VII SIMPOSIUM
ICAPEM
Jerez de la Frontera
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Cáncer de pulmón: diferencias en el perfil clínico en función del género.

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Conflictos de Interés

- Consultant :
    - Median Technologies, Sabartech, Roche, Astra Zeneca, Serum.
- Professional Fees :
    - Roche, Astra Zeneca, MSD.
- Scientific meeting collaborations, Insitutional grants :
    - Serum, Menarini, Esteve.

Introducción

- La EPOC en mujeres.
- El cáncer de pulmón en mujeres.
- Perfil clínico.
  - Implicaciones diagnósticas.
  - Implicaciones quirúrgicas.
  - Implicaciones de tratamiento.
- Conclusiones

La EPOC en mujeres

- El tabaquismo afecta mas a las mujeres.
  Ben-Zaken Cohen et al. 2007; Han et al. 2018

- La presentación clínica de la EPOC es diferente en mujeres y hombres.
  Jenkins et al. 2017; Lamprecht et al. 2015

- También los síntomas y la trayectoria clínica es diferente en mujeres.
  Han et al. 2018; Pérez et al. 2020

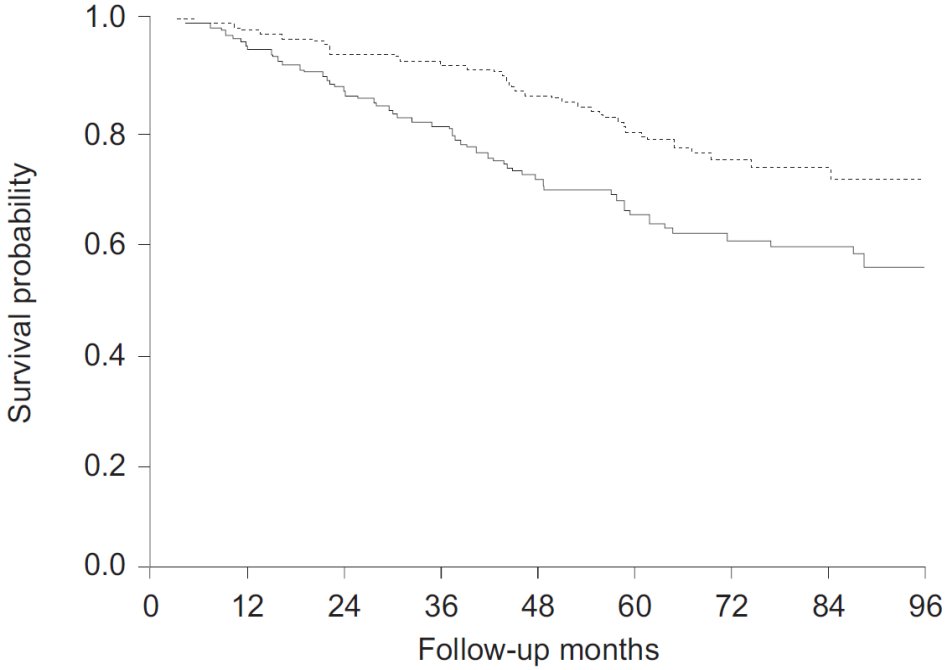
- Las mujeres desarrollan EPOC antes y tienen mas exacerbaciones que los hombres.
  Pérez et al. 2020

- La EPOC es mas prevalente en mujeres y su incidencia aumenta desproporcionadamente en ellas.
  Akinbami y Liu 2011

La EPOC en mujeres

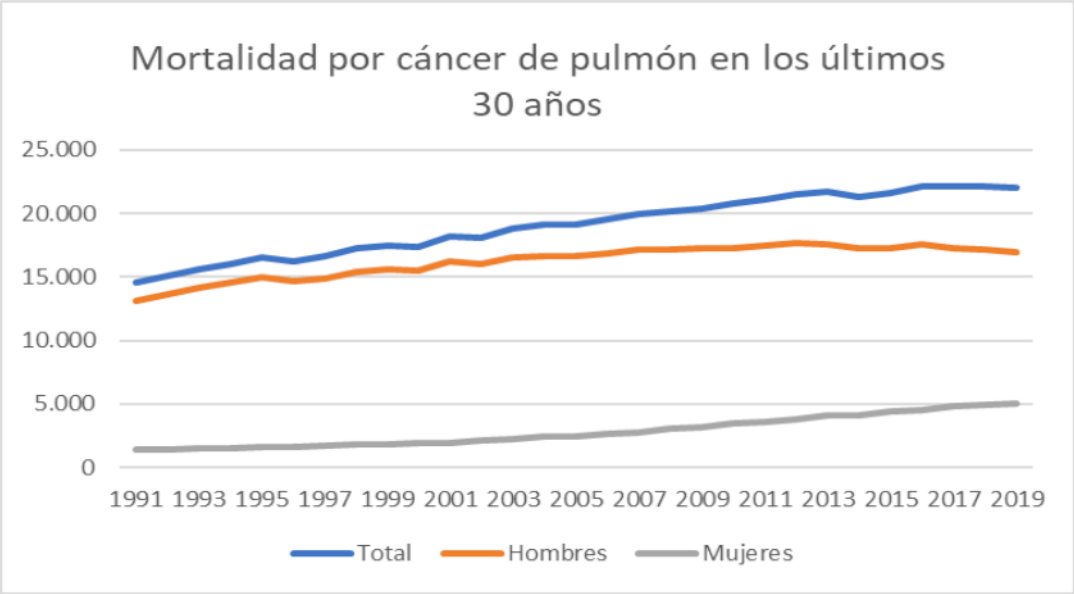
- Mas tabaquismo en las mujeres.
- Mayor esperanza de vida.
- Incorporación a profesiones de riesgo por exposición ocupacional.
- Mayor exposición a contaminación ambiental en las viviendas.
  Aryal et al. 2013
- Contribución hormonal en modelos animales ; > obstrucción/remodelación de la vía aérea y < enfisema.
  Tam et al. 2011
- El tabaquismo en mujeres activa TGF-β y conlleva una mayor estrés oxidativo.
  Tam et al. 2011

La EPOC en mujeres



Eur Respir J 2009; 33: 528–535

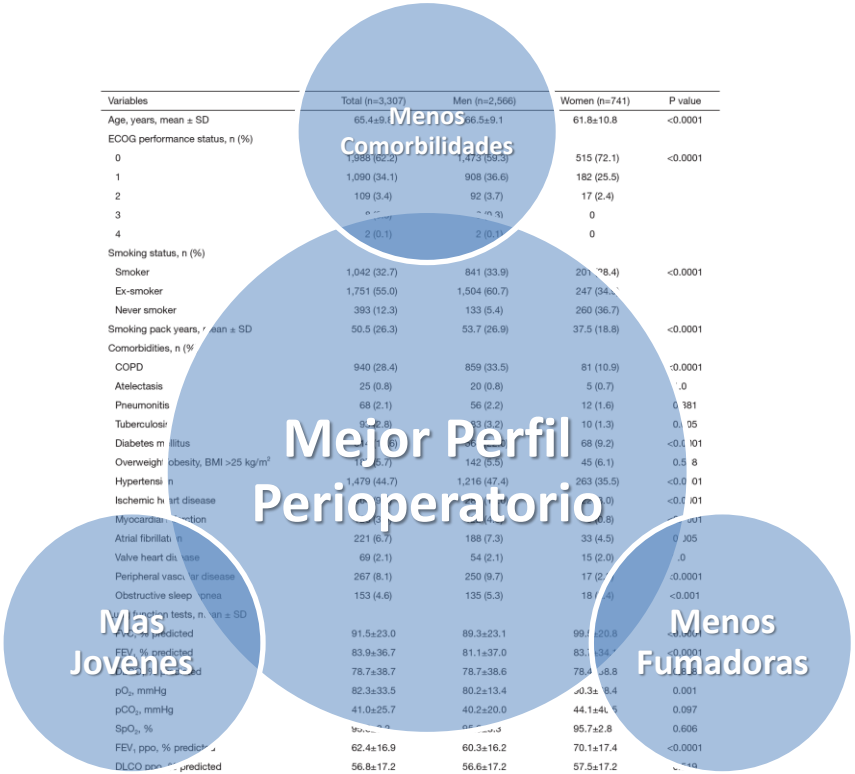
¿Y el cáncer de pulmón?



Diferencias en el Perfil Clínico

- Las mujeres con CP avanzado viven mas que los hombres.
  Wakelee et al. 2006; Schiller et al. 2002
- El CNMP tanto escamoso como adenocarcinoma expresa receptores de estrogenos.
  Olak and Colson 2004
- Mayor expresión de receptores de estrógenos en mujeres que en hombres con adenocarcinoma.
  Kadota et al. 2015
- Las mujeres con CP cuentan con menos fumadoras.
- Las mujeres con CP fuman menos.
- Las mujeres con CP tienen mas mutaciones de EGFR (20% vs 9%).
  Aryal et al. 2013

Diferencias en el Perfil Clínico



Variables	Total (n=3,307)	Men (n=2,566)	Women (n=741)	P value
Age, years, mean ± SD	65.4±9.[illegible]	66.5±9.1	61.8±10.8	<0.0001
ECOG performance status, n (%)				
0	1,988 (62.2)	1,473 (59.3)	515 (72.1)	<0.0001
1	1,090 (34.1)	908 (36.6)	182 (25.5)	
2	109 (3.4)	92 (3.7)	17 (2.4)	
3	[illegible]	[illegible]	0	
4	2 (0.1)	2 (0.1)	0	
Smoking status, n (%)				
Smoker	1,042 (32.7)	841 (33.9)	201 (28.4)	<0.0001
Ex-smoker	1,751 (55.0)	1,504 (60.7)	247 (34.[illegible])	
Never smoker	393 (12.3)	133 (5.4)	260 (36.7)	
Smoking pack years, mean ± SD	50.5 (26.3)	53.7 (26.9)	37.5 (18.8)	<0.0001
Comorbidities, n (%				
COPD	940 (28.4)	859 (33.5)	81 (10.9)	<0.0001
Atelectasis	25 (0.8)	20 (0.8)	5 (0.7)	.0
Pneumonitis	68 (2.1)	56 (2.2)	12 (1.6)	0.381
Tuberculosis	[illegible] (2.8)	83 (3.2)	10 (1.3)	0.005
Diabetes mellitus	[illegible]	[illegible]	68 (9.2)	<0.001
Overweight (obesity, BMI >25 kg/m^2)	[illegible] (5.7)	142 (5.5)	45 (6.1)	0.58
Hypertension	1,479 (44.7)	1,216 (47.4)	263 (35.5)	<0.001
Ischemic heart disease	[illegible]	[illegible]	[illegible]	<0.001
Myocardial [illegible]ction	[illegible]	[illegible]	[illegible]	[illegible]
Atrial fibrillation	221 (6.7)	188 (7.3)	33 (4.5)	0.005
Valve heart disease	69 (2.1)	54 (2.1)	15 (2.0)	.0
Peripheral vascular disease	267 (8.1)	250 (9.7)	17 (2.[illegible])	<0.0001
Obstructive sleep [illegible]nea	153 (4.6)	135 (5.3)	18 (2.[illegible])	<0.001
[illegible] function tests, n, [illegible]an ± SD				
[illegible] predicted	91.5±23.0	89.3±23.1	99.[illegible]20.8	[illegible]
FEV$_1$, % predicted	83.9±36.7	81.1±37.0	83.[illegible]34.[illegible]	<0.0001
[illegible] predicted	78.7±38.7	78.7±38.6	78.[illegible]38.8	[illegible]
pO_2, mmHg	82.3±33.5	80.2±13.4	90.3±[illegible]8.4	0.001
pCO_2, mmHg	41.0±25.7	40.2±20.0	44.1±4[illegible]	0.097
SpO_2, %	[illegible]	[illegible]	95.7±2.8	0.606
FEV$_1$, ppo, % predicted	62.4±16.9	60.3±16.2	70.1±17.4	<0.0001
DLCO ppo, % predicted	56.8±17.2	56.6±17.2	57.5±17.2	[illegible]
Exercise stress test, METS	18.4±5.7	18.5±5.6	17.7±6.7	0.428

J Thorac Dis 2019;11(4):1475-1484

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Diferencias en Histología

Variables	Total (n=3,307)	Men (n=2,566)	Women (n=741)	P value
Histological type, n=3,272 (%)				
Epidermoid	1,212 (36.8)	1,098 (43.0)	114 (15.4)	<0.0001
Adenocarcinoma	1,704 (51.7)	1,185 (46.4)	519 (70.1)	
Undifferentiated large-cell	96 (2.9)	81 (3.2)	15 (2.0)	
Undifferentiated small-cell	28 (0.9)	22 (0.9)	6 (0.8)	
Adenosquamous	55 (1.7)	48 (1.9)	7 (0.9)	
Poorly-differentiated	23 (0.7)	16 (0.6)	7 (0.9)	
Other	175 (5.3)	103 (4.0)	72 (9.7)	

J Thorac Dis 2019;11(4):1475-1484

Diferencias en Histología

Table 2A Proportion of patients diagnosed with either squamous cell carcinoma or adenocarcinoma by sex

	Adenocarcinoma		Squamous cell carcinoma	
	Men (%)	Women (%)	Men (%)	Women (%)
Moore et al. [31]	40	50	30	20
Fu et al. [14]	33	45	30	21
Visbal et al. [24]	48	59	32	22
Chen et al. [32]	42	73	41	16
Ringer et al. [26]	38	47	38	24

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Lung Cancer (2007) 55, 15—23

Diferencias en el Estadio

Variables	Total (n=3,307)	Men (n=2,566)	Women (n=741)	P value
T (tumor size), n=3,272 (%)				
T1A	871 (26.6)	632 (24.9)	239 (32.7)	<0.001
T1B	533 (16.3)	415 (16.3)	118 (16.1)	
T2A	999 (30.5)	780 (30.7)	219 (29.9)	
T2B	272 (8.3)	233 (9.2)	39 (5.3)	
T3	451 (13.8)	366 (14.4)	85 (11.6)	
T4	103 (3.1)	79 (3.1)	24 (3.3)	
Tx	43 (1.3)	35 (1.4)	8 (1.1)	
N (regional lymph nodes), n=2,345 (%)				
N0	2,449 (75.5)	1,876 (74.5)	573 (78.7)	<0.001
N1	456 (14.0)	384 (15.3)	72 (9.9)	
N2	337 (10.4)	255 (10.1)	82 (11.3)	
N3	3 (0.1)	2 (0.1)	1 (0.1)	

J Thorac Dis 2019;11(4):1475-1484

Diferencias en el Tratamiento

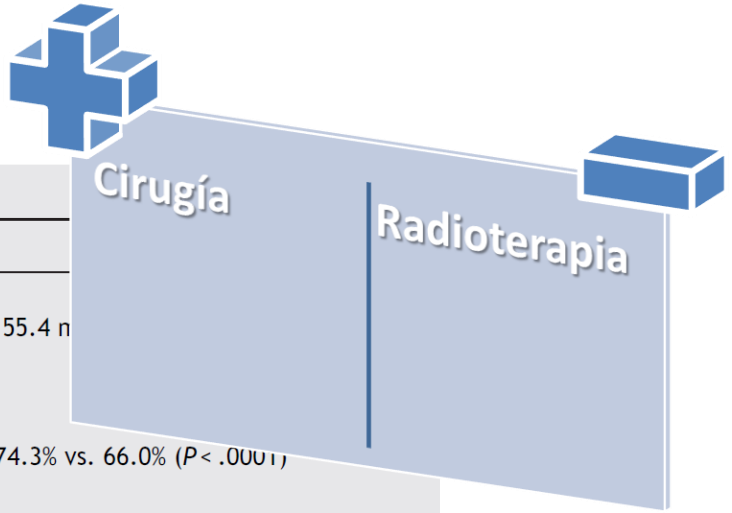

Table 3 Differences in treatment modality by sex

	Women (%)	Men (%)	*P*-value	Survival
Surgery only				
Moore et al. [31]	27.4	24.7	.031	Median: 55.4 n
Radzikowska et al. [101]	23.3	18.8	.0001	NA
Fu et al. [14]				
Local	63.7	56.4	<.0001	2-year: 74.3% vs. 66.0% (*P* < .0001)
Regional	23.4	22.2		
Radiotherapy only				
Moore et al. [31]	17.7	19.6	.031	Median: 10.1 months vs. 8.0 months (*P* = .004)
Radzikowska et al. [101]	14.5	14.6	NS	NA
Fu et al. [14]				
Local	18.2	23.4	<.0001	2-year: 12.2% vs. 15.5% (*P* < .0001)
Regional	39.4	42.5		

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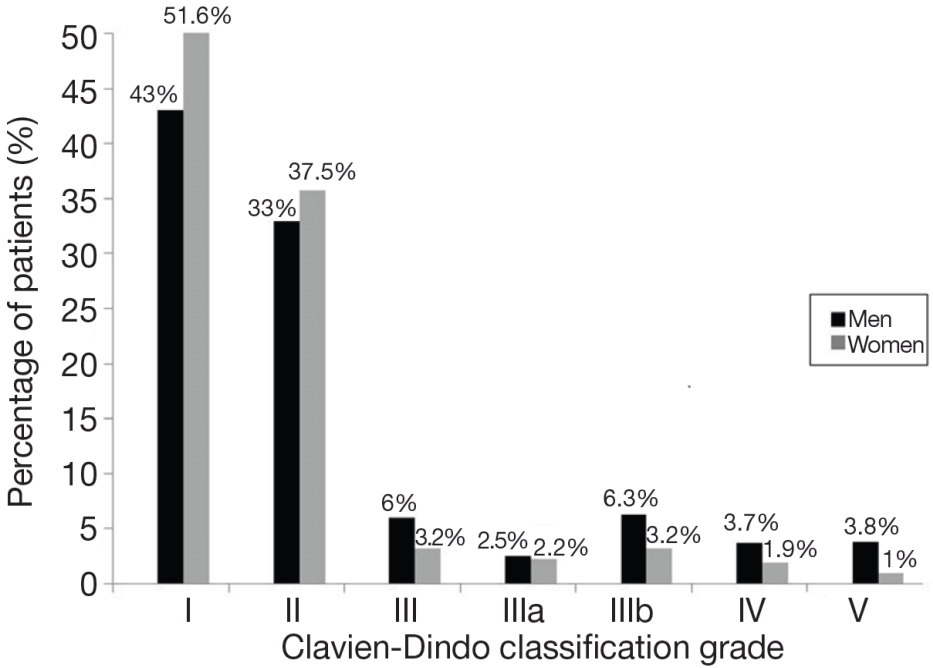
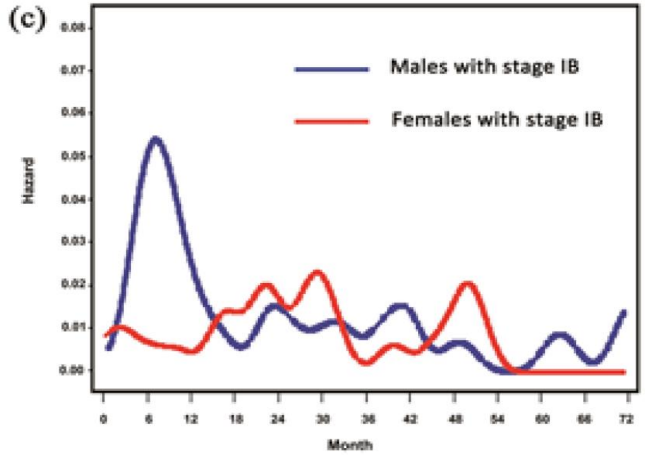
Lung Cancer (2007) 55, 15—23

Complicaciones Post Operatorias



J Thorac Dis 2019;11(4):1475-1484

Recurrencia Post Operatoria



Asian Pac J Cancer Prev, 19 (3), 719-724

Supervivencia

Table 4. Clinical Series Demonstrating NSCLC Survival Benefit in Women

	Author	Year	No. of Patients	% Female	Median Survival (Months) Male	Median Survival (Months) Female	*P* Value
Population	Radzikowska[27]	2002	20,561	14	RR, 1.15		0.001
	Wisnivesky (SEER)[71]	2007	18,67	43	38% (5-y survival)	46% (5-y survival)	0.001
	Cetin (SEER)[93]	2011	51,749	40	14% (1-y survival)	18% (1-y survival)	N/R
Surgery	Ferguson[76]	2000	451	41	26.9	41.8	0.006
	De Perrot[25]	2000	1037	19	24	30	0.004
	Minami[26]	2000	1242	27	65	121	0.05
	Alexiou[73]	2002	833	30	34% (5-y survival)	47% (5-y survival)	0.001
	Batevick[74]	2005	351	32		RR, 0.54	0.001
	Cerfolio[75]	2006	1085	38	50% (5-y survival)	60% (5-y survival)	0.001
Multimodality	Albain[83]	1995	126	36	12	21	0.08
	Werner-Wasik[84]	2000	1999	28	9.9	11.4	0.001
	Keller[94]	2002	488	42	35	41	0.12
	Albain[95]	2009	429	36	RR, 1.42		0.009
Chemotherapy	O'Connell[86]	1986	378	30	8.8	12.4	0.001
	Albain[85]	1991	2531	23	4.8	5.7	0.0005
	Paesmans[87]	1995	1052	10		RR, 0.70	0.03
	Wakelee[88]	2006	1207	37	7.3	9.2	0.004
All	Visbal[20]	2004	4618	41	12	16.8	0.01

N/R, not reported; RR, relative risk.

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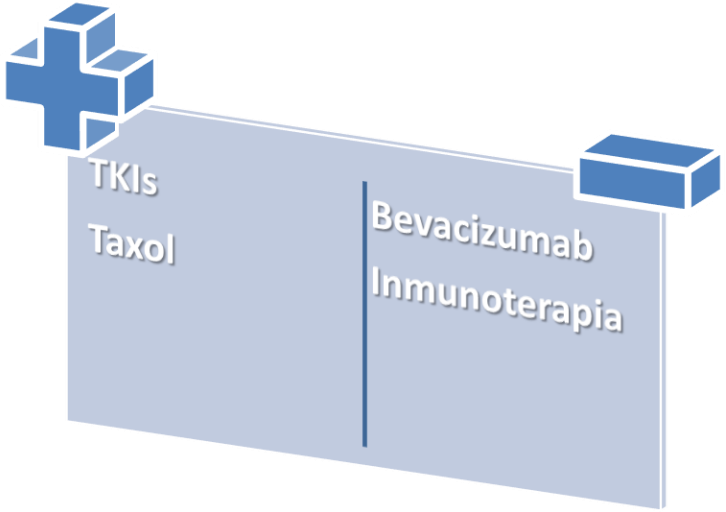
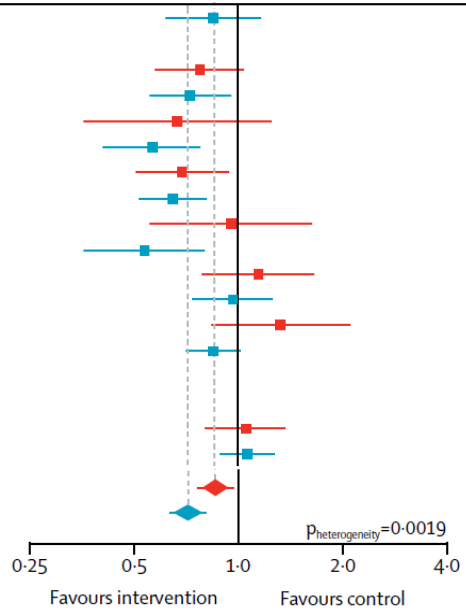
Semin Thoracic Surg 23:137-145 2011

Respuesta al Tratamiento



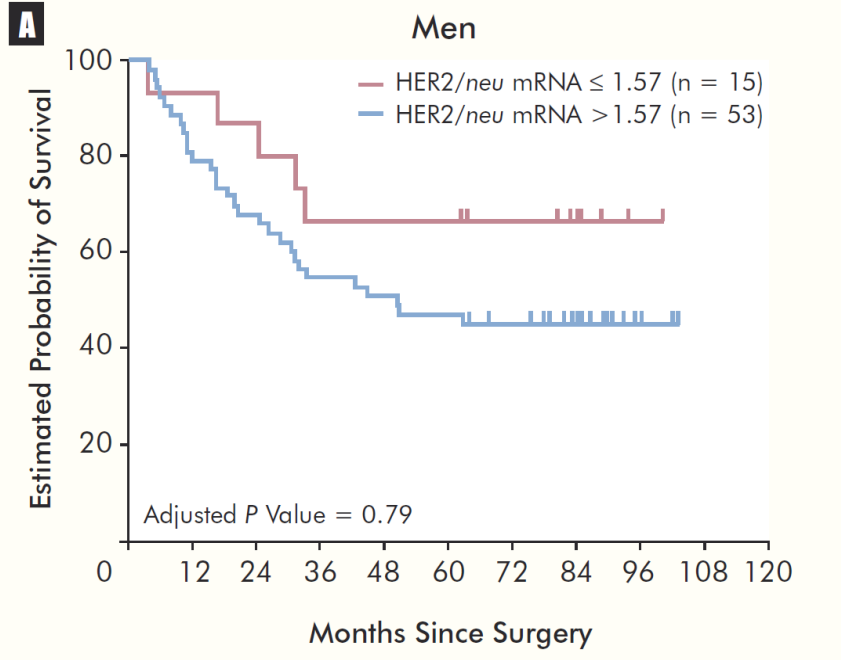
Respuesta a la inmunoterapia

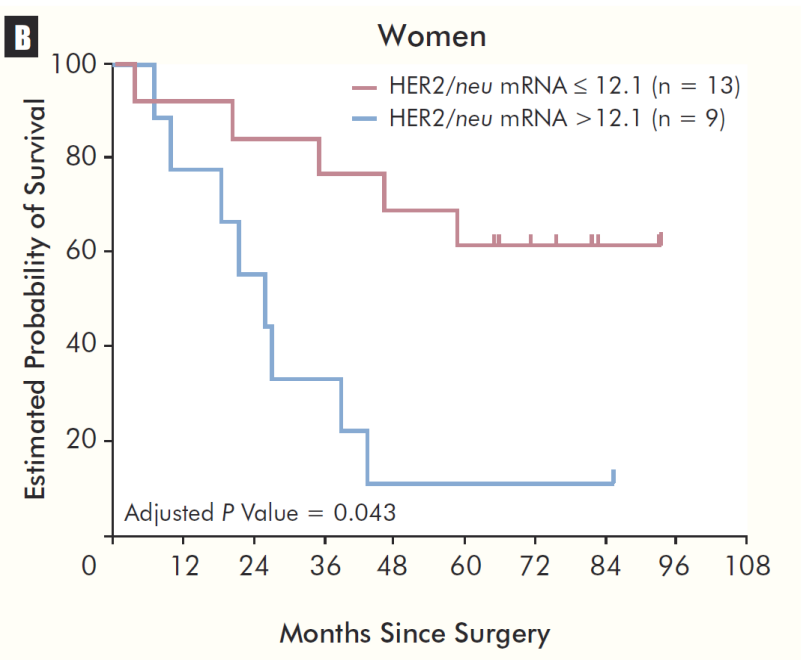
	Line of treatment	Intervention (number of patients)	Control (number of patients)	HR (95% CI)
Non-small-cell lung cancer				0·85 (0·62–1·17)
Borghaei et al (2015)[49]	>1	Nivolumab (n=292)	Docetaxel (n=290)	0·78 (0·58–1·04)
				0·73 (0·56–0·96)
Brahmer et al (2015)[47]	>1	Nivolumab (n=135)	Docetaxel (n=137)	0·67 (0·36–1·25)
				0·57 (0·41–0·78)
Herbst et al (2016)[45]	>1	Pembrolizumab (n=690)	Docetaxel (n=343)	0·69 (0·51–0·94)
				0·65 (0·52–0·81)
Reck et al (2016)[44]	1	Pembrolizumab (n=154)	ICC (n=151)	0·96 (0·56–1·64)
				0·54 (0·36–0·80)
Carbone et al (2017)[43]	1	Nivolumab (n=271)	ICC (n=270)	1·15 (0·79–1·66)
				0·97 (0·74–1·26)
Govindan et al (2017)[48]	1	Ipilimumab plus paclitaxel plus carboplatin (n=388)	Paclitaxel plus carboplatin plus placebo (n=361)	1·33 (0·84–2·11)
				0·85 (0·71–1·02)
Small-cell lung cancer				
Reck et al (2016)[42]	1	Ipilimumab plus etoposide plus platinum (n=478)	Etoposide plus platinum plus placebo (n=476)	1·06 (0·81–1·37)
				1·07 (0·89–1·28)
Pooled estimate in women				**0·86 (0·79–0·93)**
Pooled estimate in men				**0·72 (0·65–0·79)**



Lancet Oncol 2018; 19: 737–46

Marcadores Pronósticos





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Clinical Lung Cancer, Vol. 7, No. 5, 332-337, 2006

Diferencias Psicosociales

Table. Mean (SD) of psychosocial measures of patients with lung cancer, by gender.

Measure	Women (n = 47)	Men (n = 53)	*P*
Psychosocial resources			
Social network (6-pt scale)[a]	4.54 (0.85)	4.55 (0.78)	0.93
Coping effectiveness (5-pt scale)[b]	3.11 (0.54)	3.20 (0.54)	0.40
Daily spiritual experiences (6-pt scale)[c]	3.84 (0.79)	3.38 (1.09)	0.02
Religious and spiritual coping (4-pt scale)[d]	3.42 (0.40)	3.22 (0.53)	0.04
Religious support (4-pt scale)[e]	3.67 (0.40)	3.62 (0.46)	0.64
Religious meaning			
Belief in a divine plan (4-pt scale)[f]	3.47 (0.50)	3.09 (0.74)	0.01
Belief in a life mission (4-pt scale)[g]	3.19 (0.61)	2.87 (0.78)	0.03

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Gend Med. 2010;7:137–148

Diferencias Psicosociales

Table 3 EORTC QLQ-C30 and QLQ-LC29 Results

QLQ-C30	Women (n=46) Mean (Range)	Men (n=84) Mean (Range)	p-value
Global quality of life	55.75 (47.13; 64.39)	49.89 (42.63; 57.15)	0.20
Physical functioning	67.00 (58.05; 75.96)	65.28 (57.75; 72.81)	0.71
Role functioning	51.30 (39.60; 63.00)	56.39 (46.55; 66.23)	0.41
Emotional functioning	59.51 (50.15; 68.87)	61.29 (53.42; 69.16)	0.72
Cognitive functioning	74.02 (63.83; 84.22)	75.39 (66.81; 83.96)	0.80
Social functioning	56.62 (45.46; 67.81)	60.12 (50.71; 69.52)	0.55
Fatigue	51.86 (41.74; 61.97)	45.61 (37.10; 54.12)	0.24
Nausea/vomiting	17.55 (10.34; 24.76)	10.92 (4.85; 16.98)	0.08
Pain	30.24 (18.16; 42.32)	33.85 (23.69; 44.01)	0.57
Dsypnea	50.90 (39.27; 62.54)	48.84 (39.04, 58.64)	0.74
Appetite loss	38.60 (14.79; 41.99)	36.52 (15.39; 38.31)	0.76
Insomnia	28.39 (25.74, 51.47)	26.85 (25.68; 47.35)	0.83
Constipation	22.61 (10.83; 34.38)	22.96 (13.05, 32.86)	0.96
Diarrhea	14.54 (4.80; 24.28)	14.36 (6.17; 22.55)	0.97
Financial difficulties	14.84 (4.14; 25.53)	23.87 (14.86; 32.87)	0.11
QLQ-LC29	**Mean**	**Mean**	**p-value**
Cough	32.34 (21.11; 43.58)	37.11 (27.66; 46.56)	0.42
Shortness of breath	33.54 (24.39; 42.69)	37.16 (29.46; 44.86)	0.45
Hair loss	42.50 (30.13, 54.86)	25.49 (15.09; 35.89)	0.01
Fear of progression	66.51 (54.94; 78.09)	62.86 (53.12; 72.60)	0.55
Surgery related symptoms	30.60 (−0.77; 61.96)	28.27 (5.16; 51.38)	0.87
Sideeffects	20.58 (15.66; 25.50)	20.54 (16.34; 24.68)	0.99
Coughing blood	1.44 (−5.32, 8.21)	7.43 (1.74; 13.12)	0.09
Sore mouth or tongue	8.52 (0.33; 16.72)	8.68 (1.78; 15.57)	0.97

Conclusiones

- Existen importantes diferencias en el perfil clínico entre hombres y mujeres tanto en el CP como en otras enfermedades vinculadas al tabaquismo.
- Existen diferencias biológicas e histológicas.
- Las mujeres reciben diferentes tratamientos a los hombres.
- Estas diferencias suponen un mejor pronóstico en general para las mujeres con CP.