Impact of Posterior Reversible Encephalopathy Syndrome on Hospitalization and Mortality in Tyrosine Kinase Inhibitor-Treated Patients with Hematologic Malignancies: A Real-World Propensity-Matched Analysis

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SUMMARY

INTRODUCTION

- Posterior reversible encephalopathy syndrome (PRES) is an uncommon but serious neurotoxic syndrome of rapid-onset seizures, headache, visual change and confusion, driven by vasogenic cerebral edema.
- PRES has been increasingly reported with tyrosine kinase inhibitor (TKI) therapy, including BCR-ABL1 inhibitors used in CML and other hematologic malignancies.
- Despite growing recognition of TKI-associated neurotoxicity, the impact of PRES on hospitalization burden and survival remains poorly characterized.

AIM

Evaluate the association of TKI-associated PRES with inpatient hospitalization and all-cause mortality in a large real-world dataset.

METHODS

- TriNetX Global Collaborative Network; 170 healthcare organizations.
- Patients with a record of imatinib, dasatinib, bosutinib, ibrutinib or erlotinib.
- PRES cohort: ICD-10-CM I67.83 within 1 year after TKI exposure (n=135). Comparator: TKI-exposed without any PRES code (n=74,429 identified; 69,764 eligible for matching).
- Exclusions: Cocaine-related disorders and hypertensive urgency/emergency.
- Index = date the cohort definition was first met (PRES diagnosis for cases; TKI exposure for comparators).
- 1:1 propensity-score matching on 10 demographic and comorbidity covariates → 135 per cohort.
- Outcomes assessed from day 1 post-index, censored at last recorded fact: all-cause mortality (primary) and inpatient encounter (secondary), using Kaplan-Meier, log-rank and Cox models.

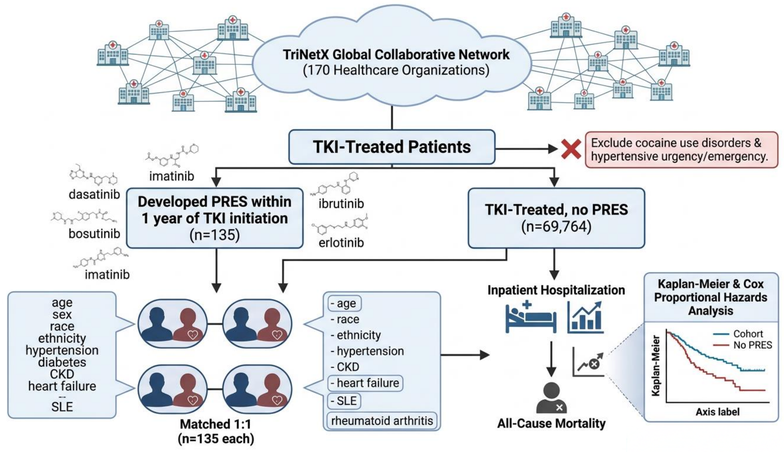
FINDINGS

45.9% vs 20.7%

all-cause mortality, PRES vs matched control

HR 2.68 (95% CI 1.72–4.19), log-rank p < 0.001

STUDY DESIGN



MATCHED COHORT CHARACTERISTICS

	TKI-PRES (n=135)	Control (n=135)	Std. diff.
Age, mean ± SD	52.5 ± 24.9	51.6 ± 25.4	0.039
Female	54.8%	51.1%	0.074
White	66.7%	67.4%	0.016
Black or African American	15.6%	15.6%	<0.001
Hispanic or Latino	13.3%	12.6%	0.022
Hypertension	51.9%	48.9%	0.059
Diabetes mellitus	20.0%	16.3%	0.096
Chronic kidney disease	12.6%	11.1%	0.046
Heart failure	11.1%	8.1%	0.101
Systemic lupus erythematosus †	≤7.4%	≤7.4%	—
Rheumatoid arthritis †	≤7.4%	≤7.4%	—

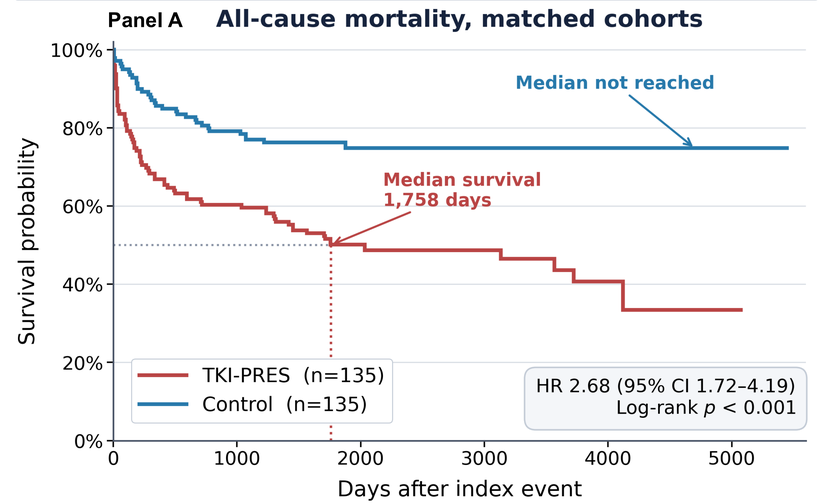
All standardized differences <0.11 except American Indian / Alaska Native race (0.40; not shown).

† TriNetX masks patient counts of 1–10 and reports them as 10. These rows are upper bounds, and their apparent perfect balance is an artefact of masking rather than a measured result.

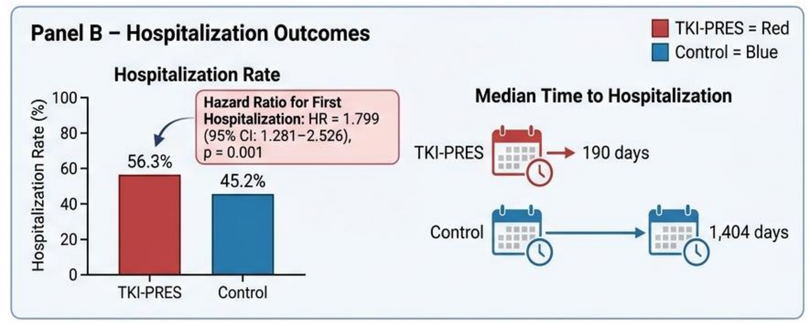
RESULTS

Outcomes:

All-cause mortality: 45.9% vs 20.7%; risk difference 25.2% (95% CI 14.3–36.0%); RR 2.21 (1.52–3.23). E-value for the hazard ratio 4.81 (2.82 for the lower confidence limit).



Hospitalization: the proportion ever hospitalized did not differ significantly (56.3% vs 45.2%; RR 1.25, 95% CI 0.98–1.58; p=0.068).



CONCLUSIONS

- Among TKI-treated patients, a PRES diagnosis identified a group with more than twice the subsequent all-cause mortality (45.9% vs 20.7%) and substantially earlier hospitalization than propensity-matched controls.
- Although PRES is characterized as clinically and radiographically reversible, the diagnosis marks a durably higher-risk trajectory rather than an isolated, self-limited event.
- The mortality difference is unlikely to be explained by a single unmeasured confounder of modest strength (E-value 4.81).
- Findings support closer post-PRES surveillance and prospective study of TKI continuation and rechallenge, for which no comparative data currently exist.

LIMITATIONS

- Retrospective coded EHR data; PRES ascertained by ICD-10-CM I67.83 without imaging confirmation or validated positive predictive value.
- Index dates differ by cohort, so follow-up begins later and at greater acuity in the PRES group, the findings are prognostic, not causal.
- Exposure spanned BCR-ABL1, BTK and EGFR inhibitors; underlying malignancy was not captured.
- Matching did not include calcineurin inhibitors, VEGF-pathway agents, transplant status, renal function or index year.
- Mortality capture in federated EHR networks is incomplete and varies with encounter frequency.

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