COGI Paris 2014 - Abstract Submission

Topic: Fetomaternal Medicine

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PREDICTION OF SHORT-TERM OUTCOME IN PREGNANT WOMEN WITH SUSPECTED PREECLAMPSIA: THE PROGNOSIS STUDY

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Do you have a preferred presentation method?: Poster

Do you wish to apply for the Young Scientist Award?: No

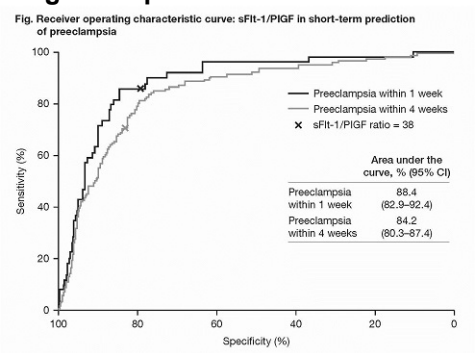
Problem Statement: Preeclampsia is a potentially life-threatening syndrome for mother/fetus, diagnosed by hypertension and proteinuria. However, clinical diagnosis is not straightforward and these signs are poor for predicting who will develop preeclampsia/associated adverse outcomes. Where preeclampsia is suspected, there is a need for reliable short-term prediction to optimize prenatal care. An imbalance of soluble fms-like tyrosine kinase-1 (sFlt-1) and placental growth factor (PlGF) has been implicated in preeclampsia pathogenesis, with high sFlt-1/PlGF ratio observed before onset. PROGNOSIS (sponsor: Roche Diagnostics) investigated the sFlt-1/PlGF ratio for short-term prediction of preeclampsia and maternal/fetal adverse outcomes in women with suspected preeclampsia.

Methods: PROGNOSIS (multicenter/prospective/double-blind/non-interventional) enrolled 1273 pregnant women (gestational age 24weeks+0days to 36weeks+6days at visit 1) with clinical suspicion of preeclampsia. A cutoff-based model for preeclampsia prediction was derived from the first 500 evaluable subjects and validated with data from a further 550 subjects. Primary objectives: to demonstrate that low sFlt-1/PlGF ratio predicts absence of preeclampsia/eclampsia/HELLP syndrome for 1 week after visit 1 (1-week rule-out), and high sFlt-1/PlGF ratio predicts diagnosis of preeclampsia/eclampsia/HELLP syndrome within 4 weeks of visit 1 (4-week rule-in). Secondary objectives included correlation of low and high sFlt-1/PlGF with absence and presence, respectively, of maternal/fetal preeclampsia-related adverse outcomes within 1 and 4 weeks. Preeclampsia and adverse outcomes were combined for an exploratory analysis. Subjects/investigators were blinded to sFlt-1/PlGF data. Diagnostic criteria were protocol-defined from international guidelines. sFlt-1 and PlGF were measured at an independent laboratory (Elecsys® system, cobas e platform, Roche Diagnostics).

Results: Preeclampsia prevalence was 19.0%. Feasibility cohort: a sFlt-1/PlGF cut-off of 38 for all gestational ages was favorable. The validation cohort had 90% power to show: a negative predictive value (NPV) of >96%, with the cut-off confirmed for 1-week rule-out of preeclampsia by a 95% CI of 97.9–99.9%; a positive predictive value (PPV) of >25%, with the cut-off confirmed for 4-week rule-in by a 95% CI of 28.4–45.7%. In the full evaluable dataset (n=1050), the sFlt-1/PlGF cut-off showed promising NPV, PPV, sensitivity and specificity (Table/Fig); primary objectives were met. Women with adverse outcomes (n=2; cerebral hemorrhage plus preeclampsia; isolated cerebral thrombosis) had high sFLt-1/PlGF ratios. sFlt-1/PlGF was correlated with fetal adverse outcomes and a combined endpoint of maternal and/or fetal adverse outcomes and/or preeclampsia. Low and high sFlt-1/PlGF ratios were associated with absence and presence of combined outcomes, respectively.

Predictive value of sFlt-1/PlGF cut-off of 38 (n=1050)		
% (95% CI)	1-week rule-out of preeclampsia	4-week rule-in of preeclampsia
NPV	99.1 (98.2–99.6)	94.9 (93.1–96.3)
PPV	16.7 (12.3–21.9)	38.6 (32.6–45.0)
Sensitivity	85.7 (72.8–94.1)	70.3 (61.9–77.8)
Specificity	79.1 (76.5–81.6)	83.1 (80.5–85.5)

Image / Graph:



Conclusion: A single sFlt-1/PlGF ratio cut-off value of 38 was validated to reliably rule-out (within 1 week) and rule-in (within 4 weeks) preeclampsia in women with suspicion of preeclampsia (gestational age 24–37 weeks), and was predictive of fetal adverse outcomes. The test may help optimize care by improving management of suspected preeclampsia.

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