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Real-World Treatment Patterns in High-Risk and Metastatic Melanoma: Evidence From the SEER-Medicare Linked Database

Debanjali Mitra,[1] Keith L. Davis,[1] Srividya Kotapati,[2] Uchenna Iloeje[2]

[1]RTI Health Solutions, 200 Park Offices Drive, Research Triangle Park, NC 27709. [2]Bristol-Myers Squibb, 5 Research Parkway, Wallingford, CT 06492, US

Background

Melanoma is the sixth most common cancer in the United States (US) and causes 1% to 2% of all cancer deaths.[1,2] Although the overall survival rate for melanoma has improved over time, advanced/metastatic melanoma remains largely a fatal disease with a median survival time of 3 to 11 months. Currently available treatments have not been able to extend the survival time among patients with advanced disease. Despite a lack of suitable therapeutic options in advanced-stage melanoma, no study has fully explored administrative data from real-world clinical settings to characterize the persistent unmet treatment need in this population. We therefore examined retrospective claims data from the Medicare system to document real-world treatment patterns in elderly patients diagnosed with high-risk or metastatic melanoma. Knowledge about treatment patterns may prove informative in the provision of optimal care and reduction of treatment gaps in malignant melanoma.

Objective

To document real-world treatment patterns of four major therapies (surgery, radiation, chemotherapy, immunotherapy) in elderly patients with high-risk (stage IIB/C, IIIA/B, IIIC) or metastatic (stage IV) melanoma.

Methods

Study design

Retrospective longitudinal analysis of the Survey, Epidemiology, and End Results (SEER)-Medicare linked database.

Database description

- SEER registry contains detailed clinical information on 98% of all new cancer cases in persons residing in SEER areas.
- Clinical information on incident cancer cases in the US between 1991 and 2002 from the SEER registry linked with longitudinal Medicare claims from 1991 to 2005 were used for this analysis.
- The registry data include (among other variables) the following
  - Patient demographics
  - Dates of diagnosis
  - Clinical data (e.g. histology, morphology, tumor stage)
  - Date first course of therapy began
  - Date and cause of death
  - Nationally representative, comprising 24% of US population
  - Captures 95% of all services and billings under Medicare Parts A and B
  - No data on prescription drugs.

Inclusion criteria

- Patients aged 65 or older.
- ≥1 diagnosis of malignant melanoma (ICD-O-2 C44.x) at stage IIB or higher.
- Index date defined as date of first stage IIB or higher diagnosis.
- Staging captured directly from SEER registry data.
- ≥6 months of continuous Medicare Part A and B benefits coverage following index date.
- Patients who died within 6 months post-index date were retained for analysis.

Disease stage

- Disease stage was assigned based on clinical criteria set forth by the American Joint Committee on Cancer (AJCC) TNM staging system for melanoma.[3]
- AJCC stage for each diagnosis was determined using an algorithm comprising the raw SEER variables HSTST (historic stage: in situ, localized, regional, or distant), E10PN (number of positive lymph nodes), E10SZ (tumor size in mm), and E10EX (extent of disease: with or without ulceration).
- High-risk (IIB/C, IIIA/B, IIIC) and metastatic (IV) stages were then identified as follows
  - Stage IV: HSTST = 'Distant'
  - Stage IIIC: HSTST = 'Regional' and E10PN ≥4
  - Stage IIIA/B: HSTST = 'Regional' and E10PN <4
  - Stage IIB/C: HSTST = 'Localized' and E10SZ >2 mm and E10EX = 'With Ulceration'.
- Index date was defined as the date of the first observed stage IIB or higher diagnosis.
- Patients were categorized into mutually exclusive categories based on the stage (IIB or higher) observed at the index date.

Treatment definitions

- Melanoma treatments were defined based on evidence of relevant Health Care Financing Administration Common Procedure Coding System (HCPCS), ICD-9-CM procedure codes, ICD-9-CM diagnostic codes, and administrative revenue codes
  - Surgical procedures: excision of skin lesions/tumors and removal of lymph nodes
  - Radiation
  - Chemotherapies: dacarbazine, vincristine, paclitaxel, cisplatin, carboplatin, vinblastine, carmustine, temozolomide, and bleomycin
  - Immunotherapies: interleukin-2 and interferon.
- Treatments received within 8 weeks for stage IIB/C and IV patients, and 6 weeks for stage IIIA/B and IIIC patients following the index date considered to be first-line therapies (based on consultation with a clinical oncologist specializing in melanoma).
- Second-line treatments identified as those received at any point beyond the first-line period.

Outcomes

- Baseline characteristics of patients diagnosed with stage IIB/C, IIIA/B, IIIC, or IV melanoma.
- Number and percentage of patients receiving surgery, radiation, chemotherapy, immunotherapy, and combinations of the four, at any point post-index date.
- Number and percentage of patients who received each treatment or combination of treatments as first- versus second-line therapy.

Results

Patient characteristics (Table 1)

- A total of 6,470 patients were identified for study inclusion.
- Disproportionately male (60%), almost exclusively white (>95%), and mostly married (>50%).
- Stage distribution
  - IIB/C: 38%; IIIA/B: 46%; IIIC: 1%; IV: 15%.
- Median follow-up time (by stage) defined as number of months between index date and earliest date of death, end of or interruption in benefits coverage, or end of study period (12/31/2005)
  - IIB/C: 56 months; IIIA/B: 39 months; IIIC: 16 months; IV: 6 months.

Table 1. Characteristics of the study sample.

	All patients		Melanoma stage at index date							
			IIB/C		IIIA/B		IIIC		IV	
	n	%	n	%	n	%	n	%	n	%
Total sample	6,470	100	2,431	37.57	2,971	45.92	88	1.36	980	15.15
Gender										
Male	3,940	60.9	1,495	61.5	1,765	59.41	61	69.32	619	63.16
Female	2,530	39.1	936	38.5	1,206	40.59	27	30.68	361	36.84
Age at index date										
65–69	1,285	19.86	534	21.97	537	18.07	25	28.41	189	19.29
70–74	1,480	22.87	594	24.43	621	20.9	25	28.41	240	24.49
75–79	1,437	22.21	528	21.72	679	22.85	20	22.73	210	21.43
80–84	1,200	18.55	429	17.65	570	19.19	12	13.64	189	19.29
≥85	1,068	16.51	346	14.23	564	18.98	6	6.82	152	15.51
Marital status										
Single	445	6.88	133	5.47	227	7.64	11	12.5	74	7.55
Married	3,388	52.36	1,191	48.99	1,580	53.18	59	67.05	558	56.94
Separated	20	0.31	7	0.29	10	0.34	–	–	3	0.31
Divorced	251	3.88	77	3.17	127	4.27	5	5.68	42	4.29
Widowed	1,454	22.47	479	19.7	721	24.27	11	12.5	243	24.8
Unknown	912	14.1	544	22.38	306	10.3	2	2.27	60	6.12
Race/ethnicity										
White	6,278	97.03	2,388	98.23	2,874	96.74	81	92.05	935	95.41
Black	57	0.88	12	0.49	29	0.98	2	2.27	14	1.43
Asian	26	0.4	8	0.33	13	0.44	1	1.14	4	0.41
Hispanic	46	0.71	11	0.45	23	0.77	2	2.27	10	1.02
Native American	4	0.06	–	–	4	0.13	–	–	–	–
Other	37	0.57	8	0.33	17	0.57	2	2.27	10	1.02
Unknown	22	0.34	4	0.16	11	0.37	–	–	7	0.71
Follow-up duration (months)										
Mean (SD)	47.82 (39.94)		64.50 (41.76)		45.42 (35.42)		28.83 (31.92)		15.37 (22.80)	
Median	40		56		39		16		6	
Range (min, max)	0, 177		0, 175		0, 177		3, 163		0, 171	
Charlson score										
Mean (SD)	1.72 (2.33)		1.67 (2.22)		1.64 (2.21)		1.58 (2.07)		2.09 (2.89)	
Median	1		1		1		1		1	
Range (min, max)	0, 16		0, 16		0, 15		0, 11		0,16	

Max = maximum; min = minimum; SD = standard deviation

Treatment options

Overall prevalence (Figure 1)

- Surgery was highly prevalent, but somewhat less common in stage IV patients. Skin lesion/tumor excision was most common surgical procedure across all stages.
- Chemotherapy was prevalent in 45% and 27% of stage IIIC and IV patients, respectively.
- Dacarbazine, the most commonly used chemotherapy, was prevalent in <5% of stage IIB/C and IIIA/B patients, 17% of stage IIIC patients, and 10% of stage IV patients.
- Low prevalence of interferon in stage IIB/C, IIIA/B, and IV patients (2%, 9%, and 8%, respectively) but highly prevalent (31%) in stage IIIC patients.

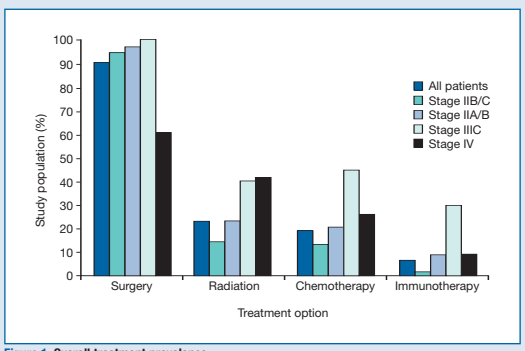

Figure 1. Overall treatment prevalence.

First-line treatment option (Figure 2)

- Surgery (primarily tumor excision) was the predominant first-line treatment, received by >85% of subjects with stage IIB/C, IIIA/B, or IIIC melanoma and 60% of stage IV cases.
- Radiation was rarely used as a first-line option, except in stage IV patients. When used as a first-line option, typically seen in combination with surgery.
- Radiation plus surgery seen as first-line option most frequently in stage IIIC and IV patients (13% and 14%, respectively).
- Chemotherapy was rare as an overall first-line option (<3% of patients) in stages IIB/C, IIIA/B, and IIIC, but somewhat more common in stage IV (12% of patients).
- 20% of stage IV patients received no active treatment (i.e. no surgery, radiation, chemotherapy, or immunotherapy) as first course of action.

Conclusions

- Results suggest that beyond surgery as a first-line approach, relatively few patients received other types of treatment as either first- or second-line therapy.
- Findings demonstrate the need for more efficacious treatment alternatives for high-risk and metastatic melanoma.
- Additional analyses of administrative data characterizing real-world treatment patterns in melanoma are needed to help inform the direction of future clinical trials.

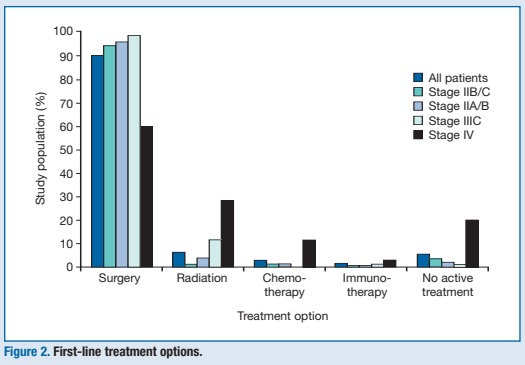

Figure 2. First-line treatment options.

Second-line treatment option (Figure 3)

- Except for stage IIIC patients, no active treatment was the most common second-line course of action.
- Surgery was generally the least prevalent second-line treatment, particularly among stage IV patients.
- Radiation was quite prevalent (~30% of cases) as a second-line treatment, especially for stage IIIC patients. When used as a second-line option, it was most commonly used alone (perhaps as palliative care).
- Chemotherapy was moderately prevalent as a second-line therapy (by respective stage, 14%, 20%, 41%, and 22% of cases). It was typically used in combination with other approaches (surgery, radiation, or immunotherapy), particularly in stage IIIC and IV patients.
- Immunotherapy was rare, except as a second-line treatment in stage IIIC (26% of cases). When used, almost always seen in combination with chemotherapy.

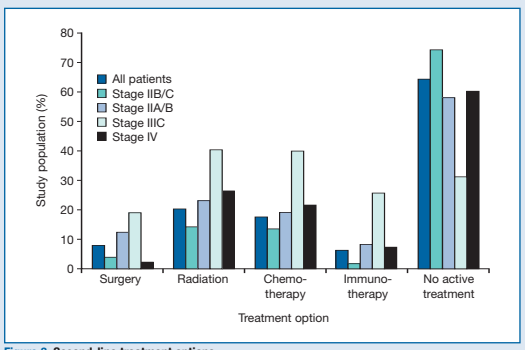

Figure 3. Second-line treatment options.

Limitations

- Because of the lack of a Part D benefit in Medicare prior to 2006, data on orally administered prescription drugs obtained at outpatient retail pharmacies are not captured in Medicare claims data currently available for research.
- Our analysis of specific systemic agents used in high-risk and metastatic melanoma is limited by the varying detail with which systemic therapies are coded for purposes of Medicare reimbursement.
- Our analysis to document receipt of treatments as first- versus second-line therapeutic approaches relies on claims-based algorithms, including calculations based on timing of treatments, which may not reflect the true intent of the attending physician.
- Our algorithms rely primarily on administrative claims submitted solely for purposes of Medicare reimbursement (and not for purposes of research) with no access to information collected from either the attending physician or the patient. The impact of misclassification bias stemming from analyses of claims data has been described in previous research.[4,5]
- This study included only patients aged 65 years or older. Findings presented here may therefore not be representative of the general population with high-risk or metastatic melanoma.

Acknowledgment

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