Oral oncolytics: adherence, cost and utilization.

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Oral oncolytics discontinuation rates and the outcomes of total medical costs and hospitalizations.

BACKGROUND

- Increasing utilization of cycled oral antineoplastic therapies (where dosages vary per monthly supply) has generated interest in examining a discontinuation metric for adherence.
- Research is needed to demonstrate whether reducing gaps in cycled medication (i.e., discontinuations) is associated with reduced total medical costs and hospitalization events in the following calendar year.

OBJECTIVES

- To identify significant associations between cycled oncolytic medication discontinuation and total medical cost and hospitalizations.

METHODS

- We used a retrospective cohort design with commercially insured patients from the MarketScan Commercial Claims and Encounters database from 2017--2019.
- Discontinuations were calculated as gap in medication supply at intervals of 1.5*last supply in the last 6 months of 2018 or 2019.
- The measure was generated among patients using 8 generic products in 6 therapy classes as a single therapy (Classes and products are presented in Table 1.).
- New to therapy/diagnosis was inferred from a look back on 2017 cancer diagnosis and medications. Possible indications for on-label end of therapy (not a discontinuation) on a subset of medications was inferred from number of fills in calendar year.
- Exclusions included those under 18 years, or without cancer diagnosis or continuous enrollment, or initiating medication within last 45 days of 6-months, or indications of death, hospice care, or transplants.
- Cancer diagnosed patients were categorized as either having a discontinuation in their medication therapy or not within the later half-year of 2018 or 2019. Medication therapy duration was calculated as days till first discontinuation or end of year.
- General linear repeated measures were used to model differences in year over year total medical costs (2018-2019). Logistic regression was used to model odds of hospitalization in 2019. Our independent variable was binary

discontinuation or covered days till discontinuation coded into 3 levels: 1-89 days, 90-149 days, and 150-182 days based on distribution.

- Models included 10 covariates of age (log transform, mean split), census region (north-east vs. other), gender (female vs. male), new to therapy/diagnosis (or not), metropolitan area (or not), mail pharmacy (all vs. other), single therapy class (or not), ratio of provider types to visits (<0.48, 0.48+), hospitalized (0,1,2+), and presence of non-cancer Charlson comorbidity index categories (yes or no).

RESULTS

- In 2018, of 4,872 patients (25.6%) had an indicated discontinuation, and a subset of 1,534 patients (31.5%) were also eligible for the 2019 discontinuation measure.
- As reported in Table 1., the most utilized therapy classes per patient were Antimetabolites (31%) followed by Immunomodulators for Myelodysplastic Syndromes (25.2%), and Cyclin-Dependent Kinases (CDK) Inhibitors (23.6%).

Table 1. Distribution of therapy classes for 2018 on total

Therapy Class	Generic Products	Patient Count	% Patients
Antimetabolites	capecitabine	1,510	31.0%
Immunomodulators	pomalidomide	207	4.2%
Multikinase Inhibitors	sunitinib, lapatinib	182	3.8%
Cyclin-Dependent Kinases Inhibitors	palbociclib, ribociclib	1,153	23.6%
Imidazotetrazines	temozolomide	591	12.1%
Immunomodulators for Myelodysplastic Syndromes	lenalidomide	1,229	25.2%

- The 25.6% discontinuation rate in 2018 was significantly reduced with residing in the north-east region (p<.02) or utilizing mail order pharmacy only (p<.02), or with a higher provider ratio (p<.002). There were increased odds of discontinuation present for new to therapy (p<.0001) and number of hospitalizations (0, 1 or 2+, p<.0001).
- In 2018, metric medication cost was significantly lower for discontinued patients (-$31,495, p<.0001). Across years, there was a trend of increased medication costs ($19,286), with a partial correlation of 0.69 (p<.0001).
- For the 2018-2019 sample of 1,534 patients, only 53 (3.5%) discontinued in both years and 361 (23.5%) discontinued in 2018 or in 2019. See Table 2 for distribution on covariates.
- Total medical costs indicated a significant overall decrease across years (-$12,757, p <.0006), with a partial correlation of 0.44 (p<.0001).
- The distribution for the 10 covariates are presented in Table 2. for the combined 2018-2019 years. To note, majority are females (66.2%), residing in a metropolitan area (87.4%), on a single therapy class (71.3%), and half used only a mail order pharmacy (50.8%).

Table 2. Distribution of 2018-2019 Dichotomous Covariates (n=1.534)

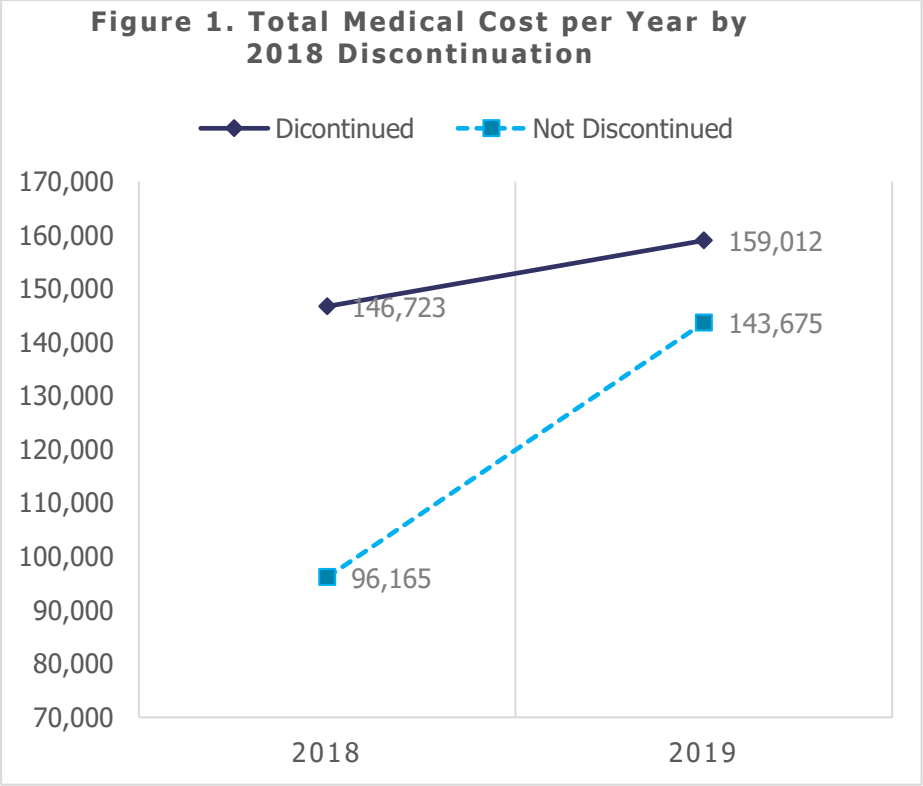
Age (56+ yrs)	Female	North-east	Metro-area	New to Tx	Single Therapy Class	Mail Order	Comor-bidity	Provider Ratio => 0.48	Hospitalized (1,2+)
49.9%	66.2%	20.7%	87.4%	37.9%	71.3%	50.8%	21.0%	18.8%	26.0%

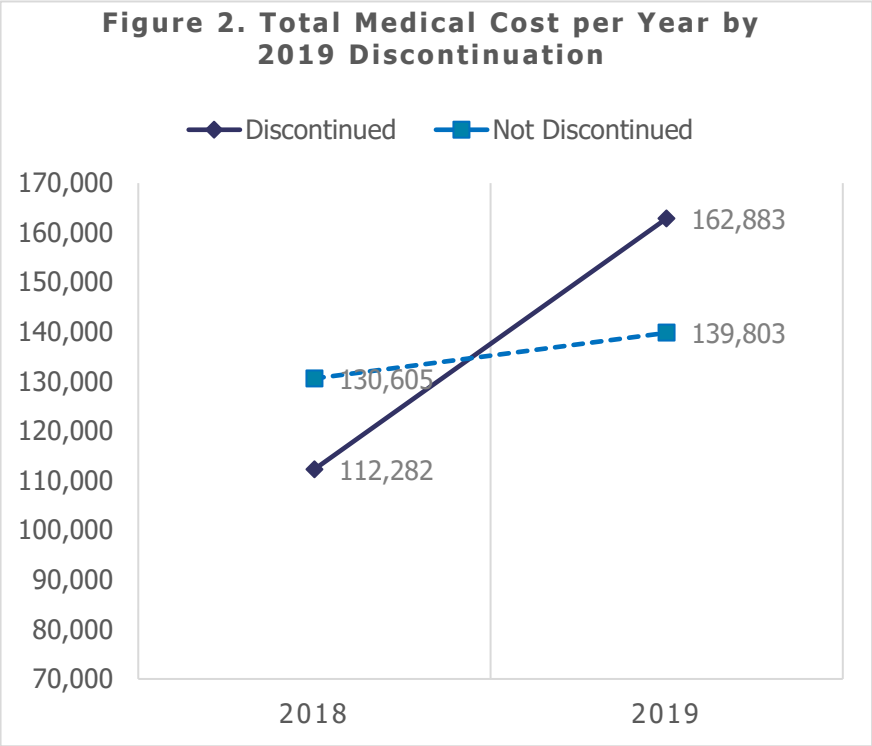
- These 10 covariates along with the discontinued indicator in either 2018 or 2018 were used to model the difference in total medical costs across years.

- The difference between total medical costs between 2018 and 2019 significantly increased among those who discontinued in 2018 compared to others ($50,558, p<.0001) and time in years ($12,289, p<.0002). See Figure 1. on adjusted total medical cost values for the interaction between 2018 discontinuation over time.

- For 2019 discontinued patients, higher estimated costs in 2019 was present compared to others ($23,080, p<.002), and there was more an increase over time in this group ($50,601, p<.0001). See Figure 2 for the interaction between 2019 discontinuation over time.

- In this repeated measure model other significant 2019 covariates where: decreased costs for younger adults (p<.002), being female (p<.0001), utilizing a single therapy class (p<.03), and having a higher provider ratio (p<.0001). Increase in cost was present for those residing in the northeast region (p<.0001), or metro-area (p<.04), being new to therapy (p<.0001), and number of hospitalizations (p<.0001).





- Odds of hospitalization in 2019 was significantly increased by 2019 discontinuation (2.32, p<.0001), and reduced by having longer medication coverage in 2018 (odds=0.66 at <61 days compared to 0.51 at 150+ days, p<.02). Hence longer therapy durations in prior year reduced odds of hospitalization in 2019.
- The only other significant covariate in this logistic model was the comorbidity indication in 2019 (odds=3.43, p<.0001).

CONCLUSIONS

- This study highlights Medication adherence (fewer gaps in medication coverage) on cycled oral antineoplastics can lead to lower medical costs and fewer hospitalization events in both current year and following year outcomes as compared to lower adherence levels.
- In addition, these results help validate the methodology presented on discontinuations. This metric can be used for yearly reporting requirements by implementing filters controlling for possible end of therapy, late medication starts in the given year, and allowing product switching within a therapy classes.

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