Development of a Disease Activity Index for the Assessment of VEXAS Syndrome (VEXAS-DAI)

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CONCLUSIONS

The VEXAS-DAI is designed to measure active inflammation in patients with VEXAS syndrome. Work is ongoing to validate this instrument in the context of the randomized PAXIS trial (Beck DB, *et al.* EULAR POS0379)[1]

INTRODUCTION

- VEXAS syndrome (Vacuoles, E1 ubiquitin-activating enzyme, X-linked, Autoinflammatory, Somatic) is a systemic disease characterized by a complex overlap of inflammatory and hematologic features[2,3]
- Inflammatory manifestations in VEXAS involve multiple organs, with clinical features that vary significantly between patients
- Presentations are highly heterogeneous, and the severity of inflammation can range widely, making disease assessment and treatment decisions challenging[4]
- Currently, no tool exists to specifically assess disease activity or response to therapy in VEXAS syndrome

OBJECTIVE

- To develop a comprehensive Disease Activity Index (DAI) to measure clinically significant inflammatory activity and provide a standardized tool for evaluating treatment response

METHODS

Step 1: Instrument development

- Clinical items representing organ involvement and degree of inflammation were selected for inclusion based on manifestations described in Weeks LD, *et al*. EULAR POS1124[5]
- Grading of severity for each clinical manifestation was adapted from the Common Terminology Criteria for Adverse Events (CTCAE) v5.0
- The VEXAS-DAI was developed based on input from a multidisciplinary group of 18 expert rheumatology and hematology physicians using modified Delphi methodology

Step 2: Instrument scoring

- Clinical validation of the VEXAS-DAI was performed by rating disease activity using Physician Global Assessment (PGA) of inflammation severity using test cases (1 case per grade per item) administered via an online polling tool
- PGA scores ranged from 0 (no active inflammation) to 100 (highest possible level of active inflammation), providing a framework for the DAI scoring system

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RESULTS

Consensus achieved on items to be included in the DAI

- The VEXAS-DAI was finalized after 4 rounds of revision, resulting in an instrument with 13 organ systems, including a total of 31 items (**Table 1**)

Table 1. VEXAS-DAI domains

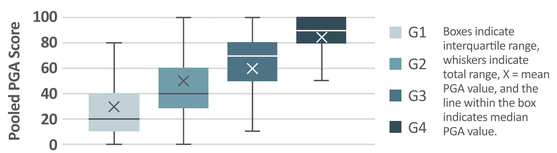
Domain	Items	Max score
Inflammatory-type rash	2	4
Chondritis	3	3
Periorbital involvement	1	2
Genitourinary involvement	1	3
Ophthalmologic involvement	5	4
Pulmonary involvement	3	4
Cardiovascular involvement	3	4
Neurologic involvement	5	4
Oral/gastrointestinal involvement	3	4
Renal involvement	1	4
New thrombosis/thromboembolism	1	0
Joint involvement	1	2
Constitutional symptoms	2	2
Total	**31 items**	**40**

DAI, disease activity index; VEXAS, Vacuoles, E1 ubiquitin-activating enzyme, X-linked, Autoinflammatory, Somatic.

Scoring developed based on PGA survey of test cases

- PGA of inflammation severity increased with increasing item grade overall (**Figure 1**) and within each organ system (**Figure 2**), justifying use of item grading to derive instrument scoring
- Minimal additive effects were observed when multiple manifestations co-occurred within the same domain (data not shown), justifying use of the highest grade within each domain to derive domain score

Figure 1. Pooled PGA responses to test cases by grade



PGA, Physician Global Assessment.

- Substantial overlap in PGA was observed between adjacent grades of the following items: episcleritis G1/2, conjunctivitis G1/2, optic neuritis G3/4, peripheral sensory neuropathy G2/3, peripheral motor neuropathy G1/2 and 3/4, and meningoencephalitis G1/2. For these items, scoring was merged, e.g., PGA scores for G1/2 episcleritis were both consistent with overall G1 scores, justifying scoring rules in which both G1 and G2 episcleritis add only 1 point to the total instrument score

Figure 2. Median PGA scores indicating inflammation severity from administered test cases

*Multiple items were queried per grade reflecting different dermatologic manifestations.
BSA, body surface area; G, grade; GI, gastrointestinal; PGA, Physician Global Assessment.

- The expert panel voted that 'New thrombosis/thromboembolism' should be captured but not scored, as isolated thrombosis may not be a reliable indicator of active inflammation, and joint involvement should be based on presence or absence of arthritis in any joint(s)
- Total score is the sum of the domain scores (range: 0–40, **Table 1**). Higher scores indicate more active inflammation

References
1. Beck DB, et al. EULAR 2025 European Congress of Rheumatology; June, 11–14, 2025; Barcelona, Spain. Poster POS0379. **2.** Beck DB, et al. *N Engl J Med* 2020;383:2628–2638; **3.** Beck DB, et al. *JAMA* 2023;329:318–324; **4.** Koster MJ, et al. *Am J Hematol* 2024 99:284–299; **5.** Weeks LD, et al. Presented at: EULAR 2025 European Congress of Rheumatology; June 11–14, 2025; Barcelona, Spain. Poster POS1124.

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