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

Background
Melanoma is the sixth most common cancer in the United States (US) and causes 1% to 2% of all cancer deaths. 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 11 to 18 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 untreated need in this population. Therefore, we examined retrospective claims data from the Medicare system to document real-world treatment patterns in elderly patients diagnosed with high-risk or metastatic melanomas.

Objective
To document real-world treatment patterns of four major therapies (surgery, radiation, chemotherapy, immunotherapy) in elderly patients with high-risk stage (IBC, IIA/B, IIC) 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 90% of all new cancer cases in persons residing in SEER areas.
• Clinical data on the incidence of cancer cases in the US between 1973 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 and death
  • 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
• ≥1 diagnosis of malignant melanoma (ICD-0-2 C44.4) at stage II/IIIA/IIIB/IIIC/IV or higher.
• Index date defined as date of first-stage II/IIIA/IIIB diagnosis.
• Staging captured directly from SEER registry data.
• ≥6 months of continuous Medicare Parts 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.
• AJCC stage for each diagnosis was determined using an algorithm comprising the raw SEER variables (HIST2: historic stage in situ, local, regional, or distant; DLMF: depth of the primary lesion; and NOA: number of positive lymph nodes), 8525 tumor (size in mm), and 8510 presence of disease with or without ulceration.
• High-risk (IBC, IIA/B, IIC) and metastatic (IV) stages were then identified as follows:
  • Stage IVA: HIST2 = ‘Distant’
  • Stage IVC: HIST2 = ‘Regional’ and 8510 = ‘d’
  • Stage IIB/1C: HIST2 = ‘Loculated’ and 8510 = ‘e’ and 8525 ≤ 2 mm and 8510 = ‘d’ (with ulceration)
• Index date was defined as the date of the first observed stage IIIB or higher diagnosis.
• Patients were categorized into mutually exclusive categories based on the stage (IIIB or higher) observed at the index date.

Treatment definitions
• Melanoma treatments were defined based on evidence of Health Care Financing Administration – Common Procedure Coding System (HCPCS), EOE-DMC procedure codes, ICD-9-CM diagnostic codes, and administrative claims review.
• Surgical procedures: excision of skin lesions/tumors and removal of lymph nodes
• Radiation
  • Chemoradiation: dacarbazine, cisplatin, paclitaxel, carboplatin, carboplatin, vinblastine, carmustine, temozolomide, and bleomycin
  • Immunotherapies: interleukin-2, and interferon
• Treatments received within 8 weeks for stage IBC, IIA/B, and IV patients, and 6 weeks for stage IIA/B and IIC patients following the index date considered for the first-line therapy (Eisen 2007). No conclusions were drawn from a clinical oncologist specializing in melanoma.
• Second-line treatments identified as those received at any point beyond the first-line treatment.

Outcomes
• Baseline characteristics of patients diagnosed with stage IBC, IIA/B, and IV melanoma.
• Number and percentage of patients receiving surgery, radiation, chemotherapy, immunotherapy, and combinations of these, 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 (63%), although exclusively white (95%), and mostly married (75%).
• Stage distribution:
  • IIA/B: 36%, IIB/C: 45%, IIIA/B: 1%, IV: 15%
  • Median follow-up time (by stage) defined as number of months between index date and earliest date of death, or of interruption in benefits coverage, or end of study period 12/31/2005:
    • IBC: 56 months; IIA/B: 30 months; IIC: 16 months; IV: 5 months.

Disease stage
• 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 IBC and IIC patients, respectively.
• Dacarbazine, the most commonly used chemotherapy, was prevalent in ≥5% of stage IBC and IIB/C patients, 17% of stage IIC patients, and 10% of stage IV patients.
• Low prevalence of interferon in stage IIB/C, IIA/B, and IV patients (2%, 8%, and 9%, respectively) but highly prevalent (31%) in stage IIC patients.

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 IBC and IIC patients, respectively.
• Dacarbazine, the most commonly used chemotherapy, was prevalent in ≥5% of stage IBC and IIB/C patients, 17% of stage IIC patients, and 10% of stage IV patients.
• Low prevalence of interferon in stage IIB/C, IIA/B, and IV patients (2%, 8%, and 9%, respectively) but highly prevalent (31%) in stage IIC patients.

First-line treatment option (Figure 2)
• Surgery (primarily tumor excision) was the predominant first-line treatment, received by >85% of subjects with stage IBC, IIA/B, and IIC melanomas and 65% of stage IV cases.
• Atezolizumab was used as an upfront first-line treatment option (15% of patients) in stage IBC, IIA/B, and IV, but somewhat more common in stage IV (21% of patients).
• 25% 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 treatments 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.

Limitations
• Because of the lack of a Part D benefit in Medicare prior to 2006, data on only administrably prescribed 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 algorithmically driven analyses 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.
• This study included only patients aged 65 years or older. Findings presented herein may therefore not be representative of the general population with high-risk or metastatic melanomas.

Acknowledgment
This study was funded by Bristol-Myers Squibb. Bristol-Myers Squibb provided medical writing assistance from Gameutter, Elam, and Ryan.

References

PCN867 Lmita Poster 25/4/08 16:15 Page 1
Debanjali Mitra, Keith L. Davis, Srividiya Kotapati, Uchenna Iloeje
101 Health Square, 330 Park Office Drive, Research Triangle Park, NC 27709; Tel: 919-506-5345; E-mail: Debanjali.Mitra@bms.com; Uchenna.Iloeje@bms.com
Presented at the International Society for Pharmacoeconomics and Outcomes Research 13th Annual International Meeting, May 2008, Toronto, Canada