

# HIGH CERVICAL PHIGFBP-1 CONCENTRATION IN ACTIM<sup>®</sup> PARTUS 1NGENI TEST IS A RELIABLE INDICATOR OF PRETERM DELIVERY WITHIN 7 DAYS

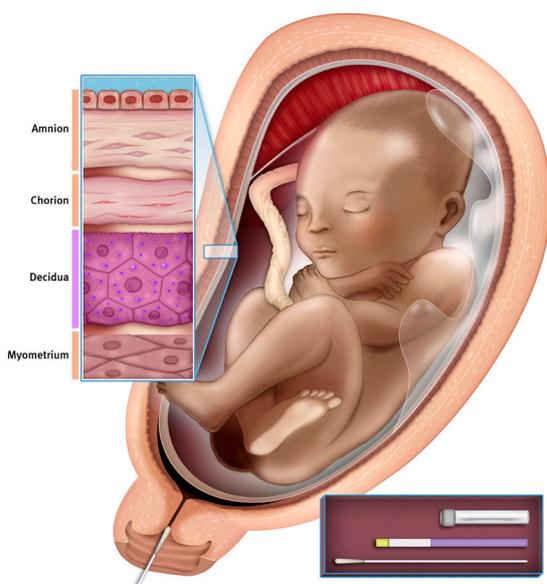
Laura Kanto<sup>1</sup>, Eivor Svens<sup>1</sup>, Juuso Juhila<sup>1</sup>

<sup>1</sup> Actim Oy, Klovinpellontie 3, FI-02180 Espoo, Finland

## Cervical phIGFBP-1 indicates preterm delivery

Preterm birth (earlier than 37 weeks of gestation) is the leading cause of neonatal morbidity and mortality, necessitating accurate predictive and preventive measures. An elevated cervical concentration of the highly phosphorylated isoform of insulin-like growth factor binding protein 1 (phIGFBP-1) is an early predictor of preterm or imminent delivery.<sup>1,2</sup>

The phIGFBP-1 phosphoisoform is produced by the decidua<sup>3,4,5</sup> and leaks into the cervix following the detachment of the decidua and chorion in the early stages of labor. The presence of phIGFBP-1 in cervical secretions predicts premature or imminent delivery in expectant mothers with intact fetal membranes, even before the occurrence of visible symptoms.<sup>1,6</sup> The concentration of cervical phIGFBP-1 can be quantified using the immunochromatographic dipstick test Actim<sup>®</sup> Partus 1ngeni (Figure 1).<sup>7,8</sup>



**FIGURE 1.** Actim Partus 1ngeni predicts preterm delivery by detecting decidual phosphoisoforms of insulin-like growth factor binding protein 1 (phIGFBP-1) in cervical secretions.

## Materials & Methods

The clinical performance of Actim Partus 1ngeni – a quantitative test employing monoclonal antibodies specific for decidual phIGFBP-1 – was evaluated retrospectively. phIGFBP-1 concentration in 120 frozen cervical swab samples from pregnant women at different gestational ages, with or without symptoms of preterm labor, was quantified using an automated Actim 1ngeni System (Figure 2).



**FIGURE 2.** phIGFBP-1 concentration was quantified from cervical swab samples using an automated and digital Actim 1ngeni System with Actim Partus 1ngeni test.

The analysis was performed under simulated use conditions according to the manufacturer's instructions and approved clinical guidelines. Median phIGFBP-1 concentration and cervical length were recorded for the clinical outcome groups: delivery within 7 days (n=60) vs. delivery after 7 days (n=60), of sample collection.

Differences in phIGFBP-1 concentration between the clinical groups were analyzed by ANOVA, and the correlation between phIGFBP-1 level and cervical length by two-tailed Pearson correlation using IBM SPSS Statistics 22.0.

## HIGH CERVICAL pHIGFBP-1 CONCENTRATION IN ACTIM® PARTUS 1NGENI TEST IS A RELIABLE INDICATOR OF PRETERM DELIVERY WITHIN 7 DAYS

### Positive Actim Partus 1ngeni test reliably predicts delivery within 7 days

The median cervical pHIGFBP-1 concentration quantified by Actim 1ngeni System with Actim Partus 1ngeni test was significantly higher in women who delivered within 7 days of sample collection as compared to women who delivered beyond the 7-day period ( $p=0.011$ ).

The median cervical length was significantly shorter in women who delivered within 7 days of sample collection, as compared to women who delivered later in the pregnancy ( $p=0.001$ ). Moreover, an elevated cervical pHIGFBP-1 concentration correlated with a shorter cervical length in women who delivered within 7 days of sample collection ( $r=0.421$ ;  $p\leq 0.05$ ). Clinical outcomes of the quantitative Actim Partus 1ngeni analysis are summarized in Table 1.

**TABLE 1.** High cervical pHIGFBP-1 concentration in Actim Partus 1ngeni and shortened cervical length predict preterm delivery within 7 days of sample collection. IGFBP-1, insulin-like growth factor-binding protein 1;  $r$ , Pearson correlation coefficient;  $n=120$ .

CLINICAL GROUPS	CLINICAL OUTCOMES			
	Days until delivery	Median pHIGFBP-1 concentration ( $\mu\text{g/L}$ )	Median cervical length (mm)	Correlation pHIGFBP-1 vs. cervical length
$\leq 7$		15.0	15.0	$r=-0.421^*$
$> 7$		4.0	30.0	$r=0.076$

Statistical significance between clinical groups

$p=0.011$

$p=0.001$

\* $p\leq 0.05$

### Conclusions

Preterm delivery is associated with a high risk of severe neonatal complications. Therefore, accurate identification of pregnant women who are at risk for preterm delivery is crucial for commencing treatment strategies that accelerate fetal pulmonary maturation and delay birth.

In this quantitative retrospective analysis, a positive Actim Partus 1ngeni result and a shortened cervical length reliably predicted delivery within 7 days of cervical sample collection in women with intact fetal membranes. Actim Partus 1ngeni is therefore a valuable clinical tool for the fast and accurate identification of women at high risk for imminent delivery. Moreover, Actim Partus 1ngeni identifies patients that are highly unlikely to give birth in the next 7 days and helps to avoid overtreatment and unnecessary medications.

### Acknowledgements

We wish to thank our Laboratory Technicians for their excellent technical assistance in this study.

### References

1. Kekki et al. Insulin-like growth factor-binding protein-1 in cervical secretion as a predictor of preterm delivery. *Acta Obstet Gynecol Scand* 2001;80:546-51.
2. Paternoster et al. Cervical pHIGFBP-1 in the evaluation of the risk of preterm delivery. *Acta Obstetrica et Gynecologica* 2007;86:151-55.
3. Rutanen et al. Radioimmunoassay of placental protein 12: Levels in amniotic fluid, cord blood, and serum of healthy adults, pregnant women and patients with trophoblastic disease. *Am J Obstet Gynecol* 1982;144:460-63.
4. Julkunen et al. Primary structure of human insulin-like growth factor binding protein/placental protein 12 and tissue expression of its mRNA. *FEBS Lett* 1988;236:295-02.
5. Martina et al. Gestational age-dependent expression of insulin-like growth factor binding protein-1 (IGFBP-1) phosphoisoforms in human extra-amniotic cavities, maternal serum, and decidua suggests decidua as the primary source of IGFBP-1 in these fluids during early pregnancy. *J Clin Endocrinol Metab* 1997;82:1894-98.
6. Tanir et al. Cervical phosphorylated insulin-like growth factor binding protein-1 for the prediction of preterm delivery in symptomatic cases with intact membranes. *J Obstet Gynaecol Res* 2009;35(1):66-72.
7. Bruijn et al. Comparison of the Actim Partus test and the fetal fibronectin test in the prediction of spontaneous preterm birth in symptomatic women undergoing cervical length measurement. *Eur J Obstet Gynecol Reprod Biol* 2016;206:220-224.
8. Vallikkannu et al. Insulin-like growth factor binding protein 1, Bishop score, and sonographic cervical length: tolerability and prediction of vaginal birth and vaginal birth within 24 hours following labour induction in nulliparous women. *BJOG* 2017;124:1274-83.
9. Kekki et al. Insulin-like growth factor binding protein-1 in cervix as a marker of infectious complications in pregnant women with bacterial vaginosis. *The Lancet* 1999;353:1494.