# MALIGNANT MESOTHELIOMA

## Diagnostic Approaches

- **No specific clinical features** of Malignant Pleural Mesothelioma (MPM).
- **Occupational history** with an emphasis on Asbestos exposure. *Usually followed by a prolonged latency period.*
- **CT of thorax with contrast**
- **Samples for diagnosis**
    - Pleural biopsy (thoracoscopic biopsy)
    - Image-guided needle core biopsies
    - Large open surgery or video-assisted thoracoscopic surgery (VATS) biopsy
    - Thoracocentesis for cytological assessment (cell block)
- **Pathology**
    - Cytology of pleural effusion controversial (not recommended)
    - Tissue biopsy specimens facilitate definite diagnosis
- A major sub-type diagnosis should be given in all cases as
    - Epithelioid
    - Biphasic
    - Sarcomatoid
    - Immunohistochemistry (IHC) diagnosis
        - At least two mesothelial markers and two markers of adenocarcinomas should be used
        - Sarcomatoid MPM often does not express mesothelial markers
        - Loss of BRCA1-associated protein 1 (BAP1)
    - Fluorescent in situ hybridization (FISH)
        - To detect homozygous deletion of p16 for MPM diagnosis.

MPM to lung vs. adenocarcinoma lung with pleural effusion as per some pathology reports

| Entity | MPM | Adenocarcinoma |
|---|---|---|
| Markers | Calretinin<br>Cytokeratin 5/6<br>WT1<br>D2-40 | TTF1<br>Napsin A<br>CEA<br>Ep-CAM |
| First Line Treatment | Platinum/pemetrexed | Platinum/pemetrexed |
| Subsequent Lines | Gemcitabine<br>Re-challenge with the initial regimen | Multiple treatment options |
| Prognosis | Poor | Far much better |

## Systemic Therapy

### First-line Therapy: The current standard

| Pemetrexed/Cisplatin | |
|---|---|
| **Pemetrexed** | 500 mg/$m^2$ day 1 |
| **Cisplatin** | 75 mg/$m^2$ day 1 |
| It is administered every three weeks. | |

| Pemetrexed/Carboplatin | |
|---|---|
| **Pemetrexed** | 500 mg/$m^2$ day 1 |
| **Carboplatin** | AUC 5 day 1 |
| It is administered every three weeks. | |

| Gemcitabine/Cisplatin | |
|---|---|
| **Gemcitabine** | 1000–1250 mg/m2 days 1, 8, and 15 |
| **Cisplatin** | 80–100 mg/m2 day 1 |
| It is administered in 3- to 4-weeks cycles. | |

- **N.B.** Maintenance therapy has not yet improved overall survival.

### Second-line Systemic Therapy

- Pemetrexed
  - Given if not administered as first-line therapy.
  - Consider to rechallenge with pemetrexed if initial administration showed response.
- Gemcitabine
  - If not administered as first-line
- Immunotherapy
  - Anti-PDL1, as a monotherapy or with anti-CTLA4 shown promising results.
- Several randomized trials are currently ongoing for frontline and later regimens.

Malignant Pleural Mesothelioma (MPM) Systemic Therapy: Immunotherapy

| Endpoints | Nivolumab | Nivolumab and Ipilimumab |
|---|---|---|
| **Median PFS (months)** | 4 | 5.6 |
| **Overall survival (OS) (months)** | 13.6 | NR |

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## Surgery

### Principles of Surgery

- The achievement of free resection margins is virtually impossible, so the aim of surgery is to obtain “macroscopic complete resection” by means of pleurectomy with decortication (P/D) or extrapleural pneumonectomy (EPP).

Randomized trials of EPP vs. no EPP after induction therapy suggest the lack of benefit, and possibly even harmful effect.

Palliation of pleural effusion when chest tube drainage is not successful.

Our surgical colleagues of the Thoracic - MDT are no more adopting surgery for MPM

### Surgical procedures:

1. Extended pleurectomy/decortication (P/D) defined as complete removal of the pleura and all gross tumor, the lung is left in situ.
2. Extrapleural pneumonectomy (EPP), implies en-bloc resection of the involved visceral and parietal pleura, including the whole ipsilateral lung.
3. If required, the diaphragm and pericardium can also be resected

## Radiation Therapy

- Short course RT is recommended as palliative treatment for relief of chest pain due to infiltration of the chest wall by MPM.

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