¿Cómo disminuir la incidencia?
OBESIDAD
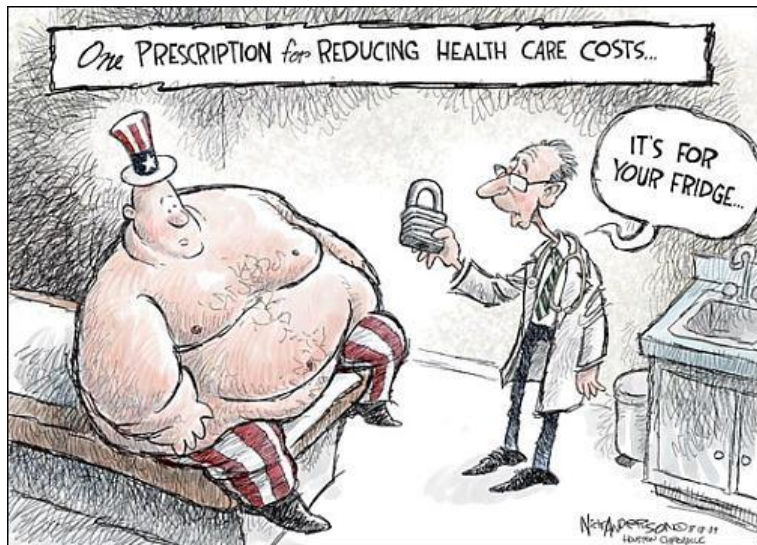
Enfermedad avanzada: histología, edad, estadio

UPSC - Uterine papillary serous carcinoma
CC - Clear cell carcinoma
G1, G2EC – Grade 1 and 2 endometrioid carcinoma
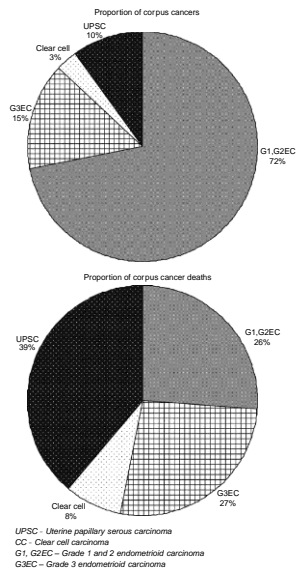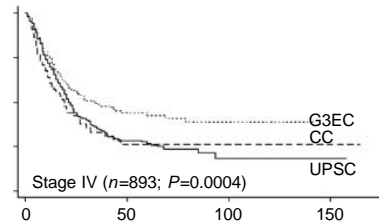G3EC – Grade 3 endometrioid carcinoma

Figure 1 Proportion of corpus cancers compared to proportion of corpus cancer deaths by histologic cell type.

Supervivencia global en estadio IV según tipo histológico

CC células claras; UPSC seroso; EG3 endometrioide G3

Factores que aumentan el riesgo de recidiva
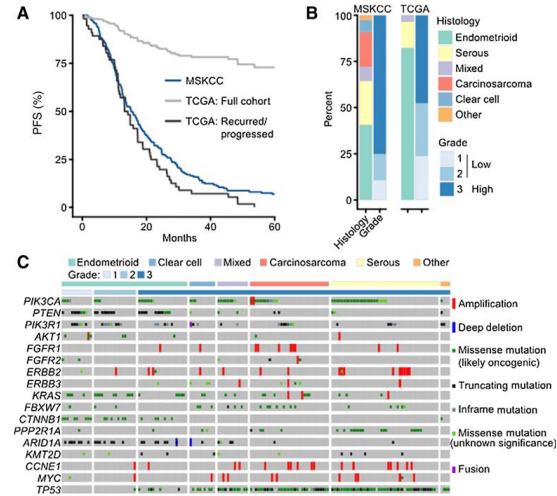
Table 2 Multivariate analysis

Factors	Hazard ratio	95% confidence interval	P-value
Stage of disease	2.05	1.93−2.17	P< 0.001
Histology[a]	1.22	1.11−1.35	P< 0.001
Age at diagnosis[b]	1.03	1.03−1.04	P< 0.001
Race[c]	1.00	0.92−1.11	P¼0.888
Adjuvant radiotherapy	0.99	0.93−1.03	P¼0.450

[a]Uterine papillary serous carcinoma vs clear cell carcinoma vs grade 3 endometrioid carcinoma. [b]As a continuous variable. [c]Whites vs Blacks vs Asians.

Hamilton et al. Uterine papillary serous and clear cell carcinomas predict for poorer survival compared to grade 3 endometrioid corpus cancers British Journal of Cancer (2006) 94, 642 – 646

Molecular classification

IMS EN cáncer de endometrio

MSI-H total	MSI-H and TMB H	MSS and TMB H	TMB High	MSS total
1.5%	82.1%	5.4%	6.6%	98.5%

B

Total   TMB-H

7,972   1,790   389

MSI-H

n = 148,803

A

Legend:
- MSI-L and TMB-H
- MSI-H and TMB-H
- MSI-H and TMB-L/I
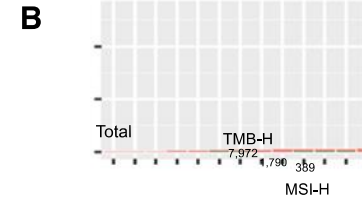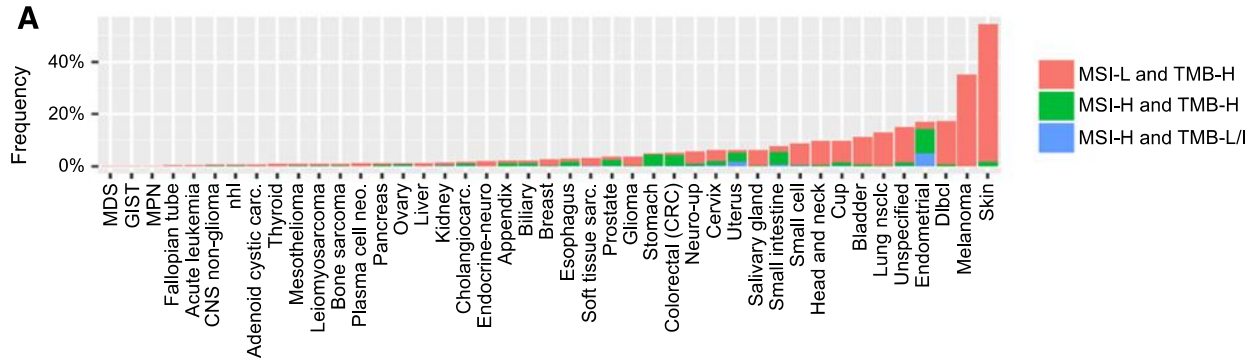
Poblaciones y criterios

- MMRd (MSI-H) vs MMRPro (MSS)

- Tiempo desde adyuvancia platino (<6 o <12 meses)

- Líneas previas en enfermedad avanzada no resecable

- Mantenimiento

Mantenimiento tras platino

TP53 WT: X-PORT

p53 wild-type

Median PFS
Selinexor (n=67): 13.7 mo (95% CI 9.20-NR)
Placebo (n=36): 3.7 mo (95% CI 1.87-12.88)
HR = 0.375 (95% CI 0.210-0.670);P value = 0.0003

Key Eligibilities
• Known p53 wild-type EC by central NGS
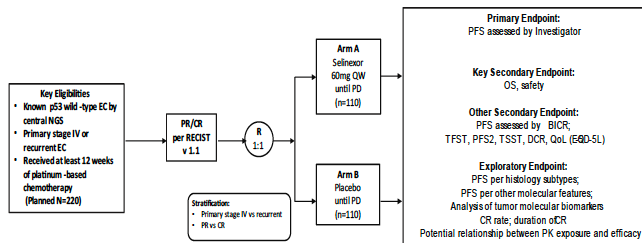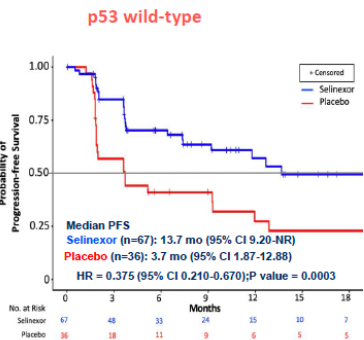• Primary stage IV or recurrent EC
• Received at least 12 weeks of platinum-based chemotherapy
(Planned N=220)

PR/CR per RECIST v 1.1

Stratification:
• Primary stage IV vs recurrent
• PR vs CR

R 1:1

Arm A
Selinexor 60mg QW until PD
(n=110)

Arm B
Placebo until PD
(n=110)

Primary Endpoint:
PFS assessed by Investigator

Key Secondary Endpoint:
OS, safety

Other Secondary Endpoint:
PFS assessed by BICR;
TFST, PFS2, TSST, DCR, QoL (EQD-5L)

Exploratory Endpoint:
PFS per histology subtypes;
PFS per other molecular features;
Analysis of tumor molecular biomarkers
CR rate; duration of CR
Potential relationship between PK exposure and efficacy

"Not exactly TP53 mutant": PARPi

	experimental	SOC	Stratification	BK	Adjuvant
Ruby P2	IO+PARP	Observation	MMR	none	
DUO-E	IO+PARP	3 arms: Obs or IO		none	>12 mo

– Unselected
– Potential BK?
– Serous histology
– P53 (IHC vs Mutation)
– GIS
– HRD mutations
– BRCA1/2

– DUO-E: all comers
– IO vs Obs
– IO vs IO+PARPi

Makker ASCO 2022

Pembrolizumab monoterapia en CE:

ESTUDIO Cohorte MSI-H todos los tumores

- •9 pacientes MSI-high recurrent or progressive endometrioid endometrial
- •Mediana tratamientos previos – 2
- •Tasa respuesta 56% (95% CI: 21-86%, N=5/9) – CR1,PR4
- •– 3 pacientes con estabilización prolongada
- •Tasa control enfermedad (RC + RP + EE) es 88.9% (8/9 pacientes) • SG a los 12 meses: 89%

ESTUDIO KEYNOTE 028 sólo CE PDL-1 +

Table 3. Best Objective Response Assessed per RECIST (version 1.1) by Investigator Review (n = 23)

Best Objective Response	No.	%	95% CI
Objective response rate*	3	13.0	2.8 to 33.6
PR†	3	13.0	2.8 to 33.6
Stable disease	3	13.0	2.8 to 33.6
Progressive disease‡	13	56.5	34.5 to 76.8
No assessment§	3	13.0	2.8 to 33.6
Nonevaluable‖	1	4.3	0.1 to 21.9
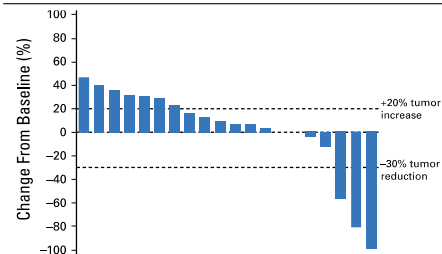
Fader, AN et.al. SGO 2016
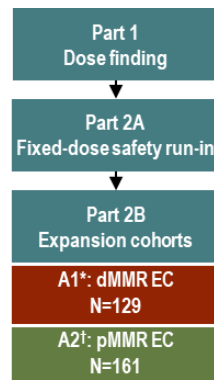Ott et al. J Clin Oncol. 2017 Aug 1;35(22):2535-2541.

Progresión durante/tras platino 1ª línea

- MSI-H Pembrolizumab /Dostarlimab

- All comers/ MSS: Lenvatinib Pembrolizumab

GARNET:
Dostarlimab in Patients with Recurrent or Advanced MMRd Disease

- **Phase 1, single-arm study across multiple tumor types**
- **In part 2B, dostarlimab was dosed at the RTD determined from Part 1 and 2A**
  - 500 mg IV every 3 wk for 4 cycles, then 1000 mg IV every 6 wk until disease progression

- **MMR status determined by local IHC**
- **Primary endpoints: ORR and DoR**

| Part 1
Dose finding |
| Part 2A
Fixed-dose safety run-in |
| Part 2B
Expansion cohorts |
| A1*: dMMR EC
N=129 |
| A2†: pMMR EC
N=161 |

Key inclusion/exclusion criteria for cohorts A1 and A2:
- Patients must have progressed on or after platinum doublet therapy
- Patients must have received ≤2 prior lines of treatment for recurrent or advanced disease
- Patients must have measurable disease at baseline
- Patients must be anti–PD-(L)1 naïve
- Patients could be screened based on local MMR/MSI testing results using IHC, PCR, or NGS performed in a certified local laboratory, but patient eligibility needs to be confirmed by MMR IHC results

Oaknin A, et al. *Ann Oncol*. 2020;31(Suppl_4): Abstract LBA36; Oaknin A, et al. *JAMA Oncol*. 2020:e204515.

GARNET: Enrollment and Outcomes

Enrolled and dosed (safety population)	dMMR EC N=126 (100%)	MMRp EC N=145 (100%)
No measurable disease at baseline or insufficient follow-up	n=23	n=3
Measurable disease at baseline and ≥6 months follow-up (efficacy population)	n=103	n=142
Discontinued treatment	70 of 126 (56%) Progression, n=49 Adverse event, n=14 Patient request, n=1 Clinical criteria, n=5 Other, n=1	127 of 145 (88%) Progression, n=89 Adverse event, n=14 Clinical criteria, n=16 Patient request, n=5 Other, n=3
Remain on treatment	n=56 of 126 (44%)	n=18 of 145 (12%)

Data cut-off date March 1, 2020. dMMR, mismatch mutation repair deficient; EC, endometrial cancer; MMRp, mismatch mutation repair proficient.

# GARNETT: tasa respuestas según inestabilidad de microsatélites de anti PD-1 dostarlimab

Best Overall Response		MSI-H EC (n=41)	MSS EC (n=79)	MSI status unknown[a] (n=5)	Total (N=125)
Overall response rate	**n (%)** (95% CI)	**20 (48.8%)** (32.9, 64.9)	**16 (20.3%)** (12.0, 30.8)	**1 (20.0%)** (0.5, 71.6)	**37 (29.6%)** (21.8, 38.4)
Complete response	n (%)	2 (4.9%)	4 (5.1%)	0 (0%)	6 (4.8%)
Partial response	n (%)	18[b] (43.9%)	12[c] (15.2%)	1 (20.0%)	31 (24.8%)
Disease control rate[d]	% (95% CI)	63.4% (46.9, 77.9)	46.8% (35.5, 58.4)	60.0% (14.7, 94.7)	52.8% (43.7, 61.8)
Response ongoing	%	85.0%	81.3%	100%	83.8%

[a]Based on central testing, MSI status could not be determined; [b]17 confirmed and 1 still on treatment and yet to be confirmed; [c]11 confirmed and 1 still on treatment and yet to be confirmed; [d]irCR+irPR+uirPR+irSD.
irCR: immune-related complete response; irPR: immune-related partial response; irSD: immune-related stable disease; uirPR: unconfirmed immune-related partial response. CI: confidence interval.

Oaknin et al. SGO 2019;

GARNET
Primary Endpoint: DoR
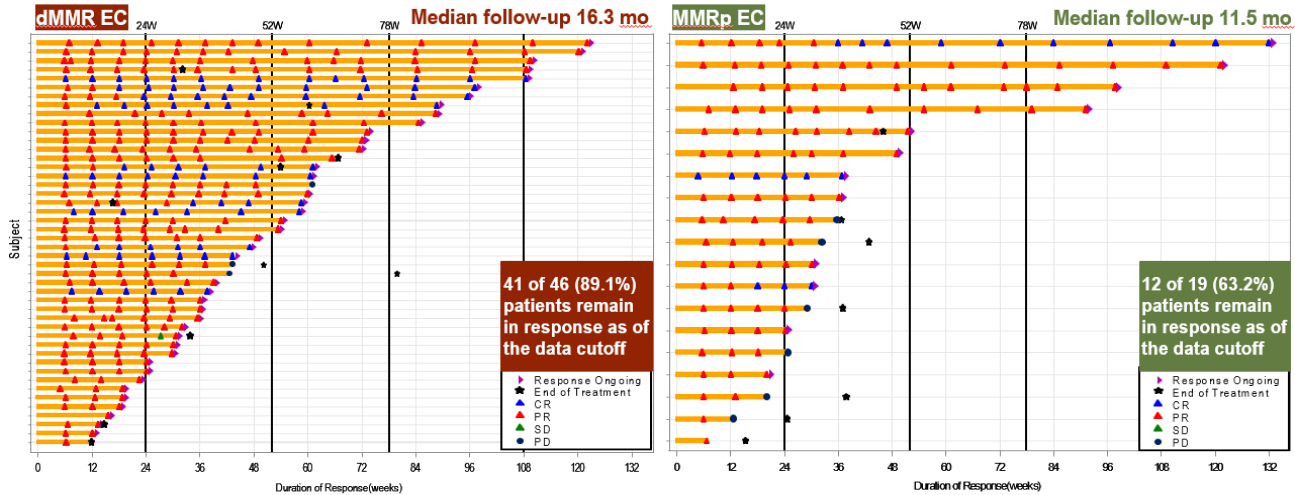
Oaknin A, et al. *Ann Oncol*. 2020;31(Suppl_4): Abstract LBA36; Oaknin A, et al. *JAMA Oncol*. 2020:e204515.

Combinaciones IO: Lenvatinib + Pembrolizumab

Fase IB/II carcinoma endometrial
Población nº líneas previas: 1 línea (48%)

Response Category	Previously Treated EC[a]			
	MSS/pMMR (n = 94)	MSI-H/dMMR (n = 11)	Total (n = 108)	All EC (N = 124)
Week 24				
Best overall response				
Complete response	2 (2.1)	1 (9.1)	3 (2.8)	3 (2.4)
Partial response	32 (34.0)	6 (54.5)	38 (35.2)	46 (37.1)
Stable disease	45 (47.9)	3 (27.3)	50 (46.3)	56 (45.2)
Progressive disease	10 (10.6)	1 (9.1)	12 (11.1)	13 (10.5)
Not evaluable	5 (5.3)	0	5 (4.6)	6 (4.8)
Objective response rate (complete response + partial response)	34 (36.2)	7 (63.6)	41 (38.0)	49 (39.5)
95% CI	26.5 to 46.7	30.8 to 89.1	28.8 to 47.8	30.9 to 48.7

Makker et al. J Clin Oncol 2020 38:2981-2992.

Keynote-775: Segunda línea lenvatinib+pembrolizumab vs QT

	LEN + pembro (n = 411)	TPC (n = 416)
Median age (range), years	64 (30-82)	65 (35-86)
MMR status: pMMR / dMMR, %	84.2 / 15.8	84.4 / 15.6
Prior history of pelvic radiation, %	40.9	41.6
ECOG 0 / 1, %[a]	59.9 / 39.9	57.9 / 42.1
Race: White / Black / Asian / other, %[b]	63.5 / 4.1 / 20.7 / 2.9	59.1 / 3.4 / 22.1 / 4.8
Histology at diagnosis, %[c]		
Endometrioid carcinoma High-grade / low-grade / not specified[d]	22.9 / 14.4 / 21.9	21.6 / 13.0 / 26.4
Serous carcinoma	25.1	27.6
Clear cell carcinoma	7.3	4.1
Mixed	5.4	3.8
Prior lines of systemic treatment 1 / ≥ 2, %	72.3 / 27.7	66.6 / 33.4
Prior lines of platinum-based treatment 1 / 2, %[e]	79.3 / 20.2	75.7 / 24.3
Prior neo-adjuvant and/or adjuvant treatment, %	54.5	60.3

Phase 3 data second line Pembrolizumab+ Lenvatinib

Efficacy according to histology (Colombo et al.)

Efficacy all comers

Efficacy pMMR

Efficacy dMMR

SGO 2021

IGCS 2021

Efficacy according to histology (Colombo et al.ESMO 2021)

Posthoc analysis

Progression-Free Survival[a] by Histology: pMMR

Endometrioid

	N	Events, n (%)	HR (95% CI)
Len + pembro	188	122 (64.9)	0.59 (0.46–0.76)
TPC	198	131 (66.2)	

Median (95% CI)
7.6 mo (5.9–9.1)
5.0 mo (3.7–5.7)

No. at risk
len + pembro 188 152 98 70 34 25 19 7 2 0
TPC 198 113 59 24 10 7 3 1 1 0

Serous

	N	Events, n (%)	HR (95% CI)
Len + pembro	99	78 (78.8)	0.54 (0.39–0.75)
TPC	112	77 (68.8)	

Median (95% CI)
5.7 mo (4.9–7.6)
3.6 mo (2.0–5.1)

99 76 45 31 16 10 7 2 2 0
112 48 22 11 3 1 0 0 0 0

Clear cell

	N	Events, n (%)	HR (95% CI)
Len + pembro	29	24 (82.8)	0.49 (0.25–0.97)
TPC	17	15 (88.2)	

Median (95% CI)
3.9 mo (2.1–7.4)
2.0 mo (1.9–4.6)

29 17 11 6 6 2 2 1 1 0
17 6 1 1 1 0 0 0 0 0

[a]Per RECIST v1.1 by BICR. Randomization was stratified by MMR status.
HRs for other histologic types: mixed cell (n = 31): HR (95% CI), 0.90 (0.35–2.29); other (n = 23): HR (95% CI), 0.38 (0.12–1.19).
Data cutoff: Oct 26, 2020.

Efficacy according to histology (Colombo et al.)

OS by Histology: All-Comers

E>CC>S   EG3 vs EG1-2?

Endometrioid

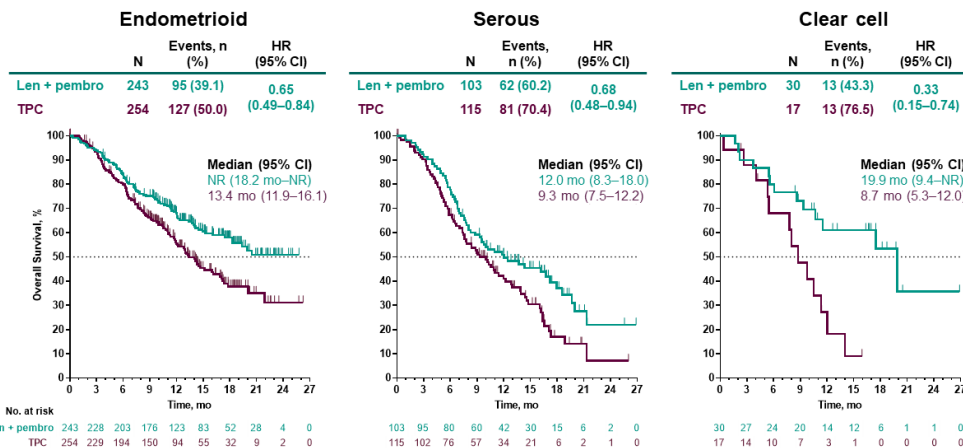|	N	Events, n (%)	HR (95% CI)
Len + pembro	243	95 (39.1)	0.65 (0.49–0.84)
TPC	254	127 (50.0)	

Median (95% CI)
NR (18.2 mo–NR)
13.4 mo (11.9–16.1)

Serous

	N	Events, n (%)	HR (95% CI)
Len + pembro	103	62 (60.2)	0.68 (0.48–0.94)
TPC	115	81 (70.4)	

Median (95% CI)
12.0 mo (8.3–18.0)
9.3 mo (7.5–12.2)

Clear cell

	N	Events, n (%)	HR (95% CI)
Len + pembro	30	13 (43.3)	0.33 (0.15–0.74)
TPC	17	13 (76.5)	

Median (95% CI)
19.9 mo (9.4–NR)
8.7 mo (5.3–12.0)

No. at risk

	0	3	6	9	12	15	18	21	24	27
len + pembro	243	228	203	176	123	83	52	28	4	0
TPC	254	229	194	150	94	55	32	9	2	0

	0	3	6	9	12	15	18	21	24	27
	103	95	80	60	42	30	15	6	2	0
	115	102	76	57	34	21	6	2	1	0

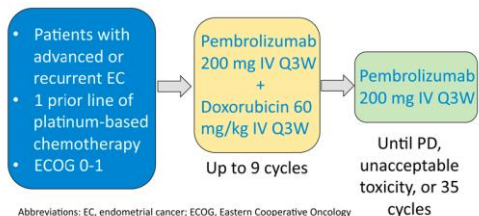|	0	3	6	9	12	15	18	21	24	27
	30	27	24	20	14	12	6	1	1	0
	17	14	10	7	3	1	0	0	0	0

HRs for other histologic types: mixed cell (n = 38): HR (95% CI), 0.37 (0.16–0.85); other (n = 27): HR (95% CI), 0.39 (0.15–1.04).
Data cutoff: Oct 26, 2020.

TOPIC: Adriamicin + Pembrolizumab Fariñas et al.

Patients with advanced or recurrent EC
- 1 prior line of platinum-based chemotherapy
- ECOG 0-1

→ Pembrolizumab 200 mg IV Q3W + Doxorubicin 60 mg/kg IV Q3W — Up to 9 cycles

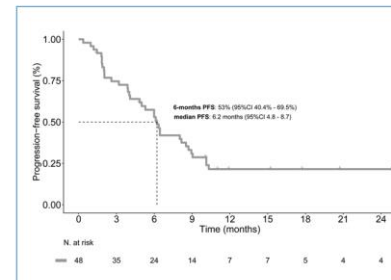→ Pembrolizumab 200 mg IV Q3W — Until PD, unacceptable toxicity, or 35 cycles

Abbreviations: EC, endometrial cancer; ECOG, Eastern Cooperative Oncology Group; IV, intravenous; PD, progressive disease; Q3W, every 3 weeks

Primary endpoint

- Progression-free survival (PFS) rate at 6 months.

Characteristics	n (%)
Median age (range), years	65.7 (37-80)
Stage at diagnostic (FIGO)	
I-II	16 (33)
III-IV	41 (65)
Histology	
Carcinosarcoma	4 (8)
Endometrioid Adenocarcinoma	31 (65)
Mixed Carcinoma	2 (4)
Serous Carcinoma	10 (21)
Other	1 (2)
ECOG performance status	
0	33 (69)
1	15 (31)
Histological Grade	
Grade 1	6 (13)
Grade 2	11 (23)
Grade 3	21 (44)
Unknown	10 (21)
Prior radiotherapy	24 (50)
Prior chemotherapy	48 (100)
Paclitaxel with carboplatin	47 (98)
Cisplatin	10 (21)
Carboplatin	9 (19)
Paclitaxel	6 (13)
Others	3 (6)
Best response with prior chemotherapy	
Complete response	4 (8)
Partial response	18 (38)
Stable disease	7 (15)
Progressive disease	7 (15)
Unknown	12 (25)
Prior surgery	34 (71)

Figure 1. Kaplan-Meier estimate of progression-free survival by investigator assessment (N=48)

6-months PFS: 53% (95%CI 40.4% - 69.9%)
median PFS: 6.2 months (95%CI 4.8 - 8.7)

N. at risk — 48 35 24 14 7 7 5 4 4

NOTE. Tick marks represent censored patients.
Abbreviations: PFS, progression-free survival.

Table 2. Best response to study treatment

Objective response rate	15 (31)
Complete response	6 (12.5)
Partial response	9 (19)
Stable disease	22 (46)
Progressive disease	10 (21)
Median duration (95% CI) of response, months	8.2 (6.2 – NR)
Median time (range) to response, months	2.1 (1.6 – 22.9)

PFS 6 mo 53 vs 24% estimated

PFS 6 mo 63% endometr vs 35% non endometr

Progresión tras platino adyuvante

MMR d: first line

	RECRUITING	Adjuvant CT	Crossover	EP	
EN13 Domenica	Yes worldwide	Yes >6mo	Yes	PFS	
EN15 C193	Yes worldwide	NO…yes	Yes in trial	PFS OS	

All comers: first line

	RECRUITING	Adjuvant CT	Crossover	EP	
LEAP001	finished	Yes >6mo			
DUO-E	finished	Yes >12mo			
RUBY Pt2	finished	Yes >6mo			

Combinaciones IO: cabozantinib + Nivolumab

**COHORTE A: nivolumab
+ cabozantinib**
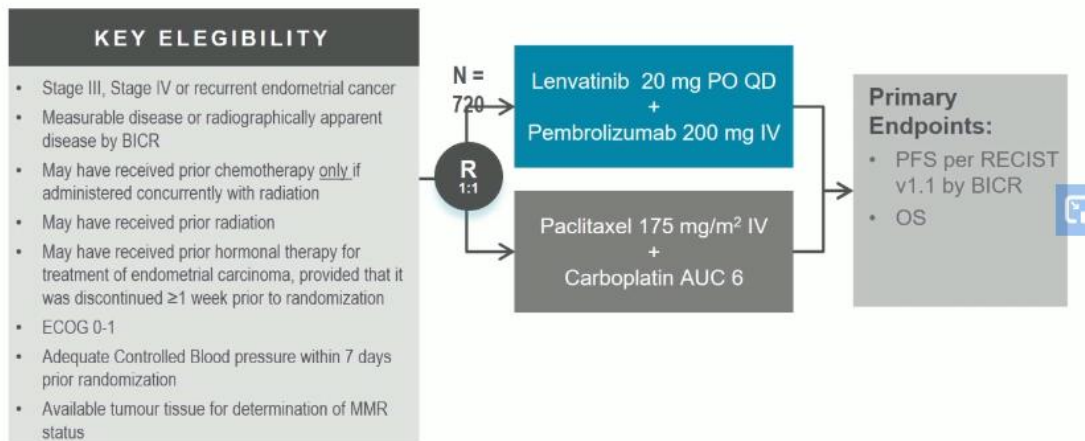N=36
Tasa respuestas: 25%

EP tras platino

COHORTE B: nivolumab
N=18
Tasa respuestas: 11.1%

Lheureux ASCO 2020
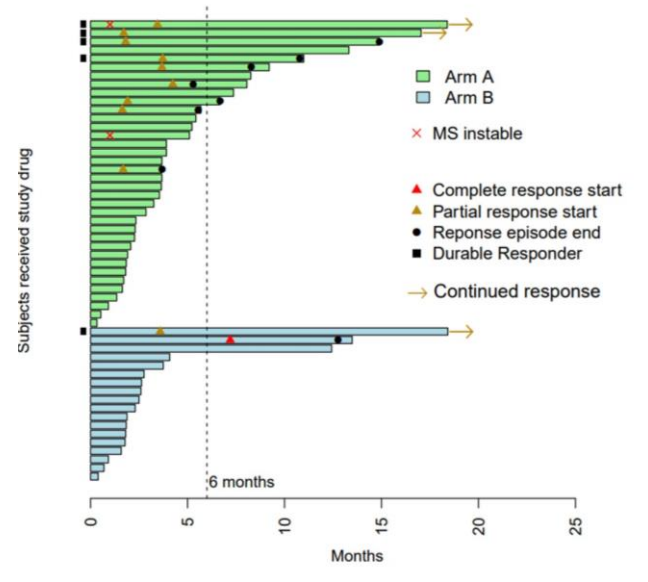
ENGOT-en9/LEAP-001: A Phase 3 randomized, open-label, study of pembrolizumab + lenvatinib vs. chemotherapy for first-line treatment of advanced or recurrent endometrial carcinoma

KEY ELEGIBILITY

- Stage III, Stage IV or recurrent endometrial cancer
- Measurable disease or radiographically apparent disease by BICR
- May have received prior chemotherapy only if administered concurrently with radiation
- May have received prior radiation
- May have received prior hormonal therapy for treatment of endometrial carcinoma, provided that it was discontinued ≥1 week prior to randomization
- ECOG 0-1
- Adequate Controlled Blood pressure within 7 days prior randomization
- Available tumour tissue for determination of MMR status

N = 720

R 1:1

Lenvatinib 20 mg PO QD
+
Pembrolizumab 200 mg IV

Paclitaxel 175 mg/m² IV
+
Carboplatin AUC 6

Primary Endpoints:
- PFS per RECIST v1.1 by BICR
- OS

BICR, blind independent central review; IV intravenous, MMR, mismatch repair. ClinicalTrials.gov: NCT03884101 (LEAP-001)
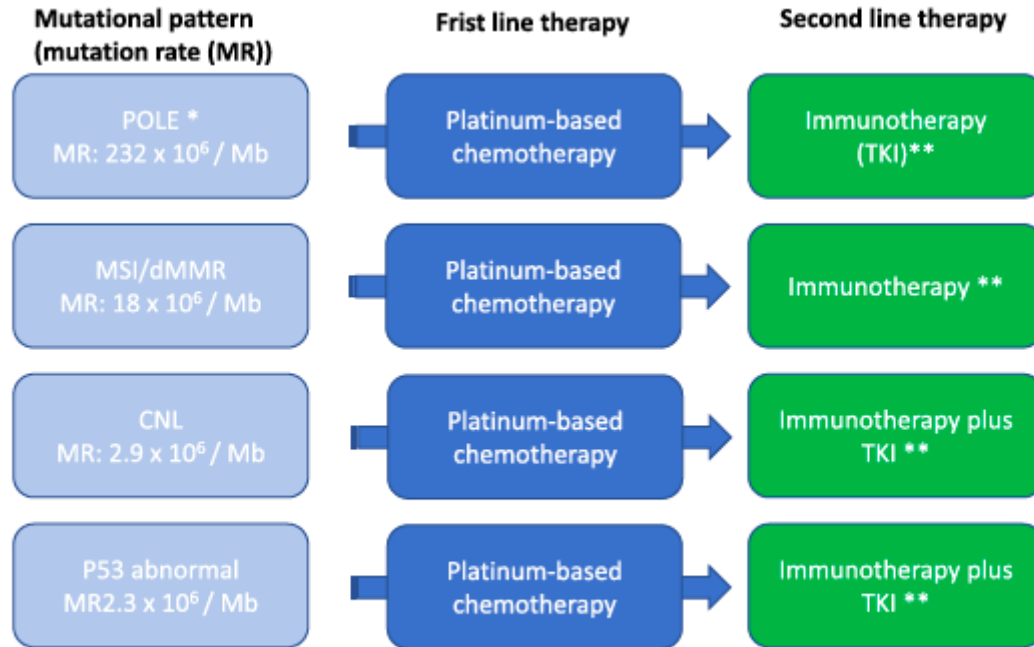
"Current" preSGO 2023 paradigm

Fig. 2. Current paradigm of treatment on the basis in advanced and recurrent endometrial cancers.

Eficacia de IO en CE MSI-H

Study	Arms	Phase	N	Biomarker selection	ORR (%)	Outcomes
KEYNOTE-158[1]	Pembrolizumab	II	49	MSI-H/MMRd	57.1	mPFS 25.7 (4.9-NR) mOS NR (27.2-NR) DOR NR (2.9-27.0+)

Study	Arms	Phase	N	Biomarker selection	ORR (%)	Outcomes
GARNET[2,3]	Dostarlimab	I/II	103	MSI-H/MMRd	44.7	mPFS 8.1 m mOS NR DOR NR

Study	Arms	Phase	N	Biomarker selection	ORR (%)	Outcomes
Konstantinopoulos[4]	Avelumab	II	15	MSI	26.7	NR

Study	Arms	Phase	N	Biomarker selection	ORR (%)	Outcomes
PHAEDRA[5]	Durvalumab	II	35	MMRd	43	NR

Study	Arms	Phase	N	Biomarker selection	ORR (%)	Outcomes
NCI-MATCH arm Z1D[6]	Nivolumab	II	13	MMRd	46.1	NR

ORR: overall response rate; PFS: profresion free-survival; OS: overall survival; DOR: duration response rate; NR: not reported
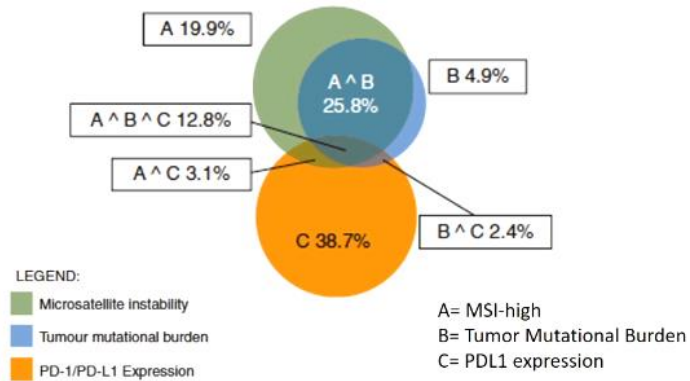
1. Marabelle et al, JCO 2019. 2.Oaknin et al,ESMO 2020. 3.Oaknin et al, JAMA oncol 2020 4.Konstantinopoulos, ASCO 2019. 5. Antill et al, ASCO 2019. 6.Azad et al,JCO 2019
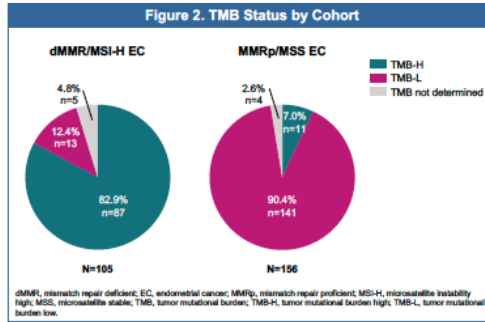
BIOMARCADORES

MSI PDL1 TMB en endometrio

A 19.9%

B 4.9%

A ^ B 25.8%

A ^ B ^ C 12.8%

A ^ C 3.1%

C 38.7%

B ^ C 2.4%

LEGEND:
- Microsatellite instability
- Tumour mutational burden
- PD-1/PD-L1 Expression

A= MSI-high
B= Tumor Mutational Burden
C= PDL1 expression

Luchini P et al. Ann Oncol 2019

Second line: Molecular Biomarker beyond MSI in IO

Garnett trial Dostarlimab and TMB Oaknin et al.

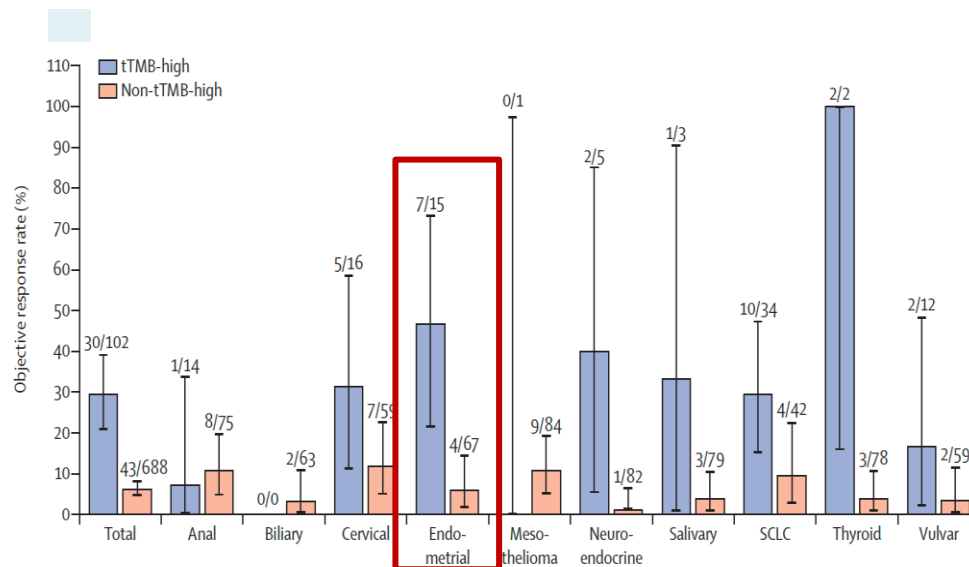Figure 2. TMB Status by Cohort

dMMR/MSI-H EC — 4.8% n=5 (TMB not determined); 12.4% n=13 (TMB-L); 82.9% n=87 (TMB-H); N=105

MMRp/MSS EC — 2.6% n=4 (TMB not determined); 7.0% n=11 (TMB-H); 90.4% n=141 (TMB-L); N=156

TMB-H, TMB-L, TMB not determined

dMMR, mismatch repair deficient; EC, endometrial cancer; MMRp, mismatch repair proficient; MSI-H, microsatellite instability high; MSS, microsatellite stable; TMB, tumor mutational burden; TMB-H, tumor mutational burden high; TMB-L, tumor mutational burden low.

Table 2. Mutations/Megabase by Cohort in Patients with a Known TMB Score Available

Parameter	dMMR/MSI-H EC (n=100)	MMRp/MSS EC (n=152)
Median (range)	20.17 (2.52–428.69)	3.78 (0–83.22)
Mean (StDev)	28.39 (45.39)	4.68 (7.28)

dMMR, mismatch repair deficient; EC, endometrial cancer; MMRp, mismatch repair proficient; MSI-H, microsatellite instability high; MSS, microsatellite stable; StDev, standard deviation; TMB, tumor mutational burden.
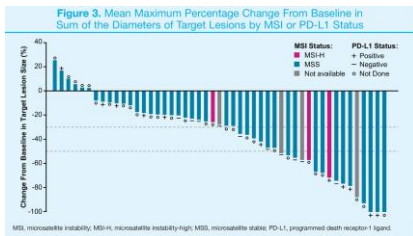

Figure 3. ORR by TMB Status (Pooled and by Cohort)

dMMR/MSI-H EC, MMRp/MSS EC, TMB-H, TMB-L

	TMB-H	TMB-L	TMB-H	TMB-L
ORR (%)	44.9	13.0	44.8 / 45.5	23.1 / 12.1
n/N	44/98	20/154	39/87 / 5/11	3/13 / 17/141

10 mutations/megabase (FDA-approved threshold) was used as the threshold for TMB-H status.

dMMR, mismatch repair deficient; EC, endometrial cancer; FDA, Food and Drug Administration; MMRp, mismatch repair proficient; MSI-H, microsatellite instability high; MSS, microsatellite stable; ORR, objective response rate; TMB, tumor mutational burden; TMB-H, tumor mutational burden high; TMB-L, tumor mutational burden low.

KEYNOTE-158 Exploratory Biomarker Objective : Association of tumour mutational burden with ORR

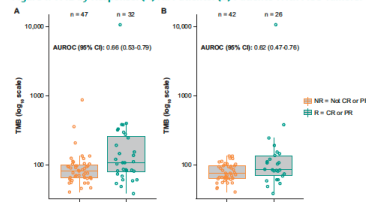Marabelle A et al;Lancet Oncol. 2020 Oct;21(10):1353-1365.

Second line biomarker

Phase 2 Lenvatinib Pembrolizumab TMB exploration (Makker et al)

No correlation to RNA signatures

Response regardless TMB

Table 2. Tumor Responses Using irRECIST (Per-Protocol Analysis set)

Figure 3. Mean Maximum Percentage Change From Baseline in Sum of the Diameters of Target Lesions by MSI or PD-L1 Status

Figure 1. TMB by Response. (A) All Patients. (B) Patients With MSS Tumors.

Table 3. ORR by TMB Subgroup

	Responders, n/N (%)
All patients	
TMB ≥175 mut/exome	10/13 (77)
TMB <175 mut/exome	22/66 (33)
Patients with MSS tumors	
TMB ≥175 mut/exome	4/4 (100)
TMB <175 mut/exome	22/64 (34)

mut, mutations.

Table 2. P Values for Association Between RNA-Sequencing Signatures and Clinical Outcomes in All Patients

	ORR		PFS	
Signature	Before Adjusting for Tcell$_{inf}$GEP	After Adjusting for Tcell$_{inf}$GEP	Before Adjusting for Tcell$_{inf}$GEP	After Adjusting for Tcell$_{inf}$GEP
Tcell$_{inf}$GEP	0.749	—	0.934	—
Angiogenesis	0.749	0.514	0.934	0.841
Glycolysis	0.888	0.915	0.878	0.968
gMDSC	0.888	0.915	0.878	0.968
Hypoxia	0.888	0.915	0.878	0.968
mMDSC	0.749	0.514	0.934	0.841
MVD	0.749	0.514	0.934	0.841
MYC	0.377	0.327	0.500	0.308
Proliferation	0.888	0.915	0.878	0.968
RAS	0.888	0.915	0.878	0.968
Stroma/EMT/TGFβ	0.749	0.514	0.934	0.841
WNT	0.888	0.915	0.878	0.968

Table 4. ORR by Select Individual Genes

	Responders, n/N	ORR, % (95% CI)
PIK3CA		
Mutation	10/27	37 (19-58)
No mutation	14/26	54 (33-73)
PTEN		
Mutation	7/17	41 (18-67)
No mutation	17/36	47 (30-65)
TP53		
Mutation	11/25	44 (24-65)
No mutation	13/28	46 (28-66)

No correlation to nonserous like (unlike TOPIC)

Situación regulatoria

Aprobación en Europa (abril 2021)

Dostarlimab* is indicated for the treatment of patients with **dMMR/MSI-H recurrent or advanced endometrial cancer** who have progressed on or following prior therapy with a platinum-containing regimen[1]

*Dostarlimab no está comercializado en España

Aprobación en US (FDA)

Pembrolizumab is indicated for the treatment of adult and pediatric patients with **unresectable or metastatic MSI-H or dMMR**
- **Solid tumors** that have progressed following prior treatment and who have no satisfactory alternative treatment options
- **Colorectal cancer** that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan[2]

Aprobación en US(FDA), Australia y Canadá

Pembrolizumab plus lenvatinib is indicated for the treatment of patients with **advanced endometrial carcinoma** that **is not** **MSI-H** or **dMMR** and who have disease progression following prior systemic therapy but are not candidates for curative surgery or radiation[3]

dMMR, deficient mismatch repair; EC, endometrial cancer; FDA, US Food and Drug Administration; MSI-H, microsatellite instability-high

1. https://ec.europa.eu/health/documents/communityregister/2021/20210421151305/anx_151305_es.pdf
2. https://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_pi.pdf
3. US Food and Drug Administration. Press Release. Available at: https://www.fda.gov/drugs/resources-information-approved-drugs/simultaneous-review-decisions-pembrolizumab-plus-lenvatinib-australia-canada-and-us. September 17, 2019. Accessed: April 30, 2021

Conclusiones

- ¿Biomarcadores? Sí

- Consideraciones clínicas
  - Adyuvancia
  - Línea de tratamiento

  - Posibilidades
    - MSI-H Dostarlimab Lenvatinib+ Pembrolizumab
    - MSS Lenvatinib+ Pembrolizumab

- Endometrio is on fire ver XAVIER, EVA Y CARMEN