#ESMOUPDATES

Iniciativa científica de:

GECP lung cancer research

LUNG CANCER UPDATES

ESMO HIGHLIGHTS

27 SEPTIEMBRE - 1 OCTUBRE 2019

Con la colaboración de:

Bristol-Myers Squibb

illumina

Lilly

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BARCELONA

SCLC (III)

Dr. Manuel Dómine Gómez

Con la colaboración de:
Bristol-Myers Squibb
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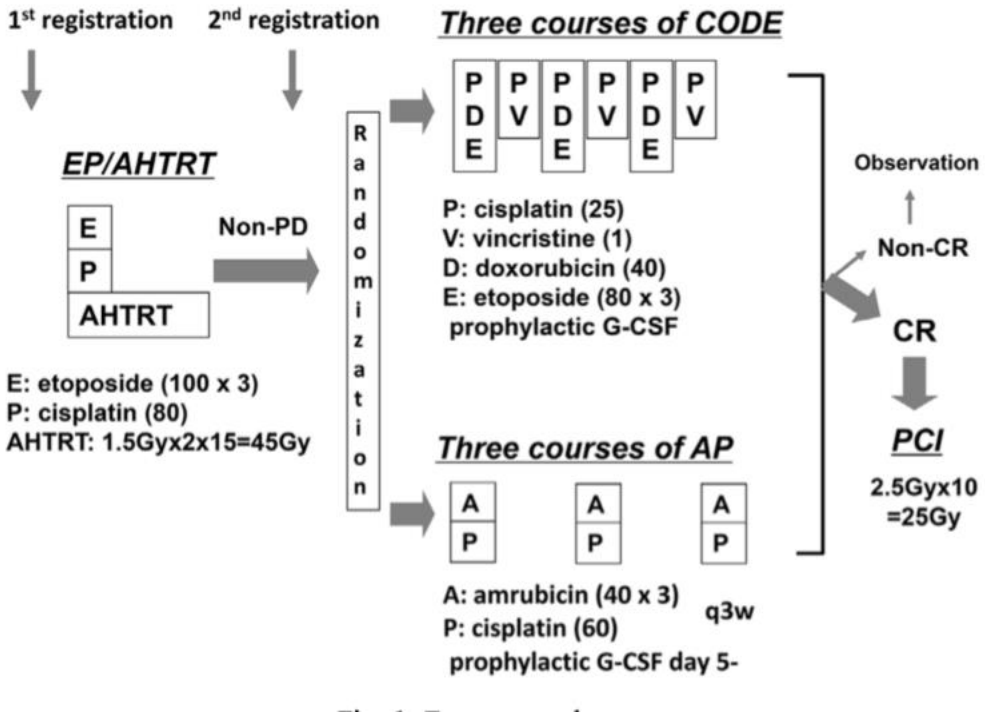
Lilly

1741PD Randomized phase II trial of CODE or AP after chemoradiotherapy for LD- SCLC: Long term survival and toxicity analysis JCOG 1011. I Sekine

OBJETIVO: Seleccionar el mejor esquema para un estudio fase III: CODE un esquema semanal intensivo o Amrubicina Platino en LD-SCLC



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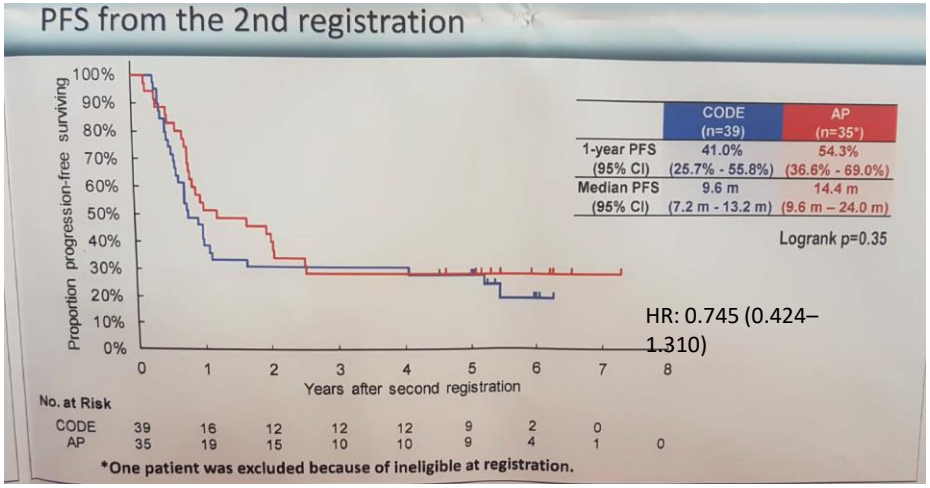

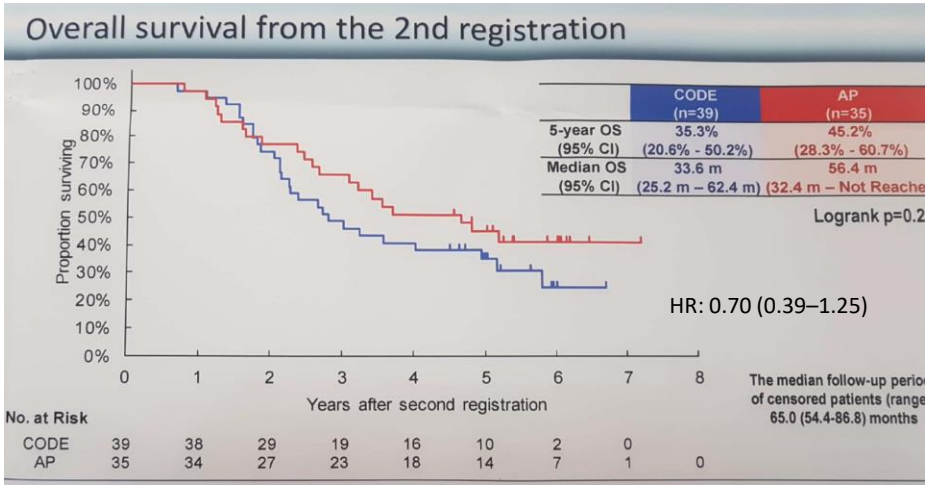

Toxicity	Toxicity grade							
	CODE (n = 38)				AP (n = 36)			
	2	3	4	3–4 (%)	2	3	4	3–4 (%)
Leukopenia	6	12	17	(76.3)	1	8	24	(88.9)
Neutropenia	4	9	18	(71.1)	1	4	28	(88.9)
Anemia	8	22	8	(78.9)	25	7	2	(25.0)
Thrombocytopenia	7	11	6	(44.7)	4	5	6	(30.6)
Febrile neutropenia	–	6	0	(15.8)	–	15	0	(41.7)
Any infection	2	1	0	(2.6)	1	1	0	(2.8)
Fatigue	5	2	-	(5.3)	5	3	–	(8.3)
Nausea	3	1	-	(2.6)	5	4	–	(11.1)
Vomiting	1	0	0	(0]	2	1	0	(2.8)
Anorexia	3	2	0	(5.3)	7	4	0	(11.1)
Diarrhea	3	1	0	(2.6)	1	0	0	(0)
Cough	0	1	–	(2.6)	0	0	–	(0)
Dyspnea	1	1	0	(2.6)	0	0	0	(0)
Hyponatremia	–	3	0	(7.9)	–	2	0	(5.6)
Hyperkalemia	4	0	0	(0)	0	0	0	(0)
Hypokalemia	–	2	0	(5.3)	–	2	1	(8.3)

AP: amrubicin and cisplatin; CODE: cisplatin, vincristine, doxorubicin and etoposide.

Aunque el perfil de supervivencia fue mejor para AP

No hubo diferencias significativas.

Ambos esquemas presentaron una toxicidad hematológica severa

Ninguno es adecuado para un fase III

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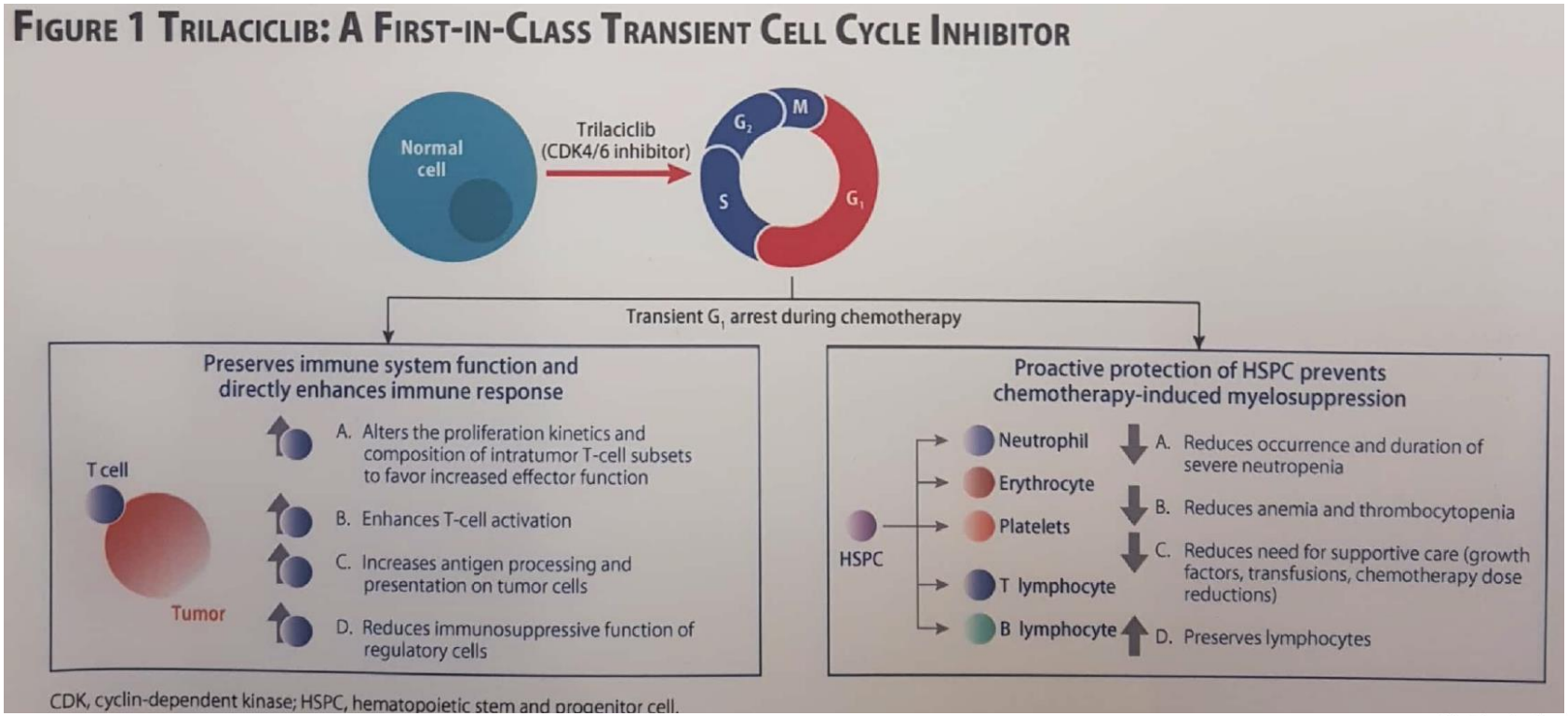
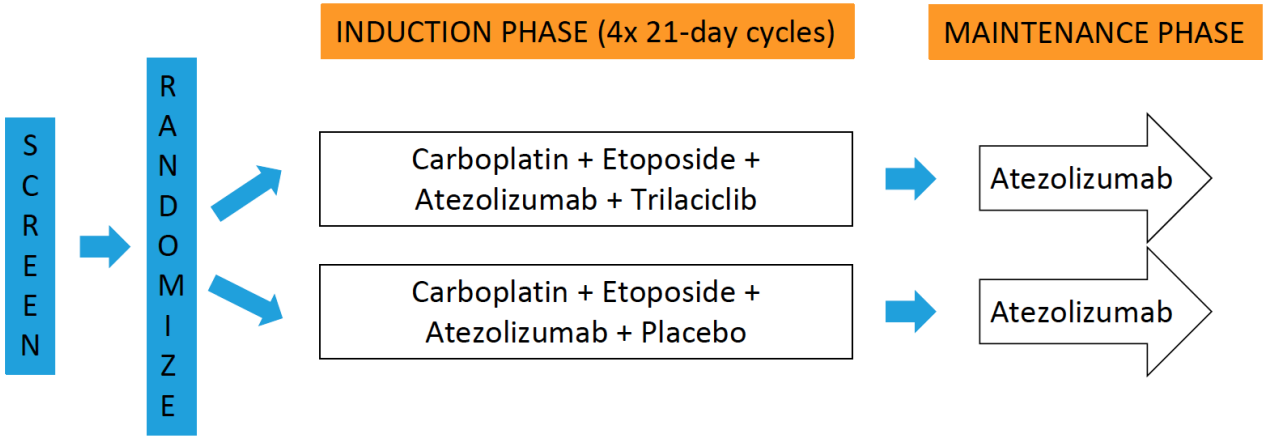
1742 PD Trilaciclib decreases myelosuppresion un ES-SCLC patients receiving first-line chemotherapy + atezolizumab. D Daniel

Trilaciclib es un potente y selectivo inhibidor de CDK4/CDK6 que inhibe de manera transitoria el ciclo celular que preserva las células hematopoyéticas progenitoras y aumenta la inmunidad antitumoral



Trilaciclib decreases myelosuppresion un ES-SCLC patients receiving first-line chemotherapy + atezolizumab. D Daniel

Trilaciclib/EP/atezolizumab in 1st-line SCLC



- Phase 2, randomized (1:1), global, double-blind, placebo-controlled
- Key objectives: PFS, OS, RR, safety in newly diagnosed ES SCLC patients
- Sample size: 100 patients
- NCT03041311

Objetivos:

Primario: evaluar el potencial de Trilaciclib de reducir la mielosupresión por quimioterapia

Secundario: Eficacia de añadir trilaciclib a atezo-carboplatino-etoposido y seguridad

Trilaciclib decreases myelosuppresion un ES-SCLC patients receiving first-line chemotherapy + atezolizumab. D Daniel

Table 4 Summary of TEAEs Occurring in ≥ 15% of Patients in Either Arm (Safety Analysis Set)

	E/P/A + Placebo (n = 53)		E/P/A + Trilaciclib 240 mg/m² (n = 52)	
	All Grades	Grade ≥ 3	All Grades	Grade ≥ 3
Any TEAE	52 (98.1)	46 (86.8)	49 (94.2)	33 (63.5)
Hematologic[a]				
Anemia	33 (62.3)	16 (30.2)	19 (36.5)	9 (17.3)
Neutropenia	40 (75.5)	32 (60.4)	22 (42.3)	11 (21.2)
Thrombocytopenia	35 (66.0)	21 (39.6)	12 (23.1)	1 (1.9)
Leukopenia	20 (37.7)	11 (20.8)	10 (19.2)	3 (5.8)
Nonhematologic[a]				
Nausea	18 (34.0)	1 (1.9)	20 (38.5)	0
Fatigue	20 (37.7)	2 (3.8)	16 (30.8)	1 (1.9)
Dyspnea	12 (22.6)	3 (5.7)	8 (15.4)	3 (5.8)
Dizziness	8 (15.1)	1 (1.9)	9 (17.3)	0
Constipation	12 (22.6)	1 (1.9)	5 (9.6)	0
Dehydration	11 (20.8)	3 (5.7)	5 (9.6)	0
Asthenia	8 (15.1)	2 (3.8)	8 (15.4)	4 (7.7)
Diarrhea	6 (11.3)	0	9 (17.3)	1 (1.9)
Cough	8 (15.1)	0	7 (13.5)	1 (1.9)
Pneumonia	8 (15.1)	8 (15.1)	7 (13.5)	4 (7.7)
Pyrexia	5 (9.4)	0	8 (15.4)	0
Decreased appetite	9 (17.0)	0	4 (7.7)	0

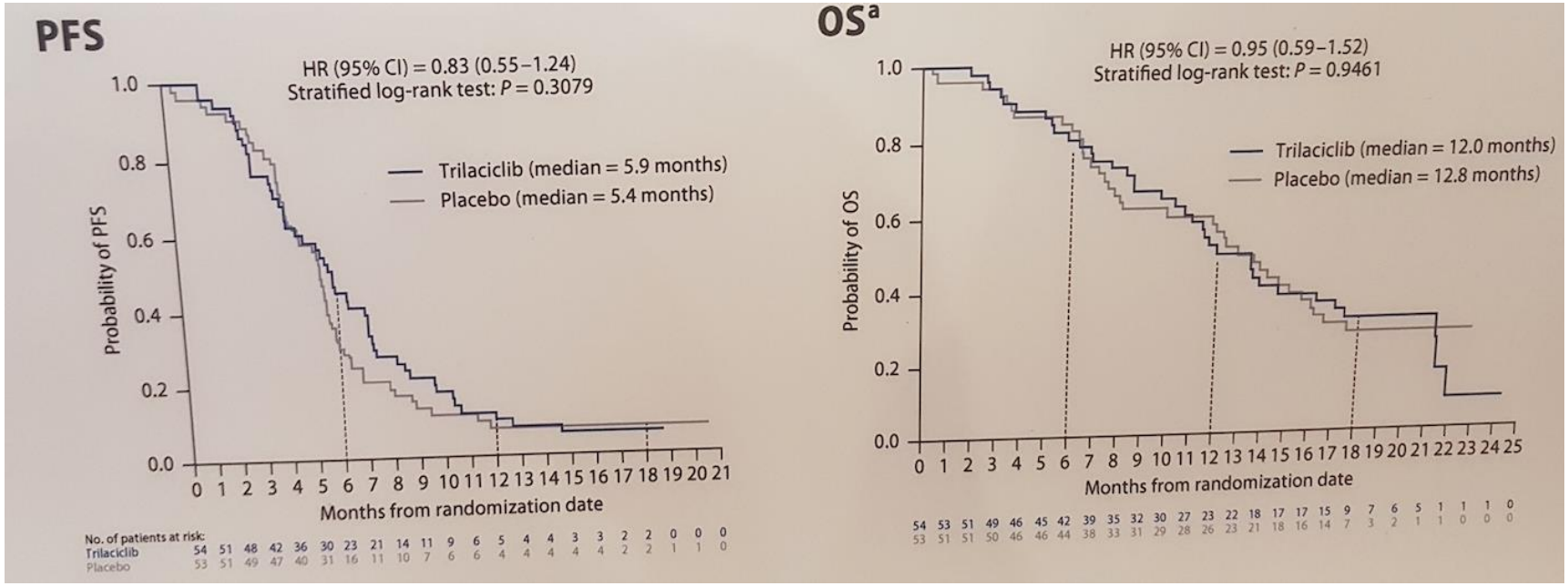
Table 3 Summary of Dose Exposure and Dose Modifications (Safety Analysis Set)

	E/P/A + Placebo (n = 53)	E/P/A + Trilaciclib 240 mg/m² (n = 52)
Duration of exposure (induction + maintenance)		
Median (range) days	182 (21–705)	205 (42–660)
Median (range) cycles	8 (1–28)	8 (2–31)
Median relative dose intensity, %		
Etoposide	92.3	98.1
Carboplatin	93.3	98.8
Atezolizumab (induction + maintenance)	95.0	96.3
Dose reductions, n (%)[a]		
Etoposide	14 (26.4)	3 (5.8)
Carboplatin	13 (24.5)	1 (1.9)
Cycle delays, n (%)	31 (58.5)	18 (34.6)
All-cause dose reductions[b]		
Event rate (per 100 cycles)	8.5	2.1

- Trilaciclib produjo menos mielosupresión en todas las líneas. Menor duración de neutropenia severa
- La toxicidad más frecuente relacionada con trilacilib fueron nauseas, fatiga y reacción en lugar de inyección. La mayoría leve, grado 3 < 6%
- El uso de trilaciclib obtuvo una mayor intensidad de dosis y menor reducción de dosis

Trilaciclib decreases myelosuppresion un ES-SCLC patients receiving first-line chemotherapy + atezolizumab. D Daniel

EFICACIA



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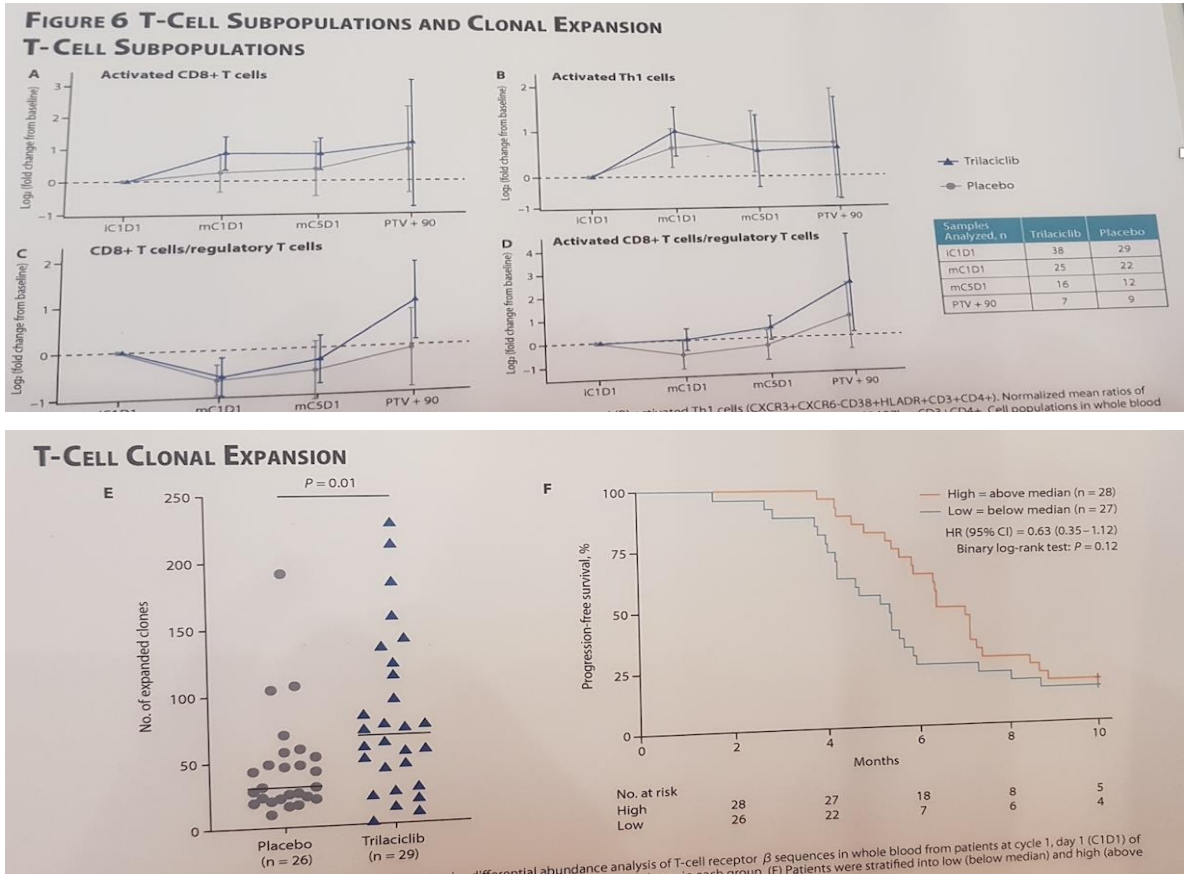
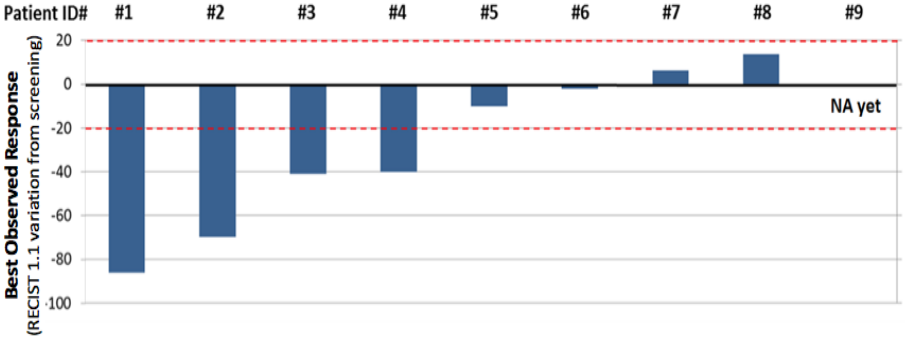


El uso de trilaciclib + carboplatino-etoposido-atezolizumab aumentó el número linfocito T CD 8 + activados y células Th1 y aumentó el ratio T CD 8 +/ Treg cells, produciendo una expansión clonal de células T

1751-TiP: CLEPSIDRA: a pilot, biomarker-guided study to assess safety, tolerability, dose finding and efficacy of iadademstat in combination with platinum-etoposide in patients with relapsed, extensive-stage small cell lung cancer

- LSD1 i overexpressed in primary SCLC (1).
- Notch-1 is a tumor suppressor repressed in SCLC. Iadademstat, a selective Lysine Specific Demethylase-1 (LSD1) inhibitor, has been shown to re-activate the NOTCH pathway in SCLC, resulting in the repression of ASCL1, a well-known non-druggable SCLC tumor driver, and to produce robust, and in some cases complete and durable, tumor regression in chemo-resistant SCLC PDX models
- 4-6 cycles of platinum etoposide + iadademstat seguido de iadademstat

	CbEt+iada	iadademstat Monotherapy
Completed cycles	**29**	**9**
Hematological toxicity*	**40**	**0**
Thrombocytopenia (≥ Grade III)	19 (65.5%)	0
Neutropenia (≥ Grade III)	11 (37.9%)	0
Anemia (≥ Grade III)	10 (34.5%)	0



8 patients: 4 PR and 3 SD (2 of the SD lasting more than 4 months)

- Iadademstat is a potential personalized therapeutic epigenetic drug for relapsed ED-SCLC patients.
- Preliminary activity of iadademstat in combination with CbEt is promising considering that standard of care topotecan in second line has shown limited activity (ORR range between 15-24%