

# Impact of Symptom Exacerbations in Patients With Medically Treated Acromegaly

E. B. GEER<sup>1</sup>, D. CLEMMONS<sup>2</sup>, J. SISCO<sup>3</sup>, M. KOOBATIAN<sup>4</sup>, J. OKEYO<sup>4</sup>, T. QUOCK<sup>4</sup>, Y. WANG<sup>4</sup>, R. COLZANI<sup>4</sup>, A. KRASNER<sup>4</sup>

<sup>1</sup>Departments of Medicine and Neurosurgery, Memorial Sloan Kettering Cancer Center, New York, NY, USA; <sup>2</sup>Department of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA;

<sup>3</sup>Acromegaly Community, Grove, OK, USA; <sup>4</sup>Crinetics Pharmaceuticals, Inc., San Diego, CA, USA

## CONTACT INFORMATION

Eliza B. Geer, MD; E-mail: geere@mskcc.org

## BACKGROUND

- Patients with medically treated acromegaly often report breakthrough disease symptoms, defined as symptom exacerbations despite receiving regular treatment<sup>1-3</sup>
- Day-to-day symptom variability and its functional life impact have not been previously studied in patients with acromegaly receiving depot injections of a somatostatin receptor ligand (SRL)

## AIMS

- To quantify symptom severity and variability in patients with acromegaly on treatment with injected depot SRLs (octreotide or lanreotide)
- To assess acromegaly symptom exacerbation frequency (ASEF), a direct measure of breakthrough symptoms, as a measure of symptom variability

## METHODS

- 58 patients were recruited from the USA, UK, and Canada; most (88%) were referred from 2 patient advocacy groups and the remainder recruited through social media
- Patients receiving injected depot octreotide or lanreotide (n=31) completed a series of 3 web-based surveys: a background survey of patient characteristics, a daily symptom survey, and an exit survey

### Online Surveys: Patients on Injected SRLs

Daily Surveys*
<ul style="list-style-type: none"> <li>Completed daily for 90 consecutive days</li> <li>7 core acromegaly symptoms: headache, joint pain, sweating, fatigue, leg weakness, swelling, numbness/tingling</li> <li>2 additional acromegaly symptoms: difficulty sleeping, difficulty with short-term memory</li> <li>Severity of each symptom rated for the previous 24 hours on a scale from 0–10</li> </ul>
Exit Survey
<ul style="list-style-type: none"> <li>Questions pertaining to multiple aspects of acromegaly and treatment, including disease burden, activities of daily living, and life satisfaction over the preceding 3-month period</li> </ul>

\*Includes 9 symptoms found to be important to patients based on qualitative research.<sup>4</sup>

- Summary statistics of symptom severity and symptom variability from the daily survey were calculated, and correlations with life impact items from the exit survey were explored
- Symptom variability was expressed as:
  - Standard deviation of the severity score (7 core symptoms)
  - ASEF defined as ≥2-point increase for any individual symptom score, comparing the 2-day average of the current period to the previous 2-day average
    - 2-point differences identified as clinically meaningful in patient interviews

## RESULTS

### Patient Characteristics

	Patients (n=31)
Age, years, mean (SD)	53.4 (13.6)
Sex, n (%)	
Female	24 (77.4)
Male	6 (19.4)
Prefer not to say	1 (3.2)
Comorbid conditions, n (%)	
Arthritis	14 (45.2)
Diabetes	12 (38.8)
Sleep apnea	3 (9.7)
Carpal tunnel syndrome	1 (3.2)
Heart failure	1 (3.2)
Previous pituitary surgery, n (%)	31 (100)
Medical treatment, n (%)	
Depot SRL monotherapy	15 (48.4)
Depot SRL + non-SRL therapy	16 (51.6)
>3 injections during the 3-month survey period, n (%)*	15 (48.4)

\*Depot SRLs not approved for administration more frequently than monthly.

### Symptom Exacerbations Occur >2×/Week

Acromegaly Symptom	Exacerbation Rate (ASEF) Mean (SE) percent of days
Any symptom*	31.6 (4.0)
Difficulty sleeping	9.1 (1.6)
Headache	7.7 (1.4)
Fatigue	6.9 (1.2)
Sweating	5.3 (1.0)
Joint pain	4.9 (0.9)
Swelling	4.1 (1.0)
Leg weakness	3.9 (0.8)
Numbness/tingling	3.7 (1.0)
Difficulty with short-term memory	3.1 (0.9)

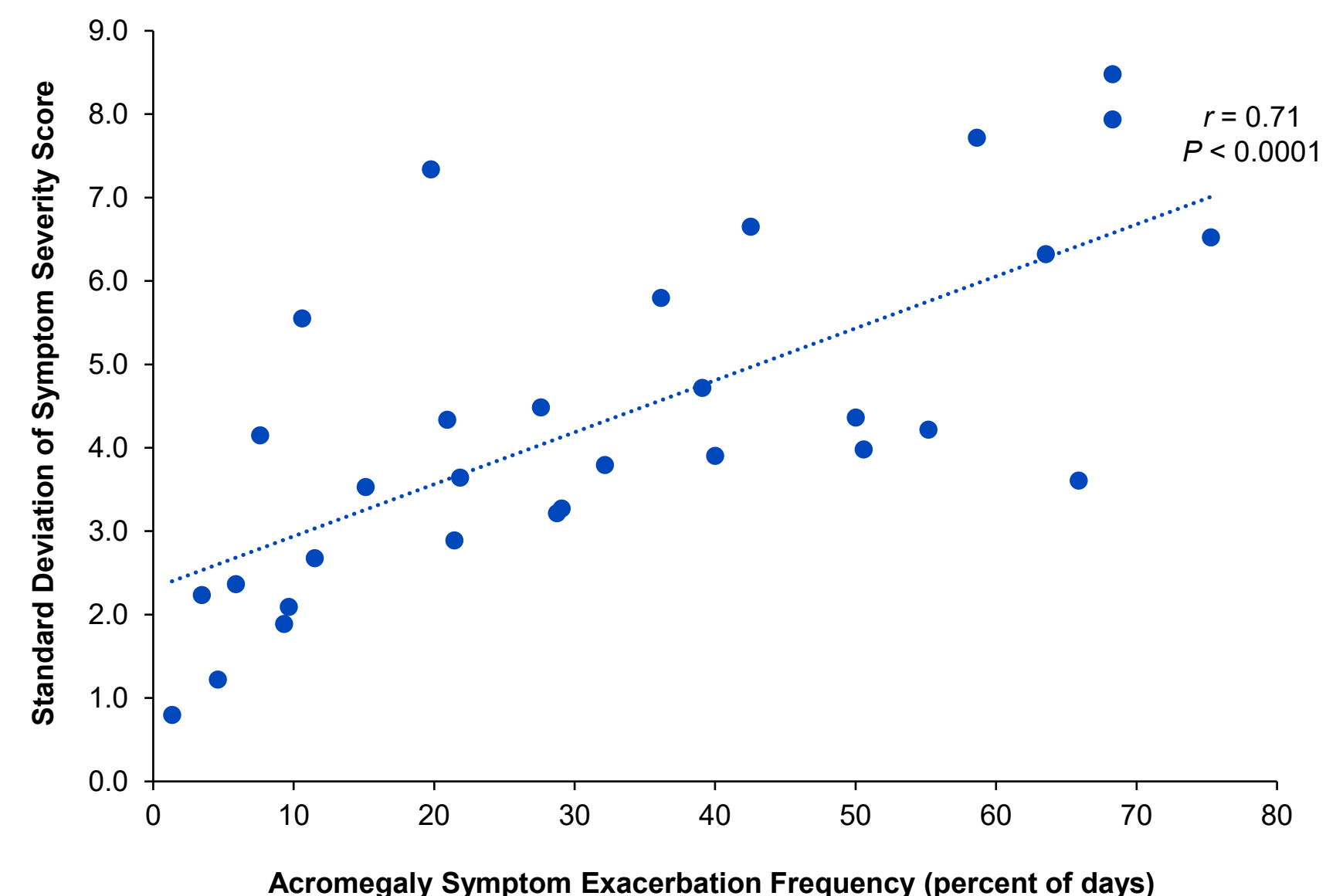
\*Of the 9 symptoms assessed in the daily survey. ASEF = acromegaly symptom exacerbation frequency.

### Symptom Severity and Variability Were Associated With Impairments in Activities of Daily Living and Life Satisfaction

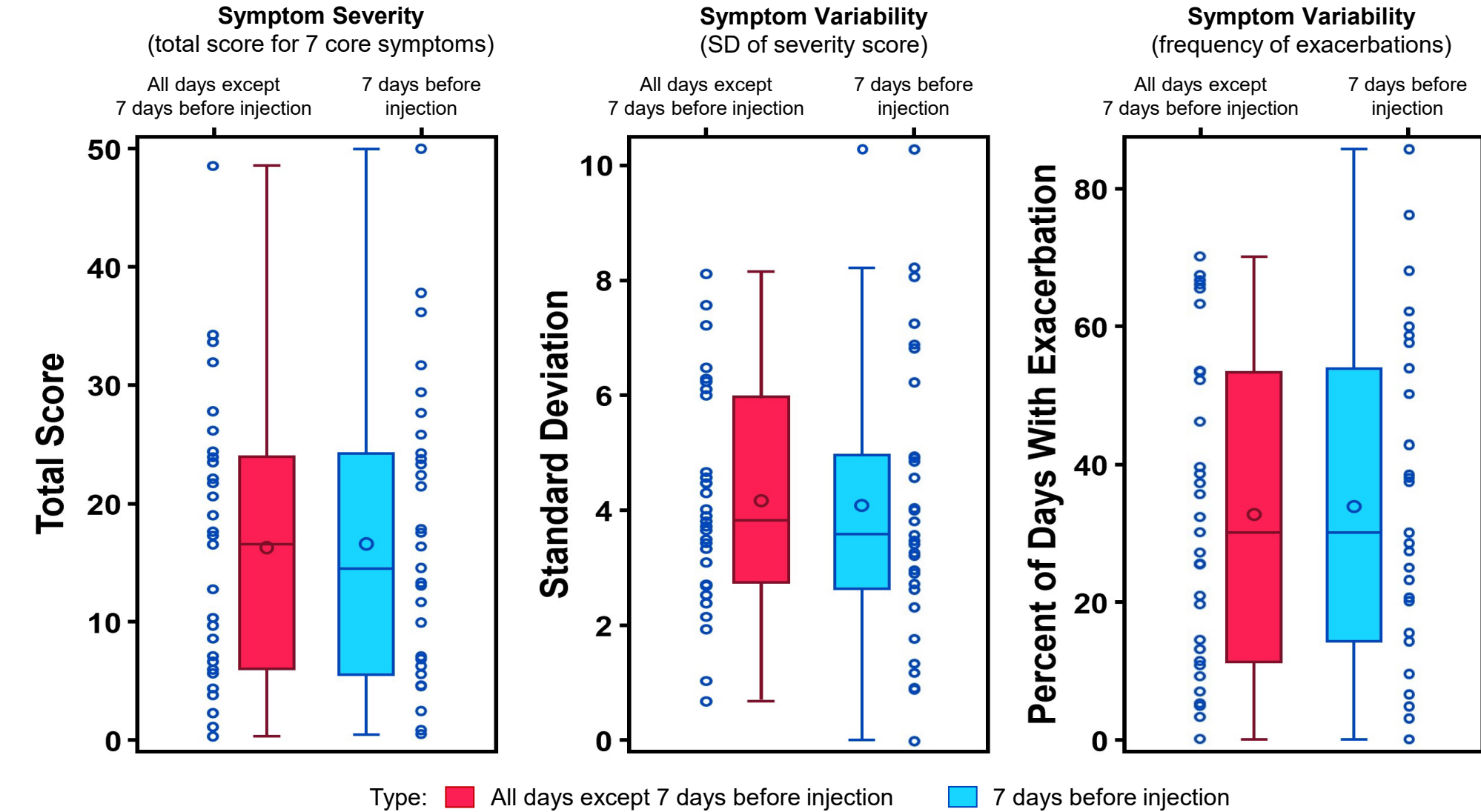
	Symptom Severity (total score for 7 items)	Symptom Variability
Interference of acromegaly with life overall	$r = 0.53$ ; $P = 0.003$	SD: $r = 0.38$ ; $P = 0.038$ ASEF: $r = 0.45$ ; $P = 0.012$
Interference with ability to work outside the home	$r = 0.55$ ; $P = 0.007$	SD: $r = 0.57$ ; $P = 0.004$ ASEF: $r = 0.39$ ; $P = 0.068$
Interference with driving a car	$r = 0.63$ ; $P < 0.001$	SD: $r = 0.43$ ; $P = 0.031$ ASEF: $r = 0.39$ ; $P = 0.052$
Daily activity affected by acromegaly	$r = 0.60$ ; $P < 0.001$	SD: $r = 0.59$ ; $P < 0.001$ ASEF: $r = 0.28$ ; $P = 0.130$
Interference with being able to enjoy the moment	$r = 0.58$ ; $P < 0.001$	SD: $r = 0.44$ ; $P = 0.014$ ASEF: $r = 0.27$ ; $P = 0.153$
Interference with taking care of children	$r = 0.69$ ; $P = 0.006$	SD: $r = 0.73$ ; $P = 0.003$ ASEF: $r = 0.56$ ; $P = 0.036$
Interference with enjoying time with family	$r = 0.47$ ; $P = 0.013$	SD: $r = 0.52$ ; $P = 0.005$ ASEF: $r = 0.47$ ; $P = 0.014$
Treatment satisfaction for improving quality of life	$r = -0.48$ ; $P = 0.005$	SD: $r = -0.32$ ; $P = 0.070$ ASEF: $r = -0.39$ ; $P = 0.031$
Number of self-reported urgent doctor visits related to acromegaly	$r = 0.24$ ; $P = 0.235$	SD: $r = 0.36$ ; $P = 0.067$ ASEF: $r = 0.39$ ; $P = 0.046$

ASEF = acromegaly symptom exacerbation frequency; SD = standard deviation of symptom severity score.

### ASEF Strongly Correlated With Standard Deviation



### Symptom Exacerbations Occurred Frequently Throughout the Injection Intervals



Horizontal lines show median value, boxes show interquartile range, open circles show mean value, and whiskers show minimum and maximum values.

## RESULTS

- Patients experienced multiple acromegaly symptoms: 83.9% of patients reported having ≥6 of the 9 assessed symptoms (symptom presence defined as individual item score >2 [range, 0-10])
- As in the larger study population, symptom exacerbations occurred randomly throughout the study in patients who received ≤3 SRL injections during the 3-month dosing period
- There were no differences in symptom severity or variability in patients using SRL monotherapy versus SRL combination therapy

## CONCLUSIONS

- In an outpatient population of patients with acromegaly treated with depot SRLs, symptom exacerbations occurred frequently throughout the injection cycle (on average, >2×/week) despite approximately 50% of patients reporting combination medical therapy or off-label increased injection frequency
- Both symptom severity and symptom variability were found to be correlated with numerous aspects of self-reported functioning, treatment satisfaction, and overall life satisfaction
- A simple daily symptom assessment can provide clinically meaningful information pertaining to adequacy of disease control during medical treatment for patients with acromegaly

## REFERENCES

- Geer EB, et al. *BMC Endocr Disord.* 2020;20(1):117.
- Geer EB, et al. *Pituitary.* 2020;23(2):140-148.
- Strasburger CJ, et al. *Eur J Endocrinol.* 2016;174(3):355-362.
- Martin S, et al. *J Patient Rep Outcomes.* 2023;7(1):15.

For acknowledgements and author disclosures, please use the QR code.



**ACKNOWLEDGMENTS**

The authors thank the study participants for their time and effort in responding to the surveys. The study was funded by Crinetics Pharmaceuticals, Inc. Technical editorial and medical writing assistance were provided under the direction of the authors by Synchrony Medical Communications, LLC, West Chester, PA, USA; funding for this support was provided by Crinetics Pharmaceuticals, Inc.

**AUTHOR DISCLOSURES**

EG reports serving as a consultant for Camurus, Crinetics Pharmaceuticals, HRA Pharma/Esteve, Recordati, and Xeris; and serving as an investigator for research grants to MSKCC from Recordati and Sparrow. DC reports serving as a consultant for Amolyt, Crinetics Pharmaceuticals, and Novo Nordisk. JS reports serving as a consultant for Alexion, Camurus, Chiesi, Debiopharm, and Recordati; and serving on advisory boards for Crinetics and Pfizer. MK, JO, TQ, YW, RC, and AK are employees of Crinetics Pharmaceuticals.