Dasatinib treatment patterns after pleural effusion among patients with chronic myeloid leukemia

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Introduction

- Choice of treatment for chronic myeloid leukemia (CML) is complex and dependent on many factors, including disease phase and drug tolerability
- The tyrosine kinase inhibitor (TKI) dasatinib is an effective long-term treatment option for most patients with newly diagnosed CML, based on deep and durable responses reported in the DASISION trial[1]
  - However, dasatinib was associated with the development of pleural effusion, an adverse event caused by the build-up of excess fluid in the pleural space outside of the lungs[2]
- Data regarding the optimal strategy for managing pleural effusion in patients treated with dasatinib are limited
  - Dose reductions, interruptions, or switching to another TKI are commonly used strategies, although patients who remained on first-line treatment had better clinical outcomes than patients who switched treatment in the SIMPLICITY trial[3]
- Here, we present results of a study examining treatment patterns, including duration of dasatinib use after pleural effusion, and healthcare resource utilization (HCRU) and costs among patients with CML treated with dasatinib who experienced a subsequent pleural effusion

Methods

Data source and study design

- Administrative claims data from the IBM MarketScan® Commercial and Medicare Supplemental Databases were used to identify patients diagnosed with CML (≥ 1 inpatient or ≥ 2 outpatient medical claims with a diagnosis code for CML: ICD-9-CM codes 205.1x, 205.8x; ICD-10-CM codes C92.1x, C92.Zx) during the study period (Jan 1, 2014 – Sep 30, 2019)

Patient identification

- Eligible patients had a confirmed diagnosis of CML, had ≥ 1 pharmacy claim for dasatinib, and experienced a pleural effusion (ICD-9-CM: 511.1, 511.89; ICD-10-CM: J90) after dasatinib during the identification (ID) period (Jan 1, 2015 – Sep 30, 2018)
  - All patients were aged ≥ 18 years on the index date (date of first pleural effusion during ID period), had ≥ 1 filled prescription for dasatinib before the index date, with dasatinib available on the index date, and did not have a code for pleural effusion during the baseline period (1 year pre-index)
  - Patients were continuously enrolled during baseline and follow-up (1 year post-index) periods

Study measures

- Treatment patterns (dose modification [interruption or reduction in dasatinib dose], switch from dasatinib to another TKI, and duration of dasatinib treatment), and HCRU (hospital visits and pleural effusion treatment) and cost measures were evaluated during follow-up

Statistical analysis

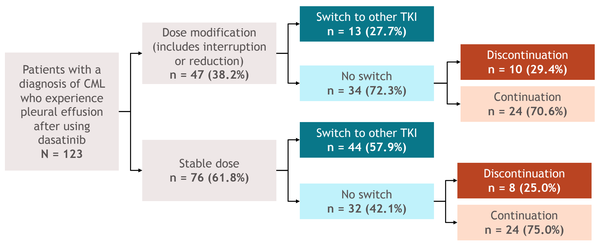
- Descriptive statistics were generated for all measures and patients were stratified by dose modification versus stable dose
  - Statistical testing was conducted using Chi-square (exact Chi-square if a cell count of < 5) or *t*-tests
- Time to switch and discontinuation in patients with and without a dose modification were compared using Kaplan-Meier estimation and plots
- All data transformations and statistical analyses were performed using SAS© version 9.4

Results

Baseline characteristics

- In total, 123 patients met the study criteria (**Figure 1**)
- Baseline characteristics were well balanced with no statistically significant differences between patients with a dose modification versus stable dose (**Table 1**)
  - The mean (standard deviation [SD]) age was 62.2 (10.9) years, 23.6% were female, the mean (SD) Charlson Comorbidity Index (CCI) was 3.8 (2.1), and the mean (SD) number of chronic conditions was 6.0 (2.4)
  - Most patients were covered by commercial/private insurance (64.2%), and treated by a physician specializing in hematology/oncology (41.5%)

Figure 1. Dasatinib treatment patterns after pleural effusion: 1-year follow-up



Dose interruption: Defined as a gap in use of 15-59 days. Reduction: Defined as reduction in average daily dose between last fill before index and first dose modification after index. Discontinuation: Defined as a gap in use of dasatinib of ≥ 60 days after exhausting current supply and among patients without a switch to another TKI; patients whose dasatinib use had a < 60-day gap were considered to have continued use. Stable dose: Defined as no modification to dasatinib dosing.

Table 1. Baseline characteristics

	Dose modification n = 47	Stable dose n = 76	All N = 123
Age, mean (SD), years	62.1 (10.3)	62.3 (11.3)	62.2 (10.9)
Female, n (%)	11 (23.4)	18 (23.7)	29 (23.6)
Insurance type, n (%)			
Commercial/private	28 (59.6)	51 (67.1)	79 (64.2)
Medicare	19 (40.4)	25 (32.9)	44 (35.8)
Primary physician specialty,[a] n (%)			
Hematologist/oncologist	21 (44.7)	30 (39.5)	51 (41.5)
Primary care physician[b]	10 (21.3)	13 (17.1)	23 (18.7)
Internist	6 (12.8)	15 (19.7)	21 (17.1)
Other[c]	10 (21.3)	18 (23.7)	28 (22.7)
CCI, mean (SD)	3.5 (1.8)	4.1 (2.3)	3.8 (2.1)
Number of chronic conditions, mean (SD)	5.7 (2.5)	6.2 (2.4)	6.0 (2.4)
Non-dasatinib TKI use prior to the first observed dasatinib fill in baseline,[d] n (%)	7 (14.9)	10 (13.2)	17 (13.8)
Days from the first observed dasatinib in the baseline period to the index date, mean (SD)	256.9 (128.2)	249.4 (123.8)	252.3 (125.0)

[a]Physician specialty with the largest number of office visits with evaluation and management services during baseline period; [b]Includes physician assistants and nurse practitioners; [c]Includes individual specialties with < 2% (other) and unknown specialties (4 with no evaluation and management claims and 6 with unspecified specialty); [d]Patients could use more than one TKI in the baseline period.

Dasatinib treatment patterns during 1-year follow-up period

- Overall, 38.2% of patients had a dose modification and 61.8% a stable dose after pleural effusion (**Figure 1**)
  - At the 1-year follow-up, most patients (72.3%) with a dose modification did not switch treatment, and, of those, 70.6% continued treatment; the majority (57.9%) of patients with a stable dose switched to another TKI
- The mean (SD) duration of dasatinib treatment (number of days from first pleural effusion to end of dasatinib treatment) was significantly greater in patients with a dose modification compared with those with a stable dose (262.0 [124.0] vs 149.1 [155.2]; *P* < 0.001) (**Figures 2 and 3**)
  - In patients with a dose modification, the mean (SD) number of days from pleural effusion to dose modification was 73.7 (77.1) days, and from dose modification to end of treatment was 188.3 (128.7) days
- Patients with a dose modification took a significantly longer time to switch from dasatinib to another TKI compared with patients with a stable dose (mean [SD]: 164.7 [105.8] vs 74.8 [76.0] days; *P* = 0.001) (**Figures 2 and 4**)

Figure 2. Time to treatment event in patients with dose modification vs stable dose

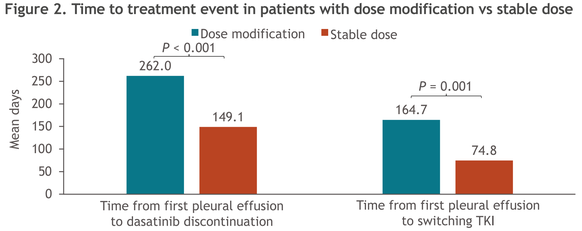
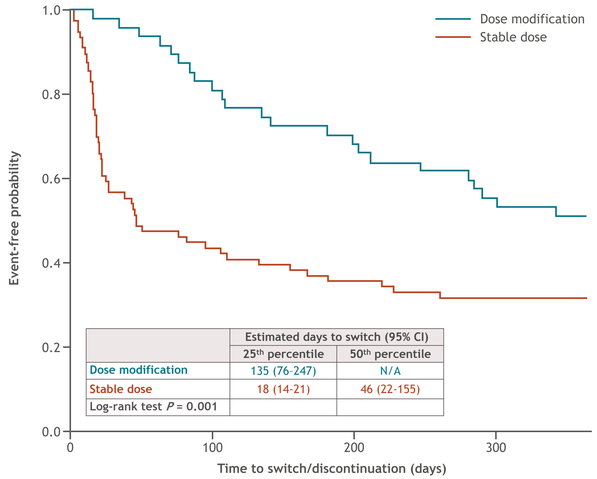
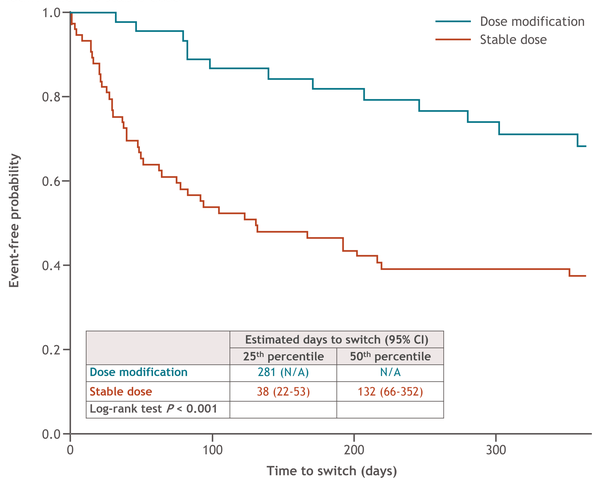


Figure 3. Kaplan-Meier estimate of the duration of dasatinib treatment in patients with dose modification vs stable dose



	Estimated days to switch (95% CI)	
	25th percentile	50th percentile
Dose modification	135 (76-247)	N/A
Stable dose	18 (14-21)	46 (22-155)
Log-rank test *P* = 0.001		

Figure 4. Kaplan-Meier estimate of time to switch to another TKI in patients with dose modification vs stable dose



	Estimated days to switch (95% CI)	
	25th percentile	50th percentile
Dose modification	281 (N/A)	N/A
Stable dose	38 (22-53)	132 (66-352)
Log-rank test *P* < 0.001		

Healthcare utilization and costs during 1-year follow-up period

- Overall, 48.0% of patients were hospitalized and 37.4% had an emergency department (ED) visit (**Table 2**)
  - The mean (SD) number of visits to the physician's office was 24.3 (16.7)
- Total mean (SD) costs were $196,797 ($143,848) (**Table 2**)
  - There were no statistically significant differences in HCRU and costs between patients with dose modification and stable dose
- Most patients who experienced pleural effusion received treatment (84.6%), including diuretics (52.0%) and corticosteroids (50.4%) (**Table 2**)

Table 2. Healthcare utilization and costs during the 1-year follow-up period

	Dose modification n = 47	Stable dose n = 76	All N = 123	*P* value
Healthcare visits				
Any hospitalization, n (%)	21 (44.7)	38 (50.0)	59 (48.0)	0.566
Total number of stays, mean (SD) [median], days	10.2 (12.8) [4]	11.8 (15.2) [6]	11.3 (14.3) [6]	0.675
Any ED visit, n (%)	20 (42.6)	26 (34.2)	46 (37.4)	0.353
No. of physician office visits, mean (SD) [median]	25.5 (16.5) [20]	23.6 (16.8) [19]	24.3 (16.7) [20]	0.529
Healthcare costs				
Total costs, mean (SD) [median]	$192,125 (143,419) [159,597]	$199,686 (144,988) [172,834]	$196,797 (143,848) [163,292]	0.778
Hospitalization costs, mean (SD) [median]	$39,885 (93,795) [0]	$41,315 (84,516) [4,096]	$40,769 (87,799) [0]	0.930
Outpatient care costs, mean (SD) [median]	$38,258 (56,468) [15,367]	$41,248 (60,315) [16,335]	$40,105 (58,658) [15,830]	0.785
Pharmacy costs, mean (SD) [median]	$113,982 (47,717) [124,969]	$117,123 (60,899) [113,546]	$115,923 (56,043) [114,607]	0.764
TKI costs, mean (SD) [median]	$106,143 (39,413) [117,407]	$107,146 (58,156) [110,967]	$106,763 (51,625) [112,167]	0.909
Pleural effusion treatment, n (%)				
Selected treatment for pleural effusion	42 (89.4)	62 (81.6)	104 (84.6)	0.246
Corticosteroids	28 (59.6)	34 (44.7)	62 (50.4)	0.110
Diuretics	23 (48.9)	41 (53.9)	64 (52.0)	0.589
Oxygen therapy	3 (6.4)	7 (9.2)	10 (8.1)	0.740
Pleural procedures (eg, thoracentesis, pleurodesis, fluid drainage)	19 (40.4)	21 (27.6)	40 (32.5)	0.141

Limitations

- Pleural effusions captured through administrative claims may only represent more severe cases (eg, cases resulting in an ED visit or hospital stay), resulting in underreporting of the true prevalence of pleural effusion following frontline dasatinib treatment
  - Results from a sensitivity analysis of the same data set supported the hypothesis that pleural effusion is potentially under-coded; a larger sample size of patients was identified when also including patients with evidence of shortness of breath along with a radiology procedure
- Administrative claims data do not allow for more comprehensive clinical data capture (eg, laboratory results) or other vitals measures (eg, body mass index)
- Furthermore, the data presented here do not provide specific details on lines of systemic therapy, which may result in inaccurate reporting of duration of therapy and related calculations

Conclusions

- These findings demonstrate that dasatinib discontinuation may not be necessary after development of pleural effusion
  - Patients who had a dose modification of dasatinib after development of pleural effusion were able to continue dasatinib treatment for a longer duration and had a lower rate of switching to another TKI (but with similar HCRU and costs) compared with patients who maintained a stable dose
- Although not all patients required a dose modification to continue dasatinib treatment after pleural effusion, these findings suggest that in some patients dose modification of dasatinib may provide continued treatment with the potential to sustain outcomes

References

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Disclosures

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