

Health-Related Quality of Life in Patients With Possible Tardive Dyskinesia Based on Patient and Clinical Assessments

ANDREW CUTLER: Hello. My name is Dr. Andrew Cutler from SUNY Upstate Medical University. Over the next few minutes, I will be discussing factors that impact health-related quality of life in patients with possible tardive dyskinesia through a review of the results from the real world RE-KINECT study. This activity sponsored Neurocrine Biosciences Inc is not certified for Continuing Medical Education. I'm presenting the data on behalf of Neurocrine. As an introduction, tardive dyskinesia, or TD, is a persistent and potentially irreversible movement disorder associated with prolonged exposure to antipsychotics or other dopamine receptor blocking agents. Evidence of the negative impact of TD on health-related quality of life and functioning, which has been studied primarily in patients with schizophrenia remains limited.

However, due to the expanding use of antipsychotics in other psychiatric disorders, research is needed to better understand the effects of TD on health-related quality of life and functioning in a broader patient population, particularly in patients with mood disorders who may be acutely aware of involuntary movements. RE-KINECT is a real world screening study of involuntary movements in psychiatric outpatients in the United States who were treated with anti-psychotic medications for any indication. All enrolled patients were asked to complete the EuroQoL dimension five level questionnaire, or EQ 5D 5L and the Sheehan Disability Scale, or SDS, before being evaluated by a clinician for possible TD. An in-depth analysis of the EQ 5D 5L and SDS data was conducted to assess the impact of possible TD on patient health-related quality of life. RE-KINECT included 37 outpatient psychiatry practices from across the United States. Adults aged 18 years and older were eligible to participate if they had three or more months of lifetime exposure to an antipsychotic, at least one clinician confirmed psychiatric disorder, and the ability to provide informed consent.

Per the study protocol patients, were assigned to one of two cohorts based on the clinician's observation and assessment of visible, involuntary movements. The protocol defined cohort 1 included 535 patients who had no visible movements or who had visible movements that assessed by the clinician as being inconsistent with possible TD. For this post hoc analysis, cohort 1 excluded all patients who had any involuntary movements, whether observed by the clinician or self-reported by the patient, resulting in a total of 450 patients.

This exclusion was done to better understand the effects of possible TD on health-related quality of life. The protocol defined cohort 2 included 204 patients with visible involuntary movements that were confirmed by the clinician as possible TD. For this post hoc analysis, a limited cohort 2 was also defined. This cohort included 111 patients who had clinician confirmed possible TD and a self-rated severity of some or a lot in at least one body region. The full protocol defined cohort 2 and the limited cohort 2 were both included in this post hoc analysis. The EQ 5D 5L included three assessments, the visual analog scale or VAS score, the mean utility score ranging from 0 defined as health state equivalent to death, to

one defined as perfect health, and dimension scores ranging from 1, defined as no problems, to 5 defined as extreme problems.

SDS assessments included domain scores ranging from 0, defined as no disruption due to illness, to 10 defined as maximum disruption due to illness. And total score, which was defined as the sum of domains scores in patients who had a score in at least two of three domains. Clinician and patient rated severity of possible TD included ratings in four body regions, ranging from 0 defined as none, to 2 defined as a lot. And summary score defined as the sum of all regions ranging from 0 to 8. The patient rated impact of possible TD included ratings on seven daily activities, ranging from 0, defined as none to 2, defined as a lot. And a summary score defined as the sum of all activities ranging from 0 to 14.

As mentioned earlier, the cohort 1 population used in this post hoc analysis only included patients with no involuntary movements, possible TD or otherwise, whether observed by the clinician or self-reported by the patient. EQ 5D 5L an SDS scores were analyzed for cohort 2 versus cohort one as follows. Mean scores were analyzed using a Welch's t-test. These analyzes were also adjusted for age, gender, and psychiatric diagnosis.

Distribution of EQ 5D 5L dimension scores were analyzed using Chi squared tests. A generalized linear regression model was used to analyze differences between cohort 2 and cohort 1 for the EQ 5D 5L utility and SDS total scores, with the following covariates to adjust for other potential confounding factors, age, gender overall health status, severity of psychiatric condition, functional status of patient, and psychiatric diagnosis.

Additional regression models were conducted using cohort 2 patients who had a rating of a lot on the following measures. Clinician rated severity of possible TD, patient rated severity of possible TD, and patient rated impact of possible TD. In the full cohort 2 of 204 patients and the limited cohort 2 of 111 patients, regression analyses were conducted to evaluate the effect of the following measures on EQ 5D 5L utility score and SDS total score.

Clinician rated severity of possible TD in four body regions and overall, which was the sum of four regions, patient rated severity of possible TD in four body regions and overall. The sum of four regions, and patient rated impact of possible TD on seven daily activities and overall the sum of seven activities. Based on unadjusted analyses as shown in this table, mean EQ 5D 5L utility and VAS scores indicated worse HRQOL and overall health state in cohort 2.

Patients with possible TD versus cohort 1, patients without possible TD or other abnormal or involuntary movements. A significant difference between cohorts was still found for EQ 5D 5L utility when the analysis was adjusted for age, sex, and psychiatric diagnosis. Mean SDS scores were not significantly different between cohorts.

The distribution of EQ 5D 5L dimension scores shown in this figure indicated that, compared to cohort 1, a higher percentage of cohort 2 patients reported moderate, severe, or extreme problems in all EQ 5D 5L dimensions. Results from the generalized linear regression model shown in this table indicated that for EQ 5D 5L utility and SDS total scores, the mean differences between cohort 2 and cohort 1 showed a significantly worse health state in cohort 2 patients who self-reported a lot of severity or a lot of impact, regardless of whether the analysis was adjusted or unadjusted.

In the analysis that included all cohort 2 patients or those with a clinician rating of a lot for severity, significant differences between cohort 2 and cohort 1 were found for EQ 5D 5L utility score but not SDS total score. As shown in this table, no significant association was found between clinician rated severity of

possible TD and EQ 5D 5L utility score or SDS total score. However, as shown in this table, patient ratings of possible TD did have statistically significant effects on health-related quality of life.

Regression coefficients between patient ratings and EQ 5D 5L demonstrated that in both cohort 2 populations, full and limited, patient rated impact scores were significantly associated with EQ 5D 5L utility score, regardless of whether the analysis was adjusted or not. In the limited cohort 2, the summary score for patient rated severity was significantly associated with EQ 5D 5L utility score. Significant associations were also found with patient rated severity in the lower extremities.

A similar pattern of results was found for SDS total score, as shown in this table. However, significance with the summary score for patient rated severity was found in the full cohort 2 rather than the limited cohort 2. In addition, significance in the full cohort 2 was found between patient rated severity in the head face region and SDS total score.

In conclusion, this post hoc analysis of reconnect data demonstrated the following points. Mean EQ 5D 5L and SDS scores indicated that possible TD had a negative impact on health-related quality of life, independent of age, sex, and psychiatric diagnosis. This impact was especially apparent in patients who self-rated themselves as having a lot of severity or a lot of impact on daily activities.

In the full cohort 2 and limited cohort 2, the summary score for patient rated impact was significantly associated with HRQoL and functioning. The summary score for patient rated severity was significantly associated with EQ 5D 5L utility in the limited cohort 2 and with SDS total score in the full cohort 2. No significant association was found between clinician rated severity and EQ 5D 5L utility or SDS total in either cohort 2, either full or limited.

These data suggests that clinicians should include specific questions at usual care visits regarding possible TD symptom's impact on daily activities to better determine the health-related impact. More research is needed to better understand the impact of TD on HRQoL in different psychiatric patient populations.