Patient-Reported Outcomes Among Patients With Steroid-Refractory or -Dependent Chronic Graft-vs-Host Disease Randomized to Ruxolitinib vs Best Available Therapy

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Stephanie J. Lee

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Introduction

- Ruxolitinib was recently approved in the US for the treatment of patients aged ≥12 years with chronic graft-vs-host disease (cGVHD) who have failed 1 or 2 lines of systemic therapy\(^1\)
  - This approval was based on data from the randomized phase 3 trial REACH3, which evaluated ruxolitinib (N=165) vs best available therapy (BAT; N=164) in patients with steroid-refractory/-dependent (SR/D) cGVHD\(^2\)
- In comparison with BAT, ruxolitinib led to\(^2\)
  - Significantly higher overall response rate at week 24 (49.7% vs 25.6%; \(P<0.001\))
  - Prolonged median failure-free survival (not reached vs 5.7 months; \(P<0.001\))
  - Greater symptom improvement at week 24 (modified Lee Symptom Scale responders, 24.2% vs 11.0%; \(P=0.001\))
- Due to the considerable effect that cGVHD has on patient quality of life (QOL), patient-reported outcomes (PROs) are an important component for determining the full measure of a drug’s efficacy
- Here we present an in-depth analysis of the impact of ruxolitinib vs BAT on various PROs in patients with SR/D cGVHD in the REACH3 study

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Methods

- **Primary endpoint**: ORR (complete response + partial response) at week 24 using NIH consensus criteria for response

- **Key secondary endpoints**
  - Failure-free survival
  - Modified Lee symptom scale response at week 24 (≥7-point reduction from baseline in the summary symptom)

- **Other endpoints**: additional PROs (FACT-BMT, EQ-5D-5L, PGIS, PGIC) collected at baseline and every 4 weeks through week 24 or until treatment failure or discontinuation from the main study period
Symptom Burden Decreased Rapidly With Ruxolitinib

- A larger proportion of patients treated with ruxolitinib than BAT were mLSS responders at week 24 and at any visit up to week 24 (Panel A)
- Ruxolitinib was associated with a rapid and continued reduction in mean summary mLSS symptom score over time (Panel B)

**Panel A**

**Patients With mLSS Response at Week 24 and at Any Visit up to Week 24**

<table>
<thead>
<tr>
<th></th>
<th>RUX (N=165)</th>
<th>BAT (N=164)</th>
<th>OR, 2.62 (95% CI, 1.42-4.82)</th>
</tr>
</thead>
<tbody>
<tr>
<td>At week 24</td>
<td>24.2</td>
<td>11.0</td>
<td></td>
</tr>
<tr>
<td>At any visit</td>
<td>41.8</td>
<td>28.0</td>
<td></td>
</tr>
</tbody>
</table>

**Panel B**

**Mean Summary Symptom Score (mLSS) Over Time**

- OR, odds ratio.
- *Mean summary symptom scores are shown for patients with data available at each time point.*

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mLSS Response Rates Were Higher With Ruxolitinib Across Subgroups

- In the ruxolitinib arm, the mLSS response rate was similar in patients with moderate and severe cGVHD (Panel A)
- Patients treated with ruxolitinib were more likely to have an mLSS response than those treated with BAT regardless of overall response (Panel B) or steroid dose at week 24 (Panel C)

CR, complete response; PR, partial response. Patients with change to or addition of new systemic cGVHD treatment were counted as nonresponders (mLSS) irrespective of the summary symptom score value. *The analysis shown was done per the intention-to-treat principle. Ninety-two patients in the RUX arm and 87 patients in the BAT arm had valid summary symptom scores at week 24. **The patient populations shown had steroid exposure data for study interval day 155 to day ≤168. Of these patients, 89 in the RUX arm and 83 in the BAT arm had valid summary symptom scores at week 24.
Improvements in mLSS Subscales Corresponded With Physician-Assessed Organ Responses

- Mean reductions in mLSS subscale scores were greater in patients receiving ruxolitinib vs BAT (Panel A).
- Greater improvements in organ-specific subscales corresponded with higher objective cGVHD responses in the respective organ at week 24 in both arms (Panel B).
- After adjusting for treatment and baseline subscale score, each of the organ-specific regression models predicted a decrease in mLSS subscale score for those who had an organ response at week 24 (Panel C).

**Panels:**

- **Panel A:** Mean change from baseline in symptom score at week 24 by mLSS subscale.
- **Panel B:** Individual organ responses at week 24.
- **Panel C:** Linear regression analysis of organ response and mLSS subscale score at week 24.

**Footnotes:**

a For the analysis pertaining to organs (skin, eye, mouth, and lung), patients were included if they had both organ response and mLSS data for the specified organ at week 24 and ≥1 of the following criteria was met: involvement of the specified organ at randomization; organ involvement at any of the cycles up to cycle 7 day 1 (week 24); baseline mLSS score for the specified organ subscale was >0; the mLSS score for the specified organ subscale changed during any time up to cycle 7 day 1.

b For the psychological, energy, and nutrition mLSS subscales, change from baseline was calculated for all patients with available data at baseline and week 24 (RUX, n=85; BAT, n=81).

c CR or PR as documented by the investigator at week 24.

d Percentage is based on the number of patients who met the inclusion criteria for each organ as stated in footnote a.
Other PROs Reflected the Positive Effect of Ruxolitinib on Symptom Burden

- At week 24, patients treated with ruxolitinib were more likely to report no or mild symptoms according to PGIS (Panel A) and greater symptom improvement by PGIC (Panel B).
- EQ-5D-5L scores were numerically higher with ruxolitinib than with BAT; no difference between arms was observed in the FACT-BMT.
  - Findings suggest that ruxolitinib treatment is not accompanied by increased toxicity and confirm that multidimensional QOL was not reduced with ruxolitinib or BAT.

Percentage is calculated based on the number of patients with PGIS or PGIC data at week 24 (RUX, n=84; BAT, n=75). Odds ratios and 95% CIs were calculated using stratified Cochran-Mantel-Haenszel test.

PGIC, Patient Global Impression of Change; PGIS, Patient Global Impression of Severity; RUX, ruxolitinib.
Conclusions

• In REACH3, ruxolitinib treatment led to greater improvements in both physician-assessed cGVHD outcomes and PROs compared with BAT

  – Unlike in the BAT arm, symptom burden decreased rapidly in the ruxolitinib arm, with continuing improvement observed over time

• An organ response at week 24 in eye, skin, mouth, or lung was predictive of a decrease from baseline in the respective mLSS subscale score at week 24

• Patients were more likely to report a feeling of improvement in their symptoms when treated with ruxolitinib vs BAT, as assessed by PGIS and PGIC

• Importantly, the patient experience of organ-specific symptom improvements was consistent with physician-assessed objective organ responses, both of which were greater with ruxolitinib than with BAT
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