5 cycles
- Placebo Q6W for 15 cycles

End Points

- Primary: PFS (per RECIST v1.1) by investigator or histopathologic confirmation and OS
- Secondary: 24-month PFS, 36-month OS, ORR, patient-reported HRQoL, and safety

[a]A 6th cycle was allowed per investigator discretion. ENGOT-cx11/GOG-3047/KEYNOTE-A18 ClinicalTrials.gov identifier, NCT04221945.

Lorusso D, et al. Lancet. 2024;403(10434):1341-1350.
Annals of Oncology (2024) 35 (suppl_2): S544-S595. 10.1016/annonc/annonc1592

KEYNOTE-A18
Caractéristiques de la population

	Pembro Arm (N = 529)	Placebo Arm (N = 531)
Age, median (range)	49 y (22-87)	50 y (22-78)
Race[a]		
White	254 (48.0%)	264 (49.7%)
Asian	156 (29.5%)	148 (27.9%)
Multiple	78 (14.7%)	86 (16.2%)
American Indian or Alaska Native	24 (4.5%)	22 (4.1%)
Black or African American	14 (2.6%)	8 (1.5%)
Native Hawaiian or Other Pacific Islander	2 (0.4%)	1 (0.2%)
PD-L1 CPS		
<1	22 (4.2%)	28 (5.3%)
≥1	502 (94.9%)	498 (93.8%)
Missing	5 (0.9%)	5 (0.9%)
ECOG PS 1	149 (28.2%)	133 (25.0%)
Squamous cell carcinoma	434 (82.0%)	451 (84.9%)

134	Pembro Arm (N = 529)	Placebo Arm (N = 531)
Stage at screening (FIGO 2014 criteria)		
IB2-IIB	233 (44.0%)	226 (42.6%)
III-IVA	296 (56.0%)	305 (57.4%)
Lymph node involvement[b]		
Positive pelvic only	327 (62.2%)	324 (61.0%)
Positive para-aortic only	14 (2.6%)	10 (1.9%)
Positive pelvic and para-aortic	104 (19.7%)	104 (19.6%)
No positive pelvic or para-aortic	84 (15.9%)	93 (17.5%)
Planned type of EBRT		
IMRT or VMAT	469 (88.7%)	470 (88.5%)
Non-IMRT and non-VMAT	60 (11.3%)	61 (11.5%)
Planned total radiotherapy dose (EQD2)		
<70 Gy	47 (8.9)	46 (8.7)
≥70 Gy	482 (91.1)	485 (91.3)

[a]3 patients (0.3%) had missing information for race, 1 (0.2%) in the pembro arm and 2 (0.4%) in the placebo arm. [b]Per protocol, a positive lymph node is defined as ≥1.5 cm shortest dimension by MRI or CT.
Data cutoff date: January 8, 2024.

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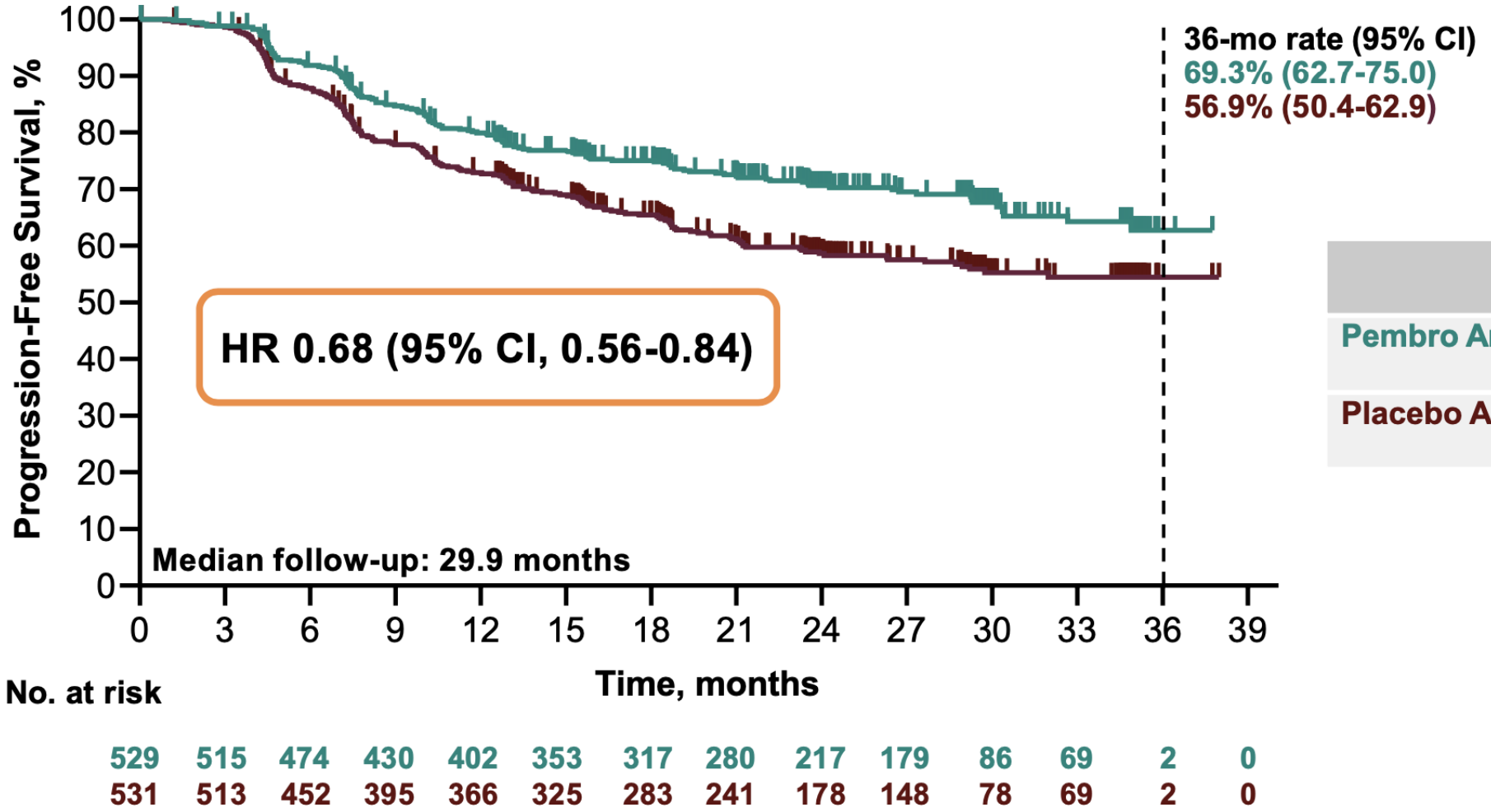
KEYNOTE-A18

Survie sans progression actualisée



	Pts w/ Event	Median, mo (95% CI)
Pembro Arm	29.3%	NR (NR-NR)
Placebo Arm	39.5%	NR (32.0-NR)

Response assessed per RECIST v1.1 by investigator review or histopathologic confirmation. Since the success criterion of the PFS hypothesis was met at IA1, no formal testing of PFS was performed at IA2. Data cutoff date: January 8, 2024.

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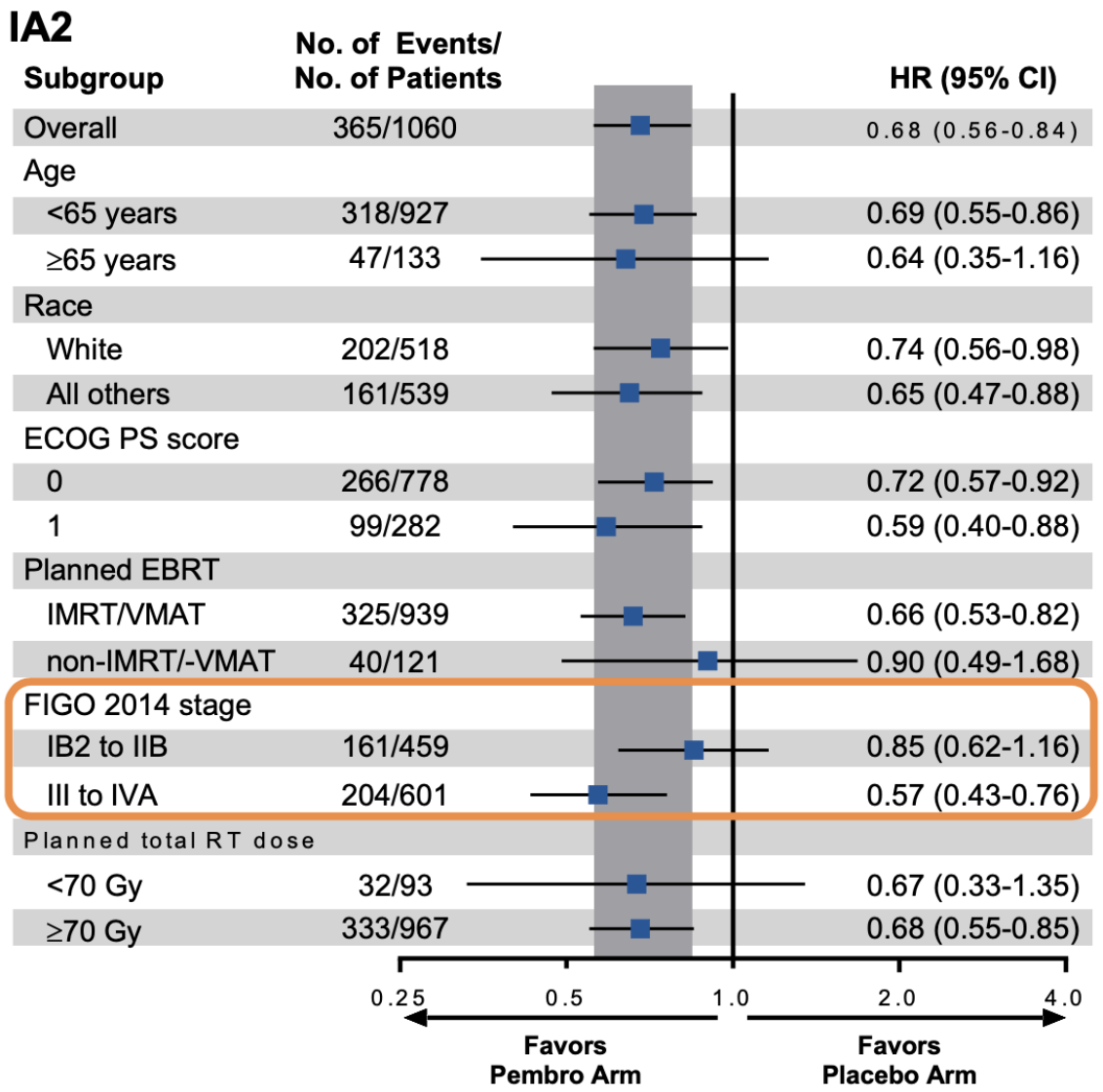
KEYNOTE-A18

Survie sans progression actualisée (sous-groupes)



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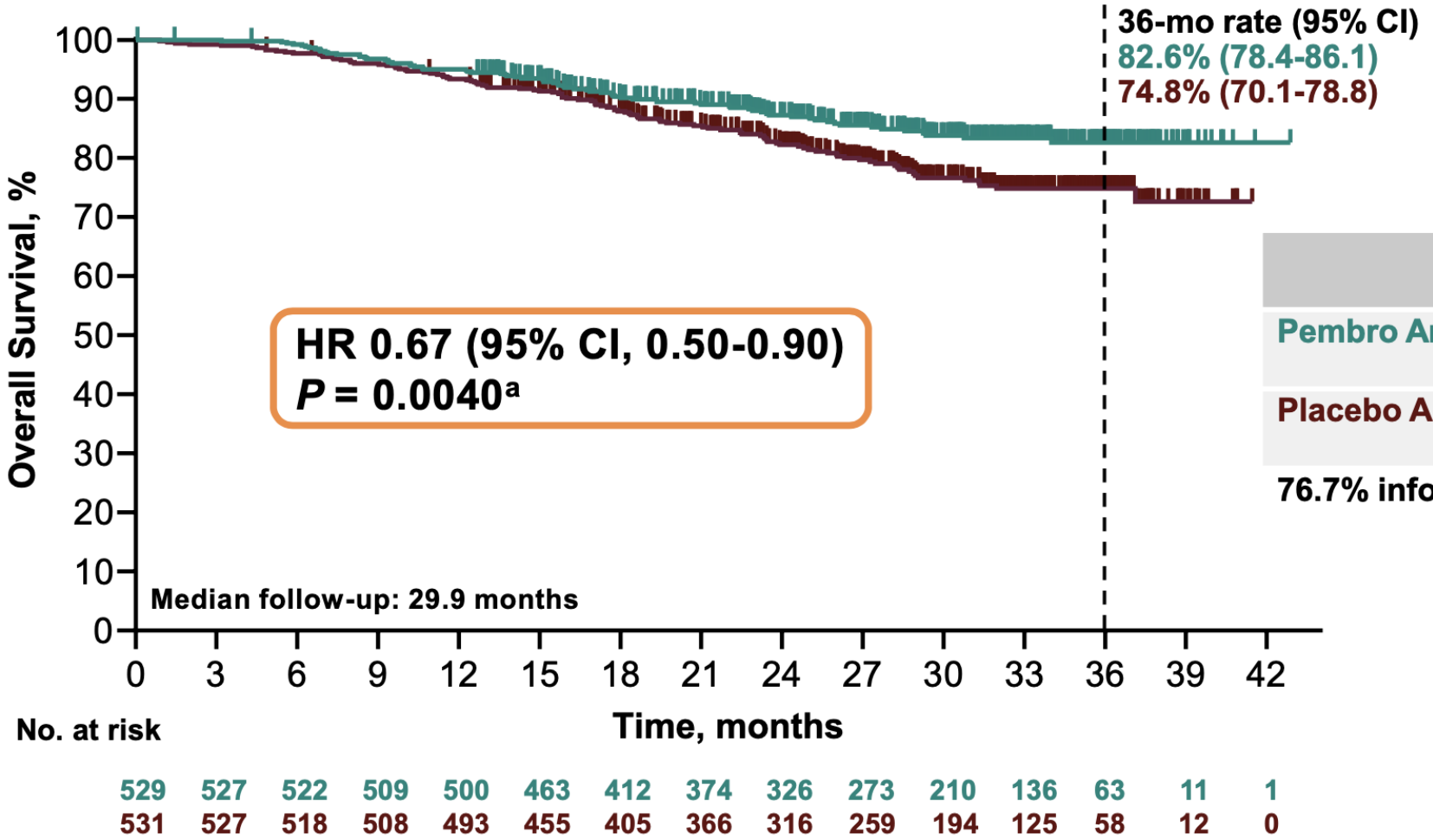
KEYNOTE-A18
Survie globale



	Pts w/ Event	Median, mo (95% CI)
Pembro Arm	14.2%	NR (NR-NR)
Placebo Arm	20.5%	NR (NR-NR)

76.7% information fraction[a]

[a]With 184 of the 240 deaths expected at the final analysis (76.7% information fraction), the observed *P* = 0.0040 (1-sided) crossed the prespecified nominal boundary of 0·01026 (1-sided) at this planned second interim analysis. At this time, 66 patients had received immunotherapy as post-progression treatment, including 15/138 patients (10.9%) in the pembro arm and 51/193 patients (26.4%) in the placebo arm; of those, 10 (7.2%) and 41 (21.2%), respectively, had received pembro. Data cutoff date: January 8, 2024.

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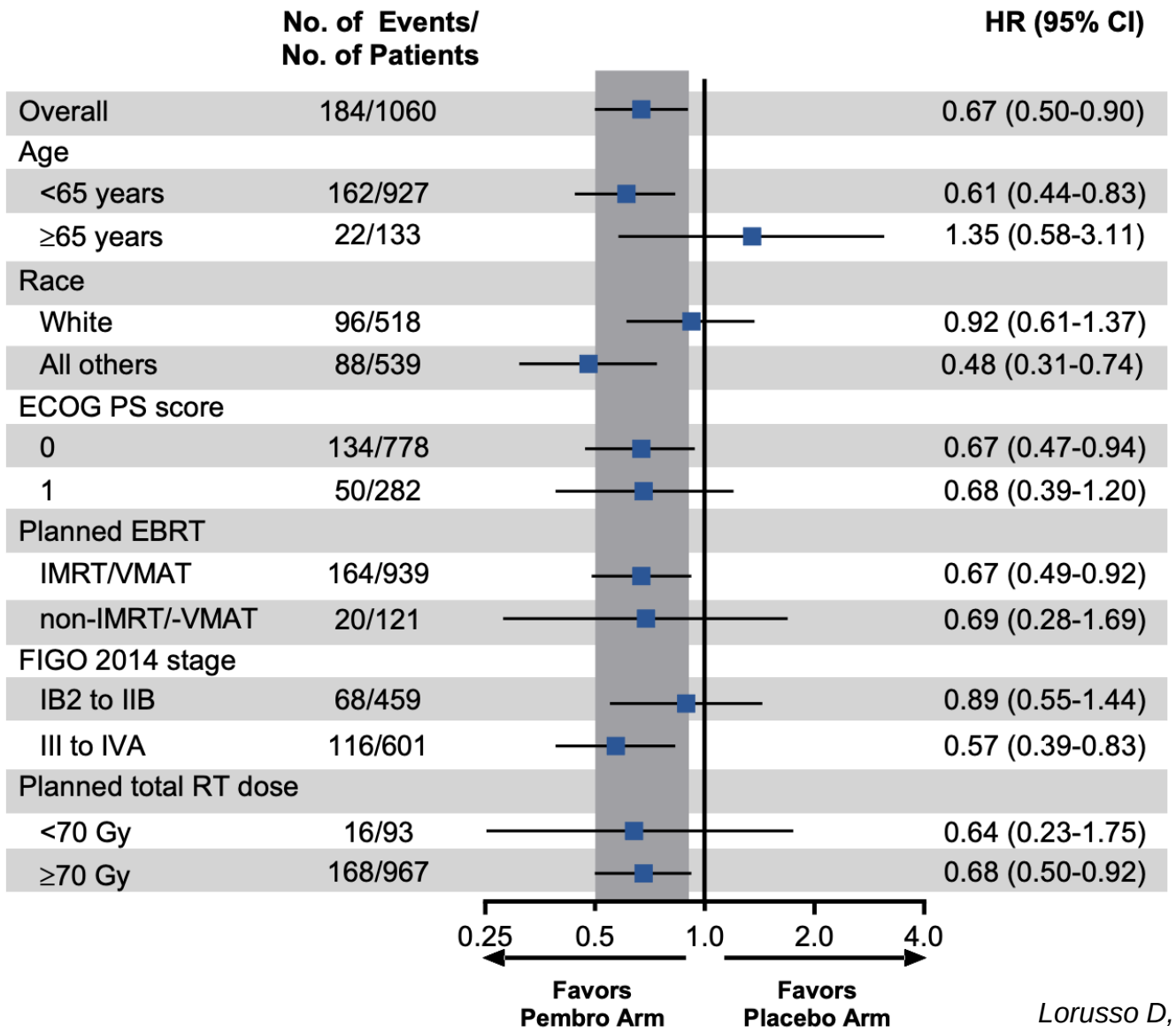
KEYNOTE-A18
Survie globale (sous-groupes)



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KEYNOTE-A18
Tolérance

	All-Cause AEs		Treatment-Related AEs[a]		Immune-Mediated AEs[b]	
	Pembro Arm (N = 528)	Placebo Arm (N = 530)	Pembro Arm (N = 528)	Placebo Arm (N = 530)	Pembro Arm (N = 528)	Placebo Arm (N = 530)
Any grade	528 (100.0%)	526 (99.2%)	512 (97.0%)	513 (96.8%)	206 (39.0%)	90 (17.0%)
Grade ≥3	413 (78.2%)	371 (70.0%)	365 (69.1%)	325 (61.3%)	25 (4.7%)	7 (1.3%)
Serious	172 (32.6%)	151 (28.5%)	102 (19.3%)	71 (13.4%)	20 (3.8%)	6 (1.1%)
Led to death	5 (0.9%)	7 (1.3%)	2 (0.4%)[c]	2 (0.4%)[d]	1 (0.2%)[e]	0
Led to discontinuation						
Any treatment	109 (20.6%)	79 (14.9%)	99 (18.8%)	69 (13.0%)	16 (3.0%)	4 (0.8%)
All treatment	1 (0.2%)	2 (0.4%)	0	1 (0.2%)	0	0

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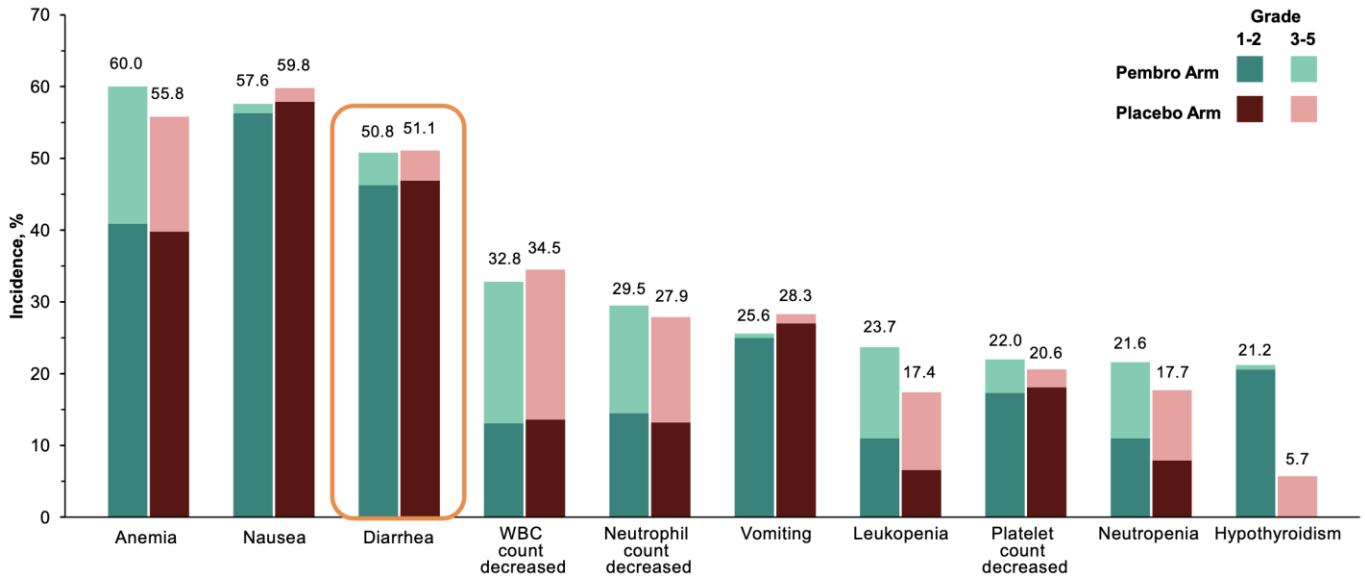
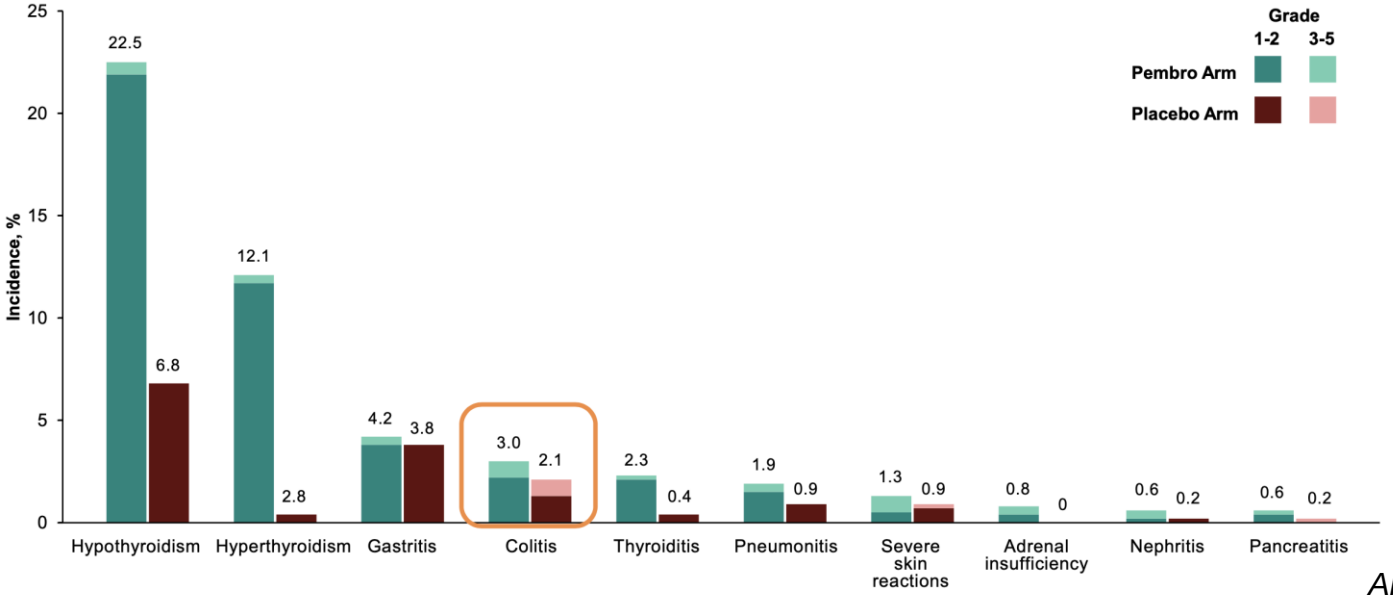
KEYNOTE-A18
Tolérance





AE ≥ 20 %

Immune-mediated AE ≥ 3 patients

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KEYNOTE-A18
Discussion

→ **Nouveau standard** de traitement chez les patientes atteintes d'un cancer du col utérin localement avancé à haut risque

Surtout chez les stades les plus avancés (III-IVA) ?

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ENDOMÈTRE

ENGOT-EN11/GOG-3053/KEYNOTE-B21: A Phase 3 Study of Pembrolizumab or Placebo in Combination With Adjuvant Chemotherapy With or Without Radiotherapy in Patients With Newly Diagnosed, High-Risk Endometrial Cancer

Toon Van Gorp,[1] Lukáš Rob,[2] Weiguo Lv,[3] Floor Backes,[4] Fırat Ortaç,[5] Kosei Hasegawa,[6] Sakari Hietanen,[7] Antonella Savarese,[8] Annouschka Laenen,[9] Yong Man Kim,[10] Lubomir Bodnar,[11] Maria-Pilar Barretina-Ginesta,[12] Lucy Gilbert,[13] Bhavana Pothuri,[14] Xiaojun Chen,[15] Jasmine Lichfield,[16] Wei Wang,[17] Robert Orlowski,[18] Alain Lortholary,[19] Brian Slomovitz[20]

[1]University Hospital Leuven, Leuven Cancer Institute, Leuven, Belgium; and BGOG; [2]3rd Faculty Medicine Charles University and Faculty Hospital Kralovske Vinohrady, Prague, Czech Republic; and CEEGOG; [3]Zhejiang University, Hangzhou, Zhejiang, China; [4]Ohio State University and James Cancer Hospital, Columbus, OH, USA; and GOG; [5]Ankara University School of Medicine, Ankara, Turkey; and TRSGO; [6]Saitama Medical University, Hidaka, Saitama Prefecture, Japan; [7]Turku University Hospital and University of Turku, Turku, Finland; TYKS Cancer Centre, FICAN West, Organization of EU Cancer Institutes, Finland; and NSGO-CTU; [8]IRCCS - Istituto Nazionale Tumori Regina Elena, Rome, Italy; and MITO; [9]Leuven Biostatistics and Statistical Bioinformatics Center, KU Leuven, Leuven, Belgium; and BGOG; [10]Asan Medical Center, University of Ulsan, Seoul, Republic of Korea; [11]Mazovia Regional Hospital, Siedlce Oncology Center, Siedlce, Poland; and ENGOT groups – PGOG; [12]Catalan Institute of Oncology and Girona Biomedical Research Institute, Medical School University of Girona, Girona, Spain; and GEICO; [13]McGill University Health Centre; Research-Institute, McGill University Health Centre; and Gerald Bronfman Department of Oncology, McGill University, Montreal, Quebec, Canada; [14]Obstetrics and Gynecology and Medicine, Gynecologic Oncology, Perlmutter Cancer Center, NYU Langone Health, New York, New York, USA; and GOG; [15]Obstetrics and Gynecology Hospital of Fudan University, Shanghai, China; and SGOG; [16]MSD, UK; [17]MSD, China; [18]Merck & Co., Inc., Rahway, NJ, USA; [19]Centre Catherine de Sienne, Hôpital Privé du Confluent, Nantes, France; and GINECO; [20]Mount Sinai Medical Center, Miami Beach, FL, USA; and GOG Foundation

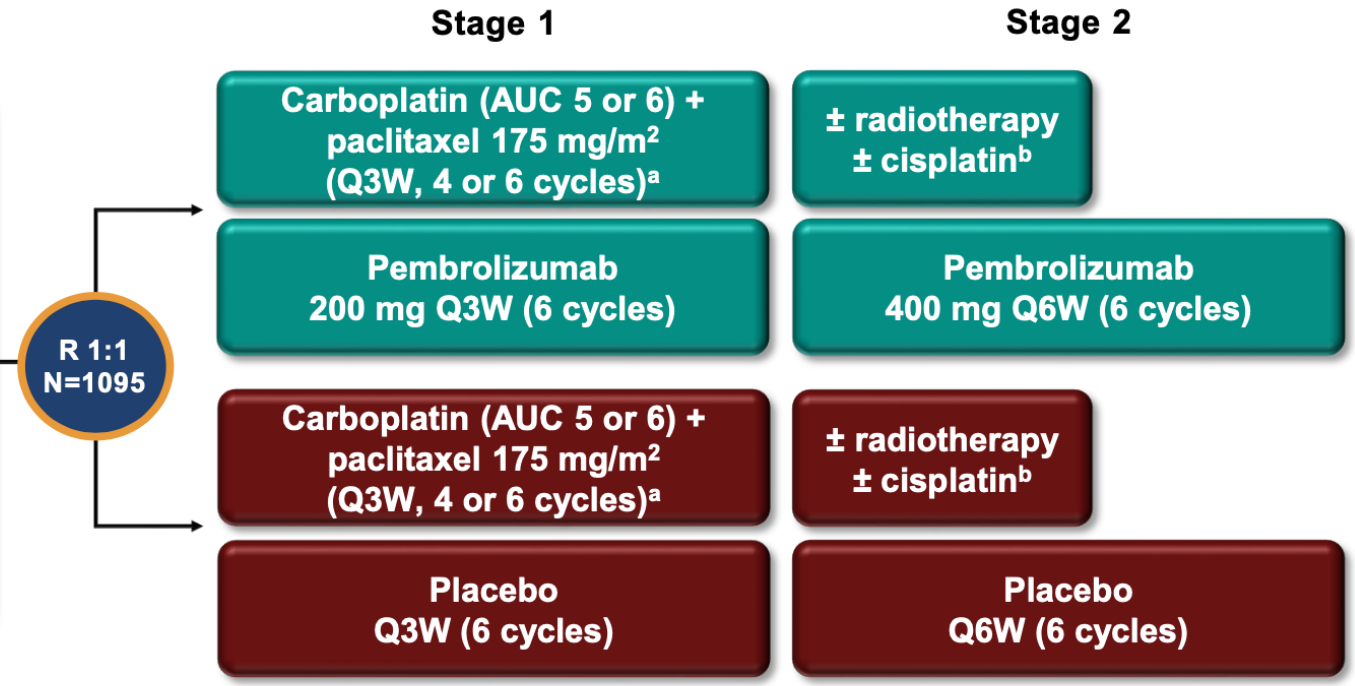
KEYNOTE-B21
Design

Key Eligibility Criteria

- Newly diagnosed EC or carcinosarcoma
- Curative surgery with no residual disease
- At high risk for recurrence:
  - FIGO (2009) surgical stage I/II, non-endometrioid with myometrial invasion
  - FIGO (2009) surgical stage I/II of any histology with known aberrant p53 expression or *TP53* mutation with myometrial invasion
  - FIGO (2009) surgical stage III/IVA of any histology
- No prior radiation or systemic therapy (including neoadjuvant) for EC

Stratification Factors

- **MMR status (pMMR vs dMMR)**, and within pMMR stratum:
  - Planned radiation (chemo-EBRT vs EBRT vs no EBRT)
  - Histology (endometrioid vs non-endometrioid)
  - FIGO (2009) surgical stage (I/II vs III/IVA)



Dual primary endpoints

- DFS as assessed radiographically by the investigator or by histopathologic confirmation
- OS

[a]Chemotherapy was administered for 4 cycles in patients planned to receive chemoradiotherapy and 6 cycles for all other patients, including those planned for radiotherapy without radiosensitizing cisplatin.
[b]Radiotherapy was optional at the discretion of the investigator, and cisplatin may have been given with EBRT as radiosensitizer; radiotherapy was started within 6 weeks after completion of carboplatin and paclitaxel (radiation may have been initiated during Stage 1 or Stage 2 depending on the number of cycles of chemotherapy that were administered).

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KEYNOTE-B21
Caractéristiques de la population

Characteristic	Pembro + Chemo (n = 545)	Placebo + Chemo (n = 550)
Age, median (range), y	62 (29–95)	62 (27–89)
ECOG PS 0	409 (75%)	416 (76%)
Race		
White	315 (58%)	362 (66%)
Asian	189 (35%)	157 (29%)
Multiple	23 (4%)	10 (2%)
Black or African American	11 (2%)	13 (2%)
American Indian or Alaska Native	2 (<1%)	3 (<1%)
Missing	5 (<1%)	5 (<1%)
Lymph node dissection	483 (89%)	502 (91%)
Lymph node status		
Lymph node involvement	223 (41%)	250 (45%)
No lymph node involvement	300 (55%)	284 (52%)
Not evaluable	22 (4%)	16 (3%)
MMR status at study entry		
dMMR	141 (26%)	140 (25%)
pMMR	404 (74%)	410 (75%)

Characteristic	Pembro + Chemo (n = 545)	Placebo + Chemo (n = 550)
FIGO 2009 stage at study entry		
IA/B	146 (27%)	144 (26%)
II	40 (7%)	41 (7%)
IIIA	109 (20%)	94 (17%)
IIIB	20 (4%)	19 (3%)
IIIC1	144 (26%)	169 (31%)
IIIC2	78 (14%)	81 (15%)
IVA/B[a]	8 (1%)	2 (<1%)
Planned radiation therapy at study entry		
EBRT[b] with cisplatin	94 (17%)	95 (17%)
EBRT[b] without cisplatin	256 (47%)	246 (45%)
Brachytherapy only	49 (9%)	52 (9%)
No EBRT or brachytherapy	146 (27%)	157 (29%)
Histology subtype		
Endometrioid	297 (54%)	297 (54%)
Non-endometrioid	248 (46%)	253 (46%)

[a]3 patients with stage IVB were randomized, including 2 in the pembro + chemo group and 1 in the placebo + chemo group. [b]With or without brachytherapy. Data cutoff date: March 4, 2024.

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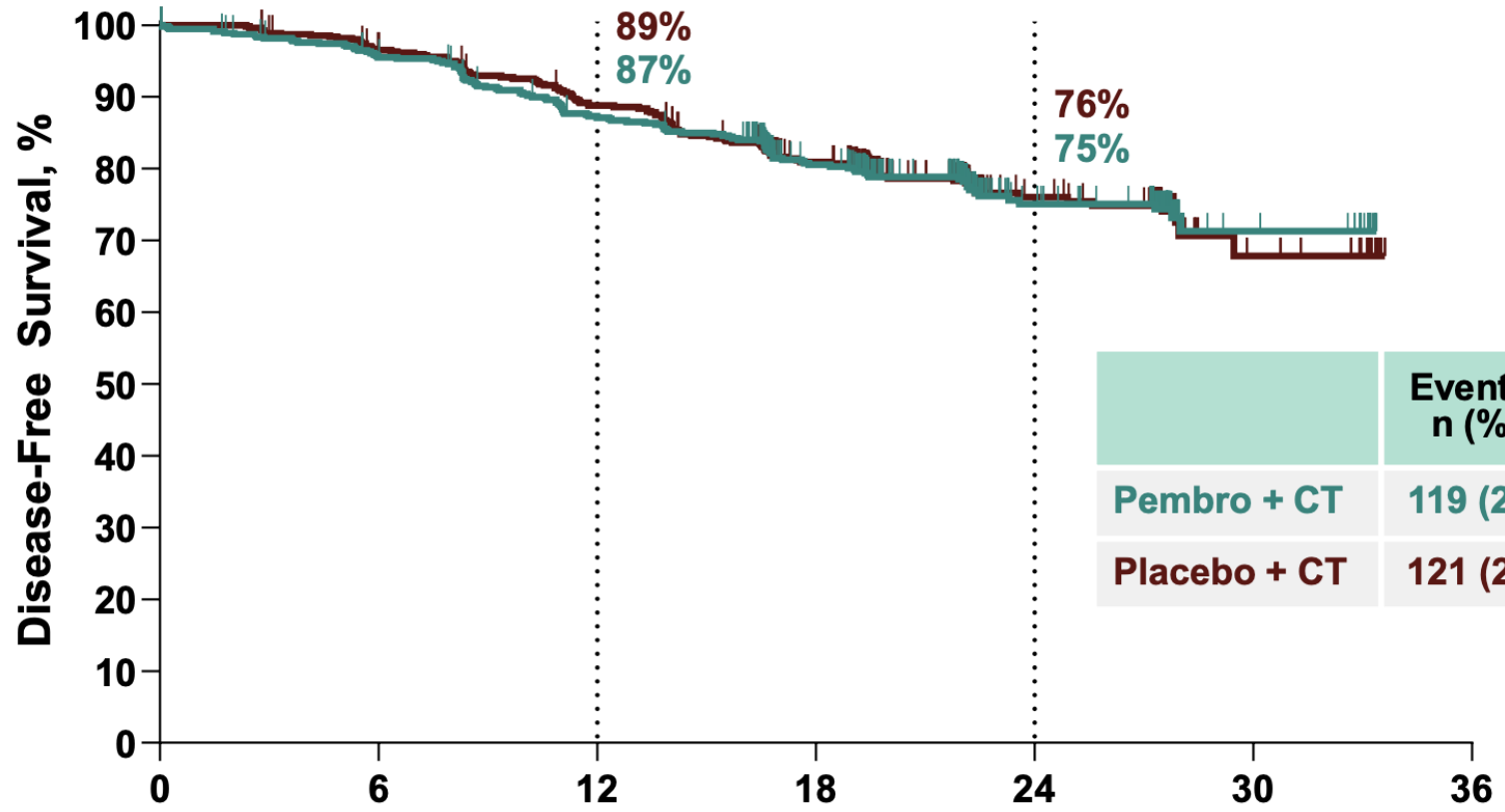
KEYNOTE-B21

Survie sans progression



	Events, n (%)	Median (95% CI), mo	HR (95% CI)	*P* value
Pembro + CT	119 (22)	NR (NR–NR)	1.02 (0.79–1.32)	0.570
Placebo + CT	121 (22)	NR (NR–NR)		

[a]DFS was defined as the time from randomization to local or distant recurrence of EC (assessed radiographically by the investigator or by histopathologic confirmation) or death from any cause.
Data cutoff date: March 4, 2024.

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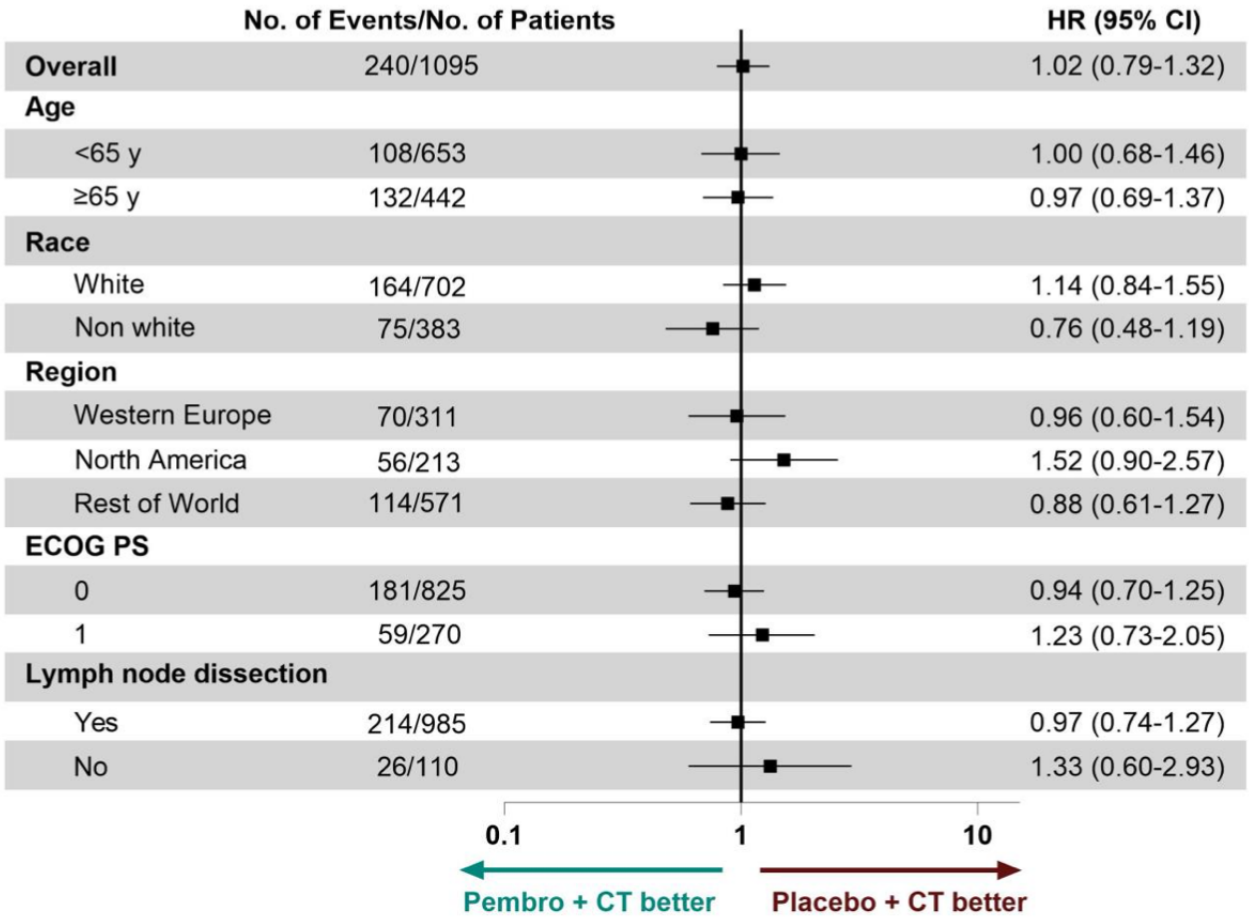
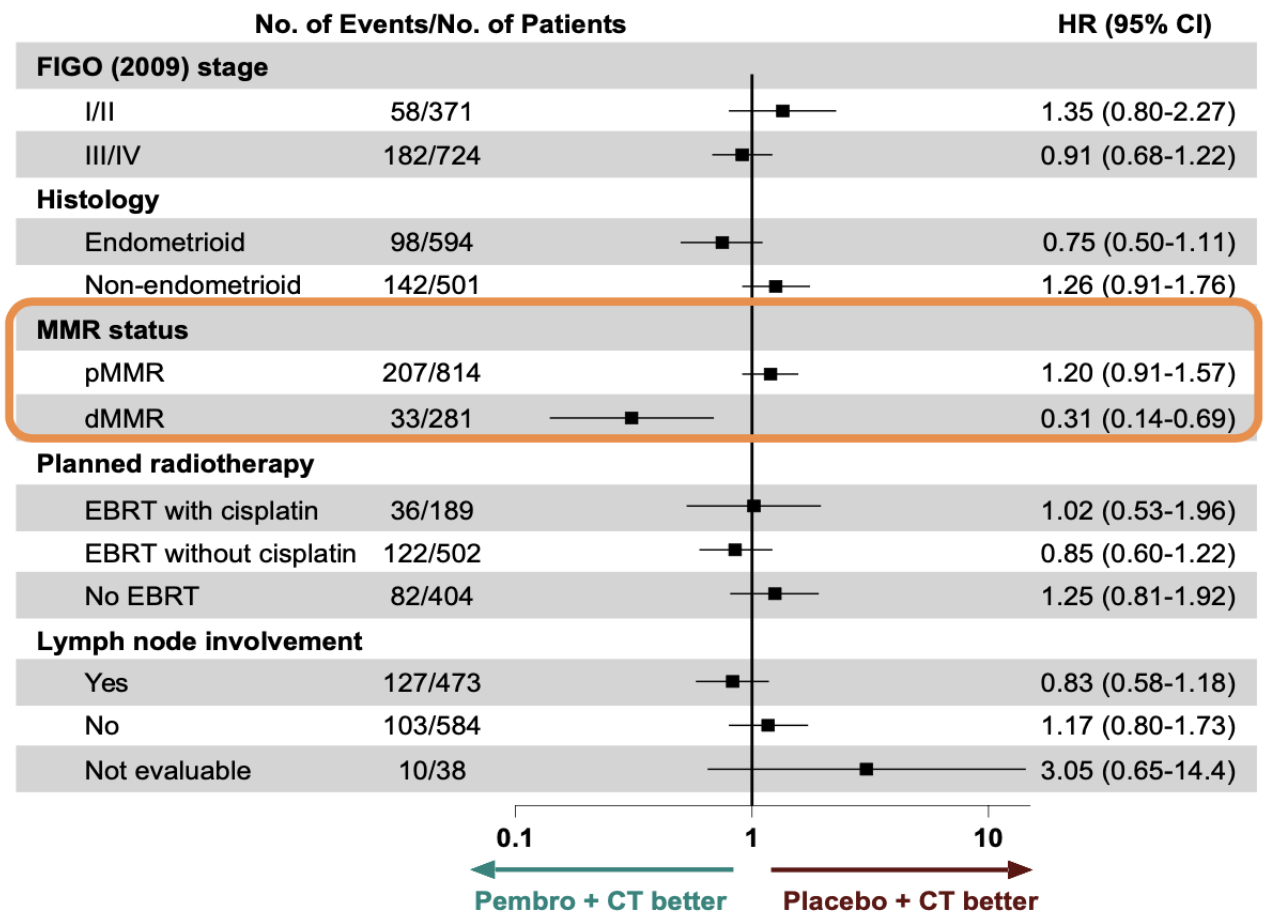
KEYNOTE-B21

Survie sans progression (sous-groupes)





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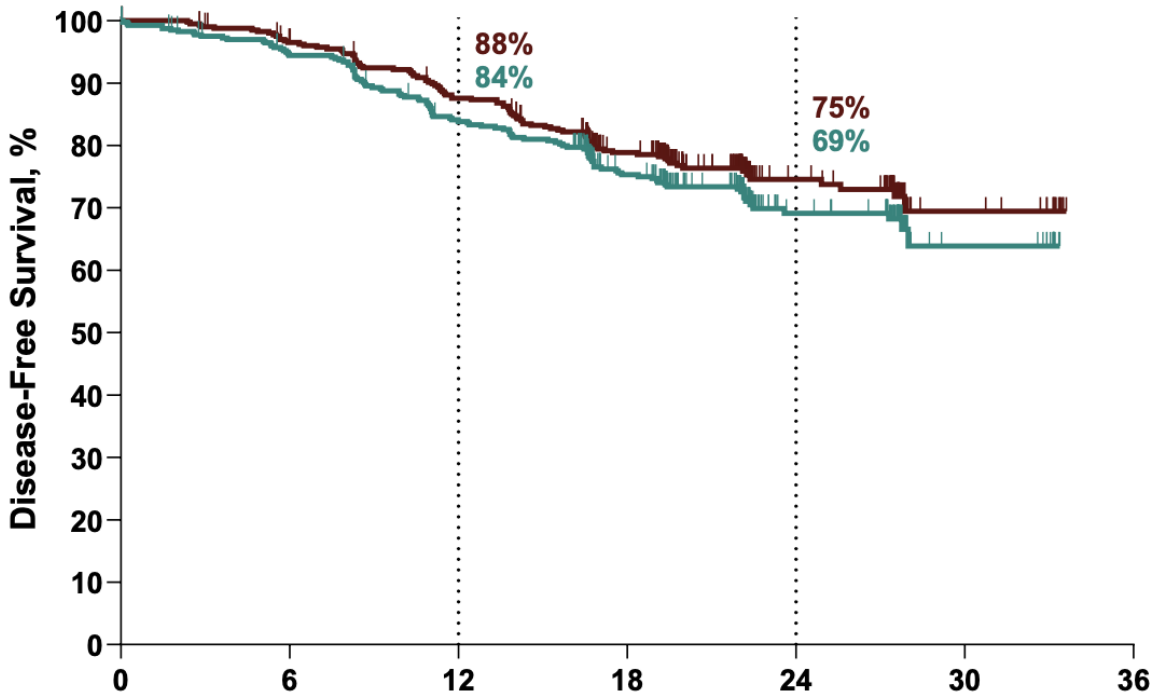
KEYNOTE-B21

Survie sans progression (pMMR vs dMMR)

pMMR Subgroup

	Events, n (%)	Median (95% CI), mo	HR (95% CI)
Pembro + CT	111 (27)	NR (NR–NR)	1.20 (0.91–1.57)
Placebo + CT	96 (23)	NR (NR–NR)	

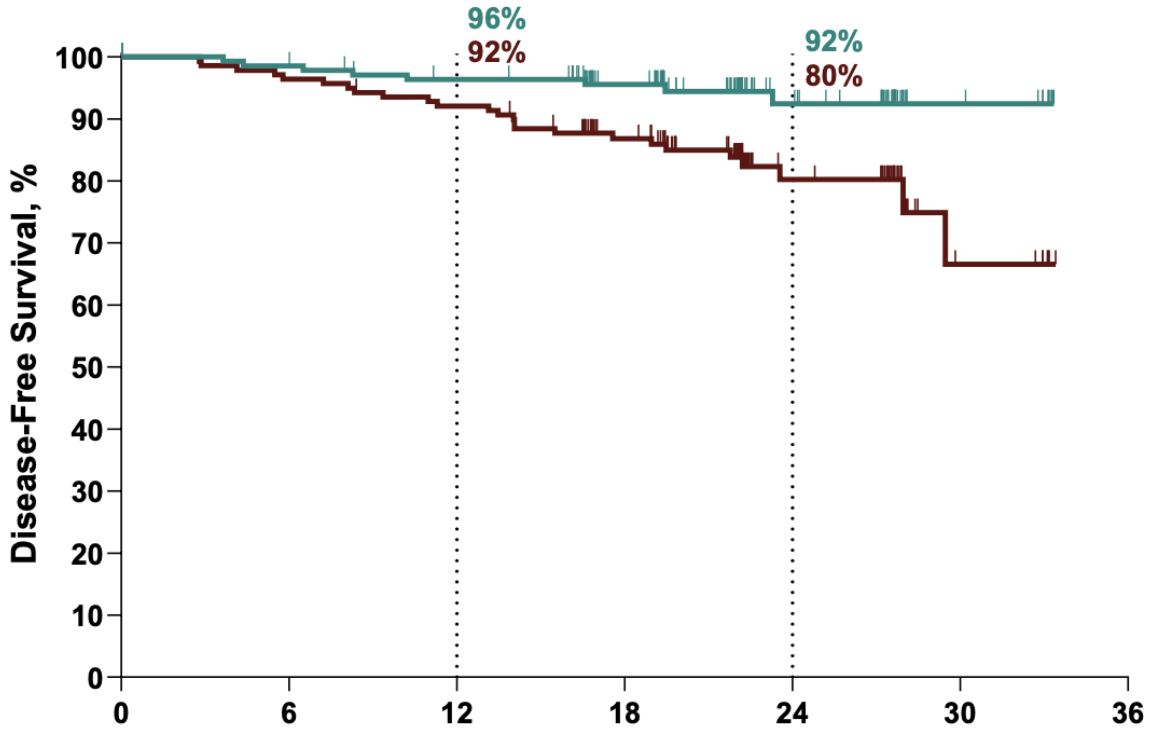


No. at risk

Pembro + CT	404	369	323	244	88	17	0
Placebo + CT	410	381	343	259	94	16	0

dMMR Subgroup

	Events, n (%)	Median (95% CI), mo	HR (95% CI)
Pembro + CT	8 (6)	NR (NR–NR)	0.31 (0.14–0.69)
Placebo + CT	25 (18)	NR (29.5–NR)	



No. at risk

	141	136	129	103	46	10	0
	140	134	127	99	38	7	0

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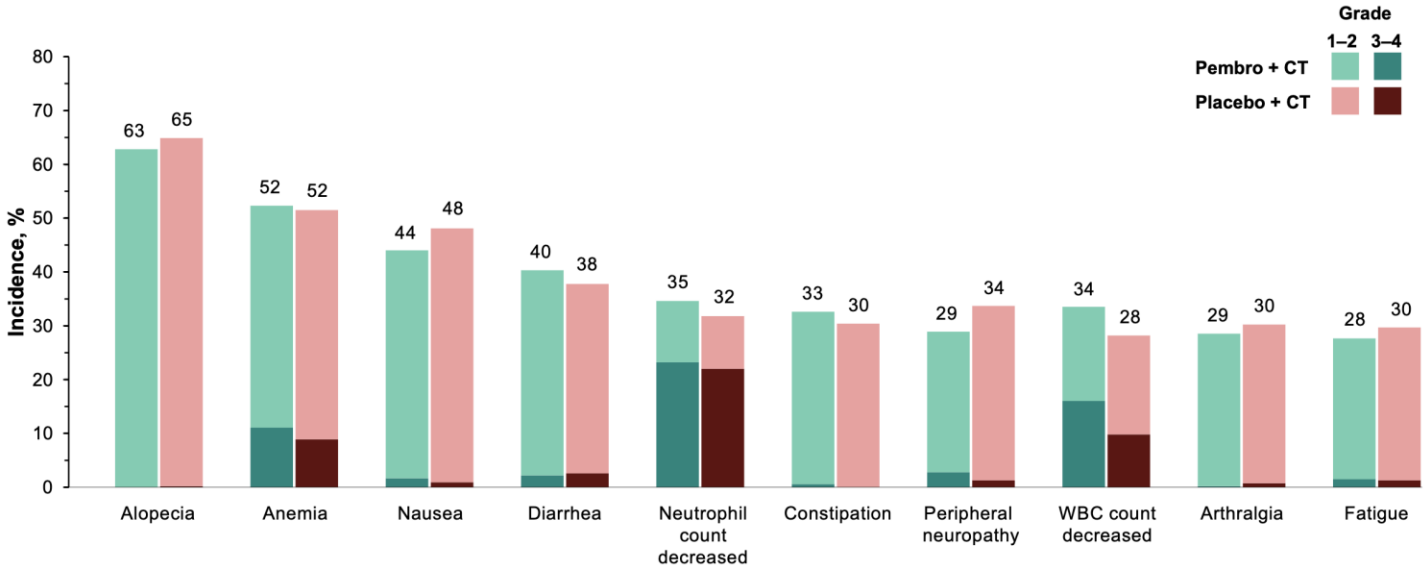
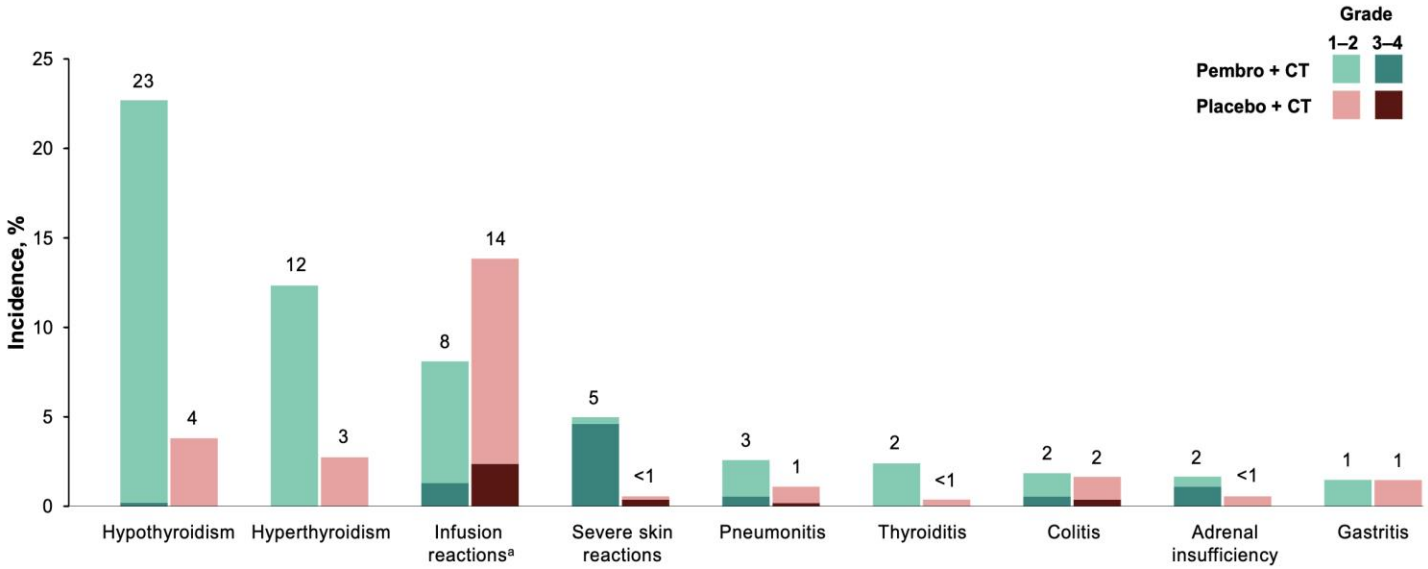
KEYNOTE-B21
Tolérance



AE ≥ 25 %



Immune-mediated AE ≥ 1 %

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KEYNOTE-B21
Discussion

- Une **étude négative** mais importante et utile
  - ➢ L'intérêt de l'immunothérapie en phase précoce (néoadjuvant/adjuvant…)
  - ➢ L'intérêt d'inclure dans les essais les patientes en les stratifiant selon leur groupe moléculaire (**études RAINBO**)

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TUMEURS TROPHOBLASTIQUES

TROPHAMET

BARCELONA 2024 ESMO congress

HCL HOSPICES CIVILS DE LYON | INSTITUT DE CANCÉROLOGIE

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Avelumab + methotrexate to eradicate low-risk gestational trophoblastic tumors in 1st-line setting: TROPHAMET trial.

Benoit YOU [1,2,3,4] ; Jean-Pierre LOTZ [1,5] ; Pierre DESCARGUES [1,6]; Florence JOLY [4,7]; Thibault DE LA MOTTE ROUGE [4,8]; Coriolan LEBRETON [4,9] ; Laurence GLADIEFF [4,10]; Philippe FOLLANA [4,11]; Mathieu JAMELOT [1,5]; Jérome MASSARDIER [1,12]; Touria HAJRI [1]; Marine ALVES-FERREIRA [13] ; Sylvie BIN [13]; Carole LANGLOIS-JACQUES [14]; Maxime BONJOUR [14] ; Adeline ROUX [13]; Christophe DESAUW [15]; Magali PROVANSAL [16]; Vérane SCHWIERTZ [17]; Francois GOLFIER [1,2,6] ; Pierre-Adrien BOLZE [1,2,6]

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TROPHAMET
Rationnel

- Tumeurs trophoblastiques gestationnelles (TTG) = **tumeurs rares** se développant pendant la **grossesse à partir du placenta** (1/10 000 grossesse, patientes jeunes)
- **80 %** des TTG diagnostiquées sont des tumeurs de **bas risque = FIGO ≤ 6**
- Taux d'hCG élevé tant que la maladie reste active.
- Standard = **monochimiothérapie jusque normalisation des hCG**
  - METHOTREXATE
  - ACTINOMYCINE D
- Guérison de 70 % des patientes en 1e ligne

- Forte expression du PD-L1 dans les TTG
- Essai de phase II **TROPHIMMUN** : **guérison > 50 %** chez des patientes résistantes à la chimiothérapie

Seckl MJ et al, Lancet. 2010;376(9742):717-729. Bolze PA et al, Int J Gynecol Cancer. 2017;27(3):554-561. Osborne RJ, et al. J Clin Oncol. 2011;29(7):825-831. You B, et al, J Clin Oncol. 2020 Sep 20;38(27):3129-3137. Lok C et al, Eur J Cancer. 2020;130:228-240. Baas IO, et al, Gynecol Obstet Invest. 2024;89(3):230-238.

TROPHAMET
Population

- Femmes ≥ 18 ans
- ECOG (performance status) ≤ 2
- TTG de bas risque (FIGO ≤ 6) avec indication d'un traitement par MTX en L1
- Absence de traitement antérieur ni de contre-indication aux IO
- Fonctions hématologiques, rénale, hépatique adéquates

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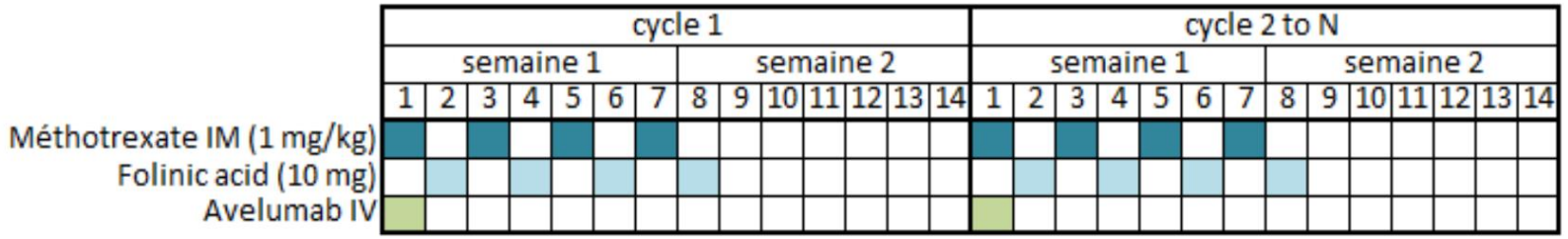
TROPHAMET
Design et méthodologie

- **SAFETY** phase I ⟺ **Effets indésirables, doses limites toxiques**
- **EFFICACY** phase II ⟺ **Taux de normalisation des hCG** permettant un arrêt des traitements

- **SAFETY** phase I ⟺ A confirmer avec 6 patientes
- **EFFICACY** phase II ⟺ **Taux de normalisation des hCG** ≥ 90 % nécessitant un recrutement de 26 patientes avec 22 patientes à guérir



→ Administration jusqu'à normalisation des hCG puis 3 cycles de consolidation

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TROPHAMET
Caractéristiques de la population

	Total	N= 26 (100%)
Age	Median (range), years	34.5 (20.0-50.0)
Disease stage	Stage I	11 (42%)
	Stage II	1 (4%)
	Stage III	**14 (54%)**
FIGO score	FIGO 1-2	8 (31%)
	FIGO 3-4	8 (31%)
	FIGO 5-6	**10 (38%)**
Pathology	Post complete mole	20 (77%)
	Post twin pregnancy & complete mole	1 (4%)
	Invasive mole	4 (15%)
	Choriocarcinoma	1 (4%)

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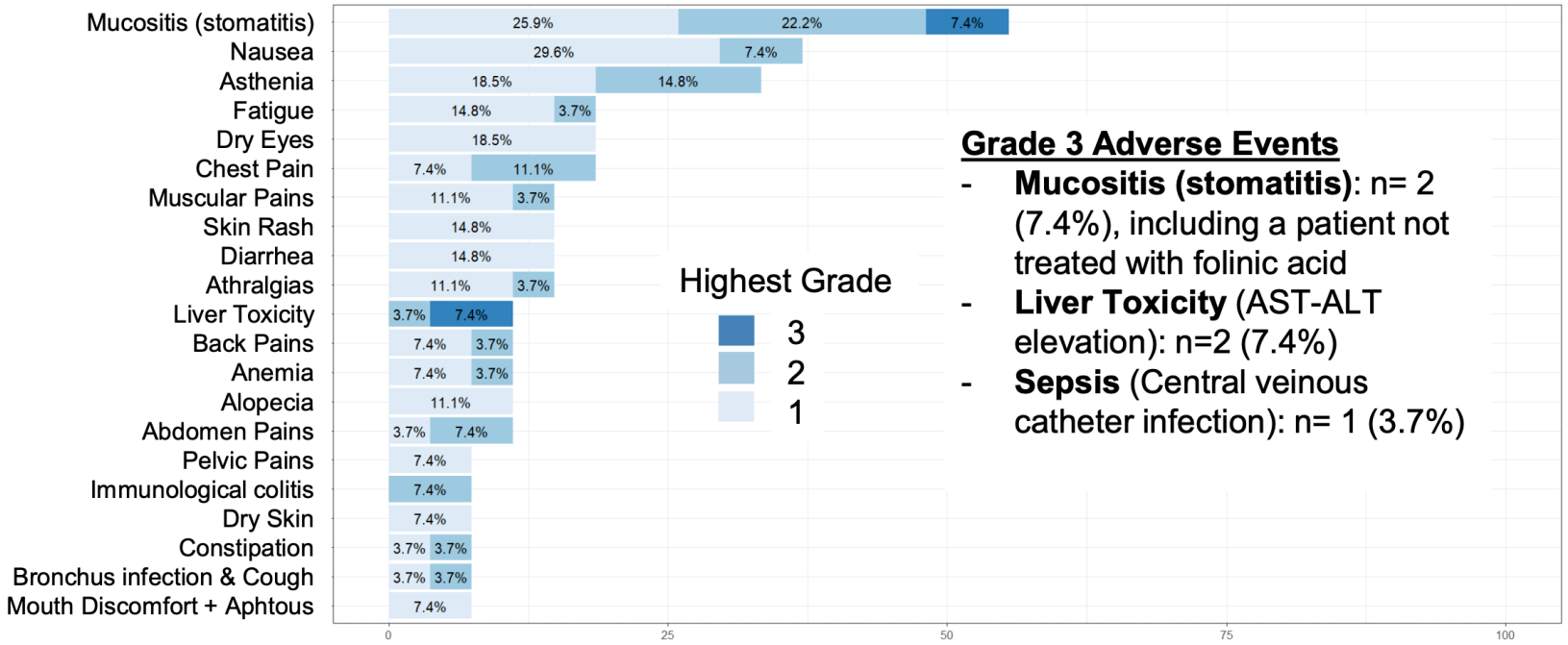
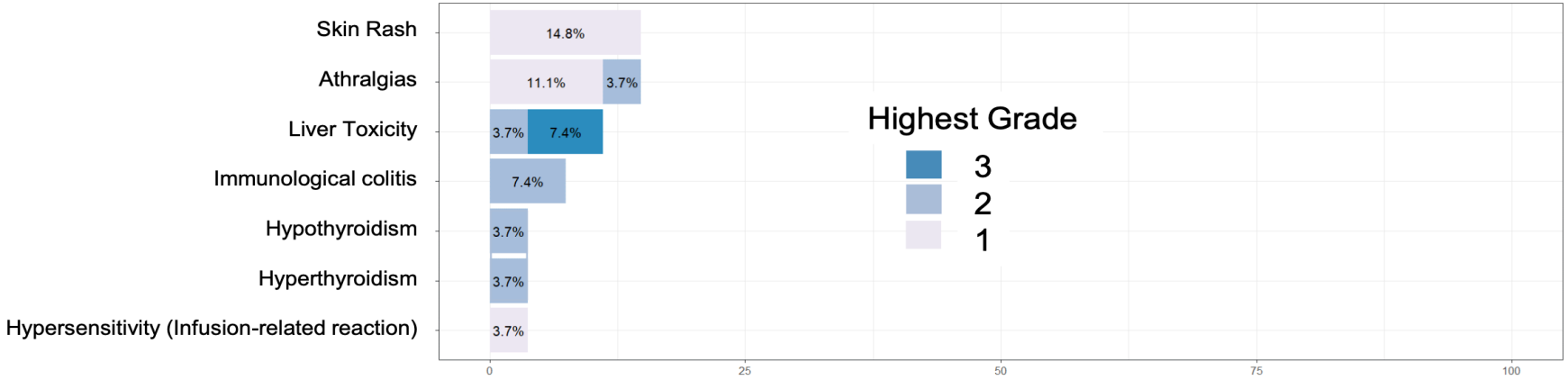
TROPHAMET
Tolérance



Grade 3 Adverse Events

- **Mucositis (stomatitis)**: n= 2 (7.4%), including a patient not treated with folinic acid
- **Liver Toxicity** (AST-ALT elevation): n=2 (7.4%)
- **Sepsis** (Central veinous catheter infection): n= 1 (3.7%)

AE ≥ 5 %



Immune-mediated AE

% of patients presenting the adverse event at least one time

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TROPHAMET
Efficacité

- Normalisation des hCG chez **96,2 % (25/26)** des patientes (95% CI [85,8-97,3])
  → Médiane de **3,32 mois** avant normalisation des hCG.
  → Nombre de cycles médians : 8 MTX (3-21) ; 8 Avelumab (2-21)
- Absence de récidive malgré 24,8 mois de suivi
- Aucun décès dans la population étudiée

	% de normalisation des hCG	
Stade	I (11/11)	100
	II (1/1)	100
	III (13/14)	92,8
FIGO	1-2 (8/8)	100
	3-4 (8/8)	100
	5-6 (9/10)	90,0

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BARCELONA 2024 ESMO congress

ANTICORPS DROGUES CONJUGUÉS

ADCs et cancer de l'ovaire

Cible	Anticorps	Payload	Linker	Ratio	ORR (%)	DOR (mois)	Référence
FRα	**Mirvetuximab Soravtansine (PICOLLO trial)**	DM4 (anti-tubuline)	Cleavable		51,9	8,25	*Annals of Oncology (2024) 35 (suppl_2): S544-S595. 10.1016/annonc/annonc1592*
	Rinatabart sesutecan	Exatecan (iTopo1)	Hydrophilic protease-cleavable	8,0	18,2-50	NR	*Annals of Oncology (2024) 35 (suppl_2): S544-S595. 10.1016/annonc/annonc1592*
HER2	**IBI354 (Trastuzumab)**	NT3 (iTopo1)	Cleaveable	8,0	40-52,5	NR	*Annals of Oncology (2024) 35 (suppl_2): S544-S595. 10.1016/annonc/annonc1592*
TROP2	**Sacituzumab Tirumotecan (MK-2870)**	KL610023 (iTopo1)	Pyrimidine-thiol	7,4	40	5,3	*Annals of Oncology (2024) 35 (suppl_2): S544-S595. 10.1016/annonc/annonc1592*
	Datopotamab Deruxtecan	Deruxtecan (iTopo1)	Cleavable tetrapeptide-based linker	4	42,9	5,7	*Annals of Oncology (2024) 35 (suppl_2): S544-S595. 10.1016/annonc/annonc1592*
Claudin 6	**TORL-1-23**	vc-MMAE		4	30-50	22-30	*Annals of Oncology (2024) 35 (suppl_2): S544-S595. 10.1016/annonc/annonc1592*

ADCs et cancer du col/endomètre

Cible	Anticorps	Payload	Linker	Ratio	ORR (%)	DOR (mois)	Référence
FRα	**Rinatabart sesutecan**	Exatecan (iTopo1)	hydrophilic protease-cleavable	8,0	30,8	8,12	*Annals of Oncology (2024) 35 (suppl_2): S544-S595. 10.1016/annonc/annonc1592*
TROP2	**Sacituzumab Tirumotecan (MK-2870)**	KL610023 (iTopo1)	Pyrimidine-thiol	7,4	34,1	5,7	*Annals of Oncology (2024) 35 (suppl_2): S544-S595. 10.1016/annonc/annonc1592*
	Sacituzumab Tirumotecan + Pembrolizumab				57,9	NR	*Annals of Oncology (2024) 35 (suppl_2): S544-S595. 10.1016/annonc/annonc1592*
	Datopotamab Deruxtecan	Deruxtecan (iTopo1)	Cleavable tetrapeptide-based linker	4	27,5	16,4	*Annals of Oncology (2024) 35 (suppl_2): S544-S595. 10.1016/annonc/annonc1592*