Malignant Pleural Mesothelioma – Current Developments

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Manchester, March 3, 2017
Mesothelioma in Europe

- Peak incidence around 2020
- British mesothelioma register and male death rates for cancer of the pleura from 6 European countries
- Statistical modeling taking into account asbestos legislation and the long latency period

Peto, BJC 1999
Stopping asbestos exposure may not modify the subsequent risk of mesothelioma

<table>
<thead>
<tr>
<th>Age at First Employment</th>
<th>Person-years</th>
<th>Observed</th>
<th>SMR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-39 years</td>
<td>30,366</td>
<td>25</td>
<td>0.4 (4287.5–9807.5)</td>
</tr>
<tr>
<td>30-39 years</td>
<td>6035</td>
<td>9</td>
<td>0.11 (3672.7–15236.1)</td>
</tr>
<tr>
<td>40+</td>
<td>2832</td>
<td>6</td>
<td>0.10 (2163.8–12853.3)</td>
</tr>
</tbody>
</table>

SMR: standardized mortality ratio

CI, confidence interval; SMR, standardized mortality ratio. From Pira et al., 2007.
Diagnosis malignant pleural mesothelioma: Video-assisted pleural biopsy for histology and immunohistochemistry

Morphology: Epithelial, sarkoid or mixed

IHC: Calretinin, mesothelin, WT-1, podoplanin
Key therapeutic considerations (1)

• Mesothelioma presents usually in a locally advanced stage not amenable to curative therapy

• Cis- or caboplatin combined with pemetrexed have emerged as the preferred chemotherapy based on one randomized trial

• Multimodality therapies including chemotherapy, pleurectomy/decortication or extrapleural pneumonectomy with or without radiotherapy continue to be explored and remain a controversial issue

Vogelzang; JCO 2003
Cisplatin and pemetrexed versus cisplatin in malignant pleural mesothelioma (fully supplemented patients)

Vogelzang, JCO 2003
Multimodality therapy of malignant pleural mesothelioma: The important questions

- EPP or no surgery?
  Impossible to answer in context of a randomized study. MARS feasibility trial failed
  Treasure, Lancet Oncol 2011

- PORT to hemithorax after neoadjuvant chemo and EPP:
  SAKK 17/04
  Stahel, Lancet Oncol 2015
MARS feasibility trial

24 randomly assigned to EPP (with radical radiotherapy)

5 EPP surgery not started
- 3 patient refusal
- 2 clinical decision

3 EPP surgery abandoned
- 1 perioperative death
- 2 unexpected disease progression

16 completed EPP surgery

13 post operative complications
- 1 reoperation plus cardiac plus pulmonary
- 1 cardiac plus pulmonary plus infection
- 1 cardiac plus pulmonary
- 1 cardiac plus urine retention
- 2 pulmonary plus other
- 1 reoperation
- 1 cardiac
- 3 other

8 radical radiotherapy not received
- 1 clinical decision
- 2 toxicity
- 2 disease progression
- 3 died

8 received radical radiotherapy

Operative mortality of EPP 18%

Treasure, Lancet Oncol 2011
Letter responding to MARS

<table>
<thead>
<tr>
<th>Stage</th>
<th>Number of patients</th>
<th>ITT median survival (95% CI)</th>
<th>EPP operative mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Chemotherapy</td>
<td>EPP</td>
<td>Radiotherapy</td>
</tr>
<tr>
<td>Weder and colleagues¹</td>
<td>T1–3, N0–2</td>
<td>19 (100%)</td>
<td>16 (84%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weder and colleagues²</td>
<td>T1–3, N0–2</td>
<td>61 (100%)</td>
<td>45 (74%)</td>
</tr>
<tr>
<td>Rea and colleagues³</td>
<td>T1–3, N0–2</td>
<td>21 (100%)</td>
<td>17 (81%)</td>
</tr>
<tr>
<td>Batirel and colleagues⁴</td>
<td>T1–3, N0–2</td>
<td>20 (100%)</td>
<td>16 (80%)</td>
</tr>
<tr>
<td>Krug and colleagues⁵</td>
<td>T1–3, N0–2</td>
<td>77 (100%)</td>
<td>57 (74%)</td>
</tr>
<tr>
<td>Van Schil and colleagues⁶</td>
<td>T1–3, N0–2</td>
<td>59 (100%)</td>
<td>42 (73%)</td>
</tr>
</tbody>
</table>

ITT=intention to treat. Median survival is in months.
Superior results of P/D and EPP in epithelial malignant mesothelioma

- Non-randomized prospective study comparing EPP (22 pts) and P/D (17 pts)
- 25 received neoadjuvant therapy, 17 adjuvant radiotherapy
Does surgery improve survival of patients with malignant pleural mesothelioma?: A multicenter retrospective analysis of 1365 consecutive patients

Survival curves according to the treatment (nonsurgical treatment versus EPP versus P/D) considering only patients with favorable prognostic factors.
Patient characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>n</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>14</td>
<td>(9.3%)</td>
</tr>
<tr>
<td>M</td>
<td>137</td>
<td>(90.7%)</td>
</tr>
<tr>
<td><strong>T Stage (clinical):</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>45</td>
<td>(29.8%)</td>
</tr>
<tr>
<td>T2</td>
<td>61</td>
<td>(40.4%)</td>
</tr>
<tr>
<td>T3</td>
<td>45</td>
<td>(29.8%)</td>
</tr>
<tr>
<td><strong>N Stage:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N0/1</td>
<td>130</td>
<td>(86.1%)</td>
</tr>
<tr>
<td>N2 (mediastinoscopy)</td>
<td>21</td>
<td>(13.9%)</td>
</tr>
<tr>
<td><strong>Histologic type:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epithelial</td>
<td>124</td>
<td>(82.1%)</td>
</tr>
<tr>
<td>Mixed histology</td>
<td>18</td>
<td>(11.9%)</td>
</tr>
<tr>
<td>Sarcomatous</td>
<td>9</td>
<td>(5.9%)</td>
</tr>
</tbody>
</table>

Patient characteristics

**Stahel, Lancet Oncol 2015**
### Chemotherapy Doses and Dose compliance

<table>
<thead>
<tr>
<th>Chemotherapy</th>
<th>Planned Dose (mg/m2)</th>
<th>Dose administered (mg/m2) (Mean (Min, Max))</th>
<th>Planned Dose administered (%) (Mean (Min, Max))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pemetrexed</td>
<td>500</td>
<td>498.4 (410.5, 555.6)</td>
<td>99.7 (82.1, 111.1)</td>
</tr>
<tr>
<td>Cisplatin</td>
<td>75</td>
<td>74.5 (61.4, 79.2)</td>
<td>99.3 (81.9, 105.6)</td>
</tr>
<tr>
<td>Carboplatin*</td>
<td>-</td>
<td>512.0 (350.0, 766.7)</td>
<td></td>
</tr>
</tbody>
</table>

* 7.3% of cycles delivered where changed to carboplatin

### Response to Chemotherapy

<table>
<thead>
<tr>
<th>Response</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>2</td>
<td>1.3</td>
</tr>
<tr>
<td>PR</td>
<td>50</td>
<td>33.1</td>
</tr>
<tr>
<td>SD</td>
<td>75</td>
<td>49.7</td>
</tr>
<tr>
<td>PD</td>
<td>20</td>
<td>13.3</td>
</tr>
<tr>
<td>NE</td>
<td>4</td>
<td>2.7</td>
</tr>
</tbody>
</table>
125 patients underwent surgery, of whom 113 had extrapleural pneumonectomy as intended; 12 patients had thoracotomy but no radical resection.

96 (64%) of 151 patients achieved complete macroscopic (R0 and R1) resection.

Five patients had died 30 days after surgery (two with pulmonary embolism and right heart failure, one with cardiac arrest, one with diaphragmatic patch failure, and one with septic multiorgan failure), a further five had died by 60 days (three had rapid tumour progression, one had cerebrovascular insult, and one had septic multiorgan failure).
SAKK 17/04: Survival from registration

All patients:
RR 30%
Median OS 15 (12.1-19.3) months

Patients randomized:

<table>
<thead>
<tr>
<th>Arm</th>
<th>Median (months)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>20.8</td>
<td>14.4</td>
</tr>
<tr>
<td>B</td>
<td>19.3</td>
<td>11.5</td>
</tr>
</tbody>
</table>

Stahel, Lancet Oncol 2015
SAKK 17/04: locoregional relapse free survival from surgery

**Graph:**

- **X-axis:** Time (months)
- **Y-axis:** Loco-regional relapse-free survival (%)

**Number at risk:**
- No radiotherapy: 27, 7, 2, 1, 0
- Radiotherapy: 27, 7, 3, 1, 0

**Arm A (No RT):**
- Median: 11.0 months
- 95% CI: 7.5 - 13.5

**Arm B (RT):**
- Median: 12.2 months
- 95% CI: 9.5 - 14.8

*Stahel, Lancet Oncol 2015*
136 patients underwent macroscopic complete resection by extrapleural pneumonectomy after induction chemotherapy for MPM. We analysed 106 patients who presented with recurrent disease until October 2014.
Accelerated hemithoracic radiation followed by extrapleural pneumonectomy for malignant pleural mesothelioma

ECOG performance status of 0 to 2, with good pulmonary function tests, a new histological diagnosis of MPM previously untreated, clinical stage T1-3N0M0, suitable for combined modality therapy,
Key therapeutic considerations (2)

- Bevacizumab added to cisplatin/pemetrexed leads to an increase in progression-free survival and overall survival
- There is no standard second line therapy, the most commonly used single agents are vinorelbine or gemcitabine
- Occasional responses occur with multitargeted TKIs

Zalcman, Lancet Oncol 2016
MAPS trial: Cisplatin/pemetrexed with or without bevacizumab

**IFT-GFPC-0701 trial: MAPS**
Mesothelioma Avastin cisplatin Pemetrexed Study

IFCT-sponsored, open-label, multi-centre randomized phase II-III trial
Roche supplied bevacizumab

- Malignant Pleural Mesothelioma (MPM)
- Histologically proven
- PS= 0-2
- No cardiovascular comorbidity
- Chemonaive

CT-scan Q.3 cycles in both arms.
Response assessed with modified RECIST criteria for mesothelioma

**Stratification:**
- center, histology (epithelioid vs. sarcomatoid/mixed), PS (0-1 vs. 2), smoking status (ever smoker vs. never-smoker)
Vinca alkaloids in the therapeutic management of malignant pleural mesothelioma

<table>
<thead>
<tr>
<th>Author [ref]</th>
<th>Regimen</th>
<th>N. pts</th>
<th>Line</th>
<th>RR</th>
<th>DCR</th>
<th>mTTP/PFS</th>
<th>mOS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stebbing [26]a</td>
<td>IV VNR</td>
<td>63</td>
<td>100% 2L</td>
<td>16%</td>
<td>84%</td>
<td>NR</td>
<td>9.6 mo</td>
</tr>
<tr>
<td>Sorensen [30]a</td>
<td>OR VNR</td>
<td>15</td>
<td>100% 2L</td>
<td>7%</td>
<td>NR</td>
<td>2.3 mo</td>
<td>2.5 mo</td>
</tr>
<tr>
<td>Zucali [27]b</td>
<td>IV VNR</td>
<td>59</td>
<td>58% 2L 42% 3L</td>
<td>15%</td>
<td>49%</td>
<td>2.3 mo</td>
<td>6.2 mo</td>
</tr>
<tr>
<td>Zauderer [28,29]b</td>
<td>IV VNR</td>
<td>45</td>
<td>53% 2L 47% 3L</td>
<td>0%</td>
<td>52%</td>
<td>2.5 mo</td>
<td>5.0 mo</td>
</tr>
<tr>
<td>Zucali [31]a</td>
<td>IV VNR + GEM</td>
<td>30</td>
<td>100% 2L</td>
<td>10%</td>
<td>43%</td>
<td>2.8 mo</td>
<td>10.9 mo</td>
</tr>
<tr>
<td>Toyokawa [32]a</td>
<td>IV VNR + GEM</td>
<td>17</td>
<td>100% 2L</td>
<td>18%</td>
<td>82%</td>
<td>6.0 mo</td>
<td>11.2 mo</td>
</tr>
</tbody>
</table>

Ref: reference; N. pts: number of patients included; IV: intravenous; OR: oral; VNR: vinorelbine; GEM: gemcitabine; Line: line of therapy (2L: second line; 3L: third line or beyond); RR: response rate; DCR: disease control rate (RR plus stable disease); mTTP/PFS: median time to progression or progression-free survival (whichever reported); mOS: median overall survival; mo: months.

a Prospective studies.
b Retrospective studies.
Sunitinib in second line for mesothelioma

- 53 patients, median of 2 6-weeks cycles
- 6 (12%) PRs
- Median time to progression 3.5 months
- 40% required dose reduction, fatigue most common side effect

Nowak, JTO 2012
Key molecular features of malignant mesothelioma

- Arises from mesothelial cells of the pleural, pericardial, and peritoneal cavities.
- Often associated with asbestos exposure. Asbestos carcinogenesis is linked to chronic inflammation that may lead to malignant mesothelial cell transformation after decades long latency.
- Consistent molecular features include:

*Bueno et al., Exp Rev Resp Med 2015*
BAP-1 mutation in mesothelioma

- BAP1 was initially identified in lung cancer cell lines as a protein that binds to BRCA1. 
  *Jensen, Oncogene 1989*

- Genetic alterations in BAP1 gene have been identified in 23% of MPM specimens. 
  *Bott, Nature Genetics 2011*
• Germline BAP1 mutations have been detected in families with a high incidence of MPM  
  *Testa, Nature Genetics 2011*

• Germline BAP1 mutations predispose to uveal melanoma, lung adenocarcinoma, meningioma, and other cancers  
  *Abdel-Rahman, Nature Genetics 2011*

• The Prevalence of BRCA-1 associated protein 1 germline mutation in sporadic malignant pleural mesothelioma is estimated around 1-2%  
  *Rusch, Lung Cancer 2014*

• Mesothelioma patients with germline BAP1 mutations have a better long-term survival as compared to patients with acquired mutation  
  *Baumann, Carcinogenesis 2015*
Vorinostat in second line malignant pleural mesothelioma

264 screened

713 screened but not randomly assigned

661 randomly assigned

329 assigned to receive vorinostat

322 discontinued
- 33 had clinical adverse events
- 12 died
- 251 had progressive disease
- 1 had laboratory-confirmed adverse event
- 15 withdrew consent
- 1 protocol deviation
- 9 other

7 received vorinostat at time of protocol-specified final analysis

329 included in intention-to-treat analysis

332 assigned to receive placebo

324 discontinued
- 11 had clinical adverse events
- 15 died
- 281 had progressive disease
- 1 lost to follow-up
- 10 withdrew consent
- 1 protocol deviation
- 5 other

8 received placebo at time of protocol-specified final analysis

332 included in intention-to-treat analysis

Krug, Lancet Oncol 2015

Vorinostat median overall survival 30.7 weeks (95% CI 26.7–36.1)
Placebo median overall survival 27.1 weeks (95% CI 23.4–31.9)
Hazard ratio (vorinostat vs placebo): 0.98 (95% CI 0.83–1.17); p=0.86
Genetic/epigenetic changes present in mesothelioma offer different possibilities for therapeutic intervention
Deaminase deprivation with pegylated arginine deiminase in patients with argininosuccinate synthetase 1-deficient malignant pleural mesothelioma

201 Patients registered

97 ASS1 negative

70 Randomized

46 Randomized to ADI-PEG20 + BSC

2 Inseligible
1 ECOG 2
1 Nonmeasurable disease

24 Randomized to BSC alone

44 Received ADI-PEG20 + BSC as randomized

22 Received BSC as randomized
2 Withdrew from study because they wanted chemotherapy

24 Analyzed for PFS and OS (intent-to-treat analysis)

25 ASS1-negative patients analyzed for OS

81 ASS1-positive patients analyzed for OS

21 ASS1 status unknown

A Alive and progression-free

No. at risk
BSC 44
ADI-PEG20 24

Median survival, mo
BSC 2.0
ADI-PEG20 • BSC 3.2

Hazard ratio, 0.56 (95% CI, 0.33–0.96)
Log rank P = .03 (1-sided P = .02)

B Alive

No. at risk
BSC 44
ADI-PEG20 24

Median survival, mo
BSC 11.1
ADI-PEG20 • BSC 11.5

Hazard ratio, 0.68 (95% CI, 0.39–1.16)
Log rank P = .15 (1-sided P = .08)
A phase I study of GSK2256098, a focal adhesion kinase inhibitor, in patients with advanced solid tumors

- In the 29 patients with recurrent mesothelioma, the median PFS was 12 (95% CI 9.1, 23.4) weeks
- (23.4 weeks merlin negative, n = 14; 11.4 weeks merlin positive, n = 9)
A phase I study of apitolisib (CDC-0980), a dual PI3K and mTOR inhibitor in patients with advanced solid tumors

Of the 27 MPM patients treated at 30 mg 28/28 schedule, 26 were evaluable by modified RECIST-independent review. Median time on study was 4 months (range, 0.5–38.9) with 8 patients (29.6%) on study for more than 6 months, including 2 patients (7.4%) for more than 12 months.
Targeting mesothelin with monoclonal antibodies and immunoconjugates

- **Amatuximab**, a chimeric monoclonal antibody
  - Combination with cisplatin/pemetrexed:
    - PRs in 33/89 (40%) and SD in 42 (51%).
    - Six month-PFS rate was 51%, median PFS 6.1 months (95% CI: 5.8, 6.4).
    - *Hassan, CCR 2014*

- **Immunotoxin SS1P** (Recombinant antibody FV and pseudomonas exotoxin)
    - *Weldon, Mol Cancer Therapeutics 2013*
Targeting mesothelin with monoclonal antibodies and immunoconjugates

• Ametumab ravtansine (maytansinoid tubulin inhibitor)

• Preclinical activity in mesothelioma
  
  *Golfier, Mol Cancer Ther 2014*

• Phase I in patients with metastatic mesothelioma
  
  *Hassen, WCLC 2015*
Phase 3 trial anetumab ravtansine plus pemetrexed and cisplatin in first line malignant pleural mesothelioma
### PD-L1 expression in malignant pleural mesothelioma

<table>
<thead>
<tr>
<th></th>
<th>Mansfield et al(^1)</th>
<th>Cedrés et al(^2)</th>
<th>Thapa et al(^3)</th>
<th>Combaz-Lair(^4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>106</td>
<td>77</td>
<td>311</td>
<td>58</td>
</tr>
<tr>
<td>Antibody used</td>
<td>5H1-A3- mouse monoclonal</td>
<td>E1L3N- Rabbit IgG (cell signalling)</td>
<td>E1L3N- Rabbit IgG (cell signalling)</td>
<td>E1L3N- Rabbit IgG (cell signalling)</td>
</tr>
<tr>
<td>Criteria of positivity</td>
<td>&gt;5% membranous and/or cytoplasmic staining</td>
<td>≥1% membranous and/or cytoplasmic staining</td>
<td>≥1% membranous and/or cytoplasmic staining</td>
<td>≥1% membranous and/or cytoplasmic staining</td>
</tr>
<tr>
<td>PD-L1 positivity</td>
<td>41.7%</td>
<td>33%</td>
<td>42%*</td>
<td>29%</td>
</tr>
<tr>
<td>All</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epitheloid</td>
<td>20%</td>
<td>33%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-epitheloid</td>
<td>38%</td>
<td>73%</td>
<td>42%*</td>
<td>37%</td>
</tr>
</tbody>
</table>

97% percent (58/60 cases) of the MPM showed a mixed infiltrate of lymphocytes, macrophages, and plasma cells (Combaz-Lair, Human Pathol 2016)

*Strong positivity predominantly in non-epitheloid tumors

\(^1\) Mansfield, JTO 2014, \(^2\) Cedres, Plos One 2015, \(^3\) Thapa, ASCO 2016, \(^4\) Combaz-Lair, Human Pathol 2016
Mesothelioma – mutational load

- Whole-exome sequencing on DNA from 22 MPMs and matched blood samples. Identification of 517 somatic mutations across 490 mutated genes
- Mesothelioma contain an average of 24 protein coding alteration per sample, a rate considerably lower than other types malignancies

Bueno, Nat Gen 2016
T-cell inflamed microenvironment by tumor entity across TCGA solid tumors
Tremelimumab in second or third line versus placebo in malignant mesothelioma

DETERMINE Study Design
Global, Randomized, Double-Blind, Placebo-Controlled, Phase 2b Trial

N=571
• Pleural/peritoneal MM
• ECOG PS 0–1
• 1–2 prior regimens (including a platinum)
• Measurable disease

2:1 randomization
Stratification:
• Pleural vs. peritoneal
• 2nd vs. 3rd line
• EORTC low vs. high risk

Tremelimumab i.v.
10 mg/kg q4w x 7 doses, then q12w
n=382

Placebo i.v.
n=189

Primary endpoint: Overall survival (OS)
Key secondary endpoints: 18-month OS, PFS, overall response rate and duration, disease control rate (DCR), durable DCR, safety
Statistics: 90% power to detect an overall HR of 0.71 (increase in median OS from 7 to 9.3 mo) using a 2-sided 0.05 level test

DETERMINE: Overall Survival (ITT Population)

<table>
<thead>
<tr>
<th></th>
<th>Tremelimumab</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>382</td>
<td>189</td>
</tr>
<tr>
<td>Events, n (%)</td>
<td>307 (80.4%)</td>
<td>154 (81.5%)</td>
</tr>
<tr>
<td>Median OS (mo)</td>
<td>7.7</td>
<td>7.3</td>
</tr>
<tr>
<td>18-mo survival</td>
<td>17.4%</td>
<td>18.2%</td>
</tr>
</tbody>
</table>

Analysis with 2 stratification factors (EORTC status and line of therapy)^

OS HR = 0.92
95% 2-sided CI = 0.76, 1.12
2-sided p-value = 0.408

*p-value for OS derived from stratifiedLog-rank test; HR and its CI derived from stratified Cox regression. HR=1 implies a lower risk of death with tremelimumab.
Summarizing available results on immune checkpoint inhibitors

<table>
<thead>
<tr>
<th>Study</th>
<th>Keynote-028 PD-L1+</th>
<th>NivoMes Unselected</th>
<th>Avelumab Unselected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Number</td>
<td>25</td>
<td>18</td>
<td>53</td>
</tr>
<tr>
<td>PR</td>
<td>7 (28%)</td>
<td>5 (27%)</td>
<td>5 (9.4%)</td>
</tr>
<tr>
<td>SD</td>
<td>12 (48%)</td>
<td>4 (22%)</td>
<td>27 (47.2%)</td>
</tr>
<tr>
<td>PD</td>
<td>4 (16%)</td>
<td>9 (50%)</td>
<td>18 (34%)</td>
</tr>
<tr>
<td>Not assessed</td>
<td>2 (8%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Level of PD-L1 expression in Keynote-028 did not correlate with response. Both PD-L1 positive and negative patients responded to Avelumab. Response to Avelumab was not associated with TIL or tumour PD-L1 staining.
Avelumab in mesothelioma cohort pretreated with platin/pemetrexed

<table>
<thead>
<tr>
<th>Response Category</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete response, n (%)</td>
<td>0</td>
</tr>
<tr>
<td>Partial response, n (%)</td>
<td>5 (9.4)*</td>
</tr>
<tr>
<td>Stable disease, n (%)</td>
<td>25 (47.2)</td>
</tr>
<tr>
<td>Progressive disease, n (%)</td>
<td>18 (34.0)</td>
</tr>
<tr>
<td>Non-evaluable, n (%)</td>
<td>5 (9.4)</td>
</tr>
<tr>
<td>Overall response rate, % (95% CI)</td>
<td>9.4 (3.1, 20.7)</td>
</tr>
<tr>
<td>Disease control rate, % (95% CI)</td>
<td>56.6 (42.3, 70.2)</td>
</tr>
</tbody>
</table>

Hassan, ASCO 2016
**Study design:**
- Multicentre, randomised, phase III trial, ETOP sponsored
- **Primary objectives:**
  - To assess safety and efficacy of pembrolizumab versus standard chemotherapy in MPM
- **Primary endpoint:**
  - Progression-free survival (based on independent radiological review)
- **Sample size:**
  - 142 randomized patients
CA209-743: A phase III, randomized, open label trial of nivolumab in combination with ipilimumab versus pemetrexed with cisplatin or carboplatin as first line therapy in unresectable pleural mesothelioma

Study design:

ClinicalTrials.gov Identifier: NCT02899299
Comprehensive genomic analysis of malignant pleural mesothelioma