6606

Disease Management and Treatment of Chronic Myeloid Leukemia (CML): Experience From the Patient (Pt) Perspective

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Background

- Chronic myeloid leukemia (CML) is a rare disease with approximately 4,500 new cases per year in the US, accounting for 15% of Leukemia cases.[1] Over the last decade, BCR-ABL inhibitors have improved clinical prognoses and outcomes for patients with CML. Despite its low incidence, the chronic nature of the condition and improved treatments have resulted in a steady increase in the number of patients living with CML
- Few studies have evaluated attributes related to CML disease and treatment and their impact on patient management in a real-world setting[2]
- The overall purpose of this study was to understand the impact of CML disease and treatment from the patient perspective with a focus on quality of life, treatment satisfaction, daily productivity and adherence to treatment. This sub-analysis was conducted to evaluate potential predictors of CML treatment satisfaction

Methods

- **Study Design**: Study Design: Cross-sectional survey of approximately 300 CML patients in chronic phase (CML-CP) conducted in the United States (US) and Europe.
- **Source Population**: CML-Chronic Phase patients, age 18 years or older have been identified from the National Health and Wellness Survey, Lightspeed Research Chronic Illness Panel, and custom recruitment in the US and Europe (UK, France, Spain, Germany, Italy)
- **Data Collection**: Data for this study was collected among patients in the US and Europe through a self-administered patient questionnaire. Methods describing the developmental process of the instrument have been described previously.[2]
- The complete instrument included five validated patient-reported outcomes questionnaires (including Short Form-12, MD Anderson Symptom Inventory, Work Productivity and Activity Impairment, Cancer Treatment Satisfaction Questionnaire, and Patient Health Questionnaire-9), along with a series of 52 questions focused specifically on CML disease and treatment burden, treatment satisfaction and adherence, and physician-provider relationship.
- The following analysis includes data captured on the US cohort (n=152). European data collection is ongoing.
- **Statistical Analysis**: Analysis on variables related to CML treatment satisfaction was conducted using data collected from the Cancer Treatment Satisfaction Questionnaire (CTSQ) and through a series of questions that were focused on doing aspects of treatment, comorbidities, and negative medication experience (defined as a composite measure of side effect occurrence, level of bothersome side effects, and impact on daily activities).
- A structural equation model was created and tested to assess the impact on CML treatment satisfaction (as measured by the Satisfaction with Therapy (SWT) scale, a component of CTSQ) of:
  - **Negative medication experiences** (NMEs), including patients' experience of them and assessment of their impact and how bothersome they are.
  - **CML Treatment burden** variables, including prescription dosing restrictions and recommendations (Rx restrictions/recommendations) and pill burden (Number of CML Medications Taken per day and
  - Number of **comorbidities** experienced
- Model components were also examined at the item level, and individual items were correlated with the SWT scale (of CTSQ) to understand how individual questions related to satisfaction.

Results

- The sample consisted of 152 CML patients in the US with an average age of 51.5 years (SD ± 11.9); 61.8% were female. Median time since diagnosis was 4 years. Clinical and demographic characteristics of the cohort are included in **Table 1**.

Table 1: Demographic and Clinical Characteristics of CML Cohort

Characteristics	CML-CP Patients (n=152) n (%)
Gender	
Male	58 (38.2%)
Female	94 (61.8%)
Mean age (standard deviation (SD))	51.5 (±11.9) years
Time since CML diagnosis	
<2 years	33 (21.7%)
2<5 years	46 (30.3%)
≥ 5 years	73 (48.0%)
Comorbidities	
High Blood Pressure/Hypertension	34 (22.4%)
Arthritis	20 (13.2%)
Insomnia/Sleeping Difficulties	18 (11.8%)
Depression	17 (11.2%)
Gastric reflux	16 (10.5%)
Thyroid Condition	13 (8.6%)
Diabetes	9 (5.9%)
Household Income	
<$25,000	9 (5.9%)
$25,000-$49,999	33 (21.7%)
$50,000-$74,999	33 (21.7%)
>$75,000	68 (44.7%)
Decline to answer	9 (5.9%)
Education Level	
<College Education	20 (13.2%)
≥ College Education	132 (86.8%)

Results (cont'd)

Cancer Treatment Satisfaction Questionnaire (CTSQ)

- Results from the individual questions of the CTSQ are presented in **Table 2**.
- Mean scores were highest for Satisfaction with Treatment (SWT) components (82.05 ± 16.74) followed by Expectations of Therapy (ET) (63.59 ± 20.85) and Feelings about Side Effects (FSE) (53.7±27.2).
- As expected, all items (*except ET item: That cancer therapy would get rid of cancer)* significantly correlated with SWT. Higher expectations of therapy and the absence of side effects were correlated with greater treatment satisfaction.
- When stratified by time from CML diagnosis, patients diagnosed <2 years ago vs 5+ years ago were more likely to:
  - Have higher ET (69.85±21.19 vs mean=60.27±20.53; p=0.0299);
  - Perceive that their therapy would get rid of their CML (3.42±1.23 vs 2.55±1.35; p=0.002)
  - Have poorer FSE and perceive that therapy limited their daily activities (non-significant trend)

Table 2: CTSQ Response Items and Correlations of each Item with Satisfaction with Therapy (SWT)

Item	Mean (SD)	Correlation with CTSQ: SWT	P-value
Expectations of Therapy (ET)	63.6 (20.9)	0.35	<.0001
That cancer therapy (IV/pills) would help you return back to a normal life?	3.4 (1.3)	0.3	0.0002
That cancer therapy (IV/pills) would get rid of the cancer?	2.7 (1.4)	0.02	0.8099
That cancer therapy (IV/pills) would help the cancer from coming back?	3.5 (1.3)	0.23	0.0042
That cancer therapy (IV/pills) would stop the cancer from spreading?	3.7 (1.2)	0.18	0.0309
That cancer therapy (IV/pills) would help you live longer?	4.4 (0.9)	0.59	<.0001
Feelings about Side Effects (FSE)	53.7 (27.2)	0.63	<.0001
That your cancer therapy (IV/pills) limited your daily activities?[1]	2.8 (1.2)	-0.54	<.0001
Upset about the side effects?[1]	3.1 (1.3)	-0.55	<.0001
Overall, was taking cancer therapy (IV/pills) as difficult as you expected?[1]	2.5 (1.3)	-0.53	<.0001
Overall, were the side effects of cancer therapy (IV/pills) as you expected?	3.0 (1.3)	0.53	<.0001
Satisfaction with Therapy (SWT)	82.1 (16.7)	1	N/A
That cancer therapy (IV/pills) was worth taking even with the side effects?	4.3 (1.0)	0.62	<.0001
In general, in the last four weeks, how often did you think about stopping your cancer therapy (IV/pills)?[1]	1.8 (1.1)	-0.68	<.0001
Overall, how worthwhile was your cancer therapy (IV/pills)?	4.6 (0.7)	0.78	<.0001
Overall, how well did the benefits of cancer therapy (IV/pills) meet your expectations?	3.9 (1.0)	0.72	<.0001
How satisfied were you with the form of your cancer therapy (IV/pills)?	4.3 (0.8)	0.76	<.0001
Overall, how satisfied were you with your most recent cancer therapy (IV/pills)?	4.2 (0.8)	0.82	<.0001
Taking everything into consideration, if given the choice again, would you decide to take this cancer therapy treatment?	4.5 (0.9)	0.79	<.0001

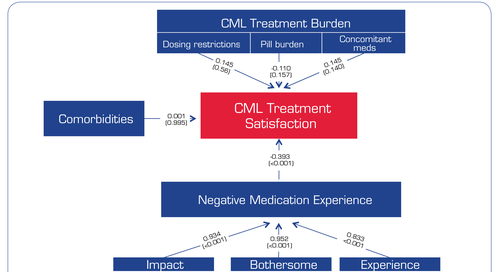
Note: Individual items are scored on a Likert scale from 1 to 5; higher scores indicate a greater degree of satisfaction.
[1]The three component scores range from 0-100.
[1]For reverse-scored items, a lower score indicates greater satisfaction.

Predictors of CML Treatment Satisfaction:

- Based on the developed structural equation model (SEM) (**Figure 1**), after adjusting for treatment burden variables and co-morbidities, negative medication experience (NME) was the strongest predictor (beta=0.4, p<0.001) of lower CML treatment satisfaction (as measured by CTSQ)
- The predictors included in the model (i.e. NME, CML dosing restrictions, CML pill burden, concomitant medications and comorbidities) accounted for 14% of the total variability in the CTSQ: SWT (indicating a good model fit)

Results (cont'd)

Figure 1: Structural Model of CML Treatment Satisfaction

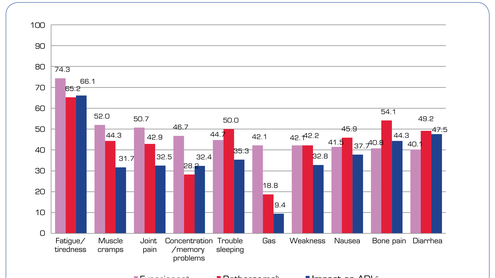


Note: Non-parenthetical values are standardized estimates (mean = 0 and standard deviation = 1) indicating strength and direction of association; these values can be compared across predictors. Associated p-values are presented in parentheses. Fit statistics indicate a great fit of the data to the model, as a non-significant χ^2 test is highly desirable, as are CFI and TLI >0.95, and RMSEA < 0.08. χ^2 Test of Model Fit: value 16.302; df 10; p-value 0.0913. CFI 0.986, TLI 0.969. RMSEA Estimate 0.064

Negative Medication Experience:

- Patients identified several Negative Medication Experiences (NMEs), including fatigue (experienced by 74% of patients) and gastrointestinal disturbances, as attributable to their CML treatment. These NMEs were cited as being bothersome and having an impact on work and activities of daily living, as well as patients' ability to enjoy hobbies and exercise. **Figure 2a** presents the top ten symptoms reported as being attributed to CML treatments
- **Figure 2b** presents the correlations of each of the components of NME with the CTSQ. Greater experience of NMEs, and greater perception of them as being bothersome and as having an impact on daily activities, were on average associated with lower satisfaction with treatment

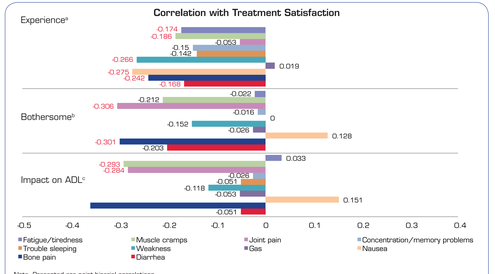
Figure 2a. Components of Negative Medication Experience – Most frequently reported symptoms attributed to CML Treatment (n=152)



[a]Patient-reported **experience** of conditions or medical issues possibly due to CML or its treatment in the past 4 weeks.
[b]Conditions experienced as most **bothersome** (presented as % of CML patients experiencing that condition and ≥2 conditions in total).
[c]Conditions experienced as having the biggest **impact** on ability to go about normal routine (presented as % of CML patients experiencing that condition and ≥2 conditions in total).

Results (cont'd)

Figure 2b. Components of Negative Medication Experience – Correlations with Treatment Satisfaction (n=152)



Note. Presented are point-biserial correlations.
Correlations in red indicate statistical significance at p<0.05
[a]Patient-reported **experience** of conditions or medical issues possibly due to CML or its treatment in the past 4 weeks.
[b]Conditions experienced as most **bothersome** (presented as % of CML patients experiencing that condition and ≥2 conditions in total).
[c]Conditions experienced as having the biggest **impact** on ability to go about normal routine (presented as % of CML patients experiencing that condition and ≥2 conditions in total).

CML Treatment Burden:

- **Table 3** presents the univariate results of the components of treatment burden (comprised of CML treatment dosing requirements, CML pill burden and concomitant medications) that were included in the final SEM
- Overall treatment burden did not have a significant impact on treatment satisfaction however CML pill burden (number of pills/treatment) was associated with poorer treatment satisfaction (r=-0.176, p<0.05)
- While treatment burden was not a predictor of treatment satisfaction 44% of patients did report that they would prefer a treatment which had fewer dosing restrictions

Table 3: CML Treatment Burden Items

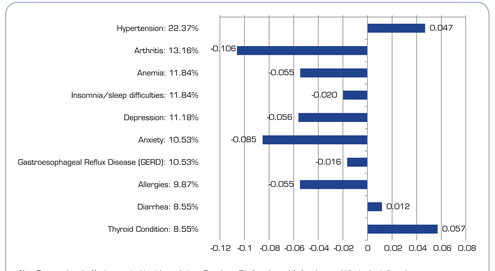
Components of CML Treatment Burden	
CML Pill Burden	**Mean (SD)**
Number of CML treatments per day	1.41 (0.62)
Number of pills per CML treatment	1.69 (1.07)
CML Treatment Dosing Restrictions/Recommendations	**N (%)**
Do not take with other non-CML medications	17 (11.2)
Take while fasting (on an empty stomach)	23 (15.1)
Take two or more pills at one time	27 (17.8)
Take twice each day	33 (21.7)
Take at specific hours apart (i.e., 12 hours apart)	47 (30.9)
Take once each day	76 (50.0)
Take at specific times of the day (i.e. in the morning or at night)	81 (53.3)
Do not take with certain foods (i.e. grapefruit juice)	86 (56.6)
Take with food	98 (64.5)
Must take with water	98 (64.5)
Concomitant medications	**Mean (SD)**
Number of Rx & OTC pills taken for non-CML conditions daily:	2.85 (3.43)
Number of pills (among those taking >0) taken for non-CML conditions:	
Once a day	3.09 (2.61)
Twice a day	0.77 (1.17)
Three times a day or more	0.19 (0.75)

Negative Medication Experience:

- **Figure 3** presents the most prevalent conditions reported by the CML cohort as comorbidities as well as corresponding correlations of each comorbidity to the CTSQ
- Based on this model, comorbidities did not significantly impact patients satisfaction with their CML treatment. As shown in Table 3, the average number of concomitant medications taken for these non-CML related conditions daily by this cohort was 2.85 (±3.43)

Results (cont'd)

Figure 3. Comorbid Conditions and Correlations with CML Treatment Satisfaction



Note: Presented on the X-axis are point-biserial correlations. Prevalence (% of total sample) of each comorbidity is also indicated.

Conclusions

- Supported by existing literature, the proposed structural model presented here emphasizes the importance of the patient experience among those with CML.
- Although patients are generally very satisfied with their treatment and do not feel substantially adversely affected by their CML, a number of negative medication effects were reported, including a high proportion of bothersome ones with a negative impact on normal daily routine (especially for fatigue, diarrhea, and bone pain).
- Overall, these NMEs had a deleterious association with patients' treatment satisfaction (beta = -0.40, p=0.0001), such that satisfaction on average decreased as level and impact of symptom burden increased.
- Although treatment burden and presence of comorbidities were not found to be associated with the level of treatment satisfaction, this may be due in part to:
  - Relatively young cohort of CML patients
  - Restricted variance on treatment burden (i.e., consistent dosing and number of pills)
  - Patients taking fewer than three additional medications for comorbidities
  - Possible underreporting of comorbidities, as implied by higher rates in previous studies[3]
- Further research and expansion of the proposed model will inform on patient reported disease and treatment specific attributes in a real-world setting.

References

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2. Talpaz M et al. Development of a cross-sectional survey to assess the experience of living with chronic myeloid leukemia (CML) from the patients' perspective. Poster session presented at: 15th Annual International Congress on Hematological Malignancies: Focus on Leukemias, Lymphomas, and Myeloma; 2011 Feb 17-20; Whistler, Canada
3. Hines P et al. Concomitant Medications and Comorbidities Among Patients with Chronic Myelogenous Leukemia Using Pharmetrics Data. Poster session presented at European Society of Hematology – International Conference; 2010 September 24-26; Washington, DC

Disclosures

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