LUNG CANCER UPDATES
ESMO HIGHLIGHTS
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GECP lung cancer research

SCLC (II)

Dr. Manuel Dómine Gómez

Con la colaboración de:
Bristol-Myers Squibb
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OVERALL SURVIVAL (OS) UPDATE IN ALTER 1202: ANLOTINIB AS THIRD-LINE OR FURTHER-LINE TREATMENT IN RELAPSED SCLC

Ying Cheng[1*], Qiming Wang[2,3], Kai Li[4], Jianhua Shi[5], Ying Liu[6], Lin Wu[7], Baohui Han[8], Gongyan Chen[9], Jianxing He[10], Jie Wang[11], Donghua Lou[12], Hao Yu[13], Haifeng Qin[14], Xiaoling Li[15]

[1,6] Jilin Cancer Hospital, Changchun, China, [2] Affiliated Cancer Hospital of Zhengzhou University, Zhengzhou, China, [3] Henan Cancer Hospital, Zhengzhou, China, [4] Tianjin Medical University Cancer Hospital, Tianjin, China, [5] Linyi Cancer Hospital, Linyi, China, [7] Hunan Cancer Hospital, Changsha, China, [8] Shanghai Chest Hospital, Shanghai Jiaotong University, Shanghai, China, [9] Harbin Medical University Cancer Hospital, Harbin, China, [10] The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China, [11] Cancer Hospital Chinese Academy of Medical Sciences, Beijing, China, [12,13] Department of Biostatistics, School of Public Health Nanjing Medical University, Nanjing, China, [14] The Fifth Medical Centre of Chinese PLA General hospital, Beijing, China, [15] Liaoning Cancer Hospital & Institute, Shenyang, China

Presented by Prof. Ying Cheng, Jilin Cancer Hospital, China

ALTER 1202 SCLC THIRD LINE
Anlotinib:TKI VEGFR, c-Kit, PDGFR, FGFR

A multicentre, randomized, double-blind phase 2 trial (ALTER1202; NCT03059797)

Eligibility Criteria
- 18-75 years
- Histological documentation of small cell lung cancer
- Previously received at least two chemotherapy regimens
- Measurable lesion (by RECIST1.1)
- ECOG PS: 0-2

R 2:1

Anlotinib 12 mg, qd, po Day 1-14, 3 weeks/cycle, N=81*

Placebo po, qd n=38*

PD

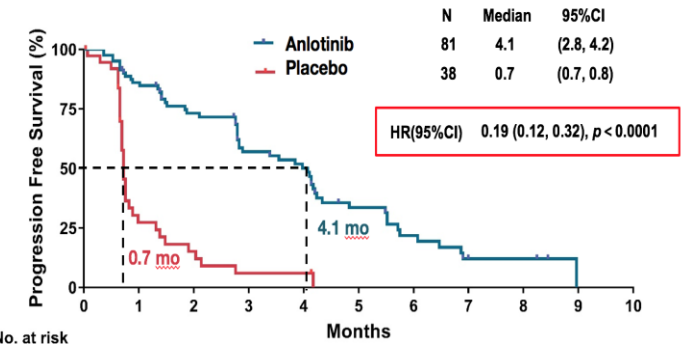
Primary Endpoint
- PFS

Secondary Endpoints
- OS
- ORR
- DCR
- Quality of Life
- Safety and Tolerability

- Enrollment period: March 2017 - May 2018
- 175 patients screen,120 patients randomized
- Data cutoff date: 30 Jun 2018
- **Stratified by:** Stage(Limited/ Extensive), Relapse(Sensitive / refractory)

Primary Endpoint: PFS (FAS)

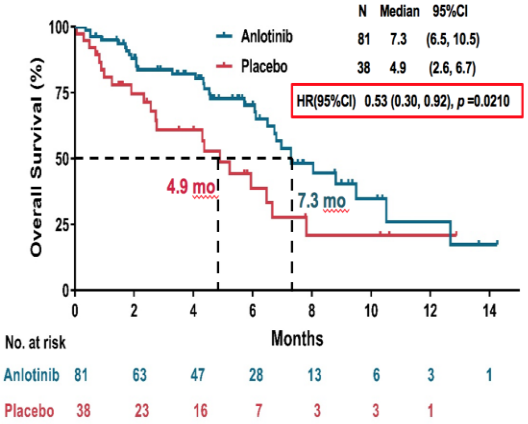
- Significantly prolonged median PFS in the anlotinib arm (4.1 months) vs. the placebo arm (0.7 months)



- OS data were not sufficiently mature (44.5% maturity)

	Anlotinib (n=81)	Placebo (n=38)
Censored, n(%)	49 (60.5)	17 (44.7)
Median, months(95%CI)	7.3 (6.5-10.5)	4.9 (2.6-6.7)
HR(95%CI)	0.53 (0.30-0.92)	

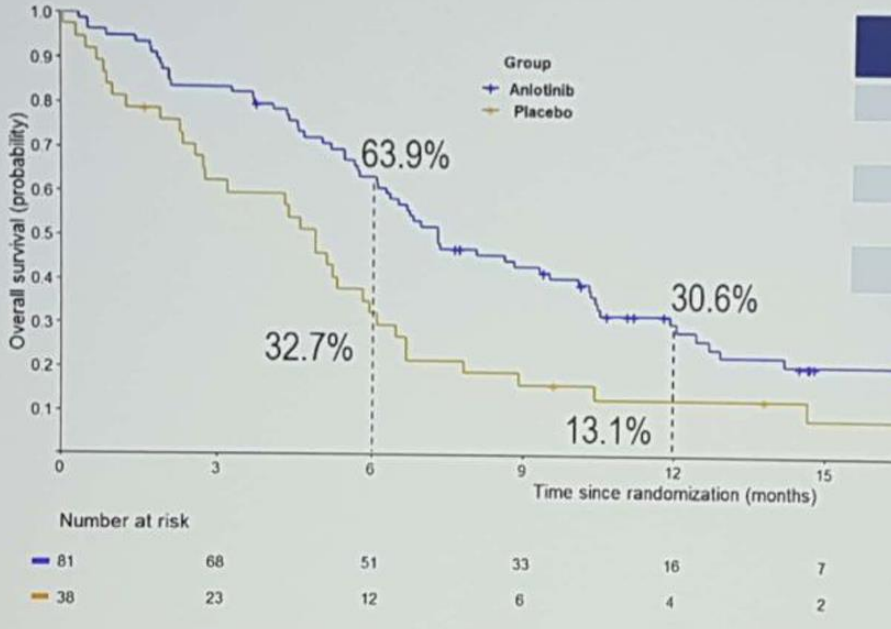
Data cutoff date: 30 Jun 2018



Selected TRAEs of Interest (SS)

TRAEs reported in ≥10% of patients , n(%)	Anlotinib , n= 81		Placebo , n=39	
	ALL	Grade 3-5	ALL	Grade 3-5
Hypertension *	32 (39.5)	11 (13.6)	2 (5.1)	1 (2.6)
Anorexia	20 (24.7)	1 (1.2)	5 (12.8)	0 (0.0)
Fatigue	20 (24.7)	1 (1.2)	5 (12.8)	0 (0.0)
Hand-foot syndrome *	17 (21.0)	4 (4.9)	0 (0.0)	0 (0.0)
TSH elevation *	14 (17.3)	0 (0.0)	0 (0.0)	0 (0.0)
Leukopenia*	13 (16.0)	0 (0.0)	1 (2.6)	0 (0.0)
ALT elevation	13 (16.0)	1 (1.2)	5 (12.8)	2 (5.1)
Lymphopenia*	13 (16.0)	2 (2.5)	0 (0.0)	0 (0.0)
Hypertriglyceridemia *	13 (16.0)	3 (3.7)	1 (2.6)	0 (0.0)
Diarrhea *	13 (16.0)	0 (0.0)	0 (0.0)	0 (0.0)
Proteinuria *	10 (12.3)	0 (0.0)	0 (0.0)	0 (0.0)

SECONDARY ENDPOINT: OS (FAS)



	Anlotinib (n=81)	Placebo (n=38)
Events , n(%)	60(74.1)	33 (86.8)
Median, months(95%CI)	7.3 (6.1,10.3)	4.9(2.7,6.0)
P value	0.0029	
HR(95%CI)	0.53 (0.34-0.81)	
6-month OS rate (95%CI)%	63.9(54.3,75.4)	32.7(20.6,51.9)
12-month OS rate (95% CI)%	30.6(21.7,43,2)	13.1(5.6,30.7)

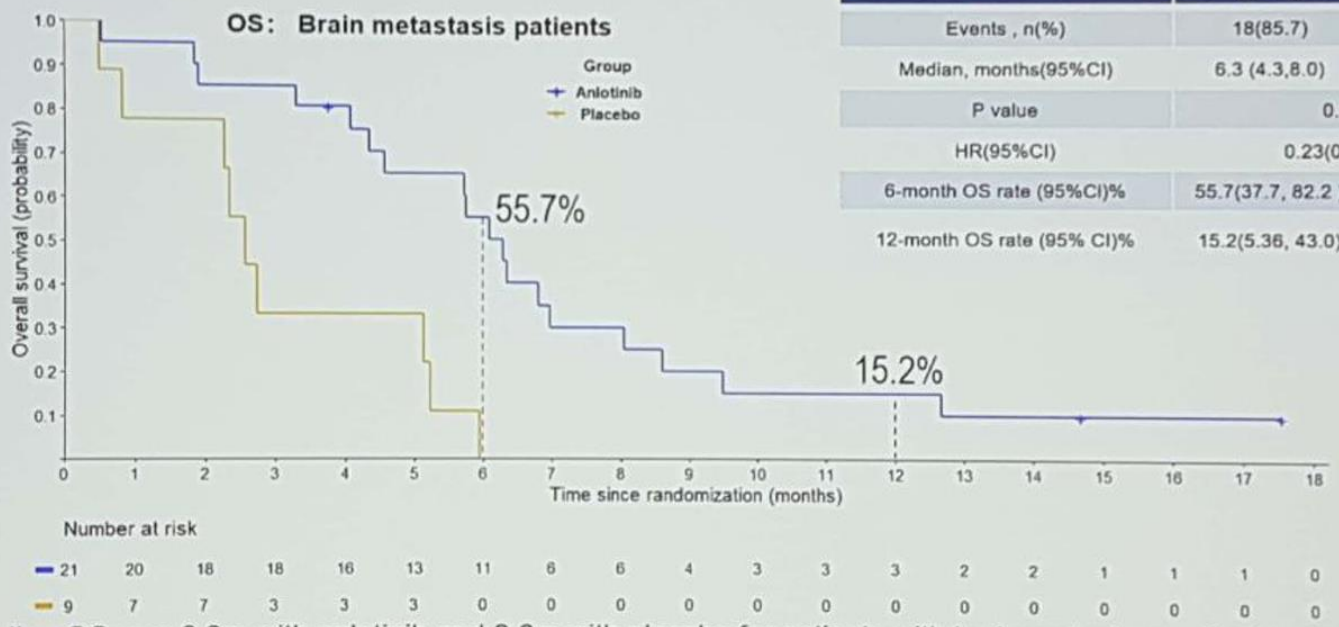
The updated OS results in final analysis by 04 April 2019 while OS events occurred in about 78.2% patients. Significantly prolonged median OS in the anlotinib arm (7.3 months) vs. the placebo arm (4.9 months).

SUBGROUP ANALYSIS OF OS (FAS)

Variable	Anlotinib N(Events)	Placebo N(Events)	Hazard Ratio(95%CI)	P-Value
All Patients	81(60)	38(33)	0.527(0.343,0.809)	0.0029
Age				
<65 years	70(51)	27(24)	0.512(0.314,0.835)	0.0063
≥65 years	11(9)	11(9)	0.609(0.238,1.560)	0.2974
ECOG performance status				
0/1	77(56)	32(28)	0.512(0.323,0.810)	0.0035
2	4(4)	6(5)	0.802(0.212,3.037)	0.7446
Disease stage				
Limited	10(6)	4(3)	0.800(0.190,3.361)	0.7573
Extensive	71(54)	34(30)	0.495(0.314,0.780)	0.0019
Type of recurrence				
Sensitive	24(18)	15(14)	0.498(0.243,1.018)	0.0510
Refreatory	53(40)	22(18)	0.611(0.349,1.070)	0.0809
Previous chemotherapy regimens. No.				
2	63(46)	28(25)	0.501(0.306,0.821)	0.0051
≥3	18(14)	10(8)	0.607(0.252,1.460)	0.2604
Response (CR and PR) to chemotherapy				
No	28(21)	21(17)	0.602(0.317,1.146)	0.1156
Yes	53(39)	17(16)	0.483(0.267,0.876)	0.0142
Brain metastase				
No	60(42)	29(24)	0.563(0.340,0.934)	0.0237
Yes	21(18)	9(9)	0.225(0.086,0.585)	0.0009

The OS benefits in favor of anlotinib were observed across most subgroups

OS BY BRAIN METASTASES (FAS)



	Anlotinib (n=21)	Placebo (n=9)
Events , n(%)	18(85.7)	9 (100)
Median, months(95%CI)	6.3 (4.3,8.0)	2.6(0.5,5.2)
P value	0.0009	
HR(95%CI)	0.23(0.09-0.59)	
6-month OS rate (95%CI)%	55.7(37.7, 82.2)	0
12-month OS rate (95% CI)%	15.2(5.36, 43.0)	0

Median OS was 6.3m with anlotinib and 2.6m with placebo for patients with brain metastases, the hazard ratio for OS favored anlotinib

Conclusiones

- ALTER 1202 es el primer estudio randomizado doble ciego que demuestra un beneficio significativo en supervivencia en tercera línea de tratamiento

- Anlotinib obtuvo un beneficio en OS de 2.4 meses (7.3 vs 4.9 meses) HR: 0.53 (0.34 -0.81)

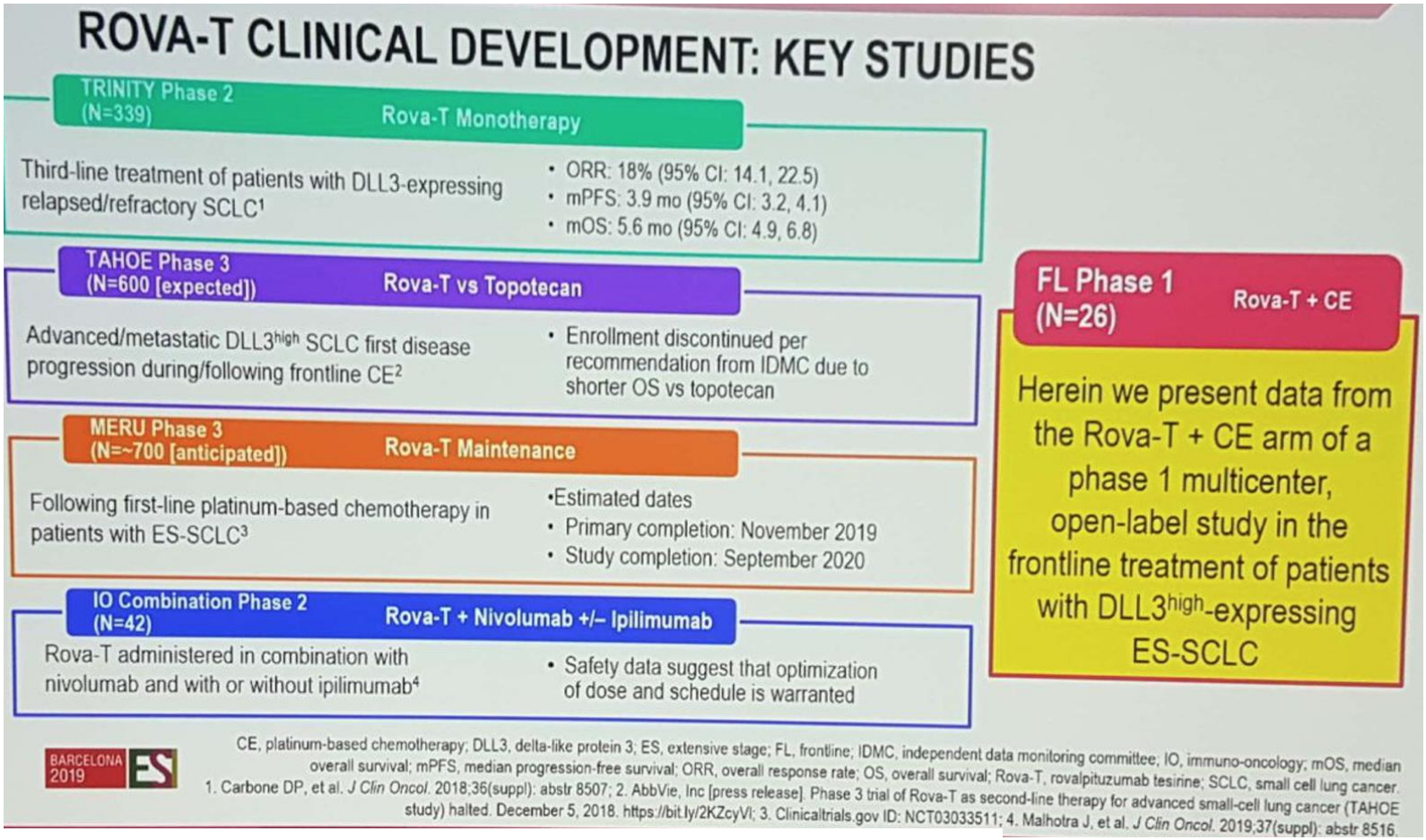
- Anlotinib debería considerarse el tratamiento estándar en pacientes que han progresado a dos líneas de tratamiento

- ES NECESARIO UN ESTUDIO CONFIRMATORIO EN POBLACIÓN OCCIDENTAL

A PHASE 1 STUDY EVALUATING ROVALPITUZUMAB TESIRINE (ROVA-T™) IN FRONTLINE TREATMENT OF PATIENTS (PTS) WITH EXTENSIVE STAGE SMALL CELL LUNG CANCER (ES-SCLC)

Christine L. Hann[1], Timothy Burns[2], Afshin Dowlati[3], Daniel Morgensztern[4], Martina Koch[5], Yu-Wei Chang[5], Philip Komarnitsky[5], Carrianne Ludwig[5], Halla Nimeiri[5], D. Ross Camidge[6]

[1]Johns Hopkins University, Baltimore, MD, USA; [2]UPMC Hillman Cancer Center, University of Pittsburgh, Pittsburgh, PA, USA; [3]University Hospitals Seidman Cancer Center and Case Western Reserve University, Cleveland, OH, USA; [4]Washington University School of Medicine, St. Louis, MO, USA; [5]AbbVie Inc., North Chicago, IL, USA; [6]University of Colorado-Denver, Aurora, CO, USA.


ROVA-T CLINICAL DEVELOPMENT: KEY STUDIES
TRINITY Phase 2 (N=339)
Rova-T Monotherapy
Third-line treatment of patients with DLL3-expressing relapsed/refractory SCLC1
• ORR: 18% (95% CI: 14.1, 22.5)
• mPFS: 3.9 mo (95% CI: 3.2, 4.1)
• mOS: 5.6 mo (95% CI: 4.9, 6.8)
TAHOE Phase 3 (N=600 [expected])
Rova-T vs Topotecan
Advanced/metastatic DLL3high SCLC first disease progression during/following frontline CE2
• Enrollment discontinued per recommendation from IDMC due to shorter OS vs topotecan
MERU Phase 3 (N=~700 [anticipated])
Rova-T Maintenance
Following first-line platinum-based chemotherapy in patients with ES-SCLC3
•Estimated dates
• Primary completion: November 2019
• Study completion: September 2020
IO Combination Phase 2 (N=42)
Rova-T + Nivolumab +/– Ipilimumab
Rova-T administered in combination with nivolumab and with or without ipilimumab4
• Safety data suggest that optimization of dose and schedule is warranted
FL Phase 1 (N=26)
Rova-T + CE
Herein we present data from the Rova-T + CE arm of a phase 1 multicenter, open-label study in the frontline treatment of patients with DLL3high-expressing ES-SCLC
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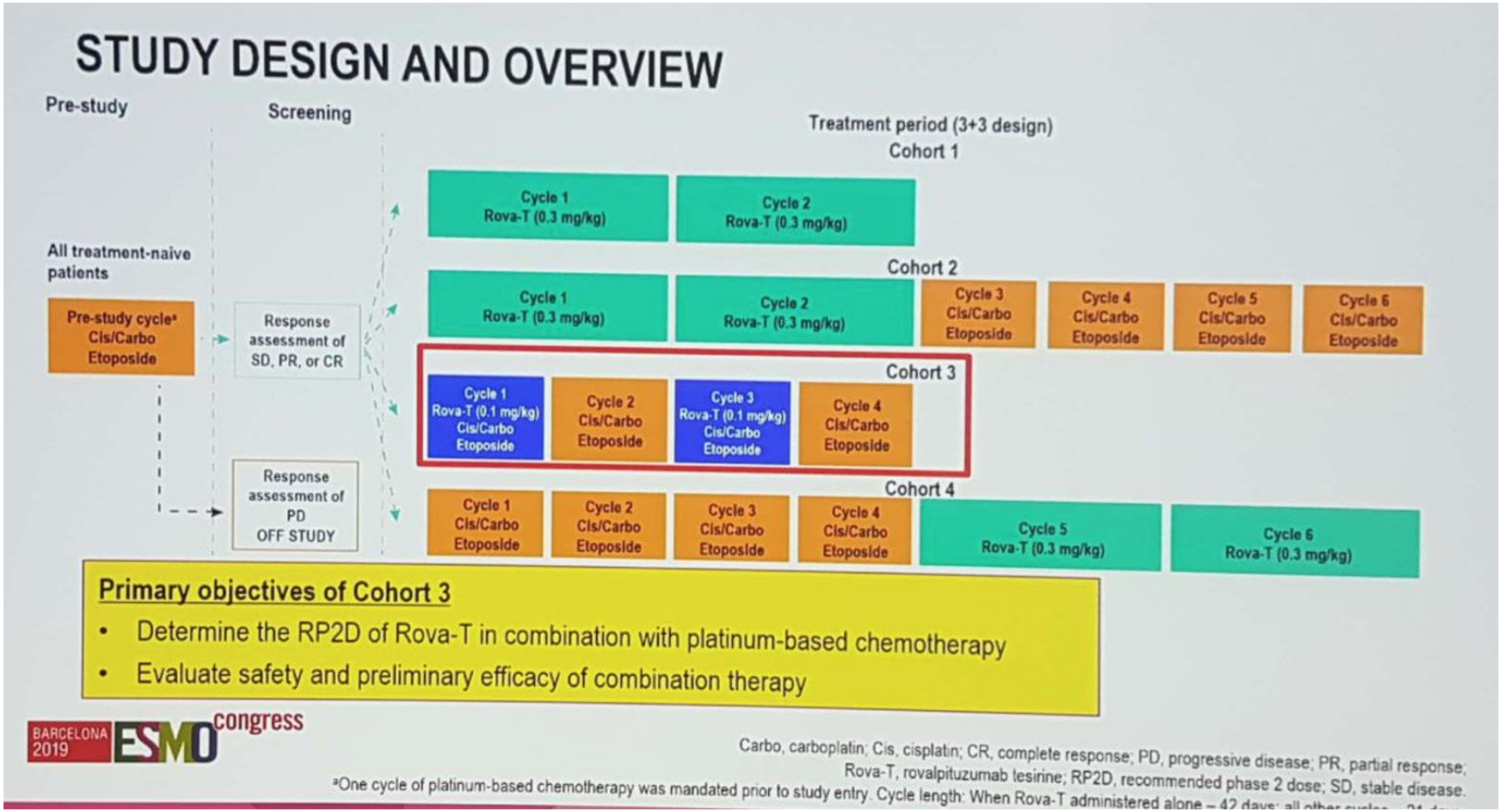
CE, platinum-based chemotherapy; DLL3, delta-like protein 3; ES, extensive stage; FL, frontline; IDMC, independent data monitoring committee; IO, immuno-oncology; mOS, median overall survival; mPFS, median progression-free survival; ORR, overall response rate; OS, overall survival; Rova-T, rovalpituzumab tesirine; SCLC, small cell lung cancer.
1. Carbone DP, et al. J Clin Oncol. 2018;36(suppl): abstr 8507; 2. AbbVie, Inc [press release]. Phase 3 trial of Rova-T as second-line therapy for advanced small-cell lung cancer (TAHOE study) halted. December 5, 2018. https://bit.ly/2KZcyVl; 3. Clinicaltrials.gov ID: NCT03033511; 4. Malhotra J, et al. J Clin Oncol. 2019;37(suppl): abstr 8516.


STUDY DESIGN AND OVERVIEW
Pre-study
Screening
Treatment period (3+3 design)
Cohort 1
Cycle 1 Rova-T (0.3 mg/kg)
Cycle 2 Rova-T (0.3 mg/kg)
All treatment-naive patients
Cohort 2
Cycle 1 Rova-T (0.3 mg/kg)
Cycle 2 Rova-T (0.3 mg/kg)
Cycle 3 Cis/Carbo Etoposide
Cycle 4 Cis/Carbo Etoposide
Cycle 5 Cis/Carbo Etoposide
Cycle 6 Cis/Carbo Etoposide
Pre-study cycle[a] Cis/Carbo Etoposide
Response assessment of SD, PR, or CR
Cohort 3
Cycle 1 Rova-T (0.1 mg/kg) Cis/Carbo Etoposide
Cycle 2 Cis/Carbo Etoposide
Cycle 3 Rova-T (0.1 mg/kg) Cis/Carbo Etoposide
Cycle 4 Cis/Carbo Etoposide
Response assessment of PD OFF STUDY
Cohort 4
Cycle 1 Cis/Carbo Etoposide
Cycle 2 Cis/Carbo Etoposide
Cycle 3 Cis/Carbo Etoposide
Cycle 4 Cis/Carbo Etoposide
Cycle 5 Rova-T (0.3 mg/kg)
Cycle 6 Rova-T (0.3 mg/kg)
Primary objectives of Cohort 3
• Determine the RP2D of Rova-T in combination with platinum-based chemotherapy
• Evaluate safety and preliminary efficacy of combination therapy
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Carbo, carboplatin; Cis, cisplatin; CR, complete response; PD, progressive disease; PR, partial response; Rova-T, rovalpituzumab tesirine; RP2D, recommended phase 2 dose; SD, stable disease.
[a]One cycle of platinum-based chemotherapy was mandated prior to study entry. Cycle length: When Rova-T administered alone = 42 days; all other

OVERVIEW OF TREATMENT-EMERGENT ADVERSE EVENTS

	Cohort 3		
	0.1 mg/kg n=8	0.2 mg/kg n=6	Total N=14
AE of any grade	8 (100)	6 (100)	14 (100)
Drug-related AE	8 (100)	6 (100)	14 (100)
Grade 3+ AEs	7 (88)	6 (100)	13 (93)
Drug-related grade 3+ AEs	7 (88)	5 (83)	12 (86)
Serious AEs	3 (38)	3 (50)	6 (43)
Drug-related serious AEs	2 (25)	2 (33)	4 (29)
AE leading to study drug withdrawal	2 (25)	2 (33)	4 (29)
Drug-related AE	2 (25)	2 (33)	4 (29)
AE leading to treatment interruption	3 (38)	1 (17)	4 (29)
Drug-related AE	3 (38)	0	3 (21)

- Eleven (79%) patients received 2 doses of Rova-T; 10 (71%) completed 4 doses of platinum-based chemotherapy
- Five (36%) patients experienced a drug-related TEAE leading to dose reduction
- One (17%) patient experienced DLT
  - Grade 3 bullous dermatitis (0.2 mg/kg)
- Two patients reported grade 5 TEAEs
  - Encephalopathy (0.1 mg/kg, drug related)[a]
  - Cardiac arrest (0.2 mg/kg, unrelated to drug)
- All patients have discontinued from study

TREATMENT-EMERGENT ADVERSE EVENTS: GRADE 3+

AEs [Cohort 3], n (%)	0.1 mg/kg n=8	0.2 mg/kg n=6	Total N=14
Neutropenia	5 (63)	1 (17)	6 (43)
Thrombocytopenia	3 (38)	1 (17)	4 (29)
Anemia	3 (38)	0	3 (21)
Fatigue	1 (13)	1 (17)	2 (14)
Febrile neutropenia	2 (25)	0	2 (14)
Pulmonary embolism	2 (25)	0	2 (14)
Leukopenia	0	2 (33)	2 (14)
Encephalopathy	1 (13)	0	1 (7)
Hyperglycemia	1 (13)	0	1 (7)
Hypokalemia	1 (13)	0	1 (7)

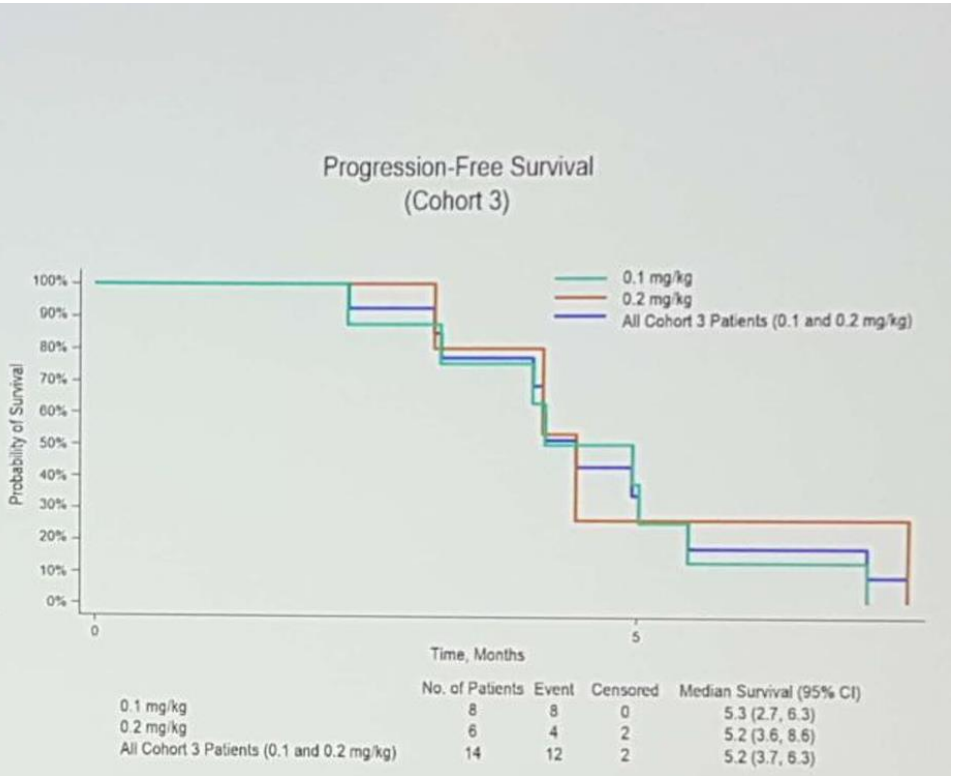
AEs [Cohort 3], n (%)	0.1 mg/kg n=8	0.2 mg/kg n=6	Total N=14
Pneumonia	1 (13)	0	1 (7)
Sepsis	1 (13)	0	1 (7)
Staphylococcal sepsis	1 (13)	0	1 (7)
Aspiration	0	1 (17)	1 (7)
Bone pain	0	1 (17)	1 (7)
Cardiac arrest	0	1 (17)	1 (7)
Dermatitis bullous	0	1 (17)	1 (7)
Hypophosphatasemia	0	1 (17)	1 (7)
Photosensitivity reaction	0	1 (17)	1 (7)
Pulmonary thrombosis	0	1 (17)	1 (7)
Spinal fracture	0	1 (17)	1 (7)

EFFICACY

	Cohort 3		All Patients (Cohort 3) N=14
	0.1 mg/kg n=8	0.2 mg/kg n=6	
Objective response rate, n (%) [95% CI]	5 (62.5) [24.5, 91.5]	2 (33.3) [4.3, 77.7]	7 (50.0) [23.0, 77.0]
Complete response, n (%)	1 (12.5)	0 (0.0)	1 (7.1)
Partial response, n (%)	4 (50.0)	2 (33.3)	6 (42.9)
Median PFS, mo (95% CI)	5.3 (2.7, 6.3)	5.2 (3.6, 8.6)	5.2 (3.7, 6.3)
Median DOR, mo (95% CI)	3.3 (1.8, 5.8)	2.8 (1.1, 6.1)	2.9 (1.1, 5.8)
Median OS, mo (95% CI)	10.3 (1.6, 15.4)	NR (2.3, NR)	10.3 (3.9, 15.4)

All patients in Cohort 3 received 1 pre-study cycle of platinum-etoposide. Baseline for response assessments was determined prior to the pre-study cycle. Response is according to RECIST version 1.1. Confirmation of CR and PR is required and changes in tumor measurements must be confirmed by repeat assessment performed in no less than 4 weeks (28 days). PFS defined as the time from the first day of platinum-etoposide therapy prior to study to the documented date of PD or death, whichever occurs first.

EFFICACY



	No. of Patients	Event	Censored	Median Survival (95% CI)
0.1 mg/kg	8	8	0	5.3 (2.7, 6.3)
0.2 mg/kg	6	4	2	5.2 (3.6, 8.6)
All Cohort 3 Patients (0.1 and 0.2 mg/kg)	14	12	2	5.2 (3.7, 6.3)

Conclusiones

- Rova T + EP fue tolerable a dosis de 0.1 y 0.2 mg/Kg

- Los efectos adversos más frecuentes fueron fatiga y neutropenia (63% cada una) para O.1 mg y fatiga (83%) para 0.2 mg

- ROVA- T no aporta beneficio en el tratamiento de primera línea de ES-SCLC añadido a EP

August 29, 2019

AbbVie Discontinues Rovalpituzumab Tesirine (Rova-T) Research and Development Program

news.abvie.com; accessed Sept. 27, 2019