Inmunoterapia y Miscelánea II

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Iniciativa científica de:

GECP

Grupo Español de Cáncer de Pulmón
Spanish Lung Cancer Group

Factores que potencialmente interfieren IT

- Antibioterapia (MA 10.01; MA 10.02): reducción eficacia?
- Tratamiento esteroideo (MA 10.05):
  - PFS: 1.98 vs 3.94 meses. HR 1.80
  - OS 4.86 vs 15.4 meses
  - Multivariante: HR 2.38
- Efectos adversos como predictores de eficacia (MA 10.06):
  - PFS: 5.7 vs 2 meses
  - OS: 17.8 vs 4.04 meses
  - Nº AEs: 8.5 vs 4.6 vs 2 meses
  - HR PFS: 0.38
  - HR OS: 0.48

Factores predictivos eficacia IT: más allá del PD-L1

- TIL y eficacia terapéutica Anti-PD1 (MA11.02):
  - Aumento TIL CD3+ (p=0.007)
  - Reducción FOXP3/CD8+ (p=0.003)
- IDO (MA11.05): 1200 p, asociación con OS
  - Univariante (p=0.006)
  - Multivariante (p=0.053)
- Determinación IHQ de proteínas del complemento en estadíos iniciales (MA11.06):
  - Altos niveles C1w, C4d, C5aR1 predictivos para inferior PFS con signif. estadística
  - Niveles PD1 asociados significativamente con PFS pero no con OS
  - Altos niveles C4d asociados con disminución significativa expresión PD-L1 en células tumorales
- Expresión LAG3 y NY-ESO-1 y duración beneficio clínico (MA11.07):
  - VPP: LAG3 (55.17%), NY-ESO-1 (57.89%), PD-L1 (71.43%)
  - Expresión LAG3: HR 0.17 para PFS, HR 0.25 para OS
- Diferencias en Tumor Neoantigen Burden entre primario y metástasis:
  - Lesiones primarias (mediana 157, 21-1156) vs lesiones metastáticas (mediana 135; 35-1902)

Segundas neoplasias broncopulmonares metacrónicas

LUNG CANCER UPDATES
IASLC HIGHLIGHTS
23-26 SEPTIEMBRE 2018 TORONTO

Baseline Patient Characteristics

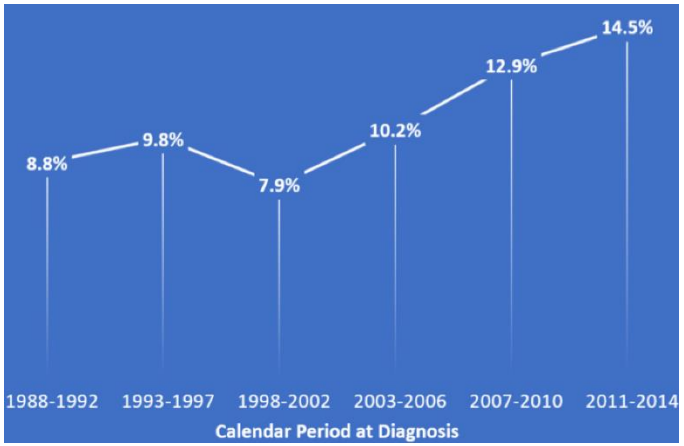
Characteristic	Lung – 1 (n = 679,541) n	%	Lung – 2 (n = 85,758) n	%
Age at diagnosis, years				
≥65	433,477	64	67,961	79
Sex				
Men	367,647	54	51,177	60
Women	311,894	46	34,581	40
Race				
White	551,851	81	71,989	84
Black	81,942	12	9,588	11
Asian	41,252	6	3,875	5
Other	4,496	1	306	0
Tumor stage				
Localized	115,704	17	22,117	26
Regional	165,322	24	21,151	25
Distant	362,823	53	38,067	44
Unknown	35,692	5	4,423	5
Histology				
Small cell	93,988	14	9,130	11
Non-small cell	463,560	68	61,884	72
Other	121,993	18	14,744	17

Associations of Lung-2 with Tumor and Clinical Characteristics

	Lung-1 OR/RRR	Lung-2 OR/RRR (95% CI) *
Tumor Characteristics		
Localized tumor	1.00	1.64 (1.61-1.67)
Tumor size ≤3 cm	1.00	1.51 (1.49-1.54)
Histology		
Small cell	1.00	0.81 (0.79-0.83)
Squamous cell	1.00	1.08 (1.06-1.10)
	OR	OR (95% CI) †
Treatment Modalities		
Radiation therapy	1.00	0.93 (0.92-0.95)
Chemotherapy	1.00	1.00 (0.98-1.02)
Surgery	1.00	1.20 (1.17-1.23)

HR, hazard ratio; OR, odds ratio; RRR, relative risk ratio; CI, confidence interval.
*The models were adjusted for age and calendar period at diagnosis, sex, race, cohabitation status, and percentile of cost of living and high-school education in county of residence. Histology and tumor grade were presented by relative risk ratio; the rest were presented with odds ratio.
†The models were adjusted for age and calendar period at diagnosis, sex, race, cohabitation status, percentile of cost of living and high-school education in county of residence, tumor stage, histology, and tumor grade

WCLC



	N of patients	From 0 to <1 year after diagnosis N (IR)	HR (95% CI) *	From 1 year to < 5 years after diagnosis N (IR)	HR (95% CI)*	From 5 years to 10 years after diagnosis N (IR)	HR (95% CI)*
Overall mortality							
Lung-1	679,541	383,208 (99.9)	1.00	135,513 (29.3)	1.00	16,821 (9.8)	1.00
Lung-2	85,758	44,288 (84.1)	0.91 (0.91-0.92)	20,073 (29.4)	1.10 (1.08-1.12)	3,133 (14.6)	1.32 (1.27-1.37)
Lung cancer specific mortality							
Lung-1	679,541	325,633 (84.9)	1.00	111,348 (24.1)	1.00	8,147 (4.7)	1.00
Lung-2	85,758	31,247 (59.3)	0.77 (0.76-0.78)	12,485 (18.3)	0.87 (0.86-0.89)	1,158 (5.4)	1.10 (1.03-1.17)

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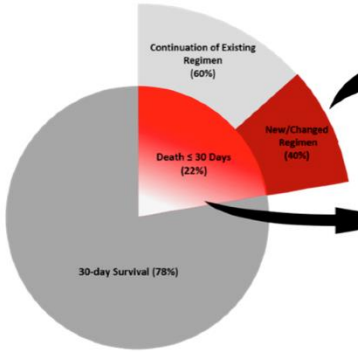
Mortalidad a los 30 días del tratamiento sistémico (Canadá)



Active intervention in patients who experience imminent death

In the Literature
30-day Mortality Rates Following Systemic Treatment

3 – 43%
For all solid tumors

8%
NSCLC Patients, England, 2014[2]

2. Wallington M, Saxon E, Bomb M, et al. Lancet 2016;17:1203-1216 doi: 10.1016/S1470-2045(16)30438-7

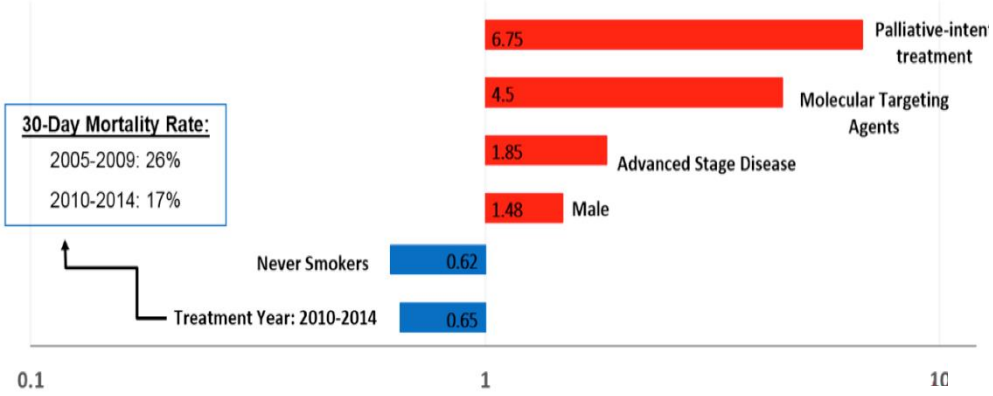
glans-look
LUNG CANCER RESEARCH

8000 NSCLC Patients
1999-2014
Demographic data
Clinical data
Pathological data
Treatment data
Outcome data

≥ 1 cycle of systemic treatment
2005 – 2014
n = 1044

30-day mortality: Death within 30 days of systemic therapy receipt

EOL Regimen Change: New/changed treatment in last 14 days of life



Multi-Year Population Based Analysis
- 22% of patients die within 30 days of systemic therapy.
- 40% of these patients had new of changed regimens in this timeframe.

Risk Factors
- Mortality associated with male gender, palliative-intent treatment, advanced stage and use of molecular targeted agents.

Benchmarks
- Study based on Canadian NSCLC patients.
- Evolving systemic treatment options and patient environment may influence 30-day mortality rate.

Tratamiento activo en el último mes de vida (Francia)

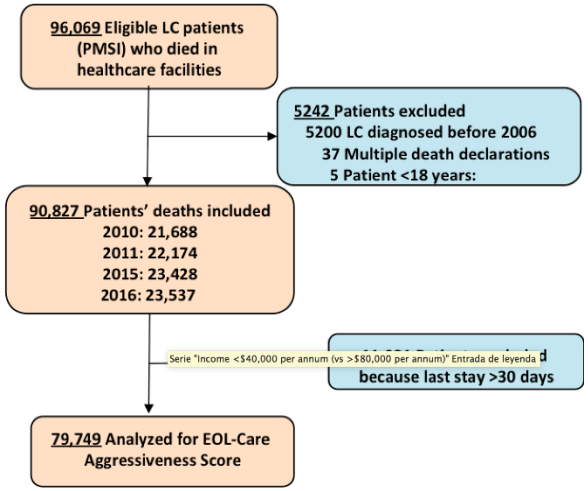
Methodology

Using a French hospital's discharge database (PMSI)

LC patients who died in healthcare facilities:
- Cohort 1: January 1, 2010 to December 31, 2011
- Cohort 2: January 1, 2015 to December 31, 2016

Inclusion criteria:
- All patients
  - with hospital-managed LC identified via ICD-10 code C34 "Lung Cancer"
  - who had died in-facility according to PMSI

Exclusion criteria:
- LC diagnosed before 2006
- Minor



Results

EOL Aggression Score

	All	Cohort 1 2010–11	Cohort 2 2015–16	p
Indicators	%	%	%	
>1 hospitalization	49%	48%	51%	<0.001
ICU admission	12%	11%	13%	<0.001
Chemotherapy ≤14 days before death	9%	10%	9%	0.33
Palliative care <3 days before death	5%	5%	5%	0.17

EOL-Care Aggressiveness	All		2010/2011		2015/2016		p
Score	n	%	n	%	n	%	
0	34,119	43%	16,884	44%	17 235	42%	
≥1	45 627	57%	21,482	56%	24 145	58%	<0.001

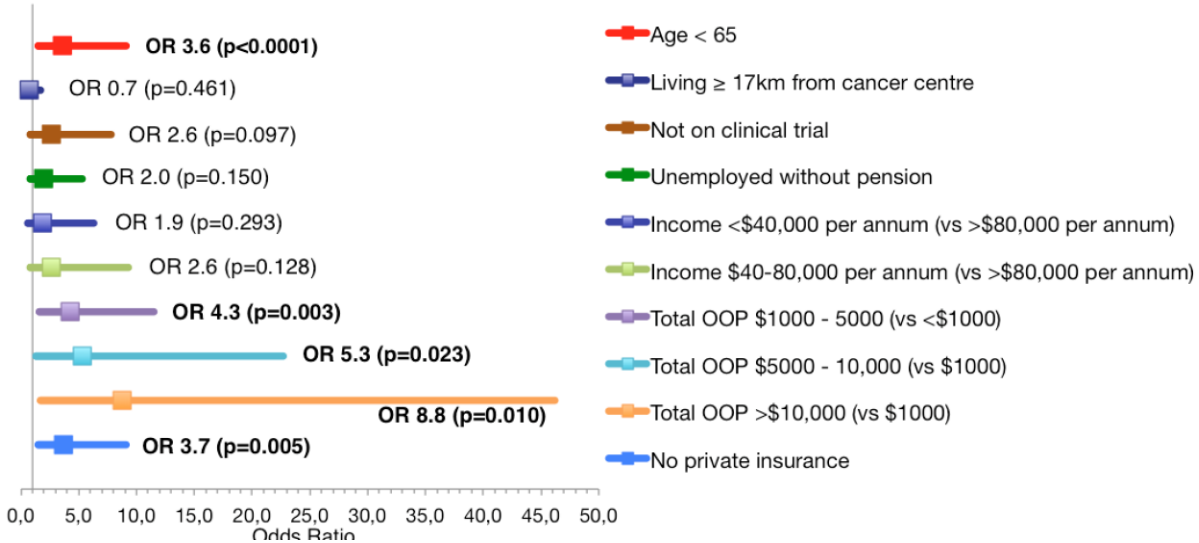
Multivariable Logistic-Regression Analysis Predicting Aggressive EOL Care

Factor	OR	95% CI	p value
Age at death (years)			<0.0001
18–55	1.00	---	
56–65	0.89	0.80–0.95	
66–75	0.76	0.71–0.82	
76–85	0.51	0.47–0.55	
>85	0.29	0.26–0.90	
Sex			<0.0001
Female	0.86	0.8–0.90	
Days since LC diagnosed			<0.0001
[0–90[	1.47	1.35–1.59	
[90–365[	1.28	1.18–1.39	
[365–730[	0.99	0.91–1.08	
[730–1095]	1.00	---	
Hypertension	1.07	1.02–1.12	0.0047
COPD	1.08	1.02–1.14	0.0070
Other lung diseases	1.08	1.01–1.15	0.0162
Cardiac history	1.08	1.02–1.14	0.0093
Malnutrition	0.72	0.68–0.76	<0.0001
Where death occurred			<0.0001
General Hospital Center	1.00	---	
University Hospital Center	1.58	1.49–1.68	
Cancer Center	2.32	2.05–2.61	
Other public institutions	1.34	1.25–1.43	
Other private institutions	1.33	1.26–1.41	
Density (no. of inhabitants/km²)			0.0013
≤90.0	1.04	0.98–1.11	
]90.0–320.3]	1.08	1.01–1.14	
]320.3–2124.5]	0.96	0.91–1.02	
>2124.5	1.00	---	
Deprivation index			0.0220
The poorest	0.92	0.87–0.98	
Deprived	0.92	0.87-0.98	
Privileged	0.93	0.87-0.99	
The most privileged	1.00	---	

Abbreviations: OR, odds ratio; COPD, chronic obstructive pulmonary disease

Toxicidad financiera USA

Patient characteristics and COST values: univariate analysis results

Patient characteristics		Number (%) N=200	COST score Median (IQR) *Lower is worse*	Univariable *P*
Age	<65 ≥ 65 Range 32-86	98 101	18 (13) 24 (14)	<0.0001
Sex	Male Female	88 (44%) 111 (56%)	20 (11) 22 (15)	0.63
Ethnicity	White Asian Other	98 (51%) 72 (37%) 23 (12%)	22 (15) 20 (12) 19 (10)	0.32
Marital status	Married Not married	146 (75%) 50 (25%)	20 (14) 22 (16)	0.38
Country of birth	Canada Other	70 (36%) 124 (64%)	22 (14) 20 (14)	0.07
Distance from PMCC	<17km ≥17km	86 (43%) 82 (41%)	23 (14) 20 (11)	0.09

Multivariable logistic regression, factors associated with greater financial toxicity, final model