Use of the Glucocorticoid Toxicity Index-Metabolic Domains Instrument to Quantify Glucocorticoid Toxicity in Adults with Chronic Inflammatory Demyelinating Polyneuropathy Using Electronic Health Records in the United States

RWD145

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INTRODUCTION

- Chronic inflammatory demyelinating polyneuropathy (CIDP) is a rare, immune-mediated peripheral neuropathy characterized by demyelination of motor and sensory nerves.[1,2]
- First-line treatment for CIDP includes corticosteroids.[3] However, with prolonged use glucocorticoids have significant toxicity risks. Side effects include osteoporosis, diabetes, obesity, cataracts, infection, and hypertension. Studies link longer treatment duration to higher toxicity.[4]
- The Glucocorticoid Toxicity Index (GTI) is the only weighted, standardized clinical outcome assessment (COA) of glucocorticoid toxicity.
- An abbreviated version, the GTI-Metabolic Domains (GTI-MD), was developed for use in clinical practice.[5] The GTI-MD correlates highly with the GTI.

OBJECTIVE

- To assess the feasibility of adapting the GTI-MD for patients with CIDP using retrospective data.

METHODS

- GTI uses 9 domains (body mass index [BMI], blood pressure [BP], glucose tolerance, lipid metabolism, bone mineral density, glucocorticoid myopathy, skin toxicity, neuropsychiatric effects and infection) to evaluate steroid toxicity in clinical trials, while GTI-MD uses 4 domains commonly collected in routine clinical practice, making it a practical COA to incorporate in datasets in less time (**Figure 1**).
- The original GTI-MD criteria include BMI, BP, glucose levels, and lipid levels lab values. However, due to the limited sample size in this study the criteria were adapted.
- In this study GTI-MD was calculated from baseline to the last available lab set in the study period.

Figure 1: Overview of GTI-MD

Definition
An abridged version that correlates highly with the GTI to quantify steroid toxicity between two time points (such as steroid use onset/index and a designated time point)

Application
A validated clinical outcome assessment of steroid toxicity for use in clinical practice and HEOR

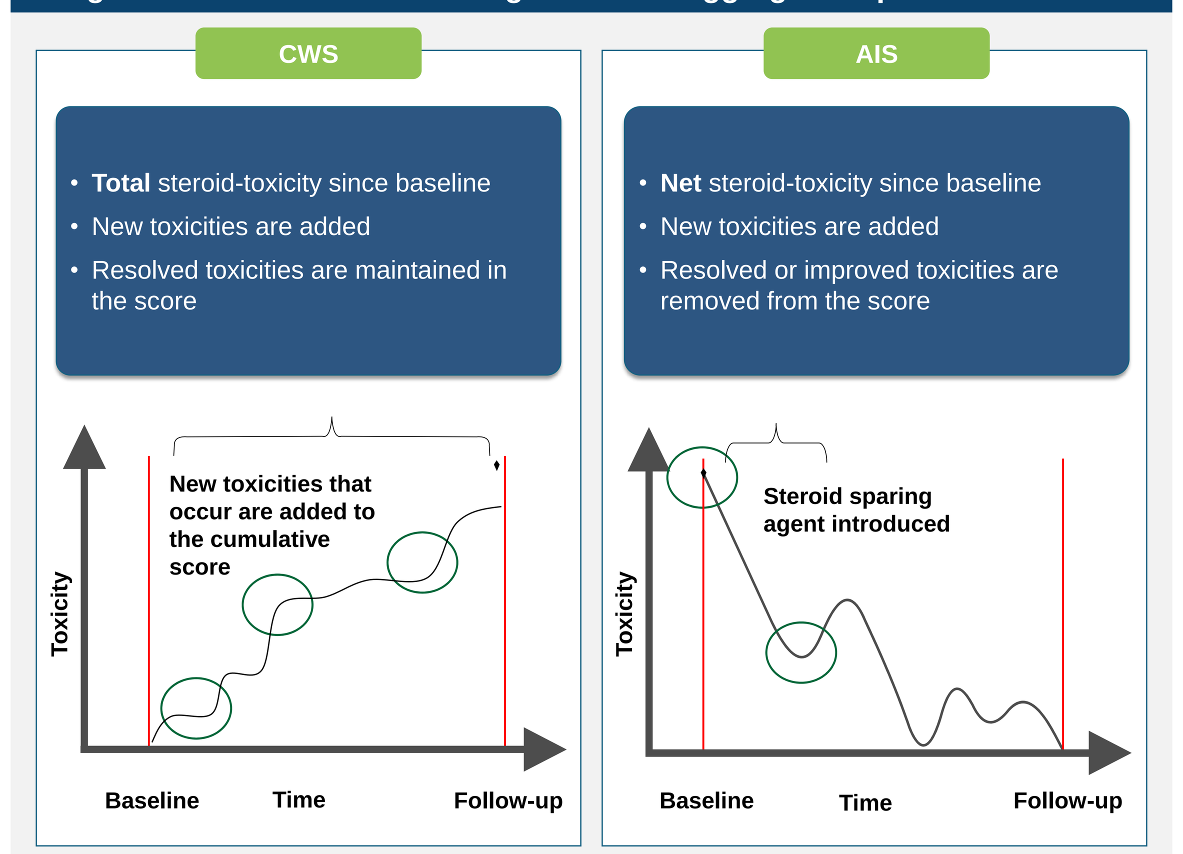
Domains assessed
- BMI
- Blood pressure
- Glucose tolerance
- Lipid metabolism

BMI, body mass index; GTI, Glucocorticoid Toxicity Index; GTI-MD, GTI-Metabolic Domains; HEOR, health economics and outcomes research.

Cumulative Worsening Score (CWS) and Aggregate Improvement Score (AIS)

- The GTI-MD measures toxicity using two scores, the CWS and the AIS (**Figure 2**).

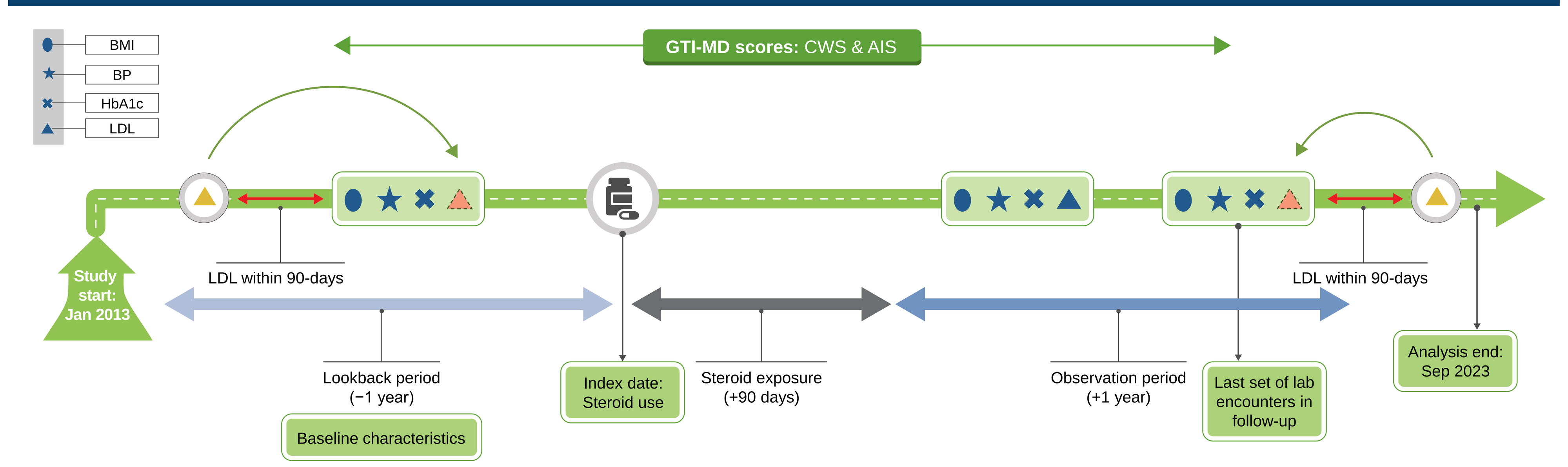
Figure 2. Cumulative worsening score and aggregate improvement score



AIS, Aggregate Improvement Score; CWS, Cumulative Worsening Score.

- This retrospective cohort study utilized Optum® Market Clarity de-identified data (Market Clarity) from January 2007 to September 2023 to identify adults with CIDP.
- CIDP patients were selected based on: ≥2 CIDP claims, ≥30–≤365 days apart, ≥1 nerve conduction test within 90 days of a confirmed CIDP diagnosis, patients with >1 CIDP claim during the selection period (Jan 2014–Jun 2022).
- Patients with 2+ exclusionary diagnosis from 1-year before CIDP diagnosis to steroid index date were excluded.
- Steroid users (SU) were defined by first steroid claim (index date) after CIDP claim in selection period. Steroid-naïve (SN) patients, defined as patients who did not receive steroids during the study period, were matched based on age, gender, days to steroid use from first CIDP diagnosis in selection period.
- Patients were not required to have low-density lipoprotein (LDL) lab value within the 14-day window for labs (BP, BMI, Hemoglobin A1C), however, they needed at least 1 LDL lab value within 90-days of the window to serve as a proxy (**Figure 3**).

Figure 3. Selection criteria



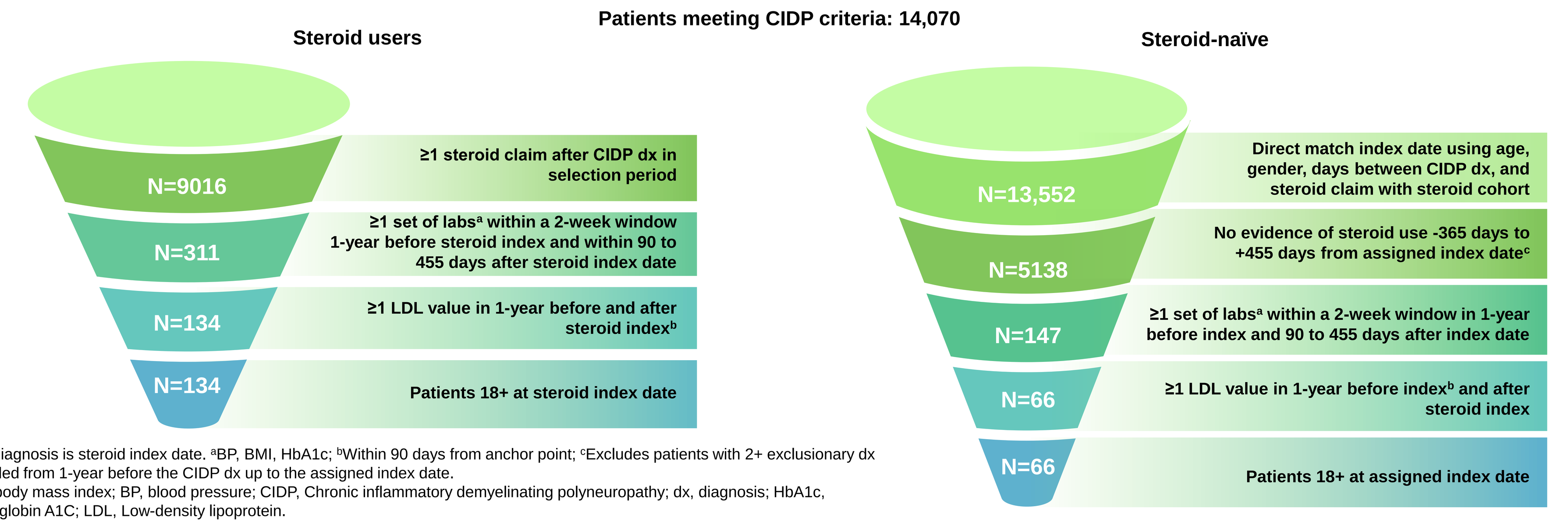
AIS, Aggregate Improvement Score; BMI, body mass index; BP, blood pressure; CWS, Cumulative Worsening Score; GTI-MD, Glucocorticoid Toxicity Index-Metabolic Domains; HbA1c, Hemoglobin A1C; LDL, Low-density lipoprotein.

RESULTS

Patient selection

- Among the 14,070 patients with CIDP, 134 were SU and 66 were SN **(Figure 4)**.

Figure 4: Patient selection



First diagnosis is steroid index date. [a]BP, BMI, HbA1c; [b]Within 90 days from anchor point; [c]Excludes patients with 2+ exclusionary dx recorded from 1-year before the CIDP dx up to the assigned index date.
BMI, body mass index; BP, blood pressure; CIDP, Chronic inflammatory demyelinating polyneuropathy; dx, diagnosis; HbA1c, Hemoglobin A1C; LDL, Low-density lipoprotein.

Table 1. Baseline demographics and characteristics

Characteristics	Steroid users n=134	Steroid naïve n=66
Age at index, mean (SD)	63.0 (11.5)	62.2 (11.4)
Gender, n (%)		
Male	77 (57.5)	52 (78.8)
Female	57 (42.5)	14 (21.2)
CCI, mean (SD)	3.5 (3.0)	3.2 (2.7)
0	21 (15.7)	12 (18.2)
1	14 (10.4)	9 (13.6)
2	28 (20.9)	8 (12.1)
3	13 (9.7)	16 (24.2)
4	15 (11.2)	5 (7.6)
≥5	43 (32.1)	16 (24.2)
Baseline GTI, mean (SD)	20.7 (22.5)	24.5 (23.5)
Presence of common CIDP comorbidities, n (%) (Top 5)		
Neuropathic pain	100 (74.6)	48 (72.7)
Hypertension	96 (71.6)	46 (69.7)
Hypercholesterolemia	81 (60.4)	33 (50)
Diabetes without chronic complications	71 (53)	41 (62.1)
Back pain	57 (42.5)	22 (33.3)

CCI, Charlson Comorbidity Index; CIDP, Chronic inflammatory demyelinating polyneuropathy; GTI, Glucocorticoid Toxicity Index; SD, standard deviation.

Baseline characteristics

- The mean (standard deviation [SD]) ages of SU and SN cohorts were 63.0 (11.5) years and 62.2 (11.4) years, respectively.
- Both the cohorts primarily comprised of male participants (SU: 57.5%; SN: 78.8%).
- The mean (SD) Charlson Comorbidity Index (CCI) scores were 3.5 (3.0) and 3.2 (2.7) in the SU and SN cohorts, respectively.
- High proportion of the patients had a CCI score of ≥5 (SU: 32.1% and SN: 24.2%, respectively) indicating towards pre-existing severe health conditions.
- The mean (SD) baseline GTI was higher in the SN (24.5 [23.5]) cohort compared to the SU (20.7 [22.5]) cohort.
- In both cohorts the most prevalent comorbidities were neuropathic pain, hypertension, and hypercholesterolemia (**Table 1**).

Steroid contraindications

- Hypertension was the most common pre-existing contraindication in both cohorts (SU:71.6%; SN: 69.7%).
- A high prevalence of other steroid contraindications was observed in the naïve cohort (diabetes without chronic complications, diabetes with chronic complications, and renal diseases) (**Table 2**).

Table 2. Steroid contraindications

Pre-existing contraindications for steroids 1-year before index date, n (%)	Steroid users, n=134	Steroid-naïve, n=66
Hypertension	96 (71.6)	46 (69.7)
Diabetes without chronic complications	71 (53)	41 (62.1)
Diabetes with chronic complications	50 (37.3)	27 (40.9)
History of severe depression, anxiety or psychosis	46 (34.3)	15 (22.7)
Osteoarthritis	41 (30.6)	9 (13.6)
Rheumatoid arthritis	41 (30.6)	1 (1.5)
GERD	37 (27.6)	10 (15.2)
Anxiety	34 (25.4)	11 (16.7)
Depression	29 (21.6)	9 (13.6)
Cataract	25 (18.7)	12 (18.2)
Renal disease	25 (18.7)	15 (22.7)
Obesity	24 (17.9)	9 (13.6)
Mild liver disease	22 (16.4)	3 (4.5)
Chronic kidney disease	18 (13.4)	12 (18.2)
Congestive heart failure	18 (13.4)	13 (19.7)
Autoimmune conditions with no steroid use advised	15 (11.2)	1 (1.5)
Glaucoma	12 (9)	6 (9.1)
Cirrhosis/liver disease	6 (4.5)	1 (1.5)
Peptic ulcer disease	5 (3.7)	1 (1.5)
History of thromboembolism	4 (3)	9 (13.6)
Epilepsy	3 (2.2)	2 (3)
AIDS/HIV	2 (1.5)	1 (1.5)
Moderate or severe liver disease	2 (1.5)	1 (1.5)
Chronic or recurrent infections	0 (0)	10 (15.2)
Tuberculosis	0 (0)	1 (1.5)

AIDS/HIV, acquired immune deficiency syndrome/human immunodeficiency virus; GERD, Gastroesophageal Reflux Disease.

GTI-MD scores

- Evidence of high steroid contraindications indicate that steroid toxicity may be biased in the naïve cohort, and thus, we present GTI-MD scores for the steroid users only.
- The mean (SD) CWS was 20.68 [22.49] and AIS was 2.4 [33.56] (**Table 3**).
- GTI-MD scores calculated for CIDP are similar to scores calculated in Myasthenia Gravis using real-world data (CWS: 22.6 [22.8]; AIS: 4.9 [34.5])[6].

Table 3. Summary of GTI-MD scores

GTI-score or domain	Steroid users (n=134)
CWS	
Mean (SD)	20.68 (22.49)
Range	0 to 98
AIS	
Mean (SD)	2.4 (33.56)
Range	−84 to 97
Minimal Clinically Important Difference (MCID)	
CWS	
≥10 points	88 (66)
≥20 points	51 (38)
≥30 points	33 (25)
AIS	
≥10 points	115 (86)
≥20 points	73 (54)
≥30 points	47 (35)

AIS, Aggregate Improvement Score; CWS, Cumulative Worsening Score; GTI, Glucocorticoid Toxicity Index; GTI-MD, Glucocorticoid Toxicity Index-Metabolic Domains; SD, standard deviation.

SUMMARY

- Evaluating GTI-MD in real-world data of patients with CIDP is feasible with certain caveats.
- Patients with CIDP who are steroid naïve have higher proportions of steroid comorbidities which could influence calculating steroid toxicity using GTI-MD.
- GTI-MD scores calculated in CIDP in the real-world are comparable to Myasthenia Gravis.

Limitations

- As CIDP is a rare disease and the strict selection criteria, the limited study sample size limits the generalizability to a wider CIDP population.
- There may be a selection bias towards patients who require frequent lab testing and received the required lab tests within a two-week period indicating a sicker cohort.
- Electronic Health Records data contains information on prescriptions. It was assumed that the patient has filled the prescription and was compliant.

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DISCLOSURES:
Cécile Blein, Clémence Arvin-Berod, and Swapna Karkare are employees of argenx. John Stone is from Harvard Medical School. Martha Stone is an employee of Steritas. Rucha Kulkarni, Yachendra Challa, Pranav Moudgalya, Anthony Nguyen, and Amit Goyal are employees of ZS Associates and serve as paid consultants for argenx.

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