FDA Approval of Pembrolizumab / Keytruda with Chemotherapy for Unresectable, Advanced, or Metastatic Malignant Pleural Mesothelioma

KEYNOTE-483 Treatment Regimen

Pembrolizumab (Keytruda)

200 mg every 3 weeks

Platinum-based Chemotherapy

Cisplatin or carboplatin and pemetrexed for up to 6 cycles

Patients received:

- **Pembrolizumab (Keytruda)** at 200 mg every 3 weeks.
- **Platinum-based chemotherapy** (cisplatin or carboplatin) and **pemetrexed** for up to 6 cycles.

Treatment with pembrolizumab continues for up to 24 months or until disease progression or unacceptable toxicity.

Key Efficacy Outcomes – Overall Survival (OS)

The **primary efficacy measure** was **overall survival (OS)**.

Outcome	Pembrolizumab + Chemotherapy	Chemotherapy Alone
Median OS	**17.3 months** (95% CI: 14.4, 21.3)	**16.1 months** (95% CI: 13.1, 18.2)

Hazard Ratio (HR): 0.79 (95% CI: 0.64, 0.98); p=0.0162.

This demonstrates a **21% reduction in the risk of death** for patients treated with pembrolizumab in combination with chemotherapy compared to chemotherapy alone.

Secondary Efficacy Outcomes

Progression-Free Survival (PFS):

- Median PFS was **7.1 months** for both treatment arms:
- **Pembrolizumab + chemotherapy** (95% CI: 6.9, 8.1).
- **Chemotherapy alone** (95% CI: 6.8, 7.7).
- **HR 0.80** (95% CI: 0.65, 0.99); p=0.0194.

Objective Response Rate (ORR):

- **52%** (95% CI: 45.5, 59.0) for pembrolizumab + chemotherapy.
- **29%** (95% CI: 23.0, 35.4) for chemotherapy alone.

Duration of Response (DoR)

6.9

Months

Median DoR for pembrolizumab + chemotherapy arm (95% CI: 5.8, 8.3)

6.8

Months

Median DoR for chemotherapy-alone arm

(95% CI: 5.5, 8.5)

Median DoR was:

- **6.9 months** (95% CI: 5.8, 8.3) in the pembrolizumab + chemotherapy arm.
- **6.8 months** (95% CI: 5.5, 8.5) in the chemotherapy-alone arm.

This shows that the duration of the response was similar between the two treatment groups, but more patients responded in the pembrolizumab arm.

KEYNOTE-483 Trial Overview

1

FDA Approval Basis

The **FDA approval** was based on findings from the **KEYNOTE-483 (NCT02784171)** trial, a **randomized, open-label phase 3 study**.

2

Patient Eligibility

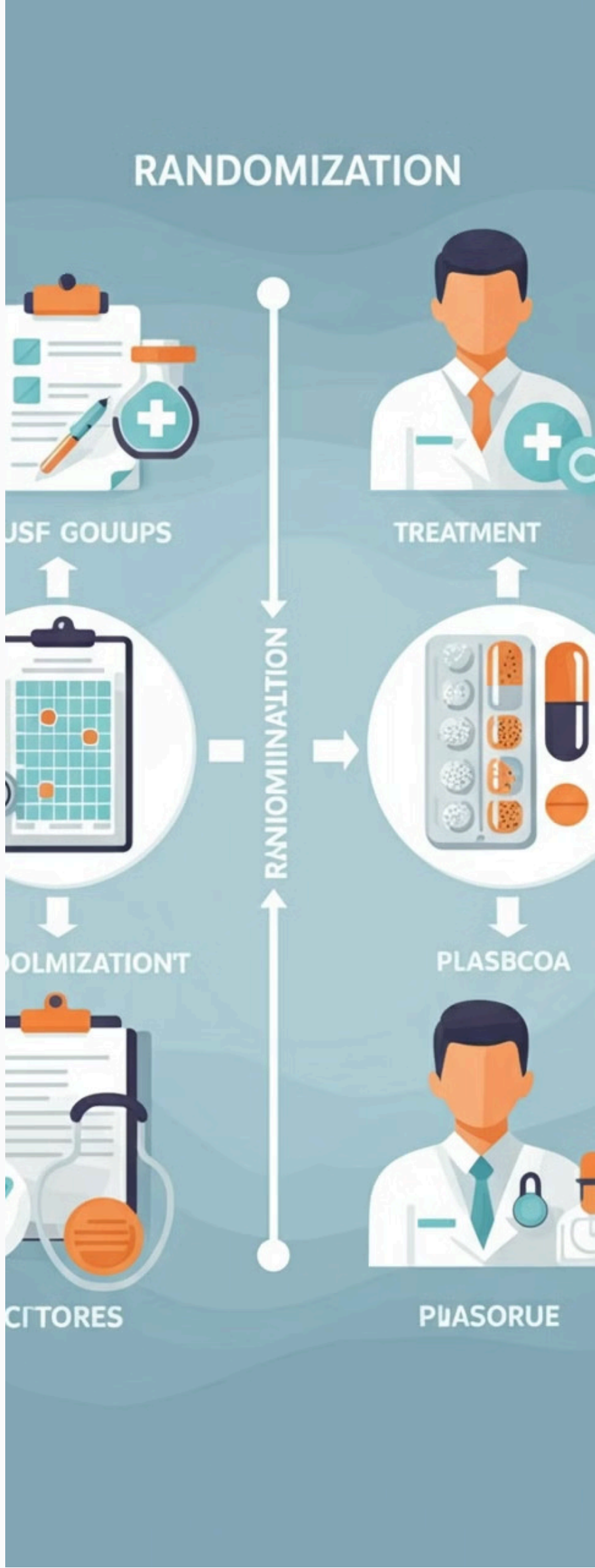
The trial involved patients with **unresectable advanced or metastatic malignant pleural mesothelioma** who had not received prior systemic therapy for advanced/metastatic disease.

3

Randomization

Patients randomized (1:1) to receive:

- **Pembrolizumab** with pemetrexed and platinum-based chemotherapy for up to 6 cycles (n=222).
- **Pemetrexed and platinum-based chemotherapy alone** for up to 6 cycles (n=218).



Safety Profile

Consistent Safety Profile

The safety profile of pembrolizumab with chemotherapy was consistent with its known risks in other cancers.

Common Adverse Reactions

- Fatigue
- Nausea
- Constipation
- Decreased appetite

Serious Side Effects

More serious side effects included immune-mediated conditions like **pneumonitis, colitis, hepatitis, and nephritis**.

Patient Monitoring

Patients must undergo regular monitoring to manage these risks effectively.

Conclusion

Pembrolizumab combined with chemotherapy offers patients with **advanced mesothelioma** a new standard of care.

The **KEYNOTE-483 trial** demonstrated significant improvements in **overall survival** and **objective response rates**, offering hope for improved outcomes.

Continued patient monitoring and further research will be key to understanding the long-term benefits of this therapy.

Impact of FDA Approval

- The **FDA approval** of pembrolizumab with chemotherapy marks an advancement in treating **unresectable, advanced, or metastatic malignant pleural mesothelioma**.
- This is the first new treatment for mesothelioma in over 15 years, offering patients improved survival outcomes and a chance at disease control.

What is Malignant Pleural Mesothelioma?

Malignant pleural mesothelioma (MPM) is a rare and aggressive cancer that develops in the thin tissue lining the lungs.

The primary cause is exposure to **asbestos**.

Unresectable mesothelioma refers to cases where surgical removal of the tumor is not possible due to its location, size, or spread.

About Pembrolizumab

Pembrolizumab (Keytruda) is an immune checkpoint inhibitor that targets **PD-1**, a protein on T cells, enhancing the immune response against cancer cells.

FDA approved pembrolizumab in combination with **platinum-based chemotherapy (cisplatin or carboplatin)** and **pemetrexed** for patients with **unresectable or metastatic malignant pleural mesothelioma**.