Organizador:

FBMS
Fundación Biomédica Miguel Servet

ASCO 2024
Tumores ginecológicos

Ana Herrero

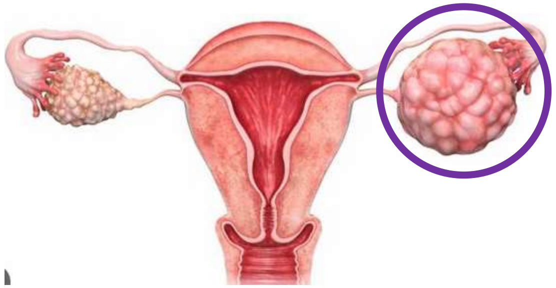
Hospital universitario Miguel Servet

Zaragoza

-

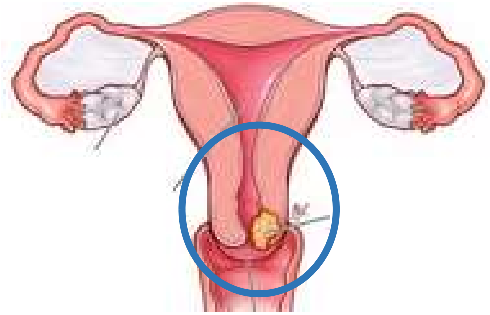
-Cáncer de ovario

NEO trial. Fase II. Sensible
AGO-OVAR 2.29/ENGOT-ov34 .Fase III. Resistente
BrUOG 354. Fase II
AXLerate-OC/GOG-3059/ENGOT OV-66.Fase III. Resistente
SCORES. Fase III. Resistente



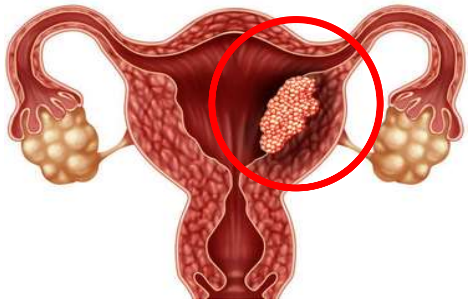
-Cáncer de cérvix

Nimotuzumab. Fase III. Locamente avanzado
RTOG 0724/GOG-0724.Fase III ady tras QT-RT
DURBAC. Fase II avanzado



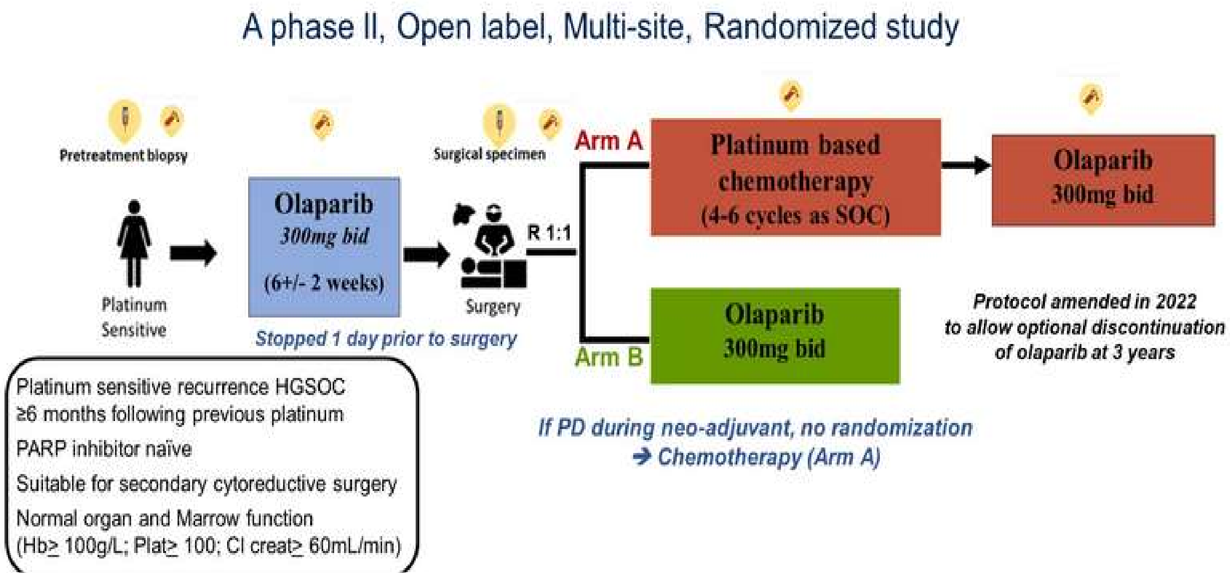
-Cáncer de endometrio

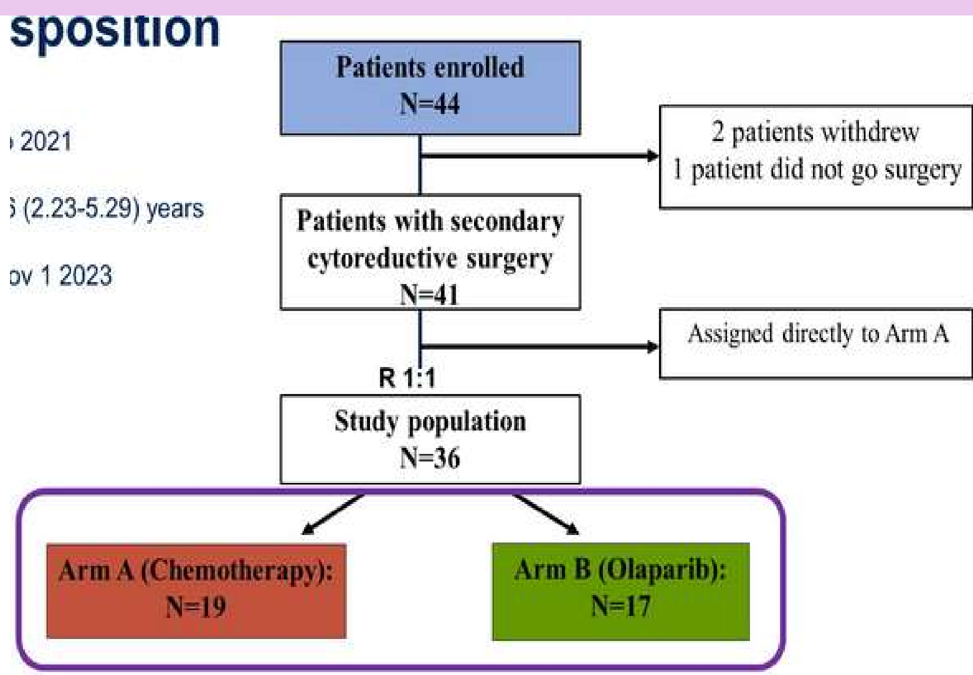
Keyvive 005.Fase II. Endometrio dMMR tras fallo a 1 línea



Phase II randomized multi-centre study of neoadjuvant olaparib in patients with platinum sensitive relapsed high grade serous ovarian cancer: The NEO trial.

Stephanie Lheureux, ASCO 24

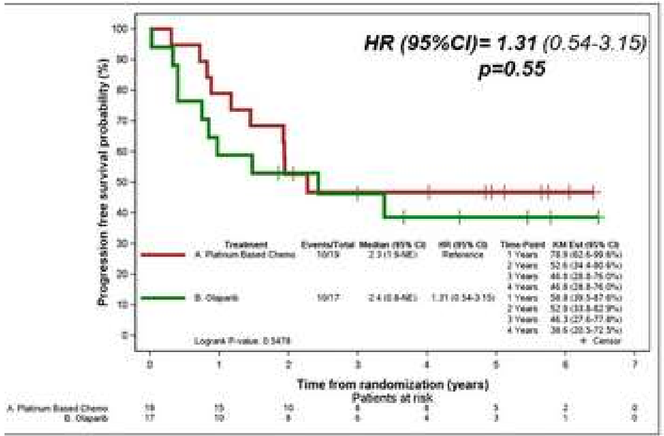




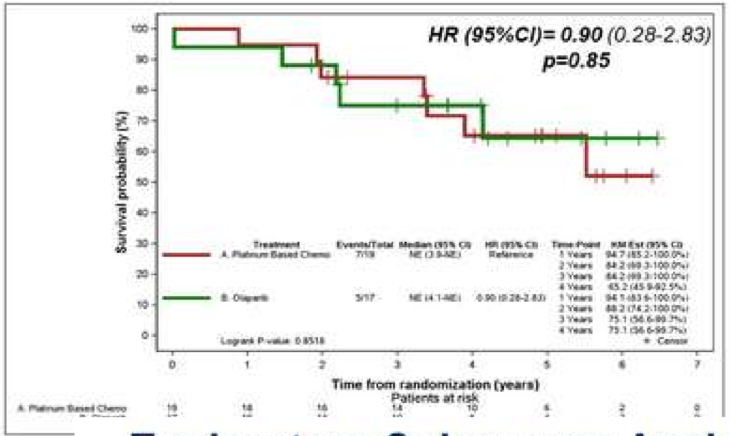
	A. Platinum Based Chemotherapy (N = 19)	*B. Olaparib (N = 17)*	*Total (N = 36)*
Age at enrollment (year)			
Median (Range)	59.0 (39.0 – 80.0)	59.0 (44.0 – 84.0)	59.0 (39.0 – 84.0)
Prior Neoadjuvant Chemotherapy			
No	12 (63.16%)	15 (88.24%)	27 (75.00%)
Yes	7 (36.84%)	2 (11.76%)	9 (25.00%)
Number of Prior Line of Therapy			
Median (Range)	1.0 (1.0 – 3.0)	1.0 (1.0 – 4.0)	1.0 (1.0 – 4.0)
Germline *BRCA* Status			
Mutated	7 (36.84%)	4 (23.53%)	11 (30.56%)
Wild-Type	5 (26.32%)	12 (70.59%)	17 (47.22%)
Unknown	7 (36.84%)	1 (5.88%)	8 (22.22%)
Race			
White	13 (68.42%)	13 (76.47%)	26 (72.22%)
Other	6 (31.58%)	4 (23.53%)	10 (27.78%)

Survival Outcomes – ITT population (N=36)

Progression Free Survival (PFS)

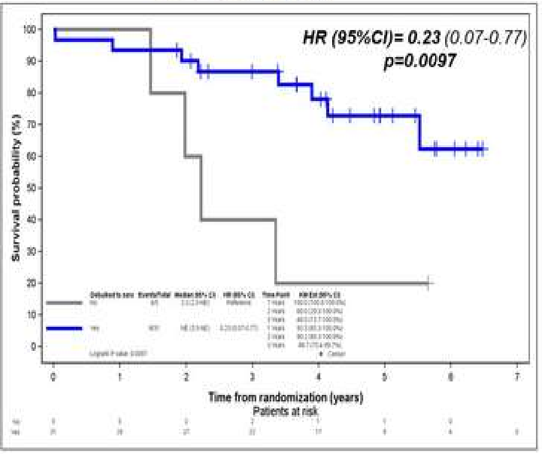


Overall Survival (OS)

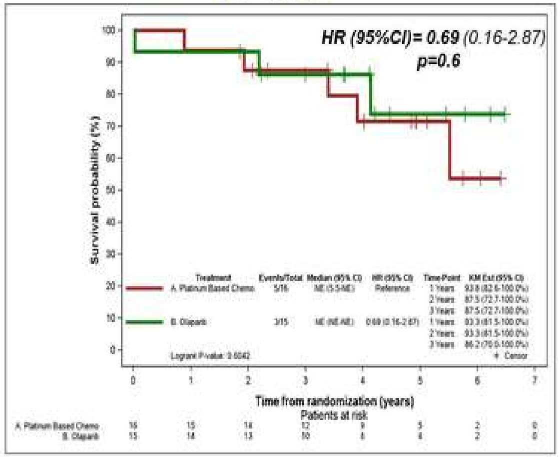


Subgroup Analyses – Residual disease status

OS: R0 vs R1

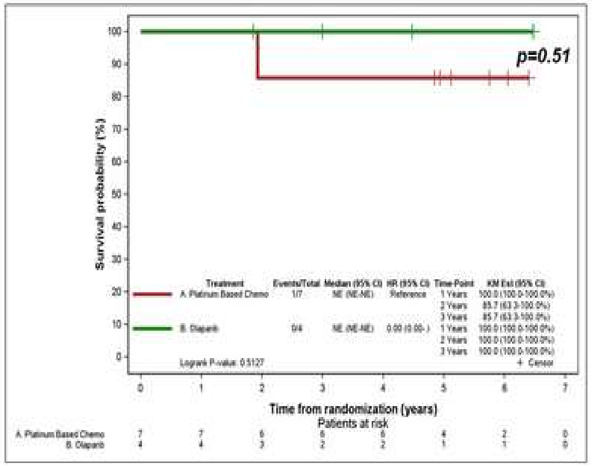


OS in R0

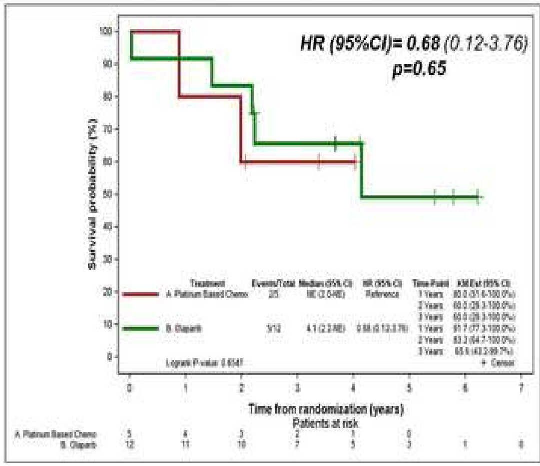


Exploratory Subgroups Analyses – g*BRCA* status

OS in g*BRCA* mut



OS in g*BRCA* WT



Surgery Period – Safety & Efficacy (N=36 patients)

- **Type of surgery:** 78% Laparotomy
- **Objective Response Rate**: 94% - Complete Response: 74% (26 patients)
- **Median time to start adjuvant therapy:** 1.2 (0.5-3.4) months
- **Surgical complications:** Grade 3 reported surgical related AE – All recovered
  - Abscess: 2 patients
  - Perforation (colonic – bladder – enterotomy): 3 patients
  - Thrombo-embolic events: 2 patients

Adjuvant Therapy post randomization

Safety: No reported MDS/AML

Treatment Exposure

- *Median cycles*

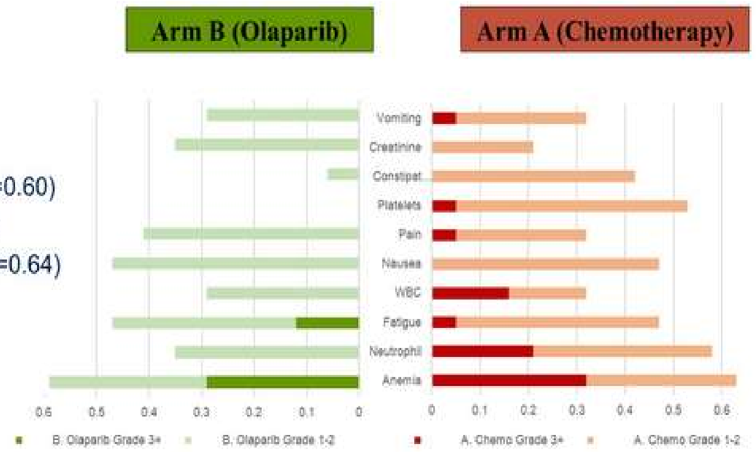
  Arm A= 21.5 – Arm B= 18 cycles (p=0.60)
- *Median time on adjuvant olaparib*

  Arm A= 13.8 – Arm B= 14.7 mths (p=0.64)
- *Dose Modification*

  Arm A = 15 pts (79%) to chemo

  12 pts (63%) to olaparib

  Arm B: 14 pts (82%)
- 13 pts off maintenance without progression



Top ten AE events during adjuvant period

Conclusion

- In patients with complete disease resection after secondary cytoreductive surgery, olaparib alone was as effective as chemotherapy followed by olaparib and associated with less toxicity.
- This study suggests the potential for a de-escalation approach with targeted therapy in this selected population.
- Further clinical & translational research is needed to investigate chemo-free option for our patients.

Atezolizumab versus placebo in combination with bevacizumab and non-platinum-based chemotherapy in recurrent ovarian cancer: Final overall and progression-free survival results from the AGO-OVAR 2.29/ENGOT-ov34 study.

Frederik Marmé. ASCO 24

RESISTENTE

Trial Design

Main Inclusion Criteria:
- Epithelial ovarian, fallopian tube or peritoneal cancer
  - 1st or 2nd relapse: TFIp < 6 months
  - OR 3rd relapse
- Recent & archival biopsy mandatory
- ECOG PS ≤ 1
- life expectancy > 3 months
- Prior Bevacizumab allowed

Stratification factors:
- Number of prior lines (1-2 vs 3)
- Planned chemotherapy (PLD vs paclitaxel)
- Prior bevacizumab (yes vs no)
- PD-L1 status (SP142 IC 1/2/3 vs 0 vs non-informative)*

- PD-L1 status was prospectively tested, but introduced as a stratification factor as part of an amendment
- Tumors with non-informative test results were to be capped at 10%

574

1:1

R

n=550

285

PLD or Paclitaxel + Bevacizumab + Placebo

Treatment until disease progression, intolerable toxicity or a maximum duration of 24 months, whatever occured first

289

PLD or Paclitaxel + Bevacizumab + Atezolizumab

PLD: 40 mg/m² d1, q28d;
Paclitaxel: 80 mg/m² d1, 8, 15, 22, q28d;
Bevacizumab: 10 mg/kg d1, q14d;
Atezolizumab OR Placebo: 840 mg d1, q14d

Primary endpoints:
- Overall survival
- Progression-free survival

Secondary endpoints:
- ORR & DOR
- Safety & tolerability
- *OS, PFS, ORR & DOR by PD-L1 status*
- *HrQoL/PROs*

Exploratory & translational endpoints

PLD, pegylated liposomal doxorubicin; PS, performance status; TFIp, treatment-free interval for platinum

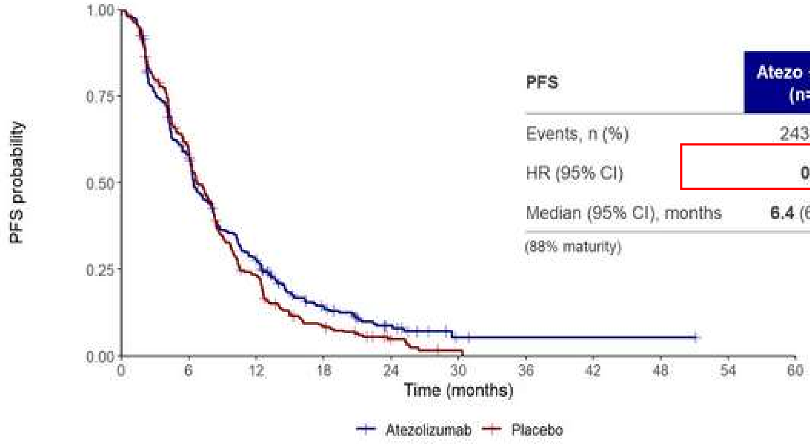
Baseline Characteristics (1)

	Atezolizumab (n=285)	Placebo (n=289)	Total (n=574)
Median patient age, years (IQR)	**62** (56-70)	**61** (53-70)	**62** (54-70)
ECOG, n (%)			
0	163 (57.2)	152 (52.6)	315 (54.9)
1	120 (42.1)	136 (47.1)	256 (44.6)
Histology, n (%)			
High-grade serous	203 (71.2)	214 (74)	417 (72.6)
other	82 (28.8)	75 (26)	157 (27.4)
Prior lines, n (%)			
1-2	183 (64.2)	182 (63)	365 (63.6)
3	102 (35.8)	107 (37)	209 (36.4)
Planned chemotherapy, n (%)			
PLD	129 (45.3)	135 (46.7)	264 (46.0)
Paclitaxel	156 (54.7)	154 (53.3)	310 (54.0)
Prior PARPi, n (%)	114 (40.0)	120 (41.5)	234 (40.8)
Prior bevacizumab, n (%)	210 (73.7)	206 (71.3)	416 (72.5)

Baseline Characteristics (2)

	Atezolizumab (n=285)	Placebo (n=289)	Total (n=574)
PD-L1 status at randomisation, n (%)*			
positive	63 (22.1)	68 (23.5)	131 (22.8)
negative	153 (53.7)	153 (52.9)	306 (53.3)
non-informative	69 (24.2)	68 (23.5)	137 (23.9)
Overall PD-L1 status, n (%)**			
positive	70 (24.6)	78 (27.0)	148 (25.8)
negative	187 (65.6)	184 (63.7)	371 (64.6)
non-informative	28 (9.8)	27 (9.3)	55 (9.6)

Primary Endpoint: Progression-free Survival (ITT)



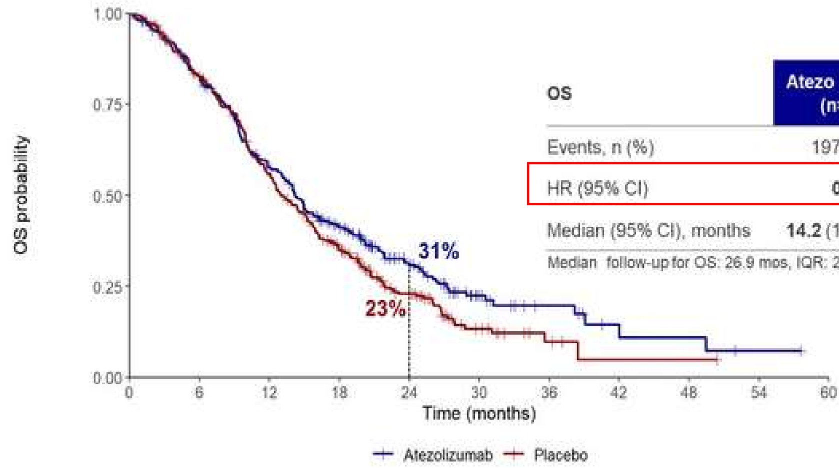
PFS	Atezo + CT/Bev (n=285)	Placebo + CT/Bev (n=289)
Events, n (%)	243 (85.3)	262 (90.7)
HR (95% CI)	**0.87** (0.73–1.04); **p=0.12**	
Median (95% CI), months	**6.4** (6.1–7.5)	**6.7** (6.2–8.1)

(88% maturity)

Number at Risk

Atezolizumab	285	158	73	31	12	2	1	1	1	0
Placebo	289	162	61	21	6	1	0	0	0	0

Primary Endpoint: Overall Survival (ITT)



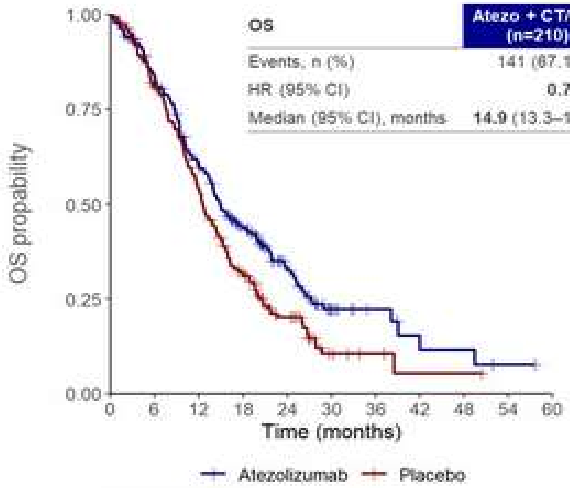
OS	Atezo + CT/Bev (n=285)	Placebo + CT/Bev (n=289)
Events, n (%)	197 (69.1)	221 (76.5)
HR (95% CI)	**0.83** (0.68–1.01); **p=0.06**	
Median (95% CI), months	**14.2** (13.0–16.1)	**13.0** (11.9–15.1)

Median follow-up for OS: 26.9 mos, IQR: 20.5-31.4 mos (73% maturity)

Response

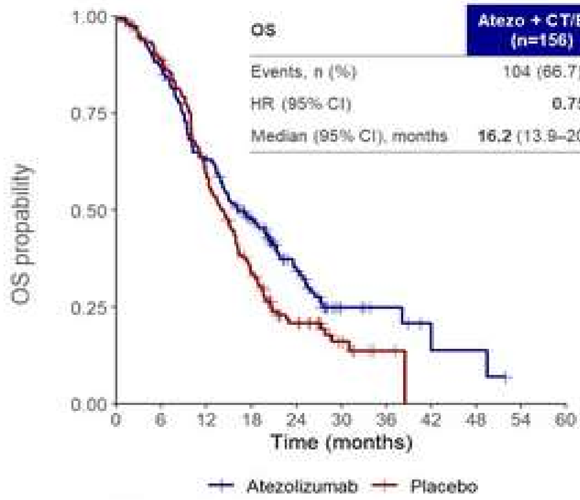
Exploratory Post-hoc Analyses

Patients with prior Bevacizumab



OS	Atezo + CT/Bev (n=210)	Placebo + CT/Bev (n=206)
Events, n (%)	141 (67.1)	161 (78.2)
HR (95% CI)	**0.74** (0.59–0.93)	
Median (95% CI), months	**14.9** (13.3–18.8)	**12.6** (11.6–14.4)

Patients receiving Paclitaxel



OS	Atezo + CT/Bev (n=156)	Placebo + CT/Bev (n=154)
Events, n (%)	104 (66.7)	119 (77.3)
HR (95% CI)	**0.75** (0.57–0.98)	
Median (95% CI), months	**16.2** (13.9–20.8)	**14.3** (12.3–15.9)

AGO-OVAR 2.29/ENGOT-ov34:
Conclusions

NUEVO GOLPE A LA INMUNOTERAPIA EN OVARIO

- The addition of atezolizumab to single-agent non-plati… based chemotherapy in combination with b… significantly improve OS or PFS
- Response rates w… nerically longer d…
- Results … biopsy (SP142)
- Safety fin… known toxicity profiles of the investigat…
- Exploratory …alyses including stool microbiome, tumor microenvironment, ctDNA and alternative PD-L1 analyses (SP263) are ongoing

Final results of BrUOG 354: A randomized phase II trial of nivolumab alone or in combination with ipilimumab for people with ovarian and other extra-renal clear cell carcinomas.

Don S. Dizon ASCO 24

LEGORRETA CANCER CENTER BROWN UNIVERSITY

Lifespan

BrUOG 354

44 p ,36 ovario

First patient in: June 2018
Last patient in: April 2023

No pause during lockdown
46 enrolled; 2 withdrew informed consent

44 treated on trial

Eligibility:
- non-renal CCC
  *stratified by ovary or extra-ovarian
- PD after at least 1 prior treatment
- No line limit
- No prior exposure to immunotherapy
- Age >18

Nivolumab 240 mg IV every 2 weeks
1 cycle = 2 weeks

Nivolumab 240 mg IV every 2 weeks
Ipilimumab 1 mg/kg IV every 6 weeks
1 cycle = 6 weeks

> Scans done every 8 weeks
> No cap on treatment duration
> Treatment until PD or unacceptable toxicity

Objectives and Statistics

- Randomized, non-comparative, phase 2
  - Primary Objective: Overall Response Rate (ORR)
  - Secondary Objectives: PFS and OS, Adverse Events
  - Exploratory: Molecular characteristics for response or non-response
- Simon's two-stage minimax design, true ORR = 30%, poor ORR = 10%
  - 86% power, alpha = 0.03

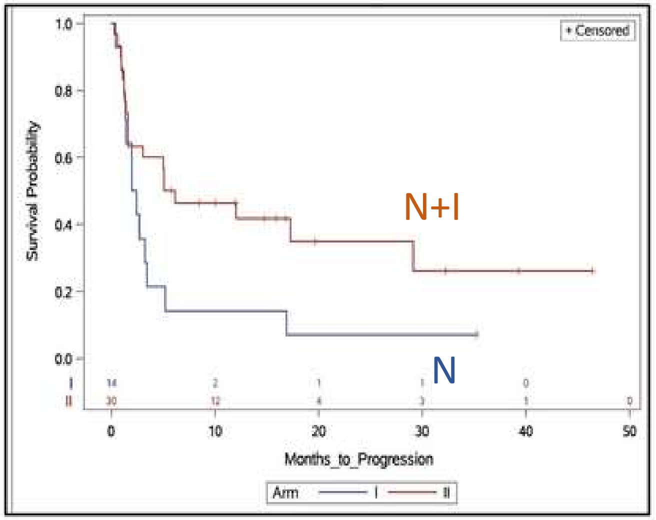
LEGORRETA CANCER CENTER BROWN UNIVERSITY

Lifespan

Demographics, n=44

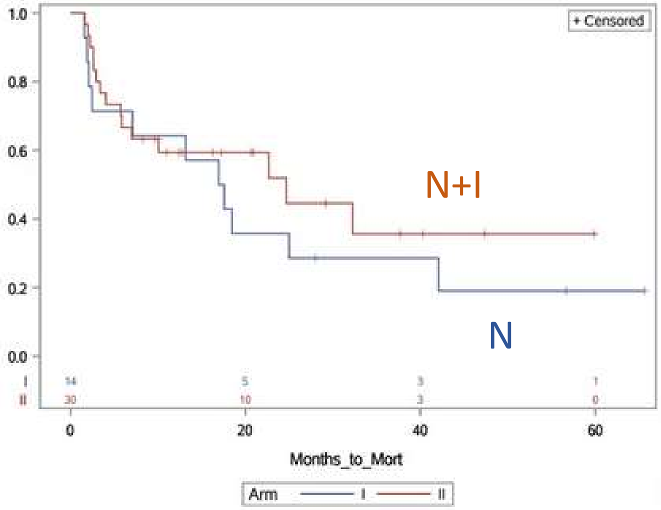
	Nivolumab (n=14)	Nivolumab/Ipilimumab (n=30)	Total (n=44)	Incidence (SEER, 2008)
Age (median, range)	54.5 (18-74)	58 (22-75)	57 (18-75)	
Diagnosis (n,%)				
Ovarian	11 (78.6)	25 (83.3)	36 (81.2)	
Uterine	3 (21.4)	3 (10)	6 (13.6)	
Other	0	2 (6.7)	2 (4.5)	
Race (n, %)				
White	12 (85.7)	21 (70)	33 (75)	82.5%
Black	1 (7.1)	3 (10)	4 (9)	3.6%
Asian	1 (7.1)	1 (3.3)	2 (4.5)	11.7%
Not Answered	0	5 (16.6)	5 (11.4)	
Ethnicity (n,%)				
Hispanic	1 (7.1)	4 (13.3)	5 (11.4)	
Not Hispanic	12 (85.7)	22 (73.3)	34 (77.3)	
Not Answered	1 (7.1)	4 (13.3)	5 (11.4)	
Prior lines (median, range)	1 (1-7)	1.5 (1-4)		

Progression-Free Survival



Arm	Median (months)	95%CI
I (Nivo)	2.2	1.2-3.4
II (Nivo/Ipi)	5.6	1.6-29.1

Overall Survival

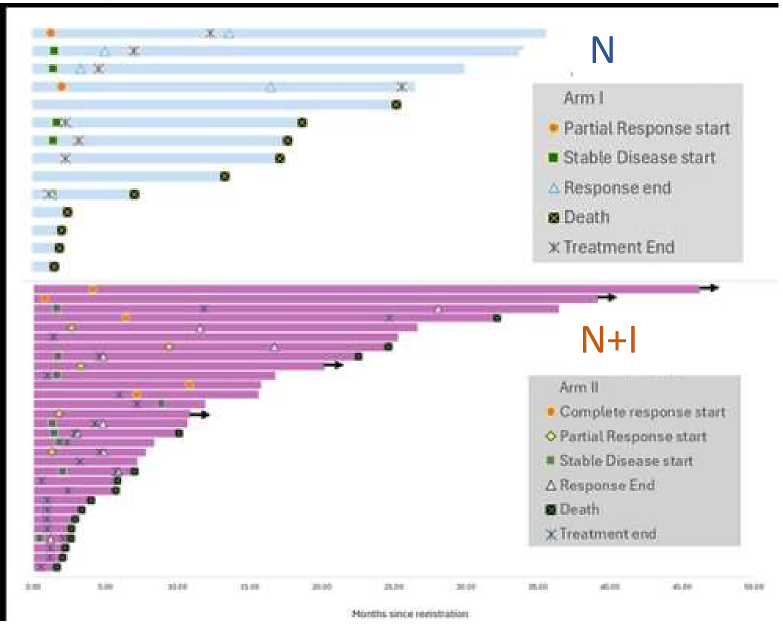


Arm	Median (months)	95%CI
I (Nivo)	17.3	2.1-42.7
II (Nivo/Ipi)	24.7	5.9-NR

Response Data

	Nivolumab n=14	Nivolumab/Ipilimumab n=30
Complete Response (n, %)	**0**	**5 (16.7)**
Partial Response (n,%)	**2 (14.3)**	**5 (16.7)**
Complete + Partial Response	**2 (14.3)**	**10 (33.3)**
Stable Disease	5 (35.7)	10 (33.3)
Progression	7 (50)	10 (33.3)
Duration of Response (months, median ± SD)	30.6 ± 4.5	22.4 ± 11.8

Timecourse on BrUOG 354



LEGORRETA CANCER CENTER
BROWN UNIVERSITY

Lifespan

Top Line Conclusions

For people with ovarian or gynecologic clear cell carcinoma, th[illegible]l activity and survival outcomes are greater when nivolumab is gi[illegible]mab vs. as a single agent.

Treatment	ORR (%)	Median PF[illegible]	[illegible] OS (range, months)
Nivolumab	14.3	[illegible]	17.3 (2.1-42.7)
Nivolumab/Ipilimumab	[illegible]	[illegible].1)	24.7 (5.7-NR)

UNA PEQUEÑA LUZ PARA LA INMUNOTERAPIA EN CÁNCER DE OVARIO

There were no [illegible] identified among volunteers with gynecologic clear cell ca[illegible] immunotherapy.

Immunotherap[illegible] presents an important and available treatment option for people with these rare and aggressive malignancies.

AXLerate-OC/GOG-3059/ENGOT OV-66: Results of a phase 3, randomized, double-blind, placebo/paclitaxel-controlled study of batiraxcept (AVB-S6-500) with paclitaxel in platinum-resistant recurrent ovarian cancer.

Katherine Cynthia Fuh. ASCO 2024

RESISTENTE

AXL es un receptor tirosin kinasa implicado en múltiples procesos biológicos esenciales para el desarrollo de metástasis.

Key Eligibility Criteria

- Platinum-resistant, high-grade serous ovarian cancer
- 1-4 prior lines
- ECOG 0-1
- Stratifications:
  - Prior bevacizumab use
  - Lines of therapy
  - Platinum-free interval

R

I: Weekly paclitaxel 80mg/m^2 on d1, 8, 15 q28 days + Batiraxcept (AVB-500)15mg/kg D1 and D15 q28 days

II: Weekly paclitaxel 80mg/m^2 on d1, 8, 15 q28 days

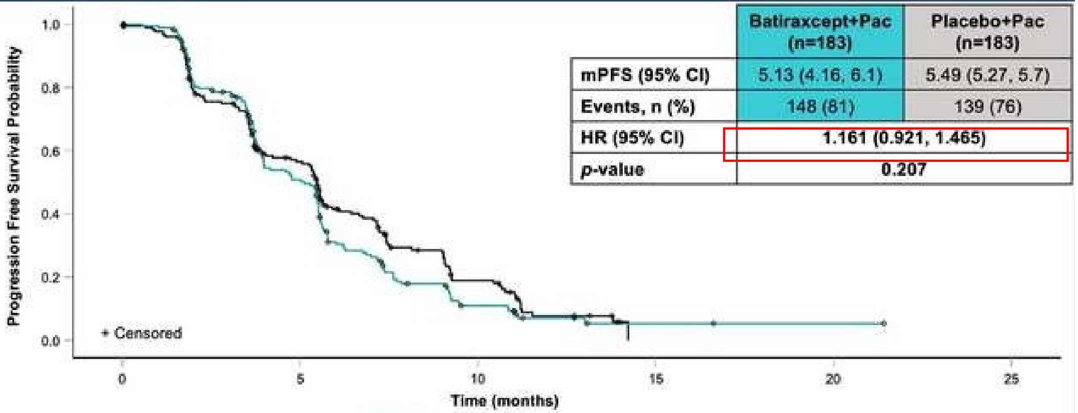
NCT04729608: Recruitment completed from April 2021 - Dec 2022

- Enrollment: 366 participants from 90 GOG Partners US sites + 70 ENGOT sites

- **Primary Endpoints:**
  1. PFS in bevacizumab naïve
  2. PFS in the total population
- **Secondary endpoint**
  1. Overall Survival
- **Exploratory endpoints**
  1. AXL expression by IHC
  2. GAS6 expression by IHC
  3. Serum Soluble AXL/GAS6 ratio

- Primary end-point: PFS
- PFS and OS tested at 0.05 significance level
- 95% power used to detect HR in PFS/OS analysis
- PFS and OS in high AXL and low AXL groups were adjusted for three covariates: prior bevacizumab, Platinum-Free Interval (PFI), and prior lines of treatment
- Multivariable model was performed including an interaction term for treatment arm and AXL expression

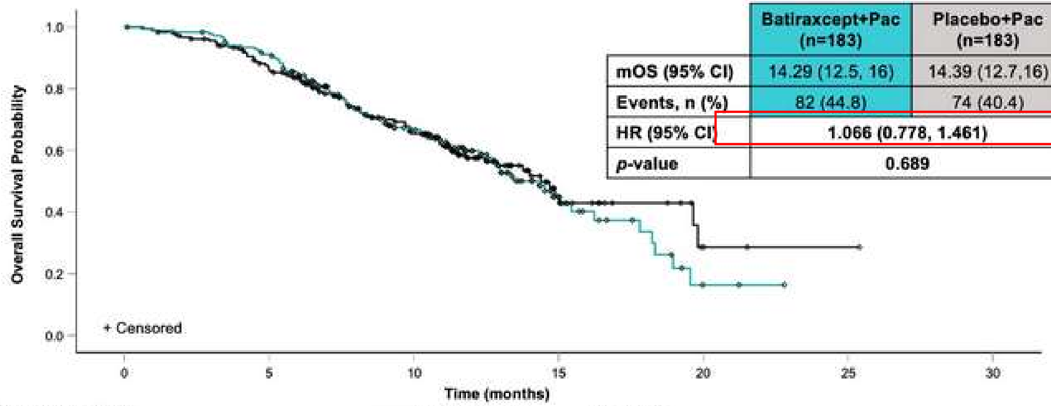
Progression Free Survival for Overall Cohort



	Batiraxcept+Pac (n=183)	Placebo+Pac (n=183)
mPFS (95% CI)	5.13 (4.16, 6.1)	5.49 (5.27, 5.7)
Events, n (%)	148 (81)	139 (76)
HR (95% CI)	1.161 (0.921, 1.465)	
p-value	0.207	

No. Participants at Risk					
Batiraxcept+Pac	183	81	12	1	0
Placebo+Pac	183	89	20	0	

Overall Survival for Overall Cohort

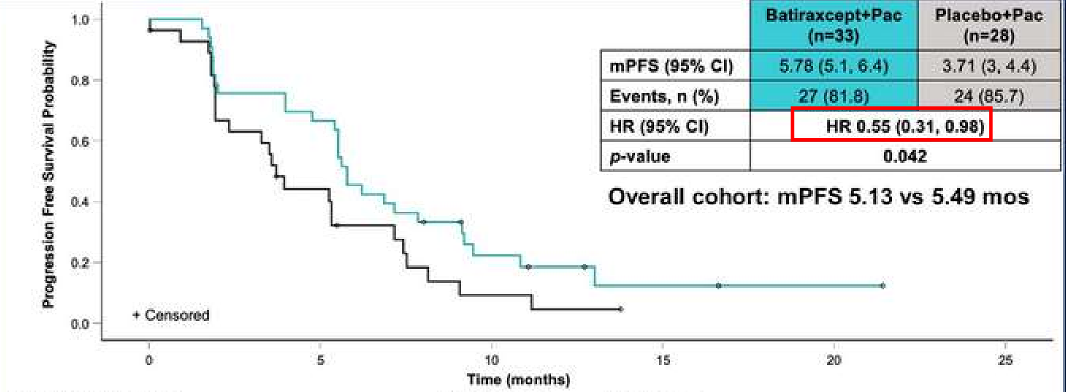


	Batiraxcept+Pac (n=183)	Placebo+Pac (n=183)
mOS (95% CI)	14.29 (12.5, 16)	14.39 (12.7,16)
Events, n (%)	82 (44.8)	74 (40.4)
HR (95% CI)	1.066 (0.778, 1.461)	
p-value	0.689	

No. Participants at Risk						
Batiraxcept+Pac	183	161	88	20	1	0
Placebo+Pac	183	146	83	18	2	0

Exploratory Endpoint: High AXL Expression by Immunohistochemistry (80% intensity and higher)

Progression-Free Survival for AXL High IHC Cohort

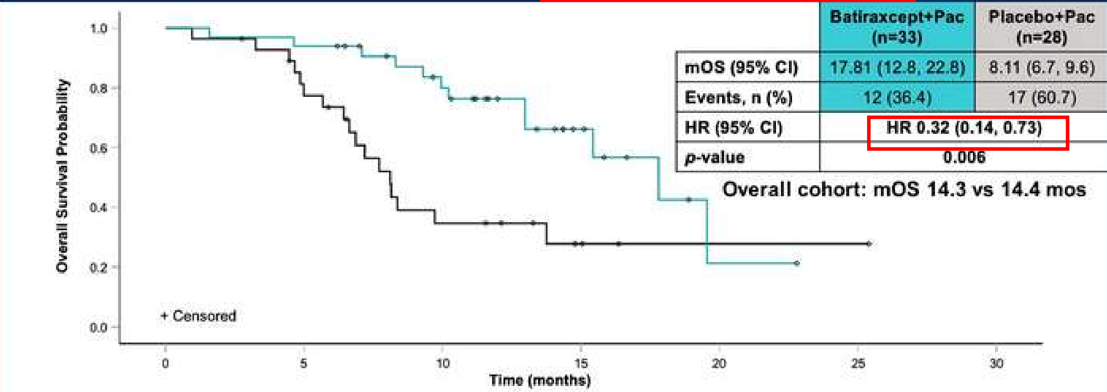


	Batiraxcept+Pac (n=33)	Placebo+Pac (n=28)
mPFS (95% CI)	5.78 (5.1, 6.4)	3.71 (3, 4.4)
Events, n (%)	27 (81.8)	24 (85.7)
HR (95% CI)	HR 0.55 (0.31, 0.98)	
p-value	0.042	

Overall cohort: mPFS 5.13 vs 5.49 mos

No. Participants at Risk					
Batiraxcept+Pac	33	21	5	1	0
Placebo+Pac	28	10	1	0	

Overall Survival for AXL High IHC Cohort



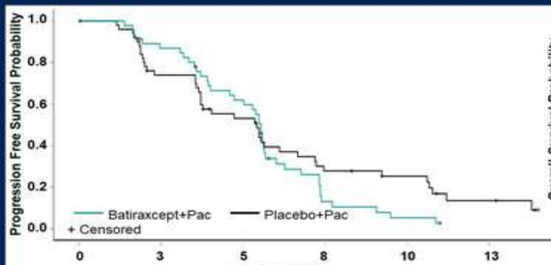
	Batiraxcept+Pac (n=33)	Placebo+Pac (n=28)
mOS (95% CI)	17.81 (12.8, 22.8)	8.11 (6.7, 9.6)
Events, n (%)	12 (36.4)	17 (60.7)
HR (95% CI)	HR 0.32 (0.14, 0.73)	
p-value	0.006	

Overall cohort: mOS 14.3 vs 14.4 mos

No. Participants at Risk					
Batiraxcept+Pac	33	30	21	7	0
Placebo+Pac	28	19	7	2	0

Progression Free Survival and Overall Survival: Medium AXL

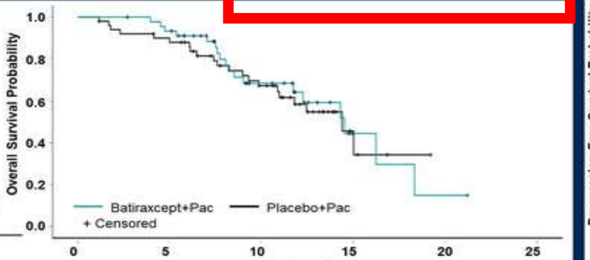
14



No. Participants at Risk						
B+P	46	39	27	4	2	0
Plac+P	51	36	24	12	9	3

	Batiraxcept+Pac (n=46)	Placebo+Pac (n=51)
mPFS (95% CI)	5.55 (5.35, 5.76)	5.42 (3.62, 7.23)
Events, n (%)	41 (89.1)	40 (78.4)
HR (95% CI)	HR 1.172 (0.903, 1.520)	
p-value	0.232	

Overall cohort: mPFS 5.13 vs 5.49 mos



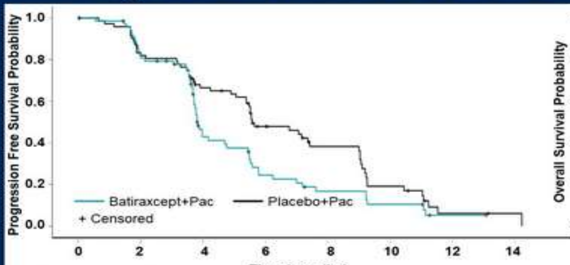
No. Participants at Risk					
B+P	42	20	3	1	0
Plac+P	43	27	4	0	

	Batiraxcept+Pac (n=46)	Placebo+Pac (n=51)
mOS (95% CI)	14.52 (11.13, 17.91)	14.39 (11.60, 17.19)
Events, n (%)	18 (39.1)	21 (41.2)
HR (95% CI)	HR 1.005 (0.709, 1.425)	
p-value	0.978	

Overall cohort: mOS 14.3 vs 14.4 mos

Progression Free Survival and Overall Survival: Low AXL

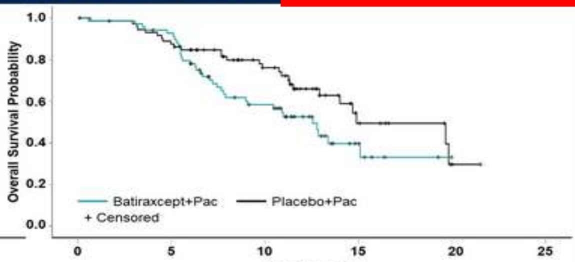
15



No. Participants at Risk								
B+P	70	54	23	12	7	4	0	
Plac+P	73	59	44	27	17	8	1	0

	Batiraxcept+Pac (n=70)	Placebo+Pac (n=73)
mPFS (95% CI)	3.84 (3.64, 4.05)	5.59 (4.17, 7.00)
Events, n (%)	55 (78.6)	56 (76.7)
HR (95% CI)	HR 1.474 (1.01, 2.15)	
p-value	0.044	

Overall cohort: mPFS 5.13 vs 5.49 mos



No. Participants at Risk						
B+P	70	62	32	6	0	
Plac+P	73	62	39	9	1	0

	Batiraxcept+Pac (n=70)	Placebo+Pac (n=73)
mOS (95% CI)	12.55 (10.17, 14.93)	14.88 (9.90, 19.86)
Events, n (%)	35 (50.0)	27 (37.0)
HR (95% CI)	HR 1.618 (0.97, 2.6[illegible])	
p-value	0.063	

Overall cohort: mOS 14.3 vs 14.4 mos

Conclusions:

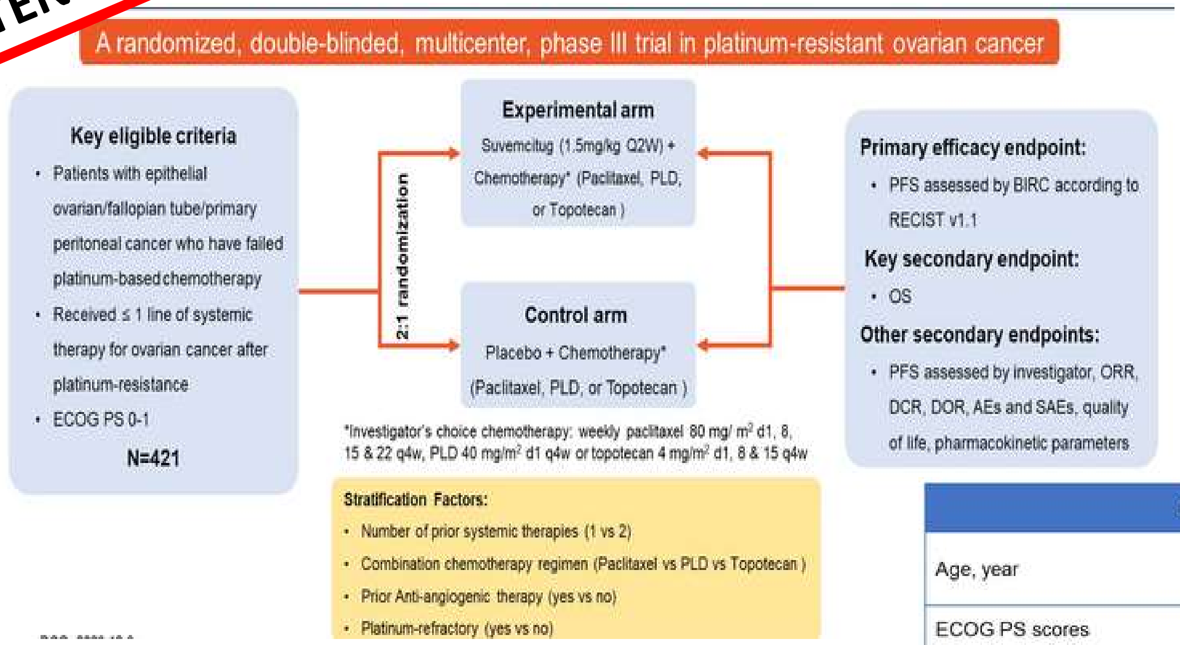
The addition of batiraxcept to paclitaxel did not improve PFS or OS. However, in AXL high tumors, the PFS and OS were higher in participants who received batiraxcept with paclitaxel compared to paclitaxel alone.

A phase III randomized, double-blinded, placebo-controlled study of suvemcitug combined with chemotherapy for platinum-resistant ovarian cancer (SCORES).

Guangwen Yuan. ASCO 2024

RESISTENTE

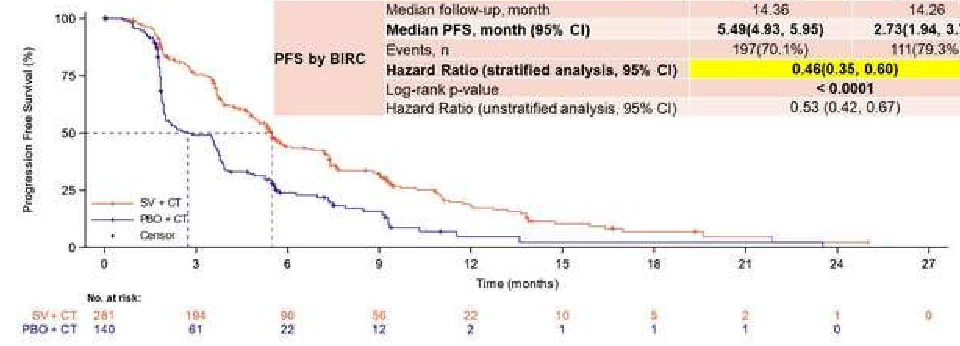
Suvemcitug (BD0801) is a next-generation humanized monoclonal antibody directed against VEGF



Characteristics		Suvemcitug + CT N = 281	Placebo + CT N = 140
Age, year	Mean (SD)	56.0(7.46)	56.0(8.14)
	Median	56.0	55.0
	Min ~ Max	36 ~ 76	34 ~ 79
ECOG PS scores	0	106(37.7%)	40(28.6%)
	1	175(62.3%)	100(71.4%)
Tumor Histologic Type, n	High-grade serous adenocarcinoma	278(98.9%)	136(97.1%)
	Endometrioid carcinoma	3(1.1%)	4(2.9%)
Number of lines of previous anti-tumor regimens, n	1	88(31.3%)	40(28.6%)
	2	105(37.4%)	52(37.1%)
	3	60(21.4%)	35(25.0%)
	≥ 4	28(10.0%)	13(9.3%)
Prior anticancer drug therapy, n	Chemotherapy	281(100%)	140(100%)
	PARP Inhibitors	136(48.4%)	70(50.0%)
	Antiangiogenic agents	141(50.2%)	70(50.0%)
	Bevacizumab	123(43.8%)	61(43.6%)
Patients with platinum-refractory ovarian cancer (IWRS), n	Yes	27(9.6%)	15(10.7%)
	No	254(90.4%)	125(89.3%)
Baseline CA-125 level, n	≤ 2×ULN	36(12.8%)	14(10.0%)
	2×ULN-1000	178(63.3%)	95(67.9%)
	> 1000	67(23.8%)	31(22.1%)

Primary Endpoint – PFS by BIRC

		Suvemcitug+ CT (N = 281)	Placebo + CT (N = 140)
PFS by BIRC	Median follow-up, month	14.36	14.26
	Median PFS, month (95% CI)	**5.49(4.93, 5.95)**	**2.73(1.94, 3.75)**
	Events, n	197(70.1%)	111(79.3%)
	Hazard Ratio (stratified analysis, 95% CI)	**0.46(0.35, 0.60)**	
	Log-rank p-value	< 0.0001	
	Hazard Ratio (unstratified analysis, 95% CI)	0.53 (0.42, 0.67)	

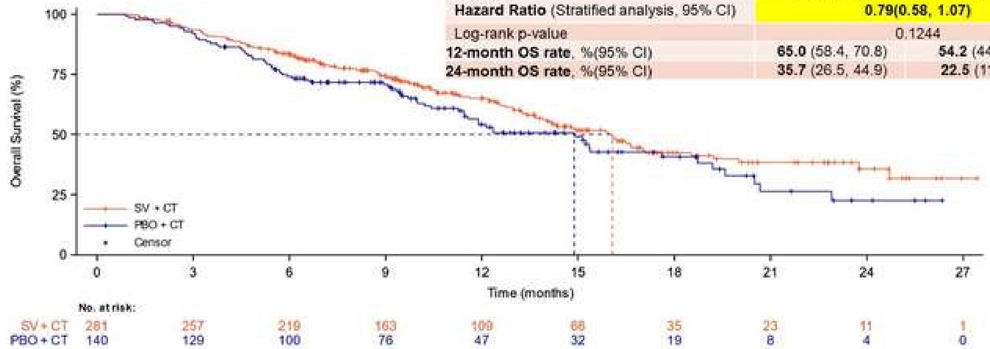


PBO, placebo
SV, suvemcitug

- ◆ SCORES has met the primary endpoint.
- ◆ Improvement of PFS (BIRC) is both statistically and clinically significant.

Key Secondary Endpoint - Overall Survival

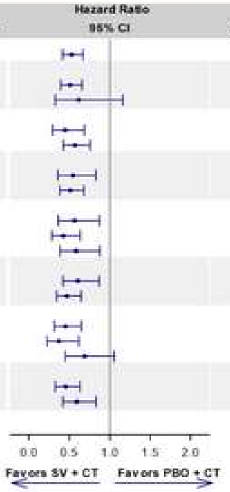
	Suvemcitug + CT (N = 281)	Placebo + CT (N = 140)
Median follow-up, month	14.36	14.26
Median OS, month (95% CI)	**16.07(13.67, 18.53)**	**14.88(11.43, 18.73)**
Events, n	120(42.7%)	71(50.7%)
Hazard Ratio (Stratified analysis, 95% CI)	**0.79(0.58, 1.07)**	
Log-rank p-value	0.1244	
12-month OS rate, %(95% CI)	**65.0** (58.4, 70.8)	**54.2** (44.5, 62.9)
24-month OS rate, %(95% CI)	**35.7** (26.5, 44.9)	**22.5** (11.4, 35.9)



◆ The OS data are immature，a trend of OS benefit is observed in the suvemcitug + CT arm.

PFS by BIRC：Forest plot

Subgroup	Events/N SV + CT	Events/N PBO + CT	Median, mo SV + CT	Median, mo PBO + CT	Hazard Rat[io] 95% CI
Overall	197/281	111/140	5.49	2.73	0.53(0.42,0.(
Age					
<=65	169/243	95/120	5.39	2.53	0.51(0.39,0.(
>65	28/38	16/20	5.65	3.78	0.62(0.33,1.1
Baseline ECOG					
0	72/106	33/40	5.42	2.73	0.45(0.29,0.(
1	125/175	78/100	5.49	2.53	0.57(0.42,0.7
Ascites					
Y	68/91	34/45	4.93	2.00	0.54(0.36,0.8
N	129/190	77/95	5.59	3.61	0.51(0.38,0.(
Number of lines of previous anti-tumor regimens					
1	58/88	32/40	5.91	3.84	0.56(0.36,0.8
2	77/105	41/52	5.39	3.52	0.42(0.28,0.(
>=3	62/88	38/48	4.00	2.00	0.58(0.39,0.8
Platinum-free interval (month)					
<3	85/109	48/59	4.63	2.00	0.61(0.42,0.8
>=3	112/172	63/81	6.83	3.65	0.47(0.34,0.(
Chemotherapy (IWRS)					
Paclitaxel	87/124	51/62	5.65	3.71	0.45(0.31,0.(
Topotecan	53/69	25/34	3.88	2.00	0.37(0.22,0.(
Doxorubicin	57/88	35/44	5.32	3.68	0.69(0.45,1.(
Received anti-angiogenic therapy (IWRS)					
Y	98/138	59/70	4.93	2.00	0.45(0.33,0.(
N	99/143	52/70	5.95	3.75	0.59(0.42,0.8



Conclusion

- SCORES met its primary endpoint.
  - Suvemcitug plus chemotherapy showed a statistically significant and clinically meaningful PFS improvement across all pre-defined sub-groups compared to chemotherapy alone.
  - Suvemcitug plus chemotherapy also improved ORR, DCR and DOR.
- The OS data are immature, a clear trend of OS benefit has been shown in the suvemcitug arm.
- The safety of suvemcitug was manageable.

CONCLUSIONES OVARIO

-Explorando (datos de un fase II) la desescalada de QT en determinados grupo de pacientes mediante el uso de iPARP.

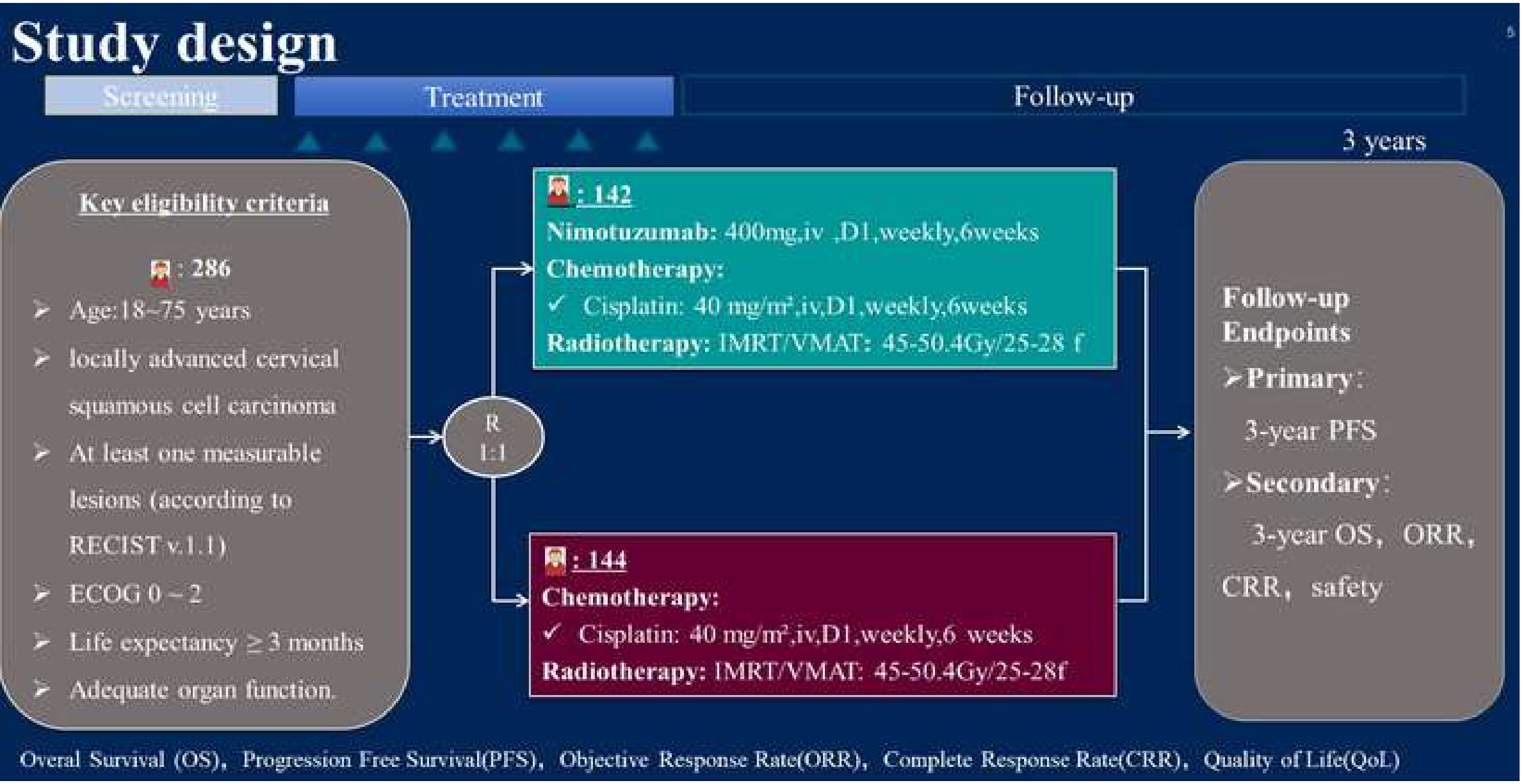
-Enésimo fracaso de la inmunoterapia en cáncer de ovario aunque quizá si en algunos subtipos seleccionados.

-El reto de las pacientes resistentes a platino, nuevos anti VEGF, búsqueda de nuevas dianas como la alta expresión de AXL.

Nimotuzumab plus concurrent chemoradiotherapy for locally advanced cervical squamous cell carcinoma: The randomized, phase 3 CC3 study.

Jun jie Wang. ASCO 2024

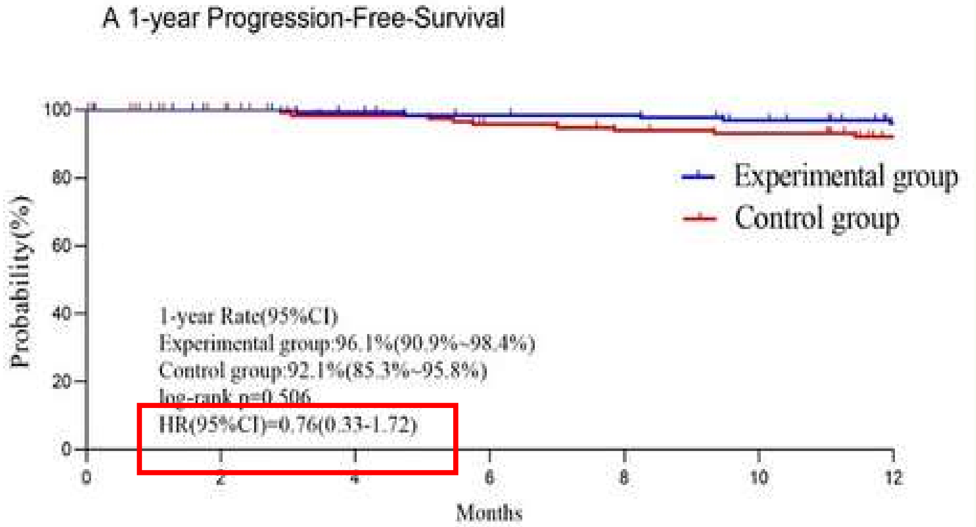
Nimotuzumab anticuerpo humanizado que reconoce al Receptor del Factor de Crecimiento Epidérmico EGFR



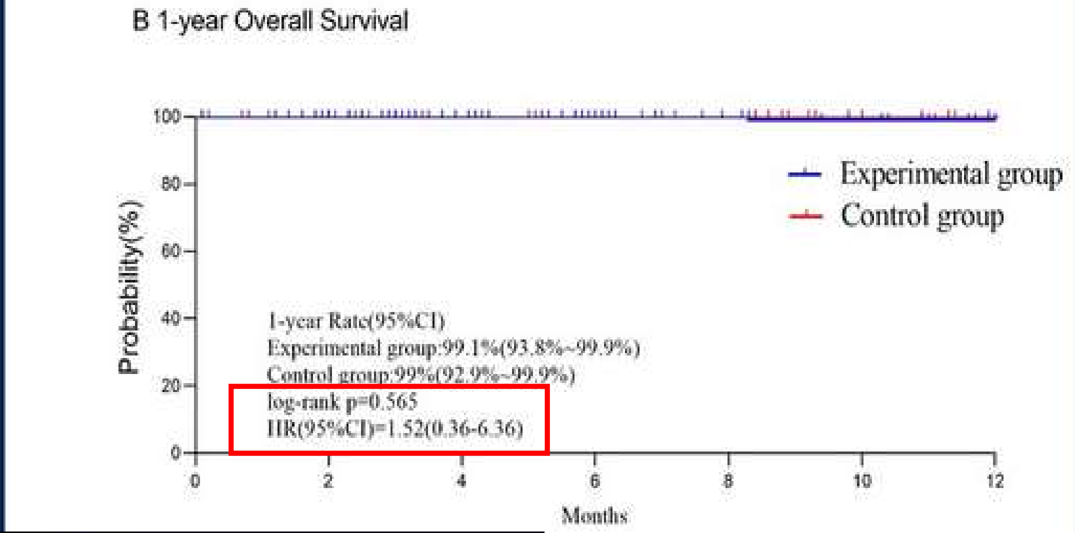
Clinical Trial Objectives

- Primary
  - 3-year PFS
- Secondary
  - 3-year OS, ORR, CRR, safety

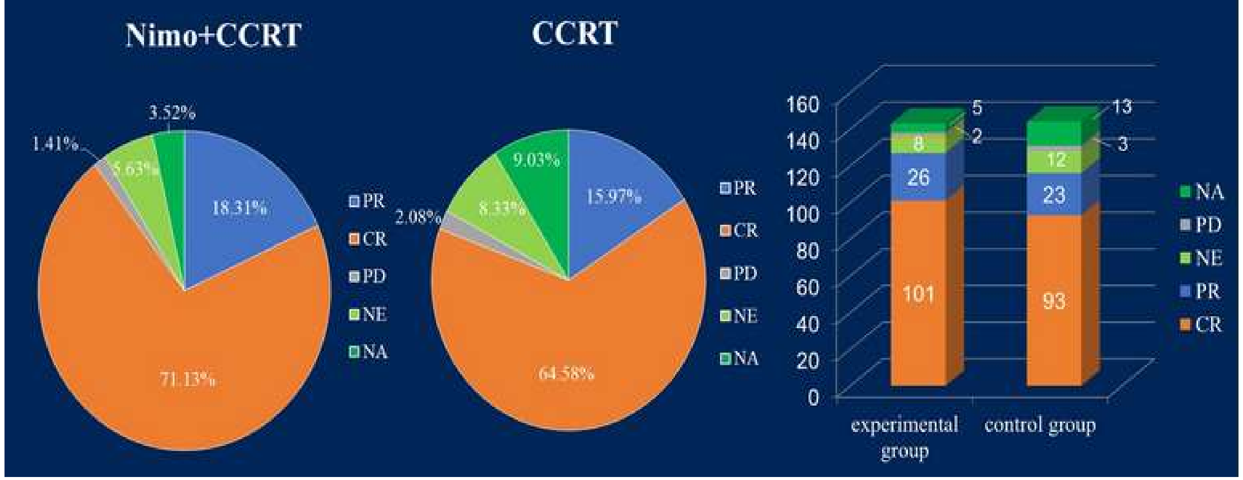
Progression Free Survival

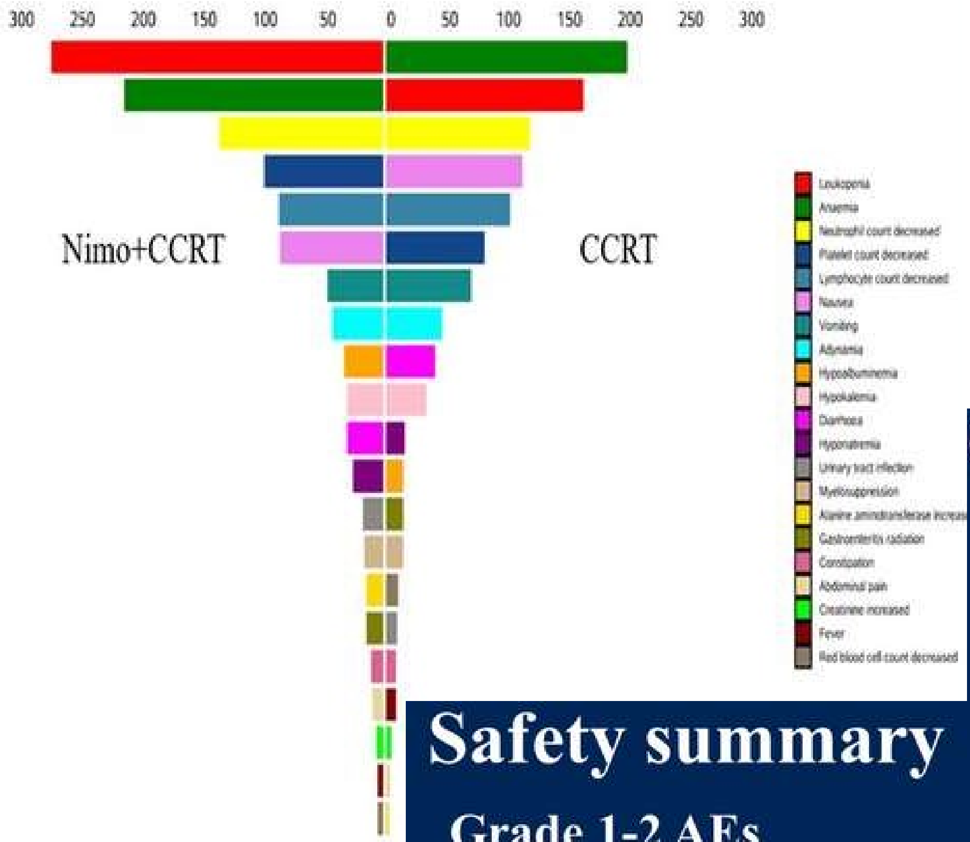


Overall Survival



Overall Response Rate





Safety summary

Grade 1-2 AEs

Conclusions

- The study verified the addition of nimotuzumab provided PFS benefit and ORR improvement.
  - 1-year PFS :(96.1% versus 92.1%, p = 0.506)
  - ORR :(89.44% versus 80.56%, p = 0.036).
- Nimotuzumab combined with chemoradiotherapy had a good safety profile.
  - The incidence of grade 1-2 AE in experimental group was similar to control group
- The trial is ongoing –final PFS, OS and other secondary results will be reported in due course.
- The combination therapy of nimotuzumab and concurrent chemoradiotherapy represents a promising option for this populations.

Adjuvant chemotherapy following concurrent chemoradiation (CRT) in patients with high-risk early-stage cervical carcinoma following radical hysterectomy: Results of NRG oncology/RTOG 0724/GOG-0724.

Anuja Jhingran ASCO 2024

Endpoints

- Primary endpoint – disease-free survival (DFS)
- Secondary endpoints - OS and AEs (CTCAE v4)

stage IA2, IB, or IIA cervical carcinoma with at least one of the following high-risk features after radical hysterectomy
-positive pelvic nodes
-positive parametrium,
-and/or positive para-aortic nodes

STRATIFY		RANDOMIZE
	Intention To Use Brachytherapy 1. No 2. Yes **RT Modality** 1. Standard RT 2. IMRT **Radiation Therapy Dose** 1. 45 Gy 2. 50.4 Gy	

Concurrent weekly cisplatin and RT ± brachytherapy

Concurrent weekly cisplatin and RT ± brachytherapy

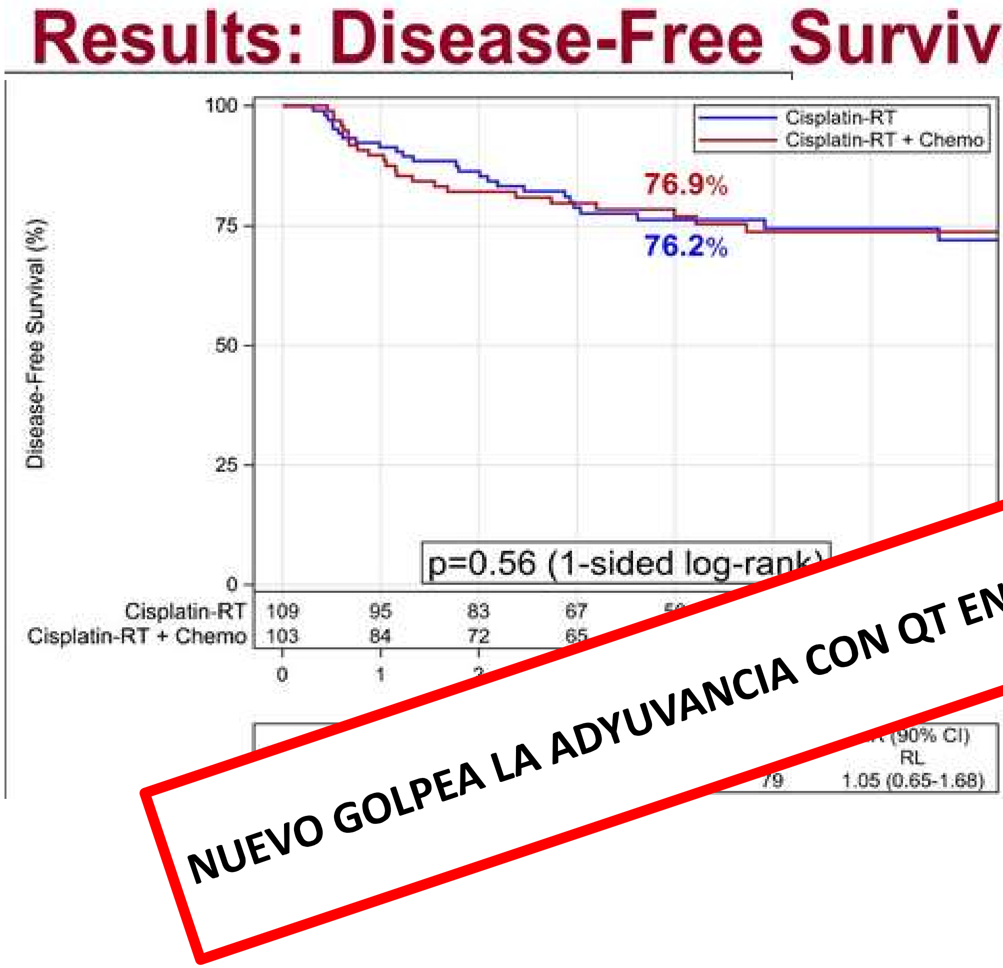
FOLLOWED BY

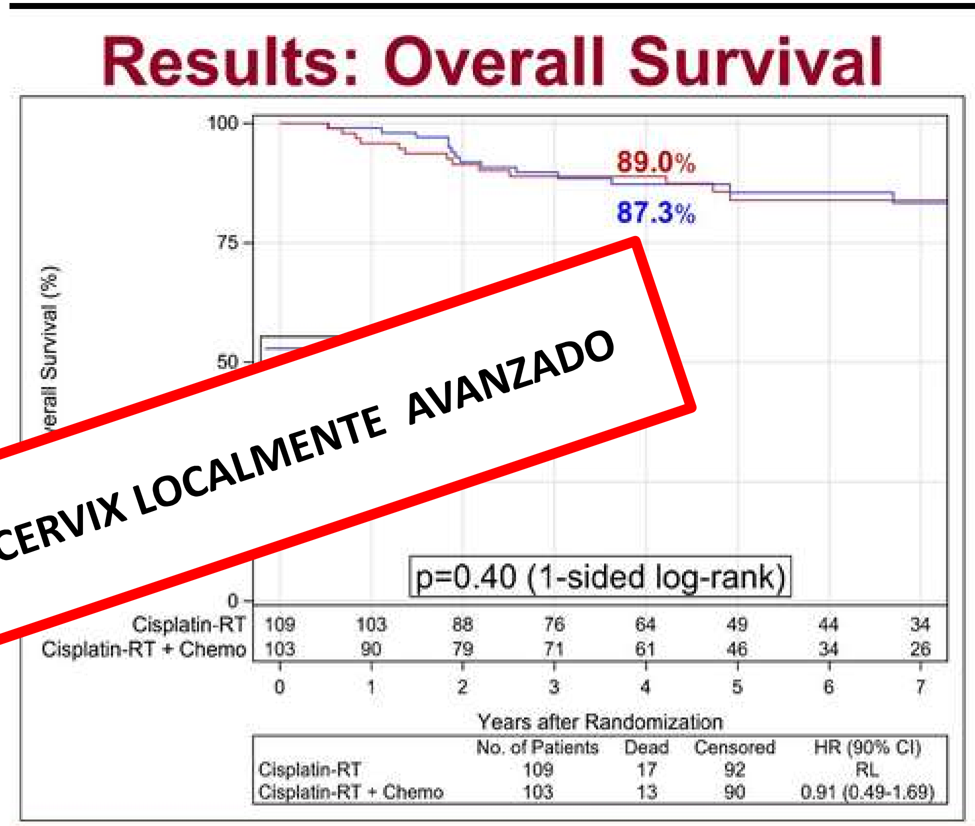
Carboplatin and paclitaxel

Results: Patient and Tumor Characteristics

	Cis + RT (n=109)	Cis + RT + chemo (n=103)	Total (n=212)
Race			
White	60 (55%)	49 (48%)	109 (51%)
Asian	42 (39%)	40 (39%)	82 (39%)
Other	7 (6%)	14 (14%)	21 (10%)
Hysterectomy			
Open	64 (59%)	54 (52%)	118 (56%)
Laparoscopic/Robotic	45 (41%)	49 (48%)	94 (44%)
Histological type			
Squamous cell	88 (81%)	74 (72%)	162 (76%)
Adenosqumous	6 (6%)	5 (5%)	11 (5%)
Adenocarcinoma	15 (14%)	24 (23%)	39 (18%)
Stage			
IA2	3 (3%)	6 (6%)	9 (4%)
IB	97 (89%)	88 (85%)	185 (87%)
IIA	9 (8%)	9 (9%)	18 (8%)
Positive pelvic nodes			
No	33 (30%)	23 (22%)	56 (26%)
Yes	76 (70%)	80 (78%)	156 (74%)
Positive para-aortic nodes			
No	54 (50%)	43 (42%)	97 (46%)
Yes	3 (3%)	5 (5%)	8 (4%)
Not dissected	52 (48%)	55 (53%)	107 (50%)
Intention to use Brachytherapy			
No	61 (56%)	58 (56%)	119 (56%)
Yes	48 (44%)	45 (44%)	93 (44%)
RT modality			
Standard RT	46 (42%)	41 (40%)	87 (41%)
IMRT	63 (58%)	62 (60%)	125 (59%)
RT dose			
45 Gy	35 (32%)	30 (29%)	65 (31%)
50.4 Gy	74 (68%)	73 (71%)	147 (69%)

- Enrollment: 9/16/2009 - 3/2/2022
- 236 patients randomized - 212 eligible
  - 109 Cisplatin-RT (Arm 1)
  - 103 Cisplatin-RT + Chemo (Arm 2)
- Median age 46 years (min-max: 25 -77)
- Median follow-up for all patients – 4.5 years (min-max: 0.02-12.8)





Conclusions

The addition of systemic chemotherapy following CRT didn't improve DFS or OS in cervical cancer patients with high-risk factors after radical hysterectomy

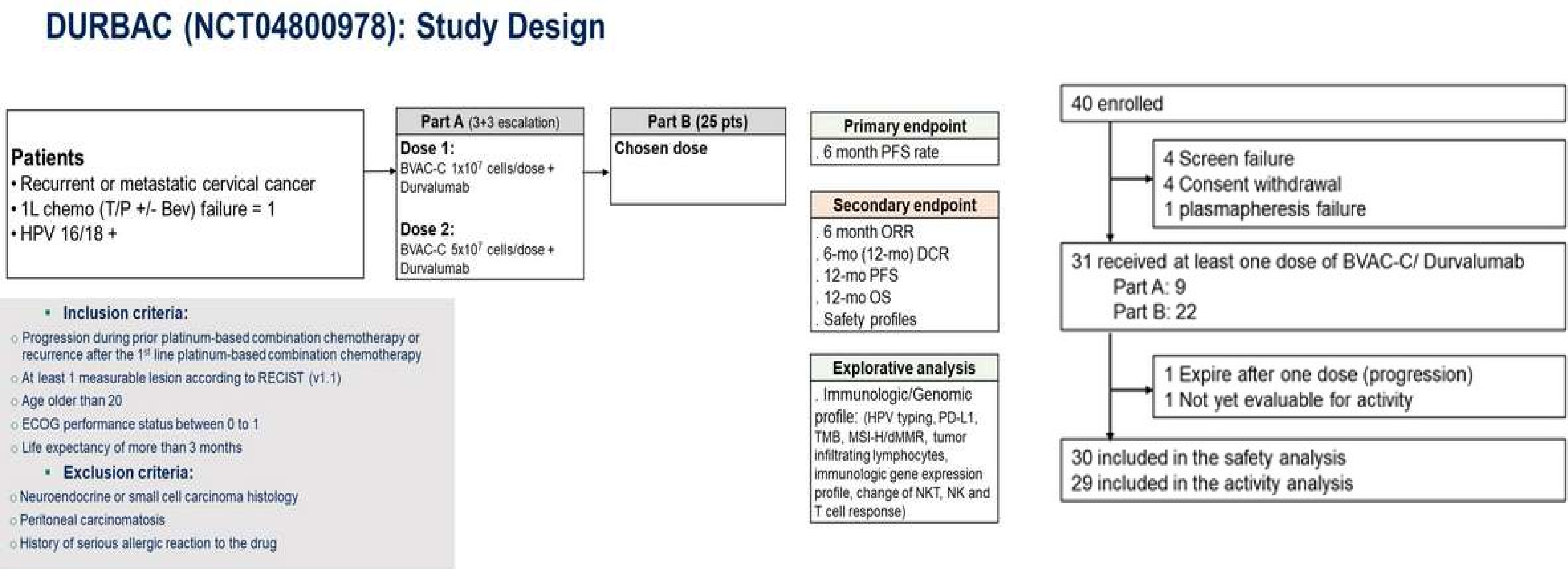
An open label, single arm phase II, multicenter trial of durvalumab and BVAC-C, in patients with HPV 16- or 18-positive cervical cancer and failure of first-line platinum-based chemotherapy (DURBAC).

Chel Hun Choi. ASCO 24

El EC consta de dos partes.

La Parte A, diseño de aumento de dosis de 3+3, evalúa BVAC-C combinado con 1500 mg de durvalumab para establecer la dosis máxima tolerada (MTD) y la dosis recomendada para la Parte B.

Parte B, de expansión con hasta 25 p , se centra en la seguridad y la eficacia clínica, medidas por la tasa de SLP a 6 meses.

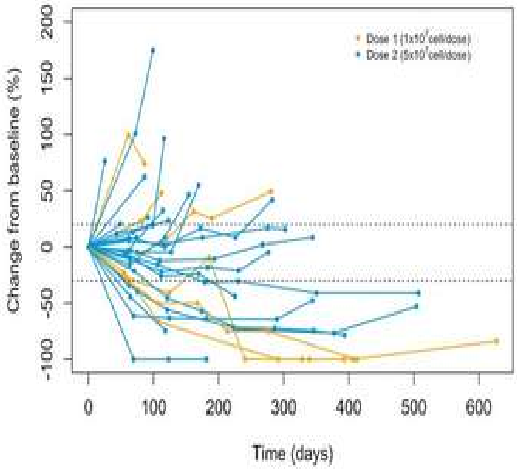


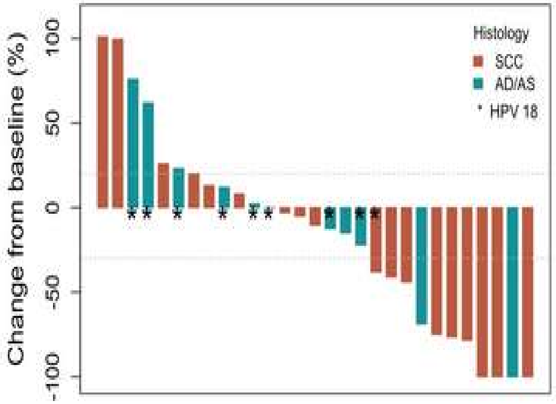
Patients characteristics (N = 30)

	N = 30
Histology	
SCC	18 (60%)
Adeno/AS	12 (40%)
FIGO stage	
I	13 (43%)
II	5 (17%)
III	9 (30%)
IV	3 (10%)
Primary treatment	
Surgery	11 (37%)
CCRT	13 (43%)
Chemotherapy	6 (20%)
Treatment free interval (mo)	7.8 (1.2 – 36.4)
Target lesion	
Lung	16 (55%)
LNs	16 (55%)
Pelvis	10 (35%)

	N = 30
Dose of BVAC-C	
1x10^7 cells/dose	6 (20%)
5x10^7 cells/dose	24 (80%)
ECOG	
0	24 (80%)
1	6 (20%)
HPV	
16	20 (67%)
18	8 (27%)
16 and 18	2 (7%)
Cycles of BVAC-C	
1-2	5 (17%)
3	6 (20%)
4	19 (63%)
Median cycles of Durvalumab	4 (1 – 25)

Maximum Percentage Change in Target Lesion from Baseline by Investigators

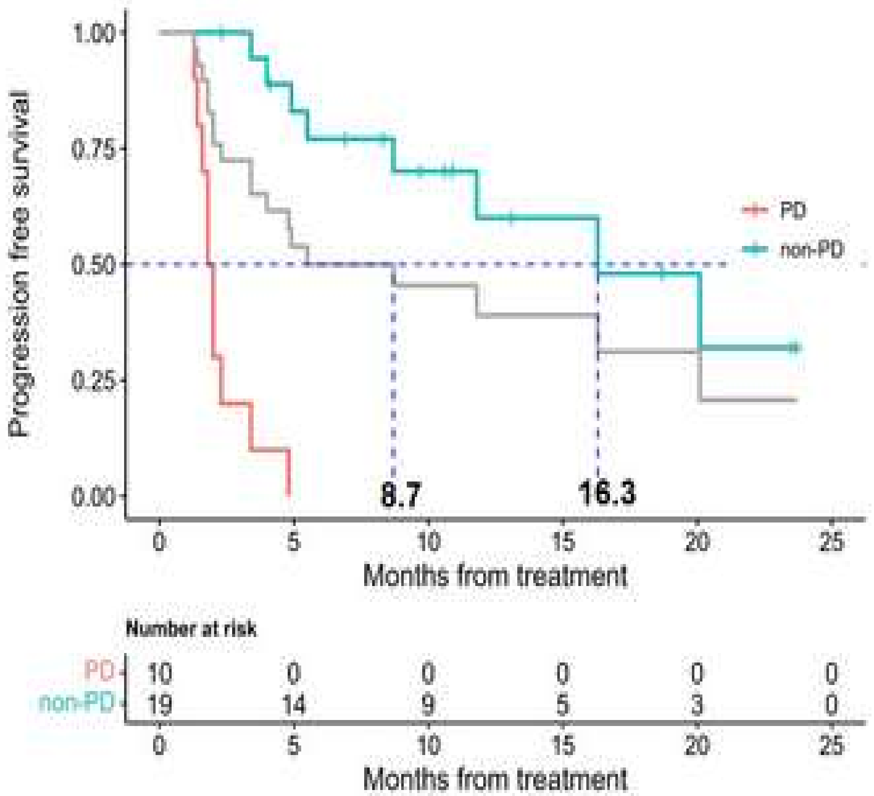


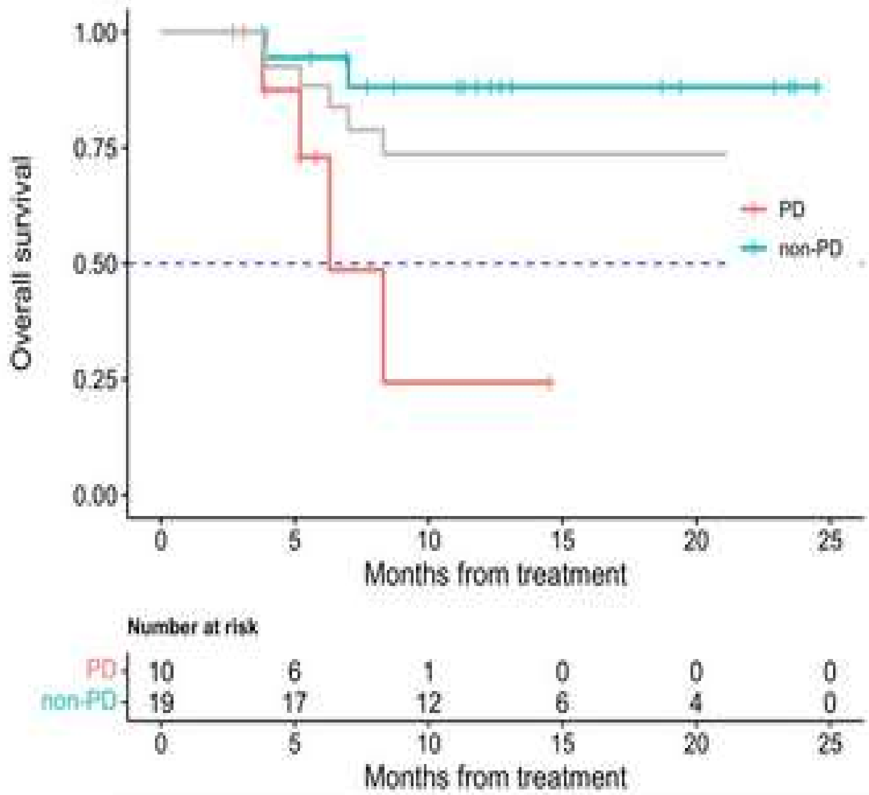


6 Month Progression-Free Survival Rate and Overall Response Rate

		HPV type		Histology	
	Activity (n = 29)	HPV 16	HPV 18	SCC (n = 18)	AD (n = 11)
6 month PFS rate	**50% (34 – 73)**				
Overall response rate	38% (20 – 56)				
CR	4 (14%)	4 (20%)	0 (0%)	3 (17%)	1 (9%)
PR	7 (24%)	6 (30%)	1 (11%)	6 (33%)	1 (9%)
SD	3 (10%)	0 (0%)	3 (33%)	0 (0%)	3 (27%)
PD	15 (52%)	10 (50%)	5 (56%)	9 (50%)	6 (55%)
Median time to response (mo)	5.1 ± 3.7				
Median duration of response (mo)	13.3 (12. 2 – NA)				

Progression-Free Survival and Overall Survival According to Response





Safety Summary (N = 30)

Grade	G1		G2	G3		Total
	Dose interruption	No change	No change	Discontinuation	Dose interruption	(%)
Fatigue	0	1	0	0	0	1 (3)
Headache	0	3	1	0	0	4 (13)
Fever/chill	1	20	3	0	0	24 (80)
Cytokine release syndrome	0	1	0	0	0	1 (3)
Cardiac marker elevation	0	0	0	1	0	1 (3)
Chest discomfort	0	0	0	1	0	1 (3)
Cough	0	1	1	0	0	2 (7)
dyspnea	0	0	1	0	0	1 (3)
Vomiting	0	1	0	0	0	1 (3)
Diarrhea	0	2	0	0	0	2 (7)
Constipation	0	1	0	0	0	1 (3)
LFT elevated	0	0	0	0	1	1 (3)
Myalgia	0	1	0	0	0	1 (3)
Rash	0	3	0	0	0	3 (10)
Thyroid dysfunction	0	7	0	0	0	7 (23)

Conclusions/ Key Takeaways

- BVAC-C is a therapeutic vaccine that activates both innate and adaptive immune effectors
- When combined with durvalumab, BVAC-C has shown durable antitumor activity in patients with HPV 16 or 18 positive recurrent cervical cancer who have failed first-line platinum-based chemotherapy
  - 6-month PFS rate: 50% (34% – 73%)
  - ORR: 38% (20% – 56%) [CR 14%, PR 24%]
  - Median PFS: 8.7 month
- BVAC-C has a manageable safety profile and can be produced within 1 day, making it a significant option for second-line treatment

CONCLUSIONES CÉRVIX

- Datos a favor de Ac anti EGFR junto a QT RT en localmente avanzado, un estándar que esta a punto de caer.

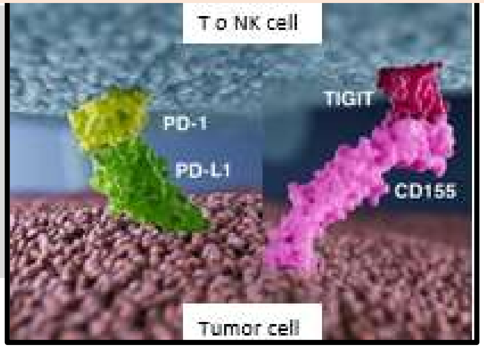
- Nuevo golpe (definitivo ??) a la adyuvancia con QT en localmente avanzado.

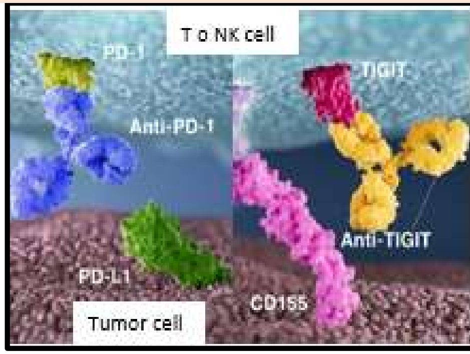
- Esperanzadores resultados mediante combinación de inmunoterapia tradicional con vacunas en 2 línea.

Vibostolimab coformulated with pembrolizumab (vibo/pembro) for previously treated advanced mismatch repair–deficient (dMMR) endometrial cancer: Results from cohort B1 of the phase 2 KEYVIBE-005 study.

Carlos Rojas. ASCO 2024

TIGIT es un checkpoin expresado en células del s immune (células T y NK),que tiene function de inhibicion.
Vibostolimab es un anticuerpo anti-TIGIT que restablece la actividad antitumoral al bloquear la unión del receptor TIGIT a sus ligandos (CD112 y CD155), activando así los linfocitos T





KEYVIBE-005 Study Design (NCT05007106)

Key Eligibility Criteria (Cohort B1)
- Aged ≥18 years
- Recurrent locally unresectable or metastatic endometrial cancer
- dMMR tumor by central assessment
- Disease progression after 1 prior platinum-based chemotherapy or ≤2 lines if 1 was given in the (neo)adjuvant setting
- No prior PD-(L)1 inhibitor therapy
- ECOG PS 0 or 1

N = 40 → **Coformulated vibostolimab 200 mg with pembrolizumab 200 mg IV Q3W for up to 35 cycles (~2 years)** → Until unacceptable toxicity, disease progression, or withdrawal decision

Primary end point: ORR per RECIST v1.1 by investigator assessment

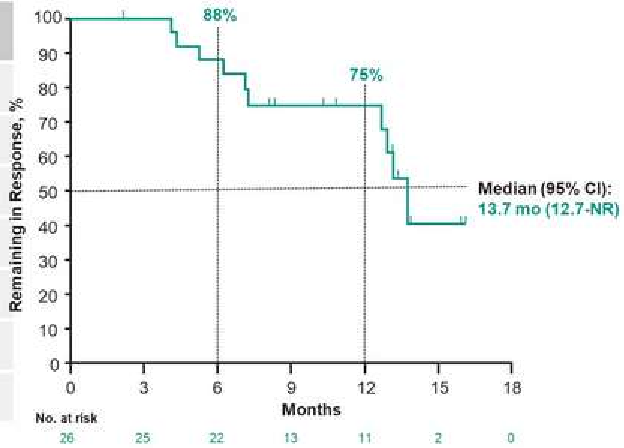
Secondary end points: DOR and PFS per RECIST v1.1 by investigator assessment, OS, and safety

Patients treated with vibo/pembro
N = 40

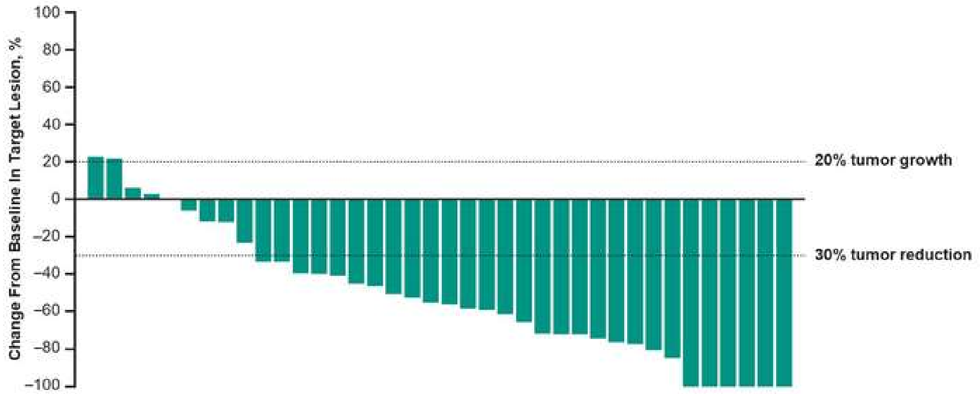
- **Ongoing, n = 17**
- **Discontinued study treatment, n = 23**
  - **11 AEs**
  - **7 progressive disease**
  - **4 clinical progression**
  - **1 patient decision to withdraw**

Response per RECIST v1.1 by Investigator Assessment

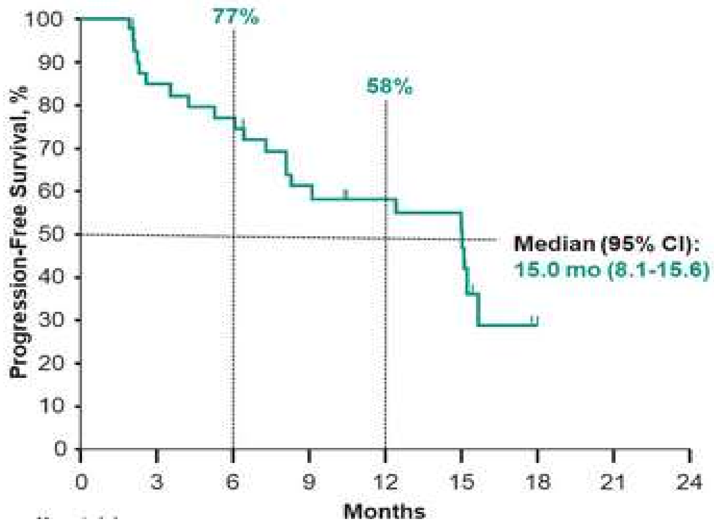
	Vibo/Pembro N = 40
ORR, % (95% CI)	65 (48-79)
Best overall response, n (%)	
CR	5 (13)
PR	21 (53)
SD	8 (20)
PD	4 (10)
No assessment[a]	2 (5)

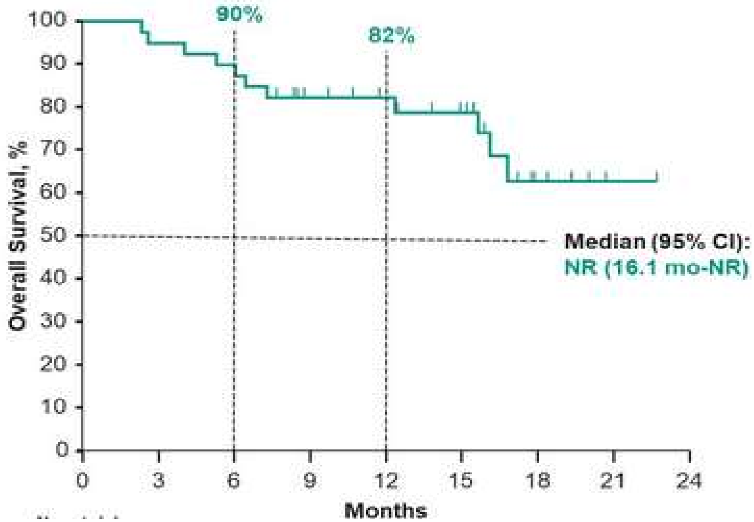


Best Change From Baseline in Target Lesion Size per RECIST v1.1

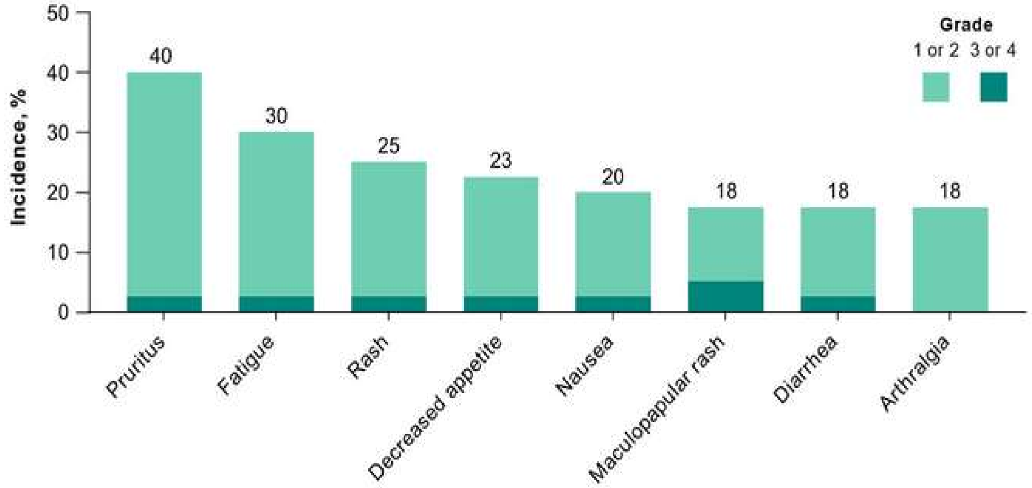


PFS per RECIST v1.1 by Investigator Assessment and OS

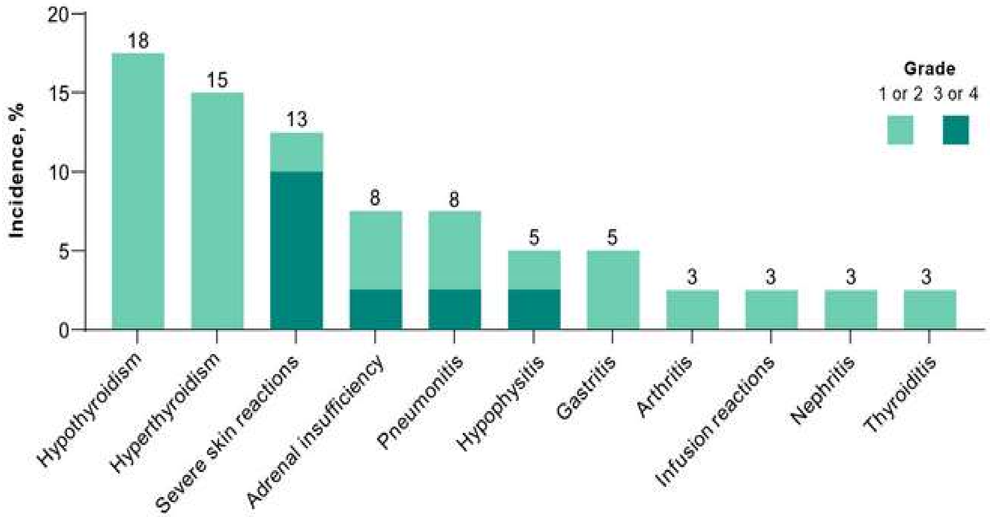




Most Common Treatment-Related Adverse Events (>15%)



Immune-Mediated AEs and Infusion Reactions



Conclusions

- After 17.2 months of follow-up, coformulated vibostolimab/pembrolizumab demonstrated durable antitumor activity and a manageable safety profile in patients with previously treated advanced dMMR endometrial cancer
  - ORR was 65%, with 75% of responders experiencing a response for ≥1 year
  - Median PFS was 15.0 months, and median OS was not reached
- The addition of vibostolimab to pembrolizumab may improve the efficacy observed with pembrolizumab monotherapy in KEYNOTE-158[1,2]
- These results support further evaluation of vibostolimab/pembrolizumab in advanced immunotherapy-sensitive tumors