Treatment Patterns in Metastatic Melanoma after Introduction of New Drug Therapies

Kennedy K[1], Murty S[2], Dye J[2], Whisman T[1] *, Worley K[2]

1. Humana Pharmacy Solutions, Humana Inc.; 2. Comprehensive Health Insights, Humana Inc., Louisville, KY; *at the time the study was conducted

Background

Since March of 2011, four novel oncolytic agents have been approved for metastatic melanoma, three of which target specific genetic mutations in melanoma cells and require companion diagnostic testing for specific genetic variants before use. All 4 products are FDA-approved for use alone and 2 (dabrafenib, trametinib) are approved for use alone or in combination with each other. Characterizing the treatment patterns that have emerged since approval of these novel agents can provide insight into better strategies for optimizing patient care in non-resectable metastatic melanoma.

Objective

To characterize initial, concurrent and/or subsequent cancer therapy for patients receiving ipilimumab (IPI), vemurafenib (VEM), dabrafenib (DAB), or trametinib (TRAM) for non-resectable metastatic malignant melanoma (MMM).

Methods

Study Design: Observational, retrospective claims analysis
Data Source: Pharmacy, medical and laboratory claims, and enrollment data, from the Humana Research Database, which is derived from approximately 7.36 million members nationwide across commercial, Medicare Advantage and prescription drug plans.
Study Period: July 1, 2010 to June 30, 2014
- Identification period was January 1, 2011 to December 31, 2013

Inclusion Criteria:
- Age 19-89 years on the index date (defined as the first metastatic diagnosis during the identification period)
- ≥2 diagnoses of malignant melanoma within 30 days with 1 occurring in the pre-index period; evidence of metastatic disease; and ≥1 prescription for IPI, VEM, DAB, or TRAM during the identification period
- Fully-insured commercial or Medicare Advantage Prescription Drug plan enrollees
- Continuous 6-month pre- and post-index eligibility; however, due to the expected high mortality rate in this population, people who died in within 6 months of index diagnosis were still included in the descriptive analysis

Measures and Statistical Analyses:
- Initial therapy was defined as the first documented cancer therapy within 90 days of the index diagnosis.
- Concurrent therapy was begun after the start and before the end of initial therapy regimen
- Subsequent therapy was provided after completion of initial therapy.
- Patients were followed until death, disenrollment or June 30, 2014, whichever came first, to track initial, concurrent and subsequent cancer therapies.
- Initiation and duration based on claims data for all cancer treatments were recorded for each patient and results were reported using descriptive statistics.

Table 1. Sample Attrition

Selection Criteria	N (%)
Diagnosis of metastasis in identification period	91,292 (100)
≥1melanoma diagnosis in pre-index period	2,461 (2.70)
2 melanoma diagnoses in 30 days, with ≥1 in pre-index	1,838 (2.01)
≥1 prescription for ipilimumab, vemurafenib, dabrafenib, or trametinib after the metastatic melanoma diagnosis	264 (0.29)
Fully-insured commercial/Medicare	243 (0.27)
Age 19 to 89 years on index date	242 (0.27)
No metastasis in pre-index period	226 (0.25)
Continuous eligibility	196 (0.21)
Final Cohort	**196 (0.21)**

Results

Table 2. Timing of Metastatic Malignant Melanoma Therapy

Days from Diagnosis to Initial Therapy	N (%)	Days from Initial to Concurrent Therapy	N (%)	Days from Initial to Subsequent Therapy	N (%)
0-30	90 (45.9)	0-30	20 (43.5)	0-30	14 (18.9)
31-60	35 (17.9)	31-60	8 (17.4)	31-60	16 (21.6)
61-90	15 (7.6)	61-90	4 (8.7)	61-90	8 (10.8)
>90	56 (28.6)	91-180	16 (34.8)	91-180	22 (29.7)
---	---	>180	13 (28.3)	>180	51 (68.9)
Total	**196**	**Total**	**46**	**Total**	**74**

While 46% of initial treatment started within 30 days of diagnosis, 69% of subsequent treatment was administered >6 months after initial therapy.

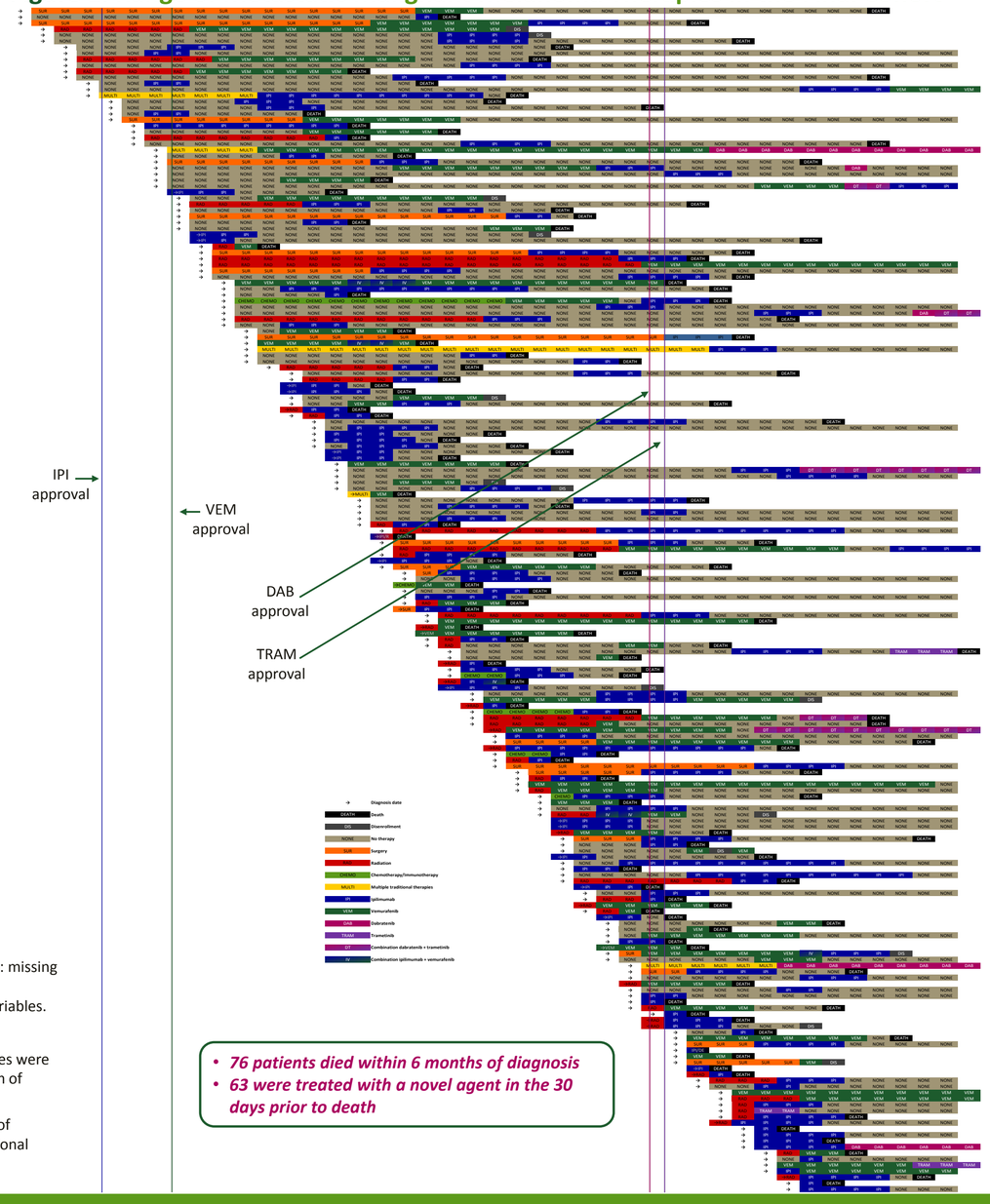
Table 3. Distribution of Metastatic Malignant Melanoma Therapy

Initial Therapeutic Category (n=196)	N (%)	Days of Therapy, Mean (SD)	Concurrent Therapeutic Category[a] (n=135)	N (%)	Days of Therapy, Mean (SD)	Subsequent Therapeutic Category[a] (n=135)	N (%)	Days of Therapy, Mean (SD)
Ipilimumab	40 (20.4)	42.1 (45.9)	Ipilimumab	15 (11.1)	67.9 (91.8)	Ipilimumab	41 (30.4)	46.0 (25.9)
Vemurafenib	17 (8.7)	223.6 (167.1)	Vemurafenib	12 (8.9)	194.9 (116.3)	Vemurafenib	19 (14.1)	174.4 (141.5)
Dabrafenib	n <10[b]	---	Dabrafenib	n <10[b]	---	Dabrafenib	n <10[b]	---
Trametinib	n <10[b]	---	Trametinib	n <10[b]	---	Trametinib	n <10[b]	---
Other immunotherapy/ chemotherapy[c]	n <10[b]	---	Other immunotherapy/ chemotherapy[b]	n <10[b]	---	Other immunotherapy/ chemotherapy[b]	25 (1.8)	---
Radiation	52 (26.5)	116.8 (159.7)	Radiation	19 (14.1)	84.6 (135.2)	Radiation	19 (14.1)	104.7 (117.6)
Surgery	21 (10.7)	78.9 (137.9)	Surgery	n <10[b]	2 (2.6)	Surgery	n <10[b]	1 (0.0)
Multiple therapies[d]	n <10[b]	---	≥1 concurrent therapy	46 (34.1)	---	≥1 subsequent therapy	74 (54.8)	---
No initial therapy[e]	56 (28.6)	---	No concurrent therapy	89 (65.9)	---	No subsequent therapy	61 (45.2)	---

Only 37.5% of patients initiated on ipilimumab were administered the full recommended duration (4 doses) and 30% received only 1 dose. Dabrafenib and trametinib were rarely used in this cohort.

[a]Patients could be included in more than one therapeutic category
[b]Data not shown for n<10 patients
[c]Interferon alfa 2b, Peginterferon alfa 2b, Interleukin - 2, BCG, Imiquimod, Imatinib, Carboplatin, Cisplatin, Dacarbazine, Nab-Paclitaxel, Paclitaxel, Temozolomide, Vinblastine, Melphalan.
[d]More than one therapy provided at treatment initiation
[e]No initial treatment provided in the first 90 days after diagnosis

Figure 1. Range of Metastatic Malignant Melanoma Therapies in the Final Cohort



- ***76 patients died within 6 months of diagnosis***
- ***63 were treated with a novel agent in the 30 days prior to death***

Conclusions

- Targeted novel agents, especially for VEM, DAB and TRAM, were used less frequently as first-line metastatic melanoma therapy, potentially due to indications limited to patients with BRAF mutations.
- New therapies were more likely to be prescribed in conjunction with other modalities of cancer care.
- Understanding how new therapies can be incorporated into current treatment regimens and implications for health outcomes are important areas for future research.

Limitations

- The very small sample size limits our ability to draw conclusions.
- This study is subject to limitations inherent to administrative claims data: missing data, coding errors, data not measured in claims (e.g., health behavior information), and the potential influence of unidentified confounding variables.
- A medication claim does not equate to taking the medication.
- Although two claims with metastatic codes and two with melanoma codes were required for inclusion, it is still possible that individuals had another form of cancer.
- The 6-month follow-up period was insufficient to observe the full range of measures or final dispositions and longer follow-up would provide additional insight.

Humana

National Comprehensive Cancer Network
21st Annual Conference | Hollywood, FL
Mar 31 - Apr 2, 2016