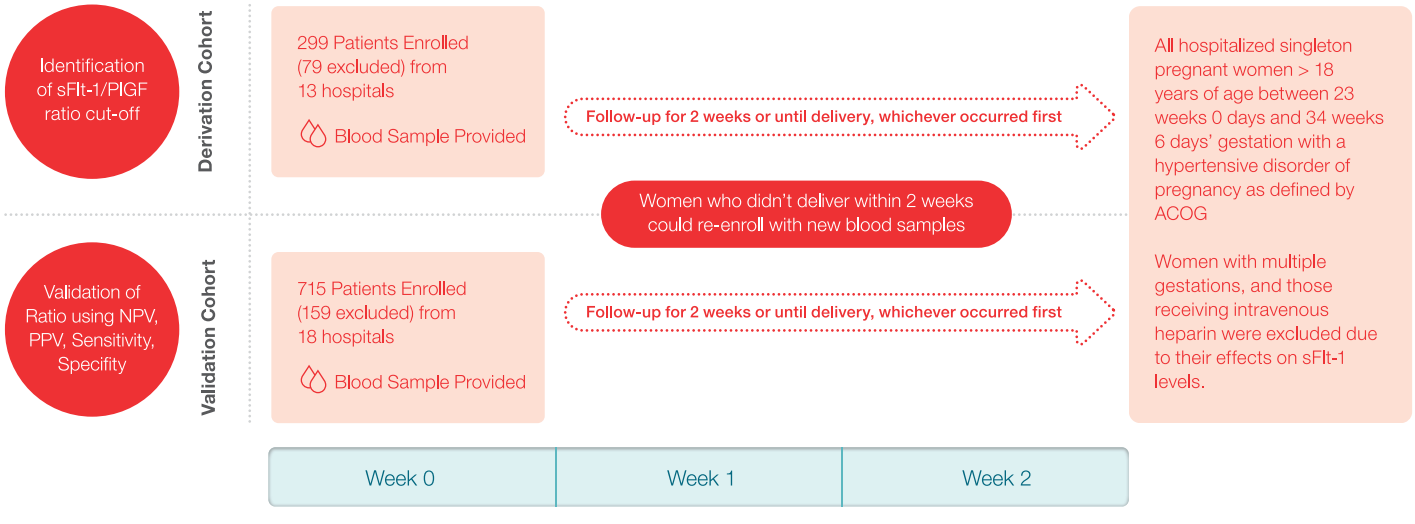
PRAECIS study[1], a large U.S. multicenter study to stratify pregnant women with preeclampsia with severe features

Goal of the PRAECIS study

PRAECIS (Preeclampsia Risk Assessment: Evaluation of Cut-offs to Improve Stratification) study was intended to identify and validate a sFlt-1/PlGF ratio to stratify the short-term risk of developing preeclampsia with severe features (sPE) in women with hypertension hospitalized in late pregnancy.

Study Design

A multicenter, blinded, prospective study was conducted in 18 US hospitals where the ratio of serum soluble Fms-like tyrosine kinase (sFlt-1) to Placental Growth Factor (PlGF) was measured in pregnant women hospitalized between weeks 23+0/7 & 34+6/7 of gestation.



Primary Outcome Development of sPE within 2 weeks after enrollment

Secondary Outcome Predicting adverse outcomes within 2 weeks.

Study population

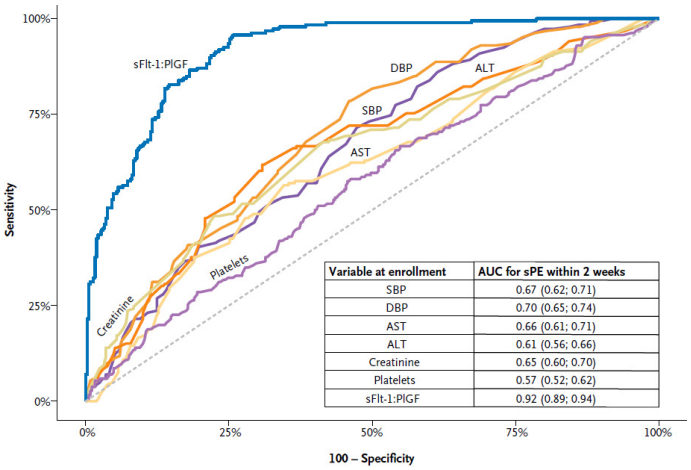
Women were recruited from 18 U.S. tertiary care and community hospitals in urban and suburban settings to reflect the heterogeneity of pregnant women in the United States. Racially and ethnically more reflective of US patient population (Approximately 32% African American, 6% Asian, 52% Caucasian and 16% Hispanic). Approximately 30% of patients were Nulliparous. And a significant number of patients with a history of chronic hypertension (47.4%), preeclampsia (25.1%), kidney disease (4.5%), and Diabetes Mellitus (13.7%).

Key results

The discriminatory ratio of 40 yielded the following results for the primary outcome:

- 65.2% PPV (95% CI, 59.3 to 70.6)
- 95.8% NPV (95% CI, 92.9 to 97.6)
- 93.5% Sensitivity (95% CI, 89.1 to 96.3)
- 74.9% Specificity (95% CI, 70.2 to 79.0)

The ratio was higher than standard clinical measures (area under the ROC, 0.92 versus <0.75 for standard-of-care tests) compared with women with a ratio <40, women with a ratio >=40 were at higher risk for adverse maternal outcomes (16.1% versus 2.8%; relative risk, 5.8; 95% CI, 2.8 to 12.2). See Figure 2.



Predictive accuracy for serum sFlt-1/PlGF ratio and ther standard-of-care tests for the development of sPE.

In the subgroup of patients who identified as Black race (n=169), the ratio ≥40 yielded positive and negative predictive values of 66% (95% CI, 51 to 67) and 99% (95% CI, 94 to 100).

	Derivation Cohort	Validation Cohort
Number of patients (Total N=1014)	N patients enrolled 299 N patients after exclusion 220	N patients enrolled 714 N patients after exclusion 556
sPE within 2 weeks	31.3%	33.5%
Median sFlt-1/PlGF ratio Developed sPE: Did not develop sPE:	 **200** (IQR 53 to 458) **6** (IQR 3 to 26) (p<0.001)	 **291** (IQR 121 to 777) versus **7** (IQR, 3 to 40) (p<0.001.
sFlt-1/PlGF ratio ≥40 w/prognostic estimate	81% sensitivity (95% CI, 70 to 90) 81% specificity (95% CI, 74 to 87)	94% sensitivity (95% CI, 89 to 96) 75% specificity (95% CI, 70 to 79)
PPV (Ratio of 40)	66% (95% CI, 55 to 76)	65% (95% CI, 59 to 71)
NPV (Ratio of 40)	90% (95% CI, 84 to 95)	96% (95% CI, 93 to 98)

Predicting Maternal and Fetal Adverse Outcomes

40x	Women who developed sPE had sFlt-1/PlGF ratios approximately 40 times higher than those who did not (291 [interquartile range, 121 to 777] versus 7 [interquartile range, 3 to 40], respectively; p,0.001).
10x	The sFlt-1/PlGF ratio was approximately 10 times higher for women who developed adverse maternal outcomes than for patients who did not (279 [IQR, 53 to 774] versus 22 [IQR, 4 to 171], respectively)
30x	The sFlt-1/PlGF ratio was 30 times higher in women with an adverse fetal and neonatal outcome compared with those without (182 [IQR, 36 to 548] versus 6 [QIR, 3 to 24], respectively)
40x	Women with an sFlt-1/PlGF ratio ≥40 were more likely to deliver (spontaneously or induced) within 2 weeks compared with women with a ratio <40

Conclusion

PRAECIS is the largest prospective U.S. study to date and included 30.4% Black and 16.2% Hispanic women. The PRAECIS study clearly demonstrated that in women with a hypertensive disorder of pregnancy presenting between 23 and 35 weeks of gestation, measurement of serum sFlt-1/PlGF provided stratification of the risk of progressing to sPE within the coming fortnight as well as a strong association with adverse outcomes.

Implications for the clinical practice

The measurement of serum sFlt-1/PlGF can be used to determine if patients require stepped up care (transfer or referral to facility with appropriate care), increased monitoring and frequency of usual tests or follow expectant management per ACOG guidelines.

References

1. Thadhani et al (2022). NEJM; https://doi.org/10.1056/EVIDoa2200161

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