XXIII JORNADA DE REVISIÓN DEL

CONGRESO AMERICANO DE ONCOLOGÍA

Actualización de tumores de SNC y tumores de cabeza y cuello

23 de junio de 2023

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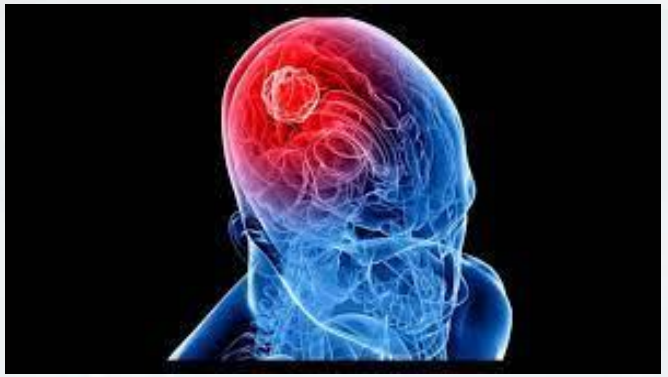
Fundación Jiménez Díaz

TUMORES DEL SNC

Destacar
- 1 comunicación de la sesión plenaria
- 6 comunicaciones orales
- 2 posters



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INDIGO: Fase 3 randomizado en gliomas de alto riesgo y bajo grado, con enfermedad residual/recurrente IDH1/2 mutados: Vorasidenib Vs placebo.

Hasta ahora…

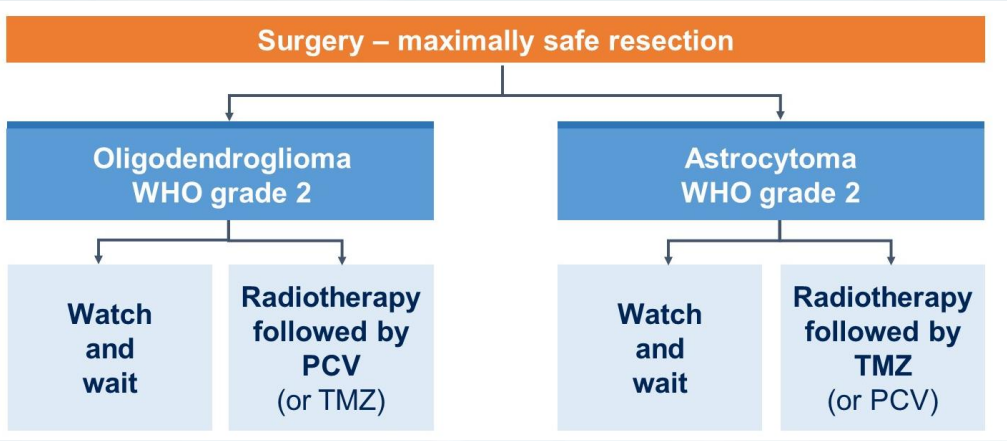
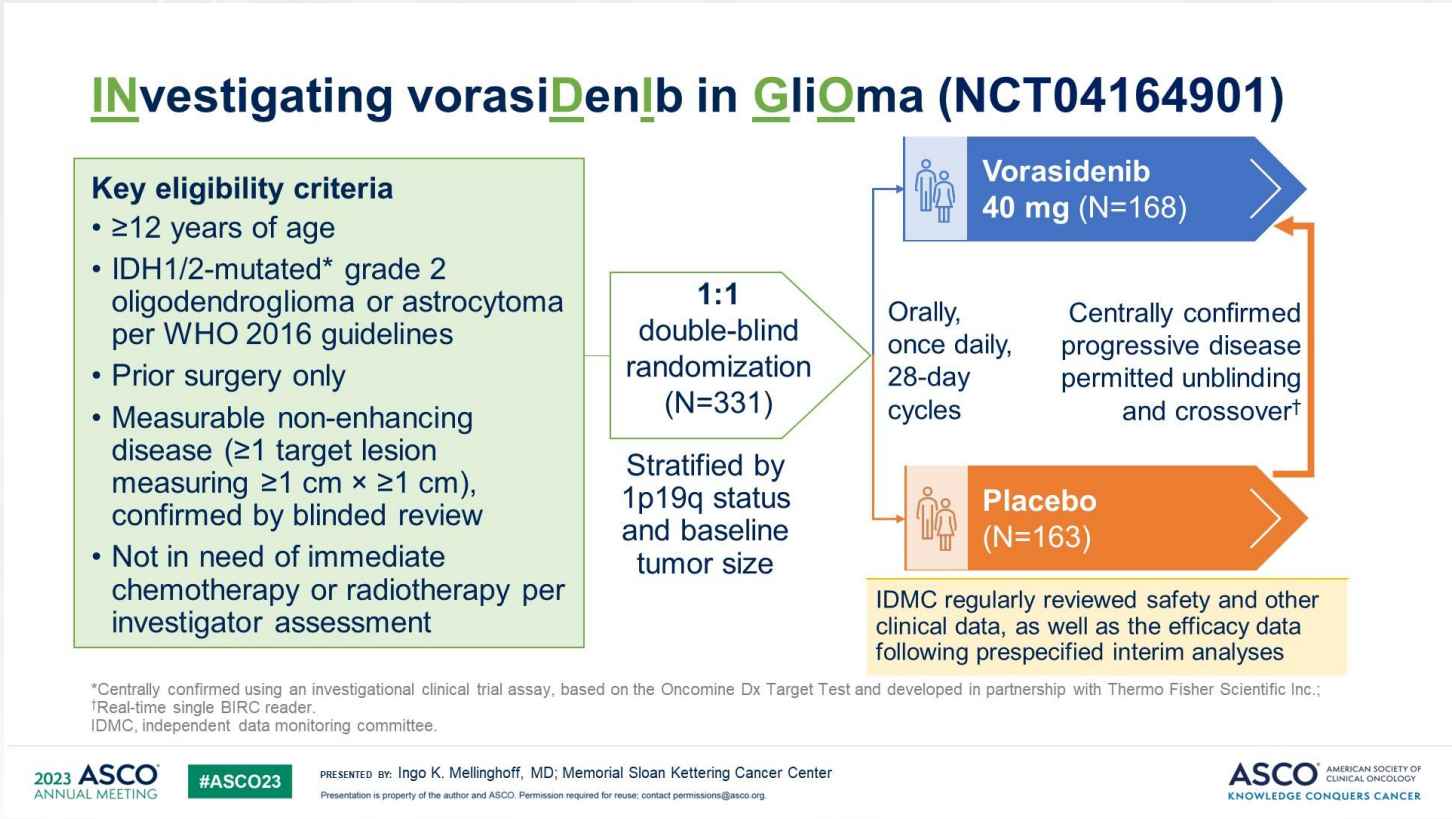


Figure modified from: Weller M *et al. Nat Rev Clin Oncol* 2021;18:170–86, with permission.
PCV, procarbazine, lomustine and vincristine; TMZ, temozolomide.

Próximamente…



1 Primary endpoint

PFS: time from randomization to the first imaging-based disease progression as assessed by BIRC or death because of any cause
- MRI every 3 months for 3 years, then every 6 months

2 Key secondary endpoint

TTNI: time from randomization to the initiation of first subsequent anticancer therapy or death because of any cause

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INDIGO: Fase 3 randomizado en gliomas de alto riesgo y bajo grado, con enfermedad residual/recurrente IDH1/2 mutados: Vorasidenib Vs placebo.

Enero/20 y Febrero/22 – 77 centros de 10 países

	Vorasidenib	Placebo
Randomized to treatment – n (%)	168 (100)	163 (100)
Received treatment (safety set)	167 (99.4)*	163 (100)
Discontinued treatment – n (%)	36 (21.4)	68 (41.7)
Centrally confirmed disease progression†	24 (14.3)	59 (36.2)
Patient decision	5 (3.0)	5 (3.1)
Adverse event	6 (3.6)	2 (1.2)
Investigator decision	1 (0.6)	1 (0.6)
Clinical disease progression‡	0	1 (0.6)
Crossed over to vorasidenib – n (%)	–	52 (31.9)

Características basales

	Vorasidenib (N=168)	Placebo (N=163)
Median age (range) – year	40.5 (21–71)	39.0 (16–65)
Sex – n (%)		
Male/female	101/67 (60.1/39.9)	86/77 (52.8/47.2)
Karnofsky performance score – n (%)		
100	90 (53.6)	87 (53.4)
90–80*	77 (45.8)	76 (46.6)
Time from last surgery for glioma to randomization – year		
Median (range)	2.5 (0.2–5.2)†	2.2 (0.9–5.0)
Chromosome 1p19q codeletion status – n (%)‡		
Codeleted/non-codeleted	88/80 (52.4/47.6)	84/79 (51.5/48.5)
Tumor size at baseline – n (%)‡		
Longest diameter of ≥2 cm/<2 cm	139/29 (82.7/17.3)	137/26 (84.0/16.0)

	Vorasidenib (N=167)	Placebo (N=163)
Any grade ≥3 AE – n (%)	38 (22.8)	22 (13.5)
Increased alanine aminotransferase	16 (9.6)	0
Increased aspartate aminotransferase	7 (4.2)	0
Seizure	7 (4.2)	4 (2.5)
Increased gamma-glutamyltransferase	5 (3.0)	2 (1.2)
Syncope	3 (1.8)	1 (0.6)
Hypertension	2 (1.2)	3 (1.8)
Decreased neutrophil count	2 (1.2)	0

- Treatment interruption due to TEAE
  - **Vorasidenib** 29.9% (n=50)
  - **Placebo** 22.7% (n=37)
- Dose reduction due to TEAE
  - **Vorasidenib** 10.8% (n=18)
  - **Placebo** 3.1% (n=5)
- Discontinuation due to TEAE
  - **Vorasidenib** 3.6% (n=6)
  - **Placebo** 1.2% (n=2)
- No fatal TEAE

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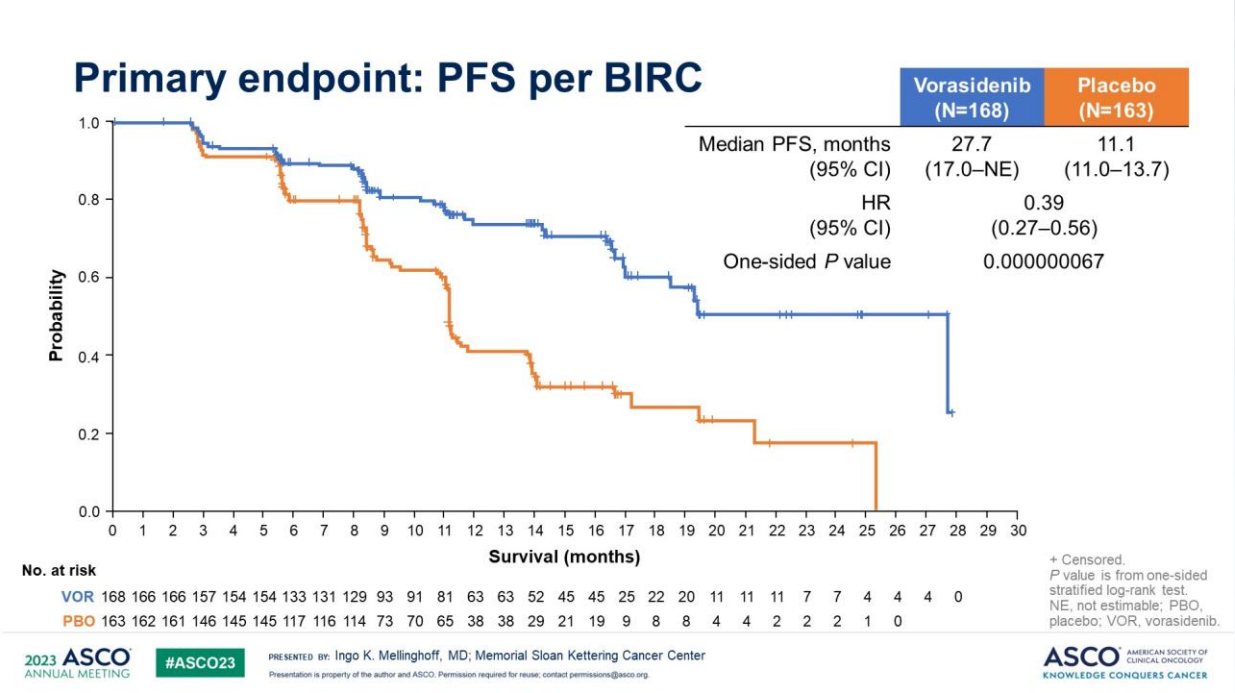
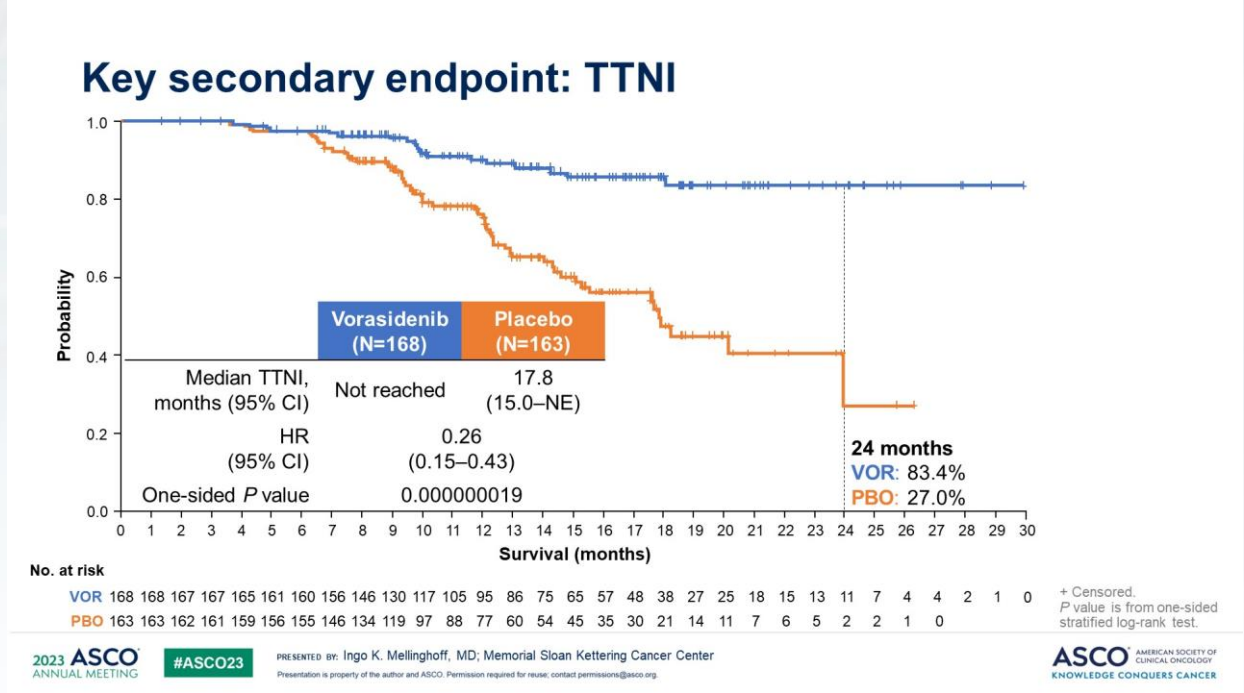
INDIGO: Fase 3 randomizado en gliomas de alto riesgo y bajo grado, con enfermedad residual/recurrente IDH1/2 mutados: Vorasidenib Vs placebo.

Objetivos 1ª





FUTURO: Mecanismos de resistencias (clonas independientes, silenciamiento epigenético de IDH), estudios de los tumores grado 3 (CODEL, CATNON…), secuencia terapéutica.

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LITESPARK-004: Fase II con Belzutifan como tratamiento del Hemangioblastoma asociado al síndrome VHL

LITESPARK-004 (NCT03401788) Study Design

Key Eligibility Criteria

- Diagnosis of VHL disease, based on germline alteration
- ≥1 measurable RCC tumor
- No RCC tumor >3 cm or other VHL tumor requiring immediate surgery
- No prior systemic anticancer therapy
- No metastatic disease
- ECOG PS 0 or 1

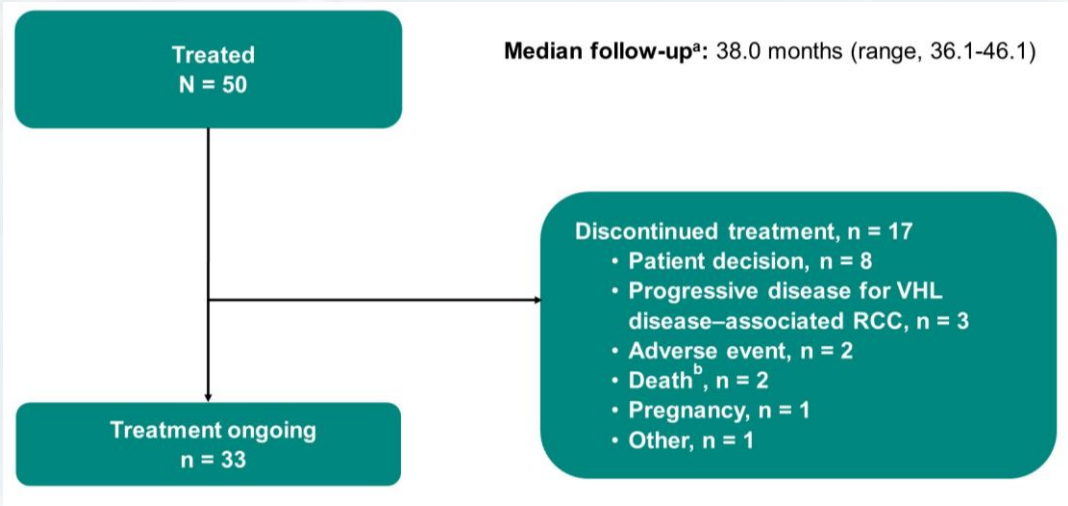
N = 61

Belzutifan
120 mg orally once daily[a]

Tumor Assessments
- At screening and every 12 weeks for a minimum of 3 years, then every 24 weeks thereafter

End points evaluated in patients with CNS hemangioblastomas
- ORR, DOR, PFS per RECIST v1.1 by (IRC); TTR, and safety

DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IRC, independent review committee; ORR, overall response rate; PFS, progression-free survival; TTR, time to response.
[a]Study treatment continued until unacceptable toxicity, disease progression, or patient withdrawal. In an event of a mixed response (ie, continuing radiographic response in RCC lesions but progression or surgical requirement for a non-RCC lesion), study treatment may be continued if patient is tolerating the study drug and no alternative treatments are available for patient's progressive VHL-associated non-RCC lesions..



Características basales

	S + C N = 50	S only N = 25
Age, median (range), years	40.5 (19-65)	34.0 (22-65)
Sex		
Male	30 (60)	19 (76)
Female	20 (40)	6 (24)
ECOG PS		
0	39 (78)	18 (72)
1	10 (20)	7 (28)
2	1 (2)	0
≥1 prior surgery for CNS hemangioblastomas	46 (92)	23 (92)

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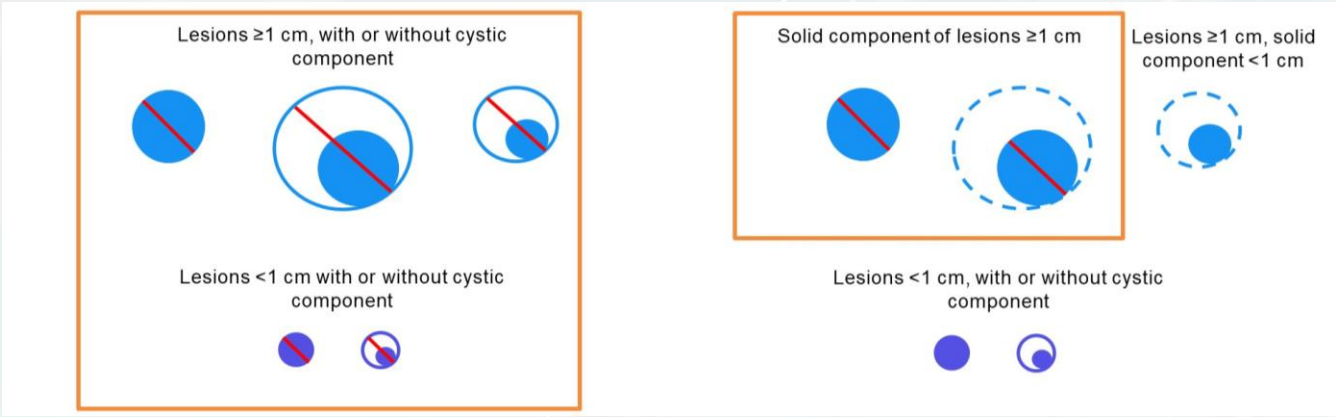
LITESPARK-004: Fase II con Belzutifan como tratamiento del Hemangioblastoma asociado al síndrome VHL

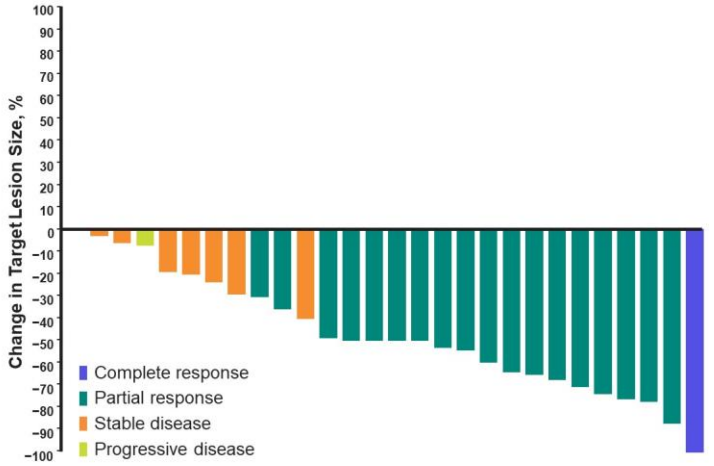


TiR – 5.4 meses
DoR (3.7-38.7m)

TiR – 3.1 meses
DoR (3.7-38.7m)

Best Overall Response and Best Percentage Change From Baseline: S + C (N = 50)

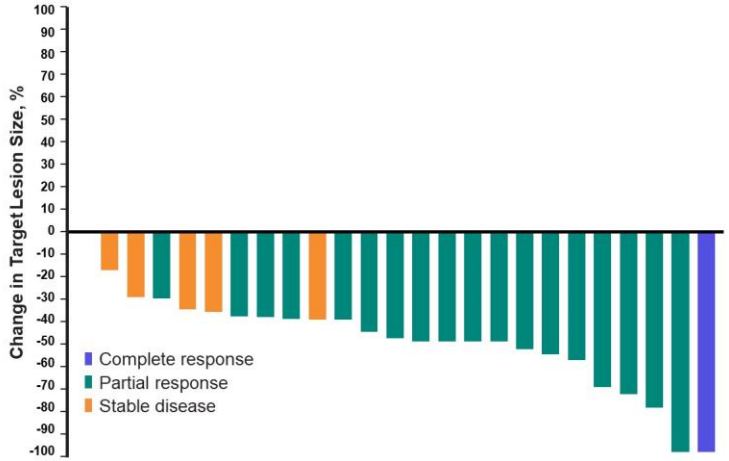
	S + C N = 50
ORR, n (%) [95% CI]	22 (44) [30-59]
DCR, n (%) [95% CI]	45 (90) [78-97]
Best overall response, n (%)	
Complete response	4 (8)
Partial response	18 (36)
Stable disease	23 (46)
Progressive disease	3 (6)
Nonevaluable	2 (4)



28 of 50 patients had evaluable postbaseline measurable disease data; 4 patients achieved complete response, including 3 patients who had nonmeasurable disease at baseline; 2 patients had progressive disease, including 1 who had only nonmeasurable disease at baseline (not shown on the waterfall plot). Data cutoff date: April 1, 2022.

Best Overall Response and Best Percentage Change From Baseline: S only (N = 25)

	S only n = 25
ORR, n (%) [95% CI]	19 (76) [55-91]
DCR, n (%) [95% CI]	24 (96) [80-100]
Best overall response, n (%)	
Complete response	1 (4)
Partial response	18 (72)
Stable disease	5 (20)
Progressive disease	0
Nonevaluable	1 (4)



Data cutoff date: April 1, 2022.

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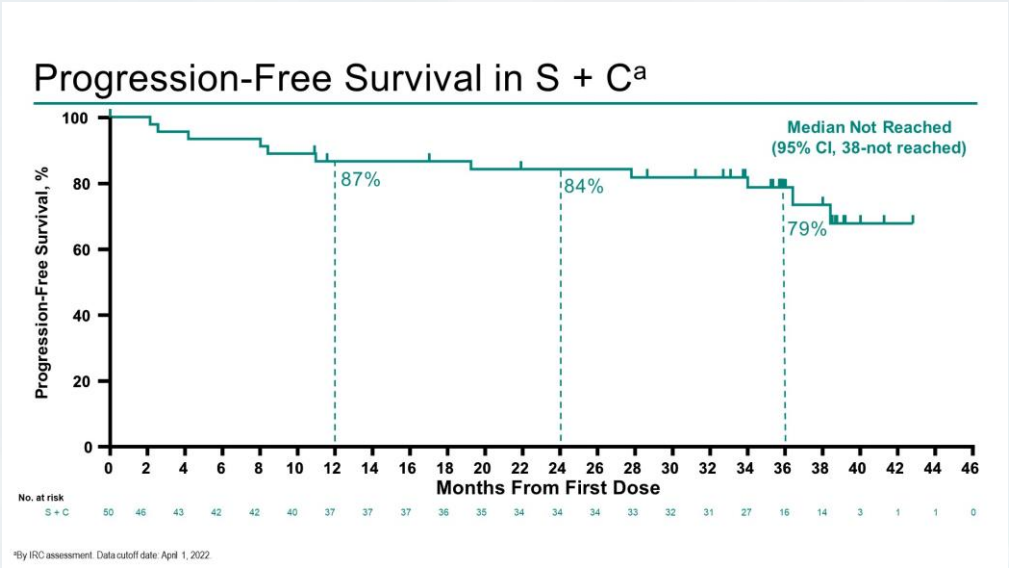
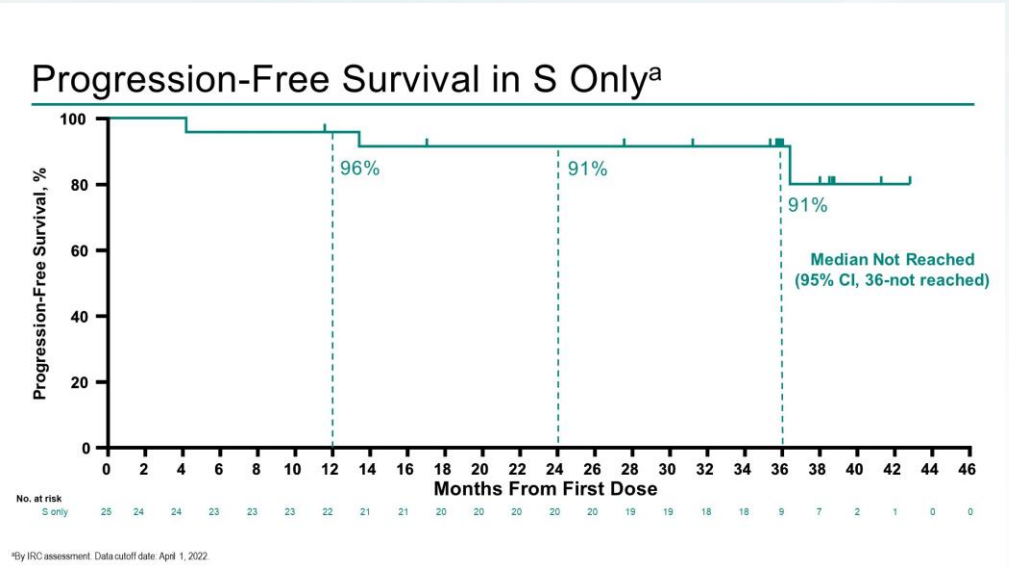
LITESPARK-004: Fase II con Belzutifan como tratamiento del Hemangioblastoma asociado al síndrome VHL





Adverse Event Summary: All Enrolled Patients

	All patients in LITESPARK-004 N = 61
Any-grade AE	61 (100)
Grade 3-5 AE	27 (44)
Treatment-related AE	61 (100)
Grade 3 treatment-related AE	11 (18)
Serious AE	18 (29)
Serious treatment-related AE	4 (7)
Treatment discontinuation because of a treatment-related AE	2 (3)[a]
Treatment interruption because of a treatment-related AE	13 (21)
Dose reduction because of a treatment-related AE	8 (13)
Death	2 (3)
Death because of a treatment-related AE	0

AE, adverse event. [a]Grade 1 dizziness and grade 2 intracranial hemorrhage. AEs were assessed in all 61 patients. Data cutoff date: April 1, 2022.

EA grado 3 relacionado – 18% - Anemia
SAE 7%
2 pacientes suspendieron el tto

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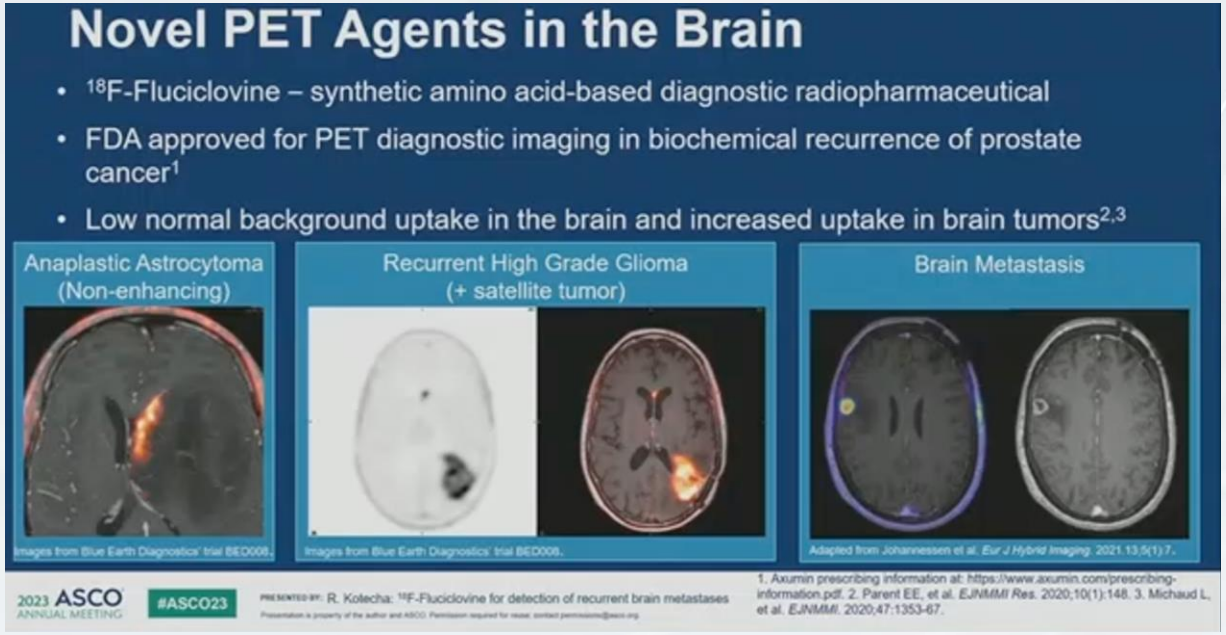
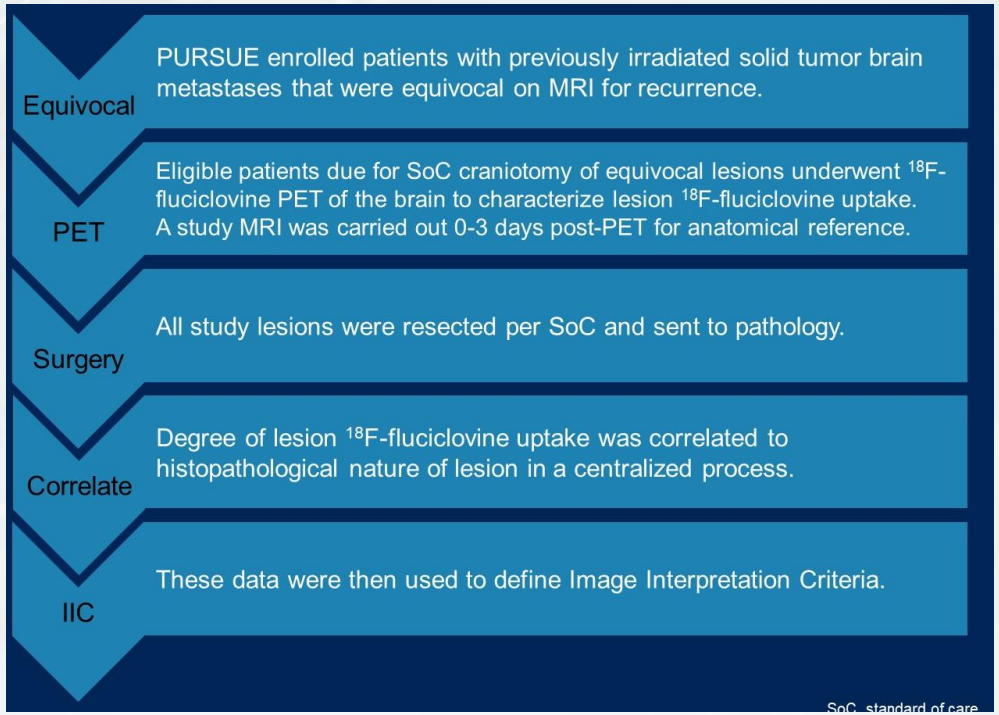
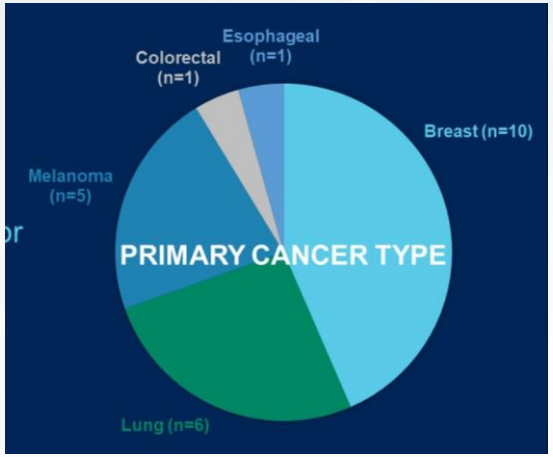
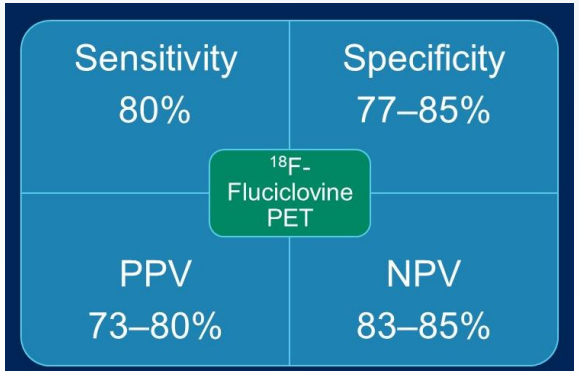
Nuevos mecanismos de evaluación de los tumores: Uso del 18F-fluciclovine para la detección de recurrencias cerebrales tras la radioterapia. PERSUE (NCT 04410367) : Fase II prospectivo #2001







43% (10/23) fueron recaídas
57% (13/23) no lo eran



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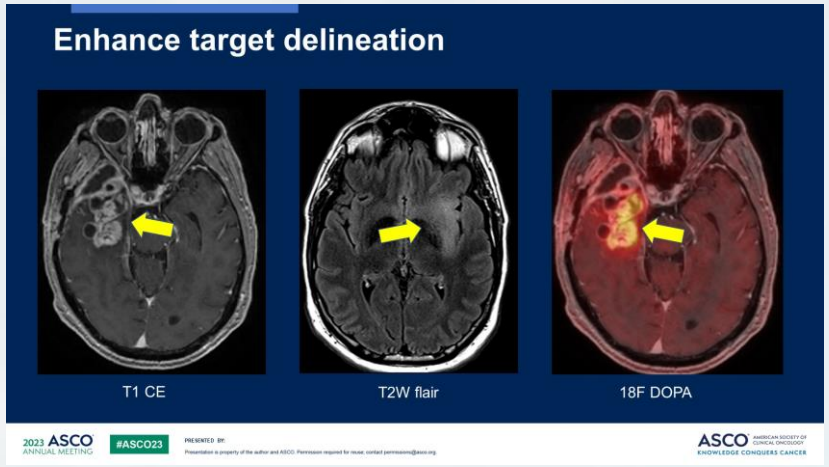
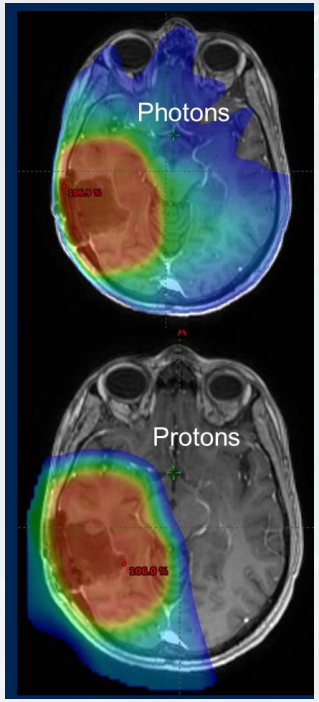
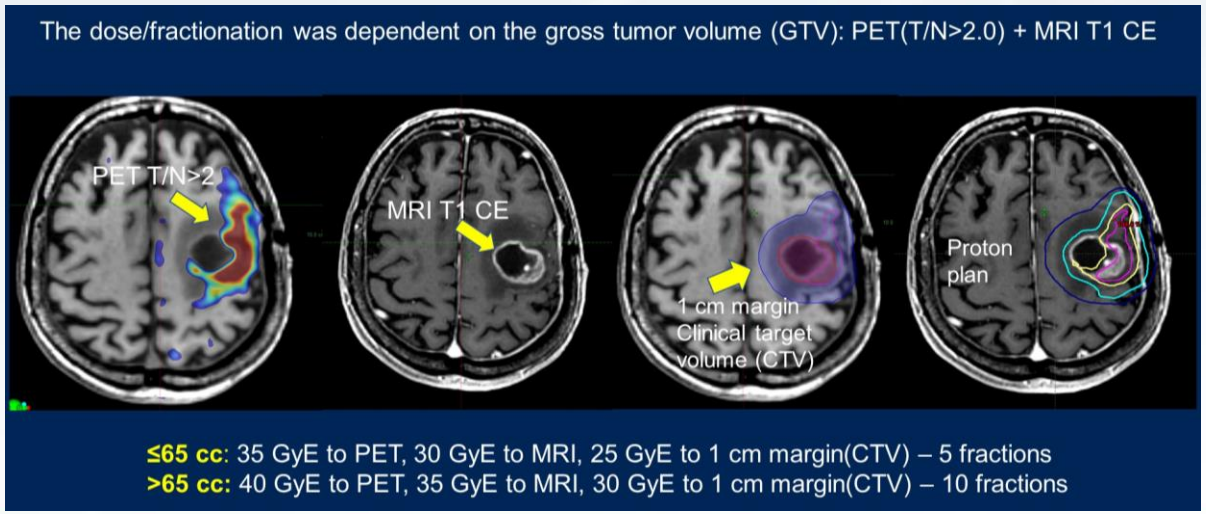
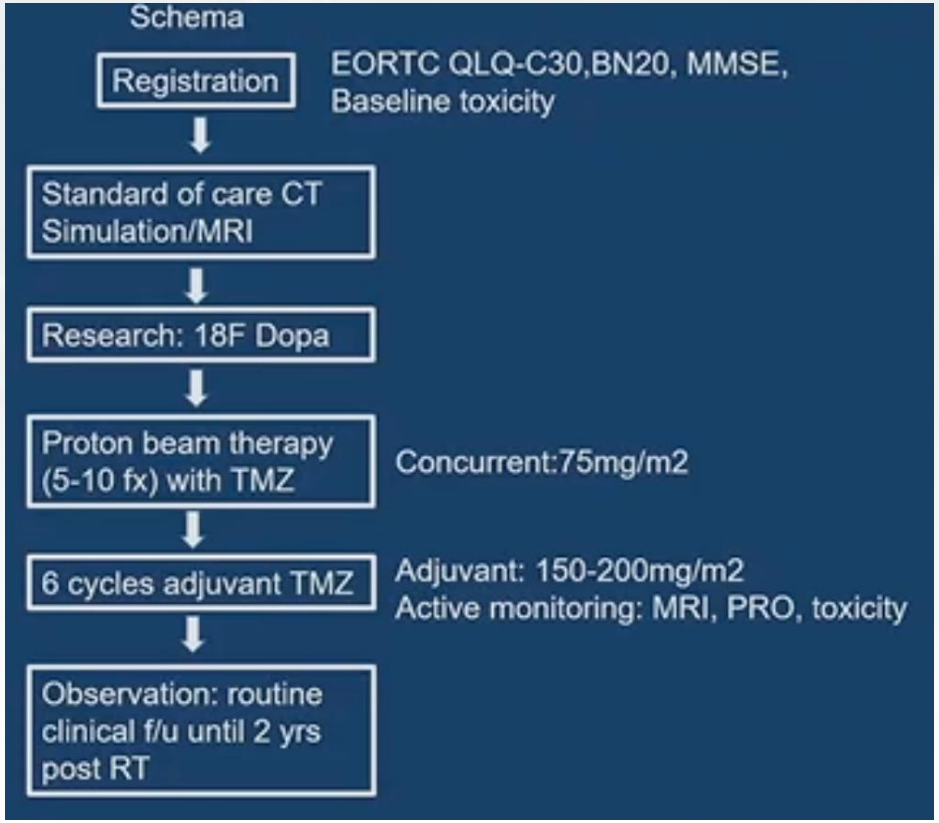
Protonterapia: Fase II con curso corto hipofraccionado con técncias de fusión de 18F-DOPA-PET/RM en paciente anciano con GBM





With improved targeting of disease with 18F-DOPA along with dosimetric advantages of proton beam therapy, can this combination offer both improved survival and quality of life?





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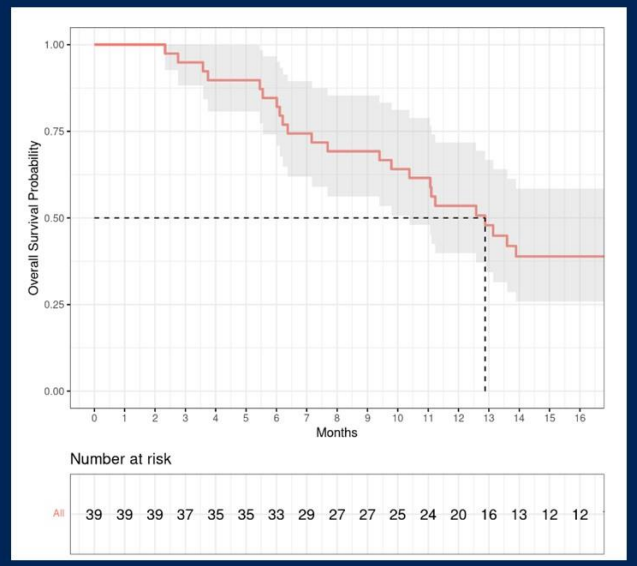
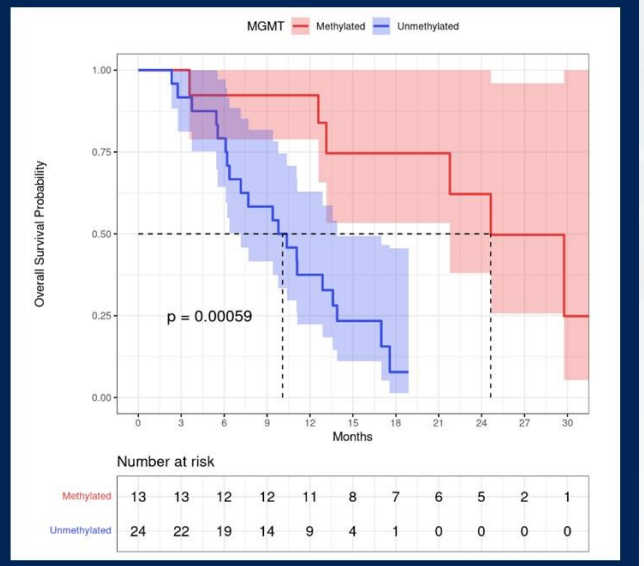
Protonterapia: Fase II con curso corto hipofraccionado con técncias de fusión de 18F-DOPA-PET/RM en paciente anciano con GBM

18/39 – 35 Gy en 5 fracciones
21/39 – 40 Gy en 10 fracciones → Todos TMZ concurrente
Media 5 ciclos adyuvantes → Varios ttos secuenciales:
BVZ, PVC, re-irradiación



Primary endpoint: Overall Survival

Median 12.9 months



Methylated MGMT: median 25 months
Unmethylated MGMT: median 10.5 months
p=0.00059

There were no grade 4 or 5 treatment related events

Grade 2+ treatment-related toxicities (N=39 pts)

- CNS necrosis 15 (38%)
- Confusion 3 (8%)
- Dysphasia 1 (3%)
- Fatigue 9 (23%)
- Headache 2 (5%)
- Seizure 5 (13%)
- Alopecia 4 (10%)

Grade 3 treatment-related toxicities (N=39 pts)

- Confusion 1 (3%)
- Fatigue 2 (5%)
- Seizure 1 (3%)
- CNS necrosis 5 (13%)
  - 2 cases of pseudoprogression vs. progression
    - 1 case tx with bevacizumab
    - 1 case tx with surgery (minimal viable tumor + extensive treatment effect)
  - 2 cases of necrosis tx with bevacizumab
  - 1 case of edema tx with bevacizumab

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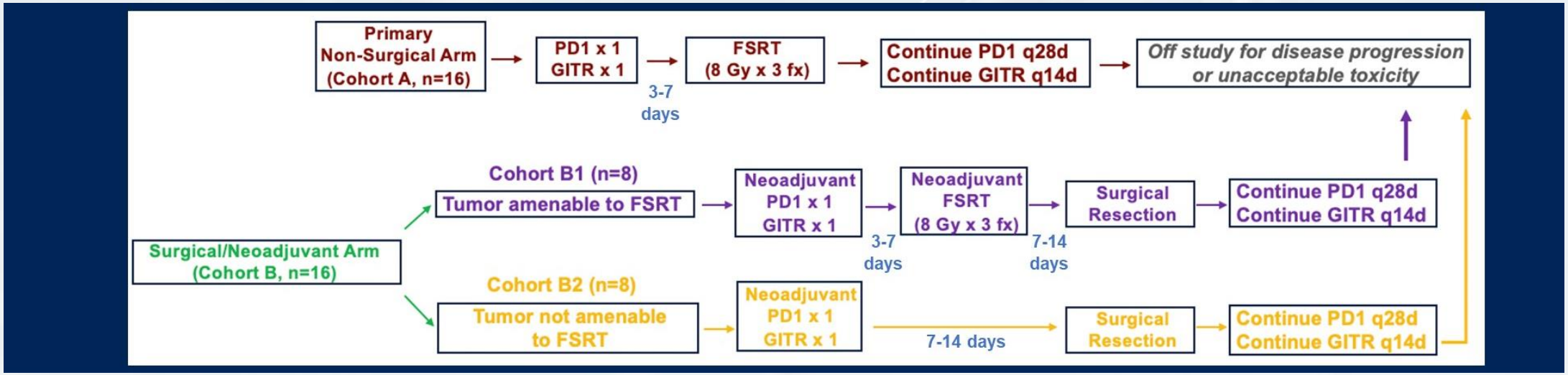
Fase II unicéntrico: Anti-PD1 + agonista GITR + radioterapia estereotáxica a la recaída del tratamiento estándar (Q+/-QTRT)



ORR

SLP

SG

Adverse Events (CTCAE v 5.0)	No. (%)
Grade 3-4 AEs at least probably related to study interventions	
Cerebral edema	11 (34)
Fatigue	5 (16)
Decreased lymphocyte count	4 (12.5)
Cognitive disturbance	4 (12.5)
Immune-related AEs	
Grade 1-2 rash	10 (31)
Grade 1-2 diarrhea	9 (28)
Grade 4 immune thrombocytopenia	1 (3)
Grade 1 AST/ALT elevation	1 (3)

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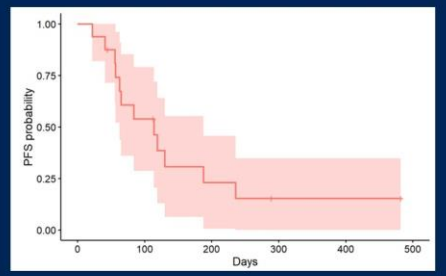
Fase II unicéntrico: Anti-PD1 + agonista GITR + radioterapia estereotáxica a la recaída del tratamiento estándar (Q+/-QTRT)

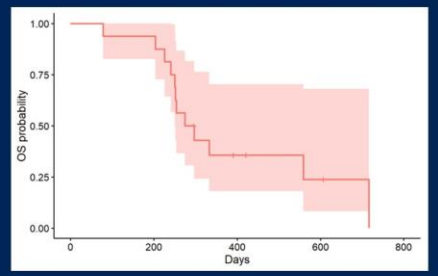
Efficacy Analysis – Cohort A (Primary/Non-Surgical, n=16)

- 0 / 16 patients achieved radiographic response per mRANO criteria (ORR, 0%)
- 9 / 16 patients (56%) achieved best response of Stable Disease

Median PFS 3.9 months (95% CI, 2.1 – 6 .2 months)



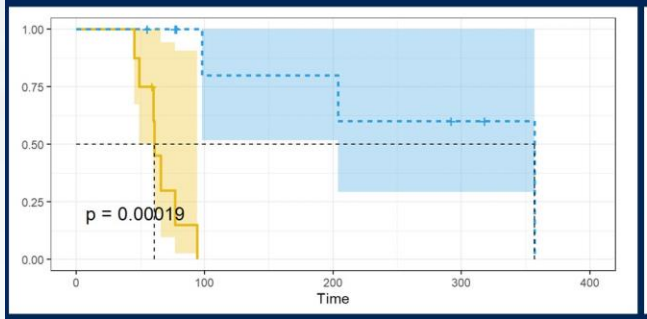
Median OS 9.4 months (95% CI, 8.2 – 10.6 months)



Efficacy Analysis – Cohort B (Surgical/Neoadjuvant Cohort)

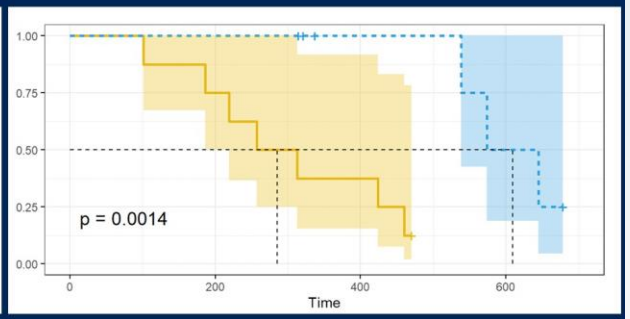
	Median PFS (*mo*)
Neoadjuvant ICB + FSRT (B1)	11.7
Neoadjuvant ICB (B2)	2.0

p=0.0002



	Median OS (*mo*)
Neoadjuvant ICB + FSRT (B1)	20.1
Neoadjuvant ICB (B2)	9.4

p=0.0014



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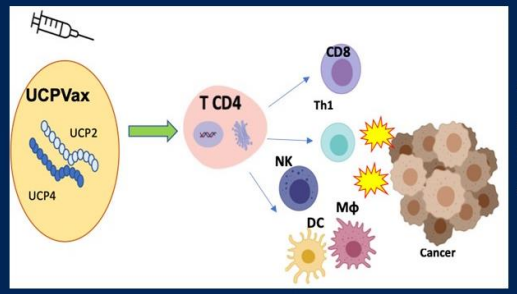
Fase II multicéntrico: Vacuna anti-telomerasa en GBM sin metilación de MGMT

UCPVax is a cancer vaccine against UCP2 and UCP4, two CD4 helper peptides derived from TERT protein (telomerase)



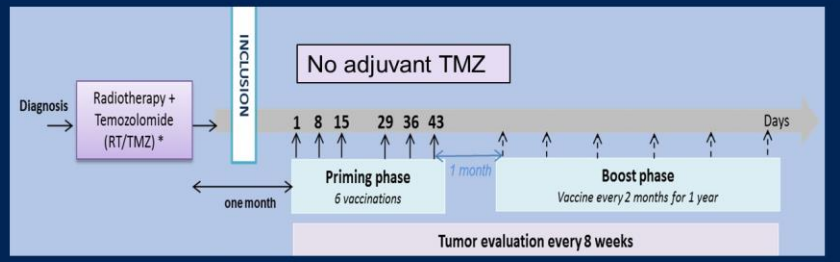
Godet et al. Clin Can Res 2012
Dosset et al. Clin Can Res 2012
Galaine et al. J Immunol 2016
Dosset et al Cancers 2020

UCPvax showed encouraging signs of efficacy in advanced NSCLC (phase I/II trial). *Adotévi et al. J Clin Oncol 2023*

UCPvax clinical trial

Design and objectives

Multi-center, prospective, non-controlled, phase II trial. (NCT04280848)

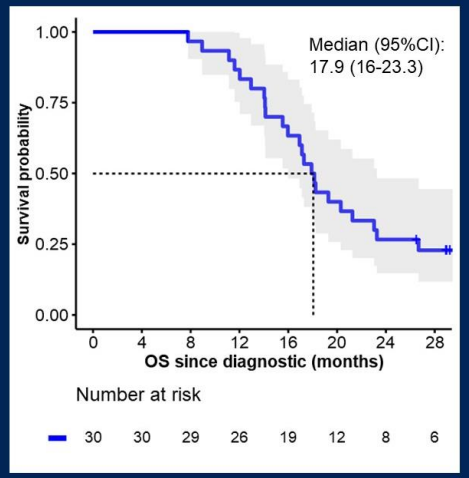


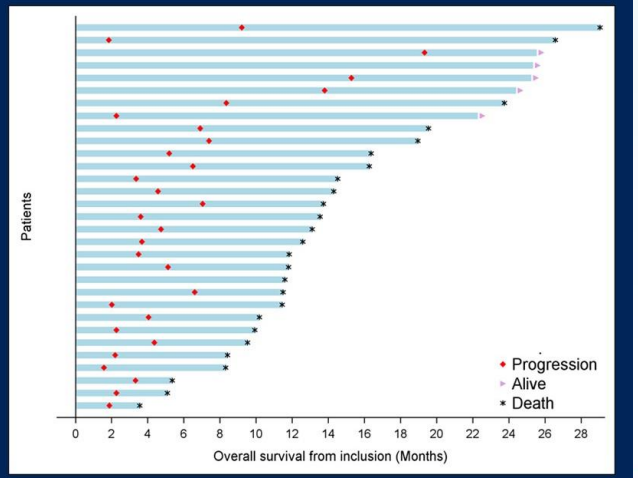
Primary endpoint:
TERT-specific CD4 T-cell response in peripheral blood (IFN-gamma ELISPOT)

Secondary endpoints:
- safety (CTCAE v 4.03)
- OS & PFS

s.c. injections : UCP2 and UCP4 (0,5mg each) + Montanide ISA-51

In the intent-to-treat population (n = 31):
Median PFS= 8.9 months , median OS: 17.9 months (No patients lost for follow-up)





Fase II multicéntrico: Pembrolizumab en pacientes con metástasis cerebrales #2006

Phase II trial of pembrolizumab in patients with brain metastases

- Baseline brain MRI and systemic staging
- Brain MRI and systemic staging every 6wks

- Previously untreated brain metastases (Cohort A)
- Progressive brain metastases (Cohort B)
- Measurable brain disease

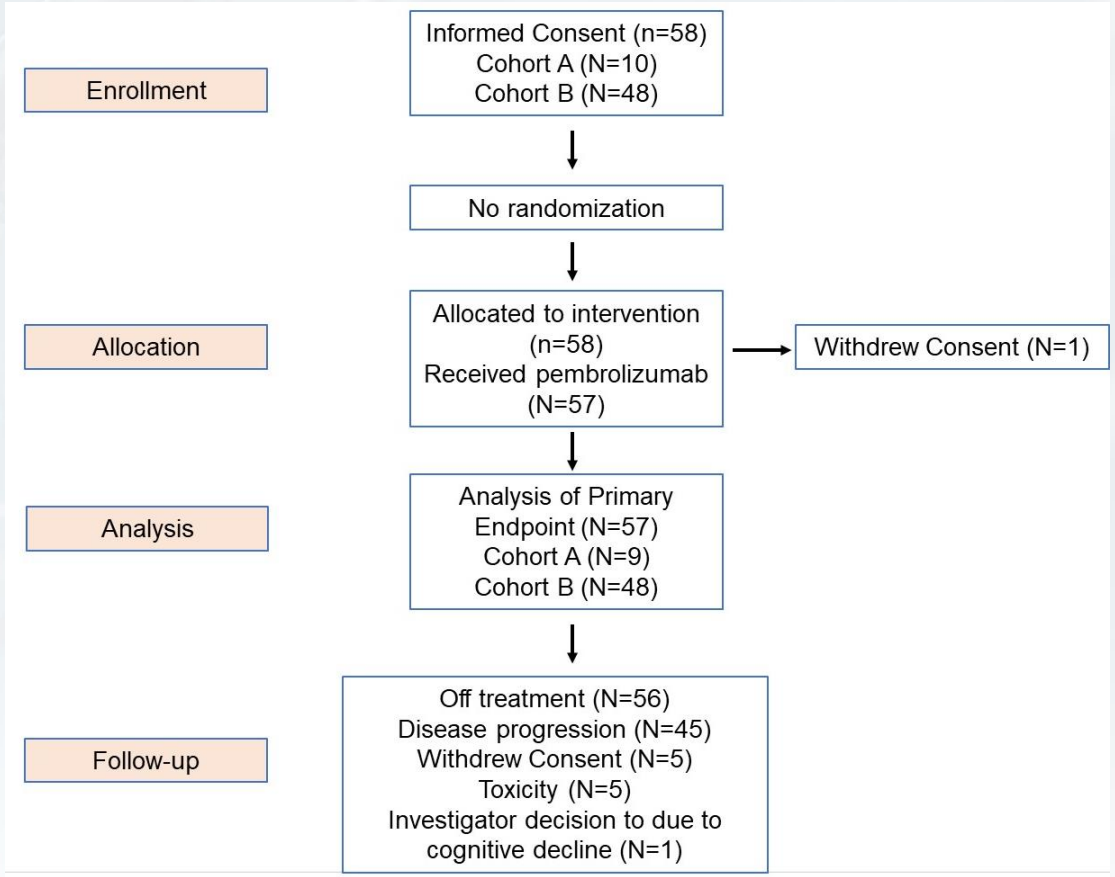
→ Pembrolizumab 200mg q3 wks → CNS or systemic progression

Primary Endpoint

- CNS benefit rate – Complete Response (CR), Partial Response (PR) or Stable Disease (SD)

Secondary Endpoints

- CNS Progression-free Survival (PFS)
- Systemic PFS
- Extracranial Response Rate
- Safety



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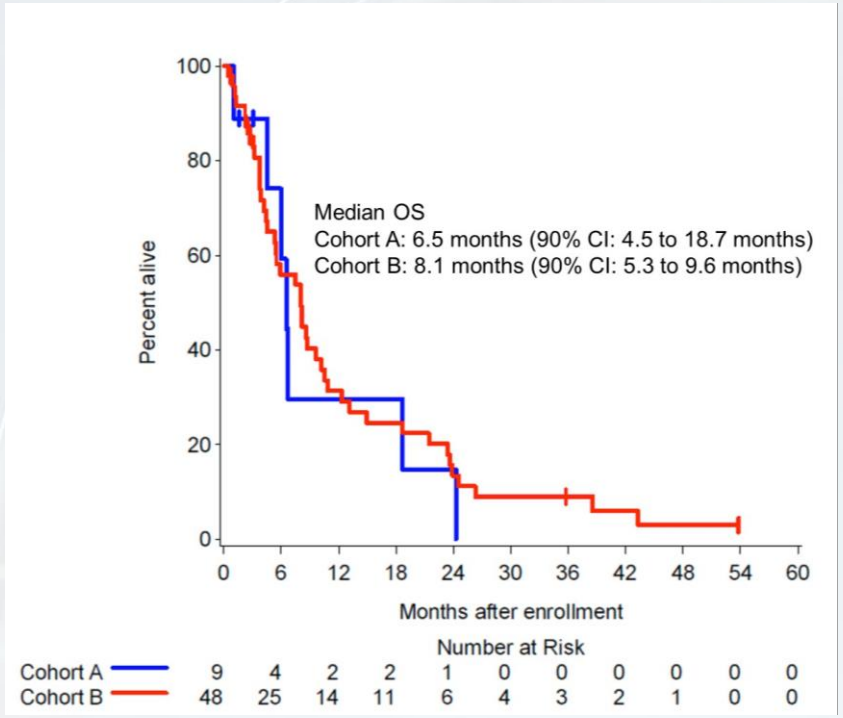
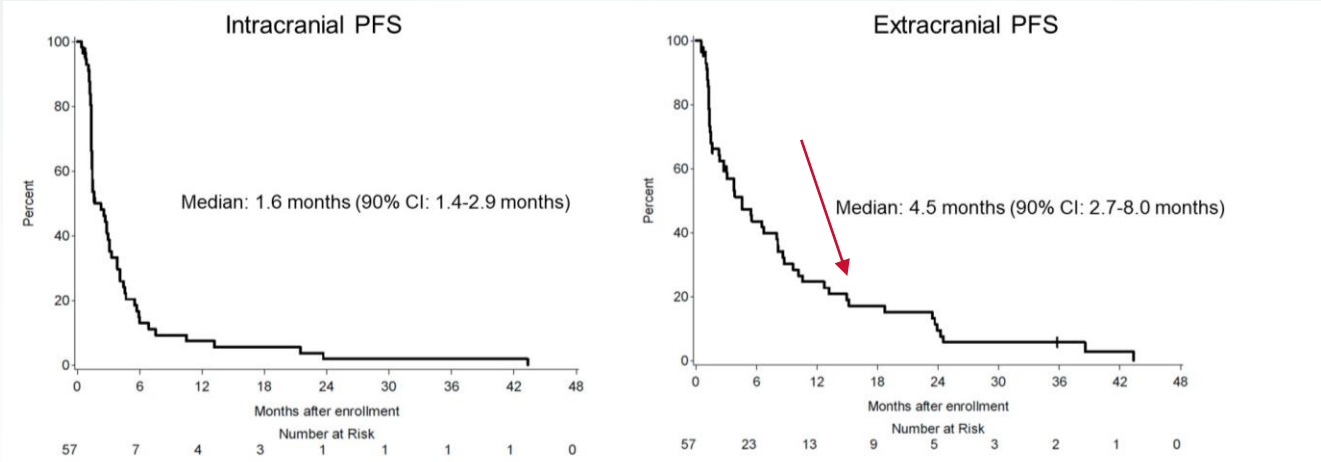
Fase II multicéntrico: Pembrolizumab en pacientes con metástasis cerebrales #2006

Respuesta por subtipo

	Clinical benefit (RANO)			
	No		Yes	
	N	%	N	%
All histologies	33	58	24	42
Breast	22	63	13	37
Melanoma			2	100
Esophageal	1	100	-	-
NSCLC NOS	4	57	3	43
SCLC	2	100	-	-
Neuroendocrine Carcinoma	1	50	1	50
Ovarian			1	100
Pituitary Carcinoma			1	100
Prostate			1	100
Renal Cell Carcinoma	1	100		
Adenocarcinoma of unknown primary	1	100		
Advanced sinonasal ACC			1	100
Alveolar soft part sarcoma			1	100
Extraosseous sarcoma	1	100		





Fase I multitumor: Seguridad y eficacia del inhibidor de BRAF (FORE8394)

- 113 patients enrolled
- 12 patients (10.6%) still on treatment
- 101 patients (89.4%) discontinued treatment
  - Disease progression* 65 (57.5%)
  - Clinical progression 18 (16%)
  - Withdrawal 9 (8%)
  - Adverse events 4 (3.5%)
    - Drug-related (n=1)
    - Underlying disease-related (n=3)
- 11 patients (9.7%) treated ≥ 2 years
- 80 patient-years of FORE8394 exposure

* *By RECIST or RANO tumor assessment criteria.*

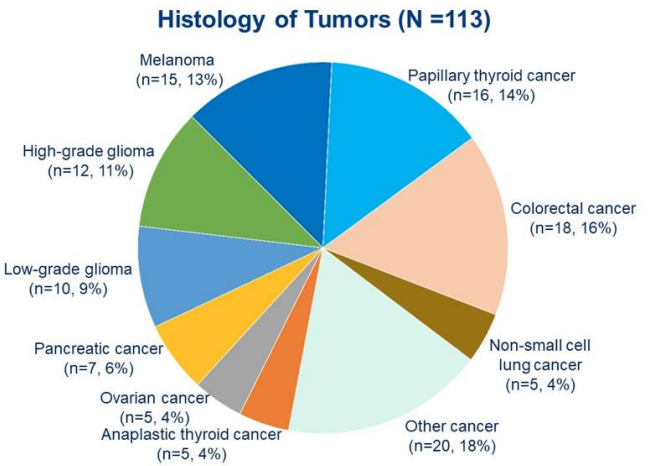
Demographics	n (%)
Age	
<18 years	5 (4.4%)
18 to <65 years	66 (58.4%)
≥65 years	42 (37.2%)
Sex	
Male	59 (52.2%)
Female	54 (47.8%)
Race	
White/Caucasian	101 (89.4%)
Black/African-American	5 (4.4%)
Asian	3 (2.7%)
Missing	4 (3.5%)
Ethnicity	
Hispanic or Latino	12 (10.6%)
Not Hispanic/Latino	99 (87.6%)
Missing	2 (1.8%)

ECOG Performance Score	n (%)
0	43 (38.1%)
1	65 (57.5%)
≥2	5 (4.4%)
CNS Metastases	**n (%)**
Solid Tumors (n=90)	12 (13.3%)
Prior Treatment	**n (%)**
Number of Lines[1]	
0	15 (13.3%)
1	28 (24.8%)
2	17 (15.0%)
3	16 (14.2%)
≥4-10	37 (32.7%)
Prior Treatment Type	
MAPK-inhibitor[2]	33 (29.2%)
BRAF-inhibitor	24 (21.2%)
Checkpoint inhibitor	30 (26.5%)

[1] *For locally advanced or metastatic disease.*
[2] *Includes patients who received a BRAF inhibitor.*

BRAF Alteration	n (%)
Class 1	64 (56.6%)
V600E	60 (53.1%)
V600K	3 (2.7%)
V600R	1 (0.9%)
Class 2	36 (31.9%)
Non-fusion	19 (16.8%)
Fusion	17 (15.0%)
Class 3	1 (0.9%)
Other[1]	3 (2.7%)
No documented BRAF alteration[2]	9 (8.0%)

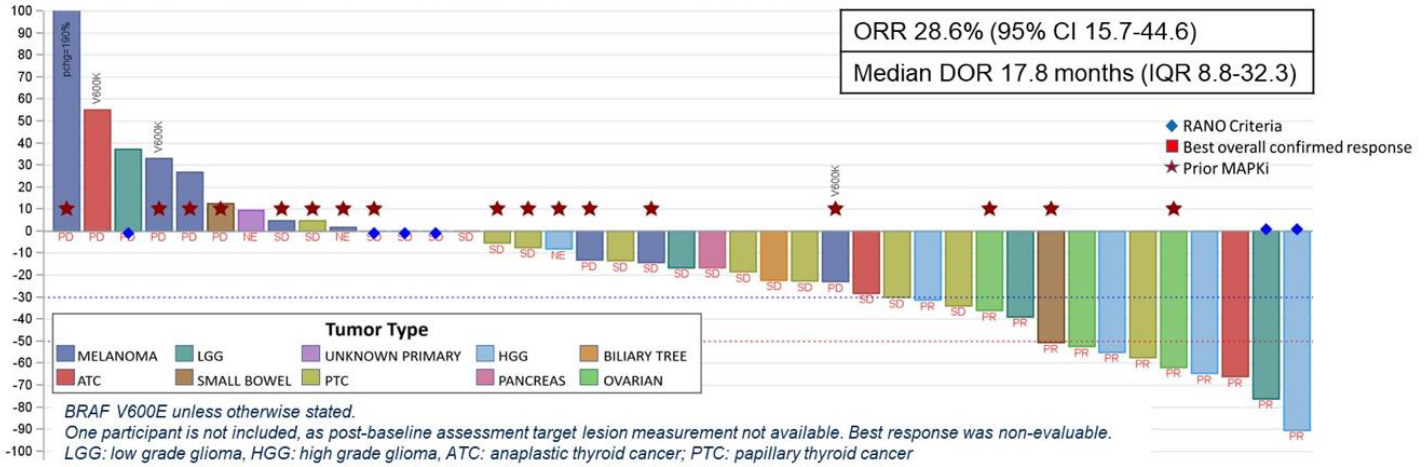
[1] *1 P708A point mutation, 1 amplification, 1 intragenic deletion*
[2] *BRAF alterations were not required for inclusion in Phase 1 component*



SNC

Fase I multitumor: Seguridad y eficacia del inhibidor de BRAF (FORE8394)

FORE8394 Best Percent Tumor Change from Baseline in V600+ Adults (N=42, mITT)
Excluding CRC Due to Known Intrinsic Resistance Through EGFR Pathway



BRAF V600E unless otherwise stated.
One participant is not included, as post-baseline assessment target lesion measurement not available. Best response was non-evaluable.
LGG: low grade glioma, HGG: high grade glioma, ATC: anaplastic thyroid cancer; PTC: papillary thyroid cancer

MAPKi Naive

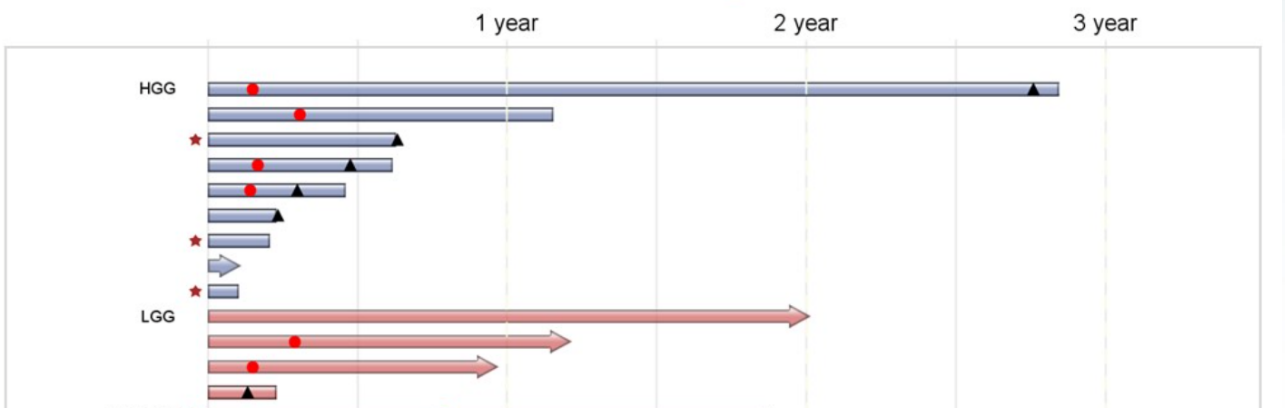
V600 Mutated Tumors (n = Naive)	ORR n (%)	CBRx24w n (%)
Primary CNS tumors (10)	6 (60%)	7 (70%)
Ovarian cancer (1)	1 (100%)	1 (100%)
Papillary thyroid cancer (6)	1 (16.7%)	4 (66.7%)
Anaplastic thyroid cancer (4)	1 (25%)	2 (50%)

MAPKi Pre-treated

V600 Mutated Tumors (n = Pre-treated)	ORR n (%)	CBRx24w n (%)
Primary CNS tumors (3)	0	1 (33.3%)
Ovarian cancer (2)	2 (100%)	2 (100%)
Small bowel cancer (2)	1 (50%)	1 (50%)
Papillary thyroid cancer (3)	0	0
Melanoma (8)	0	1 (12.5%)

3/3 confirmed PR in ovarian cancer. One with 6 prior lines of therapy, of which 4 included RAF, MEK, and/or ERK inhibitor, with documented PD.

MAPKi pretreated V600+ (N=18)
ORR 16.7%, mDOR=12.9 months



SNC

Poster SNC

A Radiomic Based Predictive Model of Lung Adenocarcinoma Brain Metastases and Molecular Subtypes

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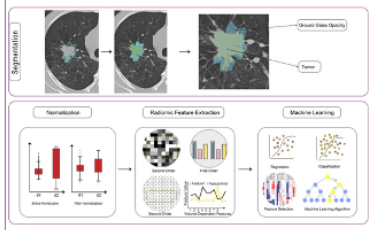
Abstract #2014

Non-small cell lung cancer (NSCLC) comprises the largest portion of brain metastases (BM) from solid cancer with 40% of patients developing BM during the course of their disease[1]. There are currently no reliable prediction tools for identifying patients at risk for BM, especially in the early-stage setting where MRI screening is not performed[2]. Furthermore, in the later stage setting, brain MRI are only performed annually. Therefore, there is a critical need to identify high-risk patients for BM that could benefit from MRI surveillance. We identified 162 lung adenocarcinoma (LUAD) patients with (N=66) or without (N=96) BM that had treatment-naive CT scans with a segmentable lesion. The tumor, surrounding ground glass opacity and necrosis were segmented via 3D slicer to create a volume of interest for radiomic texture analysis and 400 features were extracted. The Least Absolute Shrinkage and Selection Operator (LASSO) logistic regression feature selection method was used to select the most relevant features and models were built using the machine learning method XGBoost classifier[3]. Training and testing sets with random splitting was used for cross validation. We report the accuracy, sensitivity, specificity, and area under the curve (AUC) for each model. Among the extracted features that LASSO deemed as most discriminative for development of BM, we identified the most relevant features using XGBoost that predicted BM with 79% accuracy, 83% sensitivity, 72% specificity, and 79% AUC (p=0.01) in the overall population. The addition of ground glass opacity and necrosis to the model did not significantly improve performance. Furthermore, the model distinguished those with metachronous vs synchronous BM with 84% accuracy, 83% sensitivity, 86% specificity, and 83% AUC (p =0.04). Our model held up across molecular subtypes (EGFR and KRAS mutant). Importantly, the model was predictive in early-stage patients with 92% accuracy, 96% sensitivity, 83% specificity, and 95%. AUC (p=0.0005). Moreover, our model predicted for high vs. low overall survival, and was BM-specific as it was not predictive of other sites of metastases. We further developed a model from the CT features that correctly classified KRAS mutant vs. KRAS wild type LUAD with 77% accuracy, 73% sensitivity, 80% specificity, and 80% AUC (p=0.002). Utilizing a radiomics approach, we were able to predict BM from primary lung CT features including in stage I and II disease, predict synchronous vs metachronous BM, and distinguish distinct molecular LUAD subtypes. These studies will identify patients that require MRI surveillance in the early-stage setting and more intensive surveillance in the late-stage setting for BM.

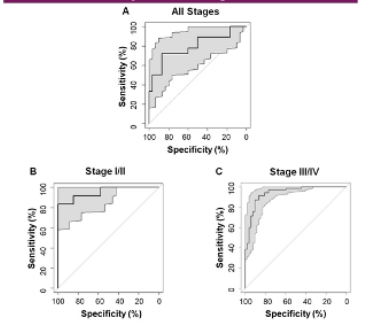
Radiomics Workflow



Patient Characteristics

Characteristics	Overall (N=162)	Brain Metastases (N=66)
Age at diagnosis, mean (SD)	65 (9.9)	65 (9.4)
Male, No. (%)	61 (38)	25 (38)
Ever smoker, No. (%)	142 (88)	59 (89)
Stage at diagnosis, No. (%)		
I	26 (16)	5 (7)
II	12 (7)	7 (11)
III	37 (23)	5 (8)
IV	85 (52)	47 (71)
Unknown	2 (1)	2 (3)
Synchronous BM, No. (%)	N/A	37 (56)
EGFR mutation, No. (%)	15 (10)	6 (10)
KRAS mutation, No. (%)	62 (41)	29 (44)
KRAS G12C, No. (%)	24 (15)	12 (18)

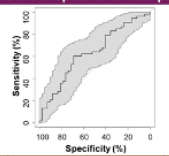
Model predicts LUAD BM development in patients with early and late stage NSCLC



Patient group	Accuracy	Sensitivity	Specificity	AUC	p-value
All stages	0.79	0.83	0.72	0.79	0.010
Stages I/II	0.92	0.96	0.83	0.95	$5.4X10^{-4}$
Stages III/IV	0.89	0.91	0.87	0.94	$1.0X10^{-14}$

Figure 1: ROC curves using 27 of 87 LASSO features from the primary tumor to predict BM in A) all stages, B) early stage (I and II) and C) late stage (III and IV) patients. Accuracy, sensitivity, specificity, AUC and p-values are reported for each model.

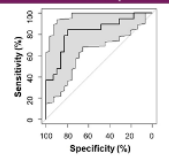
Model is more specific for BM prediction



Accuracy	Sensitivity	Specificity	AUC	p-value
0.64	0.60	0.69	0.63	0.060

Figure 2: ROC curve using 27 of 87 LASSO features to predict without metastasis vs only extra-cranial metastasis. Accuracy, sensitivity, specificity, AUC and p-values are reported.

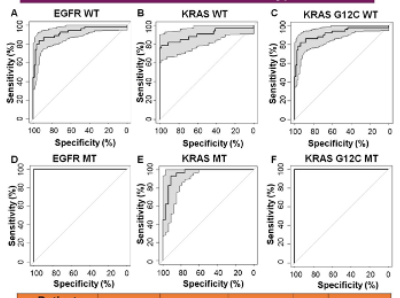
Addition of surrounding ground glass and necrosis features does not improve model



Accuracy	Sensitivity	Specificity	AUC	p-value
0.79	0.79	0.79	0.82	0.0047

Figure 3: ROC curve using 25 of 109 LASSO features from the primary tumor, surrounding ground glass and necrosis to predict BM. Accuracy, sensitivity, specificity, AUC and p-values are reported.

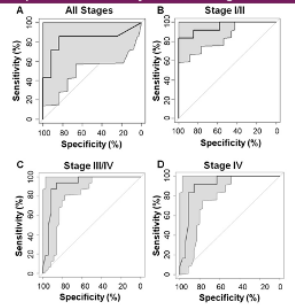
Model predicts LUAD BM development in patients with different molecular subtypes



Patient group	Accuracy	Sensitivity	Specificity	AUC	p-value
EGFR WT	0.89	0.93	0.83	0.93	$8.8X10^{-14}$
EGFR MT	1.0	1.0	1.0	1.0	$4.0X10^{-4}$
KRAS WT	0.89	0.95	0.79	0.90	$4.0X10^{-8}$
KRAS MT	0.92	0.91	0.93	0.96	$3.9X10^{-11}$
KRAS G12C WT	0.88	0.92	0.82	0.92	$6.1X10^{-12}$
KRAS G12C MT	1.0	1.0	1.0	1.0	$6.0x10^{-8}$

Figure 4: ROC curves using 27 of 87 LASSO features from primary tumor to predict BM in A) EGFR WT, B) KRAS WT, C) KRAS G12C WT, D) EGFR MT, E) KRAS MT, and F) KRAS G12C MT patients. Accuracy, sensitivity, specificity, AUC and p-values are reported.

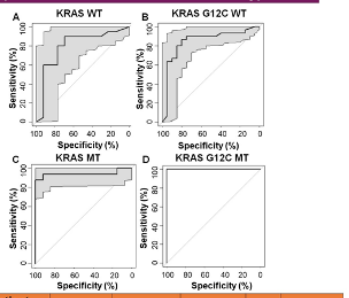
Model predicts metachronous vs synchronous BM in patients with early and late stage NSCLC



Patient group	Accuracy	Sensitivity	Specificity	AUC	p-value
All stages	0.84	0.83	0.86	0.83	0.042
Stages I/II	0.92	0.96	0.83	0.95	$5.4X10^{-4}$
Stages III/IV	0.90	0.88	0.92	0.92	$2.9X10^{-4}$
Stage IV	0.89	0.83	0.91	0.91	0.010

Figure 5: ROC curves using 7 of 40 LASSO features from the primary tumor to predict metachronous vs synchronous BM in A) all stages, B) early stage (I and II), C) late stage (III and IV), and D) stage IV patients. Accuracy, sensitivity, specificity, AUC and p-values are reported for each model.

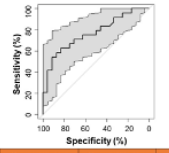
Model predicts metachronous vs synchronous BM in patients with different molecular subtypes



Patient group	Accuracy	Sensitivity	Specificity	AUC	p-value
KRAS WT	0.82	0.69	0.90	0.80	0.0080
KRAS MT	0.93	0.92	0.94	0.94	$9.5X10^{-6}$
KRAS G12C WT	0.84	0.75	0.90	0.85	$2.3X10^{-4}$
KRAS G12C MT	1.0	1.0	1.0	1.0	$2.4X10^{-4}$

Figure 6: ROC curves using 7 of 40 LASSO features from primary tumor to predict metachronous vs synchronous BM in A) KRAS WT, B) KRAS G12C WT, C) KRAS MT, and D) KRAS G12C MT BM patients. Accuracy, sensitivity, specificity, AUC and p-values are reported for each model.

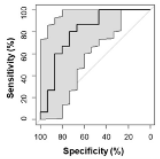
Model predicts high versus low overall survival



Accuracy	Sensitivity	Specificity	AUC	p-value
0.71	0.71	0.71	0.77	0.0028

Figure 7: ROC curve using 12 of 53 LASSO features to predict OS (cutoff 22 months). Accuracy, sensitivity, specificity, AUC and p-values are reported.

Radiomics can be used to determine KRAS status of primary lung tumors



Accuracy	Sensitivity	Specificity	AUC	p-value
0.77	0.73	0.80	0.80	0.0026

Figure 8: ROC curve using 10 of 67 LASSO to predict KRAS MT vs WT. Accuracy, sensitivity, specificity, AUC and p-values are reported.

Conclusions

- Utilizing radiomic analyses of primary lung lesions, we were able to predict the presence of BM in all stages and different molecular subtypes, and demonstrate specificity for BM prediction.
- Predicted metachronous versus synchronous BM in all stages and different molecular subtypes.
- Predicted for high vs low overall survival and determined KRAS status of primary lung tumors.

Future Directions/Clinical Relevance

- We are currently validating our BM prediction model in a large independent cohort.
- We are also developing models utilizing brain MRI scans to detect brain-specific targetable molecular alterations in LUAD-BM.
- Our model may identify patients in the clinic who would benefit from more frequent surveillance brain MRI scans, especially early-stage patients.
- Prior studies have shown frequent molecular discrepancies between primary LUAD and LUAD BM[4], and direct sampling of LUAD induces high morbidity/mortality and is often medically contraindicated.
- Accurate non-invasive identification of BM-specific targetable molecular subtypes via radiogenomics may allow for the development of a more effective BM treatment strategy.

References

1. Sørensen JB, Hansen HH, Hansen M, Dombernowsky P. Brain metastases in adenocarcinoma of the lung: frequency, risk groups, and prognosis. J Clin Oncol. 1988;6(9):1474-1480.
2. Schoenmaekers JJAO, Dingemans AC, Hendriks LEL. Brain imaging in early stage non-small cell lung cancer: still a controversial topic?. J Thorac Dis. 2018;10(Suppl 18):S2168-S2171.
3. Ak M, Toll SA, Hein KZ, Colen RR, Khatua S. Evolving Role and Translation of Radiomics and Radiogenomics in Adult and Pediatric Neuro-Oncology. AJNR Am J Neuroradiol. 2022;43(6):792-801.
4. Dono A, Takayasu T, Yan Y, et al. Differences in Genomic Alterations Between Brain Metastases and Primary Tumors. Neurosurgery. 2021;88(3):592-602.

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For questions and comments, contact Xiancheng Wu at wux11@upmc.edu

SNC

Poster SNC

Abstract 2055:

New ESMO scale for clinical actionability of molecular targets (ESCAT) for gliomas based on a multicentric real-world data cohort using next-generation sequencing

2023 ASCO ANNUAL MEETING

Authors: **Oriol Mirallas,** Gabriel Velilla, Fiorella Ruiz-Pace, Jesus Yaringaño, Ainhoa Hernandez, Daniel López-Valbuena, Diego Gomez-Puerto, Teresa Gorria, Maria Angeles Vaz, Marta Domenech, Alvaro Martinez-Monino, Macarena Gonzalez, Maria Castro, Maria Martínez-García, Estela Pineda, Joan Carles, Rodrigo Dienstmann, Carmen Balaña, Juan Manuel Sepúlveda, Maria Vieito.

BACKGROUND

- The **ESMO ESCAT** scale rank molecular alterations (MA) based on the published evidence supporting their clinical use.
- Based on our proposal for the first ESCAT classification for primary brain tumors [Mirallas *et al.* ESMO 2022], our aim was to describe the **clinical actionability of NGS** in a multicentric **glioma** cohort and gather clinical factors that enrich patients with MA to justify performing NGS.

METHODS

- A **multicentric retrospective study** included patients with molecular profiling using Next-Generation Sequencing (NGS) with different platforms (Foundation Medicine®, local NGS, Caris®, Oncomine® and fusion panels).
- Clinical actionability was classified using the **ESCAT scale:**
  - **Tier 1** → Alteration-drug match is associated with clinical benefit.
  - **Tier 2** → Alteration-drug match with antitumor activity.
  - **Tier 3** → Supported in other tumor types with similar MA.
  - **Tier 4** → Pre-clinical evidence.
- Clinical factors considered for enrichment were primary diagnosis of glioblastoma (GBM), sex, and age (cutoff of 40 years).
- Differences between groups were determined using Chi-squared test.
- The overall survival (OS) was calculated through Kaplan-Meier method and Cox hazard ratio were fitted.

Baseline Characteristics (n=361)					
Age (years)			**Histologic Grades by WHO**		
Median	52	(Range: 3 - 84)	Grade 1	8	2%
>40y	275	77%	Grade 2	38	11%
≤40y	84	23%	Grade 3	31	8%
Gender			Grade 4	284	79%
Men	219	61%	**Other Molecular Alterations**		
Women	141	39%	TP53 mutations	115	35%
WHO Group			CDK4 Gain	27	12.4%
Glioblastoma	265	73.5%	NF1 mutations	24	9%
Non-glioblastoma	96	26.5%	MDM2 Gain	15	7%
ECOG			RB1 mutations	14	5%
0-1	278	77%	POLE mutations	3	1.2%
≥2	83	23%	JAK mutations	2	0.8%

Table 1 : Cohort characteristics.

CONCLUSION

ESCAT Tier 1-2 alterations' prevalence is **high in gliomas (24%),** suggesting that molecular profiling such as **NGS** should be offered.

ACKNOWLEDGEMENTS

We would like to thank all the patients and their families. The research leading to these results has received funding from "La Caixa" Foundation (LCF/PR/CE07/50610001).

"la Caixa" Foundation

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RESULTS

ESCAT	Molecular Alterations	Number of patients	Number of patients per ESCAT group (as max. Evidence)	Tiers
I	*BRAF* V600E mutation	5	10 (2.8%)	Tier 1-2 85 (23.5%)
	NTRK (1-3) fusion	5		
II	*FGFR (1-3)* mutations	4	75 (20.8%)	
	FGFR rearrangement (FGFR-TACC)	6		
	IDH1 mutation	67		
	IDH2 mutations	3		
III	*FGFR* (1-3) amplification	1	105 (29.1%)	Tier 3-4 198 (54.9%)
	PTEN loss	12		
	BRAF fusions	6		
	H3K27M mutation	11		
	AKT1 E17K mutation	0		
	PI3K mutations (*PIK3CA / PTEN*)	98		
	MET mutation	2		
IV	*ATM* mutation	8	93 (25.8%)	
	ATRX mutation	46		
	EGFR viii rearrangement	48		
	pTERT mutation	119		
	EGFR gain	77		
	CDKN2A loss	67		
	CDKN2B loss	58		
	EGFR mutation	40		
X	No ESCAT alteration found	78	78 (21.6%)	
		Total	361 (100%)	

Table 2 : Distribution of MA according to proposed ESCAT classification.

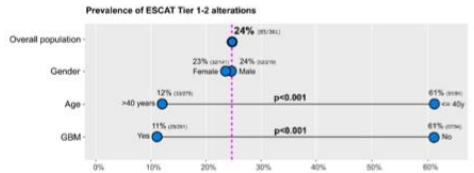


Figure 1: Tier 1-2 proportion between groups of interest.

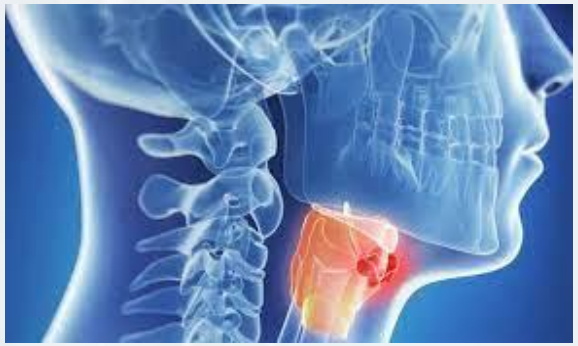
FUTURE DIRECTIONS FOR RESEARCH

Establish the ESCAT scale for gliomas and NGS in order to detect potential molecular targeted alterations. Compare molecular matched treatment with standard-of-care to quantify the clinical benefit in our real-world data cohort.

TUMORES DE CABEZA Y CUELLO

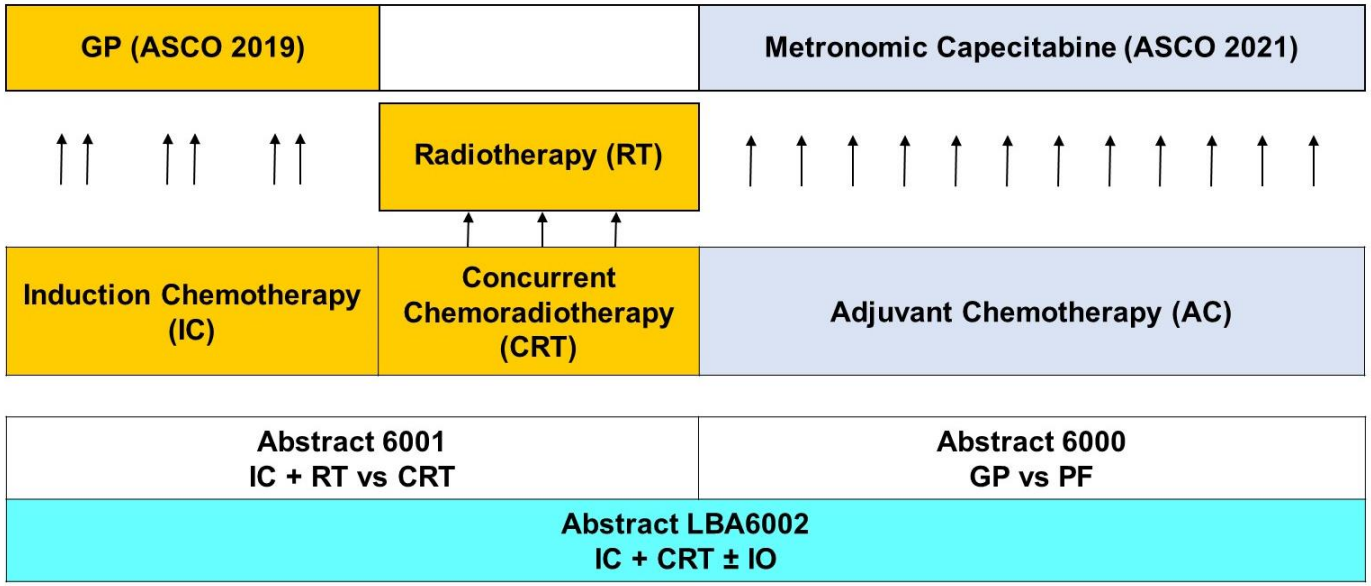
Destacar

- 3 comunicaciones orales y póster (CAVUM)
- 3 comunicaciones orales CECC – Combo QTIO (metastásico, neoadyuvante, preservación órgano y 1 póster.
- 3 comunicaciones orales sobre: Nuevas opciones terapéuticas y 2 posters



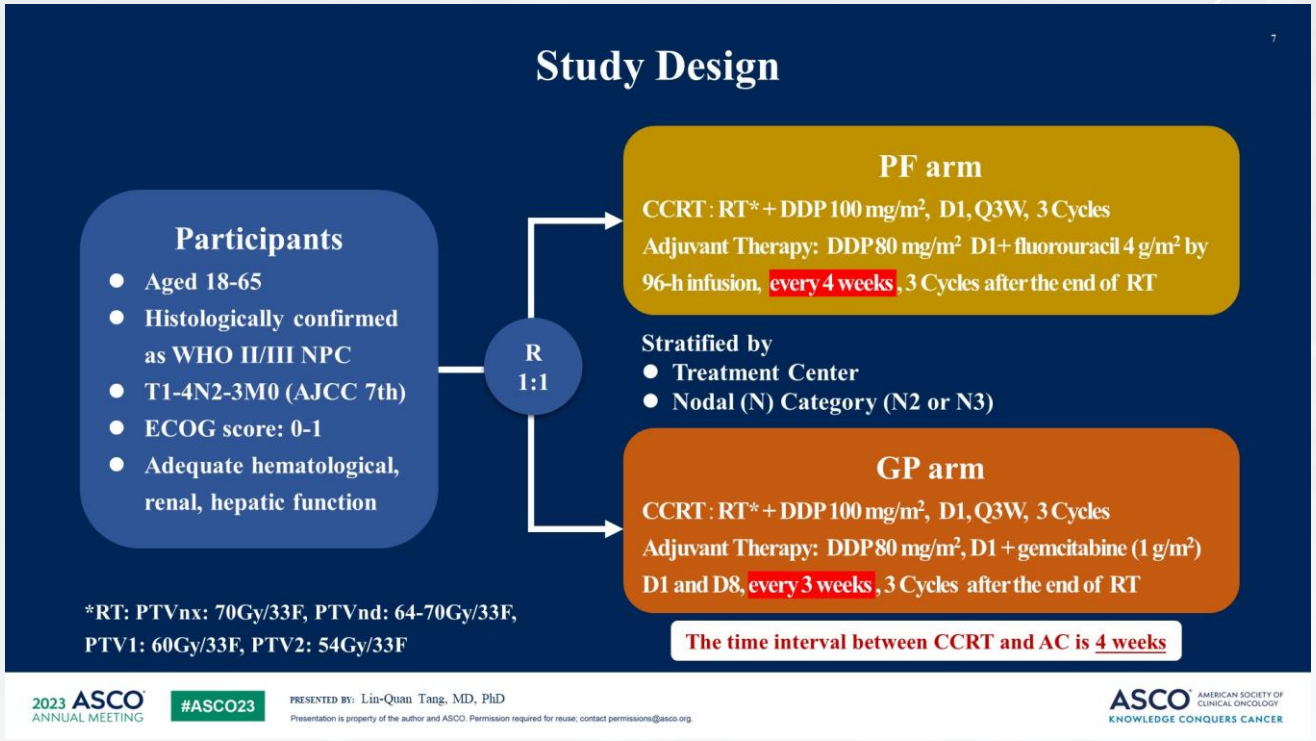
CyC - Cavum

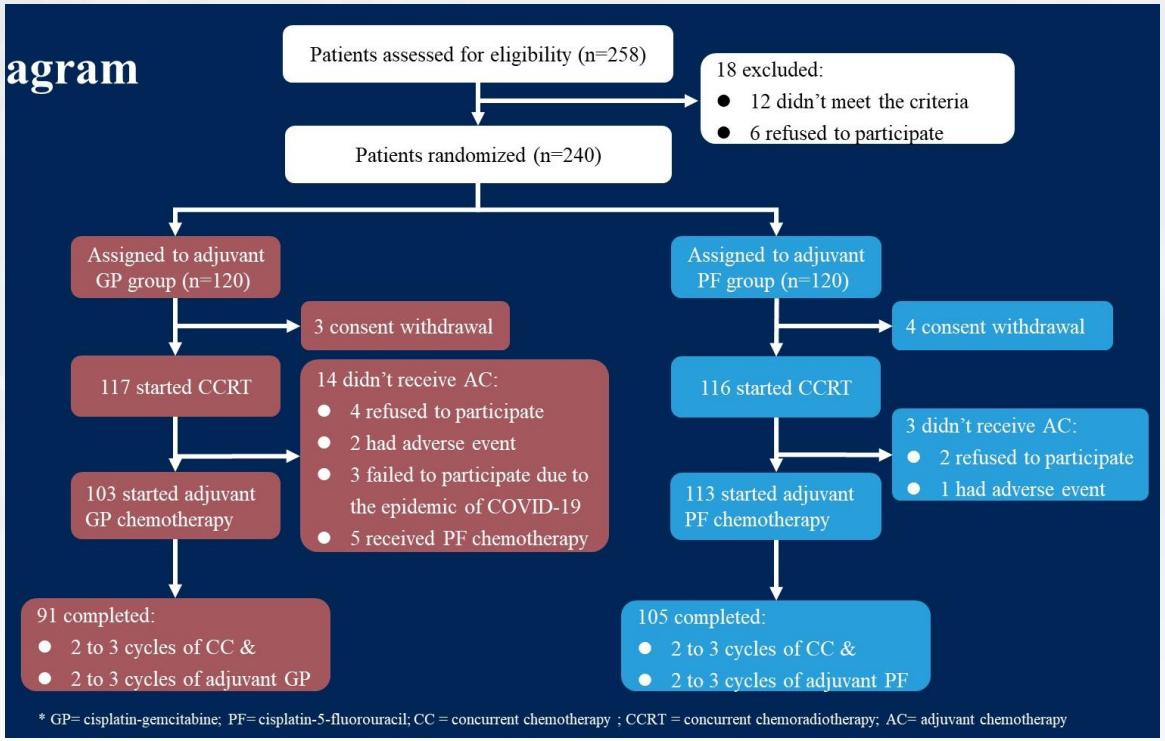
Estándar y novedades



CyC - Cavum

EC FASE III multicéntrico, randomizado en pacientes N2-3 con tratamiento adyuvante tras la QRT: Cisplatino+gemcitabina Vs PF





Objetivos: 1º - SLP a 3 años

2º - SG, SLP locorregional,Sv sin metástasis y seguridad

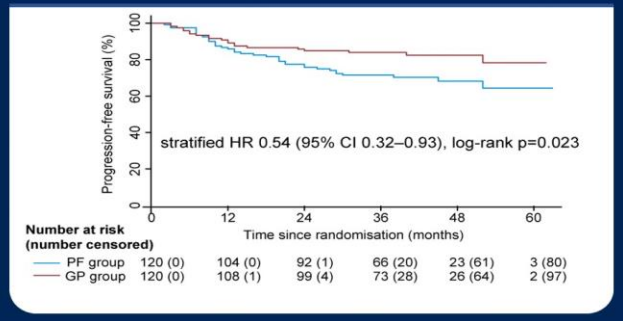
CyC - Cavum

EC FASE III multicéntrico, randomizado en pacientes N2-3 con tratamiento adyuvante tras la QRT: Cisplatino+gemcitabina Vs PF

3-year PFS for ITT analysis

13

GP group reduced risk of progression or death than that in PF group



Group	Intention-to-treat population		
	3-year PFS	95% CI	$P_{log\text{-}rank}$
PF group	**71.5%**	62.5-78.7 %	
GP group	**83.9%**	75.9-89.4 %	**0.023**

Y eso que hubo un menor cumplimiento de GP que de FP

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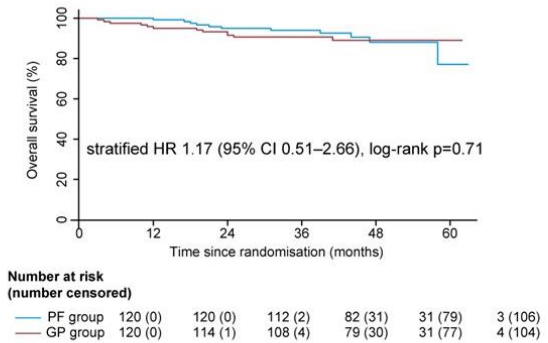
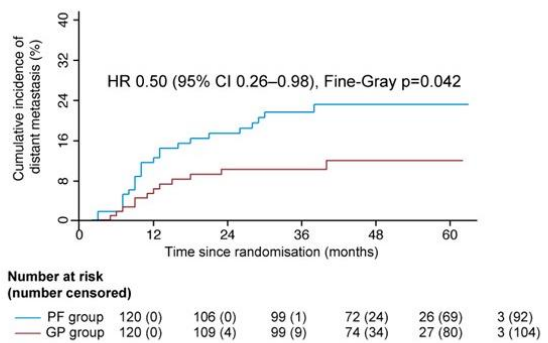
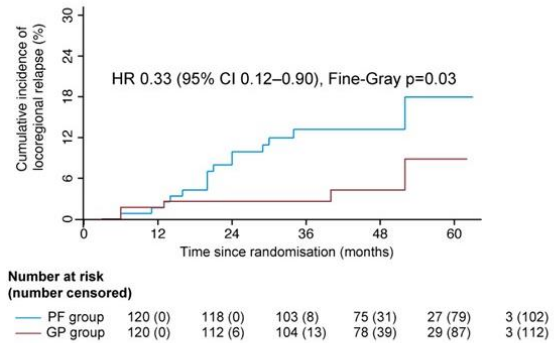
GP group exhibited no effect on 3-year OS than that in PF



GP group reduced risk of distant metastasis than that in PF



GP group reduced risk of locoregional relapse than that in PF



CyC - Cavum

EC FASE III multicéntrico, randomizado en pacientes N2-3 con tratamiento adyuvante tras la QRT: Cisplatino+gemcitabina Vs PF

Compliance of Chemotherapy

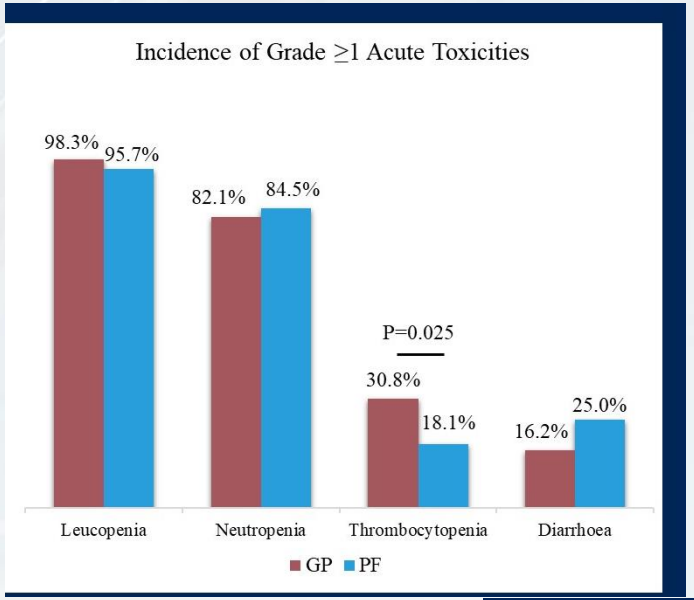
Compliance to CCRT

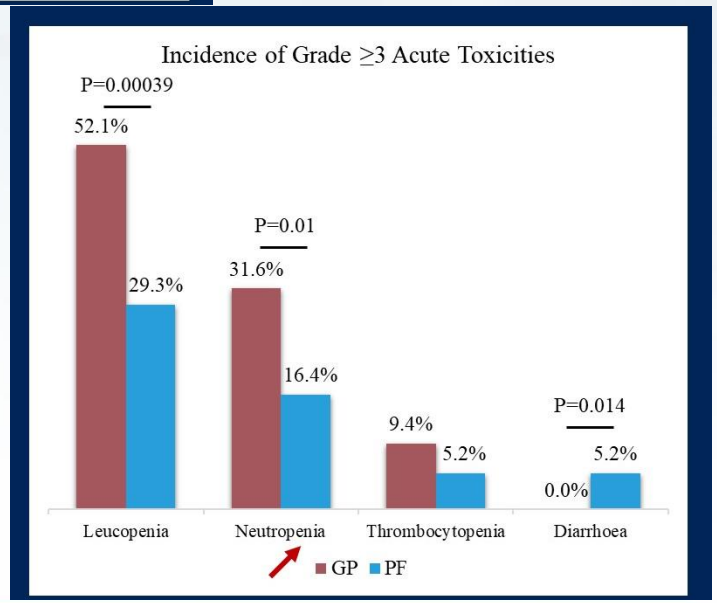
Variable	PF group (n=120)	GP group (n=120)
Completing RT, no. (%)	120 (100%)	120 (100%)
Initiating CCRT, no. (%)	116 (96.7%)	117 (97.5%)
No. of completed cycles of CC (cycles), no. (%)		
2-3	116 (96.7%)	117 (97.5%)
3	**85 (70.8%)**	**86 (71.7%)**
Concurrent cisplatin dosage received (mg/m²), no. (%)		
100 ≤ Dosage < 200	5 (4.2%)	3 (2.5%)
Dosage ≥ 200	**111 (92.5%)**	**114 (95.0%)**
300	69 (57.5%)	69 (57.5%)

Compliance to AC

Variable	PF group (n=120)	GP group (n=120)
Patients initiating protocol AC, no. (%)	113 (94.2%)	103 (85.8%)
No. of completed cycles of protocol AC, no. (%)		
2-3	106 (88.3%)	91 (75.8%)
3	**92 (76.7%)**	**74 (61.7%)**
Adjuvant cisplatin dosage received (mg/m²), no. (%)		
80 ≤ Dosage < 160	11 (9.2%)	19 (15.8%)
Dosage ≥ 160	**102 (85.0%)**	**84 (70.0%)**
240	65 (54.2%)	41 (34.2%)
Adjuvant fluorouracil dosage received (mg/m²), no. (%)		
4000 ≤ Dosage < 8000	11 (9.2%)	-
Dosage ≥ 8000	102 (85.0%)	-
12000	65 (54.2%)	-
Adjuvant gemcitabine dosage received (mg/m²), no. (%)		
2000 ≤ Dosage < 4000	-	19 (15.8%)
Dosage ≥ 4000	-	84 (70.0%)
6000	-	41 (34.2%)

* RT = Radiation therapy; GP= cisplatin-gemcitabine; PF= cisplatin-5-fluorouracil; CC = concurrent chemotherapy; CCRT = concurrent chemoradiotherapy; AC= adjuvant chemotherapy



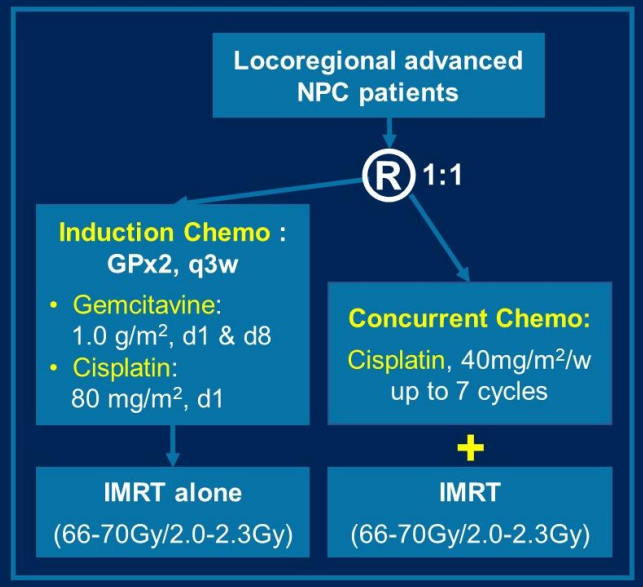


Cuidado con la toxicidad

Cavum

Fase III de no inferioridad unicéntrico de quimioterapia de inducción y RT exclusiva versus quimiorradioterapia basada en platino en ca. Cavum LA.

Flow of trial participants

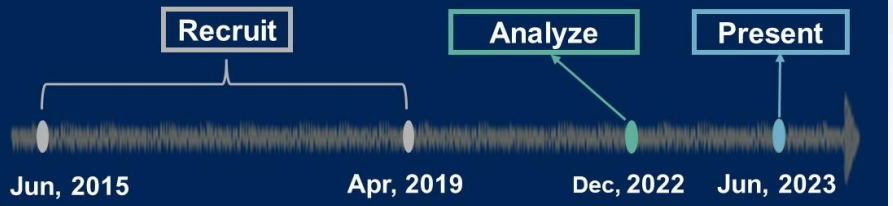


Elgibility Criteria

- ✓ WHO type II-III NPC
- ✓ Locoregionally advanced NPC (T1-4N2-3 or T3-4N0-1M0)
- ✓ 18-65 years old
- ✓ Adequate organ function
- ✓ KPS ≥ 70
- ✓ Informed consent

Sample Size Estimate (N=236)

- ✓ Primary endpoint: 2-year failure-free survival (FFS) 90% assumed in both groups
- ✓ Non-inferiority margin: 10%
- ✓ one-side α: 0.025; Power: 0.80
- ✓ 5% dropout
- ✓ 55 events observed



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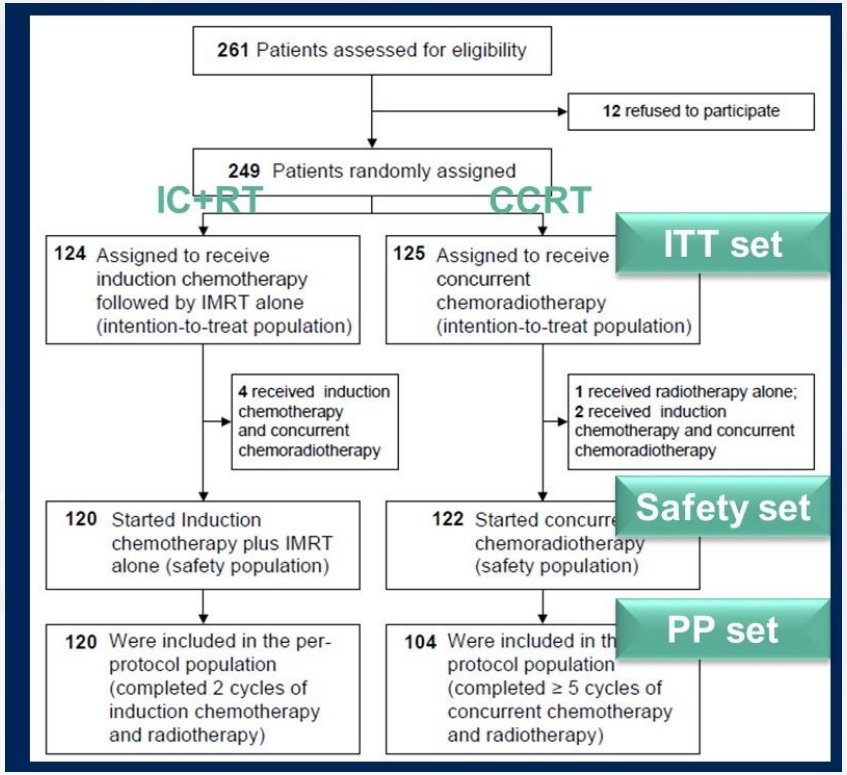
PRESENTED BY: Ming-Yuan Chen, "Induction chemotherapy plus radiotherapy alone versus CCRT in la-NPC"

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER



Cavum

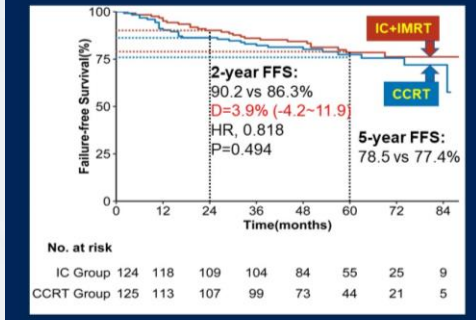
Fase III de no inferioridad multicéntrico de quimioterapia de inducción y RT exclusiva versus quimiorradioterapia basada en platino en ca. Cavum LA.

Characteristic	IC+RT N=124 (%)	CCRT N=125 (%)
Age, median (range)	45 (24-65)	46 (19-64)
Gender		
Men	84 (67.7)	81 (64.8)
Women	40 (32.3)	44 (35.2)
T classification		
T1+T2	11 (8.8)	11 (8.8)
T3	75 (60.5)	83 (66.4)
T4	38 (30.6)	31 (24.8)
N classification		
N0	3 (2.4)	4 (3.2)
N1	54 (43.5)	53 (42.4)
N2	64 (51.6)	65 (52.0)
N3	3 (2.4)	3 (2.4)
Staging		
III	85 (68.5)	92 (73.6)
IVa+IVb	39 (31.4)	33 (26.4)
Pretreatment EBV DNA*		
<4000 copy/mL	87 (73.1)	88 (72.1)
≥4000 copy/mL	32 (26.9)	34 (27.9)

INTENSIDAD DE LA QT inducción – 87.9% la completaron
INTENSIDAD DE LA QT en la QTRT – el 82.4% lo completaron

La intensidad de la RT no fue diferente en ambos subgrupos

Efficacy analysis



The median follow-up time, 60 months

	IC+RT N=124 (95%CI)	CCRT N=125 (95%CI)	P value
2y-FFS	90.2 (84.9 - 95.4)	86.3 (80.3 - 92.4)	0.494
2y-OS	97.5 (94.8 - 100)	96.0 (92.5 - 99.4)	0.080
2y-LRRFS	93.4 (88.9 - 97.8)	89.5 (84.1 - 94.9)	0.394
2y-DMFS	92.6 (88.0 - 97.3)	90.3 (85.1 - 95.5)	0.086

2y-FFS of IC+IMRT was not inferior to CCRT

Control locorregional 89.5% vs 95.2%
Control a distancia 92.8% vs 87.2%
Recaída Local y a distancia – 1.6 Vs 4%

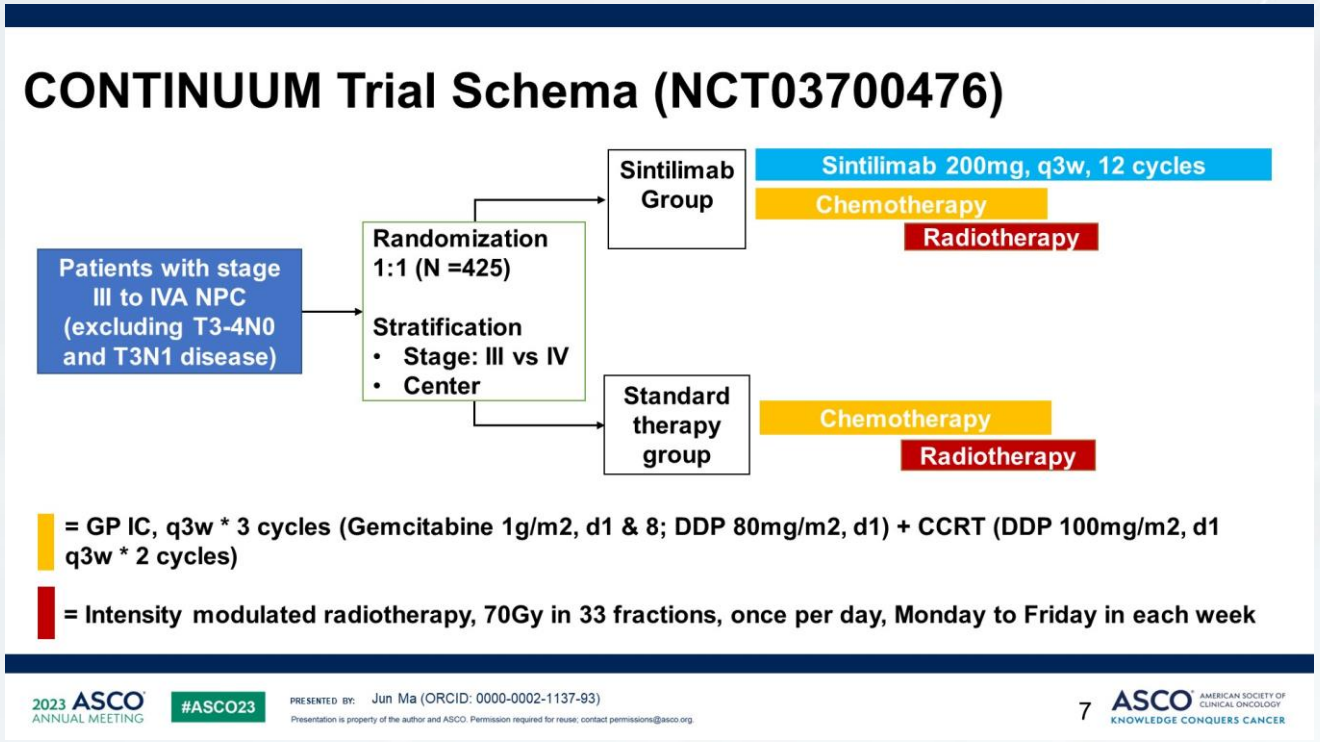
Acute adverse events

Toxicity, n (%)	IC+RT (n=120)		CCRT (n=122)		P value (grade ≥1)	P value (grade ≥3)
	grade ≥1	grade ≥3	grade ≥1	grade ≥3		
Leucopenia	66 (55.0%)	4 (3.3%)	91 (74.6%)	25 (20.5%)	0.001	<0.001
Anaemia	90 (75.0%)	0 (0)	100 (82.0%)	8 (6.6%)	0.187	0.013
Thrombocytopenia	40 (33.3%)	11 (9.2%)	46 (37.7%)	10 (8.2%)	0.477	0.789
Hypomagnesemia	23 (19.2%)	0 (0)	39 (32.0%)	5 (4.1%)	0.023	0.074
Creatinine increase	24 (20.0%)	0 (0)	41 (33.6%)	0 (0)	0.017	-
Mucositis	87 (72.5%)	7 (5.8%)	105 (86.1%)	25 (20.5%)	0.009	0.001
Nausea	85 (70.8%)	5 (4.2%)	103 (84.4%)	23 (18.9%)	0.011	<0.001
Vomiting	76 (63.3%)	3 (2.5%)	96 (78.7%)	9 (7.4%)	0.008	0.081
Dysphagia	71 (59.2%)	9 (7.5%)	81 (66.4%)	20 (16.4%)	0.245	0.033

Incidence of grade ≥3 AEs: 43.3% vs 60.7% (p=0.007)

Cavum

CONTINUUM: Fase III, multicéntrico con Sintilimab +/- (QT inducción seguido de QTRT) en ca cavum LA

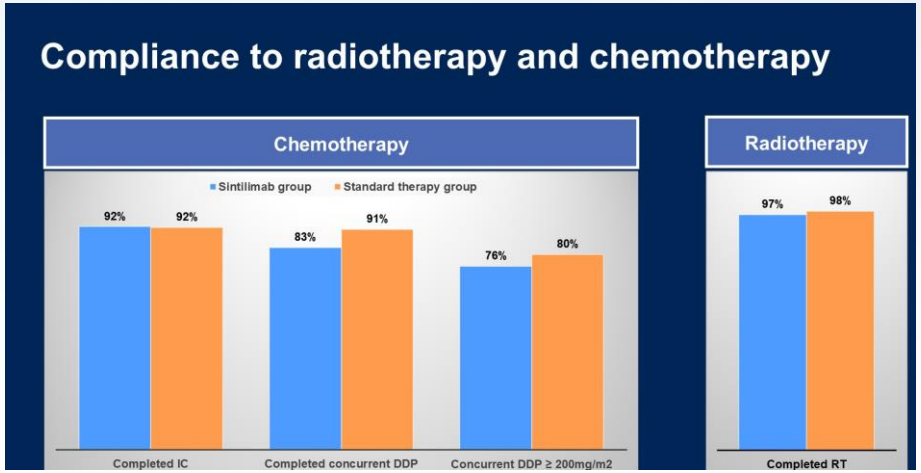


210p

215p

Characteristic (continued)	Sintilimab group n = 210	Standard therapy group n = 215
N1	43 (20.5)	48 (22.3)
N2	95 (45.2)	100 (46.5)
N3	72 (34.3)	67 (31.2)
III	62 (29.5)	64 (29.7)
IVA	148 (70.4)	151 (70.2)
Median (interquatile range)	1280 (244 – 5450)	1060 (184 – 4819)
<1	20/130 (15·4)	22/127 (17·3)
≥1	110/130 (84·6)	105/127 (82·7)
Unknown	80	88

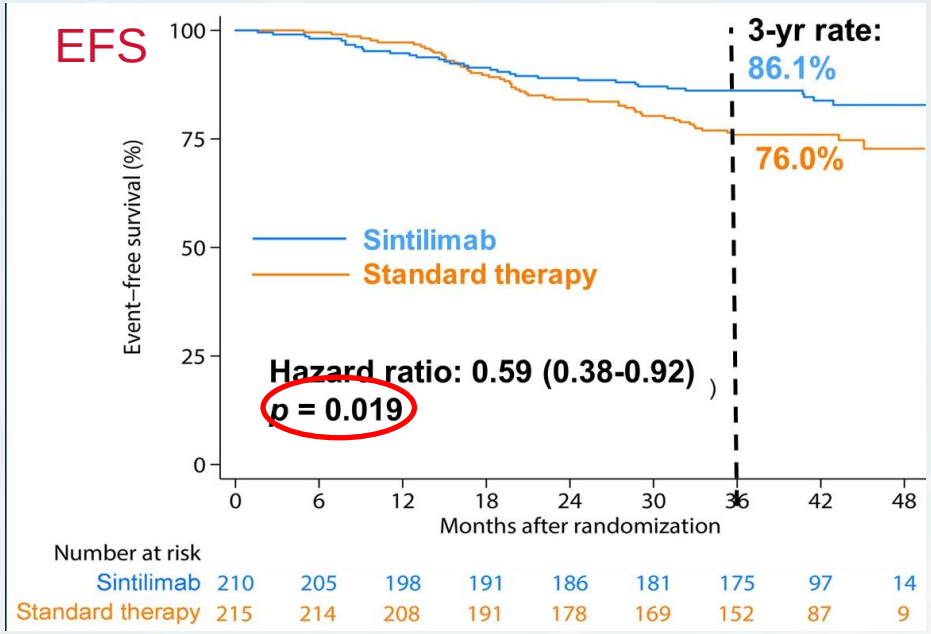
70.8% cumplimiento

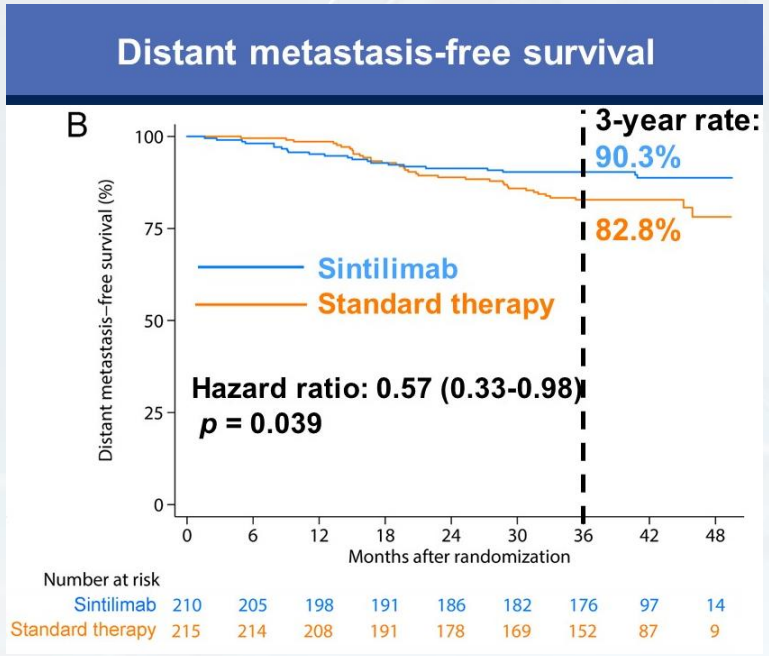


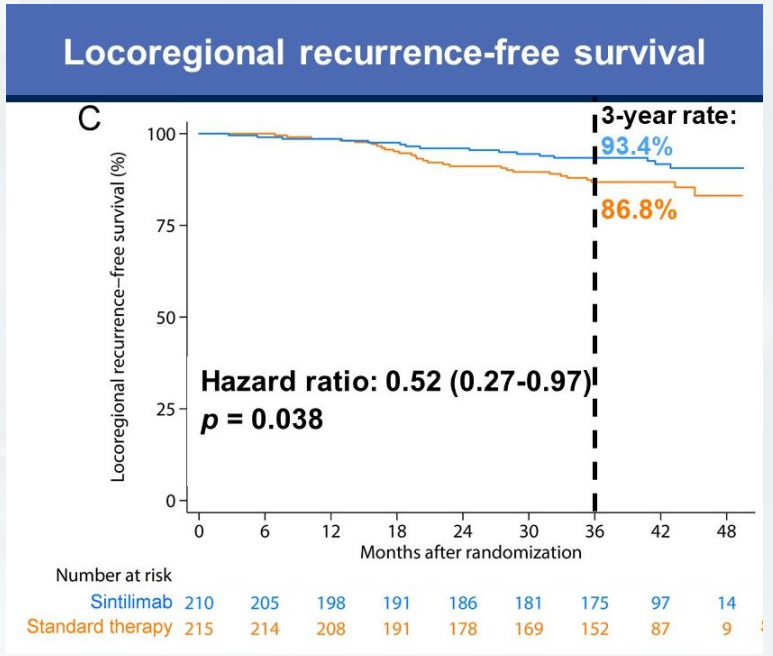
Ob 1º - SLE
Ob 2º - SG, SLP LA, SLP M, toxicidad, QoL, biomarcadores

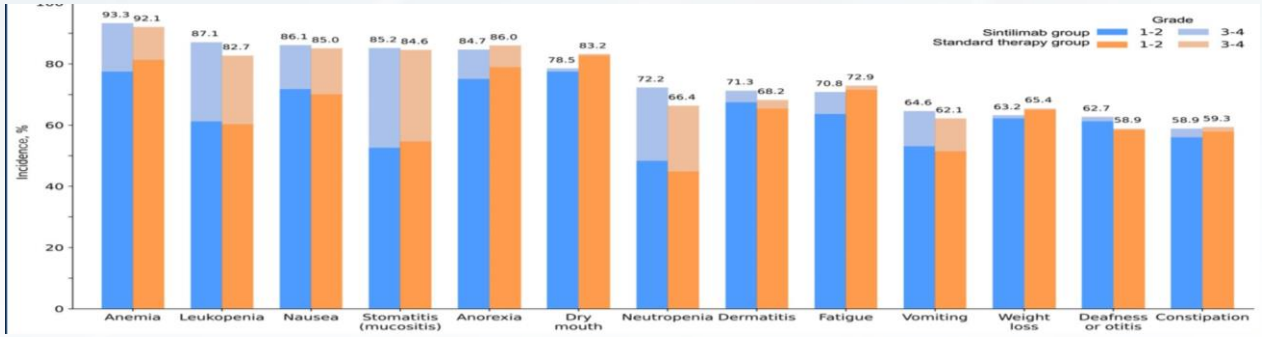
Cavum

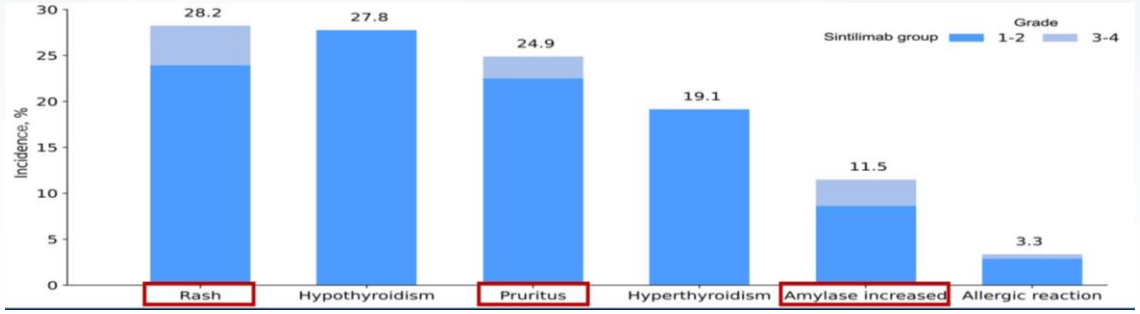
CONTINUUM: Fase III, multicéntrico con Sintilimab +/- (QT inducción seguido de QTRT) en ca cavum LA









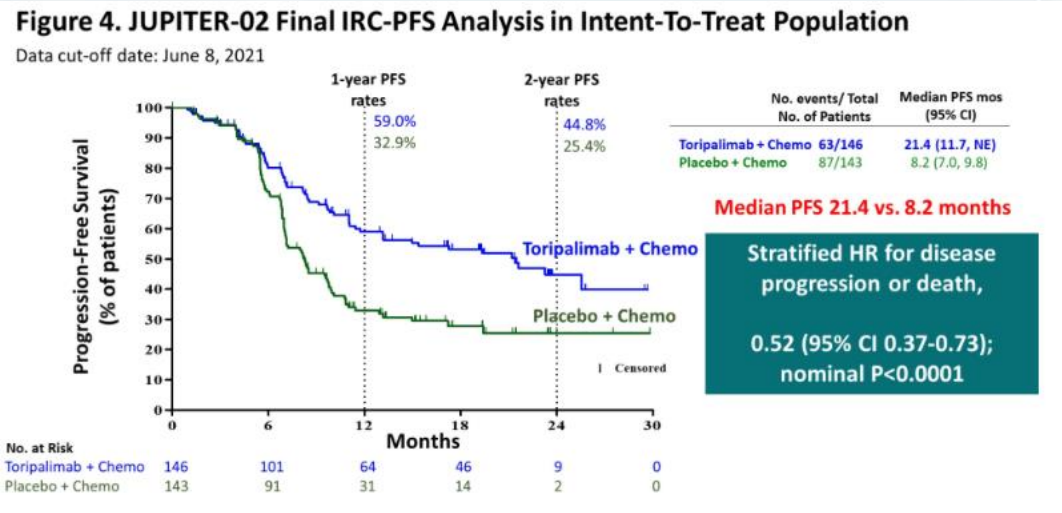


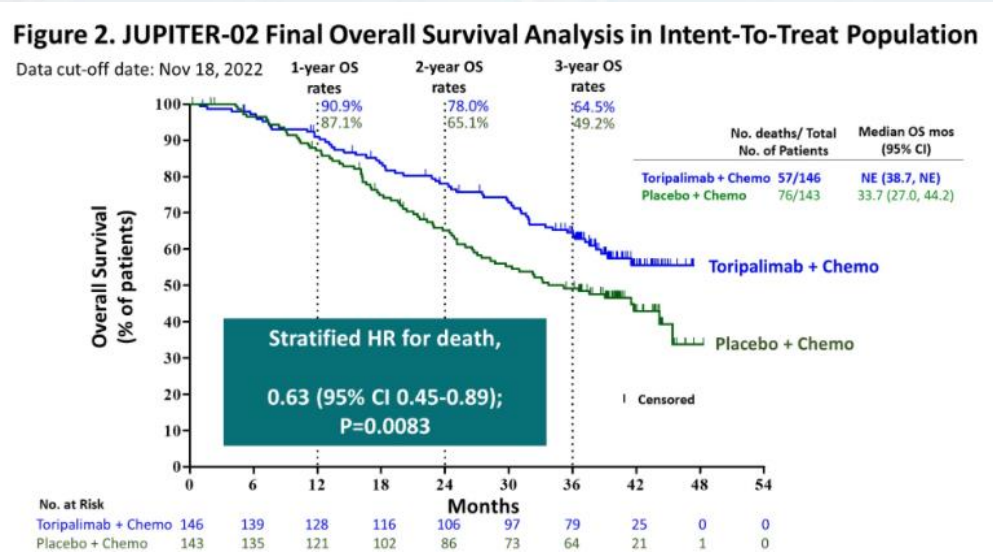
Cavum

Poster session:

Abstract #6009: Final Overall Survival Analysis of JUPITER-02: a Phase 3 study of Toripalimab versus Placebo in Combination with Gemcitabine and Cisplatin as First-line Treatment for Recurrent or Metastatic Nasopharyngeal Carcinoma (NPC)

Hai-Qiang Mai[1], Qiu-Yan Chen[1], Dongping Chen[2], Chaosu Hu[3], Kunyu Yang[4], Jiyu Wen[5], Jingao Li[6], Ying-Rui Shi[7], Feng Jin[8], Ruilian Xu[9], Jianji Pan[10], Shenhong Qu[11], Ping Li[12], Chunhong Hu[13], Yi-Chun Liu[14], Yi Jiang[15], Xia He[16], Hung-Ming Wang[17], Wan-Teck Lim[18], and Rui-Hua Xu[19]. *, Coherus Biosciences[20] and Shanghai Junshi Biosciences[21]
[1]Department of Nasopharyngeal Carcinoma, Sun Yat-Sen University Cancer Center, Guangzhou, China; [2]Affiliated Cancer Hospital & Institute of Guangzhou Medical University, Guangzhou, China; [3]Fudan University Cancer Center, Shanghai, China; [4]Union Hospital Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China; [5]Affiliated Hospital of Guangdong Medical University, Zhanjiang, China; [6]Jiangxi Cancer Hospital, Nanchang, China; [7]Hunan Cancer Hospital and the Affiliated Cancer Hospital of Xiangya School of Medicine, Changsha, China; [8]Guizhou Cancer Hospital of Guizhou Medical University, Guiyang China; [9]Shenzhen People's Hospital, Shenzhen, China; [10]Fujian Provincial Cancer Hospital, Fuzhou, China; [11]The People's Hospital of Guangxi Zhuang Autonomous Region, Nanning, China; [12]West China Hospital of Sichuan University, Chengdu, China; [13]The Second Xiangya Hospital of Central South University, Changsha, China; [14]Taichung Veterans General Hospital, Taichung, Taiwan; [15]Cancer Hospital of Shantou University Medical College, Shantou, China; [16]Jiangsu Cancer Hospital, Nanjing, China; [17]Chang Gung Memorial Hospital, Taoyuan, Taiwan; [18]National Cancer Centre, Singapore City, Singapore; [19]Department of Medical Oncology, Sun Yat-Sen University Cancer Center; State Key Laboratory of Oncology in South China; Collaborative Innovation Center of Cancer Medicine, Guangzhou, China; [20]Authoring group: Coherus Biosciences, Redwood City, California, USA; [21]Authoring group: Shanghai Junshi Biosciences, Shanghai, China *Corresponding author.



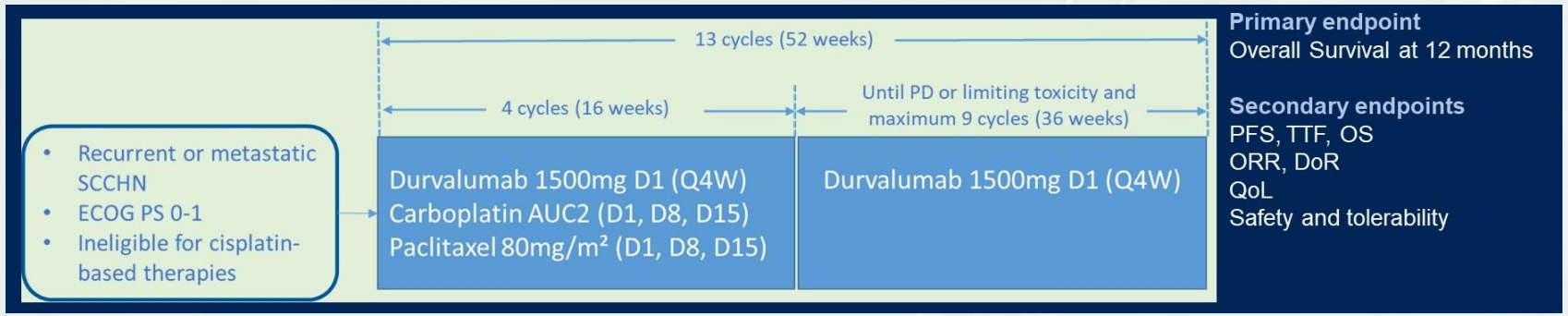


OS at 36m – NE vs 33.7 meses – HR 0.63 (0.45-0.89)
PFS +13.6m (21.4 vs 8.2 meses HR 0.52 (0.37-0.73)

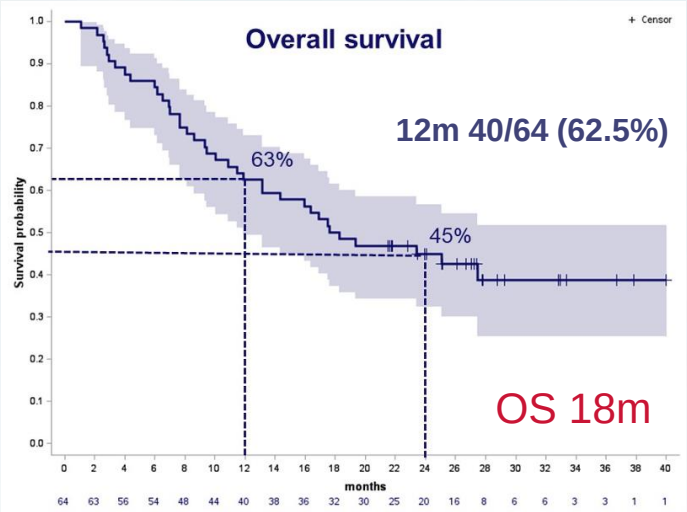
CyC

Paciente "unfit" – FRAIL IMMUNE – Fase II con durvalumab combinado con carboplatino y paclitaxel semanal en 1ºL CECC R/M no candidato a platino

64p

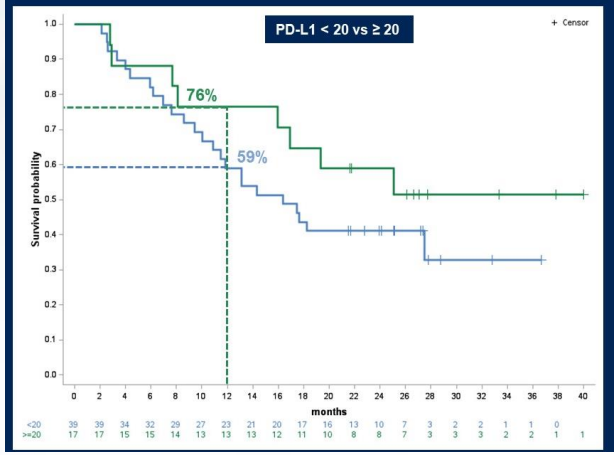


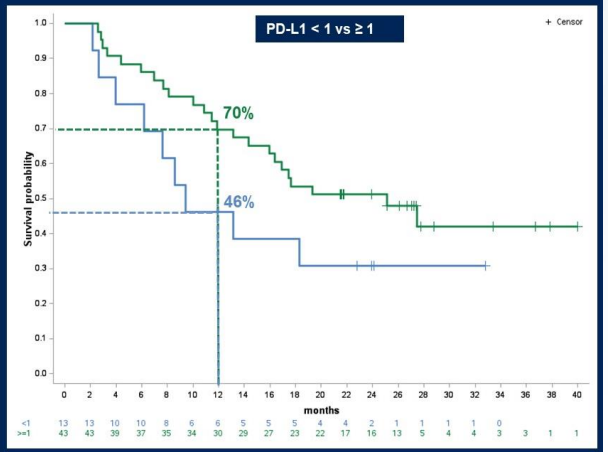
Reasons for ineligibility	
• > 70 years-old	N = 30
• Creatinine clearance (CrCl) : 40<CrCl<60 ml/min	N = 18
• Comorbidity	N > 18



Analysis population N=64	
Number of deaths (%)	37 (57.8%)
Median OS, months [min-max]	18.0 [11.9-NR]
12-month OS-rate (95%CI)	63% [49-73]
24-month OS-rate (95%CI)	45% [32-57]

Overall survival according to PD-L1 (CPS)



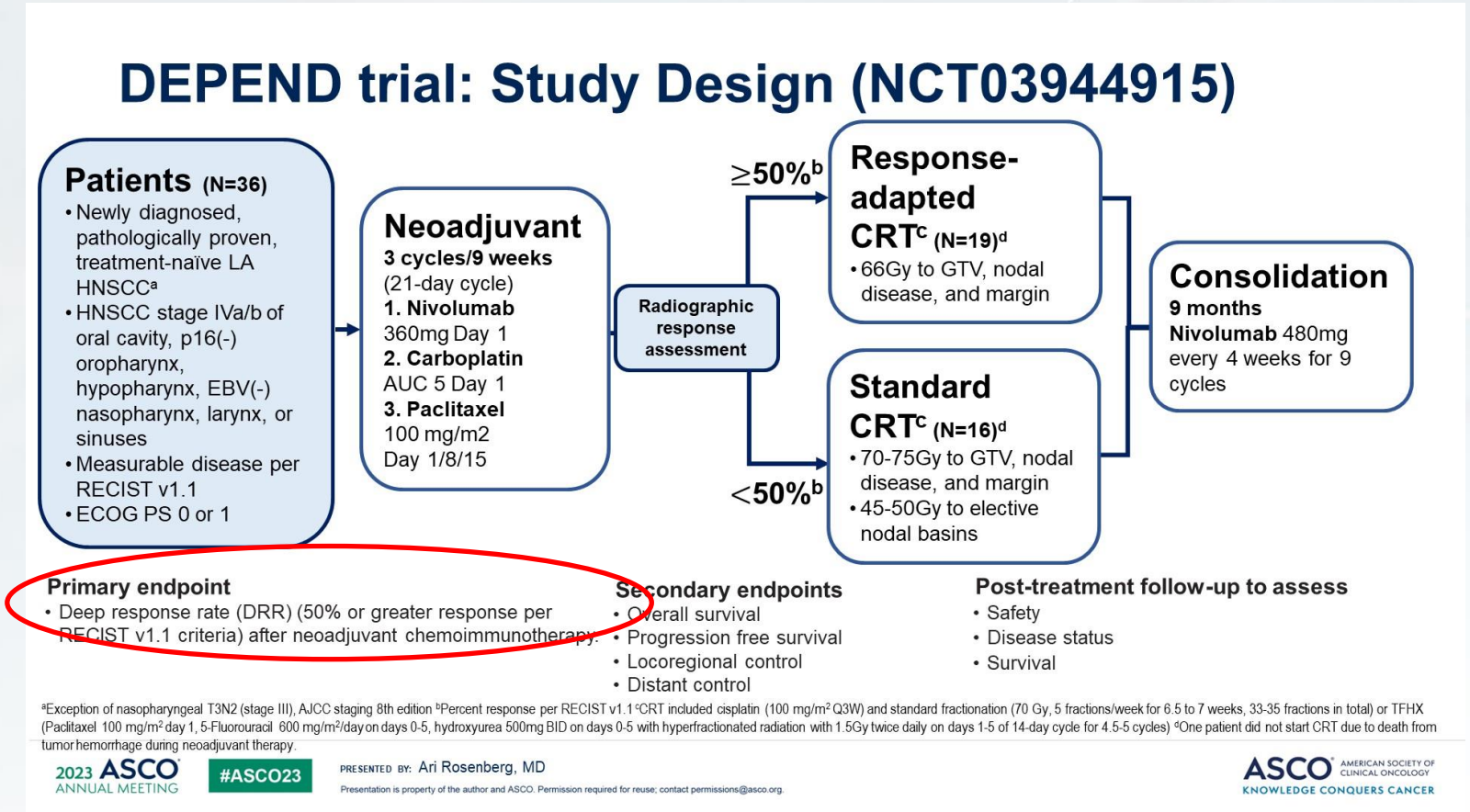


CyC

DEPEND Trial- Neoadyuvancia con carboplatino, paclitaxel y nivolumab, en CECC LA HPV-, seguido de QTRT según respuesta.

Añadir tto en ENF LA

DE-INTENSIFICAR

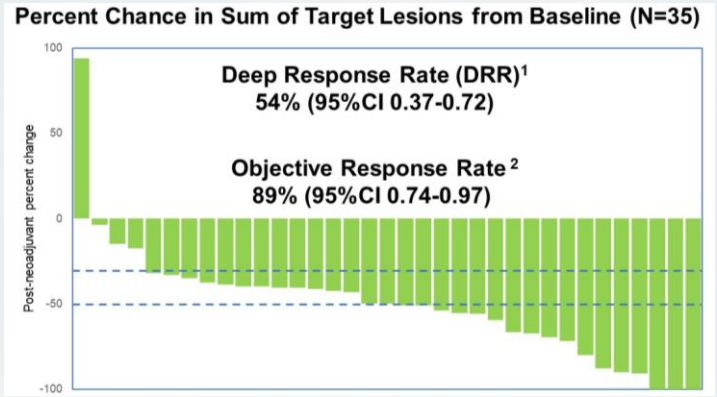


Characteristic	Total n=36[b]	Response-adapted CRT n=19	Standard CRT n=16
Tumor stage[a]			
T1	2 (5.6)	1 (5.3)	1 (6.3)
T2	6 (16.7)	2 (10.5)	4 (25.0)
T3	13 (36.1)	7 (36.8)	6 (37.5)
T4	10 (27.8)	6 (31.6)	4 (25.0)
T4a	3 (8.3)	2 (10.5)	1 (6.3)
T4b	2 (5.6)	1 (5.3)	0 (0.0)
Nodal stage[a]			
N0	4 (11.1)	3 (15.8)	1 (6.3)
N1	4 (11.1)	2 (10.5)	1 (6.3)
N2	6 (16.7)	2 (10.5)	4 (25.0)
N2b	10 (27.8)	6 (31.6)	4 (25.0)
N2c	8 (22.2)	5 (26.3)	3 (18.8)
N3	2 (5.6)	1 (5.3)	1 (6.3)
N3b	2 (5.6)	0 (0.0)	2 (12.5)
CPS ≥ 20	8 (22.2)	5 (26.3)	3 (18.8)
CPS ≥ 1	20 (55.6)	15 (78.9)	5 (31.3)

Ob 1º

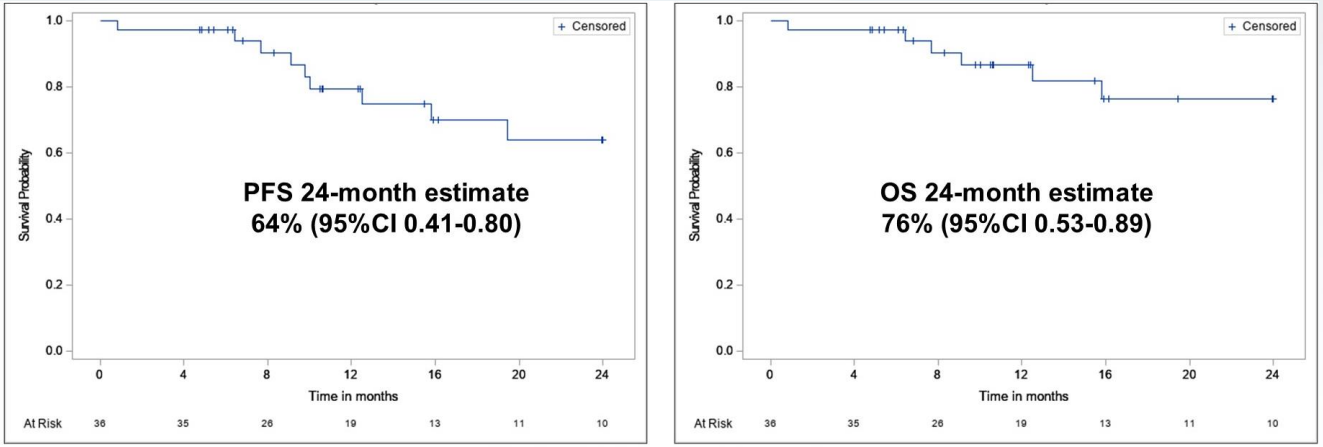
CyC

DEPEND Trial- Neoadyuvancia con carboplatino, paclitaxel y nivolumab, en CECC LA HPV-, seguido de QTRT según respuesta.

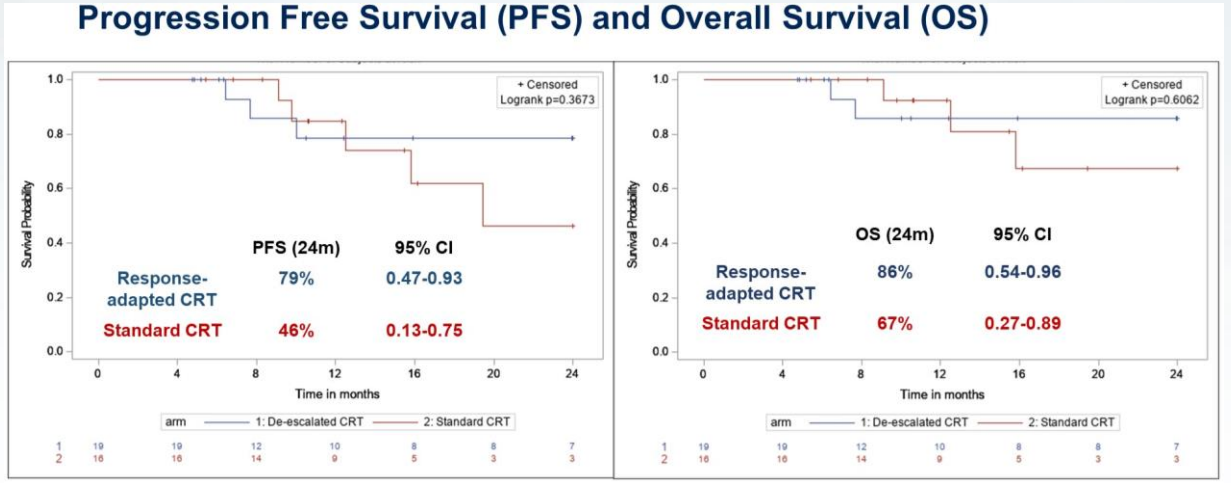


PD-L1 Combined Positive Score (CPS)	Deep Response[a] n=19	Suboptimal Response[b] n=16	Total n=35	p-value
CPS < 1, n (%)	4 (21.1)	11 (68.8)	15 (42.9)	0.006
CPS ≥1, n (%)	15 (78.9)	5 (31.3)	20 (57.1)	

36p

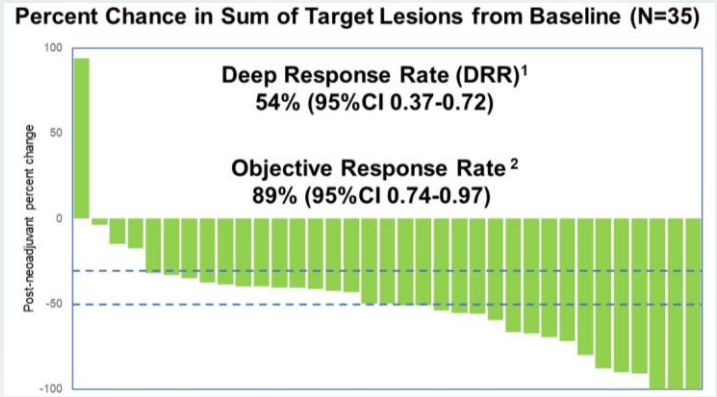


Median Follow-up 14 months
Range (5 months to 38 months)



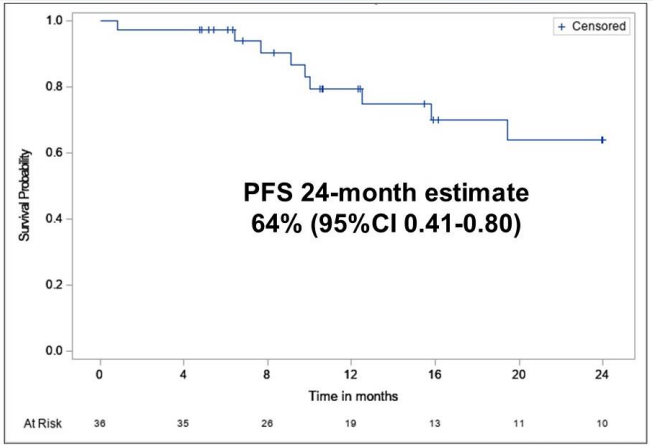
CyC

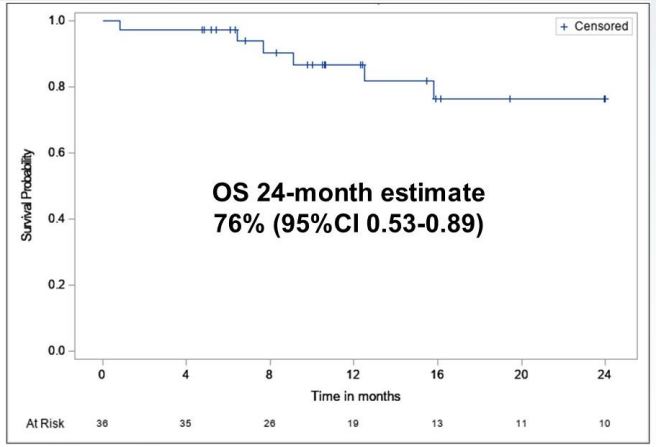
DEPEND Trial- Neoadyuvancia con carboplatino, paclitaxel y nivolumab, en CECC LA HPV-, seguido de QTRT según respuesta.



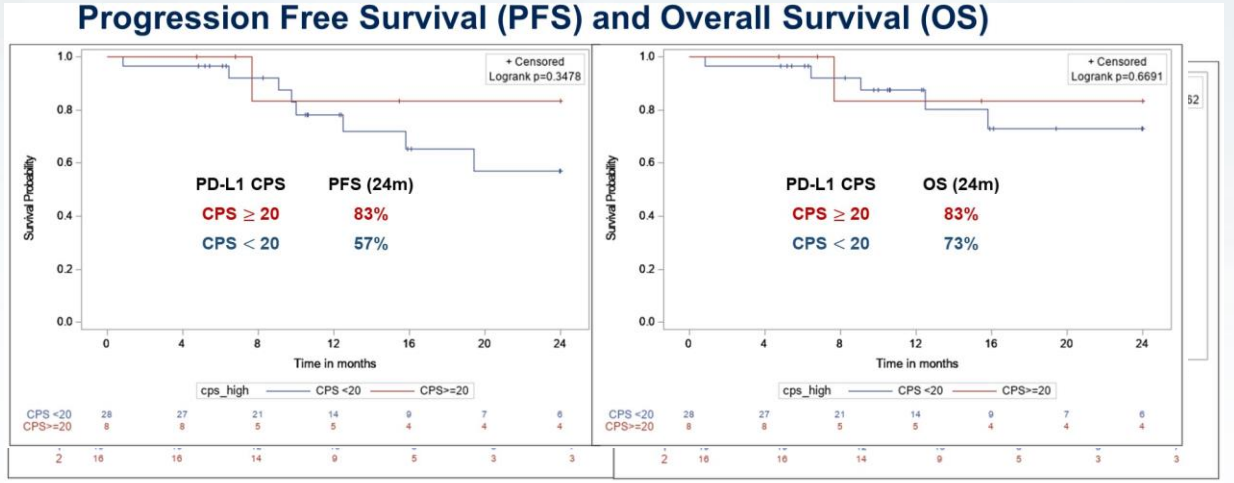
PD-L1 Combined Positive Score (CPS)	Deep Response[a] n=19	Suboptimal Response[b] n=16	Total n=35	p-value
CPS < 1, n (%)	4 (21.1)	11 (68.8)	15 (42.9)	0.006
CPS ≥1, n (%)	15 (78.9)	5 (31.3)	20 (57.1)	

36p





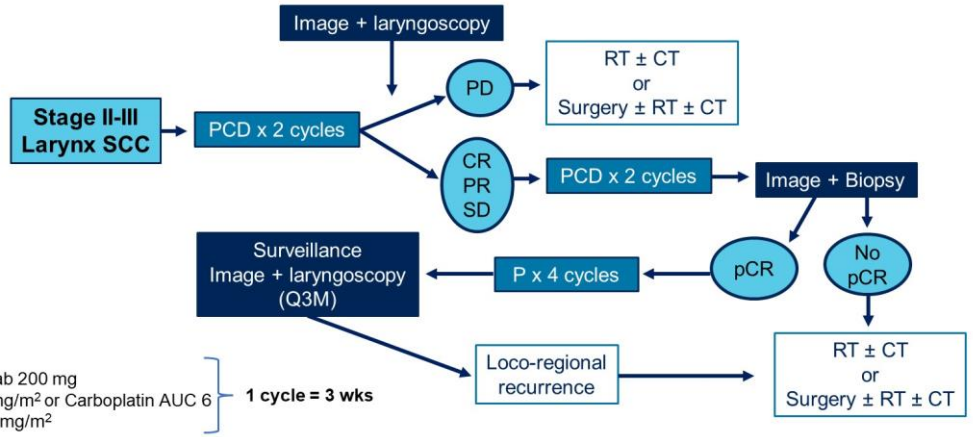
Median Follow-up 14 months
Range (5 months to 38 months)



CyC

Estudio fase II: ICoLP – Nuevas estrategias de preservación de órgano en cáncer de laringe con QTIO.

ICoLP Trial Schema



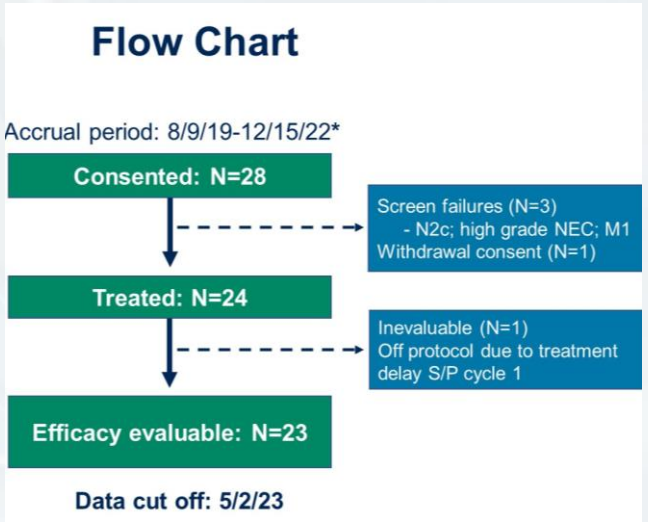
PD: progression of disease, CR: complete response, SD: stable disease; RT: photon radiotherapy, CT: concurrent chemotherapy (weekly cisplatin or carboplatin); pCR: pathologic complete response in the biopsy specimen

2023 ASCO ANNUAL MEETING #ASCO23 PRESENTED BY: Renata Ferrarotto, MD

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

Obj – Control de enfermedad (RP, RC, EE a los 2 ciclos - RCp a los 4 ciclos

Flow Chart

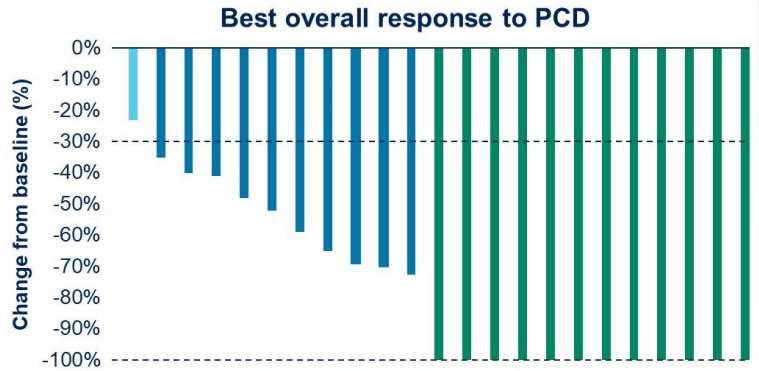


Adverse Events (AEs)	Grade 1	Grade 2	Grade 3	Grade 4	Total
Fatigue	19	3			22 (91.7%)
Anemia	8	9	2		19 (79.2%)
Diarrhea	6	5			11 (45.8%)
Nausea	8	2			10 (41.7%)
Constipation	5	2			7 (29.2%)
Peripheral sensory neuropathy	5	2			7 (29.2%)
Vomiting	6	1			7 (29.2%)
Platelet count decreased	6	1			7 (29.2%)
Neutrophil count decreased	3			3	6 (25%)
Edema limbs	4	2			6 (25%)
Myalgia	4	2			6 (25%)
Weight loss	6				6 (25%)
Alkaline phosphatase increased	5				5 (20.8%)
Hypothyroidism	5				5 (20.8%)
Palmar-plantar erythrodysesthesia syndrome	1	3	1		5 (20.8%)
Alanine aminotransferase increased	3	1			4 (16.7%)
Anorexia	3	1			4 (16.7%)
Arthralgia	4				4 (16.7%)
Blood lactate dehydrogenase increased	4				4 (16.7%)
Creatinine increased	3	1			4 (16.7%)
Lymphocyte count decreased	3	1			4 (16.7%)
Pruritus	4				4 (16.7%)

Co-Primary Endpoint: DCR S/P PCD x 2 (N=23)

100%

Response (PCD x 2)	N (%)
CR	5 (21.7%)
PR	12 (52.2%)
SD	6 (26.1%)
DCR	23 (100%)
Best Response to PCD	**N (%)**
CR	12 (52.2%)
PR	10 (43.5%)
SD	1 (4.3%)



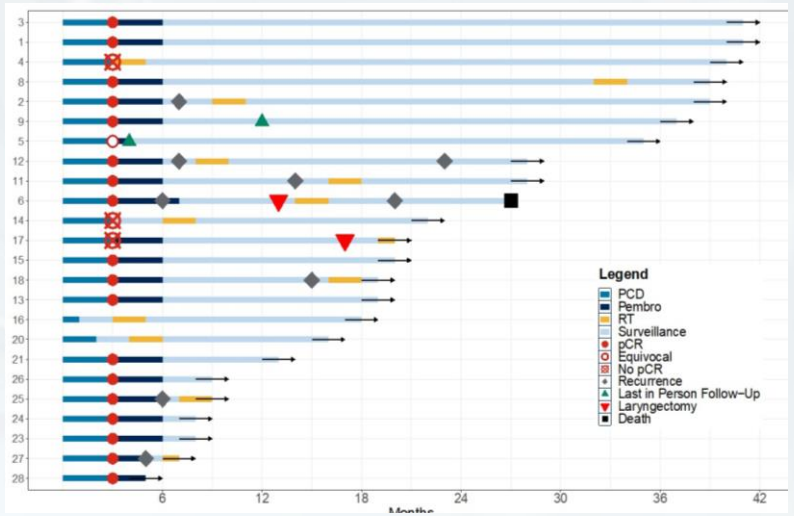
CyC

Estudio fase II: ICoLP - Nuevas estrategias de preservación de órgano en cáncer de laringe con QTIO.

Co-Primary Endpoint: pCR S/P PCD x 4 (N=23)

78.3%=18p → 4p RT o QRT o Q

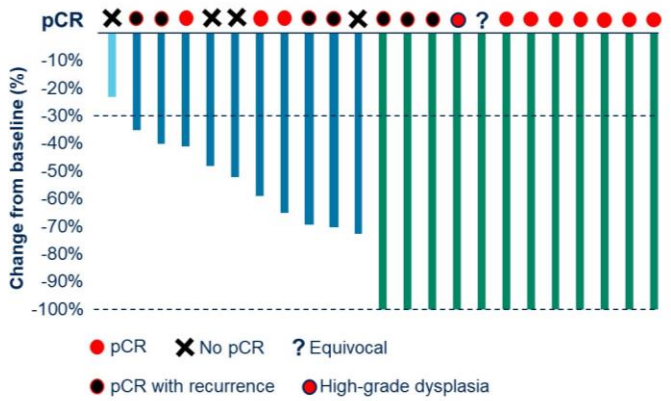
pCR	N (%)
Yes	18 (78.3%)
No	4 (17.4%)
Equivocal	1 (4.3%)



Recurrences after pCR

10 pacientes 14,5m en RC
Omitido la RT y Q

- 7 of 18 (**38.9%**) pCR pts recurred and were salvaged with local therapy
- 5 of 7 (71.4%) recurrences occurred within 5 mos and had abnormal appearance at the time of the biopsy



→ 7p RT o QRT o Q

SG 95.8%

CyC

Neoadyuvancia en CECC con Cemiplimab-QT y cetuximab

Abstract #423554: Neoadjuvant Cemiplimab with Platinum-Doublet Chemotherapy and Cetuximab to De-escalate Surgery and Omit Adjuvant Radiation in Locoregionally Advanced Head & Neck Squamous Cell Carcinoma (HNSCC)

Winston Wong, Jennifer R. Cracchiolo, Nadeem Riaz, Ian Ganly, Eric Jeffrey Sherman, Alan Loh Ho, Luc Morris, Ronald A Ghossein, Sofia Haque, Kin Wai (Tony) Hung, Anuja Kriplani, Marc Cohen, Jay Boyle, Sean Matthew McBride, Daphna Y. Gelbum, Loren S. Michel, Nancy Y. Lee, Richard J. Wong, David G. Pfister, Lara Dunn
Memorial Sloan Kettering Cancer Center, New York, NY

Fig 1: Schema

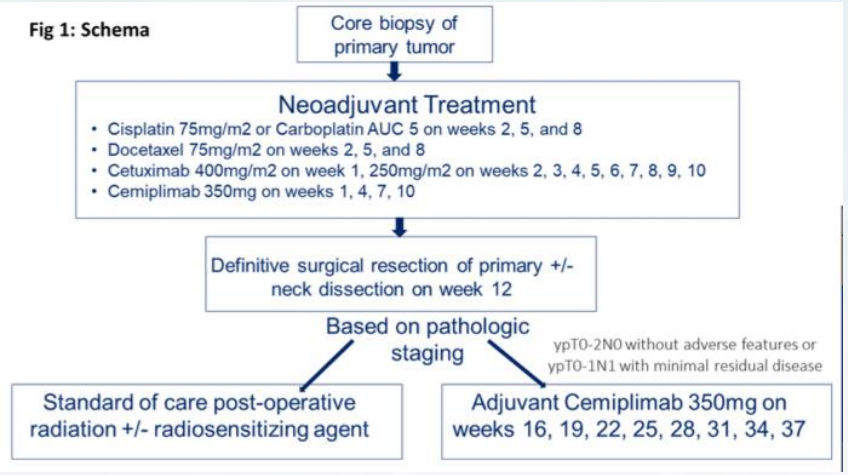


Fig 3: Disease-Free Survival

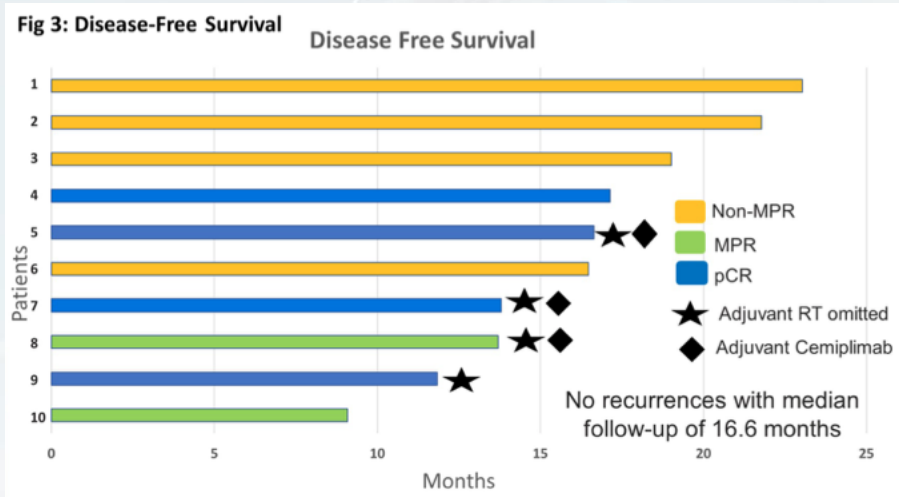
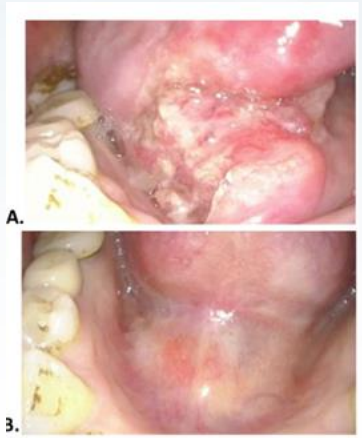


Table 3: Treatment Associated Adverse Events (TRAEs)

Adverse Event Summary	N (%)
Any TRAE	10 (100%)
Any > G3	5 (50%)
Neutropenia	3 (30%)
Diarrhea	1 (10%)
Hypomagnesemia	1 (10%)
Hypokalemia	1 (10%)
Any G5	0 (100%)
Suspected Immune-Related Adverse Events	**N (%)**
G3 Aspartate Aminotransferase Increased	1 (10%)
G4 Myocarditis	1 (10%)
G3 Myasthenia Gravis	1 (10%)

Pathologic Response	PT	Sub-site	Clinical Stage	Pathologic Stage
Pathologic Complete Response	4	Oral Cavity	cT2N1M0	ypT0N0
	5	Sinonasal	cT3N0M0	ypT0N0
	7	Oral Cavity	cT3N0M0	ypT0N0
	9	Oral Cavity	cT3N0M0	ypT0N0
Major Pathologic Response	8	Oral Cavity	cT2N1M0	ypT0N1*
	10	Oral Cavity	cT3N2cM0	ypT1N2c**
Non-Major Pathologic Response	1	Oral Cavity	cT4aN2cM0	ypT2N0
	2	Oral Cavity	cT4aN2cM0	ypT4aN3b
	3	Oral Cavity	cT3N2b/cM0	ypT2N2b
	6	Oral Cavity	cT4aN2bM0	ypT3N0



CyC

Neoadyuvancia en CECC con IO-IO (Nivolumab + relatlimab o ipilimumab)

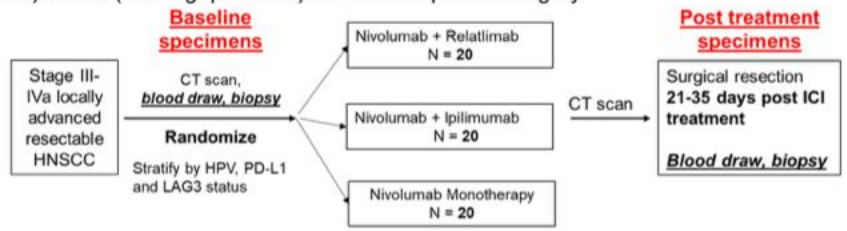
Neoadjuvant nivolumab alone or in combination with relatlimab or ipilimumab in resectable head and neck squamous cell carcinoma (HNSCC)

Robert L. Ferris[1], William Gooding[1], Simion Chiosea[1,2], Umamaheswar Duvvuri[1], Seungwon Kim[1], Mark Kubik[1], Shaum Sridharan[1], Moon Fenton[1], Heath Skinner[1], Zahra Kelly[1], Housaiyin Li[1], Lazar Vujanovic[1], Dan P. Zandberg[1]

1. UPMC Hillman Cancer Center, Pittsburgh, Pennsylvania, USA. 2. Department of Pathology, University of Pittsburgh, Pittsburgh, Pennsylvania, USA

Trial Schema

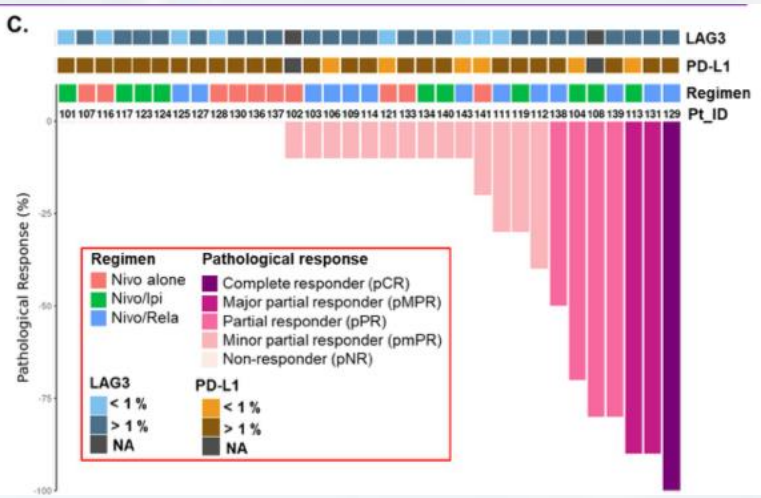
1) Previously untreated, locally advanced HPV+ and HPV- head and neck squamous cell carcinoma patients who are candidates for surgical resection.
2) Patients were stratified by p16, PD-L1, and LAG-3, with staining assessed by immunohistochemistry.
3) Patients were randomized to treat with neoadjuvant nivo alone (240 mg q2 weeks), or with ipi (1 mg/kg q3 weeks) or rela (160 mg q4 weeks) for 4 weeks prior to surgery.



A.

Characteristic (N = 33)	
Age	
Median	63
Range	32-81
Gender	
Male	20 (61%)
Female	13 (39%)
AJCC Stage	
III	14 (42%)
IV	19 (58%)
Clinical T Stage	
T1	1 (3%)
T2	5 (16%)
T3	12 (39%)
T4	13 (42%)
Clinical N Stage	
N0	10 (32%)
N1	12 (39%)
N2	9 (29%)
HPV Positive OPC	3 (9%)

C.



Los células efectoras CD8 aumentan la infiltración tumoral por la IO-IO.
Los respondedores tienen más infiltración por los CD8 y se aprecia expansión clonal.

CyC – NUEVAS? DIANAS

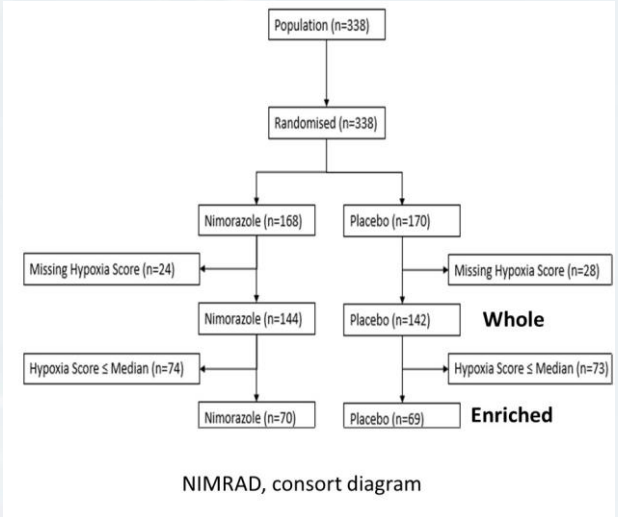
NIMRAD: Fase III randomizado, multicéntrico, de tratamiento con nimorazole y RT en tumores CECC hipóxicos mediante la evaluación de una firma génica

NIMRAD había mostrado beneficio en el tratamiento de los pacientes no candidatos a platino y cetuximab (DAHANCA 5,1990)

Whole population characteristics

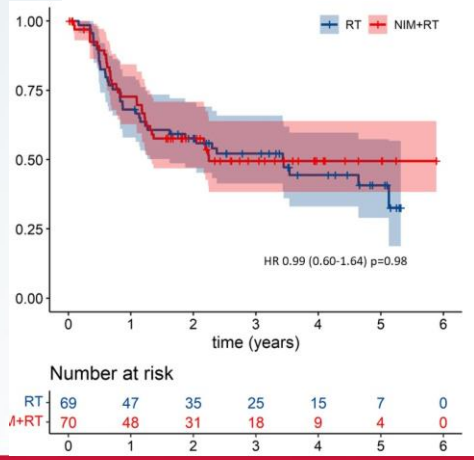
- 20 UK centres
- Recruitment May 2014 to May 2019
- 338 patients
- Median age: 73 years
- WHO PS 2: 15%
- Stage III/IV: 96%
- Oropharynx SCC HPV-positive: 66%
- Factors balanced between groups

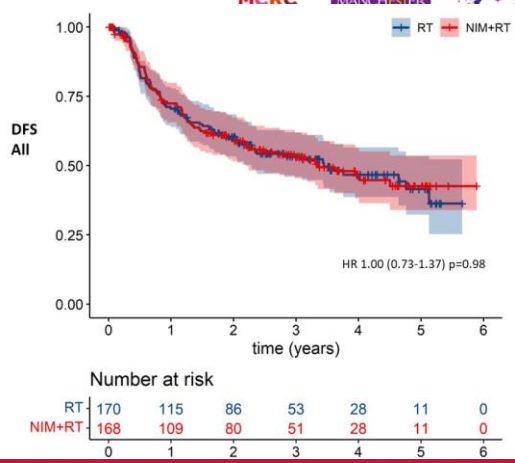
Variable		Nimorazole	Placebo	Overall
Number		168	170	338
gender (%)	Male	133 (79.2)	129 (75.9)	262 (77.5)
	Female	35 (20.8)	41 (24.1)	76 (22.5)
age (median) [range]		73.0 [44.0, 88.0]	73.0 [44.0, 88.0]	73.0 [45.0, 84.0]
tumour site (%)	Oropharynx	110 (65.5)	97 (57.1)	207 (61.2)
	Hypopharynx	25 (14.9)	26 (15.3)	51 (15.1)
	Larynx	33 (19.6)	47 (27.6)	80 (23.7)
HPV (%)	NEG	88 (52.4)	97 (57.1)	185 (54.7)
	POS	75 (44.6)	67 (39.4)	142 (42.0)
AJCC 7th Ed (%)	II	7 (4.2)	8 (4.7)	15 (4.4)
	III	52 (31.0)	51 (30.0)	103 (30.5)
	IVA	99 (58.9)	99 (58.2)	198 (58.6)
	IVB	10 (6.0)	12 (7.1)	22 (6.5)
WHO PS (%)	0	73 (43.5)	64 (37.6)	137 (40.5)
	1	69 (41.1)	80 (47.1)	149 (44.1)
	2	26 (15.5)	26 (15.3)	52 (15.4)
smoking (%)	Never Smoked	25 (14.9)	27 (15.9)	52 (15.4)
	Ex-smoker	110 (65.8)	106 (62.4)	216 (63.9)
	Current smoker	32 (19.0)	37 (21.8)	69 (20.4)



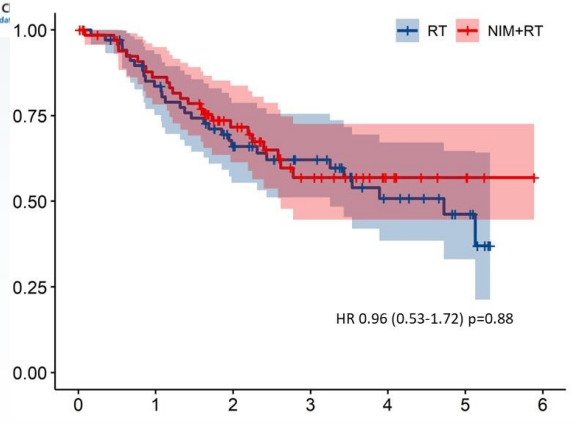
NIMRAD, consort diagram

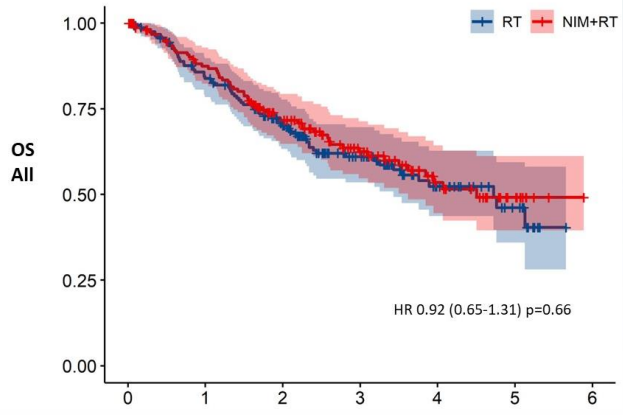
SLP





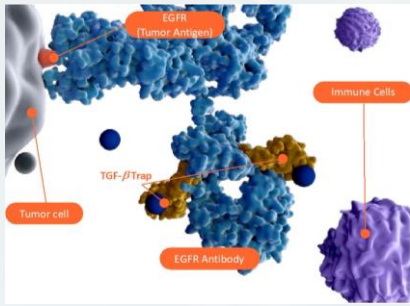
SG



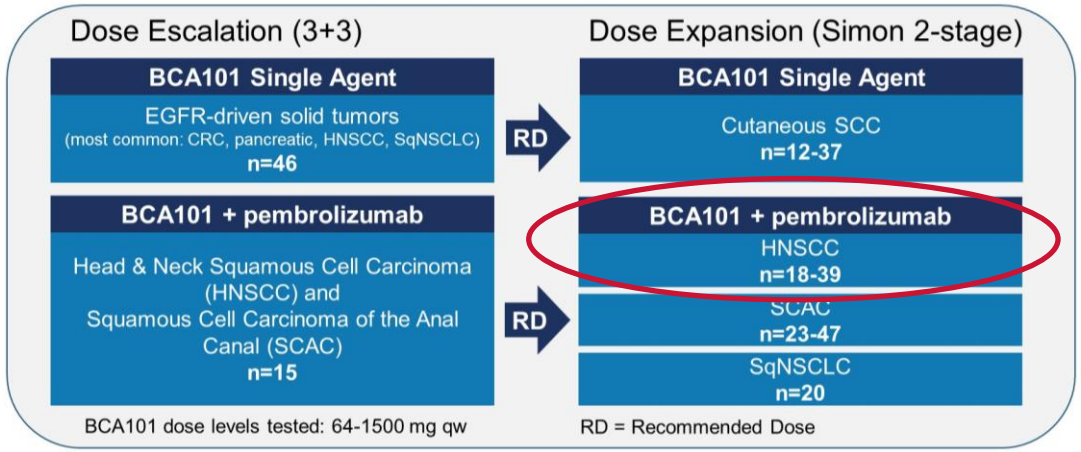


CyC – NUEVAS DIANAS

Fase I con BCA101, un inhibidor de EGFR/TGFB, combinado con pembrolizumab en pacientes con CECC R/M



BCA101 Ph1/1b study design



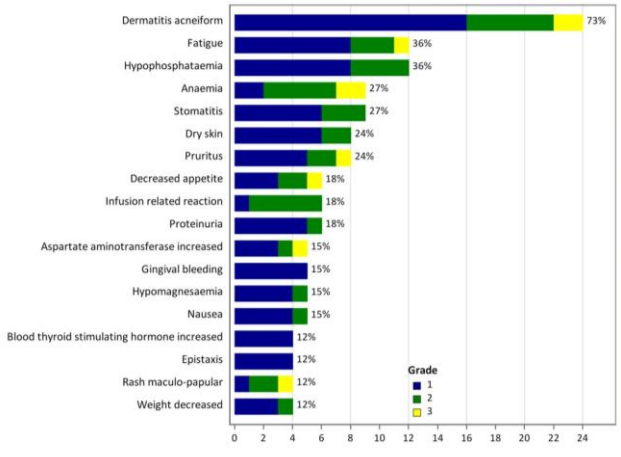
Primary Objective: Safety/Tolerability
Secondary Objectives: Preliminary efficacy, pharmacokinetics, immunogenicity

Population
- R/M HNSCC
- Oral cavity, oropharynx, hypopharynx & larynx
- HPV (p16) testing required for oropharyngeal cancer
- CPS≥1
- No prior systemic therapy in R/M setting

Simon 2-stage (H0 vs. HA, 19% vs. 38%)
- Stage 1: 18 evaluable pts, ≥4 responses required to proceed to stage 2
- Stage 2: Additional 21 patients (total n=39), 11 responses required to warrant further assessment in larger cohort

BCA101 + pembrolizumab yields manageable safety profile

AEs, treatment-related, in ≥10% of subjects, preferred term & grade

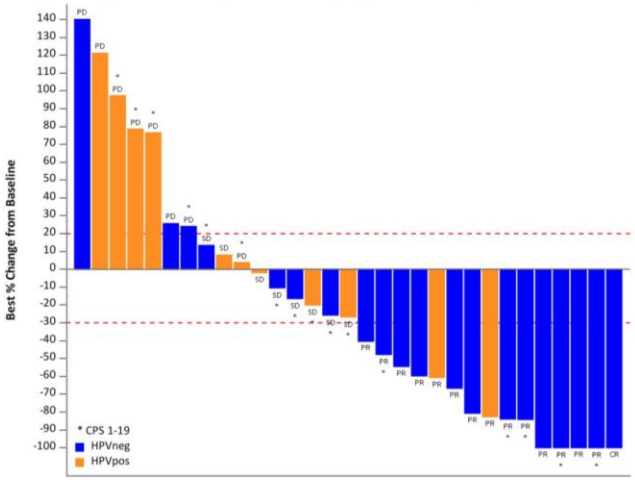


Adverse Events of Interest:
- Skin toxicity
  - Acneiform rash in 73% of subjects (two G3 events)
- Mucosal bleeding
  - Generally low-grade and manageable without the need for dose interruptions
  - One G3 drug-related tracheal hemorrhage

Treatment-related AEs leading to:
- Dose interruption: 12/33 (36%)
  - Incl. four G2 infusion related reaction
- Dose reduction: 3/33 (9%)
  - G3 acneiform rash
  - G2 blood alkaline phosphatase increased
  - G3 maculo-papular rash
- Permanent discontinuation: 3/33 (9%)
  - G3 tracheal hemorrhage
  - G4 pericarditis
  - G3 blood alkaline phosphatase increased

BCA101 + pembrolizumab in CPS≥1 R/M HNSCC (1L)

Preliminary Efficacy – Total population (N=31 evaluable)

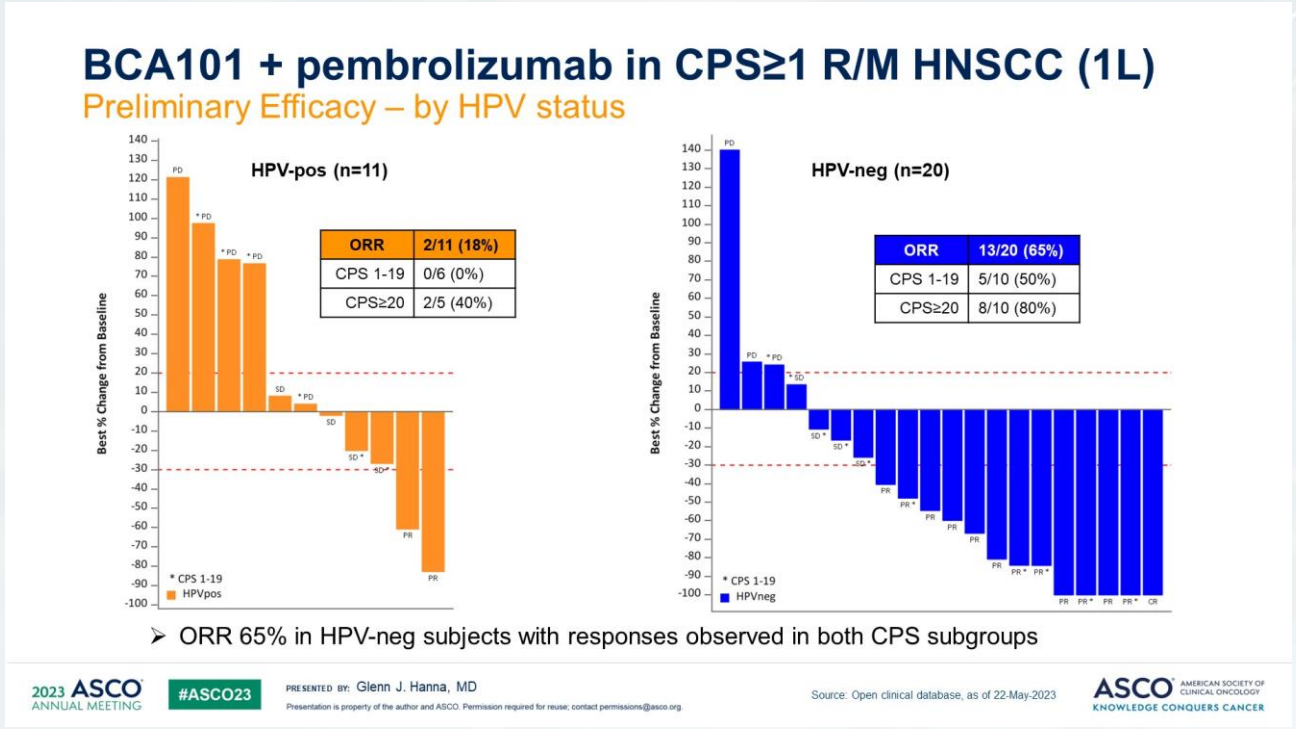


ORR	15/31 (48%)
CR	1 (3%)
PR	14 (45%)
SD	8 (26%)
PD	8 (26%)

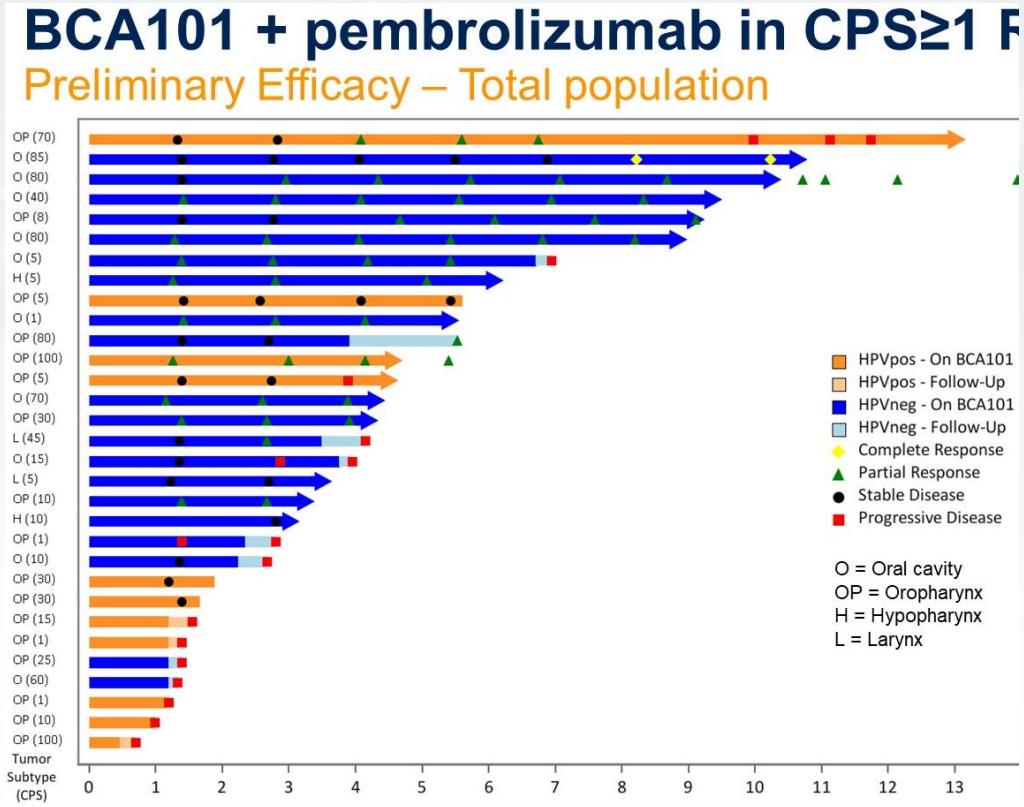
Predecible: - EGFR, PD1

CyC – NUEVAS DIANAS

Fase I con BCA101, un inhibidor de EGFR/TGFB, combinado con pembrolizumab en pacientes con CECC R/M

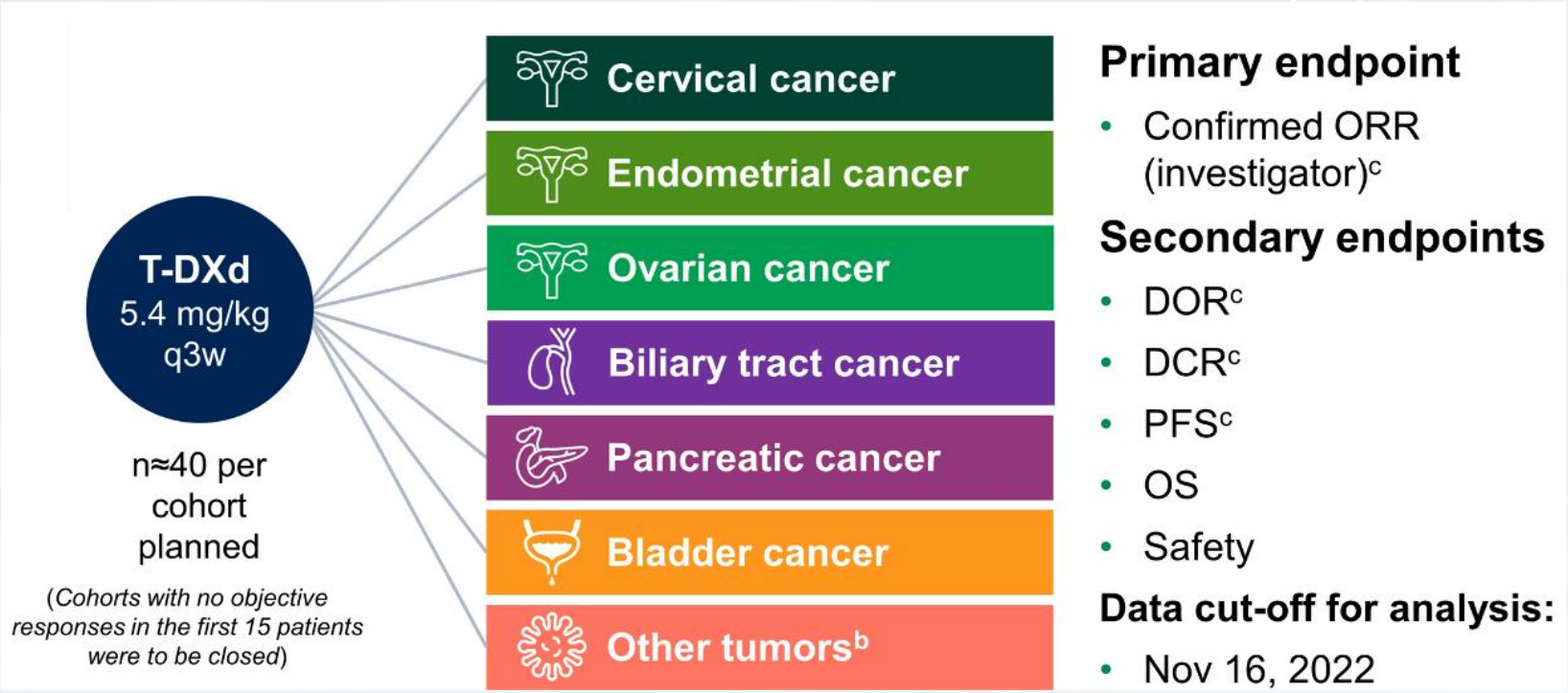


65% TR
1.4m hasta respuesta

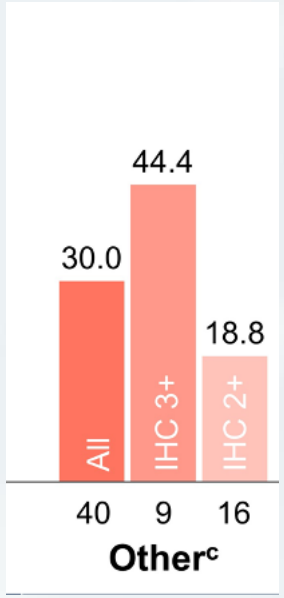


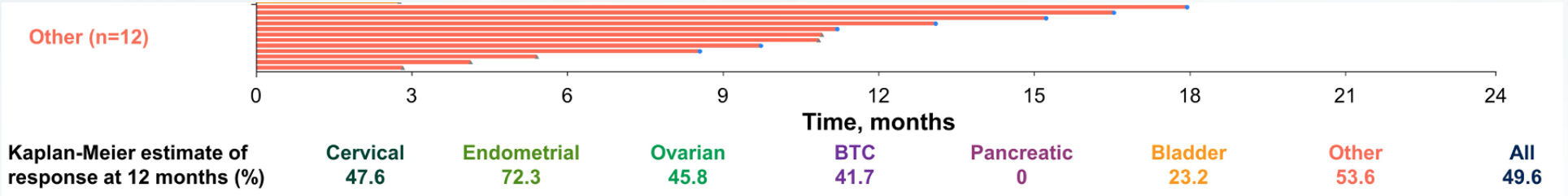
CyC – NUEVAS DIANAS

DESTINY-Pan Tumor02 - Fase II para evaluar la eficacia y seguridad de trastuzumab-deruxtecan en varios subtipos tumorales



		Other (n=40)
Investigator assessment		
ORR, n (%)		**12 (30.0)**
Best overall response, n (%)	Complete response	0
	Partial response	12 (30.0)
	Stable disease	24 (60.0)
	PD	3 (7.5)
	Not evaluable	1 (2.5)
DCR[a] at 12 weeks, n (%)		30 (75.0)
Median DOR, months (95% CI)		NR (4.1–NE)
Independent central review: ORR, n (%)		13 (32.5)





Kaplan-Meier estimate of response at 12 months (%)	Cervical	Endometrial	Ovarian	BTC	Pancreatic	Bladder	Other	All
	47.6	72.3	45.8	41.7	0	23.2	53.6	49.6

[a]Includes salivary gland cancer (n=19), malignant neoplasm of unknown primary site (n=5), extramammary Paget's disease (n=3), melanoma (n=2), oropharyngeal neoplasm (n=2), adenoid cystic carcinoma, adenocarcinoid tumor of the appendix, head and neck, intestinal adenocarcinoma, lip and/or oral cavity, oesophageal adenocarcinoma, oesophageal squamous cell carcinoma, testis and vulva (all n=1).

CyC – NUEVAS DIANAS

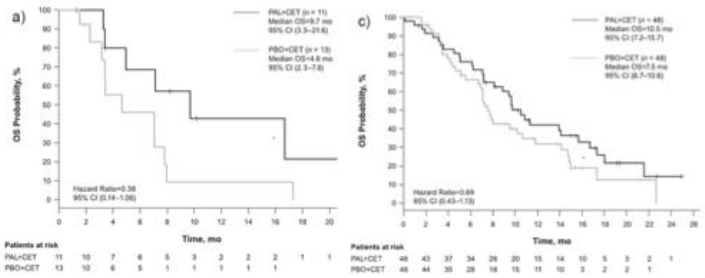
#6015: Correlation of *CDKN2A* Alterations with Tumor Response to Palbociclib Given Before Chemoradiation Therapy (CRT) to Patients with HPV-Negative, Locally Advanced Head and Neck Squamous-Cell Carcinoma (LA-HNSCC): A Single-Arm, Phase 2 Trial

Peter Oppelt, Jessica Ley, Randal C. Paniello, Sidharth V. Puram, Ryan Jackson, Patrik Pipkorn, Jason Rich, Hiram Gay, Jingxia Liu, Jared Cohen, Wade Thorstad, Douglas Adkins. Department of Medicine, Division of Oncology; Department of Otolaryngology, Division of Head and Neck Surgery; Department of Surgery, Division of Public Health Sciences; Washington University in St Louis and Alvin J Siteman Cancer Center.

Background and Rationale

- Recurrence of disease following CRT is common in HPV-negative LA-HNSCC.[1-2]
- *CDKN2A* alterations (mutations or deletions) occur in 58% of cases of HPV-negative HNSCC, and results in cell-cycle deregulation and tumor growth.[3]
- Palbociclib, a selective CDK4/6 inhibitor, results in cell cycle arrest and, in some cases, cellular senescence.
- Palbociclib resulted in target lesion decrease in 25% of patients with *CDKN2A*-altered head and neck cancers (TAPUR trial).[4]
- In biomarker-unselected, cetuximab-resistant, HPV-negative RM-HNSCC, palbociclib + cetuximab resulted in an ORR of 19%. In platinum-resistant disease, the ORR was 39%.[5]
- In patients with *CDKN2A* altered, HPV-negative RM-HNSCC, the median OS was longer in those treated with palbociclib + cetuximab vs placebo + cetuximab (9.7 vs 4.6 mos) [Palatinus Trial].[6]

***CDKN2A* Altered** | ***CDKN2A* Wild-Type**



1) NEJM 2010, 2) JCO 2014, 3) Nature 2015, 4) JCO 2021, 5) Lancet Oncol 2019, 6) Oral Onc 2021

CONCLUSIONS

- **The primary hypothesis was met: the ORR with palbociclib in HPV-negative LA-HNSCC was 42%.**
- **The ORR with palbociclib was higher in *CDKN2A*-altered vs wild-type disease (67% vs 0%, p=0.002).**

Study Design

Eligibility
- Curable LA-HNSCC
- Lx, Hpx, OC, & p16- Opx
- Measurable Disease
- NGS of tumor

Baseline Assessments
- Exam, Labs
- CT neck

Step 1 of Tx
- Palbociclib 125 mg/d orally, days 1-21 of 28 day cycle
- 2 cycles of tx, then CT neck

Step 2 of Tx
- CRT: cisplatin + RT or cetuximab + RT
- Neck CT 2 months after CRT
- FDG-PET/CT 4 months after CRT

Step 3 of Tx
- Palbociclib x 6 cycles, beginning 16-22 weeks after CRT
- Monitor for disease recurrence

Primary Endpoint: ORR
Statistical Plan: A sample size of 24 patients yielded an 80% power if the ORR was >38%, using an exact binomial test of one sample proportion comparison with an upper one-sided nominal significance level of 0.05 and null ORR of <17%.

Results

Patient and Tumor Characteristics

Characteristic		Patients n = 24 (%)
Smoking History		
	Yes	23 (96%)
	No	1 (4%)
Primary Site		
	Larynx	15 (63%)
	Hypopharynx	4 (17%)
	Oropharynx	4 (17%)
	Oral Cavity	1 (4%)
Clinical Stage		
	III	7 (29%)
	IV	17 (71%)
***CDKN2A* Status**		
Altered		15 (62%)
	Mutation	8 (33%)
	Deletion	7 (29%)
Wild-type		9 (38%)

Tumor Response

Reponse		Patients (%)
Overall		
	CR + PR	10 (42%)
	CR	1 (4%)
	PR	9 (38%)
	SD	13 (54%)
	PD	1 (4%)
By *CDKN2A* Status		
	Altered	10 (67%)
	Wild-type	0 (0%)

CyC – NUEVAS DIANAS

#6016: Olaparib, a poly (ADP-ribose) polymerase (PARP) Inhibitor, in Combination with Pembrolizumab and Carboplatin as First-Line Treatment of Recurrent or Metastatic Head and Neck Squamous-Cell Carcinoma (RM-HNSCC): A Single-Arm, Phase 2 Trial

Jared Cohen, Jessica Ley, Jingxia Lu, Emma Haselhorst, Peter Oppelt, Douglas Adkins. Department of Medicine, Division of Oncology; Department of Surgery, Division of Public Health Sciences; Washington University in St Louis and Alvin J Siteman Cancer Center.

BACKGROUND & RATIONALE

The Homologous Recombination Phenotype (HRP)

- **HRP is common in HNSCC:**

Gene	Aberration	Frequency of aberration
ATM	Loss of function mutation	16%
ATR	Loss of function mutation	10%
BRCA2	Loss of function mutation	7%
BRCA1	Loss of function mutation	6%
FANCF	Promoter hypermethylation	15%
PTEN	Homozygous deletion	12%

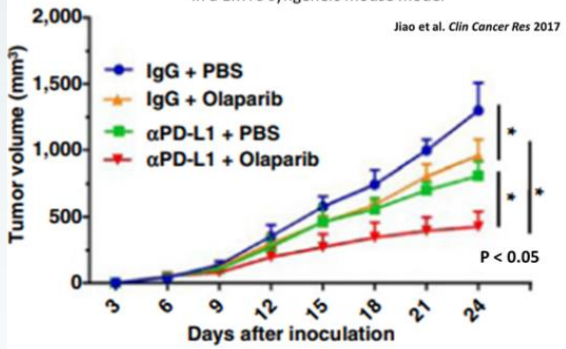
Chung et al. *Ann Oncol.* 2015; Seiwert et al. *Clin Cancer Res.* 2015; Marsit et al. *Oncogene* 2004; TCGA *Nature* 2015

- **HRP sensitizes HNSCC to PARP inhibition and platinum agents.** (Glorieux et al. *Oncotarget* 2017; Wruster et al. *Oncotarget* 2016; Lombardi et al. *Clin Cancer Res.* 2015)

- **Inhibitors of PARP and PD-1 have synergistic antitumor activity:**

Effects of olaparib and/or anti-PD-L1 antibody on tumor growth in a EMT6 syngeneic mouse model

Jiao et al. *Clin Cancer Res* 2017



- **Olaparib has been safely combined with pembrolizumab and carboplatin in patients with other cancer types.** (Rottenberg et al. *Proc Natl Acad Sci U S A* 2008, Lampert et al. *Oncotarget* 2019, Oza et al. *Lancet Oncol.* 2015).

CONCLUSIONS

- During stage 1 of this Simon two-stage phase 2 trial, first-line treatment of RM-HNSCC with olaparib, pembrolizumab and carboplatin resulted in an ORR of 67%.
- Olaparib delivery was high.
- Enrollment into stage 2 of the trial is ongoing.

CONQUER CANCER® THE ASCO FOUNDATION MERIT AWARD

Philip Francis Mulvey, III, Endowed Merit Award

Supported by Therese Marie Mulvey, MD, FASCO

STUDY DESIGN

Single-Arm, Phase 2 Trial

Eligibility
- Untreated, incurable, recurrent or metastatic HNSCC
- Oral cavity, oropharynx, larynx, and hypopharynx
- PD-L1 CPS ≥ 0
- Measurable disease
- ECOG PS 0-1
- Adequate organ function

→ **Baseline Assessments**
- Exam, labs
- CT NC
- Correlatives: Blood and archived tumor tissue

→ **Treatment**
Olaparib (200 mg bid days 1-10 of 21-day cycles for cycles 1-6 then 300 mg bid days 1-21)
+
Pembrolizumab (200 mg q21 days)
+
Carboplatin (AUC 5 q21 days for up to 6 cycles)

→ **On-Treatment Assessments**
- Exam, labs
- CT NC after every two cycles
- Correlatives: Blood at cycle 2 day 1, then at progression

Primary Endpoint: ORR
Secondary Endpoints: DoR, PFS, OS, AEs
Statistical Plan: Simon Optimal Two-Stage Design
H_0 ORR 36% H_1 ORR 62%
Type 1 error: 0.05 **Power:** 0.80 **Sample Size:** 29

Simon Two-Stage: ≥6 responses among 13 pts, accrue 16 more pts.

Reject H_0 if ≥14 responses observed in 29 pts.

Drug Delivery: At end of stage 1, assess olaparib delivery during cycles 1 and 2, with the goal of 100% delivery in ≥ 80% of patients.

RESULTS OF STAGE 1

Patient and Tumor Characteristics

Characteristic	Results (n = 12)
Median age	62 years (range 59-74)
Tobacco	
Yes	5 (42%)
No	7 (58%)
Primary site	
Oropharynx	7 (58%)
Oral cavity	4 (33%)
Larynx	1 (8%)
HPV status	
Positive	6 (50%)
Negative	6 (50%)
PD-L1 CPS status	
0	1 (8%)
1-19	4 (33%)
≥20	7 (59%)

Tumor Response and Drug Delivery

Characteristic	First-stage results (n = 12)
Best response	
CR	1 (8%)
PR	7 (58%)
SD	3 (24%)
PD	1 (8%)
Olaparib delivery (# of patients with 100% drug delivery during Cycles 1 and 2)	12 (100%)

SNC

CONCLUSIONES

- Cambio de paradigma en los gliomas de bajo grado y alto riesgo con enfermedad residual o recurrente con mutación de IDH1/2 – **Vorasidenib** – Aumenta SLP y tiempo hasta el siguiente tratamiento
- Hemangioblastomas en el contexto del sídrome VHL – **Belzutifam** – Excelente tolerancia, largas respuestas y SG no alcanzadas.
- Nuevas posibles técnicas para diferenciar PE SNC: 18F-fluciclovine
- Nuevas estrategias para el paciente anciano con GBM: Técnicas de fusión y protones
- Nuevos abordajes en GBM: Inh GITR y antiPD-1 con RT, Vacuna anti-telomerasa en GBM MGMT no metilado (POSIBILIDADES)
- Nuevas estrategias: Medicina personalizada (BRAF, IDH…)

CyC

CONCLUSIONES

- La adyuvancia del cáncer de cavum sin QT de inducción debe ser realizada con cisplatino y gemcitabina
- La QT inducción seguida de RT puede ser una alternativa a la QTRT en cáncer de cavum no candidato a inducción
- El tratamiento con sintilimab (anti-PD1) aumenta la SLP, con menor tasa de recaídas locales y a distancia, combinado con QT inducción y QTRT en cáncer de cavum.
- Se debe profundizar en esquemas de QTIO adaptada al paciente frágil en CECC, el combo de durvalumab y carboplatino-taxol semanal parece una alternativa a los esquemas actuales del pac unfit.
- Esquemas de desescalada de tratamiento tras QTIO basada en pueden ser una estrategia a plantear en el futuro para reducir dosis de RT o incluso en la preservación de laringe. QUEDA MUCHO
- Vamos avanzando hacia la medicina de precisión en los tumores de cabeza y cuello y se precisa de biomarcadores para seleccionar dianas a explorar: EGFR/TGFB, CDKN2A, HER2… (HRAS, PI3K…) Nos falta dar con la tecla correcta.

XXIII JORNADA DE REVISIÓN DEL

CONGRESO AMERICANO DE ONCOLOGÍA

Muchas gracias