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Poitiers

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1^{er} post ESMO Nouvelle-Aquitaine 2024



Liens d'intérêts

Novartis, Astra Zeneca, Daiichy Sankyo

Cancer du col de l'utérus



KEYNOTE-A18: radio-chimiothérapie +/- immunothérapie: plénière!

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

R 1:1 N = 1060

Cisplatin 40 mg/m² 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/m² QW for 5 cycles^a + EBRT followed by brachytherapy

Placebo Q3W for 5 cycles

Placebo Q6W for 15 cycles

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])





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Baseline Characteristics

	Pembro Arm (N = 529)	Placebo Arm (N = 531)
Age, median (range)	49 y (22-87)	50 y (22-78)
Racea		
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%)

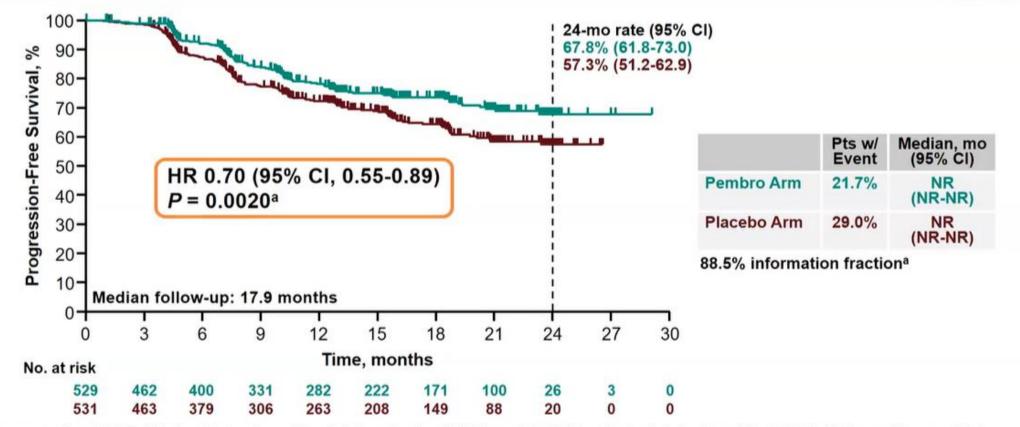
134	Pembro Arm (N = 529)	Placebo Arm (N = 531)
Stage at screening (FIGO 2014 crite	eria)	
IB2-IIB	233 (44.0%)	226 (42.6%)
III-IVA	296 (56.0%)	305 (57.4%)
Lymph node involvement ^b		
Positive pelvic only	327 (62.2%)	324 (61.0%)
Positive para-aortic only	14 (2.6%)	10 (1.9%)
Positive pelvic and para-aortic	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 (EC	QD2)	
<70 Gy	47 (8.9)	46 (8.7)
≥70 Gy	482 (91.1)	485 (91.3)



Cancer du col de l'utérus

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Progression-Free Survival at IA1



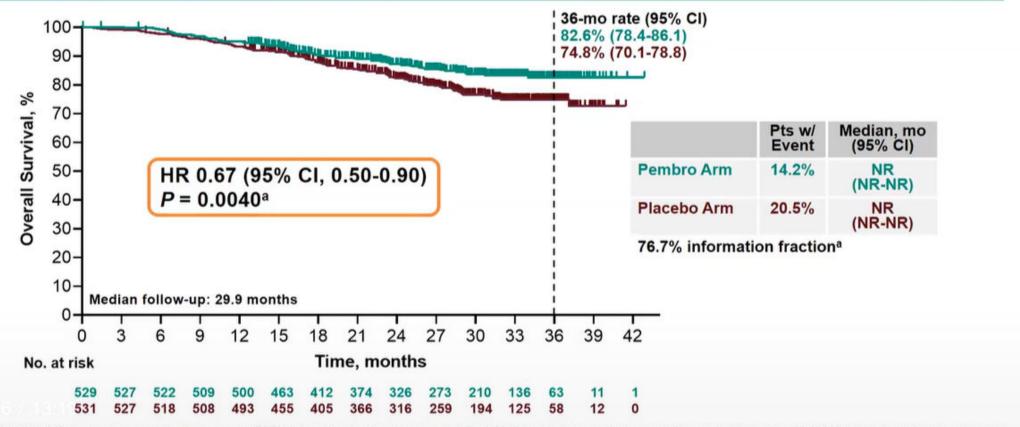
Response assessed per RECIST v1.1 by investigator review or histopathologic confirmation. "With 269 events (88.5% information fraction), the observed P = 0.0020 (1-sided) crossed the prespecified nominal boundary of 0.0172 (1-sided) at this planned first interim analysis. The success criterion of the PFS hypothesis was met, and thus no formal testing of PFS will be performed at a later analysis. Data cutoff date: January 9, 2023.



Cancer du col de l'utérus

KEYNOTE-A18: radio-chimiothérapie +/- immunothérapie: plénière!

Primary Endpoint: Overall Survival at IA2



"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.

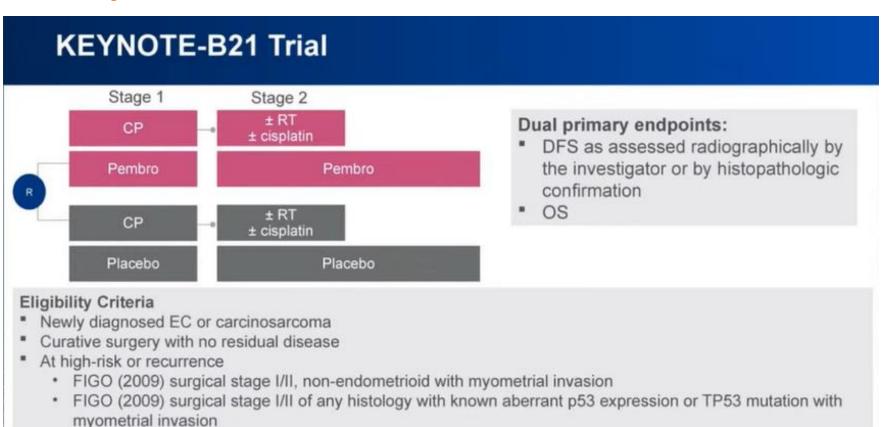


Cancer de l'endomètre

FIGO (2009) surgical stage III/IVA of any histology

No prior radiation or systemic therapy (including neoadjuvant) for EC

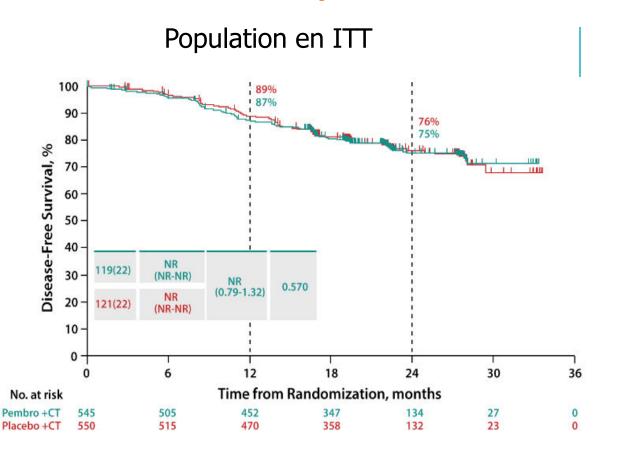
KEYNOTE-B21: Pembrolizumab adjuvant : étude négative mais résultats positifs!

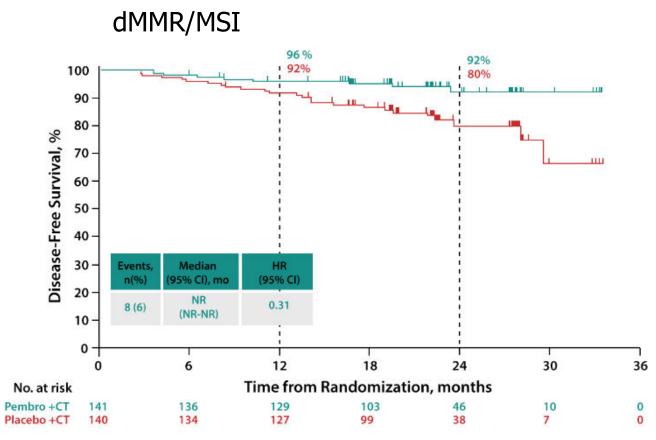




Cancer de l'endomètre

KEYNOTE-B21: Pembrolizumab adjuvant : étude négative mais résultats positifs!

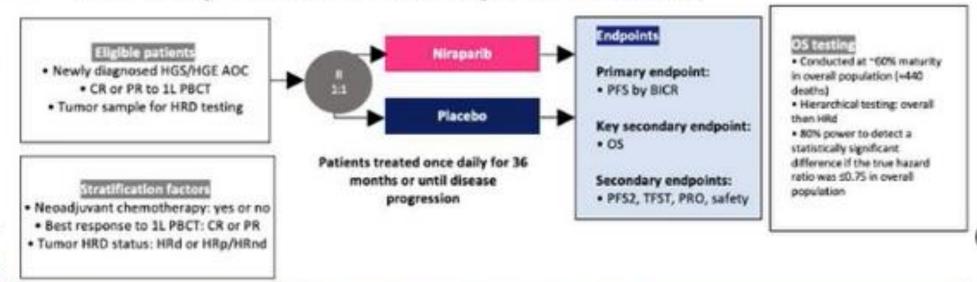






PRIMA : la déception en survie globale !

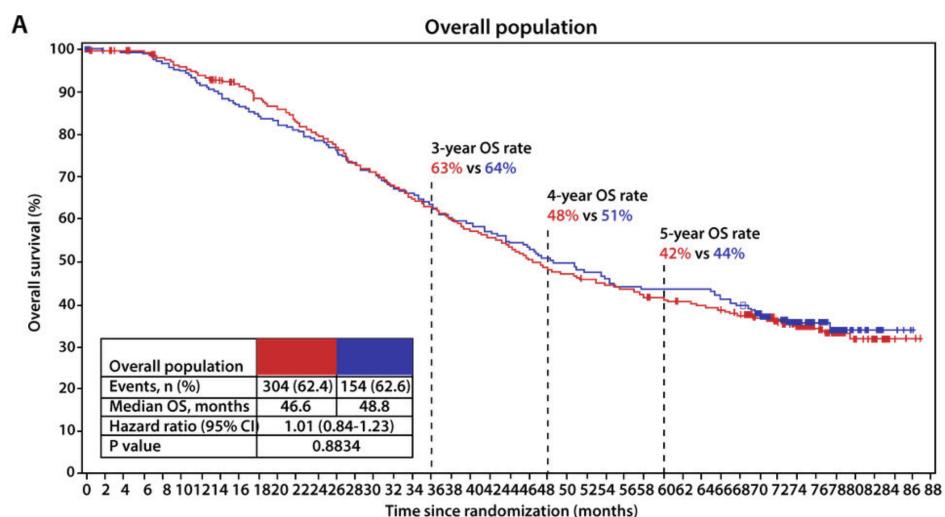
PRIMA/ENGOT-OV26/GOG-3012



The state of the s	isk characteristics of PRIMA population	T
Disease stage	Residual disease	Tumor HRD/BRCA status
35.1% stage IV disease at diagnosis	>99% stage III disease at diagnosis with residual primary debulking surgery	50.9% HRd
Initial treatment		30.4% HRd/BRCAm
66.7% received neoadjuvant chemotherapy	47.5% postoperative visible residual disease	34.0% HRp
30.6% achieved partial response to 1L PBCT		



PRIMA: la déception en survie globale!





ATHENA-COMBO: nouvel échec de l'immunothérapie

ATHENA STUDY SCHEMA

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

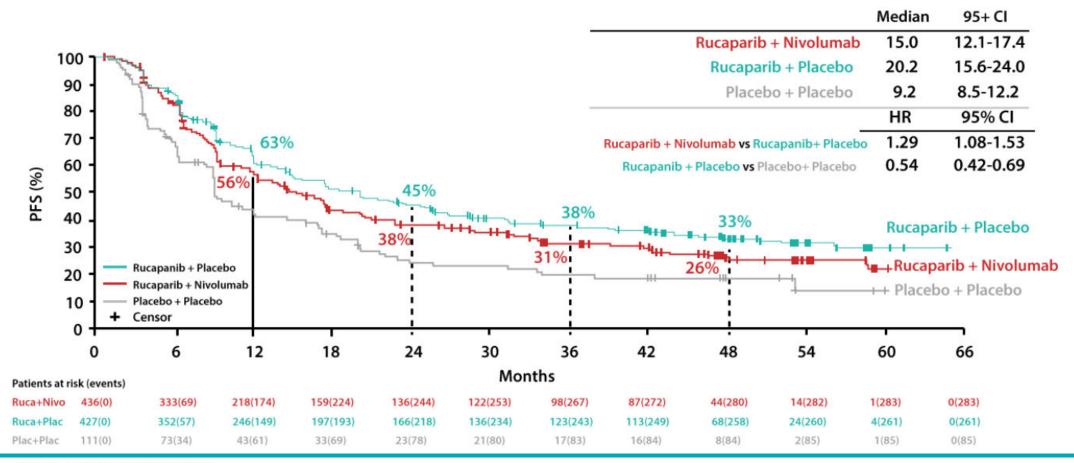
Arm D (n≈100) placebo PO + placebo IV

Primary endpoint: Investigator-assessed PFS in the ITT population



ATHENA-COMBO: nouvel échec de l'immunothérapie

ATHENA-COMBO: INVESTIGATOR-ASSESSED PFS (ITT)





ATALANTE : résultats finaux en OS

ATALANTE design and endpoints

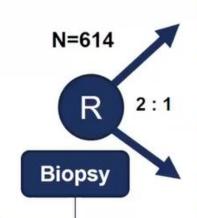




- Relapsed non-mucinous epithelial OC
- Platinum-free interval >6 mos
- 1 or 2 prior chemotherapy lines
- ECOG PS ≤1

Stratification factors:

- PD-L1 ≥ 1% on immune cells vs <1% vs unknown
- Chemotherapy: Cb-PLD or gemcitabine or paclitaxel
- Platinum-free interval: 6-12 vs >12 mos





Up to 24 months

Bevacizumab + atezolizumab

Carboplatin-based chemotherapy



Up to 24 months

Bevacizumab + placebo

- Co-primary endpoints: PFS in the ITT and PD-L1-+ populations
- Secondary endpoints:
 - Overall Survival
 - TSST, TFST, safety and HrQoL

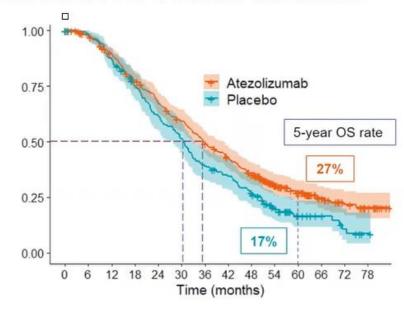


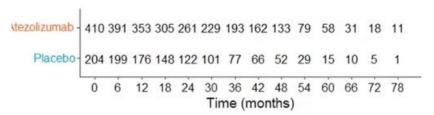
Jean-Emmanuel KURTZ



ATALANTE : résultats finaux en OS

ATALANTE overall survival









- Median OS* was:
 - 35.75 months (32.89- 41.00) in the atezolizumab arm
 - 30.62 months (27.79- 33.15) in the placebo arm
- The estimated probability of OS at 60 months was:
 - 27% (CI 95% 23%-32%) in the Atezolizumab arm
 - 17% (CI95% 12%-23%) in the placebo arm.

^{*} No formal comparison due to the hierarchical statistical plan

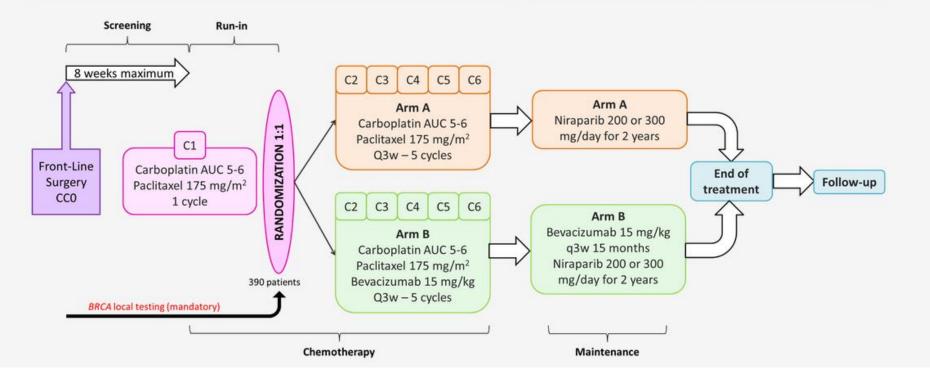


Comment choisir la maintenance? Bevacizumab, iPARP? NIRVANA

- Stage IIIA/B/C
- High-grade non-mucinous and non-clear cell epithelial ovarian, fallopian tube or primary peritoneal carcinoma
- Complete cytoreduction
- BRCA status mandatory
- PS 0/1

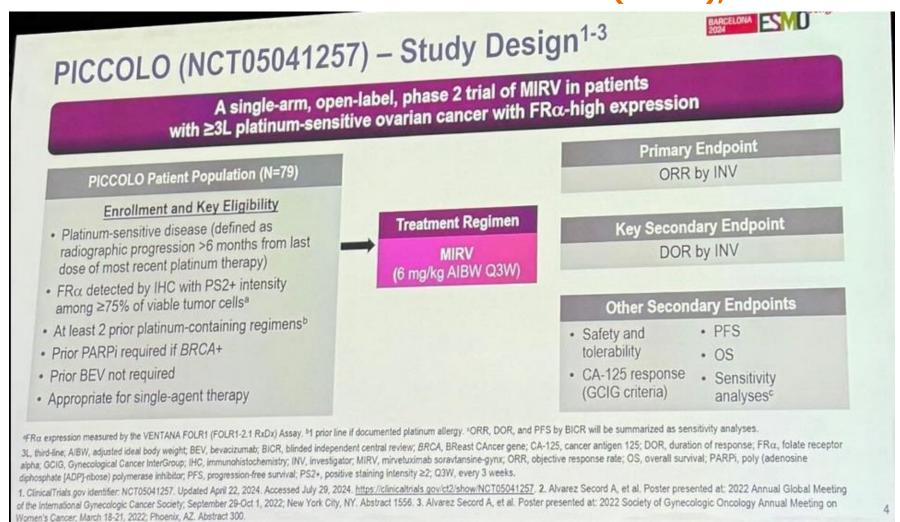
STRATIFICATION

- BRCA status (local assessment)
- FIGO stage at diagnosis (IIIA versus IIIB/IIIC).
- Previous hyperthermic intraperitoneal chemotherapy (yes/no).



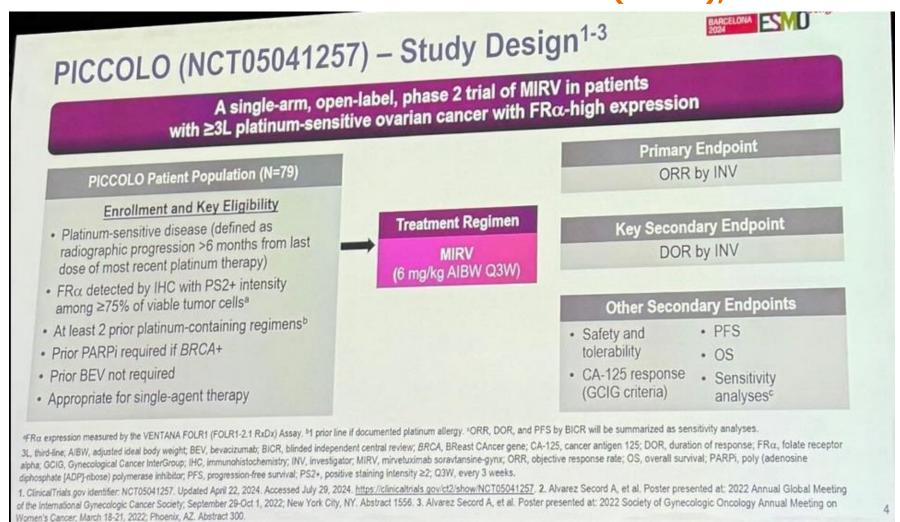


Les ADC: le mirvetuximab soravtansine (MIRV), essai PICCOLO





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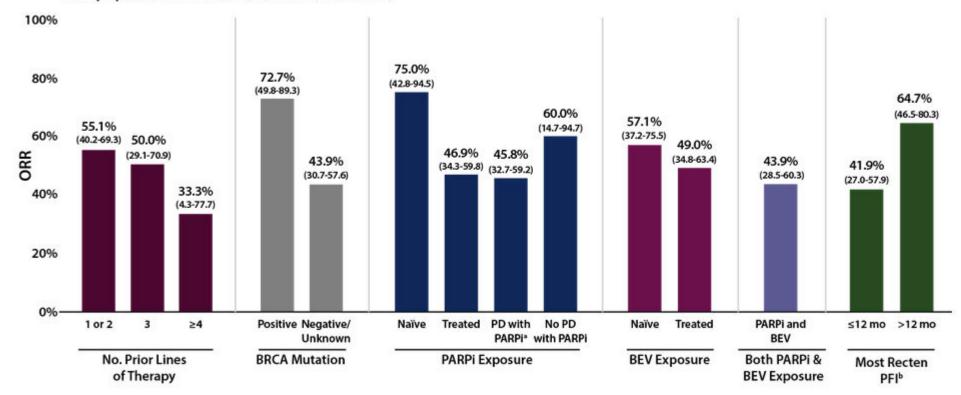




Les ADC: le mirvetuximab soravtansine (MIRV), essai PICCOLO

ORR by Subgroups

Total population ORR: 51.9% (95% CI, 40.4-63.3)



Data cutoff: January 17, 2024 ORR presented with 95% CI

'if the participant had progression of disease when 30 days after the last dosing of a PARPi or progression was isted as the reason for treatment discontinuation of a PARPi, the participant was defined as having progressive disease on prior PARPi and was included in this category. Platinum-free interval is defined as time from last dose of the latest line platinum therapy to the date of disease progression and/or relapse following that line of therapy (time rounded to whole number).



Endomètre et ovaire

Les ADC: le Datopotamab-Deruxtecan (D-Dxd), essai TROPION Pan-Tumor03

TROPION-PanTumor03: Study Design



A Phase 2, open-label, global study (NCT05489211) evaluating Dato-DXd as monotherapy and in combination with various anticancer agents across several tumour types

N = 35

Dato-DXd1

6 mg/kg IV Q3W

N = 40

Here, we present results of Dato-DXd monotherapy in the ovarian and endometrial cancer cohorts

Ovarian cancer (TROP2 expression unselected)

- High-grade serous or endometrioid ovarian, fallopian tube, or primary peritoneal carcinoma
- ECOG PS 0 or 1
- Progressed on ≥1 line of platinum chemotherapy but no more than 2 lines of therapy for advanced or metastatic disease; platinum-sensitive and resistant disease allowed'

Endometrial cancer (TROP2 expression unselected)

- Advanced/metastatic endometrial carcinoma
- All histologies (except sarcoma)
- ECOG PS 0 or 1
- Progressed on ≥1 line of platinum chemotherapy but no more than 2 lines
 of therapy for advanced or metastatic disease

Endpoints Primary

- ORR by investigator per RECIST v1 1
- . Safety & tolerability

Secondary

- PFS, DoR, DCR by investigator
- PK and immunogenicity

Exploratory

- · 0S
- Biomarker analyses

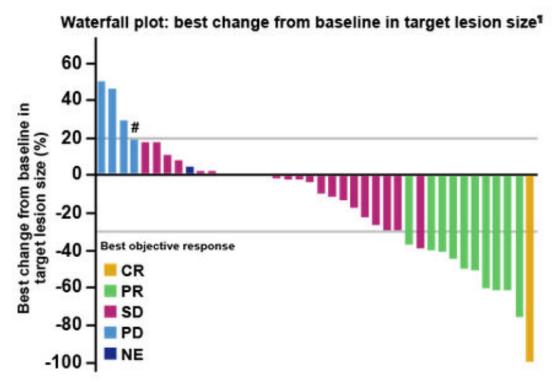


Endomètre et ovaire

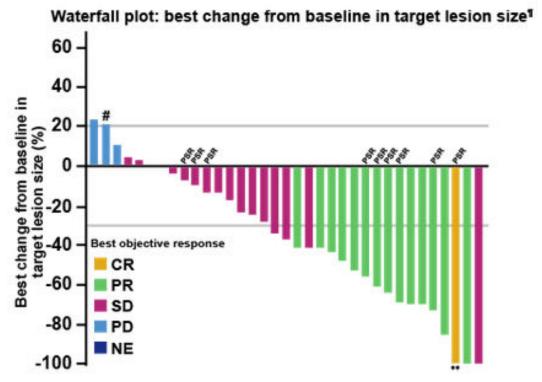
Les ADC: le Datopotamab-Deruxtecan (D-Dxd), essai TROPION Pan-Tumor03

Endomètre

Ovaire



SSP: 6,3mois (IC 95 % : 2.8-non encore atteinte)

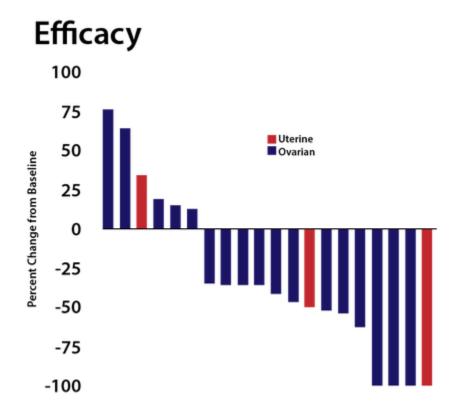


SSP: 5,8mois (IC 95 %: 4,1-7,1)



Endomètre et ovaire, cellules claires

Immunothérapie prometteuse! Phase II MoST-CIRCUIT, NIVO-IPI



Response	Total N=261	Ovarian N=22	Uterine N=4				
Objective response rate % (95% CI)	50% ² (95% CI : 29 to 56%)	50% (95% CI : 27 to 65%)	50% (95% CI : 9 to 91%)				
Best overall response							
CR	3 (12%)	3 (14%)	0				
PR	10 (38%)	8 (36%)	2 (50%)				
SD	2 (8%)	1 (5%)	1 (25%)				
PD	5 (19%)	5 (23%)	0				
No radiological assessment	6 (23%)	5 (23%)	1 (25%)				
Clinical benefit rate % (95%CI)	58% (95% CI : 35 to 71%)	55% (95% CI : 31 to 69%)	75% (95% CI : 30 to 99%)				

¹ One patient withdrew and one patient experienced grade 5 myocarcarditis prior to first assessment

² includes one patient with dMMR tumour (PSM2 mutation)

³ Six patients clinically progressed prior to their first radiological assessment and were taken off study



Tumeur trophoblastique gestationnelle à bas risque

Essai français TROPHAMET, phase I/II: nouveau standard? TROPHAMET trial design (NCT04396223)

Study Treatment

- Treatment
 - 8-day MTX regimen: Methotrexate 1 mg/kg IM on days 1, 3, 5, 7 alternating with oral Folinic acid; Q2weeks
 - Avelumab: Flat dose with IV 800 mg every 2 weeks, on days 1 before MTX

	cycle 1									cycle 2 to N												\neg						
		semaine 1					semaine 2							semaine 1							semaine 2							
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Méthotrexate IM (1 mg/kg)																												
Folinic acid (10 mg)																												
Avelumab IV																												

Administration until hCG normalization, followed by 3 consolidations cycles



Tumeur trophoblastique gestationnelle à bas risque

Essai français TROPHAMET, phase I/II: nouveau standard?

Critère largement atteint avec taux de guérison de 96,2%!

