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Treatment Patterns, Clinical Outcomes, Healthcare Resource Use and Costs in Older Adults with Malignant Pleural Mesothelioma

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Background

- Malignant pleural mesothelioma (MPM) is a rare and aggressive cancer typically attributed to occupational asbestos exposure and associated with a poor prognosis (five-year survival rate of 9%) in the United States.[1,2]
- Mesotheliomas are classified into epithelioid and non-epithelioid (biphasic and sarcomatoid) histologies, with the former making up over 70% of mesotheliomas and associated with better prognosis than the other subtypes.[7]
- Management of MPM is challenging, with limited treatment options available: usually surgery for resectable disease and radiation and systemic therapy for unresectable disease.[4,5]
- Poor survival outcomes have been associated with historical chemotherapies, with the median overall survival (OS) for the standard treatment for MPM i.e., platinum-pemetrexed, shown to be 12 to 18 months.[4,6]
- Immunotherapy has been approved in first-line treatment (1L) of advanced MPM with nivolumab plus ipilimumab approval in 2020 based on CheckMate-743 followed by approval of pembrolizumab plus platinum and pemetrexed chemotherapy based on KEYNOTE-483 in 2024.
- There is limited real-world evidence on clinical and economic outcomes among patients treated with systemic chemotherapy for advanced MPM. Furthermore, these outcomes are infrequently reported by the main histological subtypes.

Objectives

- To examine treatment patterns and clinical outcomes [real-world time to treatment discontinuation (rwTTD) and real-world OS (rwOS) among patients who initiated 1L for advanced MPM.
- To summarize the disease management health care resource use (HCRU) and costs among these patients.

Methods

Data Source

The National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) registry data (2007-2017) and linked Medicare claims (2007-2019)

Eligibility Criteria

Patients were included in the study if they had been diagnosed with advanced MPM, initiated 1L, with continuous enrollment in Medicare from diagnosis date to ≥3 months after 1L start date (index date) and ≥6 months follow-up period.

Study Outcomes and Measures

- rwTTD was defined as the time from the index date to the date of 1L (including maintenance therapy) discontinuation. Treatment was deemed discontinued at the last administration date if patients died during the therapy or initiated a next line of therapy or had a gap of ≥120 days between the last administration and the last known activity date.
- rwOS is defined as the time from the index date to the date of death.
- MPM-related HCRU and costs were estimated using Medicare claims for medical services associated with a diagnosis of MPM, excluding claims for the administration of MPM treatments. All costs were adjusted to 2023 US dollars.

Statistical Analysis

- Patient characteristics, treatment patterns, and MPM-related HCRU and costs were presented using descriptive statistics.
- Kaplan-Meier method was used to estimate rwTTD and rwOS.

Results

Patient Characteristics

- A total 554 patients met the eligibility criteria. Of the total patients, 78.9% (n=437) had epithelioid and 21.1% (n=117) had non-epithelioid histology.
- Majority of patients were White (95%) and male (74%), with a median age of 74 years (range: 70-78 years).
- About 50% resided in the South, with most patients living in Metropolitan areas (>86.6%).

MPM-Related HCRU and costs

- Most (92.2%) had at least one outpatient visit, 34% had at least one inpatient stay and 59% had at least one emergency department (ED) visit during the follow-up period [Table 1]. In PPPM terms, patients on average had 0.85 outpatient visits, 0.03 inpatient stays and 0.08 ED visits [data not shown]
- The MPM-related cost of all medical services exceeded $100,000 with higher costs for those with non-epithelioid histology compared to those with epithelioid [Table 1]. The PPPM medical service cost was $5,639 for patients with at least 1 visit [data not shown]

Table 1. Treatment Patterns, HCRU and Costs by Histology

	Overall (n=554)		Epithelioid (n=437)		Non-epithelioid (n=117)	
1L Therapy	**N**	**%**	**n**	**%**	**n**	**%**
Platinum-pemetrexed	419	75.6	330	75.5	89	76.1
Pemetrexed	47	8.5	**	**	**	**
Bevacizumab-Platinum-Pemetrexed	45	8.1	**	**	**	**
2L Therapy	**300**		**236**		**64**	
Platinum-pemetrexed	75	25	63	26.7	12	18.8
Pembrolizumab	58	19.3	43	18.2	15	23.4
Gemcitabine	52	17.3	**	**	**	**
3L Therapy	**120**		**97**		**23**	
Gemcitabine	30	25	63	26.7	12	18.8
Vinorelbine	20	16.7	**	**	**	**
Pembrolizumab	16	13.3	**	**	**	**
MPM-related HCRU	**n**	**%**	**n**	**%**	**n**	**%**
≥1 outpatient visit	511	92.2	404	92.4	107	30.8
≥1 inpatient stay	190	34.3	154	35.2	36	30.8
≥1 ED visit	328	59.2	250	57.2	78	66.7
≥1 medical service	546	98.6	431	98.6	115	98.3
MPM-related Costs	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
Inpatient stays, $	16,608.78	50,687.43	16,850.44	43,930.26	15,703.08	70,726.79
Outpatient visit, $	68,163.43	159,148.26	61,712.21	136,794.52	92,341.50	223,061.02
All medical services, $	102,657.52	173,495.05	95,980.49	151,026.62	127,681.84	238,887.66

**=not reported to ensure patient privacy according to the data use agreement for SEER-Medicare data

Treatment Patterns

- Of all 554 1L patients, 54.2% initiated second-line therapy (2L), and 21.7% initiated third-line therapy (3L) [Table 1].
- Platinum-pemetrexed (75.6%) was the most common 1L regimen followed by pemetrexed (8.5%) and bevacizumab-platinum-pemetrexed (8.1%) [Table 1].
- Platinum-pemetrexed (25.0%) was the most common 2L regimen followed by pembrolizumab (19.3%) and gemcitabine (17.3%) [Table 1].

Real-World Time to Treatment Discontinuation and Overall Survival

- Median rwTTD was 5.3 mo (95% CI 4.2-6.3), 5.3 mo (95% CI 4.2-6.7) and 4.8 mo (95% CI 3.7-7.9) in the overall population, epithelioid and non-epithelioid subgroups, respectively [Figure 1].
- Median OS in the overall population was 16.3 mo (95% CI 15.4-17.8) and 5-year OS rate was 8% (95% CI 5.5-10.9%). In the epithelioid and non-epithelioid subgroups median OS was 17.8 mo (95% CI 16.3-19.2) and 13.5 mo (95% CI 11.1-14.9) with corresponding 5-year OS rate of 8.9% (95% CI 6.0-12.4%) and 4.4% (95% CI 1.3-10.5%), respectively [Figure 2].
- In a sensitivity analysis that did not require continuous Medicare enrollment and min. follow up period median OS in the overall population was 10.8 mo (95% CI, 9.5-12.5) with 5-year OS rate of 5.4% (95% CI, 3.4-8.1%). In the epithelioid and non-epithelioid subgroups median OS was13.6 mo (95% CI, 12.1-15.5) and 5.7 mo (95% CI, 4.5-6.5), respectively [data not shown]

Figure 1. Kaplan-Meier Curve for rwTTD by Histological Subtype

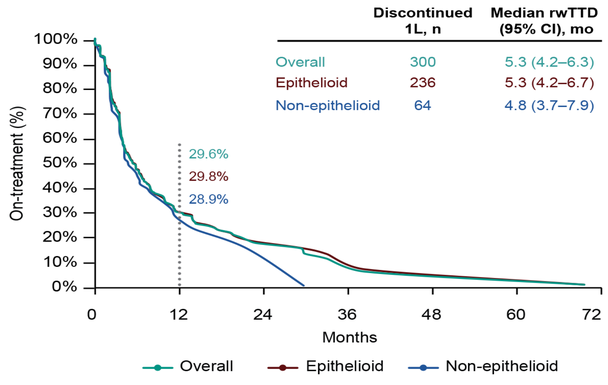
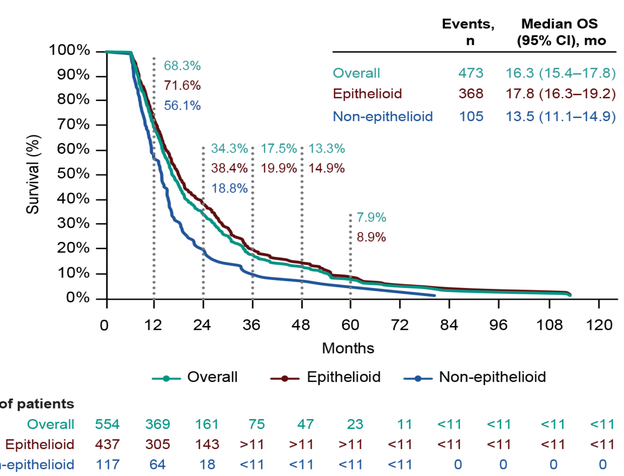


Figure 2. Kaplan-Meier Curve for rwOS by Histological Subtype



Limitations

- These results may not reflect the most current treatment patterns because of the time lag in data refreshes. The latest data is through 31 Dec. 2019 which is before the approval of immunotherapy in 2020.
- Given that the Medicare population is ≥65 years, the study results may not reflect outcomes in younger patients.
- Treatment switching used to derive lines of therapy could be due to toxicities rather than disease progression, which could not be assessed in this study.
- The requirements of continuous Medicare enrollment and min. follow-up after 1L may have introduced immortal time bias, resulting in longer survival estimates in the main analyses. In a sensitivity analysis without these requirements, survival estimates were lower than those for the main analyses

Conclusion

- This study demonstrated a substantial unmet need for patients treated with 1L systemic chemotherapy for MPM. A little over half (54%) of patients continued to 2L and only 22% initiated 3L. The 5-year survival rate was only 8%, highlighting the need for a more effective therapy.
- MPM was associated with significant healthcare resource and economic burden, particularly in patients with non-epithelioid histology.
- These findings underscore the importance to treat patients with MPM with more effective therapies such as immune checkpoint inhibitors which have become the new standard of care in 1L.

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Disclosures

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