Enhancing Drug Safety Surveillance: Signal Identification in the Sentinel System

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OBJECTIVE

To demonstrate the concurrent application of two distinct study designs leveraging tree-based scan statistics (TBSS) for the identification of safety signals in the U.S. FDA's Sentinel System.
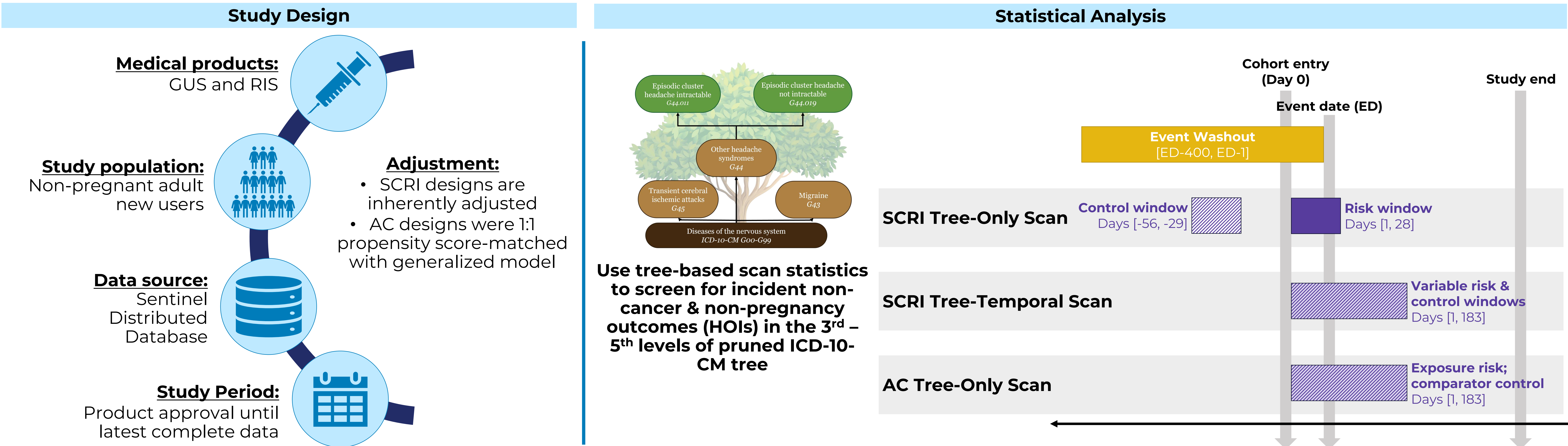
BACKGROUND

- Sentinel Distributed Database (SDD) is a national distributed data network of electronic healthcare databases used for surveillance by the U.S. FDA.
- TBSS (TreeScan™) are used in the SDD as one method of performing drug safety signal identification.

METHODS

- TBSS use a hierarchical outcome tree with simultaneous adjustment for multiple scanning of correlated outcomes.
- TreeScan™ analyses were conducted for monoclonal antibodies guselkumab (GUS) and risankizumab-rzaa (RIS) using self-controlled risk interval (SCRI) and active comparator (AC) designs.

CASE EXAMPLES

Study Design

Medical products: GUS and RIS

Study population: Non-pregnant adult new users

Adjustment:
- SCRI designs are inherently adjusted
- AC designs were 1:1 propensity score-matched with generalized model

Data source: Sentinel Distributed Database

Study Period: Product approval until latest complete data

Statistical Analysis

Use tree-based scan statistics to screen for incident non-cancer & non-pregnancy outcomes (HOIs) in the 3rd – 5th levels of pruned ICD-10-CM tree

Cohort entry (Day 0) | Event date (ED) | Study end

Event Washout [ED-400, ED-1]

SCRI Tree-Only Scan — Control window Days [-56, -29] | Risk window Days [1, 28]

SCRI Tree-Temporal Scan — Variable risk & control windows Days [1, 183]

AC Tree-Only Scan — Exposure risk; comparator control Days [1, 183]

Findings

Drug	Study Design	Scan Type	New Use Episodes	Significant HOI Clusters in the Inpatient/Emergency Department Setting
RIS	SCRI	Tree-Only	29,815	0 alerts
	SCRI	Tree-Temporal	21,095	2 transient alerts for gallstones without inflammation
	AC	Tree-Only	16,096	0 alerts
GUS	SCRI	Tree-Only	27,827	0 alerts
	SCRI	Tree-Temporal	23,251	0 alerts
	AC	Tree-Only	16,096	0 alerts

DISCUSSION & CONCLUSIONS

- Few statistical alerts for risankizumab-rzaa and guselkumab were identified across both study designs.
- Upon follow-up record review, codes contributing to alerts for gallstones appeared to be incidental to orders for imaging given by diagnostic radiology; the alerts were deemed not to represent a new safety signal.
- TBSS are compatible with several epidemiological study designs in the Sentinel System's real-world database to perform active drug safety surveillance for the U.S. FDA.

ACKNOWLEDGEMENTS