Healthcare Costs Associated with Locoregional and Distant Recurrence in Patients with Non-metastatic Melanoma

Ahmad Tarhini,[1] Sameer R. Ghate,[2] Raluca Ionescu-Ittu,[3] Briana Ndife[2], Ameur M. Manceur,[3] Philippe Jacques,[3] François Laliberté,[3] Antonio Nakasato,[2] Mei Sheng Duh[4]

[1]Cleveland Clinic, Taussig Cancer Center, Cleveland, OH, US; [2]Novartis Pharmaceuticals Corporation, East Hanover, NJ, US; [3]Groupe d'analyse, Ltée, Montréal, QC, Canada; [4]Analysis Group Inc, Boston, MA, US

Background

- Most patients with non-metastatic melanoma are managed with surgical excision and/or lymph node surgery (dissection or lymphadenectomy), but up to half of patients surgically treated for melanoma will have a recurrence in their lifetime[1,2], particularly among those with higher stages of non-metastatic melanoma.
- Published economic studies generally focus on patients with metastatic/advanced melanoma or patients with distant recurrence[3-8].
- There are few, if any, pharmacoeconomic studies focusing on non-metastatic melanoma, or on patients with locoregional recurrences (including lymph node metastasis).
- Real-world information on the costs of both locoregional and distant recurrences in patients with non-metastatic melanoma would be useful to payers, especially since the treatment landscape is currently changing with the advent of new adjuvant therapies[9,10].

Objective

- To quantify healthcare costs associated with locoregional and distant recurrence in patients with non-metastatic melanoma who underwent lymph node surgery (or, for a minority of cases, surgical excision with a diagnosis of secondary malignancy in the lymph nodes surgical).

Methods

Data Source

- The study used the Truven Health Analytics MarketScan® Commercial Claims and Encounters, and Medicare Supplemental databases (Truven) from January 1, 2008 to July 31, 2017
- Truven has data on more than 240 million unique patients since 1995 from approximately 100 employers and several health plans, and includes enrollment history, demographic variables, and claims for medical (provider and institutional) and pharmacy services
- Data are de-identified and comply with the confidentiality requirements of the Health Insurance Portability and Accountability Act

Sample Selection

- From January 2008 to July 2017, there were 265,421 patients with a melanoma diagnosis in the Truven database, of which 68,032 adult patients did not have an indicator of other primary cancer, and had >15 months of continuous healthcare coverage.
- Patients with a melanoma-related surgery (lymph node surgery; for a minority of cases, with a diagnosis of secondary malignancy in the lymph nodes surgical excision was also allowed) were selected, and patients with indicators of metastatic melanoma excluded.
- The study sample included 6,400 patients with non-metastatic melanoma who underwent surgery.

Study Design

- The study used a retrospective claims design. The study period spanned from the index surgery until the earliest date between end of eligibility (due to disenrollment or death), or end of data availability (Jul 31, 2017).
- Locoregional and distant recurrence episodes
  - Recurrences were identified based on post-surgery recurrence indicators derived from patterns of melanoma therapy (i.e., initiation of new pharmacotherapy, radiotherapy, or new skin excision/lymph node surgery) and secondary malignancy diagnoses.
  - Distant recurrences were distinguished from locoregional recurrences based on indicators that were specific to metastatic disease (e.g., antineoplastic agents and regimens not listed as adjuvant therapies in the NCCN melanoma guidelines, including systemic therapies and ipilimumab before 2015)
  - Recurrence episodes were defined from 30 days prior to first indicator of a locoregional/distant recurrence to 30 days after last indicator for recurrence (locoregional recurrences) or end of follow-up (distant recurrences).
- Healthcare costs were (a) reported during episodes of locoregional/distant recurrence and (b) compared in the year post-recurrence between
  - patients with locoregional/distant recurrence(s) and
  - recurrence-free matched controls (1:1 matching on propensity scores percentiles,[11] insurance coverage with Medicare supplemental, and time between index lymph node surgery and beginning of first recurrence; among patients with at least 3 months of insurance coverage after the beginning of the first recurrence, a matched control was found for 950/977 patients with locoregional recurrence and 87/90 patients with distant recurrence)
- Patient baseline characteristics were measured in the six months before the index surgery and included demographics, melanoma tumor site, baseline costs, the Quan-Charlson comorbidity index[12] (excluding cancer diagnosis) and a cancer-specific index[13] (excluding melanoma diagnosis).

Outcomes

- Healthcare cost outcomes, reported per patient per month (PPPM), were inflated to 2017 US dollars (USD; commercial payer perspective), and included:
  - All-cause healthcare costs, by component: inpatient admission (IP), emergency department admission (ED), outpatient visits including medication administration (OP), other (e.g., durable medical equipment), and pharmacy prescription costs.
  - Melanoma-specific costs in real world, defined as costs associated with medical services for melanoma, including treatments (pharmacological: antineoplastic whether in NCCN guidelines or not, and other including injection of steroid, pain control medication, anesthesia [for surgery]; surgery; radiotherapy) and disease monitoring.
- For the description of all-cause and melanoma-specific healthcare costs during episodes of recurrence, all episodes were included (1,524 locoregional and 102 distant recurrence episodes) and a patient could contribute more than one locoregional recurrence episode. Costs were measured between the start and end date of the episodes of recurrence
- For the comparison of all-cause healthcare cost between recurrence and recurrence-free cohorts, only the first recurrence episode was included for the recurrence cohorts. Costs were measured in the year after the first recurrence for the patients in the recurrence cohorts and in the year following a randomly selected index date for the recurrence-free cohorts

Statistical Analyses

- Descriptive analyses relied on frequencies and proportions for categorical variables and means (standard deviations) for continuous variables.
- For the comparison of the matched recurrence and recurrence-free cohorts non-parametric bootstrap procedure methods (B=549 resamples) were used to obtain the 95% confidence interval (CI) of the difference in all-cause healthcare costs between cohorts, and the p-value.

Results

Table 1. Baseline Characteristics: Study Sample and Matched Recurrence and Recurrence-free Cohorts

	Study sample	Matched cohorts: locoregional recurrence		Matched cohorts: distant recurrence	
Variable	**N = 6,400**	**Recurrence N=950**	**Recurrence-free N=950**	**Recurrence N=87**	**Recurrence-free N=87**
BASELINE CHARACTERISTICS					
Age (years), Mean ± SD	53.8 ± 13.5	59.6 ± 13.2	59.6 ± 12.7	62.1 ± 12.9	61.0 ± 13.6
Females, N (%)	2,924 (45.7%)	370 (38.9%)	377 (39.7%)	32 (36.8%)	29 (33.3%)
Insurance plan type, N (%)					
Commercial insurance only	5,354 (83.7%)	689 (72.5%)	689 (72.5%)	55 (63.2%)	55 (63.2%)
Commercial insurance + Medicare supplemental	1,046 (16.3%)	261 (27.5%)	261 (27.5%)	32 (36.8%)	32 (36.8%)
All-cause healthcare costs, $US 2017 PPPM, Mean ± SD					
Total healthcare cost	$1,225 ± 2,636	$1,989 ± 4,202	$1,720 ± 2,779	$2,210 ± 2,740	$2,357 ± 6,439
Total medical	$1,103 ± 2,547	$1,768 ± 4,035	$1,513 ± 2,612	$1,979 ± 2,624	$2,087 ± 6,250
Inpatient admission	$193 ± 1,731	$244 ± 1,354	$225 ± 1,385	$369 ± 1,316	$239 ± 894[†]
Emergency department	$39 ± 272	$37 ± 304	$44 ± 231	$71 ± 265	$55 ± 248
Outpatient visits, including drug administration	$864 ± 1,668	$1,479 ± 3,699	$1,233 ± 2,073	$1,506 ± 1,941	$1,781 ± 6,105
Other	$7 ± 78	$8 ± 65	$11 ± 67	$34 ± 211	$12 ± 96[†]
Pharmacy prescriptions	$122 ± 540	$221 ± 676	$207 ± 734	$230 ± 848	$270 ± 613
Melanoma tumor site, N (%)					
Face	473 (7.4%)	78 (8.2%)	89 (9.4%)	8 (9.2%)	10 (11.5%)
Neck	346 (5.4%)	48 (5.1%)	51 (5.4%)	11 (12.6%)	4 (4.6%)*
Trunk	2,232 (34.9%)	338 (35.6%)	329 (34.6%)	27 (31.0%)	33 (37.9%)[†]
Limb	2,873 (44.9%)	414 (43.6%)	403 (42.4%)	33 (37.9%)	38 (43.7%)[†]
Other	133 (2.1%)	19 (2.0%)	19 (2.0%)	2 (2.3%)	0 (0.0%)*
Unspecified	774 (12.1%)	115 (12.1%)	124 (13.1%)	18 (20.7%)	5 (5.7%)*
Quan-Charlson comorbidity index[12], Mean ± SD	0.2 ± 0.6	0.2 ± 0.6	0.2 ± 0.6	0.4 ± 0.8	0.4 ± 0.7
Cancer-specific comorbidity index[13], Mean ± SD	1.2 ± 1.5	1.0 ± 1.3	1.0 ± 1.3	1.2 ± 1.4	1.0 ± 1.0[†]
Comorbidities					
Hypertension	2,405 (37.6%)	344 (36.2%)	365 (38.4%)	31 (35.6%)	31 (35.6%)
Actinic keratosis	960 (15%)	238 (25.1%)	245 (25.8%)	16 (18.4%)	12 (13.8%)[†]
Diabetes, uncomplicated	745 (11.6%)	124 (13.1%)	127 (13.4%)	5 (5.7%)	19 (21.8%)*
Cardiac arrhythmias	615 (9.6%)	69 (7.3%)	76 (8.0%)	13 (14.9%)	11 (12.6%)
OTHER COVARIATES					
Study period (months), Mean ± SD	29.8 ± 23.1	-	-	-	-
Index lymph node surgery to first recurrence (months), Mean ± SD	-	15.3 ± 16.6	16.0 ± 16.6	19.3 ± 14.4	18.6 ± 15.3

PPPM, per patient per month; SD,standard deviation
*Standardized difference >20%| between recurrence group within cohort after matching. †Standardized difference >10%| between recurrence group within cohort after matching.

- Mean age in the study sample for description of recurrences was 53.8 years and approximately 46% of the patients were female; mean duration of the study period was 29.8 months.
- Most baseline covariates were balanced after matching between the recurrence and recurrence-free cohorts (i.e., standardized differences <|20%|), with a few exceptions for the distant recurrence versus recurrence-free cohorts, where some melanoma sites, and diabetes presented a standardized difference superior to |20%|, and the IP costs as well as some comorbidities a standardized difference superior to |10%|.

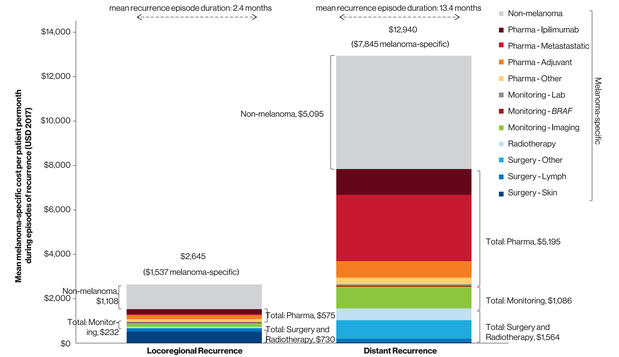
Table 2. All-cause Healthcare Costs During Episodes of Recurrence and During Recurrence-free Period

	During episodes of locoregional recurrence	During episodes of distant recurrence	During recurrence-free period[a]
	N=1,524 episodes N=1,116 patients	N=102 episodes N=102 patients	N=6,400 patients
Duration recurrence episode/recurrence-free period, Mean ± SD	2.4 months ± 1.3	13.4 months ± 11.5	25.4 months ± 21.8
All-cause healthcare costs (PPPM during recurrence episode/recurrence-free period; 2017 USD), Mean ± SD			
Total healthcare	$2,645 ± 6,638	$12,940 ± 16,341	$$1,076 ± 3,661
Total medical[b]	$2,340 ± 6,538	$11,549 ± 16,118	$$893 ± 3,502
Inpatient	$341 ± 2,021	$3,446 ± 8,902	$177 ± 1,126
Emergency	$70 ± 447	$492 ± 2,553	$40 ± 198
Outpatient, total	$1,942 ± 5,914	$7,603 ± 12,621	$665 ± 3,163
Outpatient, antineoplastic treatment[c]	$423 ± 4,467	$3,206 ± 9,772	$150 ± 2,257
Other	$11 ± 101	$7 ± 28	$11 ± 81
Pharmacy prescriptions, total	$306 ± 1,047	$1,392 ± 3,519	$183 ± 659
Pharmacy, antineoplastic treatment[d]	$159 ± 960	$1,171 ± 3,485	$60 ± 550

PPPM, per patient per month; SD, standard deviation
[a]The recurrence-free period included the time between the index date and the first recurrence for patients with a recurrence, or the time between the index date and the end data of data availability or end of insurance coverage/death for those patients with no recurrence.
[b]For the costs during episodes of locoregional recurrence, the components of the 'Medical' may not sum to the 'Medical' row as only the episodes pertaining to the component were used to derive the component PPPM.
[c]Outpatient visits associated with administration of antineoplastic treatments, whether in the NCCN guidelines for melanoma or not; cost of the visit included both the provider fees for the drug administration and the cost of the medication.
[d]Included antineoplastic agents (whether in the NCCN guidelines for melanoma or not) some of which may be used for multiple purposes (e.g., methotrexate).

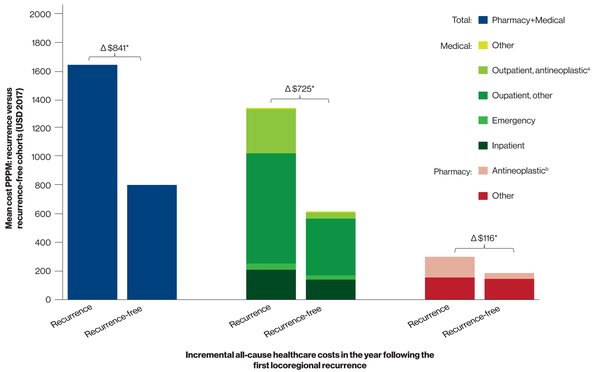
- Mean duration of locoregional recurrence episodes was 2.4 months vs. 13.4 months for distant recurrence episodes.
- The all-cause healthcare costs PPPM during episodes of recurrence were more expensive compared to the costs during recurrence free-period, especially when compared to episodes of distant recurrence ($1,076 vs $12,940 PPPM).
- During episodes of distant recurrence approximately half of the OP costs were associated with antineoplastic treatment administration, and nearly all of the pharmacy costs were associated with antineoplastic treatment.

Figure 1. Melanoma-specific Healthcare Costs Per Patient Per Month During Episodes of Recurrence



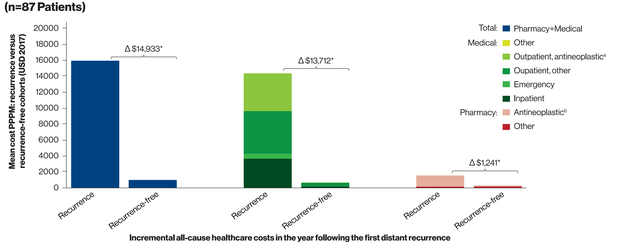
- In both recurrence types, more than half of the total costs were associated with melanoma.
- During episodes of locoregional recurrence, the total melanoma-specific costs were $1,537 PPPM, with 47% accounted by cost of melanoma surgery and radiotherapy (among patients who underwent surgery, the cost of surgery varied from $73 to $1,476 PPPM; the mean cost for radiotherapy was $659 PPPM).
- During episodes of distant recurrence, the total melanoma-specific costs were $7,845 PPPM, with 66% accounted by the costs of pharmacological antineoplastic therapy (among treated, the cost of pharmacological antineoplastic therapy varied from $645 to $13,219 PPPM).

Figure 2. All-cause Healthcare Costs in the Year Following First Locoregional Recurrence Between Matched Cohorts (N=950 patients)



*Significant at a Type I error rate of 0.05
PPPM, per patient per month
[a]Outpatient visits associated with administration of antineoplastic treatments, whether in the NCCN guidelines for melanoma or not; cost of the visit included both the provider fees for the drug administration and the cost of the medication.
[b]Included antineoplastic agents (whether in the NCCN guidelines for melanoma or not) some of which may be used for multiple purposes (e.g., methotrexate).

Figure 3. All-cause Healthcare Costs in the Year Following First Distant Recurrence Between Matched Cohorts (n=87 Patients)



*Significant at a Type I error rate of 0.05
PPPM, per patient per month
[a]Outpatient visits associated with administration of antineoplastic treatments, whether in the NCCN guidelines for melanoma or not; cost of the visit included both the provider fees for the drug administration and the cost of the medication.
[b]Included antineoplastic agents (whether in the NCCN guidelines for melanoma or not) some of which may be used for multiple purposes (e.g., methotrexate).

- Patients with recurrences, in particular distant recurrences, incurred significantly higher total all-cause healthcare costs PPPM in the year following the start of the first episode of recurrence compared to recurrence-free matched controls.

Limitations

- Potential inaccuracies in the database, common to studies based on healthcare claims, are expected to affect cohorts to a similar extent. Residual confounding due to factors unobserved in claims data cannot be ruled out.
- The recurrence algorithm used treatment pattern indicators to detect recurrences; although previous studies have shown that claims-based algorithms may be used to identify cancer recurrences[14-15], misclassifications may have occurred.
- The first melanoma diagnosis captured in the current study could have corresponded to the locoregional after an earlier melanoma diagnosis. A 12-month washout period was applied to minimize the chance of capturing recurrences at the first melanoma diagnosis in the data.

Conclusions

- This real-world study from the commercial payer perspective highlights the significant cost burden associated with melanoma recurrences after lymph node surgery, which can increase all-cause healthcare costs by nearly $15,000 PPPM in the first year post-recurrence for patients with a distant recurrence. Although less expensive (i.e., increase of $841 PPPM in the first year post recurrence), locoregional recurrences are more frequent and may significantly affect costs at the population level.
- The impact of new treatments, notably new adjuvant therapies[9,10], with potential to reduce recurrences and thereby costs, remains to be seen, and would constitute an interesting topic of future research.

References

1. Benvenuto-Andrade C, *et al. Dermatol Ther.* 2005;18(6):423-435.
2. Leiter U, *et al. J Surg Oncol.* 2004;86(4):172-178.
3. Chang CL, *et al. Melanoma Res.* 2015;25(4):312-320.
4. Harries M, *et al. Int J Clin Pract.* 2017;71(5).
5. Johnston K, *et al. Eur J Cancer.* 2012;48(14):2175-2182.
6. McKendrick J, *et al. J Med Econ.* 2016;19(6):587-595.
7. Reyes C, *et al. Melanoma Res.* 2013;23(2):159-166.
8. Toy EL, *et al. Curr Med Res Opin.* 2015;31(8):1561-1572.
9. Weber J, *et al. N Engl J Med.* 2017;377(19):1824-1835.
10. Long GV, *et al. N Engl J Med.* 2017;377(19):1813-1823.
11. Austin PC. *Multivariate Behav Res.* 2011;46(3):399-424.
12. Quan H, *et al. Am J Epidemiol.* 2011;173(6):676-682.
13. Sarfati D, *et al. J Clin Epidemiol.* 2014;67(5):586-595.
14. Chubak J, *et al. J Natl Cancer Inst.* 2012;104(12):931-940.
15. Deshpande AD, *et al. Annals of epidemiology.* 2015;25(4):297-300.
16. Livaudais-Toman J, *et al. eGEMs.* 2016;4(1).

Presented at AMCP Annual Meeting 2018, April 23-26, Boston, MA

This study was sponsored by Novartis Pharmaceuticals Corporation.

Text: Qd7209
To: 8NOVA (86682) US Only
+18324604729 North, Central and South Americas; Caribbean; China
+447860024038 UK, Europe & Russia
+46737494608 Sweden, Europe
Visit the web at:
http://novartis.medicalcongressposters.com/Default.aspx?doc=d7209

Copies of this poster obtained through Quick Response (QR) Code are for personal use only and may not be reproduced without permission from the author of this poster.

Scan this QR code