¿Qué hay de nuevo en el tratamiento de los tumores de glándulas salivares?

III REUNIÓN DE TRABAJO EN CÁNCER DE CABEZA Y CUELLO.
Controversias en el manejo del paciente con cáncer de cabeza y cuello.

22 de marzo de 2021
Dra Teresa García Manrique
FEA HU Virgen Macarena


Poquito
MakeAGIF.com

TUMORES MALIGNOS DE GLANDULAS SALIVARES MAYORES

Actualización según OMS 2005

Carcinoma de células acinares
Carcinoma mucoepidermoide
Carcinoma adenoide quístico
Adenocarcinoma polimorfo de bajo grado
Carcinoma epitelial-mioepitelial
Carcinoma de células claras (sin otra especificación)
Adenocarcinoma de células basales
Carcinoma sebáceo
Linfoadenocarcinoma sebáceo
Cistoadenocarcinoma
Cistoadenocarcinoma cribiforme de bajo grado
Adenocarcinoma mucinoso
Carcinoma oncocítico
Carcinoma del ductus salivar
Adenocarcinoma (sin otra especificación)
Carcinoma mioepitelial
Carcinoma sobre adenoma pleomórfico
Carcinosarcoma adenoma pleomórfico metastásico
Carcinoma de células pequeñas
Carcinoma de células gigantes
Carcinoma linfoepitelial
Sialoblastoma

El-Naggar AK, et al. World Health Organization Classification of Tumors of Head and Neck. IARC. Lyon 2017

epidemiologia de tumores glándulas salivares

- Incidencia: 1-3/100.000/año
- no preferencia por sexo
- edad media 55-65 (45)
- Factores riesgo: radiación, tabaquismo, VEB, VIH, HPV, factores ambientales (queroseno..)
- PARÓTIDA: malignos 15-20%
- GS menores: malignos 80%

epidemiologia de tumores malignos de glándulas salivares

Afectación ganglionar al diagnóstico 25%

A distancia

pulmón 80% hueso e hígado

epidemiologia de tumores malignos de glándulas salivares

supervivencia 5 años según estadios SEERS 1995

ESTADIO	SUPERVIVENCIA
I	75 %
II	59 %
III	57 %
IV	28 %

epidemiologia de tumores malignos de glándulas salivares

supervivencia 5 años según estadios SEERS 1995

ESTADIO	SUPERVIVENCIA
I	75 %
II	59 %
III	57 %
IV	28 %

MAYOR CAPACIDAD DE DISEMINACION A DISTANCIA
Carcinoma adenoide quístico
Carcinoma indiferenciado
Carcinoma mixto
Carcinoma ductal

Tratamiento inicial

CIRUGÍA

T1 y T2 bajo grado

RADIOTERAPIA ady

T3 y T4

Adenoides quísticos *

Salivares menores

- de nasofaringe
- profundos de parotida
- no R0
- margen quirúrgico estrecho o afecto
- indiferenciado o alto grado
- recurrentes
- afectación de hueso, tejido conectivo
- afectación ganglionar
- afectación perinerual
- afectación extracapsular

QUIMIOTERAPIA ady

No estudios prospectivos

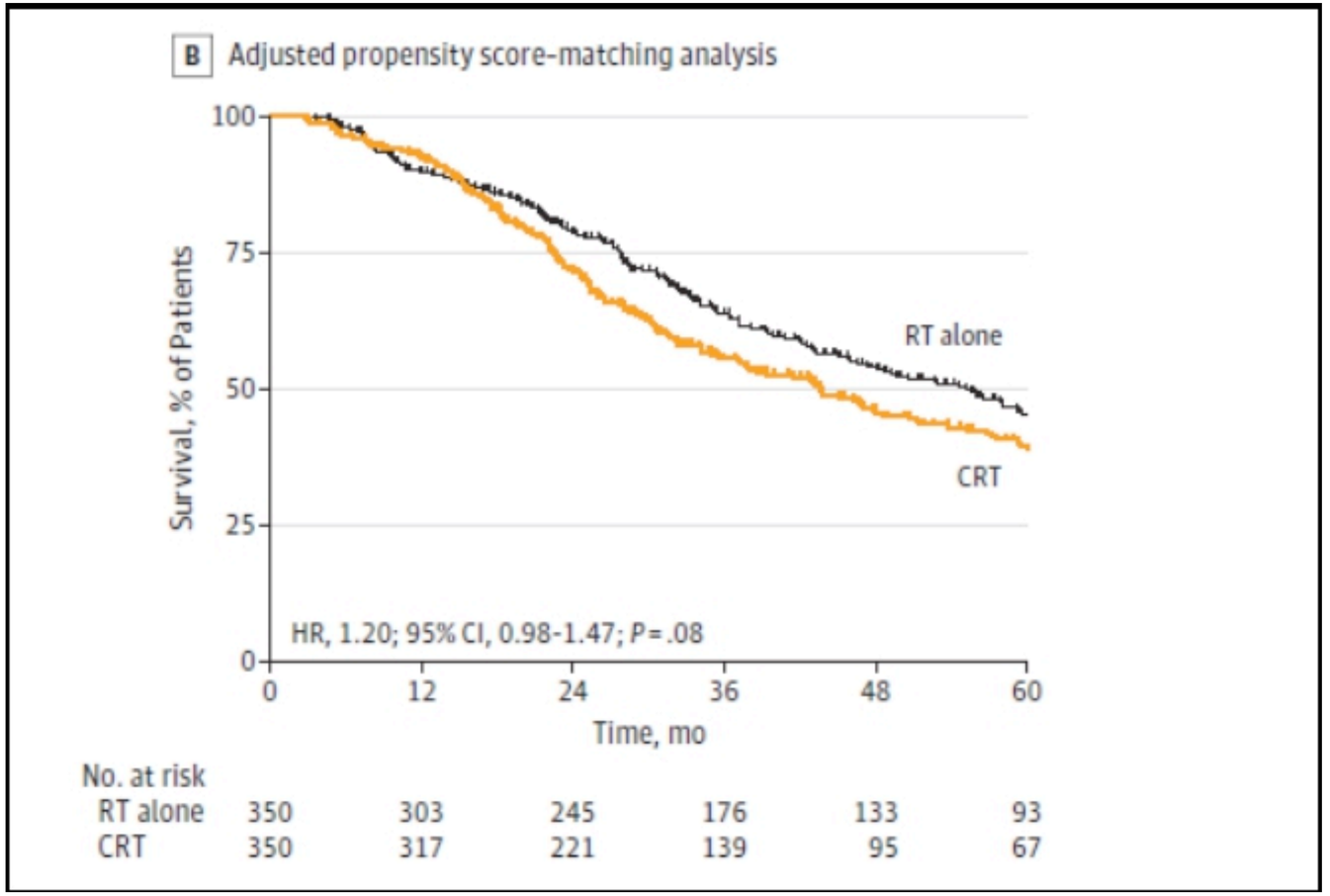
Series retrospectivas sin beneficio

JAMA Otolaryngology–Head & Neck Surgery | Original Investigation

Association of Adjuvant Chemoradiotherapy vs Radiotherapy Alone With Survival in Patients With Resected Major Salivary Gland Carcinoma

Data From the National Cancer Data Base

Arya Amini, MD; Timothy V. Waxweiler, MD; Jeffrey V. Brower, MD, PhD; Bernard L. Jones, PhD; Jessica D. McDermott, MD; David Raben, MD; Debashis Ghosh, PhD; Daniel W. Bowles, MD; Sana D. Karam, MD, PhD



2016

Ensayos prospectivos en adyuvancia

TABLE 1 Clinical trials in the adjuvant setting

NCT ref	Title	Population	Intervention	Primary outcome	Enrolment
02998385	Chemo-radiotherapy vs radiotherapy in the treatment of salivary gland and nasal tumours	High risk resected sinus or salivary gland cancer (any histopathology) or Unresectable salivary gland cancer (high risk sub-types)	*Arm A*: Radiotherapy *Arm B*: Radiotherapy + cisplatin (3 weekly)	Progression-free survival	260
01220583	Radiation therapy with or without chemotherapy in treating patients with high-risk malignant salivary gland tumours that have been removed by surgery	High risk resected salivary gland cancer (adenoid cystic; mucoepidermoid; acinic cell; adenocarcinoma).	*Arm A*: Radiotherapy *Arm B*: Radiotherapy + cisplatin (weekly)	Progression-free survival	120
02776163	Post-operative concurrent chemo-radiotherapy in treating patients with high-risk malignant salivary gland tumours	High risk resected salivary gland cancer (any histopathology)	*Arm A*: Radiotherapy + cisplatin (3 weekly x2, day 1-3) *Arm B*: Radiotherapy + cisplatin + docetaxel (3 weekly x 2)	Disease-free survival	53

RECLUTAMIENTO ACTIVO

RECLUTAMIENTO ACTIVO

RECLUTAMIENTO ACTIVO

Oral Oncology 90 (2019) 30–37

Contents lists available at ScienceDirect

Oral Oncology

journal homepage: www.elsevier.com/locate/oraloncology

Prognostic value of programed death ligand-1 and ligand-2 co-expression in salivary gland carcinomas

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[a] Department of Head and Neck Surgery, National Kyushu Cancer Center, Notame 3-1-1, Minami-ku, Fukuoka 811-1395, Japan
[b] Department of Pathology, National Kyushu Cancer Center, Notame 3-1-1, Minami-ku, Fukuoka 811-1395, Japan

- Primer estudio que examina microambiente inmune tumoral del cáncer de glándulas salivares (PDL1, PDL2, inestabilidad de microsatélites y TILs)
- PD-L2 + implica fenotipo agresivo (más que PDL1+)
- Co-expresión de ambos ligandos implica peor pronóstico
- Vía antiPD1/PDL1-2 podría ser una buena opción de tratamiento

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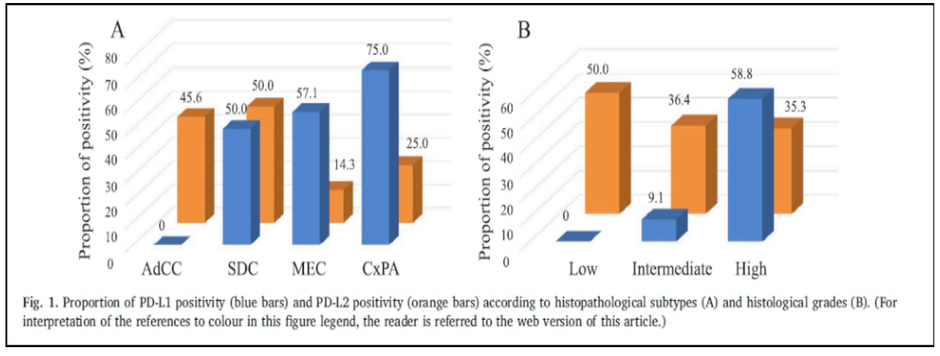
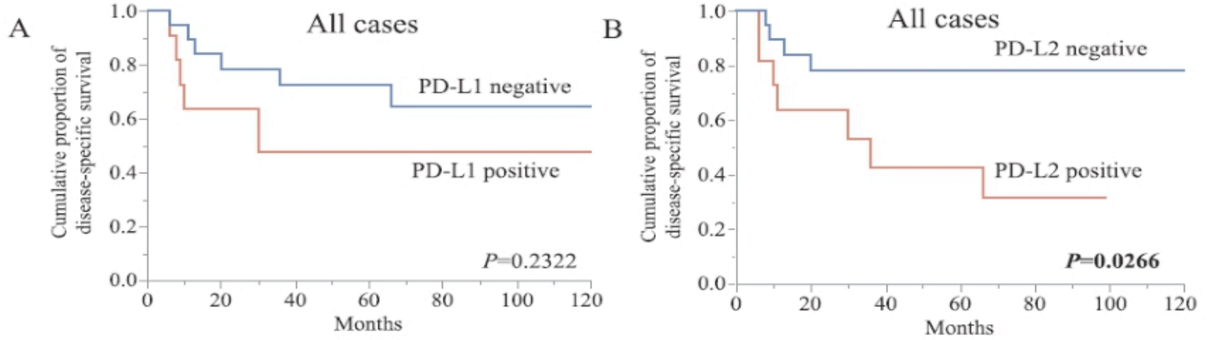


Fig. 1. Proportion of PD-L1 positivity (blue bars) and PD-L2 positivity (orange bars) according to histopathological subtypes (A) and histological grades (B). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)



Quimioterapia en enfermedad recurrente/metastásica

⚠️ Casos y series retrospectivas

Table 3. Treatments for Which Antitumor Activity Has Been Reported in Salivary Gland Carcinoma

Treatment	Adenoid Cystic Carcinoma			Mucoepidermoid Carcinoma			Adenocarcinoma		
	Response	No. of Patients Responding	Total No. of Patients	Response	No. of Patients Responding	Total No. of Patients	Response	No. of Patients Responding	Total No. of Patients
Cisplatin[84]	R	2	13	R	1	5	NR	0	5
Paclitaxel[25]	NR	0	14	R	3	12	R	4	17
Vinorelbine[24]	R	2	13	—	—	—	R	2	5
Epirubicin[22]	R	2	20	—	—	—	—	—	—
Mitoxantrone[21,23]	R	5	50	—	—	—	—	—	—
Methotrexate*[59]				R	2	5	—	—	—
CAP (various)[26,28-30,59,63] or CAP-FU[27]	R	12	43	R	5	6	R	23	37
Anthracycline/cisplatin ± FU[31-33,85]	R	6	19	R	1	4	R	8	14
Cyclophosphamide/doxorubicin*[58,59]	R	2	6	NR	0	6	R*	1	1
Cisplatin/methotrexate/bleomycin*[58,59]	NR	0	3	R	2	3	—	—	—
Cisplatin/vinorelbine[24]	R	4	9	—	—	—	R	1	5
Carboplatin/paclitaxel[86,87]	R	2	10	—	—	—	R*	1	1

Abbreviations: R, objective response; NR, no response; CAP, cyclophosphamide/doxorubicin/cisplatin; FU, fluorouracil.
*Data derived mainly from case reports/retrospective series rather than prospectively performed clinical trials.

Laurie and Licitra JCO 2006

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Vinorelbine[24]	R	2	13	—	—	—	—	2	5
Epirubicin[22]	—	—	—	—	—	—	—	—	—
Mitoxantrone[21,23]	—	—	—	—	—	—	—	—	—
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SG m poliQT: 14- 25 meses
SG m monoQT: 8-67 meses

SLP: 6 meses

Laurie and Licitra JCO 2006

-YA NO
ME ESCUCHAS

-YO TAMBIÉN

Tratamiento dirigido

Table 2. Genetic alterations in salivary gland tumors

Tumor	Genetics
Secretory carcinoma	*ETV6-NTRK3* fusion (minority *ETV6-X)*
Clear cell carcinoma	*EWSR1-ATF1* fusion
Basal cell adenoma	*CYLD* LOH/mutation *CTTNB1* mutation [84]
Mucoepidermoid carcinoma	*CRTC1-MAML2* fusion *CRTC3-MAML2* fusion (minority) *CDKN2A* deletion
Adenoid cystic carcinoma	*MYB* and *MYBL1* fusion *NOTCH1* mutation
Salivary duct carcinoma	*ERBB2* amplification *AR* copy gain/overexpression
Pleomorphic adenoma	*PLAG1* and *HMGA2* rearrangements
Carcinoma ex pleomorphic adenoma	*PLAG1* and *HMGA2* rearrangements *p53* and *RB* alterations *MDM2* amplification
Polymorphous adenocarcinoma, cribriform adenocarcinoma of minor salivary gland origin	*PRKD1* mutation/rearrangement, *PRKD2* and *PRKD3* rearrangement
Epithelial myoepithelial carcinoma	*HRAS* mutation?

ESMO GOOD SCIENCE BETTER METHODS BEST PRACTICE

Annals of Oncology 28: 2539–2546, 2017
doi:10.1093/annonc/mdx399
Published online 4 August 2017

ORIGINAL ARTICLE

Comprehensive genomic profiles of metastatic and relapsed salivary gland carcinomas are associated with tumor type and reveal new routes to targeted therapies

J. S. Ross[1,2*†], L. M. Gay[1†], K. Wang[3], J.-A. Vergilio[1], J. Suh[1], S. Ramkissoon[1], H. Somerset[4], J. M. Johnson[5], J. Russell[6], S. Ali[7], A. B. Schrock[7], D. Fabrizio[8], G. Frampton[8], V. Miller[7], P. J. Stephens[8], J. A. Elvin[1] & D. W. Bowles[9*]

Table 1. Clinical characteristics and genomic alterations in 10 different salivary gland cancer histologic subtypes

	Typically low-grade salivary gland cancers ($n = 264$)					Typically higher grade salivary gland cancers ($n = 359$)				
	Adenoid cystic carcinoma	Acinic cell carcinoma	Polymorphous low grade adenocarcinoma	Myo-epithelial carcinoma	Mammary analog secretory carcinoma	Muco-epidermoid carcinoma	Salivary duct carcinoma	Adenocarcinoma, not otherwise specified	Carcinoma, not otherwise specified	Carcinoma ex pleomorphic adenoma
Patients (*N*)	154	73	5	20	12	57	44	117	119	22
GAs/tumor	1.6	2.8	1.6	3.6	2.8	4.2	3.6	4.1	5.2	3
Median age in years	55	55	72	56	62	58	67	61	63	62
Gender (% female/% male)	50% F 50% M	54% F 46% M	80% F 20% M	42% F 58% M	38% F 62% M	46% F 54% M	18% F 82% M	26% F 74% M	35% F 65% M	50% F 50% M
Significant GAs (%)	MYB-NFIB (65)	PTEN (10) BRAF (5) NF1 (5)	PTEN (20) TSC2 (20) FGFR1 (20)	PIK3CA (15) RICTOR (15) PTCH1 (10) PDGFRB (5)	ETV6-NTRK3 (100)	PIK3CA (20) ERBB2 (13) BRCA2 (17) FGFR1 (7)	ERBB2 (32) PTEN 17) BRAF (5) PIK3CA (27)	ERBB2 (17) BRAF (5) EGFR (5) PIK3CA (24)	ERBB2 (15) PIK3CA (20) NF1 (8) PTEN (8) NF1 (8)	ERBB2 (32) FGFR1-PLAG (9)
TP53 GA frequency (%)	4	10	0	13	17	43	67	55	48	46
ERBB2 GA frequency (%)	0	0	0	0	0	13	32	17	15	2
PIK3CA GA frequency (%)	5	3	0	15	0	20	27	24	20	0
BRAF GA frequency (%)	0	3	0	5	0	4	5	4	4	0
Tumor mutational burden >10 mut/Mb (%)	1	3	0	5	0	10	14	10	2	12
Potential for targeted therapies	Low	Limited	Moderate	High	High	Moderate	High	Moderate	Moderate	High

GA, Genomic alterations.

Ross J.S. et al. Annals of Oncology 2017, 28: 2539-2546

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Ross J.S. et al. Annals of Oncology 2017, 28: 2539-2546

Alteraciones moleculares en carcinoma de glándulas salivares NO adenoide quístico

Table 2. Overview of associations between potentially druggable molecular targets and non-ACC SGC histotype [7,8,17].

Druggable molecular target	AcCC	ADC NOS	Ca ex pleom. ad	MASC	MEC	MyoepiC	PLGAC	SDC
AR		21%						75–99%
HER-2		17%	17%		13% (HG)			32–73%
PI3K		24%			4.3% (LIG) 52% (HG)	15%		27%
TRK				100%				
CDK/Cyclin	71%	35%			20% (AG)	33%		
FGFR			9%		7% (AG)		20%	
BRCA					10.5% (AG)			
RAS/RAF/MAPK	5%	5%						5%
Hedgehog						10%		
MET		CR				CR		
High TMB		10%	12%		10% (AG)			14%
PD1/PD-L1		8%	36%					30%

Expert Opin Investig Drugs 2019

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TRK				100%				
CDK/Cyclin	71%	35%			20% (AG)	33%		
FGFR			9%		7% (AG)		20%	
BRCA					10.5% (AG)			
RAS/RAF/MAPK	5%	5%						5%
Hedgehog						10%		
MET		CR				CR		
High TMB		10%	12%		10% (AG)			14%
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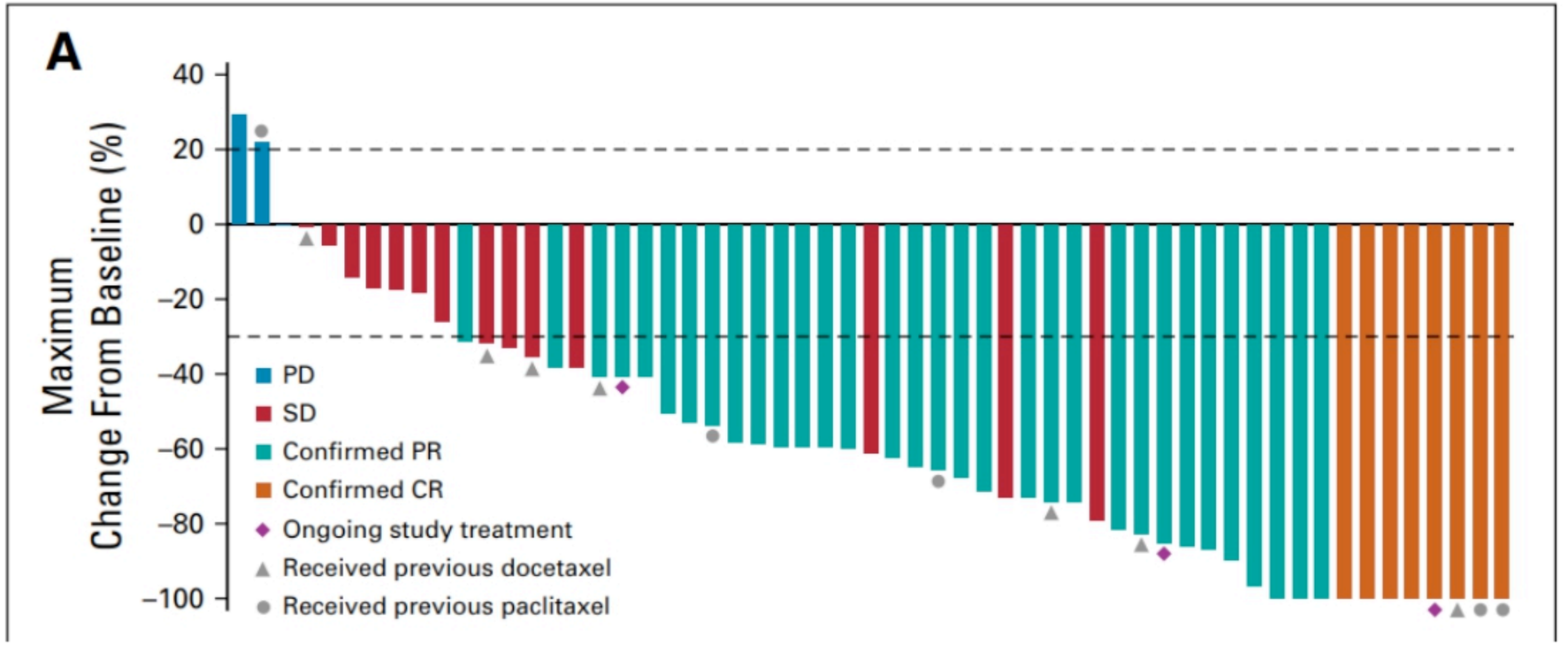
Expert Opin Investig Drugs 2019

J Clin Oncol. 2019 Jan 10;37(2):125-134. doi: 10.1200/JCO.18.00545. Epub 2018 Nov 19.

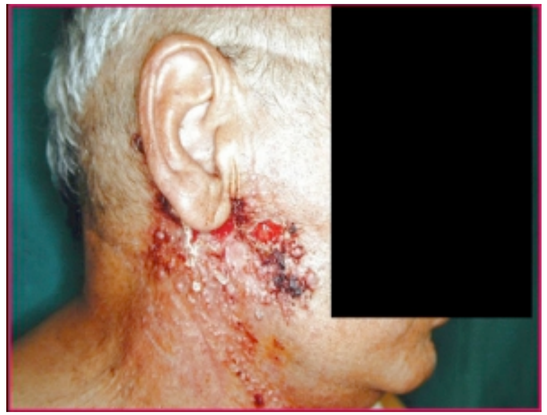
Phase II Trial of Trastuzumab and Docetaxel in Patients With Human Epidermal Growth Factor Receptor 2-Positive Salivary Duct Carcinoma.

Takahashi H[1], Tada Y[1], Saotome T[2], Akazawa K[3], Ojiri H[4], Fushimi C[1], Masubuchi T[1], Matsuki T[1], Tani K[3], Osamura RY[5,6], Hirai H[7], Yamada S[8], Kawakita D[9], Miura K[1], Kamata SE[1], Nagao T[7].



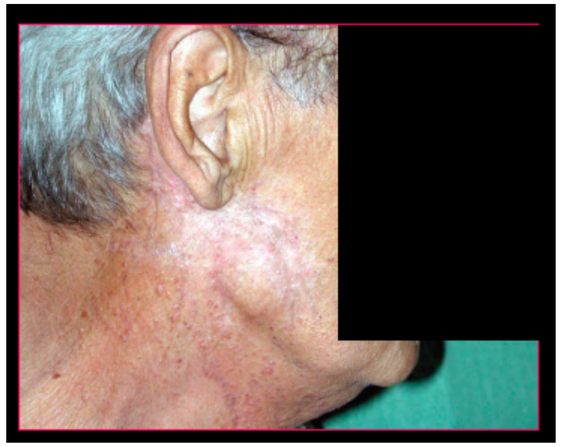
- Tasa de respuesta 70.2%
- SLP m 8.9 meses
- SG m 39.7 meses

Expresión de receptores androgénicos y terapia hormonal



Tras dos meses de tratamiento

Licitra et al. JCO 2003



JOURNAL OF CLINICAL ONCOLOGY | DIAGNOSIS IN ONCOLOGY

Androgen Receptor–Positive Salivary Duct Carcinoma: A Disease Entity With Promising New Treatment Options

Jaspers HJC et al. JCO 2011

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Annals of Oncology 29: 979–984, 2018
doi:10.1093/annonc/mdx771
Published online 1 December 2017

ORIGINAL ARTICLE

A prospective phase II study of combined androgen blockade in patients with androgen receptor-positive metastatic or locally advanced unresectable salivary gland carcinoma

C. Fushimi[1], Y. Tada[1*], H. Takahashi[1], T. Nagao[2], H. Ojiri[3], T. Masubuchi[1], T. Matsuki[1], K. Miura[1], D. Kawakita[4], H. Hirai[2], E. Hoshino[5], S. Kamata[1] & T. Saotome[6]

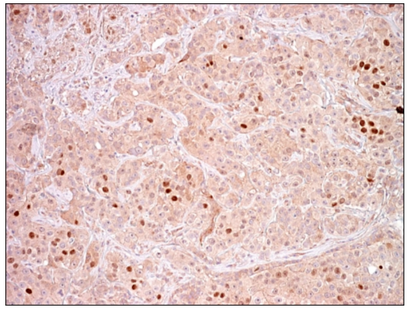
Table 4. Reported cases of hormone therapy for androgen positive–salivary gland carcinoma

Author (year)	Study design	*N*	Treatment	Efficacy			
				CR	PR	SD	PD
Hulst (1994) [13]	Case report	1	LH-RH analogue		1		
Jaspers (2011) [14]	Retrospective	10	9: bicalutamide, 1: CAB		2	3	5
Yajima (2012) [15]	Retrospective	8	LH-RH analogue		2	3	3
Soper (2013) [16]	Case report	1	CAB + IMRT	1			
Yamamoto (2014) [17]	Case report	1	Bicalutamide	1			
Agbarya (2014) [18]	Case report	1	Bicalutamide + letrozole	1			
Locati (2016) [19]	Retrospective	17	CAB	3	8	4	2
Boon (2016) [20]	Retrospective	31	ADT[a]		4	10	17
Present study	Phase II	36	CAB	4	11	16	5

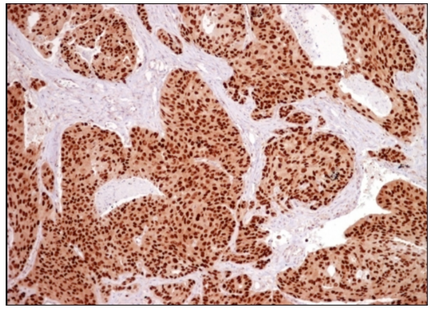
[a]Drug: unknown.

CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; LH-RH analogue, luteinizing hormone–releasing hormone analogue; CAB, combined androgen blockade; IMRT, intensity modulated radiation therapy; ADT, androgen deprivation therapy.

¿quienes son los candidatos a hormonoterapia?



RA negativos



RA positivos

- Enfermedad avanzada
- RA con alta expresión, independiente de histología (ca de ductos salivar, adenocarcinomas, mucoepidermoide alto grado…)
- tipo de hormonoterapia:
    - bicalutamida 150 mg?
    - bicalutamida 50 mg + LHRH c/28?
- Durante cuánto tiempo?

BEDSIDE TO BENCH REPORT

Cancer Biology & Therapy 15:6, 1–5; June 2014; © 2014 Landes Bioscience

Activity of abiraterone in rechallenging two AR-expressing salivary gland adenocarcinomas, resistant to androgen-deprivation therapy

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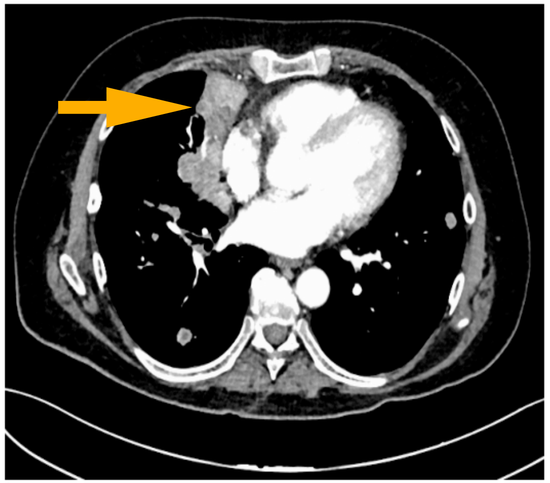

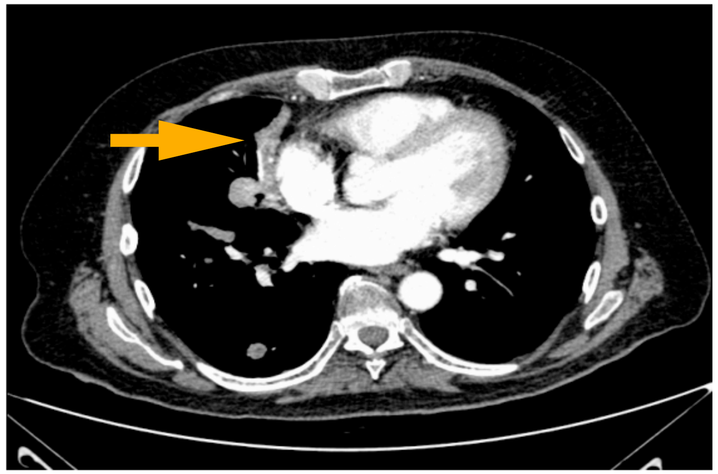

Phase II trial of abiraterone acetate in patients with relapsed and/or metastatic, castration resistant salivary gland cancers (NCT02867852)

ensayos clínicos sin clasificación molecular

TABLE 2 Clinical trials without molecular stratification

NCT Ref	Title	Population	Intervention	Primary outcome	Enrolment	
03132038	Nivolumab in recurrent or metastatic salivary gland carcinoma of the head and neck	Salivary gland cancer (any histopathology)	Nivolumab	Non-progression rate	92	reclutamiento cerrado
03012581	Secured access to nivolumab for adult patients with selected rare cancer types	Salivary gland cancer (any histopathology)	Nivolumab	Response rate	20-50 (salivary gland cohort)	reclutamiento activo
03172624	Study of nivolumab plus ipilimumab in patients with salivary gland cancer	Salivary gland cancer (any histopathology)	Nivolumab + Ipilimumab	Response rate	64	reclutamiento activo
02834013	Nivolumab and ipilimumab in treating patients with rare tumours	Salivary gland cancer (any histopathology) and Adenoid cystic carcinoma	Nivolumab + Ipilimumab	Response rate	16 (per salivary gland cohort)	reclutamiento activo
03146650	Nivolumab and ipilimumab in treating patients with metastatic/recurrent adenoid cystic carcinoma (ACC) of all sites and non-ACC salivary gland cancer	Salivary gland cancer (any histopathology)	Nivolumab + Ipilimumab	Progression-free survival	63	reclutamiento cerrado
03360890	Pembrolizumab with chemotherapy for poorly chemo-responsive thyroid and salivary gland tumours	Salivary gland and thyroid cancer (any histopathology)	Pembrolizumab + Docetaxel	Response rate	23 (salivary gland cohort)	reclutamiento activo
03087019	Pembrolizumab with or without radiation in patients with recurrent or metastatic adenoid cystic carcinoma	Adenoid cystic carcinoma	*Arm A:* Pembrolizumab *Arm B:* Pembrolizumab + Radiotherapy (palliative)	Objective response in non-irradiated lesions	44	reclutamiento cerrado
02883374	Chidamide for advanced cephalic and cervical adenoid cystic carcinoma: evaluation of efficiency and safety	Adenoid cystic carcinoma	Chidamide	Disease control rate	30	desconocido. dos años sin datos

ensayos clínicos con clasificación molecular

TABLE 3 Studies of drug therapy in molecular sub-groups of salivary gland cancer including basket studies

NCT Ref	Title	Molecular groups	Intervention	Primary outcome	
02749903	Enzalutamide for patients with androgen receptor positive salivary cancers	Androgen receptor over-expression	Enzalutamide	Response rate	
01969578	Androgen deprivation therapy in advanced salivary gland cancer	Androgen receptor over-expression	*Arm A:* Cisplatin/ Doxorubicin OR Carboplatin/Paclitaxel *Arm B:* Bicalutamide + triptorelin	Progression Free Survival	reclutamiento activo
02867852	Abiraterone acetate in patients with relapsed and/or metastatic salivary gland cancers	Androgen receptor over-expression	Abiraterone acetate	Response rate	desconocido. dos años sin datos
02568267	Basket study of entrectinib (RXDX-101) for the treatment of patients with solid tumours harbouring NTRK 1/2/3 (Trk A/B/C), ROS1, or ALK gene rearrangements	NTRK1/2/3, ROS1, ALK gene rearrangement	Entrectinib	Response rate	reclutamiento activo
02576431	Study of LOXO-101 (Larotrectinib) in subjects with NTRK fusion positive solid tumours	NTRK1/2/3	Larotrectinib	Response rate	reclutamiento activo
03215511	Phase 1/2 study of LOXO-195 in patients with previously treated NTRK fusion cancers	NTRK1/2/3	LOXO-195	Response rate	reclutamiento activo
02465060	MATCH: Targeted therapy directed by genetic testing in treating patients with advanced refractory solid tumours, lymphomas, or multiple myeloma	EGFR, HER2, MET, ALK, ROS1, BRAF, PIK3CA, mTOR, TSC1/2, GSK, PTEN, NF1, GNAQ, GNA11, SMO, PTCH1, NF2, KIT, FGFR, DDR2, AKT, NRAS, CCND1/2/3, CDK4/6, MLH1, MSH2, NTRK1/2/3, BRCA1/2	Afatinib; Crizotinib; Osimertinib; Dabrafenib; Taselisib; Pertuzumab/ Trastuzumab; Sapanisertib; GSK2636771; Trastuzumab Emtansine; Vismodegib; Defactinib; Sunitinib; AZD4547; Dasatinib; Capivasertib; Binimetinib; Palbociclib; Nivolumab; Larotrectinib; Adavosertib	Response rate	reclutamiento activo
02693535	TAPUR: Testing the use of FDA approved drugs that target a specific abnormality in a tumour gene in people with advanced stage cancer	VEGFR, Bcr-abl, SRC, LYN, LCK, ALK, ROS1, MET, CDKN2A, CDK4/6, CSF1R, PDGFR, VEGFR, mTOR, TSC, ERBB2, BRAF, KRAS, NRAS, SRC, KIT, PDGFRB, EPHA2, FYN, LCK, YES1, RET, VEGFR1/2/3, PDGFRB, RAF-1, BRCA1/2, ATM, POLE, POLD1, MSI, Mutational burden,	Axitinib; Bosutinib; Crizotinib; Palbociclib; Sunitinib; Temsirolimus; Trastuzumab/Pertuzumab; Vemurafenib/Cobimetinib; Cetuximab; Dasatinib.	Response rate	reclutamiento activo
03297606	CAPTUR: Canadian profiling and targeted agent utilisation trial	NRG, EGFR, ERRB2/3/4, VEGFR1/2/3, Bcr-abl, SRC, ALK, ROS1, MET, KIT, PDGFRA/B, ABL1, POLE, POLD1, BRCA1/2, CDKN2A, CDK4/6, CCND1, CSF1R, FLT3, RET, FGFR1/2/3, VHL, AKT1/2/3, FBXW7, FLCN, mTOR, NF1/2, NTRK3, PIK3CA, PIK3R1, PTEN, RHEB, STKII, TSC1/2, BRAF, PTCH1, SMO, Mutational burden.	Afatinib; Axitinib; Bosutinib; Crizotinib; Dasatinib; Erlotinib; Nivolumab/Ipilimumab; Olaparib; Palbociclib; Sunitinib; Temsirolimus; Trastuzumab/Pertuzumab; Vemurafenib/Cobimetinib; Vismodegib.	Response rate	reclutamiento activo

tratamiento dirigido para carcinoma adenoide quístico

Carcinoma adenoide quístico y terapia dirigida

Author, aa	Drug	Ph	N° ACC	RR	SD	mPFS, mos
Guigay, 2007	Imatinib (KIT)	II	21	2/17	6/17	NA
Ghosal, 2010	Imatinib + plat KIT	II	28	3/28	19/28	NA
Ramalingam, 2010	Vorinostat (HDAC inh)	I	5	1/5	4/5	NA
Hoover AC, 2013	Nelfinavir (AKT)	II	15	0	7	5.5
Dillon PM, 2013	Dovitinib (FGFR)	II	21	2/19	9	NA
Thomson DJ, 2013	Sorafenib (BRAF; VEGFR)	II	23	0	13/19	11.3
Locati LD, 2016	Sorafenib	II	19/37	2/19	11/19	8.9
Wong SJ, 2013	Dasatinib (Src)	II	40	0	21	4.8
Ho A, 2016	Axitinib (VEGFR)	II	33	3	25	NA
Guigay, 2016	Pazopanib	II	49	0		
Rodriguez, 2018	Eribulin	II	29 (11 ACC)	3/29 (2 ACC)	8	3.5
Locati LD, 2018	Lenvatinib (VEGFR2, FGFR, PDGFR)	II	28	3/26	20/26	9
Tchekmedyian V, 2018		II	33	5/33	24/33	16.4

No respuesta con gefitinib, cetuximab, trastuzumab, sunitinib, bortezomib; everolimus…;

Compound	Target	Site
Axitinib (R)	VEGFR	South Korea
Apatinib	VEGFR	China
Chidamide	HDAC	China
Pembrolizumab plus radiation	PD-1 immunotherapy	USA
MYB vaccine plus BGB-A317	Vaccine and PD-1 immunotherapy	Australia
AL101	NOTCH1	USA
RAD001	mTOR	South Korea
Apatinib + particle therapy	VEGFR2 + hadrotherapy	China
Cabozantinib	RET, MET	Netherlands

Interesting targets under evaluation in phase I trials: CDK9, MDM2, NOTCH1

conclusiones

- Son tumores con muy baja incidencia y marcada heterogeneidad histológica
- El tratamiento local se debe adaptar al tipo histológico, presentación clínica, riesgo de recidiva… lo que conlleva falta de unificación
- La quimioterapia tiene actividad muy modesta, pero hay un espacio para el tratamiento hormonal en subgrupos seleccionados.
- Contamos con evidencia preliminar con terapias dirigidas y estudios prospectivos con garantías para estos tumores.

molaría verse
después de un
“hay que verse”.

Muchas gracias.