GLP-1 receptor agonist-associated thrombocytopenia: A Novel/Extensive Pharmacovigilance Evaluation From Southern Network on Adverse Reactions (SONAR-AI)

Demir C. Uslu, BS[1]; Charles L. Bennett, MD, PhD[1]; Gretchen L. Watson, PhD[1]; Mia Lynch[1] *on behalf of SONAR*
[1]University of South Carolina College of Pharmacy, Columbia, SC, USA

RWD133

At a Glance

Clinical Signal

7	2,000 /µL	54	$500
Clinician-confirmed cases	Median platelet nadir	Additional FAERS cases	Total Study Cost

SONAR-AI Performance

6 Weeks	95%
Time to Study Completion	Case Data Completeness

Background

- GLP-1 receptor agonists (semaglutide, tirzepatide, liraglutide, exenatide) are widely prescribed for type 2 diabetes and obesity
- Thrombocytopenia is **NOT LISTED** in regulatory-approved product labels across the US, EU, Canada, Australia, Japan, or New Zealand
- No prior clinician-adjudicated case series of GLP-1RA–associated thrombocytopenia existed
- Pre-marketing trials are underpowered to detect rare hematologic toxicities
- Cumulative GLP-1RA exposure has increased among individuals without diabetes, younger patients, and those with fewer cardiometabolic comorbidities, heightening importance of post-marketing surveillance
- Prior RADAR/SONAR investigations identified thrombocytopenia associated with clopidogrel (NEJM, 2000) and COVID-19 vaccines (Lancet Haematology, 2022)

Objectives

- Clinically characterize GLP-1RA–associated thrombocytopenia using clinician-confirmed cases
- Evaluate the efficacy, completeness, cost, and timeliness of AI-assisted pharmacovigilance compared to prior surveillance methodologies
- Compare data collection metrics across three generations of pharmacovigilance: RADAR, SONAR, and SONAR-AI

Methods

Case Identification
- 3 initial cases identified by hematologists at a Manhattan center; 4th reported by Seattle hematologist
- AI identified 2 cases from conference presentations; 1 from a scoping review article
- Cases included if: thrombocytopenia developed after GLP-1RA initiation, alternative causes reasonably excluded, and sufficient clinical detail available

Data Sources
- Clinician reports, FAERS, eHealthMe, social media, international product labels
- AI-assisted literature searches (ChatGPT 4.0)
- Data abstracted included: demographics, platelet counts, bleeding manifestations, treatments, outcomes, and rechallenge information

Comparator Investigations
- RADAR (clopidogrel-associated TTP)
- SONAR (COVID-19 vaccine-associated thrombocytopenia)

Limitations

- Observational case series; population-level incidence, relative risk, and causality not established
- Clinician-based case identification may preferentially capture more severe clinical presentations
- Social media and patient-reported sources lacked sufficient detail for independent validation and were excluded from primary analysis
- Absence of denominator data precludes risk comparison across individual GLP-1RA agents or patient subgroups
- Drug-dependent platelet antibody testing available in only one patient

First-ever GLP1-RA Associated Thrombocytopenia Case Series

Table 1. Clinical characteristics of patients with GLP-1RA-associated thrombocytopenia

Case	Age	Time to Onset	Platelet nadir (/µL)	Bleeding Manifestations	Key Treatments	Outcome
1	31	~3 months after switch	31,000	None	Drug discontinuation	Partial recovery over 6 months
2	47	Weeks after dose escalation	106,000	Epistaxis, bruising	Drug interruption; rechallenge attempted	Recurrent thrombocytopenia; drug discontinued
3	31	~1 month	8,000	Severe bruising, menorrhagia	Steroids, IVIG, rituximab, TPO-RA	Persistent/refractory ITP
4	41	~10 weeks	2,000	Diffuse ecchymoses	IVIG, dexamethasone	Complete recovery
5	69	Weeks	< 2,000	Epistaxis	Steroids, IVIG, TPO-RA, splenectomy	Resolution post-splenectomy
6	62	~5 weeks	2,000	Petechiae, mucosal bleeding	Steroids, IVIG	Recovery by 50 days
7	55	~11 weeks	1,000	Mucosal, GI bleeding	Steroids, IVIG, rituximab, splenectomy	Recovery after drug clearance; DDAb positive

Abbreviations: IVIG = intravenous immunoglobulin; TPO-RA = thrombopoietin receptor agonist; DDAb = drug-dependent antibody.

Additional Pharmacovigilance Signals

Figure 1. FAERS Reports by Year for Semaglutide and Tirzepatide + Thrombocytopenia and Immune Thrombocytopenia

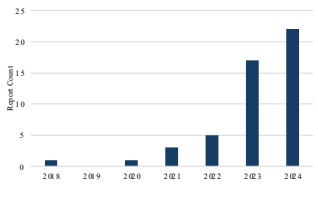

Table 2. FAERS Reports by Age Group

Semaglutide and Tirzepatide FAERS Reports 2018-2024 For Thrombocytopenia and Immune Thrombocytopenia	
18-64 Years	26
65-84 Years	10
85+ Years	1
Not Specified	17

SONAR-AI Performance

Table 3. Aggregate Metrics for all Pharmacovigilance Methods

	RADAR (20th century Method)	SONAR (21st century method without AI)	SONAR-AI (21st century method)
Prototype ADR	Clopidogrel-associated thrombotic thrombocytopenic purpura (FDA approval 1989)	COVID-19 vaccine associated thrombocytopenia (FDA approval 2020)	Semaglutide-associated thrombocytopenia (FDA approval 2017)
% of initial cases reported by clinicians	100%	100%	100%
Time to complete FDA query	3 months	1 month	30 minutes to query FAERS
Research assistant time to review literature for additional cases	3 weeks	2 weeks	8 hours (ChatGPT partially supported)
Time to synthesize data summary	3 weeks	3 weeks	5 seconds
Number of additional cases identified in AI-based web-sites	Not available	Not available	77 (2025)
Number, training, and annual salary of research assistants	4 college graduates with training in literature review and in statistics. $45,000 per year	1 medical student, 1 PhD data aggregator, and FDA analyst $50,000 per year	1 high school graduate, 3 college freshman and sophomores with extensive training in social media. $6,000 per year
Overall estimated cost and time	$100,000 over 1 year	$10,000 over 6 months	$500 over 4 months
Time from initial signal to public dissemination as peer-reviewed manuscript or as a pre-print	2 years	1.5 years	6 months

Conclusions

First Documented Case Series

Seven clinician-confirmed cases of GLP-1RA—associated thrombocytopenia identified across semaglutide, tirzepatide, liraglutide, and exenatide. Median platelet nadir was 2,000/µL (range <2,000–106,000). Four patients required thrombopoietin receptor agonists, corticosteroids, plasmapheresis, and/or splenectomy, highlighting the potential severity of this adverse event.

Immune-Mediated Mechanism Supported

A drug-dependent platelet-reactive IgG antibody specific to exenatide was demonstrated in one patient, providing direct immunologic evidence of causality. In a second patient, rechallenge led to recurrent thrombocytopenia, further supporting an immune-mediated mechanism consistent with drug-induced immune thrombocytopenia.

Critical Gap in Product Labeling

Despite 54 FAERS reports including 1 death and 50 serious cases, and 175 eHealthMe reports, thrombocytopenia remains absent from GLP-1RA product labels across the US, EU, Canada, Australia, Japan, and New Zealand, representing a significant unaddressed post-marketing safety signal.

AI Transforms Pharmacovigilance

SONAR-AI completed this comprehensive evaluation in 6 weeks at $500 while achieving 95% case data completeness. Compared to 1 year, $500,000, and 90% completeness for RADAR, and 3 months, $20,000, and 90% for SONAR, this is a significant increase in speed and quality of work. AI-assisted pharmacovigilance represents a faster, cheaper, and more complete approach to post-marketing drug safety surveillance.

Clinical & Regulatory Implications

Practitioners should consider recent GLP-1RA exposure when evaluating new-onset thrombocytopenia, particularly when severe or refractory to standard therapies. Early drug discontinuation, diagnostic evaluation, and timely reporting to regulatory authorities are recommended. Notably, while conventional approaches improve two of three quality metrics, SONAR-AI uniquely improved all three making the pharmacovigilance process faster, cheaper, and more complete, thus establishing a new benchmark for AI-assisted pharmacovigilance.

References
For all references, supplementary data tables, citations, and digital copies of the poster. citations, please see the QR code.

Funding
Supported by the National Cancer Institute and National Institutes of Health.

Conflicts of Interest
No authors reported or disclosed any conflicts of interest

To Contact
Please email demiruslu@gmail.com for any questions regarding the abstract

Key References
1. Bennett CL, Connors JM, Carwile JM, et al. Thrombotic thrombocytopenic purpura associated with clopidogrel. N Engl J Med 2000; 342(24): 1773-7.
2. Aster RH, Bougie DW. Drug-induced immune thrombocytopenia. *N Engl J Med* 2007; 357(6): 580-7.
3. Bennett CL, Gondabolu K, Kwah LW, et al. Using Twitter for the identification of COVID-19 vaccine-associated haematological adverse events. *Lancet Haematol* 2022; 9(1): e12-e3.
4. Wong CH, Bennett CL, Magagnoli J, Richardson C. Post-Marketing Safety Assessment for Glucagon-Like Peptide-1 and Dual Incretin Therapies in Diabetes and Obesity. *J Clin Pharmacol* 2025.