LUNG CANCER UPDATES
IASLC HIGHLIGHTS
7-10 DE SEPTIEMBRE 2019
BARCELONA
Cáncer de pulmón de célula pequeña
Mesotelioma/Timoma (2)

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

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**

![OS Kaplan-Meier Curve]

<table>
<thead>
<tr>
<th></th>
<th>Durvalumab + EP (n=268)</th>
<th>EP (n=269)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events, n (%)</td>
<td>155 (57.8)</td>
<td>181 (67.3)</td>
</tr>
<tr>
<td>mOS, months (95% CI)</td>
<td><strong>13.0</strong> (11.5–14.8)</td>
<td><strong>10.3</strong> (9.3–11.2)</td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>0.73 (0.59–1.00)</td>
<td>0.80 (0.59–1.09)</td>
</tr>
<tr>
<td>p-value</td>
<td>0.0047</td>
<td>0.121</td>
</tr>
</tbody>
</table>

**PFS**

![PFS Kaplan-Meier Curve]

<table>
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<th>Durvalumab + EP (n=268)</th>
<th>EP (n=269)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events, n (%)</td>
<td>226 (84.3)</td>
<td>233 (86.6)</td>
</tr>
<tr>
<td>mPFS*, months (95% CI)</td>
<td><strong>5.1</strong> (4.7–6.2)</td>
<td><strong>5.4</strong> (4.8–6.2)</td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>0.78 (0.64–0.93)</td>
<td>1.0 (0.81–1.24)</td>
</tr>
</tbody>
</table>
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

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

Fase 3 nal-Iri vs topotecan en 2L.
Relapse or progression at least 90 days after completion 1L.

<table>
<thead>
<tr>
<th>Esquema</th>
<th>n</th>
<th>ORR (%)</th>
<th>PFS (m)</th>
<th>OS (m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cb-VP16</td>
<td>82</td>
<td>49</td>
<td>4.7</td>
<td>7.5</td>
</tr>
<tr>
<td>Topotecán VO</td>
<td>82</td>
<td>25</td>
<td>2.7</td>
<td>7.4</td>
</tr>
</tbody>
</table>

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