LUNG CANCER
UPDATES
ASCO HIGHLIGHTS
31 MAYO - 4 JUNIO 2019

Iniciativa científica de:
GECP
lung cancer research

Carcinoma microcítico pretratados

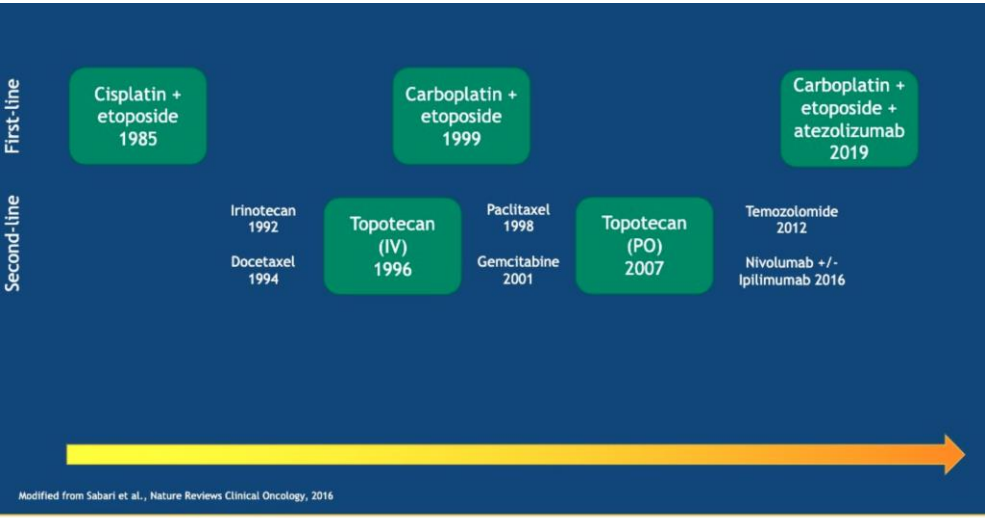
Dr. Delvys Rodríguez-Abreu

Día 1

Con la colaboración de:

Bristol-Myers Squibb
illumina
Lilly

Carcinoma microcítico en recaída



Modified from Sabari et al., Nature Reviews Clinical Oncology, 2016

Efficacy/Safety	1997: Single-arm Topotecan[1]	1999: Randomized Topotecan vs CAV[3,4] *Sensitive disease*	2014: Randomized Topotecan vs Amrubicin[5]	2018: CheckMate 331 Randomized chemotherapy[6] vs Nivolumab[7]
Response rate	21.7%	24.3%	16.9%	16.5%
mTTP/mPFS	2.8 months[2]	3.1 months[2]	3.5 months	3.8 months
mOS	5.4 months	5.8 months	7.8 months	8.4 months
Grade 3-4 neutropenia	74.9%	88.5%	53.8%	45%
Grade 3-4 thrombocytopenia	29.5%	57.4%	54.3%	21%
Grade 3-4 anemia	11.8%	42.3%	30.5%	26%

[1]Ardizzoni et al., JCO 1997; [2]Median time to progression; [3]Von Pawel et al., JCO 1999; [4]Eligibility required progression at least 60 days after completion of first-line chemotherapy; [5]Von Pawel et al., JCO 2014; [6]chemotherapy: topotecan (IV or oral) or amrubicin IV (where locally approved); [7]Reck et al., ESMO IO 2018, abstract 489.

Hospital Universitario 12 de Octubre SaludMadrid

cnio Centro Nacional de Investigaciones Oncológicas

UNIVERSIDAD COMPLUTENSE MADRID

EFFICACY AND SAFETY PROFILE OF LURBINECTEDIN IN SECOND-LINE SCLC PATIENTS:

Results from a phase II single-agent trial

Paz Ares L.[1]; Trigo JM.[2]; Besse B.[3]; Moreno V.[4]; Lopez R.[5]; Sala MA.[6]; Ponce S.[1]; Fernandez C.[7]; Siguero M.[7]; Kahatt C.[7]; Zeaiter A.[7]; Zaman K.[8]; Boni V.[9]; Arrondeau J.[10]; Martinez M.[11]; Delord JP.[12]; Awada A.[13]; Kristeleit R.[14]; Olmedo ME.[15]; Subbiah V.[16]

Hospital Universitario 12 de Octubre, CNIO, Universidad Complutense & Ciberonc, Madrid, Spain[1]; Hospital Universitario Virgen de la Victoria, Málaga, Spain[2]; Gustave Roussy Cancer Campus, Villejuif, France[3]; Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain[4]; Hospital Clínico Universitario de Santiago de Compostela, Santiago De Compostela, Spain[5]; Hospital Universitario de Basurto, Bilbao, Spain[6]; PharmaMar, Colmenar Viejo, Spain[7]; University Hospital CHUV, Lausanne, Switzerland[8]; START Madrid-CIOCC, Hospital Universitario Sanchinarro, Madrid, Spain[9]; Hôpital Cochin, Paris, France[10]; Complejo Hospitalario de Navarra, Pamplona, Spain[11]; Institut Claudius Regaud, Toulousse, France[12]; Institut Jules Bordet, Université Libre de Bruxelles, Brussels, Belgium[13]; UCL Cancer Institute, London, United Kingdom[14]; Hospital Universitario Ramón y Cajal , Madrid, Spain[15]; Md. Anderson Cancer Center, Houston, USA[16]

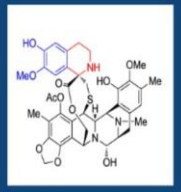
Lurbinectedin

Lurbinectedin is a synthetic analog of trabectedin

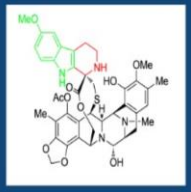
Natural marine-based tetrahydroisoquinoline antitumor agent

Inhibitor of activated transcription in preclinical studies

Signals of activity in SCLC with lurbinectedin/chemo combination phase 1 studies[1, 2]



TRABECTEDIN



LURBINECTEDIN

[1]Calvo et al., Ann Oncol. 2017 Oct 1;28(10):2559-2566; [2]Olmedo et al., ESMO 2017.

Carcinoma microcítico en 2da o 3era línea

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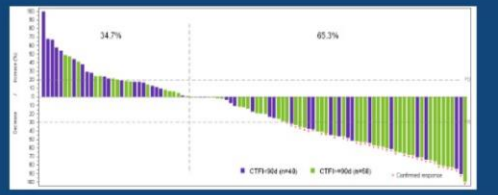
N-105

Key points

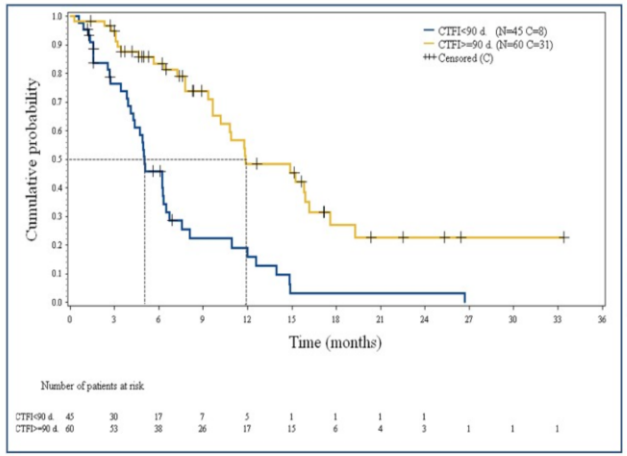
This study met its primary endpoint
- ORR 35.2%

Other efficacy endpoints:
- mDOR 5.3 months
- mPFS 3.9 months
- mOS 9.3 months



How do these numbers compare to historical topotecan data?

Overall Survival: Sensitive and Resistant SCLC Populations



	n	OS mo median (95% CI)	OS at 12 mo % (95% CI)
All	105	9.3 (6.3-11.8)	34.2 (23.2-45.1)
Resistant CTFI< 90d	45	5.0 (4.1-6.3)	15.9 (3.6-28.2)
Sensitive CTFI≥ 90d	60	11.9 (9.7-16.2)	48.3 (32.5-64.1)

Safety and Tolerability: Related or Unknown Adverse Events (AE)

n=105	n (%)
AEs	89 (84.8)
- Grade ≥3	36 (34.3)
SAEs	11 (10.5)
Related AEs leading to death	0 (0.0)
Related AEs leading to treatment discontinuation	2 (1.9)
Dose delays treatment related	21 (22.1*)
Dose reductions #	25 (26.3*)
G-CSF	23 (21.9)
Transfusions (red blood cells and/or platelets)	10 (9.5)

* Per protocol: dose had to be reduced in case of grade 4 neutropenia

* Based on 95 patients who received ≥ 2 cycles of treatment

	Lurbinectedin (n=105)	Von Pawel 2014: Topotecan (n=213)[1]	Von Pawel 2014: Amrubicin (n=424)[1]	CheckMate 331: Chemotherapy (n=285)[2]	CheckMate 331: Nivolumab (n=284)[2]
ORR (%)	35.2	16.9	31.1	16.5	13.7
ORR sens (%)	45.0	23.1	40.9		
ORR res (%)	22.2	9.4	20.1		
mPFS	3.9 m	3.5 m	4.1 m	3.8 m	1.4 m
mPFS sens	4.6 m	4.3 m	5.5 m		
mPFS res	2.6 m	2.6 m	2.8 m		
mOS	9.3 m 95% CI 6.3-11.8	7.8 m 95% CI 6.6-8.5	7.5 m 95% CI 6.8-8.5	8.4 m 95% CI 7.0-10.0	7.5 m 95% CI 5.6-9.2
mOS sens	11.9 m	9.9 m	9.2 m	11.1 m	7.6 m
mOS res	5.0 m	6.2 m	5.7 m	5.7 m	7.0 m

✓ Efficacy appears comparable, if not superior, to historical studies.

[1]Von Pawel et al., JCO 2014: 32(35) 4012-2019; [2]Reck et al., ESMO IO 2018, abstract 489. Chemotherapy control arm was topotecan or amrubicin.

Carcinoma microcítico en 2da o 3era línea
Trilaciclib

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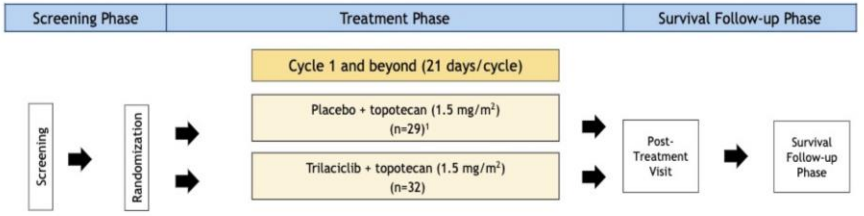
Effect of Trilaciclib, a CDK 4/6 Inhibitor, on Myelosuppression in Patients with Previously Treated Extensive-Stage Small Cell Lung Cancer

Lowell L. Hart[1,2,3], Zoran Gojko Andric[4], Maen A. Hussein[1,5], Renata Ferrarotto[6], J. Thaddeus Beck[7], Janakiraman Subramanian[8], Davorin Z. Radosavljevic[9], Dragana Jovanovic[10], Krishna Kishore Pachipala[11], Miroslav Samarzija[12], Bojan Zaric[13], Wahid Tewfik Hanna[14], Raid Aljumaily[1,15], Taofeek Kunle Owonikoko[16], Rajesh K. Malik[17], Shannon R. Morris[17], Misha L. Johnson[17], Zhao Yang[17], Steven Adler[17] and David R. Spigel[1,18]

Sarah Cannon Research Institute, Nashville, TN[1]; Florida Cancer Specialists and Research Institute, Fort Myers, FL[2]; Wake Forest University School of Medicine, Winston-Salem, NC[3]; Clinical Hospital Center, Bezanijska Kosa, Belgrade, Serbia[4]; Florida Cancer Specialists and Research Institute, Tavares, FL[5]; The University of Texas MD Anderson Cancer Center, Houston, TX[6]; Highlands Oncology Group, Rogers, AR[7]; Hanna Cancer Associates, Knoxville, TN[8]; Institute for Oncology and Radiology of Serbia Clinic for Medical Oncology, Belgrade, Serbia[9]; Clinic for Pulmonary Diseases, Clinical Center of Serbia, Belgrade, Serbia[10]; Millennium Oncology, Woodlands, TX[11]; University Hospital Centre Zagreb, Zagreb, Croatia[12]; Faculty of Medicine, University of Novi Sad Institute for Pulmonary Diseases of Vojvodina, Sremska Kamenica, Serbia[13]; University of Tennessee Graduate School of Medicine, Knoxville, TN[14]; Stephenson Cancer Center, University of Oklahoma HSC[15]; Emory University, Atlanta, GA[16]; G1 Therapeutics, Inc., Research Triangle Park, NC[17] and Tennessee Oncology, Nashville, TN[18]

G1T28-03 Study Design: Extensive-Stage SCLC (2L/3L)

N-61



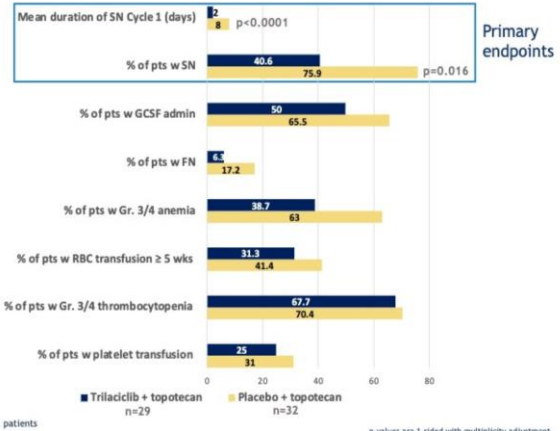
- Randomized, double-blind, placebo-controlled, Phase 2 study stratified by ECOG status (0 to 1 versus 2) and sensitivity to 1L treatment (sensitive versus resistant)
- Trilaciclib administered IV on Days 1-5 prior to topotecan
- Patients treated until disease progression, unacceptable toxicity or withdrawal of consent
- Use of primary prophylactic colony stimulating factors in Cycle 1 was not allowed; supportive care measures per institution were permitted throughout the study
- A trilaciclib + 0.75 mg/m² topotecan arm was also enrolled (n=30); data not shown

ES-SCLC, Extensive-Stage Small cell lung cancer; L, Line

† One patient randomized to placebo was not treated

Trilaciclib Demonstrates Myelopreservation Benefit Across Multiple Lineages

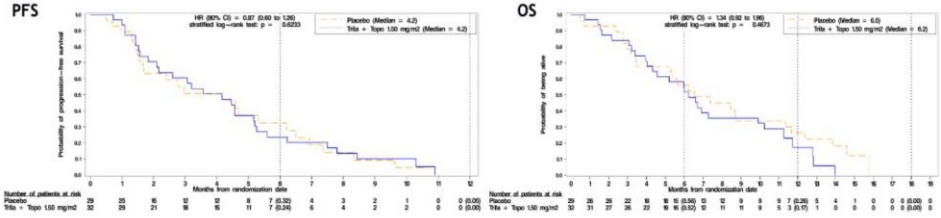
- Duration of severe neutropenia is a surrogate for an increased risk of febrile neutropenia, infection, IV antibiotic use and hospitalizations
- Chemotherapy-induced anemia in cancer patients correlates with fatigue and a compromised quality of life



SN, Severe neutropenia, FN, febrile neutropenia, Gr, grade, RBC, red blood cell, %, percent, pts, patients
Data are based on laboratory values

p-values are 1-sided with multiplicity adjustment

Trilaciclib Does Not Impair Chemotherapy Efficacy



- ORR was comparable in placebo and trilaciclib arms: 6/26 (23.1%) for placebo and 5/30 (16.7%) for trilaciclib
- PFS was comparable in placebo and trilaciclib arms
- OS was comparable in the placebo and trilaciclib arms
  - OS was impacted by regional differences (ex-US placebo OS was longer than historical data)