#IASLCUPDATES

Iniciativa científica de:

GECP lung cancer research

LUNG CANCER UPDATES

IASLC HIGHLIGHTS

7-10 DE SEPTIEMBRE 2019

Con la colaboración de:

Bristol-Myers Squibb

illumina

Lilly

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IASLC HIGHLIGHTS
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BARCELONA
Iniciativa científica de:
GECP lung cancer research

Cáncer de pulmón de célula pequeña Mesotelioma/Timoma (2)

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Con la colaboración de:
Bristol-Myers Squibb
illumina
Lilly

CPCP/MPM/Timoma – L09/M10.09.2019

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7-10 DE SEPTIEMBRE 2019

Cáncer pulmón célula pequeña

PL02 – Presidential Symposium including Top 7 Rated Abstracts

OA15 - Targeted Agents and Immunotherapy for Small Cell Lung Cancer

P2.12 – Small cell Lung Cancer / NET (26 posters)

Mesotelioma pleural

MA12 - New Frontiers from Pathology to Genomics

MA23 - Preclinical Models and Genetics of Malignant Pleural Mesothelioma

P2.06 – Mesotelioma (26 posters)

Timoma

MA20 - Thymic Tumors: From Molecular to Clinical Results and New Challenges in Other Rare Thoracic Tumors

P2.15 – Timoma (5 posters)

Iniciativa científica de:
GeCP
lung cancer research

Cáncer de pulmón de célula pequeña

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7-10 DE SEPTIEMBRE 2019

PL02 – Presidental Symposium including Top 7 Rated Abstracts

PL02.11 - Overall Survival with **Durvalumab Plus Etoposide-Platinum** in First-Line Extensive-Stage SCLC: Results from the CASPIAN Study (L. Paz-Ares)

OA15 – Targeted Agents and Immunotherapy for Small Cell Lung Cancer

OA15.01 - Combination **Olaparib** and **Temozolomide** in Relapsed Small Cell Lung Cancer: Updated Results from Phase 1/2 Clinical Trial (AF Farago)

OA15.02 - **Carboplatin-Etoposide** Versus **Topotecan** as Second-Line Treatment for Sensitive Relapsed Small-Cell Lung Cancer: Phase 3 Trial (I Monnet)

OA15.04 - Genomic and TCR Intratumor Heterogeneity of Small-Cell Lung Cancer by Multiregion Sequencing: An Association with Survival (J Zhang)

OA15.05 - BIOLUMA: A Phase II Trial of Nivolumab and Ipilimumab in Lung Cancer – Prospective Evaluation of TMB in SCLC Patients (J George)

Iniciativa científica de:
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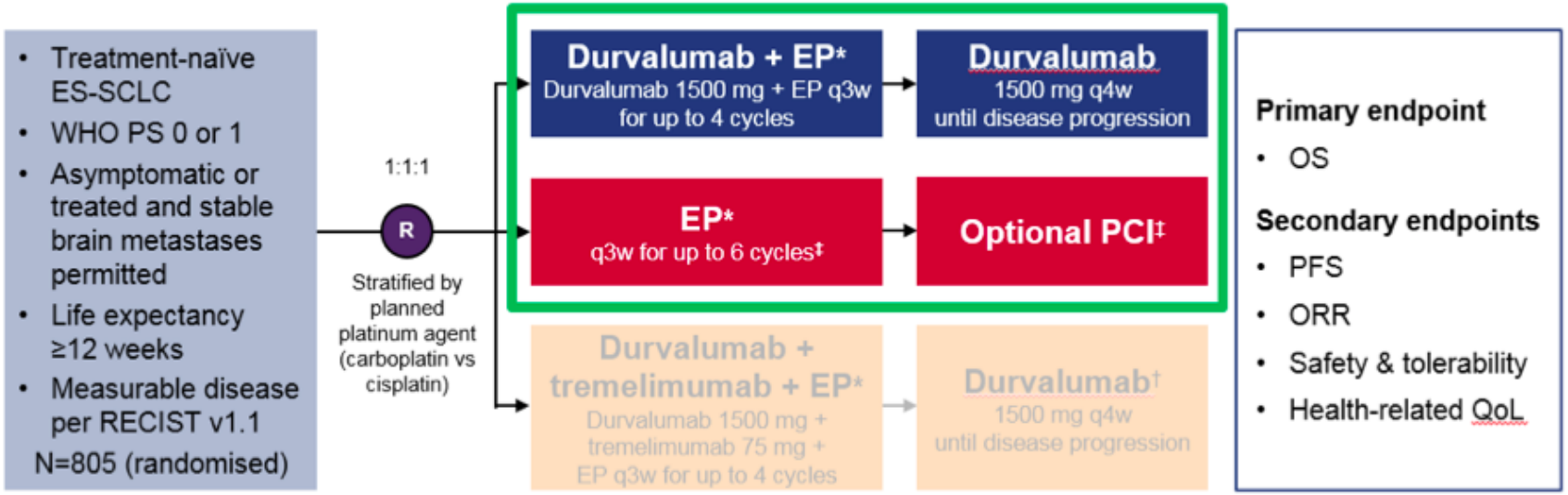
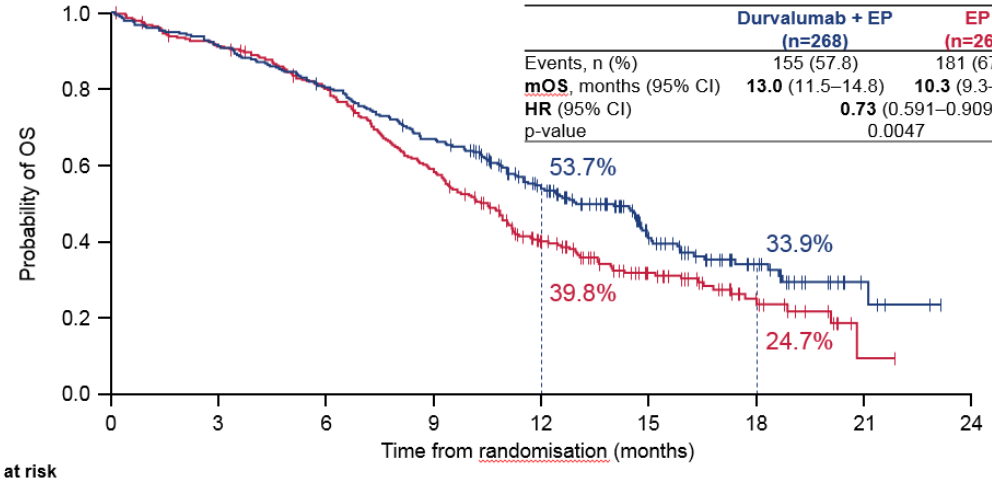
CASPIAN Study Design

Phase 3, global, randomised, open-label, sponsor-blind multicentre study



PL02.11 - Overall Survival with Durvalumab Plus Etoposide-Platinum in First-Line Extensive-Stage SCLC: Results from the CASPIAN Study (L. Paz-Ares)

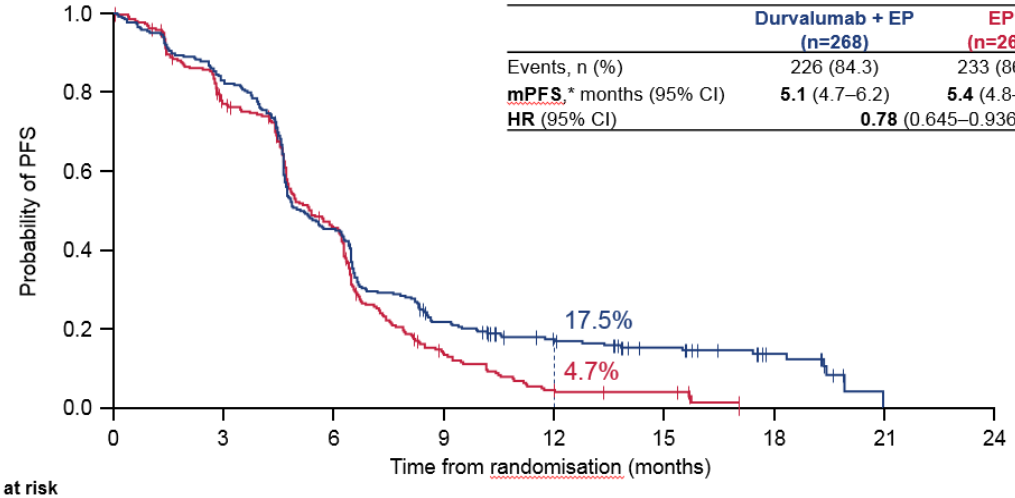
OS



	Durvalumab + EP (n=268)	EP (n=269)
Events, n (%)	155 (57.8)	181 (67.3)
mOS, months (95% CI)	**13.0** (11.5–14.8)	**10.3** (9.3–11.2)
HR (95% CI)	**0.73** (0.591–0.909)	
p-value	0.0047	

No. at risk									
Durvalumab + EP	268	244	214	177	116	57	25	5	0
EP	269	242	209	153	82	44	17	1	0

PFS



	Durvalumab + EP (n=268)	EP (n=269)
Events, n (%)	226 (84.3)	233 (86.6)
mPFS,* months (95% CI)	**5.1** (4.7–6.2)	**5.4** (4.8–6.2)
HR (95% CI)	**0.78** (0.645–0.936)	

No. at risk									
Durvalumab + EP	268	220	119	54	34	22	10	0	0
EP	269	194	109	30	9	7	0	0	0

OA15.01 - Combination Olaparib and Temozolomide in Relapsed Small Cell Lung Cancer: Updated Results from Phase 1/2 Clinical Trial (AF Farago)

Cohorte 1: O + T d1-7/21d

Cohorte 2: O d1-21/21d + T d1-7/21d

Esquema	n	ORR (%)	DOR (m)	PFS (m)	OS (m)
Lurbinectidina	105	35.2	NR	2.0	8.7
Lurbinectidina + Doxorrubicina	27	37	?	3.4	7.9
Temozolamida + Veliparib	55	39	4.6	3.8	8.2
Temozolamida + Olaparib (cohort 1)	50	41.7	4.3	4.2	8.5
Temozolamida + Olaparib (cohort 2)					
nal-Iri (70)	25	44	?	?	?

Fase 3 nal-Iri vs topotecan en 2L.

OA15.02 - Carboplatin-Etoposide Versus Topotecan as Second-Line Treatment for Sensitive Relapsed Small-Cell Lung Cancer: Phase 3 Trial (I Monnet)

- Relapse or progression at least 90 days after completion 1L.

Esquema	n	ORR (%)	PFS (m)	OS (m)
Cb-VP16	82	49	4.7	7.5
Topotecán VO	82	25	2.7	7.4

- El retratamiento con Cb-VP16 puede considerarse un estándar en 2ª línea en enf platino-S (>3m).

Mesotelioma pleural

MA12 - New Frontiers from Pathology to Genomics

MA12.01 - Redefining MPM Types as a Continuum Uncovers Immune-Vascular Interactions

MA12.02 - Growth Patterns in Epithelioid MPM: A Clinicopathological Review of 614 Cases Over 15 Years

MA12.03 - PARP Inhibitor Sensitivity Does Not Depend on BAP1 but Is Enhanced by Temozolomide in MGMT Deficient Human Mesothelioma Cells

MA12.05 - Genomic Analysis of Long Term MPM Patients Treated with Palliative Chemotherapy

MA12.06 - Patient-Derived Organotypic Tumor Spheroids (PDOTS) Facilitate Therapeutic Screening for MPM

MA12.07 - **Integrative Transcriptome Analysis** of MPM Reveals a Clinically-Relevant **Immune-Based Classification**

MA12.09 - Checkpoint Inhibitors Synergize with Dendritic Cell-Therapy in Pre-Clinical Models and Mesothelioma Patients

MA12.10 - **Novel Germline Mutations** in DNA-Damage Repair and DNA Replication Identified in Patients with MPM

MA12.11 - Anti-Tumor Efficacy of Mesothelin Targeted Immunotoxin LMB-100 Plus Pembrolizumab in Mesothelioma Patients and Mouse Models

Mesotelioma pleural

MA23 - Preclinical Models and Genetics of Malignant Pleural Mesothelioma

MA23.01 - Phase II Trial of an Oral FGFR Inhibitor AZD4547 as Second or Third Line Therapy in MPM: Final Results of FRAME Study

MA23.02 - **CDK4/6 Inhibitors** Show Antitumor Effects in Preclinical Models of MPM

MA23.03 - BAP1 Loss Induces Genome Instability Through BRCA1-Dependent and Independent Mechanisms in MPM

MA23.05 - A Phase II Trial of Nintedanib in Recurrent MPM

MA23.06 - Development of a Novel Genetically Engineered Mouse Model of MPM

MA23.07 - Loss of Expression of BAP1 and/or MTAP Aids in the Diagnosis of MPM Metastatic to Lymph Nodes

MA23.09 - **Fusion Genes** Identified from WGS/WES of MPM Tumours

MA23.10 - Low Number of Mutations and Frequent Co-Deletions of CDKN2A and IFN Type I Characterize MPM

MA23.11 - Analysis of **Immune Phenotype** Composition in MPM Using Bulk RNA Sequencing

Mesotelioma pleural

MPM genetics

MA12.01 - Redefining MPM Types as a Continuum Uncovers Immune-Vascular Interactions

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MA23.11 - Analysis of **Immune Phenotype** Composition in MPM Using Bulk RNA Sequencing

Somatic mutations

MA12.05 – UQCRC1 mutations → Factor de mal pronóstico

Germline mutations

MA12.10 – **4 Novel Germline Mutations** in DNA-Damage Repair and DNA Replication Identified in Patients with MPM

Mesotelioma pleural

Preclinical activity of targeted therapies

MA12.03 - PARP Inhibitor Sensitivity Does Not Depend on BAP1 but Is Enhanced by Temozolomide in MGMT Deficient Human Mesothelioma Cells

MA23.03 - BAP1 Loss Induces Genome Instability Through BRCA1-Dependent and Independent Mechanisms in MPM → Sensitize to DNA damaging agents and PARP inhibitors.

MA23.02 - **CDK4/6 Inhibitors** Show Antitumor Effects in Preclinical Models of MPM

New preclinical models of disease

MA12.06 - Patient-Derived Organotypic Tumor Spheroids (PDOTS) Facilitate Therapeutic Screening for MPM

MA23.06 - Development of a Novel Genetically Engineered Mouse Model of MPM

Clinical trials

MA12.09 - Checkpoint Inhibitors Synergize with Dendritic Cell-Therapy in Pre-Clinical Models and Mesothelioma Patients

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MA23.05 - A Phase II Trial of Nintedanib in Recurrent MPM

Timoma

MA20 - Thymic Tumors: From Molecular to Clinical Results and New Challenges in Other Rare Thoracic Tumors

MA20.01 - Global Quantitative Mass Spectrometry Reveals Potential Novel Actionable Targets in Thymic Epithelial Tumors (TET)

MA20.02 - **GAD1** Expression and Its **Methylation** Become Indicators of Malignant Behavior in Thymic Epithelial Tumor (S. Soejima).

MA20.03 - DNA Methylation of **MT1A** and **NPTX2** Genes Predict Malignant Behavior of Thymic Epithelial Tumors (K. Muguruma).

MA20.05 - Follow-Up Update of 2 Phase II Studies of **Pembrolizumab** in Thymic Carcinoma

MA20.06 - Neutrophil to Lymphocyte Ratio Is an Independent Prognostic Predictor in Thymoma

MA20.07 - Thymomectomy and Total Thymectomy or Simple Thymomectomy for Early Stage Thymoma Without Myasthenia Gravis: An ESTS Thymic Working Group Study

MA20.09 - Breast Implant Associated Anaplastic Large Cell Lymphoma: Outcomes of a Newly-Recognized Malignancy of the Thoracic Wall

MA20.10 - Long-Term Prognostic Factors After Minimally Invasive Esophagectomy (MIE) for Esophageal Cancer

MA20.11 - Surgical Treatment for Metastatic Lung Tumors from Sarcomas of Soft Tissue and Bone

Timoma

High-throughput proteomics (Guha):

- High expression of GSTP1 in carcinomas.
- Growth inhibition of GSTP1+ cells lines by specific inhibitors (ezatiostat)

DNA methylation of GAD1, MT1A and NPTX2 (Soejima, Muguruma)

- Higher promoter methylation in carcinomas.
- Poor prognostic factor

Update two F2 trials of ICI in thymic carcinoma (G. Giaccone)

- 26-40 pts, mF/u: 3-4 años.
- ORR 20% (DoR: 3.2y in NCI trial!!)
- Severe irAE 15-19%
- Ongoing research with IO combos.