

foro debate oncología

Zaragoza 26-29 septiembre 2023



Novedades en tumores de cabeza y cuello localmente avanzado

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26 de Septiembre de 2023

Tumores de cabeza y cuello localmente avanzados (estadios III-IVb)

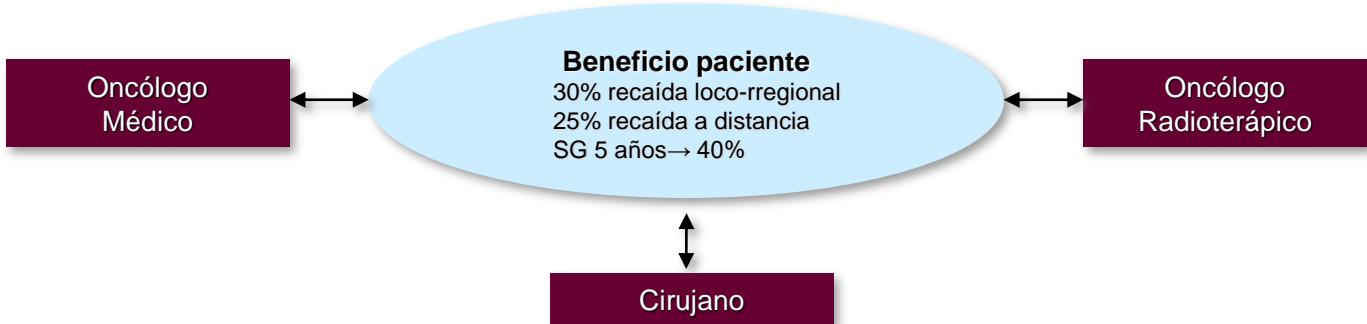


Alta complejidad

- ECOG
- Comorbilidad
- Preferencias paciente
- Localización
- Resecabilidad

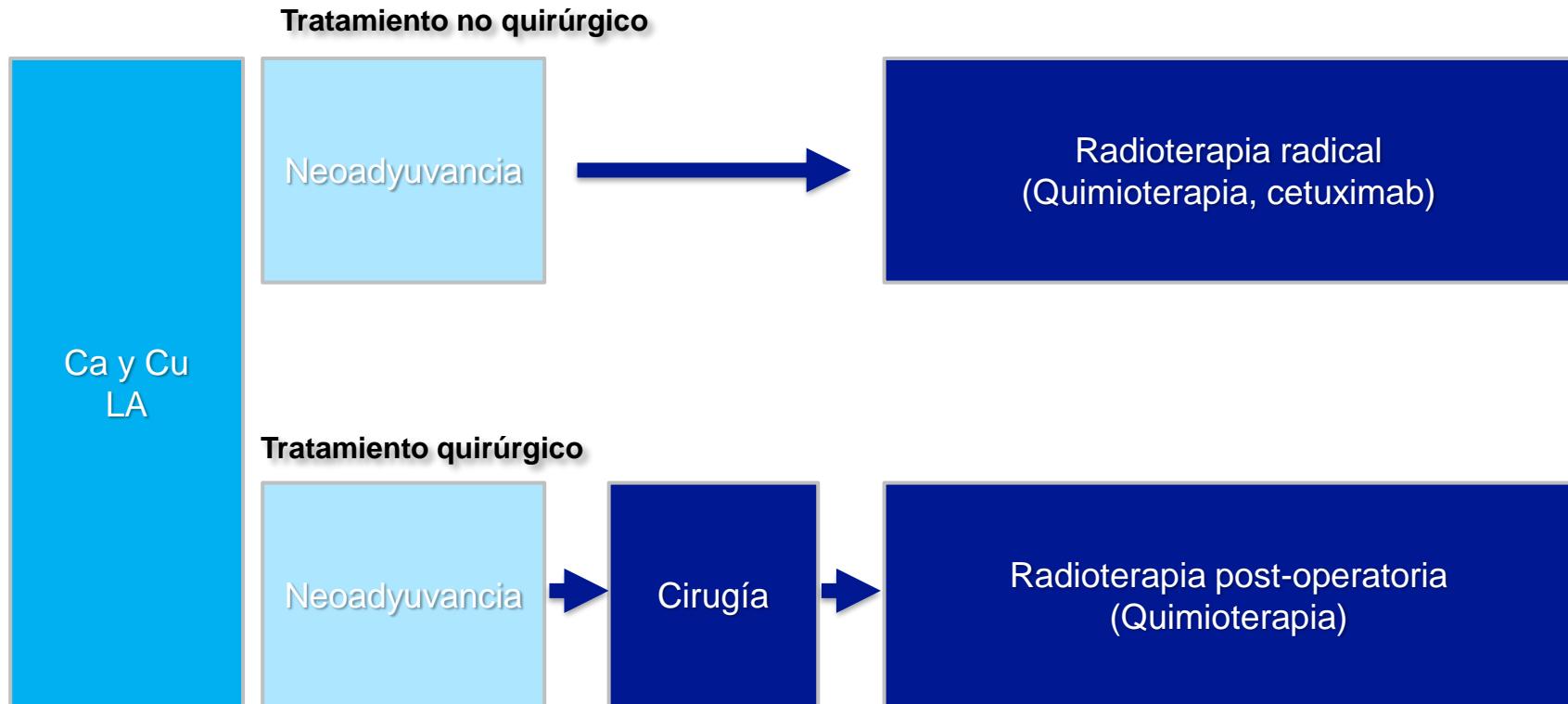
Objetivos

- Curación, aumento de supervivencia
- Preservación órgano (tumores resecables)





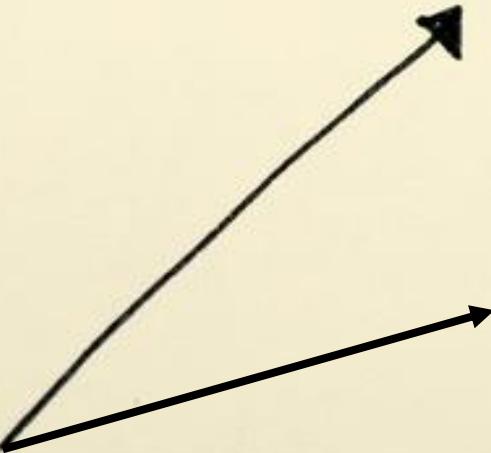
Este es el escenario terapéutico en el que nos movemos (más o menos...)





¿Novedades en tumores de
cabeza y cuello localmente
avanzado?

Expectations





“A la vida le basta el espacio de una grieta para renacer”
Ernesto Sábato





Tratamiento no quirúrgico

Ca y Cu
LA



Radioterapia radical
(Quimioterapia, cetuximab)

- Quimio-radioterapia con cisplatino a dosis altas sigue siendo el tratamiento estándar¹
- Radioterapia concomitante con cetuximab en pacientes unfit cisplatino²

1. NCCN Clinical Practice Guidelines Head and Neck Cancer 2020
2. Bonner JA, et al. Lancet Oncol 2010



Tratamiento no quirúrgico



Radioterapia radical
(Quimioterapia, cetuximab)

- Quimio-radioterapia con cisplatino a dosis altas sigue siendo el tratamiento estándar¹
- Radioterapia concomitante con cetuximab en pacientes unfit cisplatino²
- Quimioterapia de inducción en pacientes seleccionados, si se usa TPF³

1. NCCN Clinical Practice Guidelines Head and Neck Cancer 2020
2. Bonner JA, et al. Lancet Oncol 2010
3. locca O, et al. Oral Onol 2018



Tratamiento no quirúrgico



Ca y Cu
LA

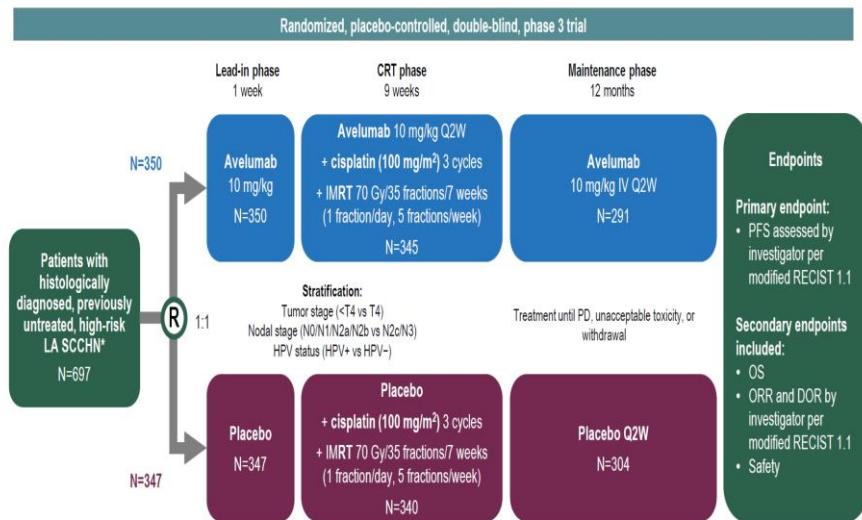
Radioterapia radical
(Quimioterapia, cetuximab)

Inmunoterapia

- Quimio-radioterapia con cisplatino a dosis altas sigue siendo el tratamiento estándar¹
- Radioterapia concomitante con cetuximab en pacientes unfit cisplatino²
- Anti-PD1 han demostrado beneficio en enfermedad recurrente o metastásica^{3,4,5}

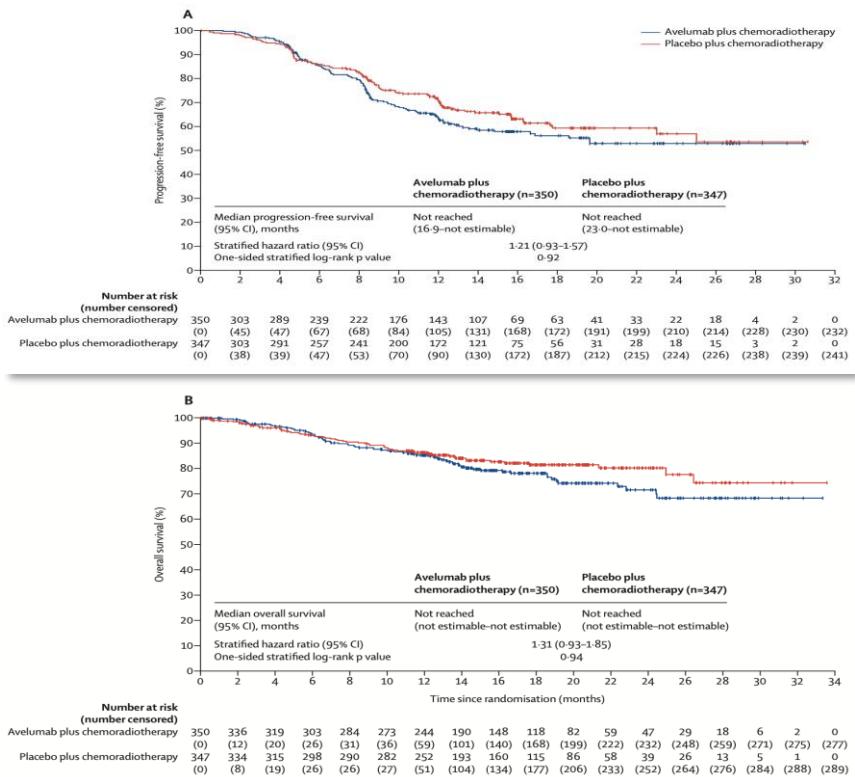
1. NCCN Clinical Practice Guidelines Head and Neck Cancer 2020
2. Bonner JA, et al. Lancet Oncol 2010
3. Burtness B, et al. Lancet 2019
4. Cohen E W, et al. Lancet 2019
5. Ferris RL, et al. Ann Oncol 2020

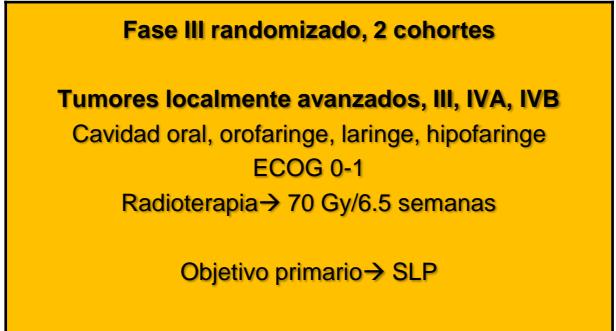
Avelumab plus standard-of-care chemoradiotherapy versus chemoradiotherapy alone in patients with locally advanced squamous cell carcinoma of the head and neck: a randomised, double-blind, placebo-controlled, multicentre, phase 3 trial



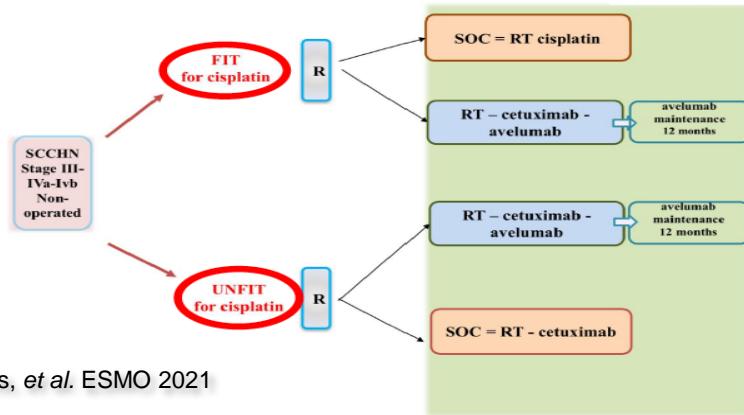
DOR, duration of response; HPV, human papillomavirus; IMRT, intensity-modulated radiation therapy; IV, intravenously; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; Q2W, every 2 weeks; R, randomized; RECIST 1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

* High-risk LA SCCHN (oral cavity, oropharynx, larynx, or hypopharynx); HPV-negative disease stage III, IVa, IVb; nononcopharyngeal HPV-positive disease stage III, IVa, IVb; HPV-positive oropharyngeal disease T4 or N2c or N3 (TNM staging per AJCC, 7th edition).





Study design (II) & run in safety phase



Bourhis, et al. ESMO 2021

Cohort fit : summary

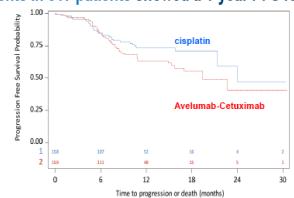
430 patients randomized

The number of PFS events was not reached, at the time of analysis

The planned interim analysis for futility based on 89 events in 317 patients showed a 1-year PFS rate of :

73% (95%CI 65%-81%) in SOC-cisplatin-RT
vs
64% (95%CI 54%-72%) in Avelumab-Cetuximab-RT

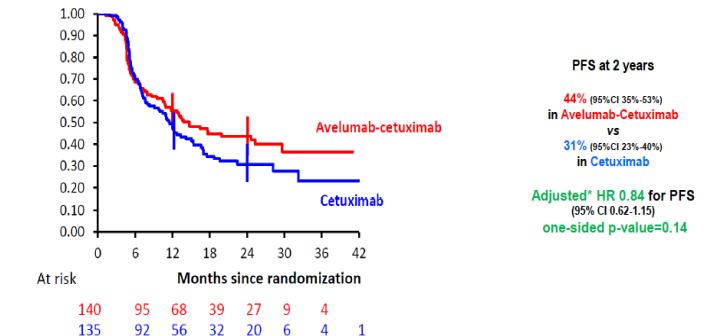
→ HR 1.27 (95%CI 0.83-1.93),
crossing the futility boundary



Unfit Cohort : Primary endpoint

Kaplan Meier estimate of progression free survival (PFS)

Median follow-up = 21.3 months (IQR 14.6-28.3) (similar in both arms)

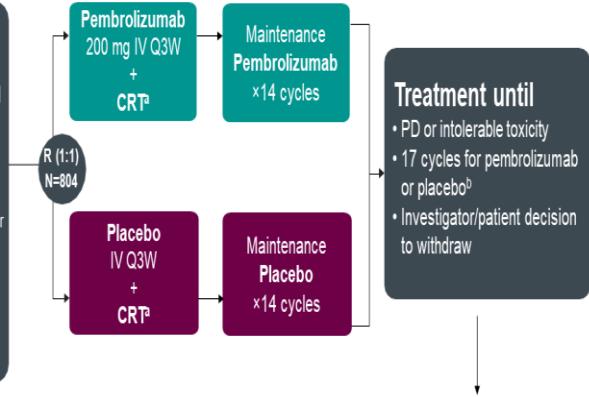




KEYNOTE-412 Study Design (NCT03040999)

Patients

- Newly diagnosed, pathologically proven, treatment-naïve unresected LA HNSCC
- T3-T4 [N0-N3] or any N2a-3 [T1-T4] larynx/hypopharynx/oral cavity/ p16-negative oropharynx cancers
- T4 or N3 p16-positive oropharynx cancer
- Evaluable tumor burden per RECIST v1.1
- ECOG PS 0 or 1
- Candidates for definitive high-dose cisplatin-based CRT



Stratification Factors

- Radiotherapy regimen (AFX vs SFX)
- Tumor site/p16 status (oropharynx [p16+ vs p16-] or larynx/hypopharynx/oral cavity)
- Disease stage (III vs IV)

Primary endpoint

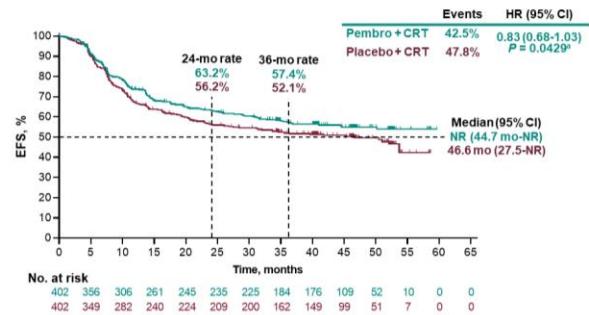
- Event-free survival (EFS)

Secondary endpoints included:

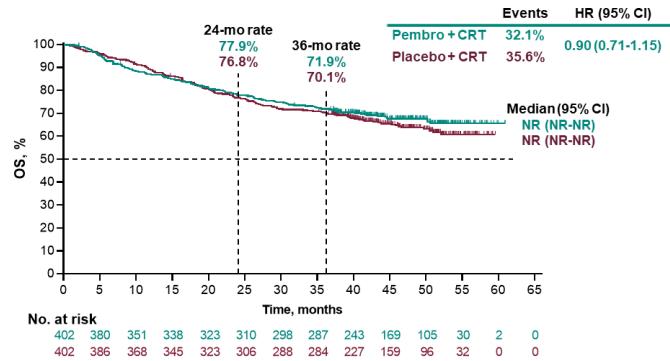
- OS
- Safety/tolerability

Machiels J-P, et al. ESMO 2022

Event-Free Survival, ITT Population

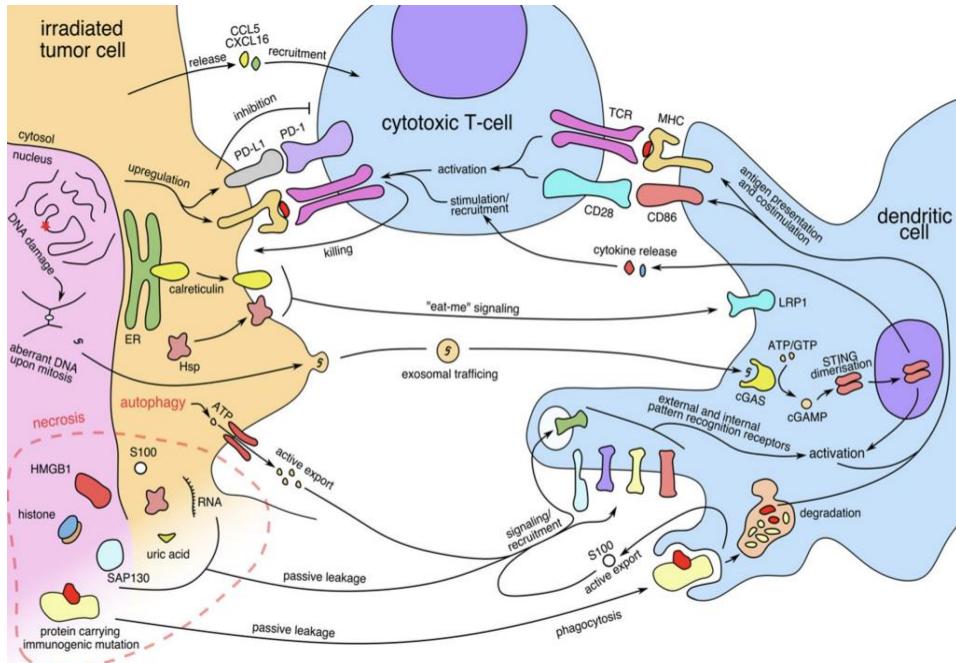


Overall Survival, ITT Population





Radioterapia + Inmunoterapia



Radiotherapy as a Backbone for Novel Concepts in Cancer Immunotherapy.
Kabiljo J, et al. Cancers 2020

1. Liberación de DAMPs (ATP, calreticulina y HMGB)
2. Liberación de DNA citosólico → STING → INF tipo 1
3. Presentación antigenica → péptidos intracelulares
4. Regulación positiva MHC
5. Liberación citocinas inmunoestimuladoras

Favorecen el desarrollo respuesta inmune específica





Tratamiento no quirúrgico

Ca y Cu
LA





IAP (XIAP, cIAP1/2)

Bloquean la apoptosis → Supervivencia

Sobre-expresión → Tumores de cabeza y cuello, mal pronóstico, resistencia fármacos antitumorales

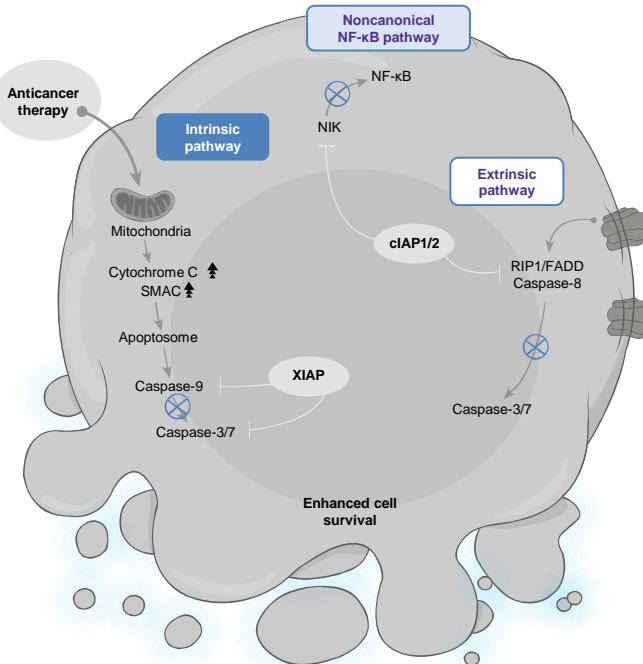
Intrinsic pathway

- XIAP directly blocks caspase-9 and caspase-3/7

Extrinsic pathway

- cIAP1/2 prevent formation of the pro-apoptotic signaling complex (extrinsic pathway) and block NIK activity (noncanonical NF-κB pathway)

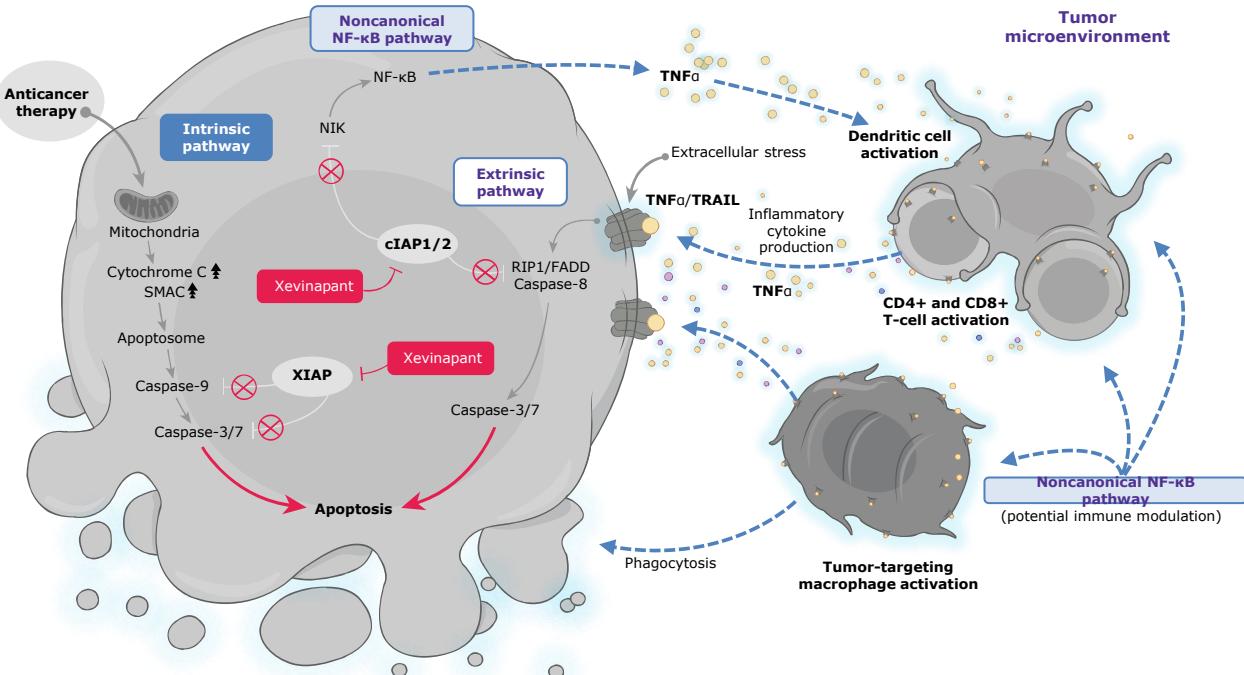
IAP activity is blocked by
the endogenous antagonist **SMAC**,
which promotes apoptotic signaling^{1,2,7-9}



Xevinapant → Pequeña molécula, first-in-class, oral Inhibidor de IAP Promueve la apoptosis Mejora eficacia radioterapia y cisplatino



- Inhibiting **XIAP**, which releases the blockade on downstream caspase activity in the **intrinsic apoptotic pathway**
- Inhibiting **cIAP1/2**, which promotes pro-apoptotic TNF receptor signaling via the **extrinsic apoptotic pathway** and induces TNF α expression via the **noncanonical NF- κ B pathway**



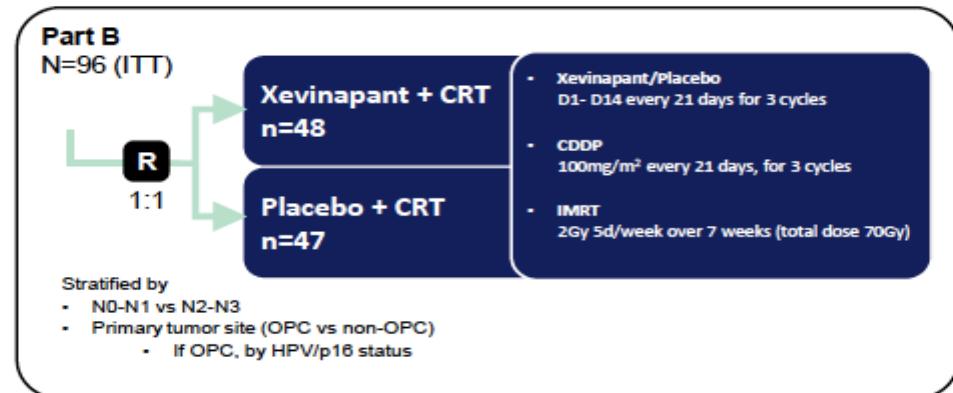


STUDY DESIGN

Double-blind, placebo-controlled, Randomized Phase II

Part A
N=14
Dose escalation
Phase I*
Primary endpoint
Definition of MTD/RP2D

RP2D
200mg QD

**Main inclusion criteria:**

- Previously untreated, unresectable stage III, IVA & IVB LA-SCCHN
- Oral cavity
- Hypopharynx
- Larynx
- Oropharynx-HPV/p16 both negative or positive

Primary endpoint

- Locoregional control rate at 18 months after CRT
(Δ>20% between arms with 0.8 power at 0.2 significance level)

Main secondary endpoints

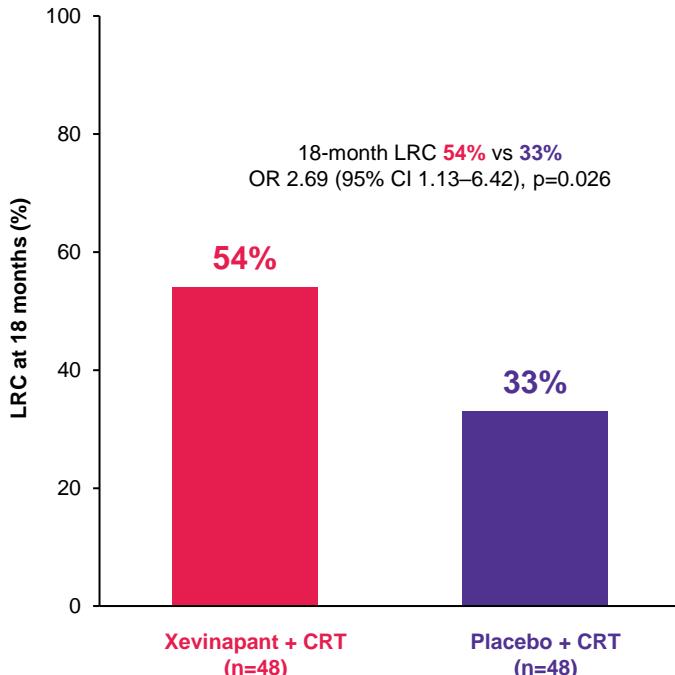
- PFS
- Duration of LRC
- Overall survival

ClinicalTrials.gov Identifier: NCT02022098.
* Tao et al. ESTRO 2016

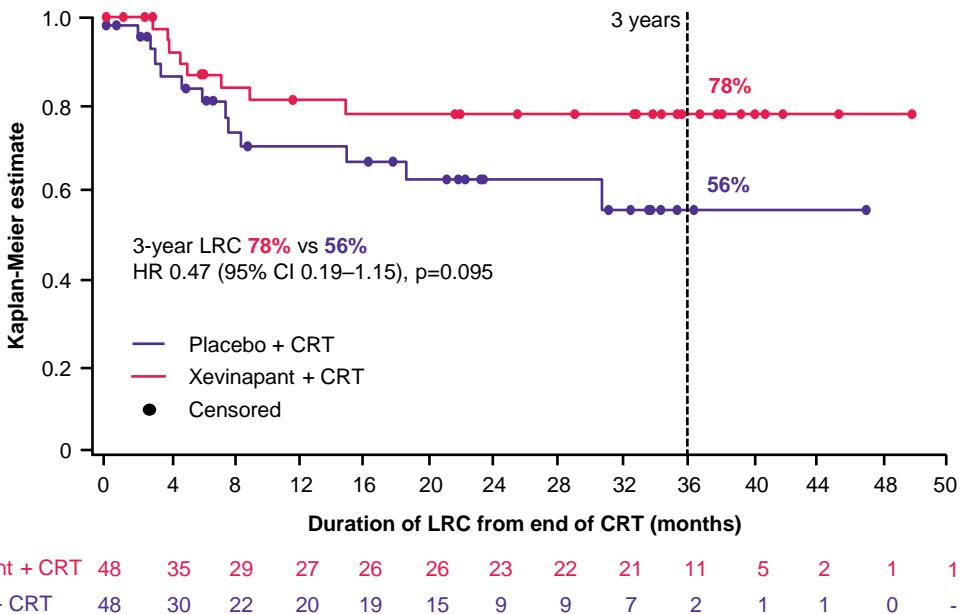


Xevinapant (Debio 1143) → Control locoregional

Primary endpoint: proportion of patients with LRC at 18 months after CRT (ITT population)



Secondary analysis: LRC after 3 years (ITT population)



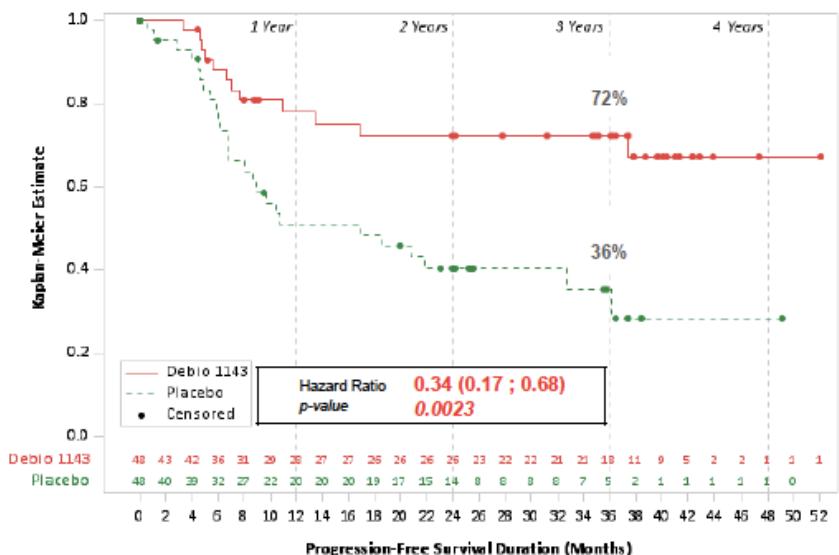


Xevinapant (Debio 1143) → SLP

VIRTUAL
2020 ESMO congress

Duration of PFS - 3-year follow up

As per investigator, with censoring for late events* – ITT



Median PFS

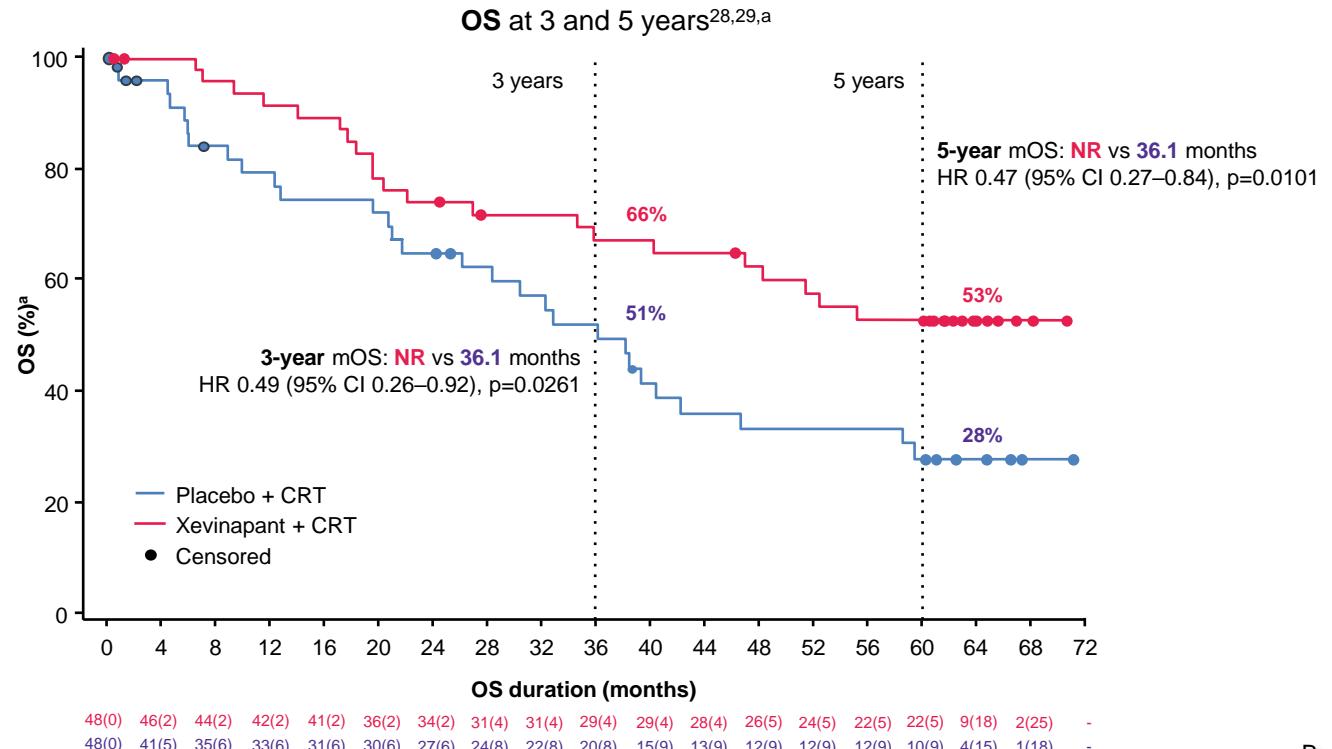
- Placebo: 16.9 months
(95%CI: 6.8 - 36.1)
- Xevinapant: Not reached (95%CI: 37.4- NR)

Statistically significant, clinically compelling PFS improvement

* Late events: those occurring after missed assessments: censored to avoid assumption of non-PD for long periods before PD identified (FDA guidance)



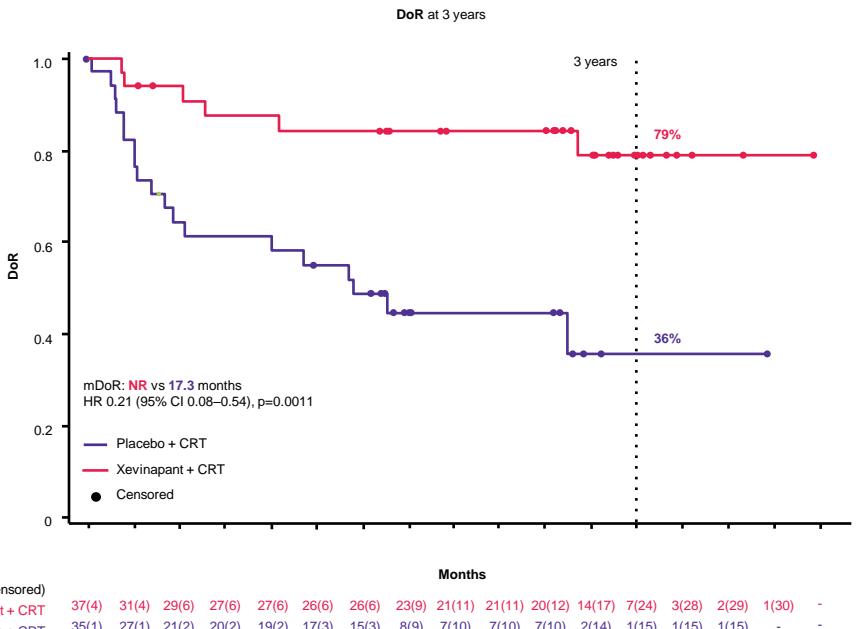
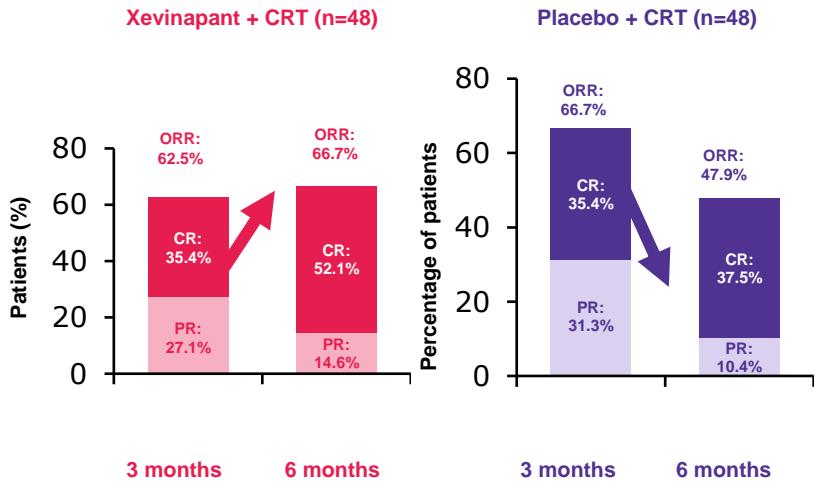
Xevinapant (Debio 1143) → SG



Bourhis J, et al. ESMO 2022



Xevinapant (Debio 1143)→ Respuestas



Sun X-S, et al. Lancet Oncol 2020

Bourhis J, et al. Ann Oncol 2022. Abstract LBA 33



Xevinapant (Debio 1143)→ Toxicidad

Most common TEAEs	Xevinapant + CRT (n=48), n (%)			Placebo + CRT (n=47 ^b), n (%)		
	Grade 1–2	Grade 3	Grade ≥4	Grade 1–2	Grade 3	Grade ≥4
Any	7 (15)	41 (85)	9 (19)	6 (13)	29 (62)	12 (25)
Mucositis	21 (44)	15 (31)	0	22 (47)	10 (21)	0
Dysphagia	10 (21)	24 (50)	0	19 (40)	10 (21)	0
Anemia	12 (25)	17 (35)	0	15 (32)	11 (23)	0
Weight loss	27 (56)	0	0	22 (47)	0	0
Radiation skin injury	24 (50)	1 (2)	0	17 (36)	3 (6)	0
Nausea	19 (40)	2 (4)	0	16 (34)	1 (2)	0
Xerostomia	19 (40)	1 (2)	0	18 (38)	0	0
Dermatitis	16 (33)	2 (4)	0	17 (36)	1 (2)	0
Neutropenia	4 (8)	7 (15)	4 (8)	4 (9)	11 (23)	2 (4)
Tinnitus	15 (31)	0	0	10 (21)	0	0
ALT increased	7 (15)	6 (13)	0	6 (13)	2 (4)	0
AST increased	6 (13)	3 (6)	0	2 (4)	1 (2)	0
Acute kidney injury	8 (17)	2 (4)	0	3 (6)	4 (9)	0
Blood creatinine increased	4 (8)	0	0	5 (11)	1 (2)	0
Renal failure	3 (6)	1 (2)	0	5 (11)	0	0
Chronic kidney disease	2 (4)	1 (2)	0	0	2 (4)	0

**Estudio Fase III (Trilynx)
en marcha...**



Tratamiento no quirúrgico





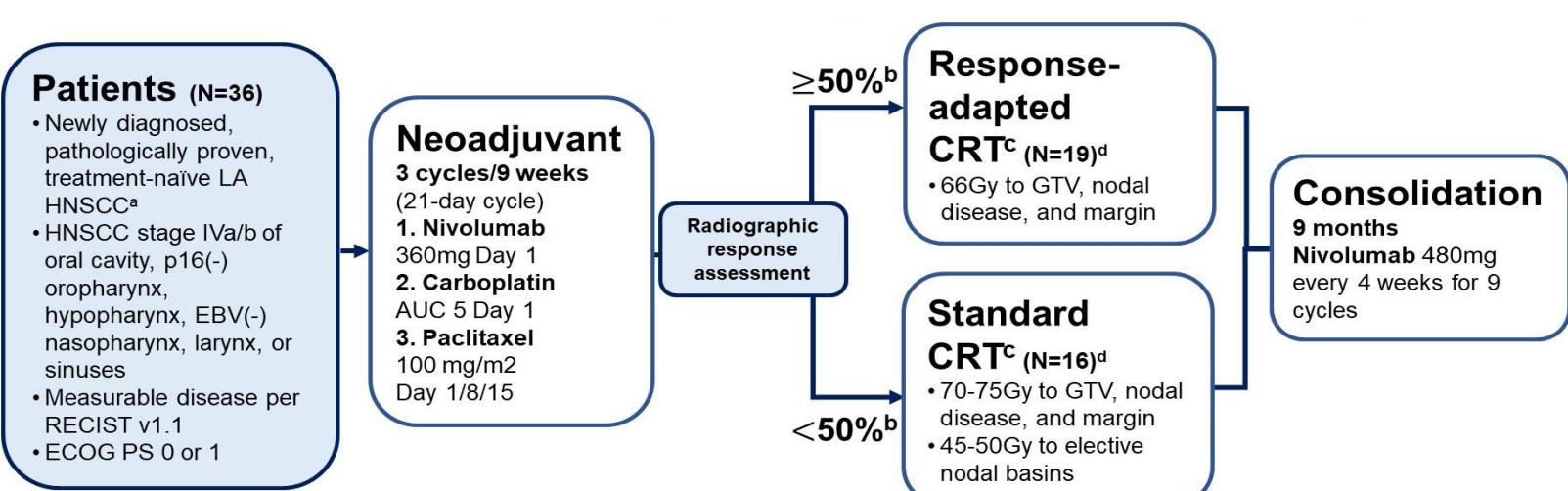
Ensayos clínicos neoadyuvancia (Inmunoterapia + Quimioterapia)

Autor/ Estudio	Pacientes	N	Inmunoterapia	Quimioterapia	Objetivo primario	Resultados
Zinner, ESMO 2020/ NCT03342911	Estadio III-IV Orofaringe HPV+	32	Nivolumab	Carboplatino- Paclitaxel x 6	pCR	42% pCR HPV- 50% pCR HPV+
Rosenberg, ASCO 2021/ NCT03107182 Estudio OPTIMA II	Orofaringe HPV+ T3-4, N2-3	72	Nivolumab	Carboplatino-Nab- paclitaxel x 3	Respuestas profundas ($\geq 50\%$) RECIST 1.1	70%
Hecht, ASCO 2021/ NCT03426656 CheckRad-CD8	Estadios III-IV	80	Durvalumab + Tremelimumab	Cisplatino- Docetaxel	Factibilidad Cambios CD8 intratumoral	82% SLP 2 años → 73% SG 2 años → 86%

Adaptado de Argiris A, ESMO 2021



Neoadjuvant nivolumab, paclitaxel, and carboplatin followed by response-stratified chemoradiation in locoregionally advanced HPV negative head and neck squamous cell carcinoma (HNSCC): The DEPEND trial.



Primary endpoint

- Deep response rate (DRR) (50% or greater response per RECIST v1.1 criteria) after neoadjuvant chemoimmunotherapy.

Secondary endpoints

- Overall survival
- Progression free survival
- Locoregional control
- Distant control

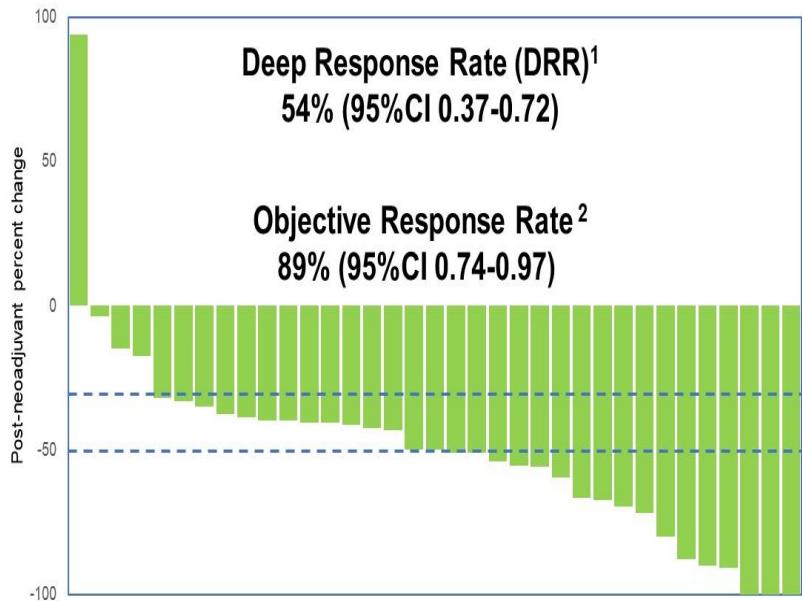
Post-treatment follow-up to assess

- Safety
- Disease status
- Survival



DEPEND Trial → Respuestas

Percent Change in Sum of Target Lesions from Baseline (N=35)



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)	

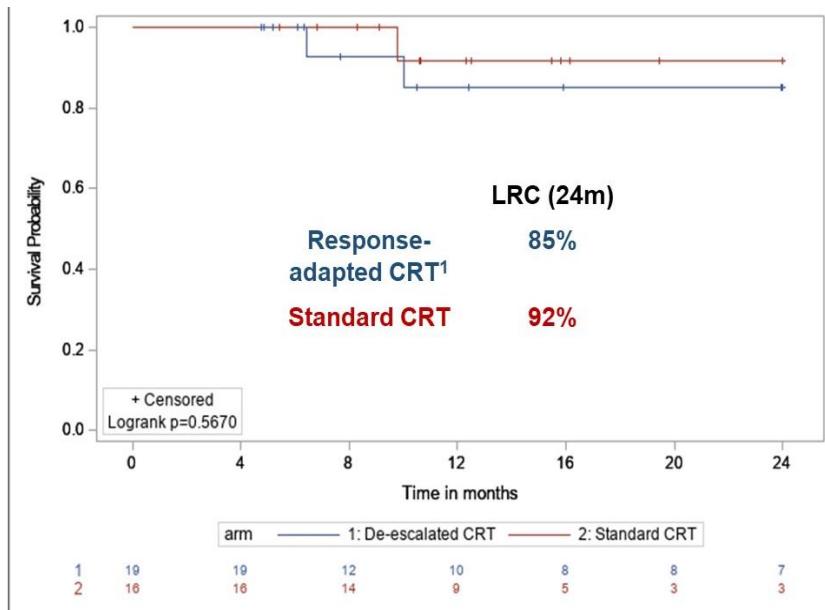
PD-L1 Combined Positive Score (CPS)	Deep Response ^a n=19	Suboptimal Response ^b n=16	Total n=35	p-value
CPS < 20, n (%)	14 (73.7)	13 (81.3)	27 (77.1)	0.77
CPS ≥ 20, n (%)	5 (26.3)	3 (18.8)	8 (22.9)	

^aDeep Response ($\geq 50\%$ tumor shrinkage per RECIST v1.1)

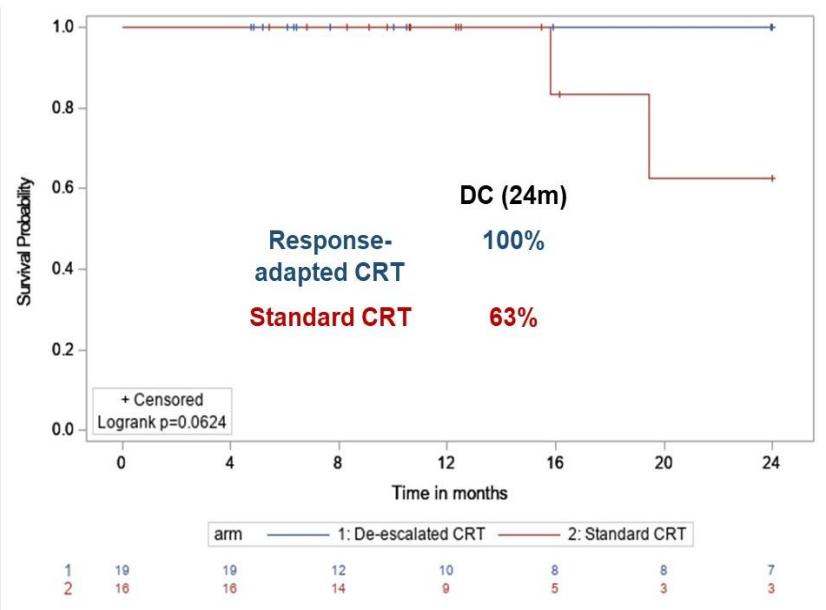
^bSuboptimal Response (<50% tumor shrinkage per RECIST v1.1)



DEPEND Trial → Control locoregional y a distancia

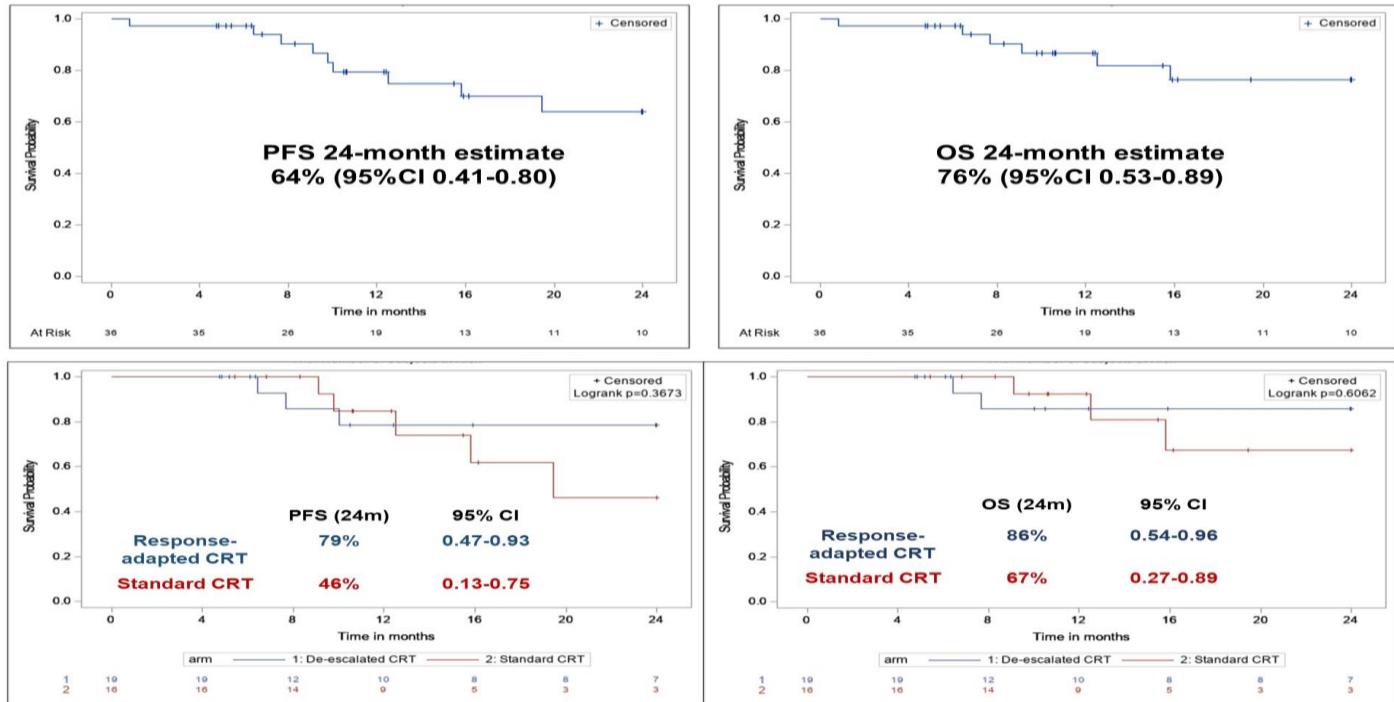


¹No nodal failures in omitted nodal regions





DEPEND Trial → SLP y SG



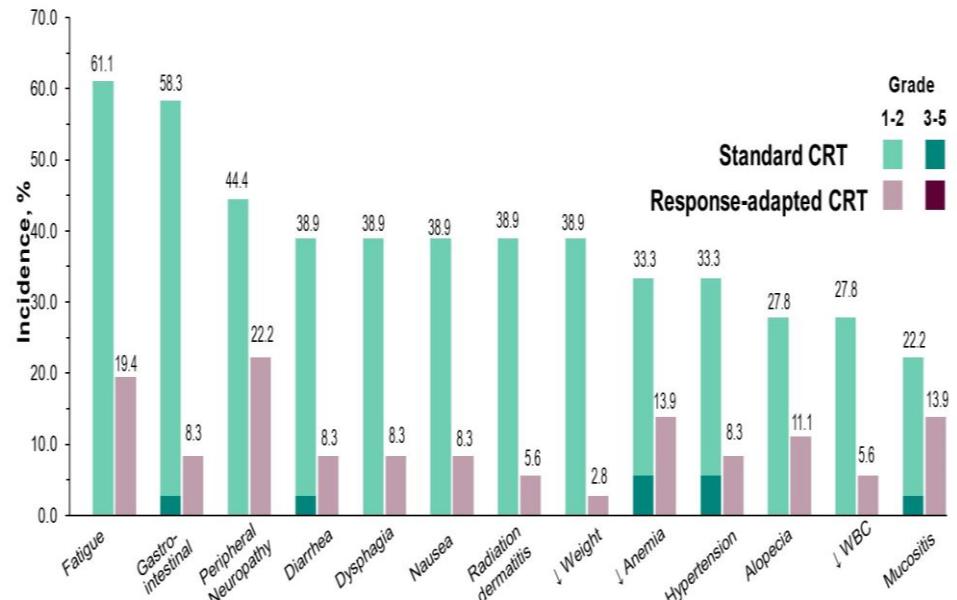


DEPEND Trial → Toxicidad

Quimio-inmuno inducción

Adverse event (CTCAE v5)	All Grades (N=36)	Grades 3-5 (N=36)
N patients with ≥1 AE (%)	36 (100)	17 (47)
Gastrointestinal toxicity	33 (92)	1 (3)
Fatigue	28 (78)	0 (0)
Peripheral neuropathy	25 (69)	0 (0)
Anemia	22 (61)	2 (6)
Neutropenia	2 (6)	2 (6)

Quimio-radioterapia





Ca y Cu
LA

Tratamiento quirúrgico

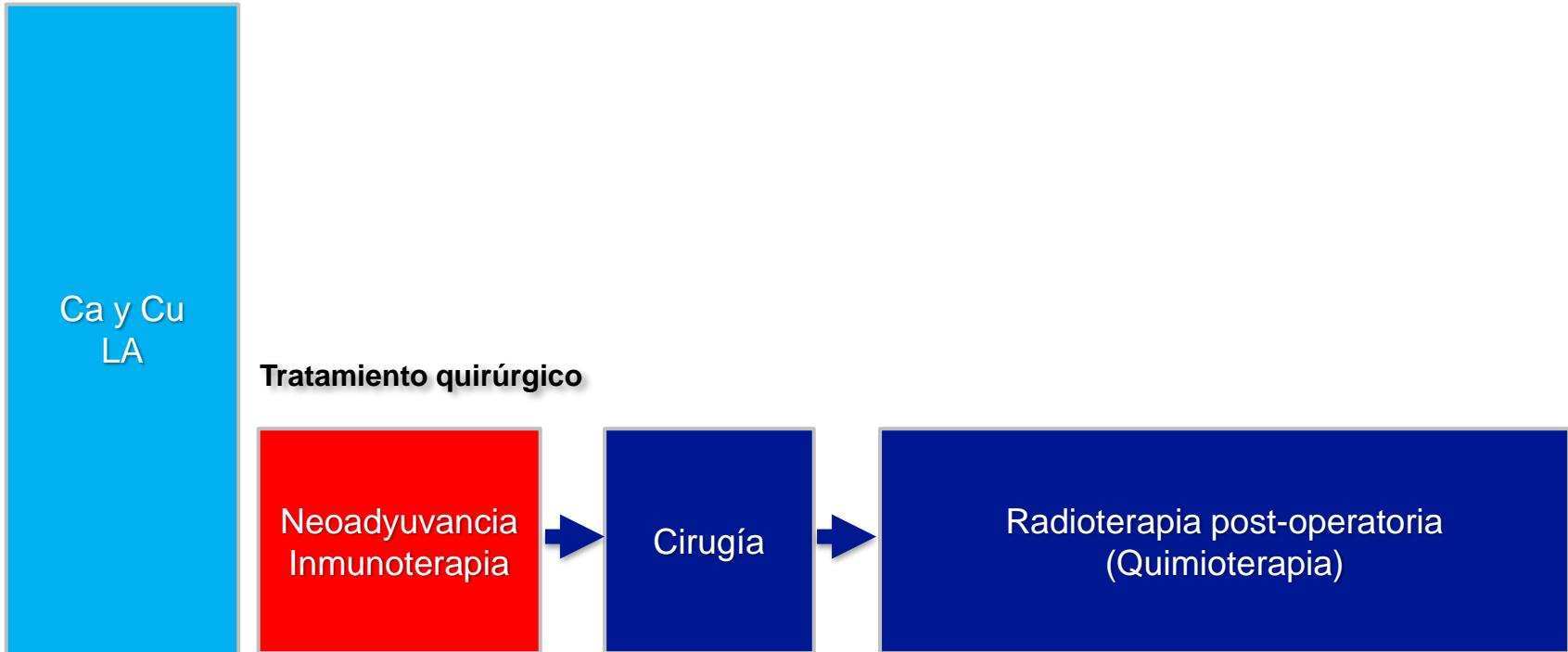
Cirugía



Radioterapia post-operatoria
(Quimioterapia)

- Tratamiento elección algunas localizaciones o no respuesta inducción como preservación órgano¹
- Tratamiento adyuvante pacientes alto riesgo → Cisplatino 100 mg/m²/3 s + RT 66 Gy
- Alto riesgo → Margen afecto y/o afectación ganglionar extracapsular
- 2 estudios pivotales (RTOG95-01² y EORTC22931³) y su análisis combinado⁴ confirman la eficacia

1. NCCN Clinical Practice Guidelines Head and Neck Cancer 2020
2. Cooper JS, *et al.* N Engl J Med 2004
3. Bernier J, *et al.* N Engl J Med 2004
4. Bernier J, *et al.* Head Neck Cancer 2005





Ensayos clínicos neoadyuvancia (agente anti-PD-1)

Autor/ Estudio	Pacientes	Fármaco Dosis	Adyuvancia	N	Criterios de respuesta	Respuestas
Ferris JTC 2021/ CheckMate 358	Estadio III-IVB HPV+/HPV-	Nivolumab 2	No	52	pPR→ 10-50% RTV MPR→ ≤ 20% RTV pCR→ 0% RTV	HPV+→ 23.5% (3pPR/1MPR) HPV-→ 6% (1pPR)
Uppaluri CCR 2020/ NCT02296684- Cohorte 1	Estadios III/IVB HPV-	Pembrolizumab 1	Pembrolizumab en alto riesgo	36	pTR-0→ < 10% pTR-1→ 10-49% pTR-2→ ≥ 50%	pTR-1→ 22.2% pTR-2→ 22.2% 2 MPR
Uppaluri ASCO 2021/ NCT02296684-Cohorte 2	Estadios III-IVB HPV-	Pembrolizumab 2	No	28	pTR-0→ < 10% pTR-1→ 10-49% pTR-2→ ≥ 50%	pTR-1→ 7.1% pTR-2→ 42.9%
Wise-Draper ASCO 2018 & 2021 NCT02641093	Estadios III-IVB HPV-	Pembrolizumab 1	Pembrolizumab	92	NPR < 20% pPR 20-89% MPR ≥ 90%	pPR 30% MPR 8% 1/34 pCR

PR→ Respuesta parcial

MPR→ Respuesta mayor patológica

RVT→ Tumor residual viable

TR→ Respuesta tumoral

NPR→ No respuesta patológica

pPR→ Respuesta parcial patológica

pCR→ Respuesta completa patológica

Adaptado de Argiris A, ESMO 2021



Ensayos clínicos neoadyuvancia (Combinaciones)

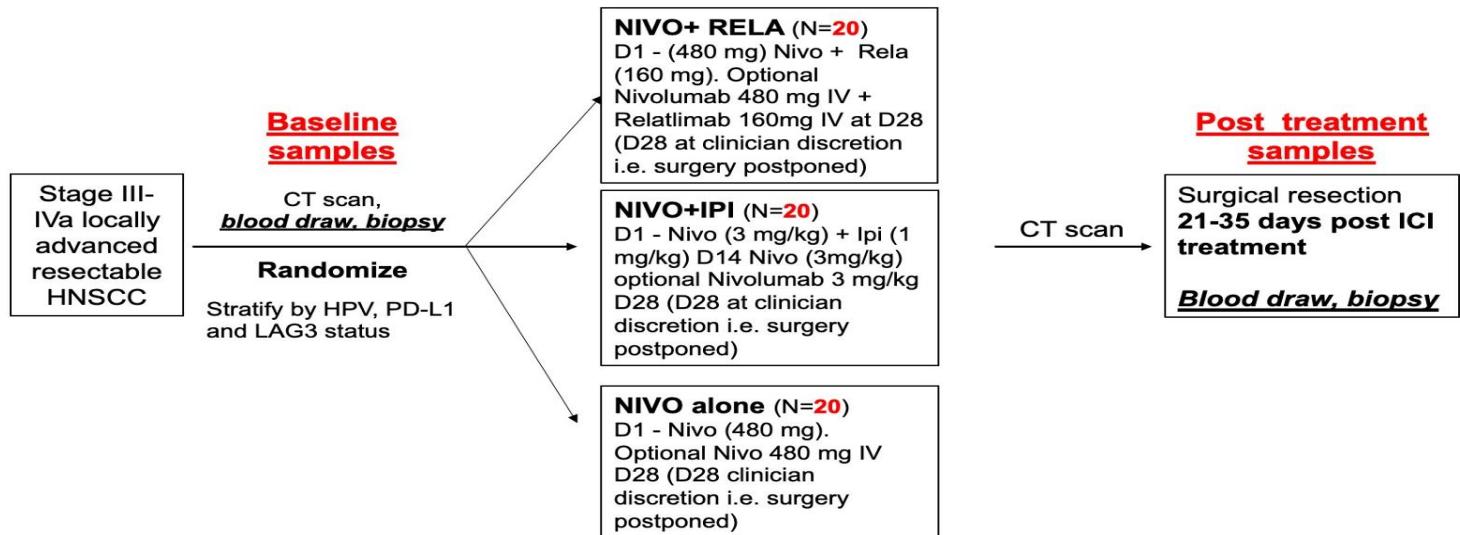
Autor/ Estudio	Pacientes	N	Tratamiento	Objetivo primario	Definición Respuesta	Respuestas	Toxicidad grados 3-4
Zurr ESMO 2020/ IMCISION (2 cohorts)	Estadio II-IVB Recurrentes HPV-	32	Nivolumab, Nivolumab + IpiLimumab	Retraso en cirugía; respuestas, impacto hipoxia en linfocitosT	NPR → < 20% pPR → 20-89% MPR → ≥ 90%	62% (1/6 MPR Nivo y 8/26 MP Nivo +Ipi)	34%
Schoenfeld, JAMA 2020/ NCT02919683 Randomizado	Cavidad oral Estadios II-IVA	30	Nivolumab +/- IpiLimumab	Respuestas; TRAEs, DLTs y retraso en cirugía	pTR-0 → <10% pRT-1 → 10- 49% pTR-2 → 50%	(54%, 1 MPR Nivo y 73%, 3 MPR Nivo +Ipi)	10%
Ferrarotto CCR 2021/ NCT03144778-CIAO Randomizado	Estadios II/IVA Recurrentes	29	Durvalumab +/- Tremelimumab	Cambio en densidad CD8	MPR → 90%	MPR 8% No diferencia añadir Tremelimumab	14%

Adaptado de Argiris A, ESMO 2021



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

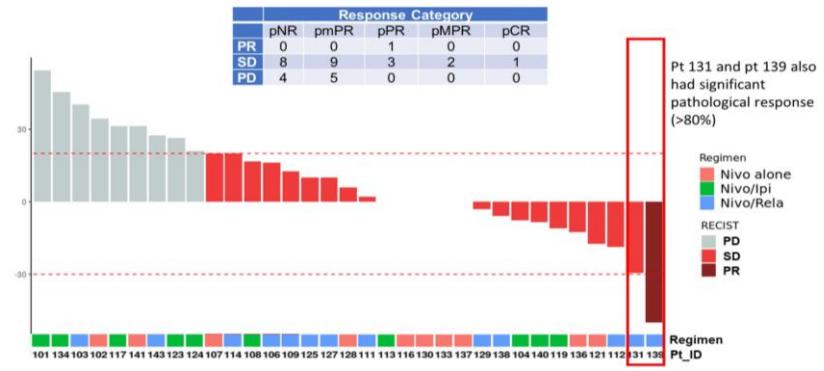
18-139 Trial Schema



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Clinical outcome: Radiographic response (N=33)

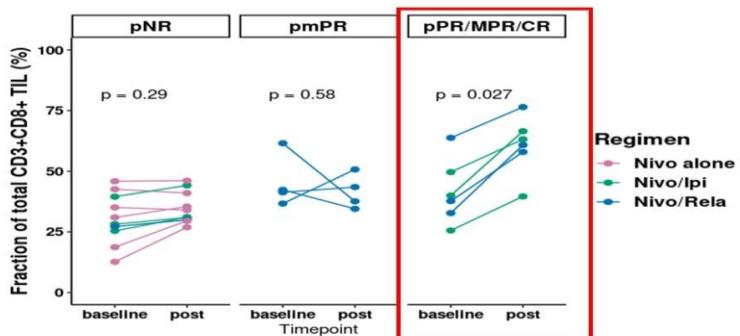


Nivolumab plus Relatlimab treatment may be associated with better pathological response

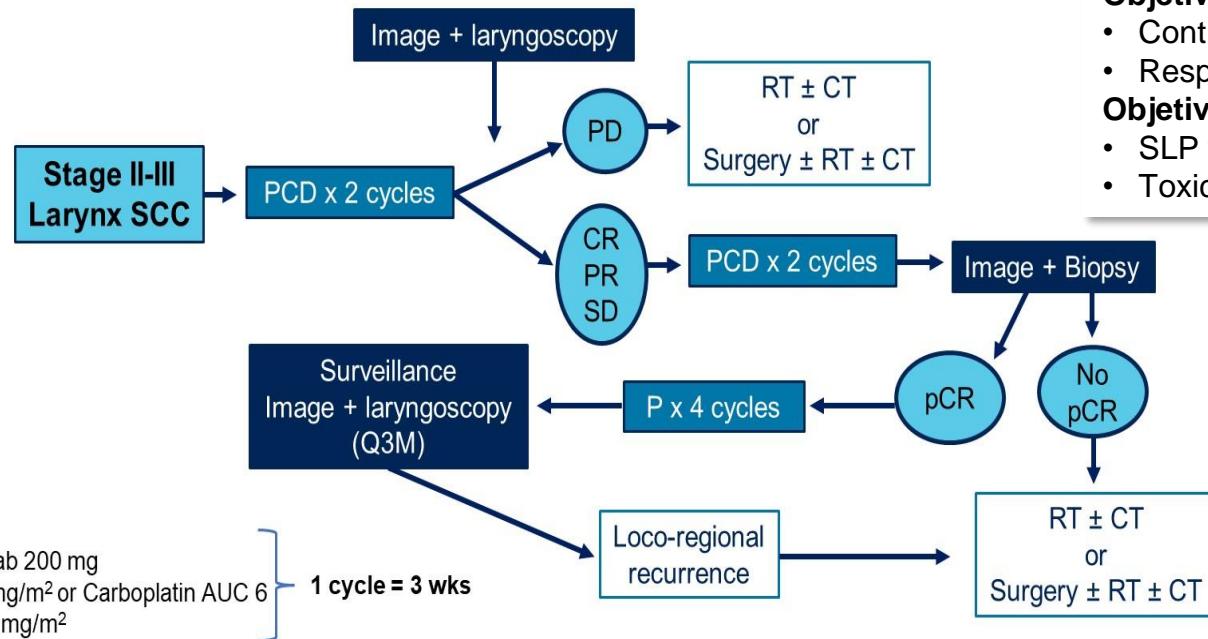
Pathologic Parameter	All Patients	Pathological response category					p-value
		pNR	pmPR	pPR	pMPR	pCR	
Treatment (n=33)							
Nivolumab alone	6	4	0	0	0	0	
Nivolumab + Ipilimumab	4	3	2	1	0	0	
Nivolumab + Relatlimab	2	7	2	1	1	1	0.0667
PD-L1(n=32)							
<1%	0	4	1	1	0	0	
>1%	12	9	2	2	1	1	0.1817
LAG3 (n=32)							
<1%	4	4	0	0	0	0	
>1%	8	9	3	2	1	1	0.2385
PD-L1 >1% & LAG3 >1 % (n=13)							
Yes	1	4	2	1	1	1	0.2126
No	1	3	0	0	0	0	

Nivo/Rela in >1 PD-L1 and >1LAG3 which is that more patients with combined positivity had a > 50% path response (4 vs. 0)

Biomarcadores
Respuesta completa → Aumento TILs
Expresión LAG3 → Respuesta



Immuno-Chemotherapy as single treatment modality for Larynx Preservation (ICoLP)



Objetivos primarios

- Control locorregional tras 2 ciclos
- Respuesta completa tras 4 ciclos

Objetivos secundarios

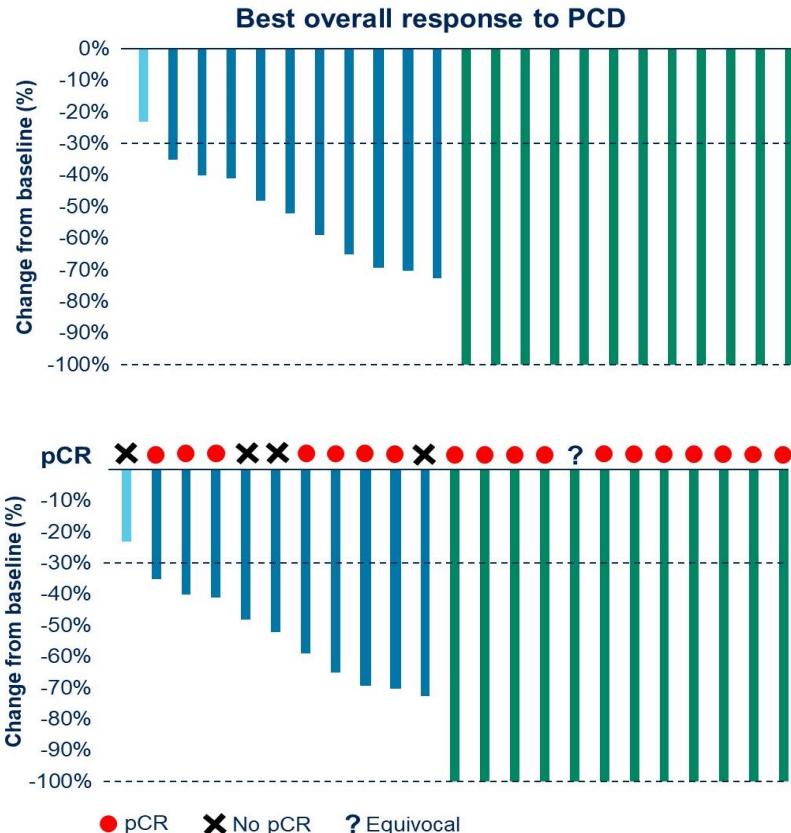
- SLP y SG
- Toxicidad

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Tras 2 ciclos

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%)



Tras 4 ciclos

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

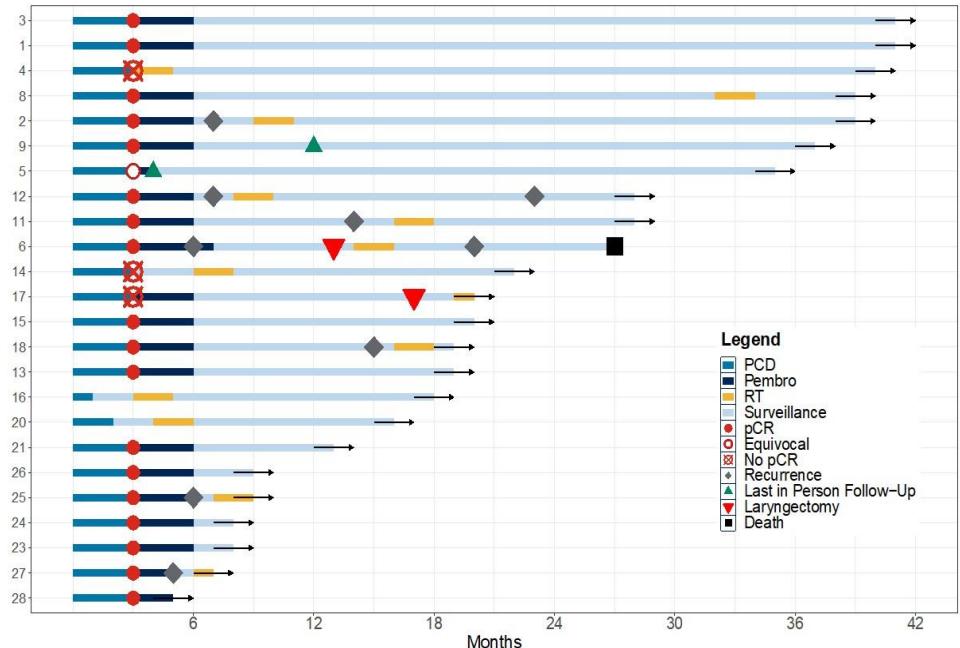
Tratamiento de rescate

- Non-pCR (N=4)
 - RT (N=1); CRT (N=2)
 - Laryngectomy and post-op SBRT (N=1) (S/P CRT for BOT SCC)
- Recurrent pCR (N=7)
 - CRT (N=5), RT (N=1)
 - Laryngectomy and post-op CRT (N=1)
 - refusal of CRT at recurrence and LOF for 4 mos;
 - presented to the ER with stridor, tumor no longer amenable to CRT



Larynx preservation, Recurrence, and Survival

- Median FU: 20.4 mos (4.6 – 41.4 mos)
- LPR: 91.7% (22/24)
- Recurrence rate: 8.3% (2/24)
 - 1 locoregional
 - 1 distant (lung)
- Survival rate: 95.8% (23/24)
- 48% pacientes tratados sólo quimio-inmunoterapia
- Ninguno de estos traqueostomía o gastrostomía
- pRC sólo con biopsias subóptimo





Ca y Cu
LA

Tratamiento quirúrgico

Cirugía

Radioterapia post-operatoria
(Quimioterapia)

Adyuvancia
Inmunoterapia





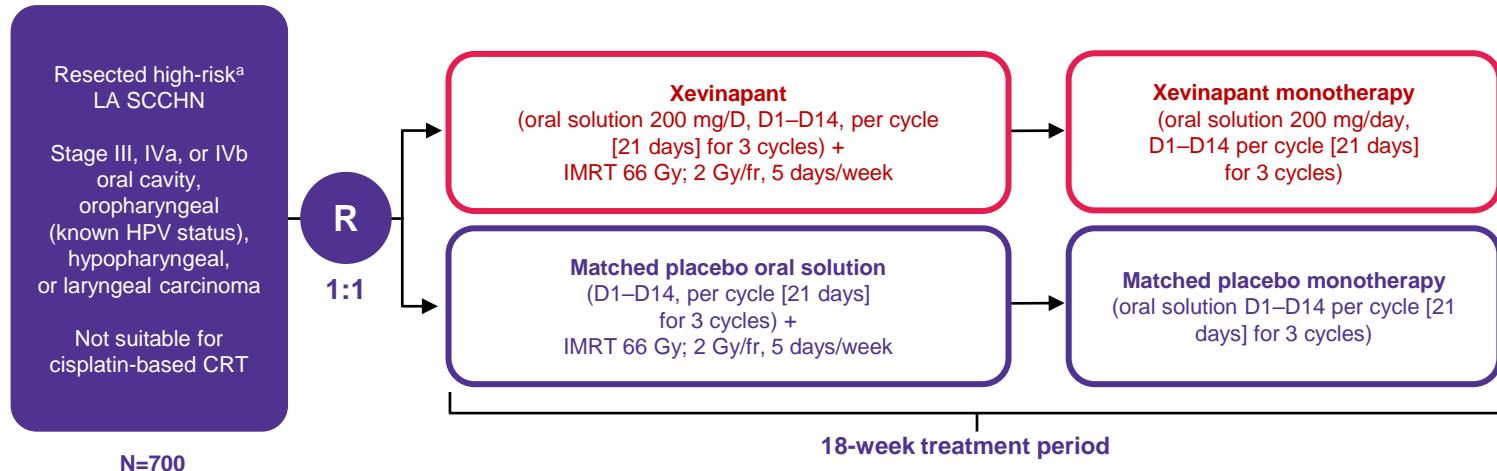
Ensayos clínicos adyuvancia (más otras cosas...)

NCT Number	Study Name	Eligible Disease	Description	Outcome
Sequential Immunotherapy after Definitive Chemoradiation				
NCT0811015	EA3161	Intermediate-risk p16-positive oropharyngeal cancer	1: SOC definitive CRT 2: SOC definitive CRT with adjuvant nivolumab	Pending
Immunotherapy with Surgery and Chemoradiation				
NCT01810913	RTOG 1216	Resected p16-negative LAHNSCC	1: SOC surgery and adjuvant CRT (cisplatin) 2: SOC surgery and adjuvant CRT (docetaxel and cetuximab) 3: SOC surgery and adjuvant CRT (cisplatin) with atezolizumab. Atezolizumab is concurrent and sequential with CRT	Pending
NCT03576417	NIVOPOSTOP	Resected LAHNSCC	1: SOC surgery and adjuvant CRT 2: SOC surgery and adjuvant CRT with nivolumab. The nivolumab is concurrent with and sequential to the CRT	Pending
NCT03452137	IMvolve010	Definitively treated LAHNSCC (CRT or surgery as the definitive local therapy)	Definitive local therapy followed by: 1: Placebo 2: Atezolizumab	Pending
Immunotherapy as a Neoadjuvant Therapy Prior to Surgery and also with Adjuvant CRT				
NCT03765918	MK-3475-689	Resectable LAHNSCC	1: SOC surgery and adjuvant CRT 2: Neoadjuvant pembrolizumab, surgery, and adjuvant CRT with pembrolizumab. Pembrolizumab is a neoadjuvant prior to surgery, concurrent with adjuvant CRT and sequential following CRT	Pending
NCT03700905	IMSTAR-HN	Resectable LAHNSCC	1: SOC surgery and adjuvant CRT 2: Neoadjuvant nivolumab, surgery, and adjuvant CRT, followed by sequential nivolumab or adjuvant nivolumab and ipilimumab	Pending

Tabla extraída de Rao YJ, et al. Cancers 2023



Phase III, randomized study of xevinapant + RT vs placebo + RT in patients with resected high-risk LA SCCHN who are ineligible for cisplatin



Primary endpoint: Disease-free survival^b

Secondary endpoints: OS, time to subsequent cancer treatments, safety, HRQoL

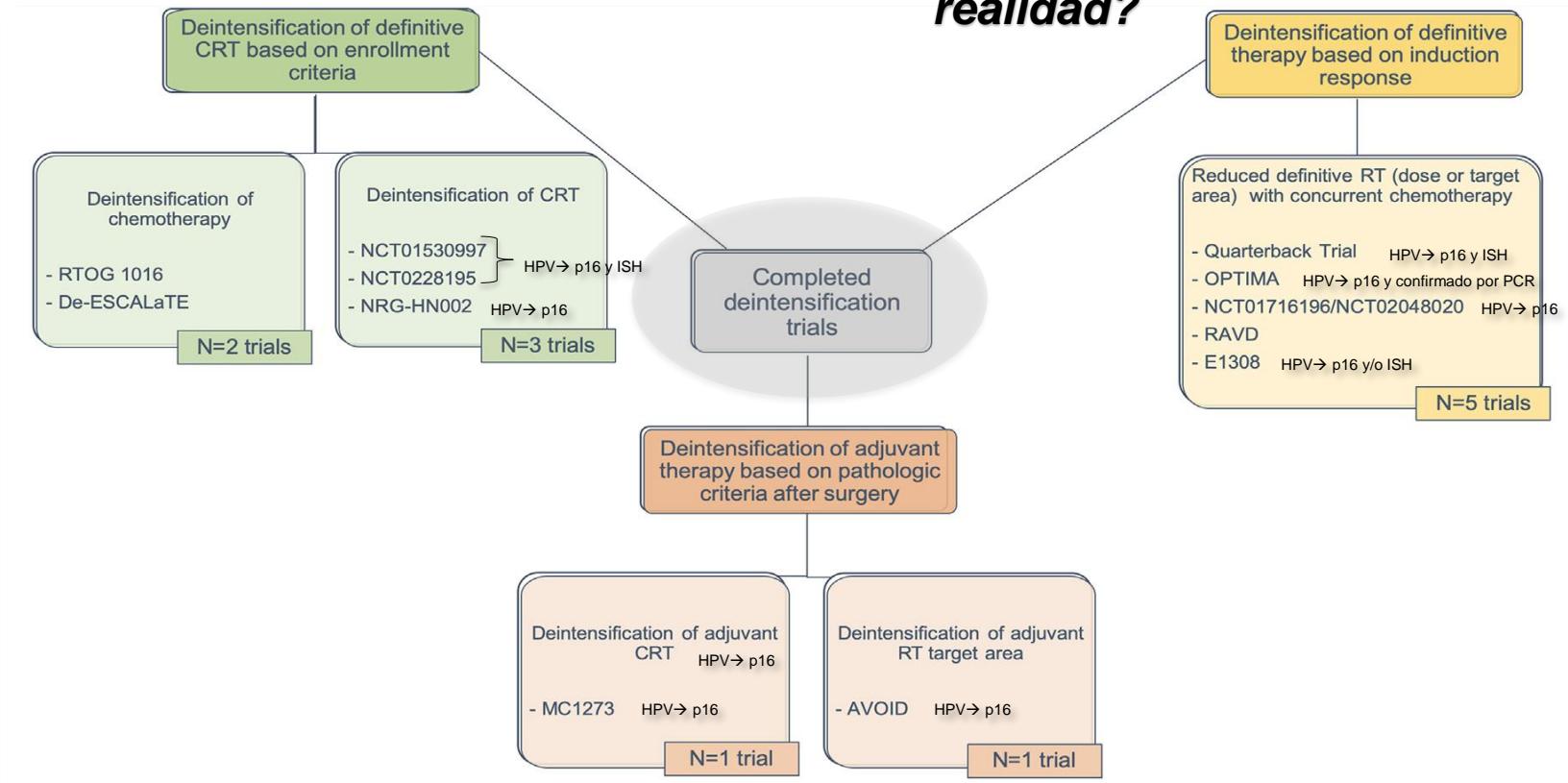


Carcinoma orofaringe

HPV



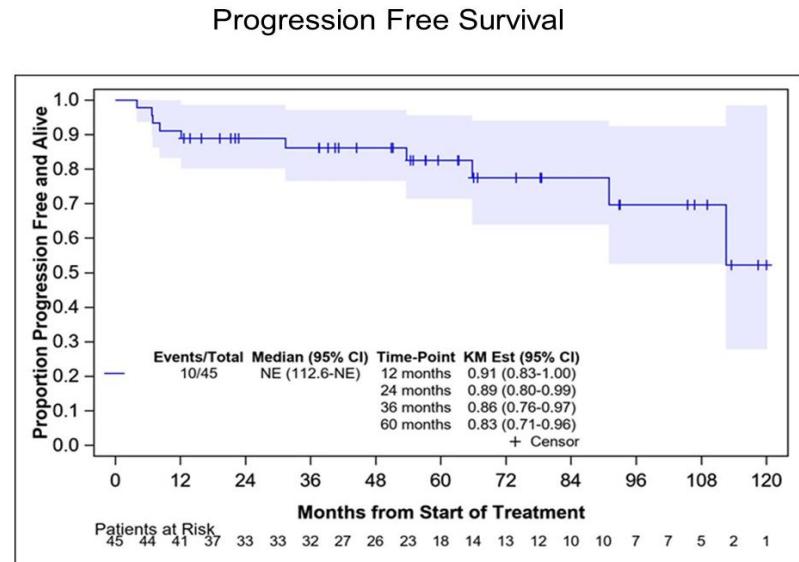
¿La desescalada es una realidad?





Abstract #6020: The Quarterback Trials - Phase 2 Sequential Study of Induction Chemotherapy and Reduced Dose Chemoradiation for HPV Positive Oropharynx Cancer

- HPV alto riesgo
EEC, T4, N2c, Genotipo no HPV16
- 3 ciclos quimio inducción TPF
- Si respuesta → RT (56 Gy) + Carboplatino semanal
- Objetivos primarios→ Control locorregional y SLP 3 años
- Comparado con RTOG 1029→ 85% y 80%



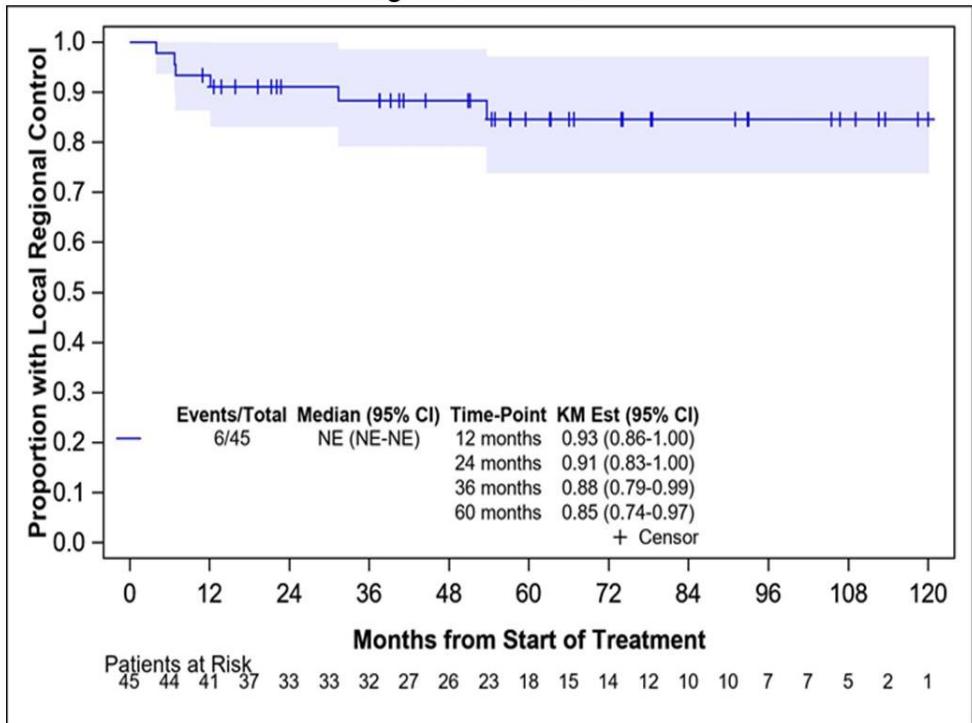


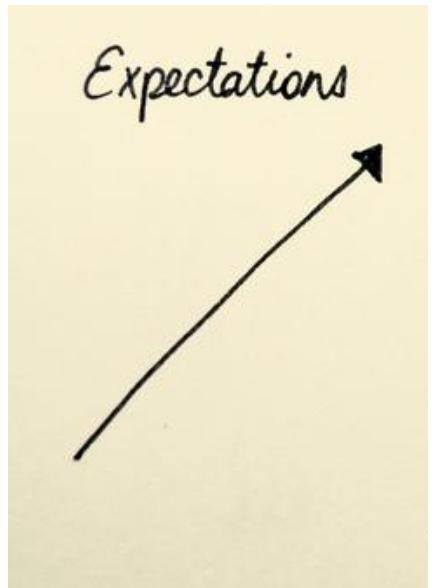
Quarterback Trials

Outcomes 5-2023

Total subjects	45
HPV Disease Specific Outcomes	
Locoregional Control	39 (86.7%)
Metastatic Disease	2 (4.4%)
Status HPV specific survival	
HPV Specific Death	4 (8.9%)
Alive	39 (86.7%)
Alive with Disease	3 (6.6%)
Salvaged Immunotherapy	1 (2.2%)
Death from second primary	1 (2.2%)
Death from SLE	1 (2.2%)
Disease Specific Survival	39 (91%)
Median of Follow-up (Months)	69 (18-126)
Progression Free Survival	35 (77.8%)
Overall Survival	39 (86.7%)
Patients with Second Primary	5 (11.1%)
SCC in-Field Head and Neck	2 (4.4%)
Renal cell, myeloma, MDS	3 (6.7%)

Local Regional Control





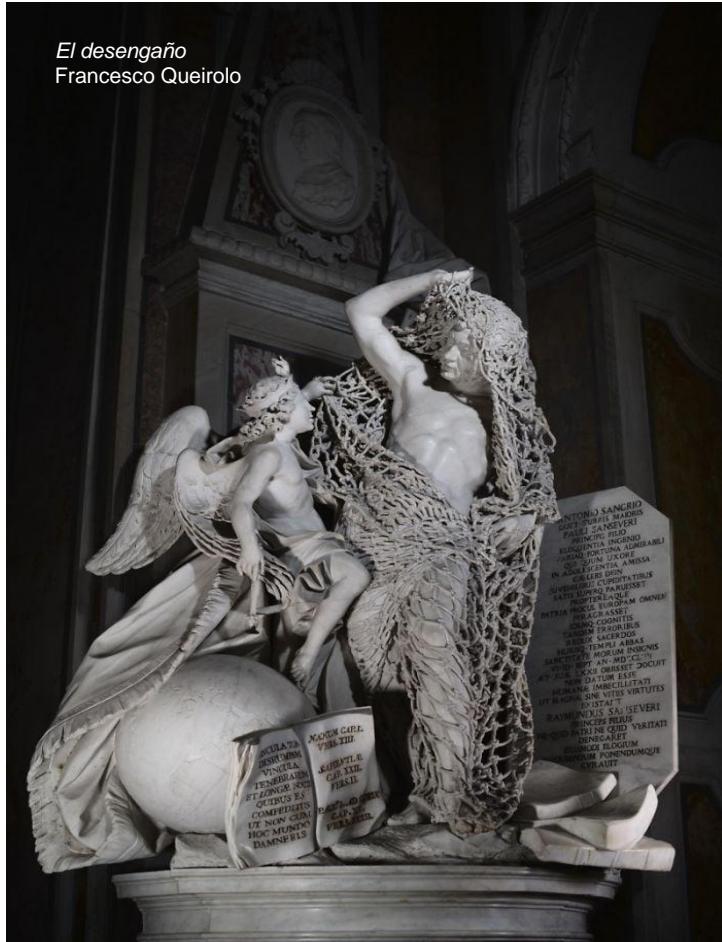
3 conclusiones

Xevinapant
Quimio-inmuno de inducción
Desescalada

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“Romperé tu cadena, la cadena de las tinieblas y de la larga noche de la que eres esclavo para que no seas condenado en este mundo”

El desengaño
Francesco Queirolo



**Gracias por vuestra
atención**

