2345

Herpes Zoster Incidence & Disease Burden among Patients Undergoing Autologous Hematopoietic Stem Cell Transplant in a Large US Population

Jianbin Mao, PhD[1]; Jeffrey T McPheeters, BA[1]; Dongmu Zhang, PhD[2], Camilo J Acosta, MD, PhD[2], Lynn Finelli, DrPH[2]
[1]Optum, Eden Prairie, MN USA [2]Merck & Co. Inc., Kenilworth, NJ, USA

ABSTRACT

BACKGROUND: Autologous Hematopoietic Stem Cell Transplant (Auto-HSCT) is used to treat cancers. Conditioning regimens cause immunosuppression increasing risk for herpes zoster (HZ). More than 25% of Auto-HSCT recipients developed HZ compared to 0.3-0.5% of the general population. HZ may increase healthcare resource utilization (HRU) and cost and antiviral prophylaxis can mitigate risk of HZ. However, real world data are lacking on AP use, HZ risk, HRU and cost in Auto-HSCT patients.

METHODS: Claims were analyzed for patients in the Optum Research and Impact National Benchmark Databases. Adults aged ≥18 years with an Auto-HSCT procedure between 1/2006—12/2011 were included; those with HZ pre-Auto-HSCT or received Zostavax during the study period, or had <12 months of enrollment were excluded. HZ incidence was calculated as cases observed after Auto-HSCT over accrued time-at-risk in person-years (PY). To assess HRU and all-cause costs, HZ onset date was set for HZ cases, and a random date was selected for those w/o HZ; all patients required 365 days of follow-up. Costs were assessed, after excluding the top 5% of most expensive outliers, from 21 days pre-onset date through 364 days post-onset date and compared by t-test and generalized linear model.

RESULTS: There were 223 HZ cases among 2,350 Auto-HSCT recipients; HZ incidence was 62.18/1,000 PY (95% CI: 54.28-70.90). The mean time-at-risk was 405 (SD=340) vs. 529 (SD=458) days for those with HZ vs. w/o HZ. Incidence increased with age; females had higher incidence (72 vs 56/1,000 PY, p=0.061). Receiving corticosteroids was associated with a higher risk of HZ (odds ratio [OR]: 1.40, 95% CI: 1.00-1.95). HZ incidence was higher among patients without antiviral prophylaxis; but even those prophylaxed had incidence 6-fold higher than the immunocompetent population . One-year costs for those with HZ (n=122) vs. w/o HZ (n=562) did not differ significantly in bivariate (($71,818 (SD $77,299 vs. $70,377 (SD $72,222) (p=0.844)), or multivariate analyses (cost ratio: 1.07, 95% CI: 0.86-1.32, p=0.566).

CONCLUSIONS: Auto-HSCT recipients have high incidence of HZ despite antiviral prophylaxis. Costs incurred among Auto-HSCT recipients with HZ were not significantly different from those without HZ but variance was large. Further evaluation of inpatient and outpatient costs is ongoing.

BACKGROUND

- Conditioning chemotherapy causes severe immunosuppression, thus increases patients' risk of HZ. [1]
- In one year, more than 25% of Auto-HSCT recipients develop HZ [1-5] compared to 0.3-0.5% of the general population.[6]

OBJECTIVES

- To determine annual HZ incidence among Auto-HSCT recipients
- To evaluate HZ-associated health care resource utilization (HRU) and cost among Auto-HSCT recipients

METHODS

Study Design

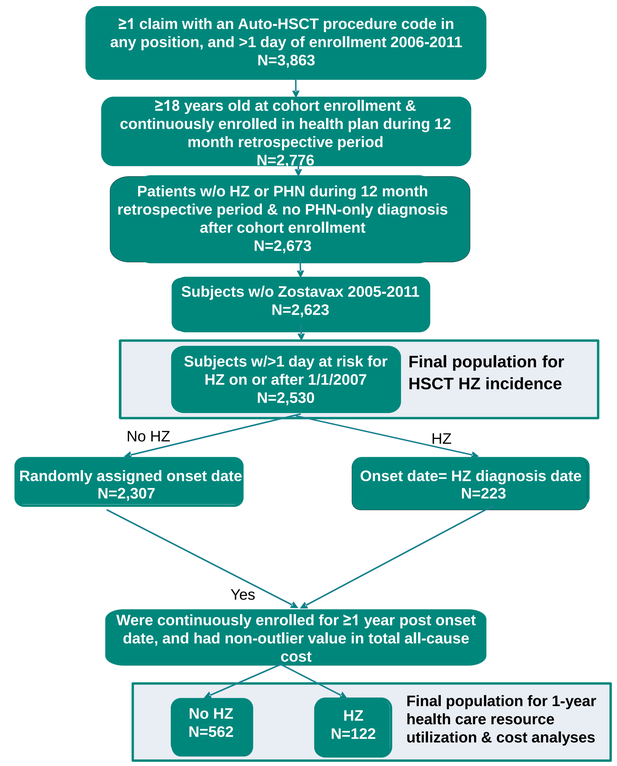
- Administrative claims databases from Optum Research Database and Impact National Benchmark Database in the United States.
- Retrospective study containing both commercial and Medicare Advantage enrollees with both medical and pharmacy insurance coverage from Jan. 01, 2006 to Dec. 31, 2011.
- Patient selection criteria are shown in Figure 1.
- Key definitions for the HZ-incidence analysis:
  - Incident HZ case: first claim with a diagnosis code for HZ (ICD-9-CM: 053.00-053.11, 053.14-053.9) at any time after Auto-HSCT procedure. Patients were considered no longer at risk for HZ after first HZ diagnosis.
  - HZ time-at-risk started on the date of Auto-HSCT procedure per Current Procedural Terminology (CPT: 39241) and ICD-9-CM procedural codes: 41.01, 41.0441.07 & 41.09) occurred from Jan01, 2006 to Dec. 31, 2011
  - HZ time-at-risk ended at the earliest of four possible events: development of HZ, disenrollment, death, and study-end date (Dec. 31, 2011).
  - Antiviral prophylaxis (AP): use of acyclovir, famciclovir, ganciclovir, valacyclovir and valganciclovir at any time from 21 days prior to Auto-HSCT through the end of time-at-risk.
- Key definitions for the 1-year all-cause HRU and cost analysis:
  - Patients with HZ were compared to patients without HZ; onset date for patients with HZ was first HZ-diagnosis date; onset date for patients without HZ was a randomly-selected claim date after Auto-HSCT procedure.
  - 1-year HRU and cost were measured from 21 days prior to the onset date through 365 days post onset date.
  - The 5% of most costly patients were excluded separately from both cohorts

Statistical Analyses

- HZ incidence rate was calculated as a ratio of HZ cases observed over total time-at-risk per 1,000 PY,
- Odds ratios and associated 95% confidence intervals (CI) were calculated for baseline Quan-Charlson comorbidity score and type of hematopoietic cancer.
- Difference in HRU and costs were assessed with t-tests (for continuous measures) or Chi-square tests (for categorical measures).
- Difference in all-cause total cost was analyzed using a generalized linear model with gamma distribution and log rank (MVA).

RESULTS

Figure 1. Patient Attrition



Auto-HSCT= hematopoietic stem cell transplant; HZ = herpes zoster; PHN= post-herpetic neuralgia

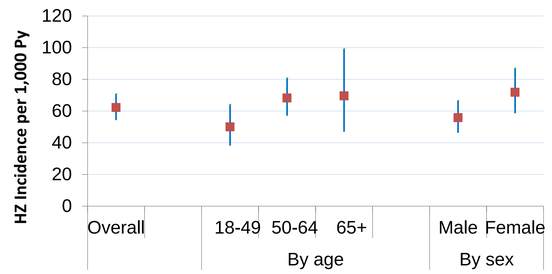
Table 1. Patient Demographics and Time-at-risk Days

	Total	Patients with HZ	Patients without HZ	P-value
Overall, n (%)	2,530 (100)	223 (8.8)	2307 (91.2)	
Age, mean (SD)	53.4 (12.1)	53.5 (11.7)	53.4 (12.1)	0.832
Age category, n (%)				
18-49	783 (31.0)	61 (27.4)	722 (31.3)	0.224
50-64	1,375 (54.4)	132 (51.2)	1,243 (53.9)	0.128
65+	372 (14.7)	30 (13.5)	342 (14.8)	0.581
Geographic region*, n (%)				
Northeast	777 (30.7)	66 (29.6)	711 (30.8)	0.705
Midwest	593 (23.4)	60 (26.9)	533 (23.1)	0.201
South	914 (36.1)	79 (35.4)	835 (36.2)	0.820
West	240 (9.5)	16 (7.2)	224 (9.7)	0.216
Sex				
Male, n (%)	1,501 (59.3)	120 (53.8)	1,381 (59.9)	0.079
Female, n (%)	1,029 (40.7)	103 (46.2)	926 (40.1)	
Time-at-risk (days)				
Mean	517.8	404.6	527.7	
Standard deviation	449.9	340.0	457.8	
Median	384.5	302.0	391.0	

* 6 subjects with "Other" geographic region not shown in Table 1

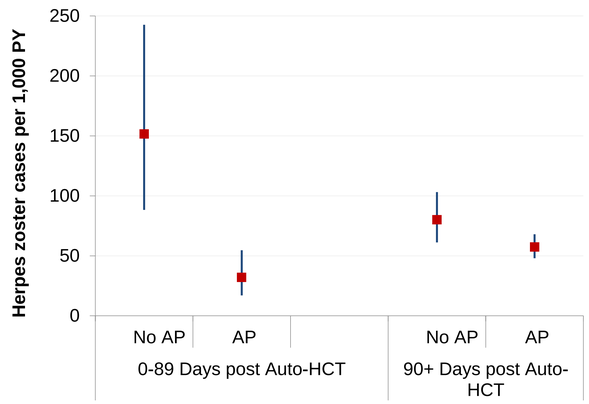
- A total of 2,530 Auto-HSCT recipients were included in the HZ incidence analysis. 223/2,530 patients (8.8%) patients developed HZ. Patients with HZ did not differ from patients without HZ in age, gender and geographic region distribution
- 2,063 (81.5%) patients received antiviral prophylaxis (AP) at any point between 21 days prior to Auto-HSCT and the end of time-at-risk for HZ; no difference in AP by HZ status (82.1% vs 81.5% for patients with vs without HZ, *p*=0.834).
- 684 patients were included in the HRU and cost analysis: 122 patients with HZ were compared with 562 patients without HZ

Figure 2. Herpes Zoster Incidence Overall and by Age and Sex



- Overall HZ incidence was 62.2 cases per 1,000 PY overall and increased with increasing age.
- HZ incidence point estimate was higher in females than males , though this difference is not significant (71.8 vs 55.8 cases per 1,000 PY, p>0.05).

Figure 3. Herpes Zoster by Antiviral Prophylaxis (AP)

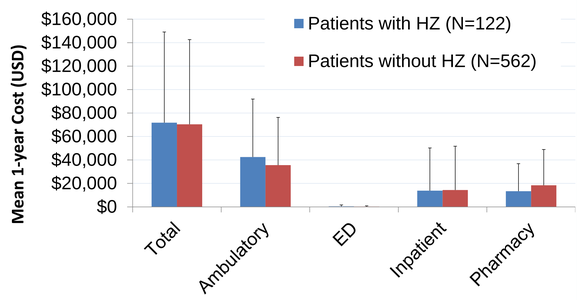


- 30 cases observed within the first 90 days of Auto-HSCT: Rate 151.6 cases per 1,000 PY among patients without AP and 32.0 cases per 1,000 PY among patients with AP.
- 193 cases were observed 90+ days post Auto-HSCT: Rate 62.9 cases per 1,000 PY among patients without AP and 57.4 cases per 1000 PY among patients with AP.

Table 2. Odd Ratios (OR) by Quan-Charlson and by Hematopoietic Cancer (HM) Type

	Total (N=2,530)		Patients with HZ (N=223)		Patients without HZ (N=2,307)		Odds of developing HZ		
	n	%	n	%	n	%	OR	Lower 95% CI	Upper 95% CI
Modified Quan-Charlson comorbidity score (excluding cancer)									
0	97	3.83	2	0.9	95	4.12	ref	-	-
1-2	820	32.4	69	30.9	751	32.6	4.36	1.05	18.09
3-4	625	24.7	50	22.4	575	24.9	4.13	0.99	17.26
5+	988	39.1	102	45.7	886	38.4	5.47	1.33	22.51
HM	1,685		159		1,526				
Multiple myeloma	1,033	61.3	99	62.3	934	61.2	ref.	–	–
Non-Hodgkin's lymphoma	510	30.3	49	30.8	461	30.2	1	0.7	1.44
Hodgkin's lymphoma	62	3.68	4	2.52	58	3.8	0.65	0.23	1.83
Leukemia	75	4.45	7	4.4	68	4.46	0.97	0.43	2.17
All other HM cancers	5	0.3	0	0	5	0.33	0	0	I

Figure 4. Comparison of 1-year Total, Ambulatory, Emergency Department (ED), Inpatient and Pharmacy Cost



- Mean total costs were high and comparable between cohorts (p=0.844), even after excluding the most expensive outliers, variance remains high.
- Ambulatory, Inpatient, Outpatient, ED costs did not differ significantly between cohorts (all p>0.05). Patients without HZ had higher mean pharmacy costs (p=0.042)
- MVA confirmed that the two study cohorts did not significantly differ in total cost (cost ratio: 1.065, 95% CI: 0.858-1.323, p=0.566).

LIMITATIONS

- These data represent the insured population and may not be generalizable to the population of the US.
- It's possible that HZ may have not been recorded as a diagnoses if a patient presented with severe HZ-related complications in a healthcare encounter.
- Patients with mild HZ may not have sought medical care, thus be not recorded in administrative claims, which may lead to underreporting.
- The health care resource utilization and cost were measured among Auto-HSCT recipients who survived at least one year after Auto-HSCT procedure, thus it's possible patients with more advanced cancer were excluded.

CONCLUSIONS

- This is the first report of HZ incidence, HCU and cost among Auto-HSCT recipients using real-world administrative claims data.
- Most patients (81.5%) received antiviral prophylaxis for some time from three weeks pre-transplant to post transplant.
- HZ incidence was higher among patients undergoing Auto-HSCT than in the general population (62 vs 3-5 per 1,000 PY), even among Auto-HSCT recipients receiving antiviral prophylaxis (32-57 cases per 1,000 PY).
- Overall costs were high among Auto-HSCT recipients. However, the development of HZ did not significantly increase total, ambulatory care, ER or inpatient costs. The lack of significance may be due to high overall costs with large variance in cost among patients.

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Contact Information

Lynn Finelli, DrPH
Merck & Co., Inc.
lynn.finelli@merck.com

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