

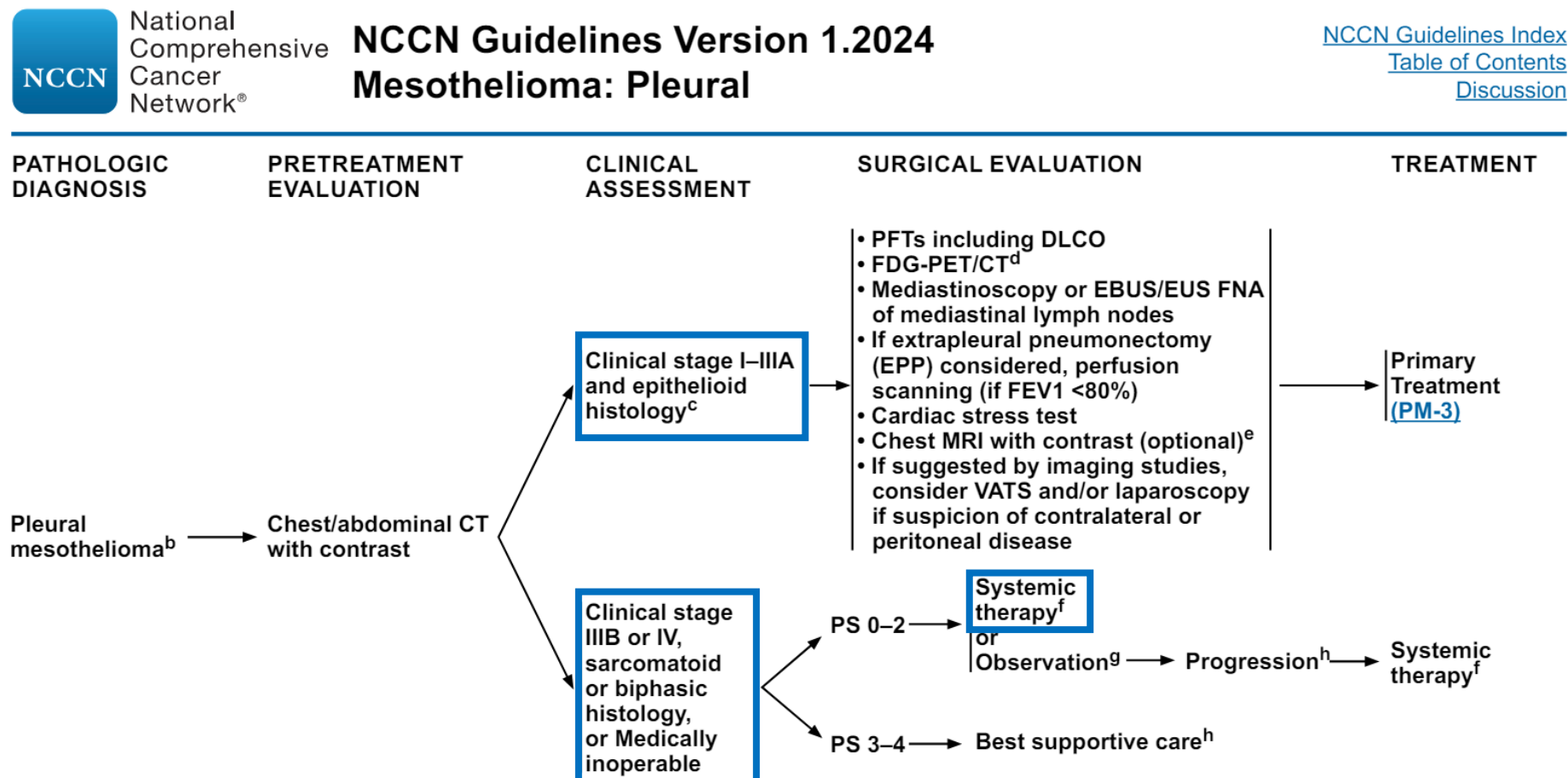
Immunotherapy in malignant pleural mesothelioma & thymic malignancies

Jeonghwan Youk

Seoul National University Hospital

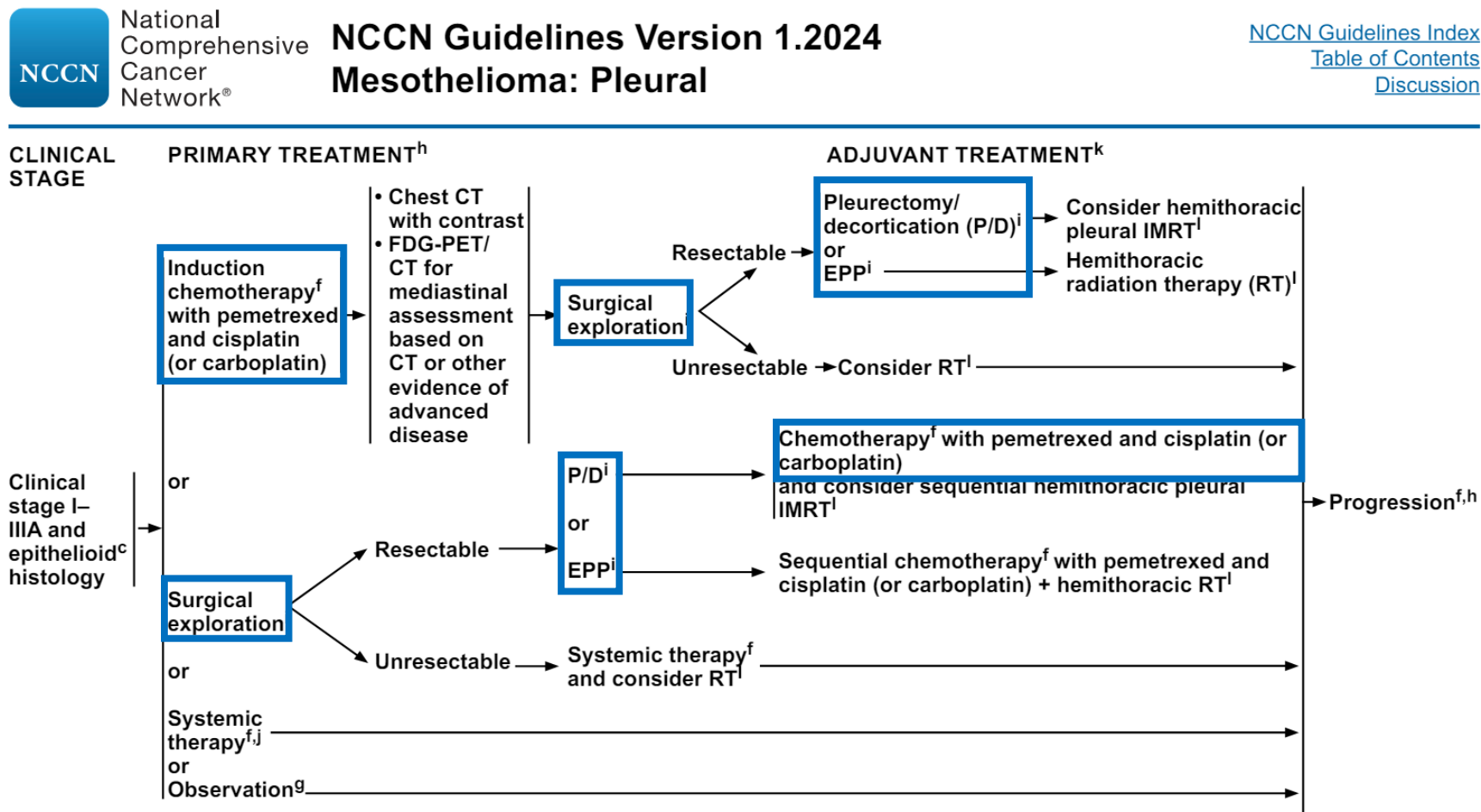
Treatment for malignant mesothelioma

- NCCN guidelines



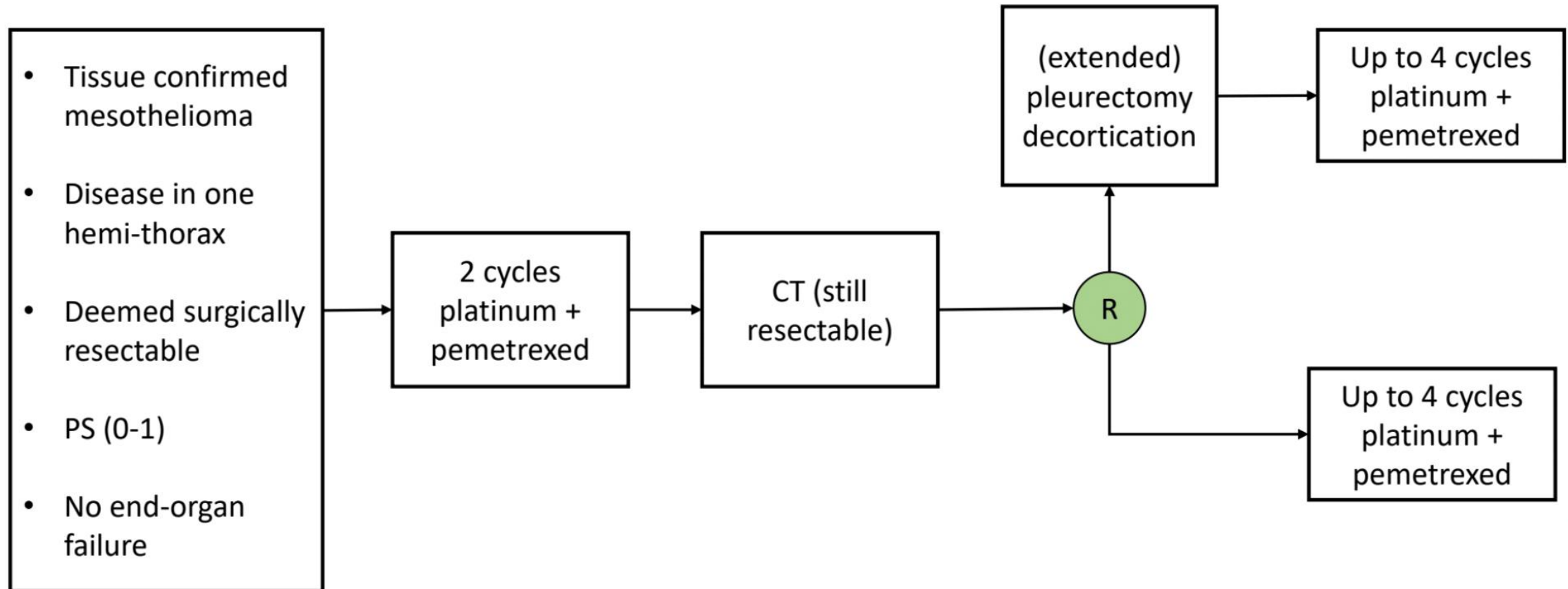
Treatment for malignant mesothelioma

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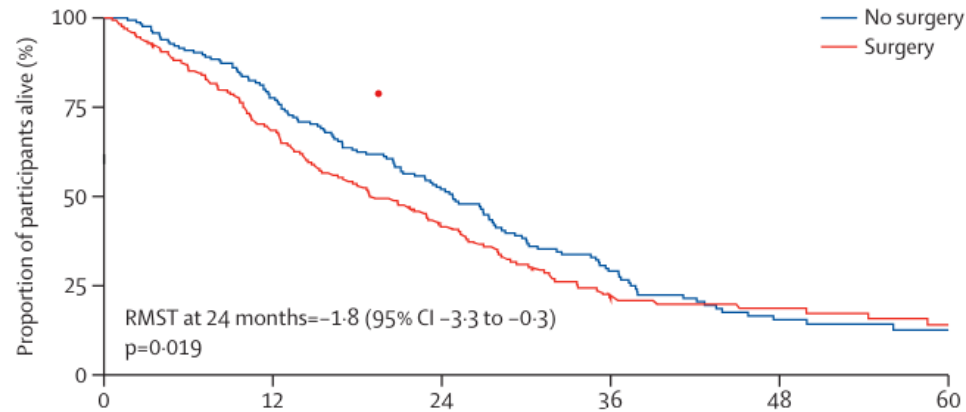
Treatment for malignant mesothelioma

- MARS 2 trial

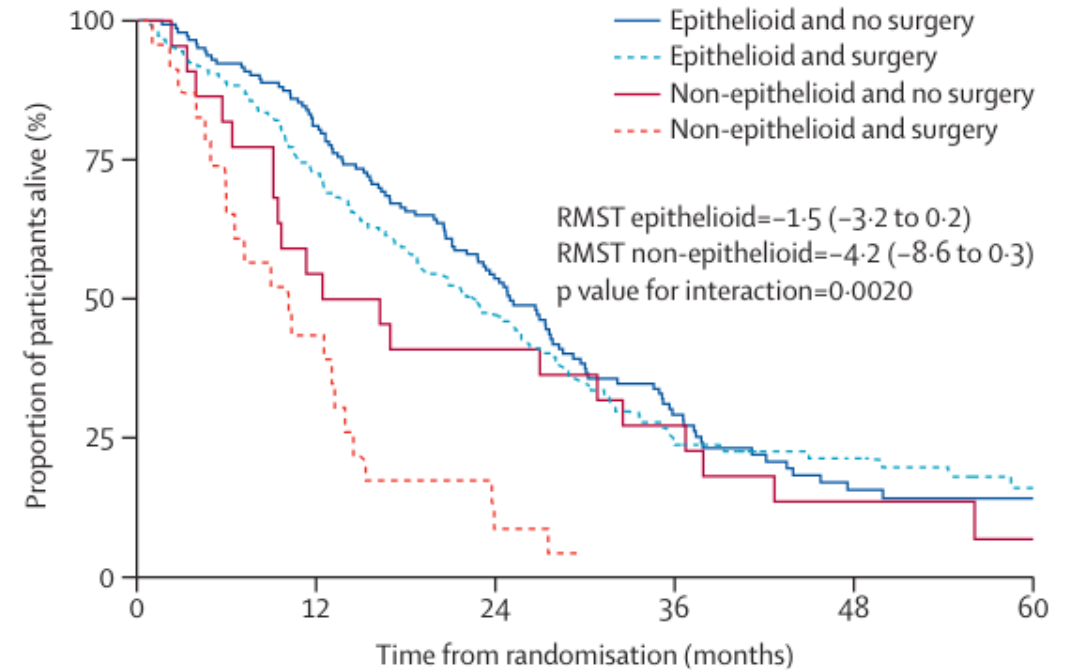
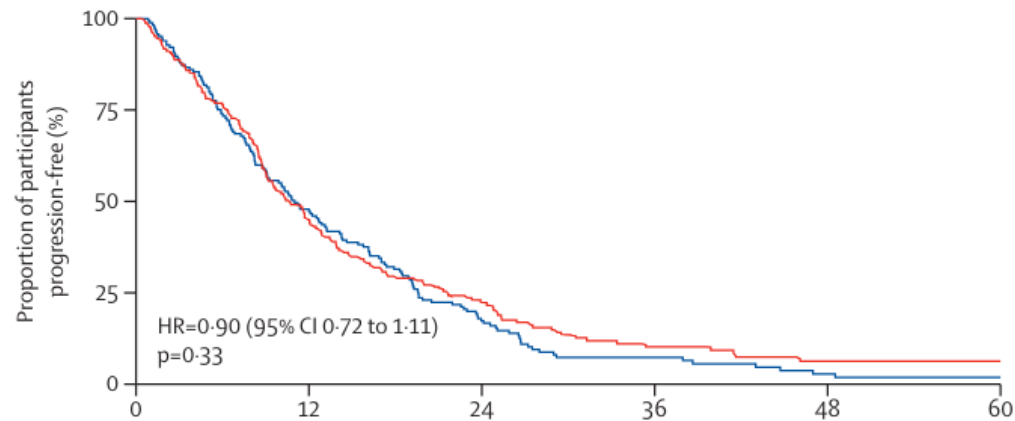


Treatment for malignant mesothelioma

- MARS 2 trial
 - OS



- PFS



Treatment for malignant mesothelioma

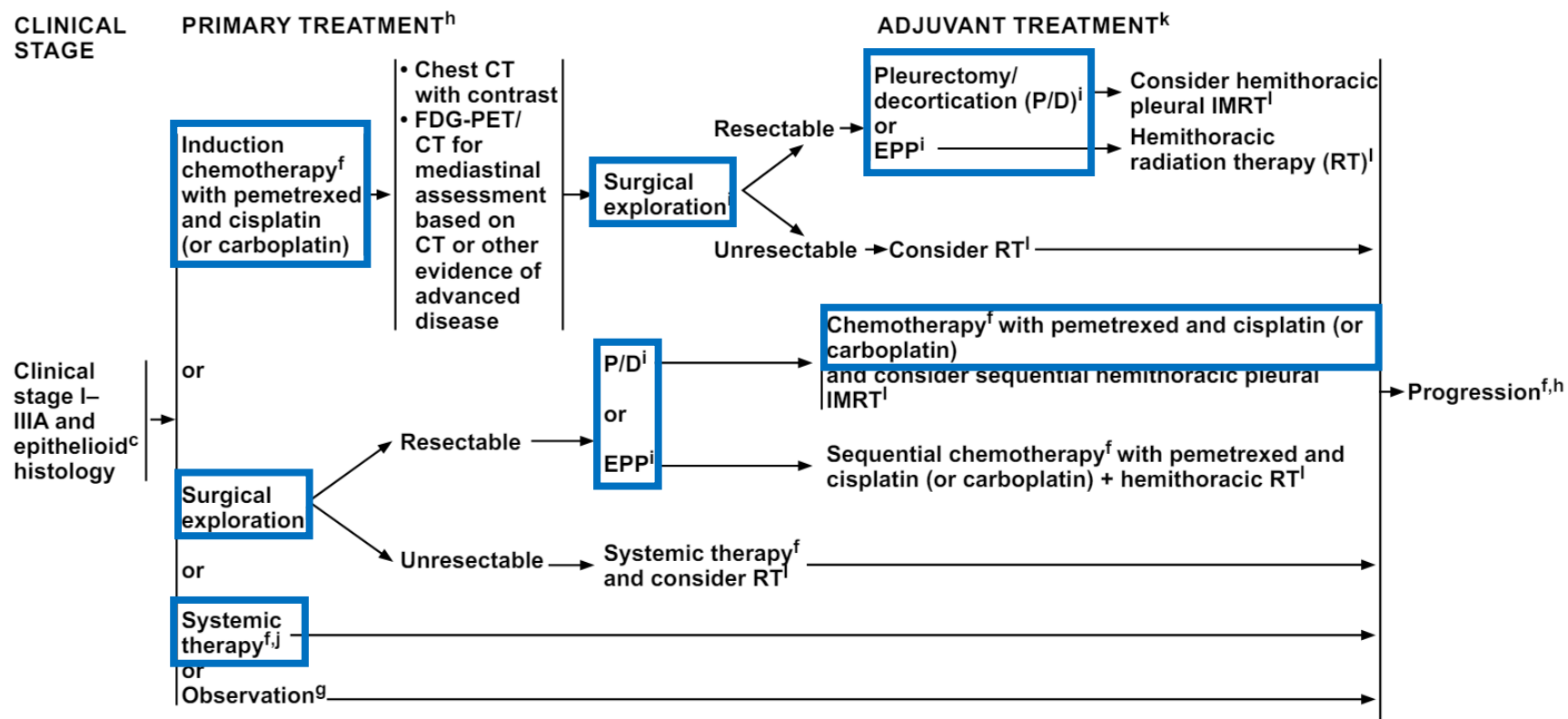
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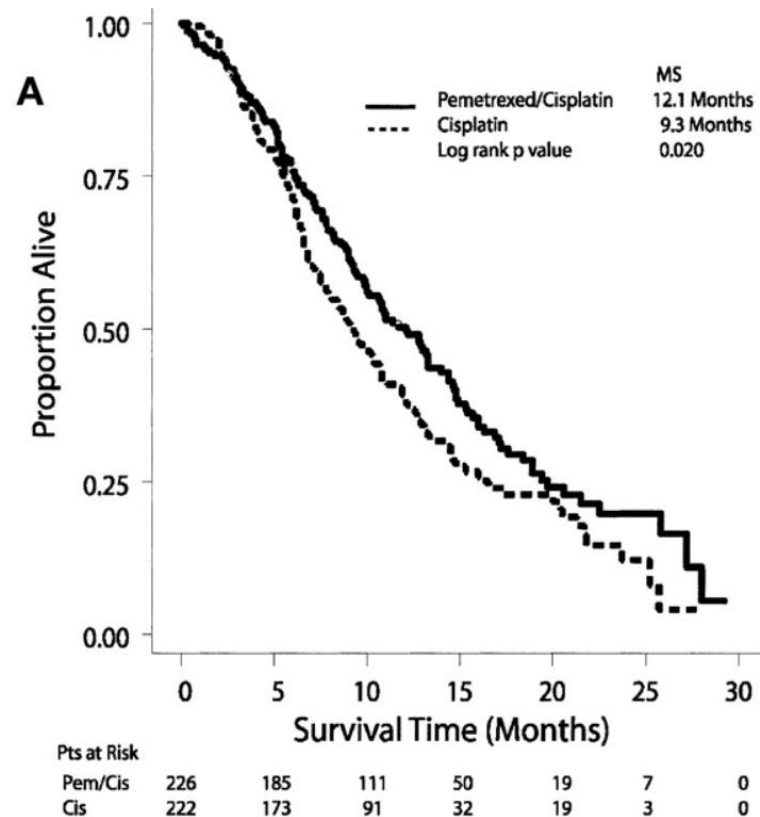
NCCN Guidelines Version 1.2024 Mesothelioma: Pleural

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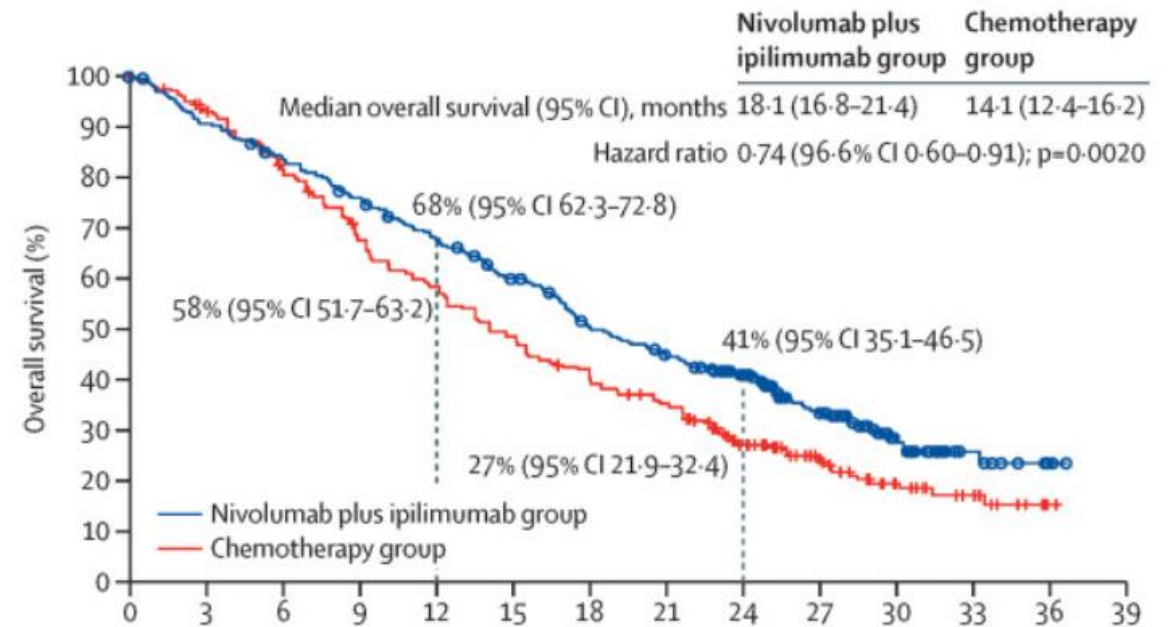
Treatment for malignant mesothelioma

- Previous trial (Before 2021-06-10 in KOR)
 - Phase III, chemotherapy-naïve
 - Pemetrexed/cisplatin > cisplatin alone



N J Vogelzang et al, Phase III study of pemetrexed in combination with cisplatin versus cisplatin alone in patients with malignant pleural mesothelioma *J Clin Oncol.* (2003)

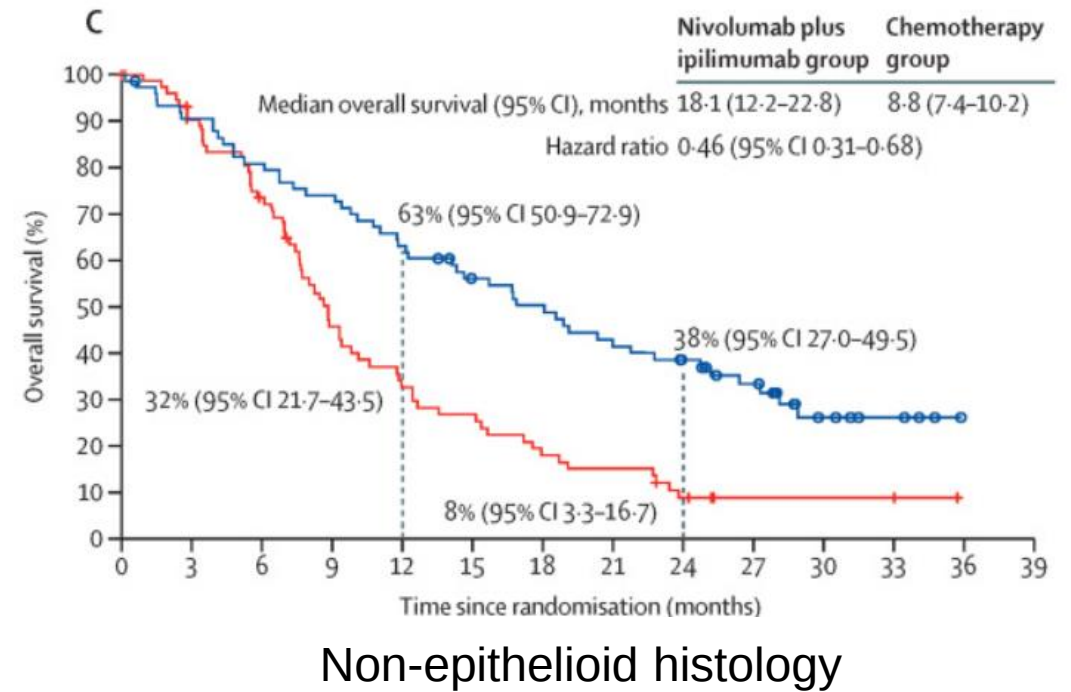
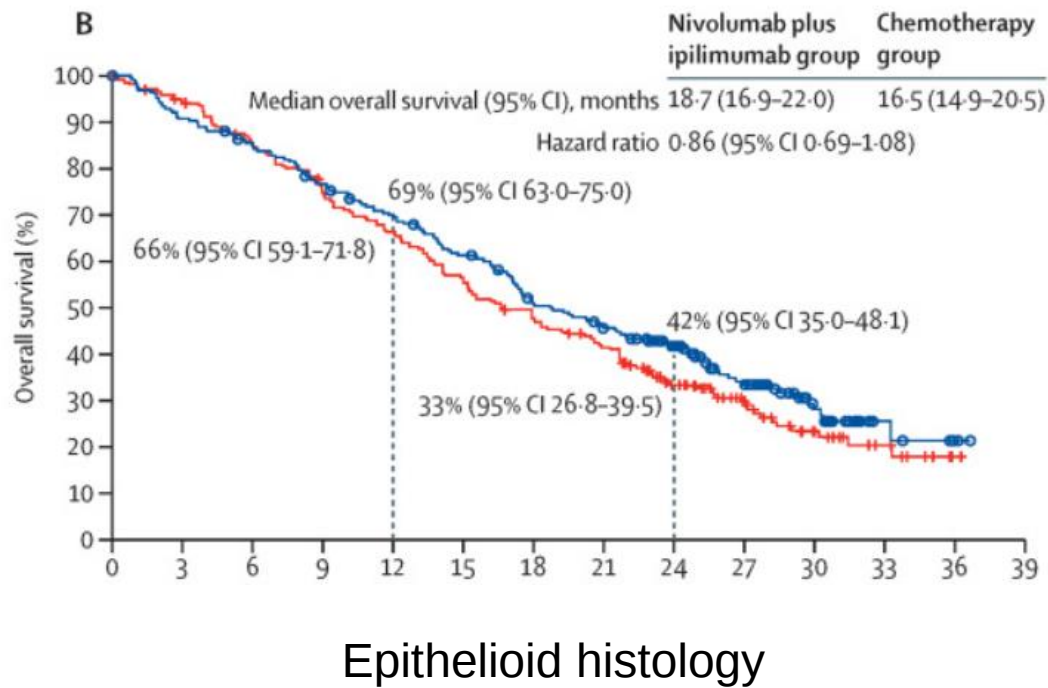
- CheckMate 743
 - Phase III, chemotherapy-naïve
 - Nivolumab/ipilimumab > chemotherapy



P Bass et al, First-line nivolumab plus ipilimumab in unresectable malignant pleural mesothelioma (CheckMate743): a multicenter, randomized, open-label, phase 3 trial *Lancet* (2021)

Treatment for malignant mesothelioma

- CheckMate 743
 - Phase III, chemotherapy-naïve
 - Nivolumab/ipilimumab > chemotherapy



Treatment for malignant mesothelioma

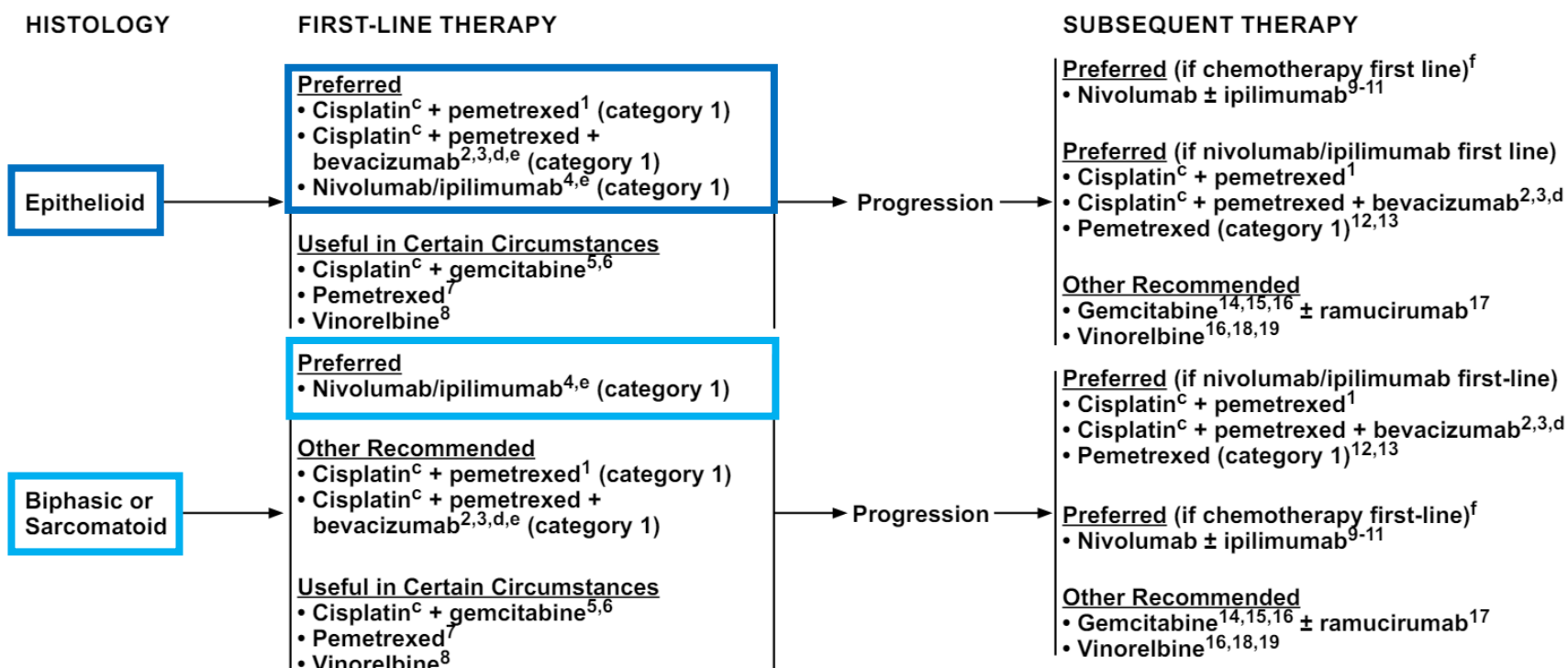
- NCCN guidelines



NCCN Guidelines Version 1.2024 Mesothelioma: Pleural

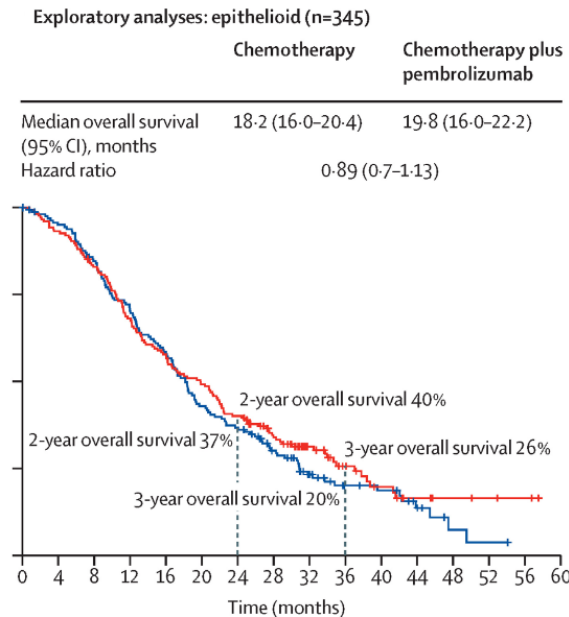
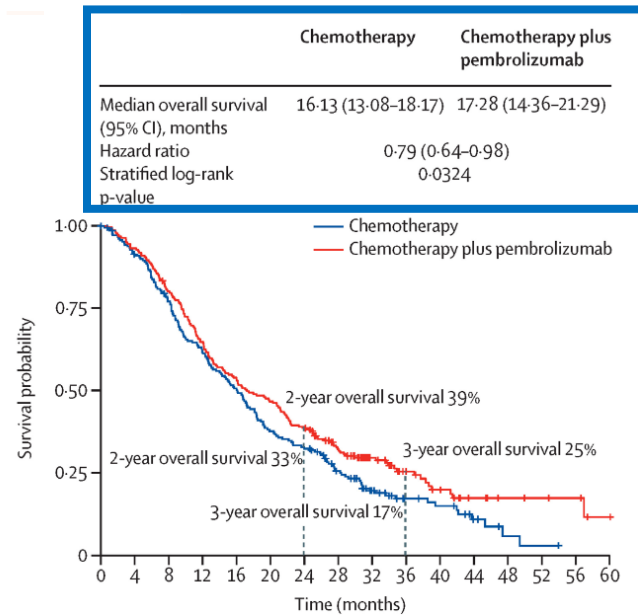
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PRINCIPLES OF SYSTEMIC THERAPY^{a,b}

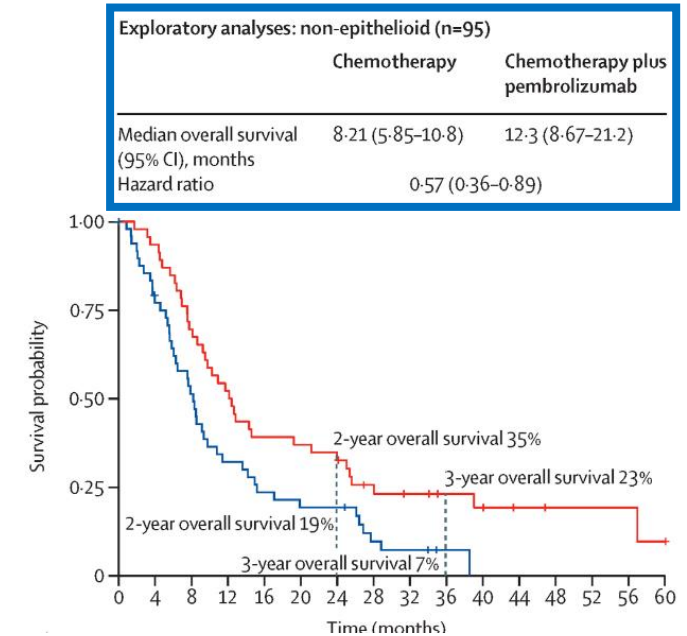


Treatment for malignant mesothelioma

- IND227
 - Phase III, chemotherapy-naïve
 - Pembrolizumab/placebo +/- pemetrexed/platinum



Epithelioid histology



Non-epithelioid histology

Treatment for thymoma & thymic carcinoma

- NCCN guidelines



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NCCN Guidelines Version 1.2024 Thymomas and Thymic Carcinomas

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PRINCIPLES OF SYSTEMIC THERAPY

FIRST-LINE COMBINATION CHEMOTHERAPY REGIMENS^a

THYMOMA

Preferred (Other Recommended for Thymic Carcinoma)

- CAP¹
Cisplatin 50 mg/m² IV day 1
Doxorubicin 50 mg/m² IV day 1
Cyclophosphamide 500 mg/m² IV day 1
Administered every 3 weeks

THYMIC CARCINOMA

Preferred (Other Recommended for Thymoma)

- Carboplatin/paclitaxel^{6,7,b}
Carboplatin AUC 6
Paclitaxel 200 mg/m²
Administered every 3 weeks

SECOND-LINE SYSTEMIC THERAPY

THYMOMA

Other Recommended

- Etoposide^{4,8}
- Everolimus⁹
- 5-FU and leucovorin¹⁰
- Gemcitabine ± capecitabine^{11,12}
- Ifosfamide¹³
- Octreotide^c (including LAR) (if octreotide scan or dotatate PET/CT positive) +/- prednisone^{14,15}
- Paclitaxel¹⁶
- Pemetrexed¹⁷

THYMIC CARCINOMA

Preferred

- Pembrolizumab^{d,18,19}
- Sunitinib²⁰
- Lenvatinib^{e,21}
- Gemcitabine ± capecitabine^{11,12}

Other Recommended

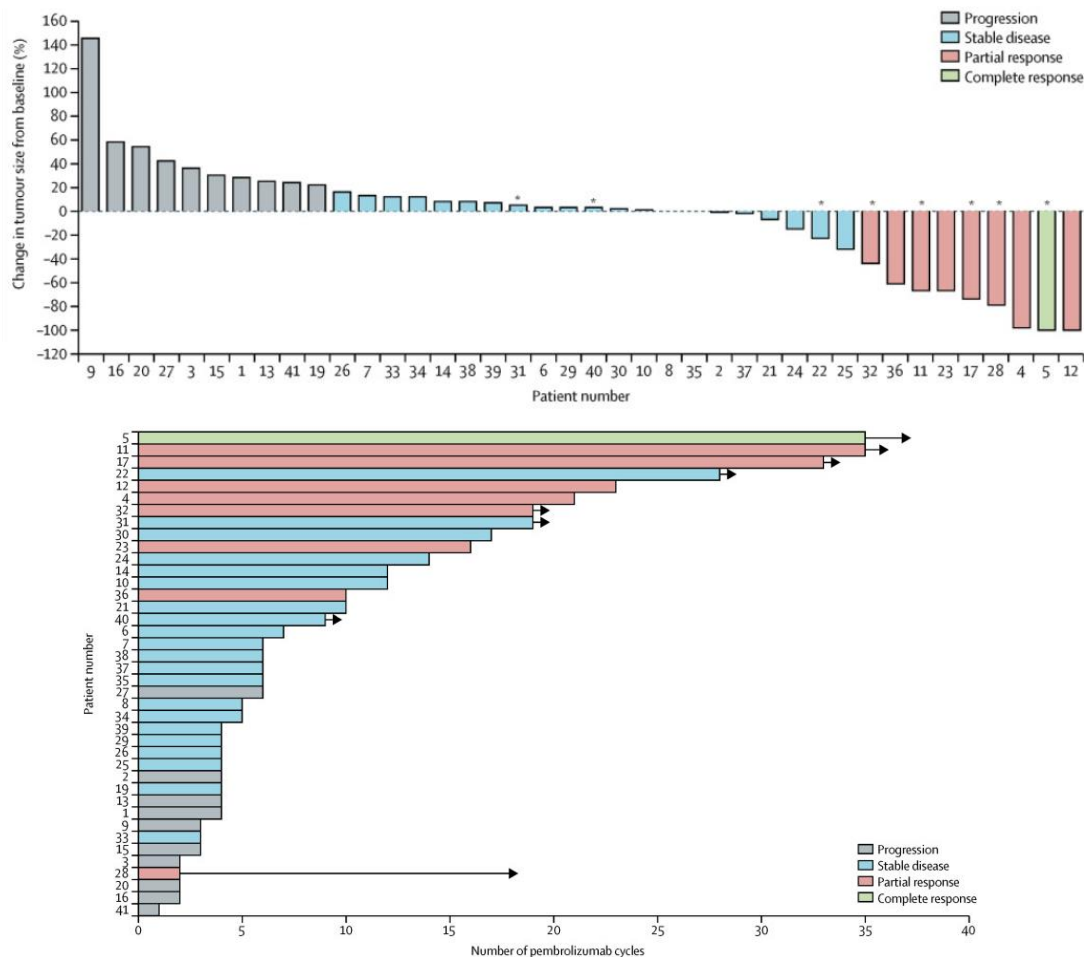
- Everolimus⁹
- 5-FU and leucovorin¹⁰
- Paclitaxel¹⁶
- Pemetrexed¹⁷

Useful in Certain Circumstances

- Etoposide^{4,8}
- Ifosfamide¹³

Treatment for thymoma & thymic carcinoma

- Pembrolizumab in phase II, single-arm



G Giaccone et al, Pembrolizumab in patients with thymic carcinoma: a single-arm, single-centre, phase 2 study. *Lancet Oncol.* (2018)

- Pembrolizumab in phase II, single-arm (KOR)

Adverse Event	Thymoma (n = 7)		Thymic Carcinoma (n = 26)	
	Grade 1-2	Grade 3-4	Grade 1-2	Grade 3-4
Hepatitis	0	2 (28.6)	0	2 (7.7)
Myasthenia gravis	1 (14.3)	0	0	2 (7.7)
Myocarditis	0	3 (42.9)	0	0
Thyroiditis	1 (14.3)	1 (14.3)	1 (3.8)	0
Dermatitis	2 (28.6)	0	0	0
Colitis	0	1 (14.3)	0	0
Conjunctivitis	0	1 (14.3)	0	0
Nephritis	0	1 (14.3)	0	0
Subacute myoclonus	0	0	0	1 (3.8)
Pruritus	0	0	3 (11.5)	0
Skin rash	0	0	2 (7.7)	0

J Cho et al, Pembrolizumab for Patients With Refractory or Relapsed Thymic Epithelial Tumor: An Open-Label Phase II Trial. *J Clin Oncol.* (2019)

Summary

- Immunotherapy has not been incorporated in perioperative treatment for MPM & thymic neoplasm
- Malignant pleural mesothelioma
 - 1st line palliative chemotherapy regimen
 - Nivolumab/ipilimumab
 - Alternatively, pembrolizumab/pemetrexed/carboplatin
 - Pemetrexed (Alimta) / cisplatin
 - Immunotherapy is more effective in non-epithelioid histology
- Thymic carcinoma
 - Subsequent palliative treatment regimen
 - Does not recommend patients with thymoma because of high rate of immune-related adverse events
 - tissue agnostic (no tissue specificity)