SITUACIONES ESPECIALES EN CANCER DE PULMON. SEGUNDA LÍNEA EN CPM

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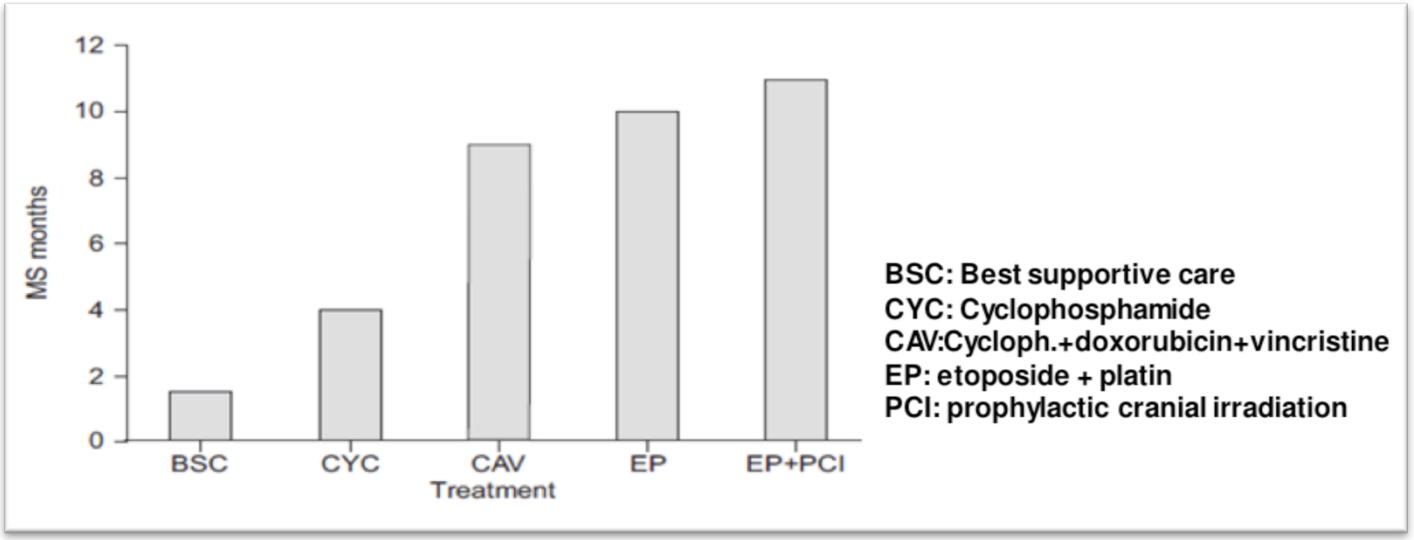
	Median Survival – Untreated Patients (wk)	Median Survival – Treated Patients (mo) plateau	5-Year Survival (%)
Limited disease	**12**	**14-20**	**10%-20%**
Extensive disease	**5**	**8-12**	**3%-5%**

- Extensión
- Tiempo desde fin de primera línea

- Probabilidad de Respuesta Objetiva en 2º línea:
  - Tiempo desde el fin de 1º línea
  - Respuesta al tto inicial
  - PS



- Platino-Etopósido es el gold standard desde 1985!!!
- Esquemas con 3-4 drogas
- Regimenes con intensificación de dosis
- Mantenimiento -Consolidación

} **INEFICACES**

TIPOS DE RECAIDAS

En función del grado de quimiosensibilidad:

- **Quimiosensibles**: PE > 90 días desde fin QT
- **Quimioresistentes**: PE≤ 90 días
- **Refractarios**: Tumor progresa o no responde al tto inicial

EL objetivo del tto : Control de síntomas y mejorar QoL

QT vs BSC

- O'Brien ME (JCO 2006): 141 ptes Topotecan oral vs BSC
  - Todos recaidas ≥ 45d
  - MOS 26 sem vs 14. 7% Respuestas objetivas. 44% EE
  - Mayor beneficio en recaidas ≥ 60 días
  - Beneficio en QoL

- Estudio SPEAR, (Ciuleanu, JCO 2010): 401 ptes Picoplatino vs BSC
  - No diferencias en SG (21 vs 20 sem)
  - SG mayor en ptes con enf refractaria o recaída quimiorresistente (21.3 vs 18.4 sem)

Owonikoko
JTO 2012

Study	Total (Sensitive/Refractory)	PS (0/1/2)	Study Design	Therapy	RR (%)		OS (months)	
					Sensitive	Refractory	Sensitive	Refractory
Eckardt et al. 2009[17]	77 (6/71)	9/51/17	Phase II single arm	Picoplatin	17	8	NR	NR
Jalal et al. 2009[18]	43 (20/23)	14/18/11	Single arm phase II	Pemetrexed	5	4	4.4	2.7
Gronberg et al 2009[19]	34 (25/9)	5/18/11	Multicenter phase II	Pemetrexed	0	11	5.7	3.8
Rocha-Lima et al. 2007[20]	71 (35/36)	19/41/11	Phase II single arm	Irinotecan Gemcitabine	31	11	7.1	3.5
Ardizzoni et al. 2003[21]	110 (68/42)	17/75/18	Multicenter single arm phase II	Topotecan + Cisplatin	29	24	NR	NR
Naka et al. 2002[22]	29 (16/13)	0/16/13	Single arm phase II	Irinotecan + Carboplatin	38	23	6.1	5.7
Sculier et al. 2002[23]	45 (29/16)	NR	Randomized phase II	Cisplatin-etoposide/carboplatin	49	19	7.7	7.4
Kosmas et al. 2001[24]	33 (13/20)	NR	Single arm phase II	Paclitaxel, Ifosfamide and Cisplatin	77	70	NR	NR
Sonpavde et al. 2000[25]	46 (32/14)	NR	Single arm phase II	Doxorubicin + Paclitaxel	53	14	NR	NR
Ardizzoni et al. 1997[26]	92 (45/47)	NR	Single arm phase II	Topotecan	37.5	6.4	6.9	4.7
Schuette et al. 2005[27]	35 (20/15)	9/21/5	Single arm phase II	Gemcitabine + Irinotecan	10	26	4.5	4.5
Ichiki et al. 2003[28]	34 (24/10)	7/16/11	Single arm phase II	Irinotecan + Ifosfamide	62.5	30	NR	NR
Hensing et al. 2006[29]	37 (20/17)	NR	Single arm phase II	BBR 3464 (Triplatin)	NR	NR	6.8	2.5
Domine et al. 2001[30]	20 (10/10)	NR	Multicenter phase II	Gemcitabine + Paclitaxel	60	50	NR	NR
Dongiovanni et al. 2006[31]	31 (21/10)	3/20/8	Single institution phase	Gemcitabine + Paclitaxel	28.6	20	NR	NR
Hoang et al. 2003[32]	27 (15/12)	25/0/2	Single arm phase II	Gemcitabine	NR	NR	8.8	4.2
Hainsworth et al. 2003[33]	29 (12/17)	NR	Single arm phase II	Gemcitabine and Vinorelbine	25	0	NR	NR
Sessa et al. 2000[34]	66 (37/29)	15/39/12	Single arm phase II	GI147211 (Camptothecin)	21.6	10.3	NR	NR
Huber et al. 2006[35]	169 (111/58)	34/92/37	Multicenter single arm phase II	Topotecan	17.2	8.6	5.04	5.33
Von Pawel et al. 2011[36]	**Amrubicin (225/199)**	NR	Multicenter phase III trial	Amrubicin	NR	NR	9.2	6.2
	Topotecan (117/96)			Topotecan	NR	NR	9.9	5.7
Vigano et al. 2011[37]	27	NA	Single arm phase II	NGR-hTNF + Doxorubicin	27	19	NR	NR
Overall	1692 (901/764)	157/407/156			27.7	14.8	7.73	5.45

Table 1 Summary of phase II trials of cytotoxic agents for relapsed SCLC

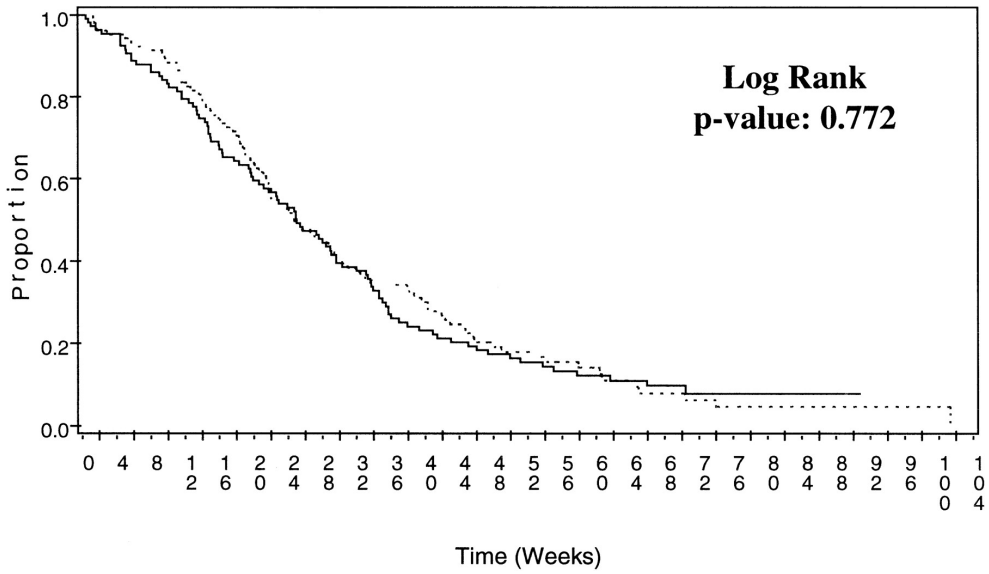
Study	Regimen	*n* of patients	Overall RR (%)	Median survival (mos)	Median response duration (mos)
Ando et al. [26]	Irinotecan (60 mg/m^2) + cisplatin (30 mg/m^2) on days 1, 8, and 15	25	80	7.9	3.6
Masuda et al. [27]	Irinotecan (70 mg/m^2) on days 1, 8, and 15 + etoposide (80 mg/m^2) on days 1–3	25	71	9	4.6
Naka et al. [28]	Irinotecan (50 mg/m^2) + carboplatin (AUC, 2) on days 1, 8, and 15	29	31	6.1	3.5
Yamamoto et al. [29]	Paclitaxel (80 mg/m^2) weekly	21	24	NA	NA
Kosmas et al. [30]	Paclitaxel (175 mg/m^2) on day 1 + ifosfamide (5 mg/m^2) on days 1 and 2 + cisplatin (100 mg/m^2) on days 1 and 2 (every 21 days)	35	73	7	5.2
Kakolyris S et al. [31]	Paclitaxel (200 mg/m^2) + carboplatin (AUC, 6) every 28 days	32	25	7	3
Sonpavde et al. [32]	Paclitaxel (175 mg/m^2) + doxorubicin (40 mg/m^2) every 21 days	46	41	NA	NA
Fennell et al. [33]	Irinotecan (100 mg/m^2) + cisplatin (100 mg/m^2) on days 1 and 15 + mitomycin (6 mg/m^2) on day 1 every 28 days	21	57	7.8	4.5
Rocha-Lima et al. [34]	Gemcitabine (1,000 mg/m^2) + irinotecan (100 mg/m^2) on days 1 and 8 every 21 days; group A, sensitive; group B, refractory	75	Group A, 31; group B, 11	Group A, 7.1; group B, 3.5	PFS: group A, 3.1; group B, 1.6
Inoue et al [35]	Amrubicin (40 mg/m^2) on days 1–3 versus topotecan (1 mg/m^2) on days 1–5 every 21 days	59	38 versus 13	8.1 versus 8.4	3.5 versus 2.2
Schmittel et al. [36]	Bendamustine (120 mg/m^2) on days 1 and 2 every 21 days	21	29	7	4

Abbreviations: AUC, area under the concentration–time curve; NA, not available; PFS, progression-free survival; RR, response rate; SCLC, small cell lung cancer.

Hurtwitz, The Oncologist 2009

Topotecan

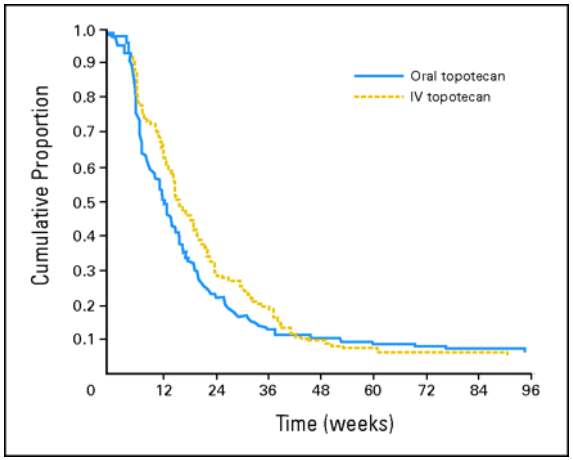
- Único fármaco aprobado en 2 línea para CPM refract/recaída
- Von Pawel, JCO 1999: Topotecan vs CAV
  - 211 ptes quimiosensibles
  - ORR (24% vs 18%), MTTP (13 vs 12 sem) y MOS (25 vs 24.7 sem)similares
  - **Mejor control sintomático** y menor toxicidad con Topotecan



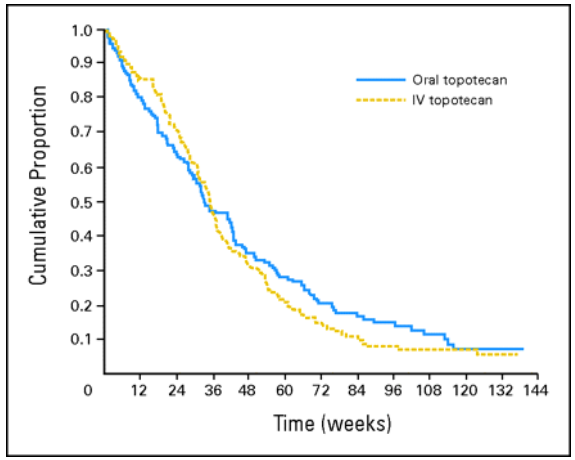
Topotecan

- Topotecan oral similar eficacia y toxicidad que iv (Eckardt JR, JCO 2007)
  - Avalado ensayo fase III de no inferioridad
  - 2.3mg/m2 diario x 5 días vs 1.5mg/m2 iv diario x 5 días
  - Pacientes quimiosensibles

TTP



SG



- Topotecan en > 65 años tiene similar eficia y toxidad (Garst, Clin Lung Cancer 2005)
- Topotecan es util en metástasis cerebrales

Otros fármacos

- IRINOTECAN: 16-47% respuestas objetivas. Nula respuesta en resistentes/refractarios
- PACLITAXEL: 29% RP, pero con corta duración de respuesta (mediana 100 días)
- DOCETAXEL: ORR 25%, con *71% neutropenia G4*
- ETOPOSIDO ORAL: ORR 23% (96% ptes VP16 previo en 1º línea)
- VINORELBINA
- GEMCITABINA

AMRUBICINA

AMRUBICINA:
Phase III 2nd-line SCLC: ACT-1 Trial

- Antraciclina 3º generación y un inhibidor potente de la Topoisomerasa II

- Small Cell Lung Cancer (SCLC)
- Extensive or Limited Disease
- Sensitive or refractory disease (Progression ≥90 or <90 days after completion of 1st-line chemotherapy, Response to 1st-line chemo)
- 1 prior chemotherapy regimen
- ECOG performance status 0-1
- Stratified: Sensitive/Refractory; Extensive/Limited

→ **RANDOMIZE 2 to 1**

→ AMR IV
40 mg/m²
1x daily on
d 1-3 q 3 w

→ Topotecan IV
1.5 mg/m²
1x daily on
d 1-5 q 3 w

- **Primary endpoint:** Overall survival
- **Secondary endpoints:** ORR, PFS, TTP, quality of life, safety, sparse PK
- **Analyses:** Interim (deaths = 294), Final (deaths = 490)

[97.5% power: 6.0 vs. 8.7 months (HR: 0.69)]

Jotte, JCO 2011

- Características de los pacientes

	AMR, N=424 n (%)	Topo, N=213 n (%)
Age (Median)	62	61
Range	22-81	30-81
Age ≥ 65 years	169 (39.9)	74 (34.7)
Sex		
Male	244 (57.5)	127 (59.6)
Female	180 (42.5)	86 (40.4)
Performance Status		
0	126 (29.7)	72 (33.8)
1	289 (68.2)	137 (64.3)
2	9 (2.1)	4 (1.9)
Sensitivity to first-line therapy		
Sensitive	225 (53.1)	117 (54.9)
Refractory	199 (46.9)	96 (45.1)

Jotte, JCO 2011

PFS

RR = 31.1 (A) vs 16.6% (T) p= 0.0001

	Amrubicin N=424	**Topotecan N=213**	**HR**	***p*-value***
N/Events	424/367	213/167		
Median PFS (months)	4.1	3.5	0.802	0.0182
95% CI	3.5 – 4.3	2.9 – 4.2	0.667 – 0.965	

* Unstratified log-rank test

Jotte, JCO 2011

OS

	AMR	Topo	HR	p-value*
N/Events	424/336	213/175		
Median OS (months)	7.5	7.8	0.880	0.1701
95% CI	6.8 – 8.5	6.6 – 8.5	0.733 – 1.057	

* Unstratified log-rank test

Jotte, JCO 2011

MOS

Sensitive Patients

	AMR	Topo	HR	p-value*
N/events	225/168	117/89		
OS (mo)	9.2	9.9	0.936	0.6164
95% CI	8.5-10.6	8.5-11.5	0.724 – 1.211	

Refractory Patients

	AMR	Topo	HR	p-value*
N/events	199/168	96/86		
OS (mo)	6.2	5.7	0.766	0.0469
95% CI	5.5-6.7	4.1-7.0	0.589 – 0.997	

* Unstratified log-rank test

Toxicidad G3-4

System Organ Class Preferred Term	Number (%) of Patients	
	Amrubicin (N=408)	Topotecan (N=197)
Patients with at least 1 Grade 3 or 4 TEAE	296 (72.5)	174 (88.3)
Blood and Lymphatic System Disorders	216 (52.9)	152 (77.2)
Anemia	65 (15.9)	60 (30.5)
Febrile Neutropenia	38 (9.3)	7 (3.6)
Leukopenia	62 (15.2)	43 (21.8)
Neutropenia	168 (41.2)	105 (53.3)
Thrombocytopenia	86 (21.1)	107 (54.3)
General Disorders and Administration Site Conditions	74 (18.1)	30 (15.2)
Fatigue	43 (10.5)	24 (12.2)
Infections	54 (13.2)	17 (8.6)
Pneumonia	22 (5.4)	5 (2.5)
Metabolism and Nutrition Disorders	67 (16.4)	24 (12.2)
Hyponatremia	21 (5.1)	11 (5.6)
Respiratory, Thoracic, and Mediastinal Disorders	43 (10.5)	19 (9.6)
Dyspnea	18 (4.4)	13 (6.6)
Transfusions		
Blood and related products	131 (32.1)	104 (52.8)

P<0.05 for highlighted values.

BENDAMUSTINA

- Alquilante con eficacia demostrada en primera línea combinado con carbo (RR 73%, TTP 5.2 months and OS 8.3 months [Köster, JTO 2007].
- Ensayo fase II, 2ª y 3ª lineas
  - Bendamustina 120mg/m^2 IV d1-2, cada 3 sem
  - 48 ptes.: 1 RC, 9 RP, 13 EE (Tasa control enf 48%)
  - MTTP 3.7m, MOS 4.77m
  - Toxicidad 3-4: astenia 18%, disnea 15%, infección 12.5%
- Ensayo abierto combinado con VP16

Lovely, et al ASCO 2012

- Inhibidor de Topoisomerasa 1

Phase II Multicenter Trial of Voreloxin as Second-Line Therapy in Chemotherapy-Sensitive or Refractory Small Cell Lung Cancer

Lee M. Krug, MD, Jeffrey Crawford, MD,† David S. Ettinger, MD,‡ Geoffrey I. Shapiro, MD,§ David Spigel, MD,‖ Tony Reiman, MD,¶ Jennifer S. Temel, MD,# Glenn C. Michelson, MD,** Donald Y. Young, MS,** Ute Hoch, PhD,†† and Daniel C. Adelman, MD‡‡*

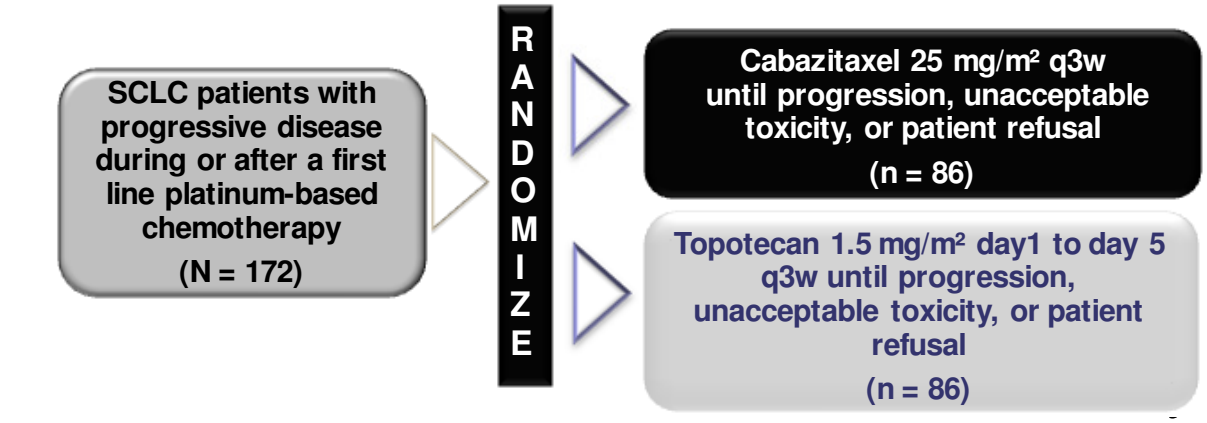
Journal of Thoracic Oncology -Volume 6,Number 2,February 2011

Conclusion: Voreloxin has minimal activity in relapsed SCLC when administered at 48 mg/m^2 in a 3-week schedule.

Cabazitaxel

- Agente antimicrotúbulo con actividad en tumores resistentes a docetaxel

ARD 12166 Phase II design



Stratification factors (IVRS)

- Brain metastasis: yes vs. no
- LDH level: ≤ upper limit vs. > upper limit

Primary

- *Progression free survival (PFS):* time interval from the date of randomization to the date of occurrence of the first documented tumor progression or death due to any cause, whichever comes first.

Secondary

- *Disease progression free rate at 12 weeks*: proportion of patients that are free of disease progression at the 12 week assessment.
- *Objective response rate (ORR) and duration (RECIST 1.1)*
- *Overall survival (OS)*
- *Safety*
- *HRQOL*

Agentes diana en estudio en CPM

Matrix Metalloproteinase Inhibitors
Marimastat
Tanomastat
c-Kit Receptor Tyrosine Kinase Inhibitors
Imatinib
Vaccines
Mitumomab
Autologous dendritic cell–Adenovirus p53 vaccine
Anti–Bcl-2 Family Protein Inhibitors
Oblimersen
AT-101 (R-(-)-gossypol)
Antiangiogenic Inhibitors
Bevacizumab
Cediranib
Vandetanib
Sorafenib
Thalidomide
Mammalian Target of Rapamycin Inhibitors
Temsirolimus
Everolimus
Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitor
Gefitinib
Farnesyltransferase Inhibitor
Tipifarnib
Multidrug Resistance Inhibitor
Biricodar
Anti-CD56 Monoclonal Antibody
BB-10901

>900 ensayos realizados

Antiangiogénicos

	Phase	Population	Pts, n	Conclusion	Reference
Bevacizumab (anti-VEGF)	II	• Extensive stage • Untreated • With combination chemotherapy	63	Promising results (pts progression-free at 6m: 33%)	*J Clin Oncol 2009*
	II		72	Primary end-point (12m OS) not reached – OS: 11m and PFS: 7m	*J Clin Oncol 2011*
	II	Relapsed, in combination with paclitaxel	34	No improvement in PFS and OS	*J Thor Oncol 2010*
	II	1st line in combination with chemotherapy	52	Improved PFS – no difference in OS	*J Clin Oncol 2011*
Vandetanib (anti-VEGFR-2)	II	Maintenance after 1st line chemotherapy for pts at CR or PR	107	No efficacy as maintenance therapy	*J Clin Oncol 2007*
Sorafenib	II	Relapsed, 2nd line	89	No clinical activity	*J Thor Oncol 2010*
Thalidomide	III	Extensive stage, after response to 2 cycles of chemotherapy	119	No significant improvement in survival	*J Clin Oncol 2007*
	III	Untreated pts, in combination with carboplatin/etoposide	724		*Lung Cancer 2008*
Cediranib (anti-VEGFR-1, 2, 3)	II	Relapsed	25	No clinical activity	*J Thor Oncol 2010*

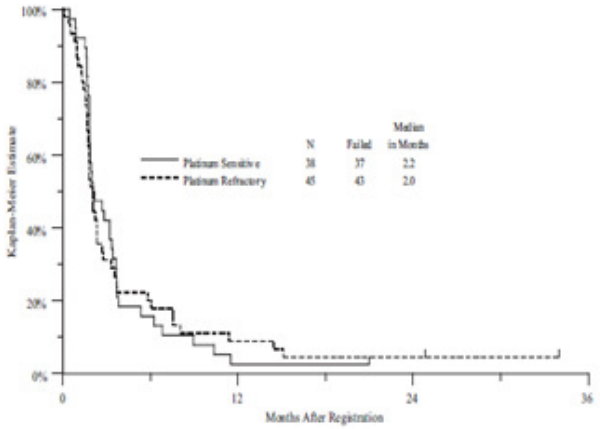
Sorafenib

Sorafenib in Platinum-Treated Patients with Extensive Stage Small Cell Lung Cancer

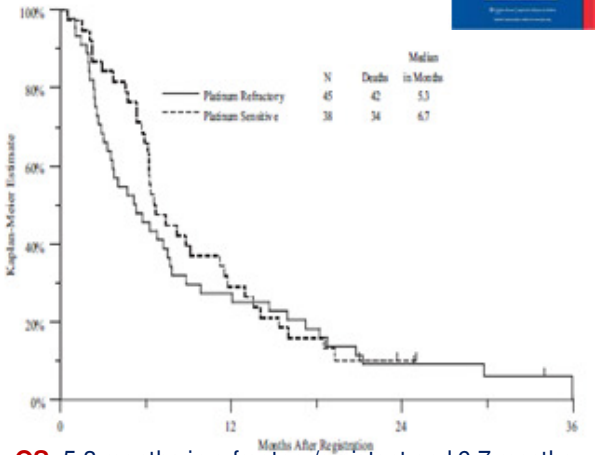
A Southwest Oncology Group (SWOG 0435) Phase II Trial

Barbara J. Gitlitz, MD, James Moon, MS,† Bonnie S. Glisson, MD,‡ H. Joachim Reimers, MD, PhD,§ Martin J. Bury, MD,‖ Justin D. Floyd, DO,¶ Thomas K. Schulz, MD,# P. Kothai Sundaram, MD,** Christopher Ho, MD,* and David R. Gandara, MD††*

- **Sorafenib:** inhibitor of B-raf, VEGFR-1, 2, 3, PDGFRβ, c-kit, FLT3, RET.
- **Primary objective:** objective response rate
- **Secondary objectives:** OS, PFS, toxicities



PFS: 2.0 months in refractory/resistant and 2.2 months in platinum-sensitive pts



OS: 5.3 months in refractory/resistant and 6.7 months in platinum-sensitive pts

(*J Thorac Oncol.* 2010;5: 1835–1840)

•Sorafenib induce una ORR 35%. MOS sin diferencias con los controles históricos

ITKs

Molecule	Phase	Population	Pts, n	Conclusion	Reference
Gefitinib (anti-EGFR)	II	Relapsed, 2nd line single-agent	18	No clinical activity	*Lung Cancer 2006*
Imatinib	II	Relapsed, 2nd line single-agent	29	No clinical activity	*Ann Oncol 2005*
	II		12	No clinical activity	*Cancer 2005*
	II		19	No clinical activity	*Clin Cancer Res 2003*
	II	Maintenance therapy, single-agent	8	No clinical activity	*Clin Lung Cancer 2010*
	II	1st line with carboplatin/ irinotecan	68	No benefit versus chemotherapy alone	*J Thorac Oncol 2007*
Sunitinib	II	Maintenance after 4 cycles of chemotherapy in pts with SD or response	16	No improvement in PFS or OS	*Journal of Thoracic Oncology, 2011*

BRIEF REPORT

Epidermal Growth Factor Receptor Mutations in Small Cell Lung Cancer

A Brief Report

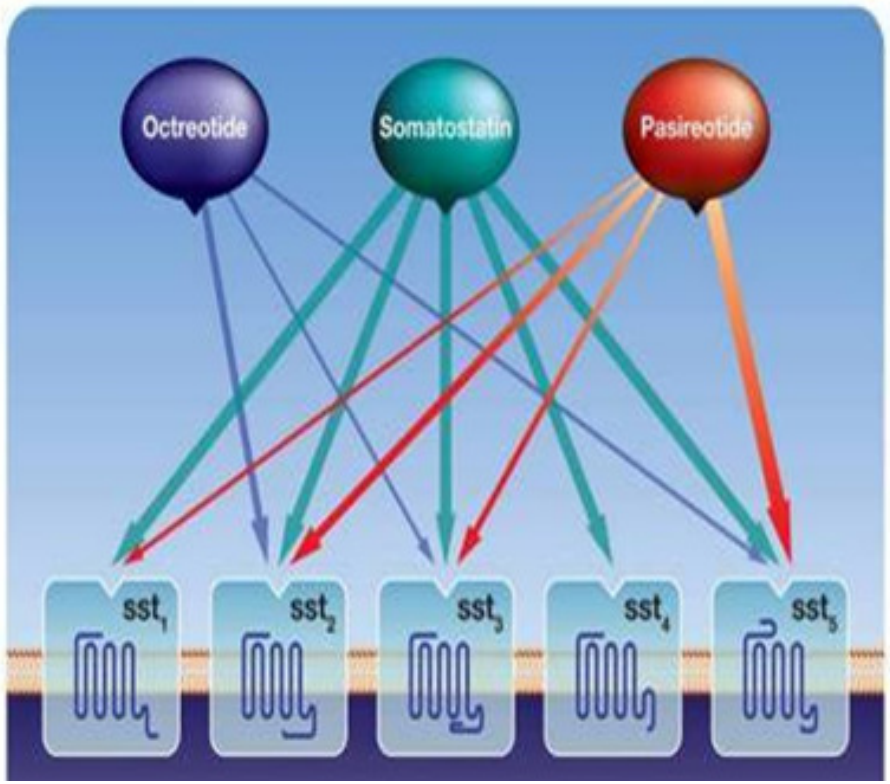
Tsu-Hui Shiao, MD, Yih-Leong Chang, MD,† Chong-Jen Yu, MD, PhD,* Yeun-Chung Chang, MD, PhD,‡ Ya-Chieh Hsu, MS,* Shih-Han Chang, MS,* Jin-Yuan Shih, MD, PhD,* and Pan-Chyr Yang, MD, PhD**

Journal of Thoracic Oncology -Volume 6,Number 1,January 2011

Conclusions: The *EGFR* mutation is rare in SCLC patients. Despite the presence of the *EGFR* mutation, gefitinib may not be effective in treating SCLC patients.

Pasireotida

A Multi-Receptor Targeted Somatostatin Analogue



- A multi-receptor targeted somatostatin analogue with a unique receptor profile, with highest affinity for sst5 as well as binding sst1,2 and 3.
- Somatostatin receptors are overexpressed in a range of tumors

PASIPHAE:Pasireotide maintenance therapy in ES- SCLC

Randomized, single blind, two-arm, placebo controlled, Phase II study

ES-SCLC pts

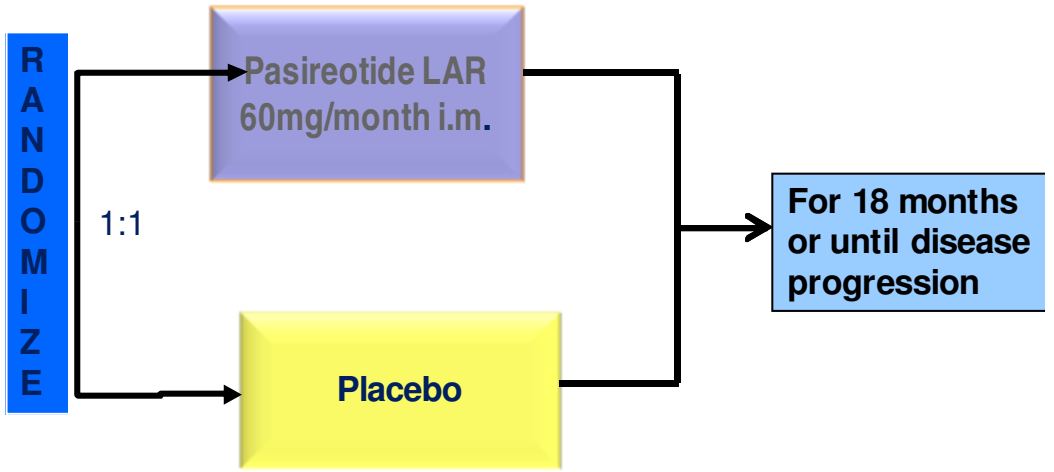
SD/PR/CR

after 4 cycles of

platinum + etoposide

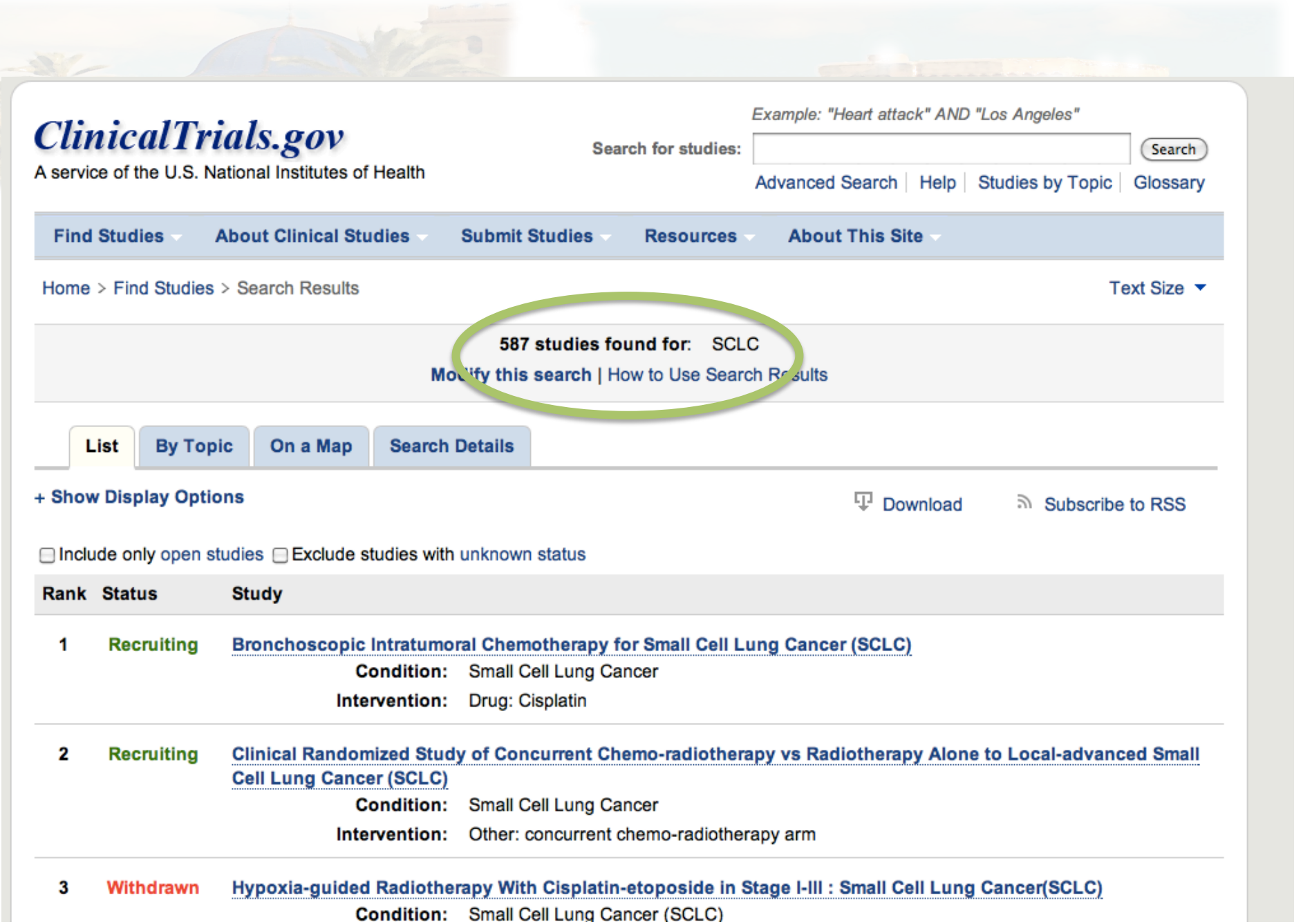
N= 160

Stratified by:
- **WHO P.S. (0 or 1 vs 2)**
- **SD versus PR and CR**



Primary endpoint:
- **PFS**

Secondary endpoints:
- **Safety of Pasireotide**
- **OS**
- **Response rate by Recist 1.1.**



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Rank	Status	Study
1	Recruiting	Bronchoscopic Intratumoral Chemotherapy for Small Cell Lung Cancer (SCLC) **Condition:** Small Cell Lung Cancer **Intervention:** Drug: Cisplatin
2	Recruiting	Clinical Randomized Study of Concurrent Chemo-radiotherapy vs Radiotherapy Alone to Local-advanced Small Cell Lung Cancer (SCLC) **Condition:** Small Cell Lung Cancer **Intervention:** Other: concurrent chemo-radiotherapy arm
3	Withdrawn	Hypoxia-guided Radiotherapy With Cisplatin-etoposide in Stage I-III : Small Cell Lung Cancer(SCLC) **Condition:** Small Cell Lung Cancer (SCLC)

ClinicalTrials.gov

A service of the U.S. National Institutes of Health

Example: "Heart attack" AND "Los Angeles"

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65 studies found for: refractory SCLC

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Rank	Status	Study
1	Unknown †	Topotecan for Irinotecan-Refractory SCLC **Conditions:** Lung Cancer; Refractory to Chemotherapy **Intervention:** Drug: topotecan
2	Active, not recruiting	Study of Hsp90 Inhibitor, STA-9090 for Relapsed or Refractory Small Cell Lung Cancer **Condition:** Small Cell Lung Cancer **Intervention:** Drug: STA-9090
3	Completed	A Study of IRESSA in Relapsed and Refractory Small Cell Lung Cancer **Condition:** Small Cell Lung Cancer **Intervention:** Drug: Gefitinib
4	Terminated	Pemetrexed in Patients With Chemosensitive and Chemoresistant Relapsed Small Cell Lung Cancer **Condition:** Small Cell Lung Cancer **Intervention:** Drug: Pemetrexed

Estudios Fase III negativos CPNM 2000-2010

Compound	Mechanism of action	N° trials	N	End point
Gefitinib	**EGFR TKI**	**8**	**5975**	**OS**
Erlotinib	**EGFR TKI**	**4**	**3661**	**OS**
Afatinib	**EGFR/HER2 TKI**	**1**	**585**	**OS**
Cetuximab	**EGFR antibody**	**1**	**676**	**PFS**
Prinomastat	**Matrix metalloprotease inhibitor**	**2**	**1048**	**OS**
Rebimastat	**Matrix metalloprotease inhibitor**	**1**	**774**	**OS**
PF-676	**Toll-like receptor 9-activating oligodeoxynucleotide**	**2**	**1667**	**OS**
Aprinocarsen	**Protein kinase C-alpha antisense oligonucleotide**	**2**	**1286**	**OS**
Bexarotene	**Retinoid X receptor activator**	**2**	**1235**	**OS**
Lonafarnib	**Farnesyl-transferase inhibitor**	**1**	**675**	**OS**
Figitumumab	**IGF-1R antibody**	**1**	**681**	**OS**
Celecoxib	**Cox2 inhibitor**	**1**	**561**	**OS**
IL-2	**Cytokine**	**1**	**241**	**OS**
Total		27	**19 065**	

Estudios con antiangiogénicos

Compound	Mechanism of action	N° trials	N	End Point
Thalidomide	**Anti-angiogenic**	**2**	**1267**	**OS**
Cediranib	**VEGFR TKI**	**1**	**296**	**OS**
Vandetanib	**Multikinase TKI**	**3**	**2698**	**PFS/OS**
AE-941	**Anti-angiogenic**	**1**	**379**	**OS**
Sorafenib	**Multikinase TKI**	**2**	**1830**	**OS**
Sunitinib	**Multikinase TKI**	**1**	**960**	**OS**
Aflibercet	**VEGF/PlGF**	**1**	**913**	**OS**
Total		11	8343	

CONCLUSIONES

- Se han desarrollado múltiples ensayos clínicos en CPM con resultados decepcionantes.
- Topotecan es el único fármaco aprobado por la FDA en 2ª línea de tratamiento (2012)
- Amrubicina es un fármaco prometedor en segunda línea en recaídas mal pronóstico