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Aneuploidy Screening

Study overview on adding Placental Growth Factor (PIGF) to first trimester sreening strategies

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Adding PlGF to T21 screening strategies

This literature review provides an overview why and how to implement PlGF as a third biomarker into today's first trimester screening strategies for trisomy 21.

Two main findings are supported in the studies:

- In the first trimester, **PlGF levels are significantly decreased** in pregnancies with a fetus affected by trisomy 21 compared to healthy controls.
- Implementation of PlGF in different screening strategies for trisomy 21 can either **increase the detection rate** or **decrease the false-positive rate**. In consequence, an improved false-positive rate results in a reduced number of women who will require an invasive test.

First-trimester studies on PlGF	Trisomy 21			Combined screening			
				Without PlGF		With PlGF	
	n	GA (weeks)	Median PlGF-MoM	FPR (%)	DR (%)	FPR (%)	DR (%)
Prospective							
Pandya et al. (cf. p. 10)	44	11–13	0.61	2.7	85	2.6	88
Retrospective							
Zaragoza et al. (cf. p. 5)	90	11–13	0.71	3.0	60	3.0	67
Cowans et al. (cf. p. 6)	70	11–13	0.76	3.0	91	3.0	92
Koster et al. (cf. p. 8)	91	11–13	0.78	3.0	71	3.0	73
Kagan et al. (cf. p. 11)	100	11–13	0.73	2.7	85	2.6	87
Koster et al. (cf. p. 8)	60	8–10	0.84	3.0	79	3.0	80

Table 1 Median placental growth factor multiples of the median in trisomy 21 and impact on performance of combined first-trimester screening in selected studies (Kagan et al., 2013)

Therefore, the implementation of PlGF measurements in the screening of pregnant women during first trimester can be beneficial in order to improve risk assessment for fetal trisomy 21.

This improved screening performance can also be considered as an added benefit when screening for pre-eclampsia, where PlGF is used as a routine biomarker.

Maternal serum placental growth factor at 11-13 weeks in chromosomally abnormal pregnancies

Zaragoza E, Akolekar R, Poon LC, Pepes S, Nicolaides KH
Ultrasound Obstet Gynecol 2009 Apr;33(4):382-6

Rationale

To investigate the potential value of maternal serum PlGF in first-trimester screening for trisomy 21 and other major chromosomal abnormalities.

Patients/Methods

In this retrospective case-control study, the maternal serum concentration of PlGF at 11 + 0 to 13 + 6 weeks was measured in 609 euploid and 175 chromosomally abnormal pregnancies, including 90 cases with trisomy 21, 28 cases with trisomy 18, 19 cases with trisomy 13, 28 cases with Turner syndrome, and 10 cases with triploidy. The levels of PlGF were compared in cases and controls, and were assessed for association with Free β-hCG and PAPP-A.

Results

In the euploid group logistic regression analysis demonstrated that significant independent contributions for log PlGF were provided by fetal crown-rump length, maternal weight, cigarette smoking and ethnic origin. After correction for these variables the median MoM for PlGF in the control group was 0.991.

Significantly lower PlGF values were observed in pregnancies with

- Trisomy 21 (0.707 MoM)
- Trisomy 18 (0.483 MoM)
- Trisomy 13 (0.404 MoM)
- Turner syndrome (0.534 MoM)
- Triploidy (0.531 MoM)

Maternal age, serum PlGF, PAPP-A and Free β-hCG provided significant contributions in the prediction of trisomy 21. The detection rates of screening with the combination of these variables were 70% and 80% at respective false-positive rates of 3% and 5%.

KEY FACTS

- **PlGF levels are significantly lower in pregnancies affected by fetal T21 when compared to unaffected controls in first trimester.**
- **In both the euploid and trisomy 21 pregnancies there was a significant association between serum levels of PlGF and PAPP-A.**
- **Maternal serum PlGF concentration at 11-13 weeks of gestation is potentially useful in first-trimester screening for trisomy 21 and other major chromosomal abnormalities.**

First trimester maternal serum placental growth factor in trisomy 21 pregnancies

Cowans NJ, Stamatopoulou A, Spencer K
Prenat Diagn 2010 May;30(5):449-53

Rationale

To examine PlGF levels in first trimester maternal serum in trisomy 21 pregnancies and to investigate the potential value of PlGF in a first trimester screening test.

Patients/Methods

In this retrospective case-control study, first trimester maternal serum from 70 trisomy 21 cases and 375 euploid controls were retrospectively analyzed for PlGF. Results were expressed as multiples of medians for comparison.

Results

Median concentration of PlGF levels was 28.4 pg/mL in the euploid group and 21.4 pg/mL in the trisomy group, resulting in significantly decreased MoM values (0.76 MoM in T21 vs 0.98 MoM in controls).

Detection rates for trisomy 21 using maternal age plus maternal serum markers PAPP-A, Free β-hCG and PlGF and NT were estimated using two different modeling software. Inclusion of PlGF into the first trimester combined test would increase the detection rate by 0.5% at a 5% false-positive rate.

- **KEY FACTS First trimester samples affected by trisomy 21 have significant lower PlGF levels than compared to unaffected controls.**
- **PlGF at 11 weeks to 13 weeks 6 days has the potential to be included as a marker for the detection of pregnancies with trisomy 21.**

Early first-trimester maternal serum placental growth factor in trisomy 21 pregnancies

Cowans NJ, Stamatopoulou A, Tørring N, Spencer K
Ultrasound Obstet Gynecol 2011 May;37(5):515-9

Rationale

To measure maternal serum PlGF levels in trisomy 21 cases and controls in samples drawn before 11 weeks' gestation.

Patients/Methods

In this retrospective case-control study, early first-trimester maternal serum samples, drawn between 8 + 0 and 10 + 6 weeks' gestation, were retrieved from frozen storage. PlGF was retrospectively measured and PlGF levels were converted to multiples of the median. Trisomy 21 (n= 37) and unaffected groups (n=244) were compared.

Results

Raw PlGF and MoM levels were significantly higher in the maternal serum of trisomy 21 cases than in controls over the 3-week gestational window (unaffected 1.0 MoM compared with trisomy 21 1.3 MoM ($p<0.0001$)). However, at 8 completed weeks of gestation the increase was most significant and at 10 completed weeks there was no significant difference between trisomy 21 and unaffected PlGF levels.

KEY FACTS

- **Early PlGF levels in maternal serum in trisomy 21 cases may be increased relative to unaffected controls.**
- **The authors discuss that during freezing bound PlGF dissociates from sFlt-1 and that this might be an explanation for their findings.**
- **However, the relationship between PlGF levels and gestational age in trisomy 21 and unaffected pregnancies in the first two trimesters of pregnancy appears to be complex and requires further study.**

Modeling Down syndrome screening performance using first-trimester serum markers

Koster MP, Wortelboer EJ, Stoutenbeek P, Visser GH, Schielen PC
Ultrasound Obstet Gynecol 2011 Aug;38(2):134-9

Rationale

To evaluate the modeled predictive value of three current screening markers PAPP-A, free β-hCG and NT and four potential screening markers ADAM12, total hCG, PP13, and PlGF for Down syndrome using different screening strategies.

Patients/Methods

All markers were measured in stored first-trimester serum of 151 Down syndrome cases and 847 controls. All marker levels were expressed as gestational age-specific MoMs and comparisons were made.

Results

Significantly different median MoMs for Down syndrome cases compared to controls were found for

- PAPP-A (0.49 vs. 1.00)
- free β-hCG (1.70 vs. 1.01)
- ADAM12 (0.89 vs. 1.00)
- total hCG (1.28 vs. 1.00)
- PlGF (0.80 vs. 1.00)
- NT (1.74 vs. 1.01)

The lower PP13 MoM in Down syndrome cases (0.91 vs. 1.00) was not statistically significant (p=0.061). Adding the four new markers to the current screening strategy (i.e. first-trimester combined test) led to an increase in DR from 77% to 80% at a 5% FPR. The modeled application of a two-sample screening strategy (with some markers assessed early and others later in the first trimester) increased the DR to 89%. In a two-step contingent screening model, using an intermediate risk range of 1 in 100 to 1 in 2000 at biochemical screening (using all markers), the overall DR was 77%, but it was predicted that only 33% of women would require referral for NT measurement.

KEY FACTS

- **First-trimester Down syndrome screening may be improved by adding new markers to the current screening test and by applying different screening strategies.**
- **The application of a two-sample screening model resulted in the highest predicted DR, but this should be confirmed in population-based prospective studies.**

Antenatal screening for Down syndrome using serum PIGF with the combined, quadruple, serum integrated and integrated tests

Wald NJ, Bestwick JP, George LM, Huttly WJ
PLoS One 2012;7(10):e46955

Rationale

To estimate the value of first or second trimester placental growth factor (PIGF) as an additional antenatal screening marker for Down syndrome.

Patients/Methods

In this retrospective case-control study, stored maternal serum samples (-40°C) were assayed for PIGF. Monte Carlo simulation was used to estimate the screening performance of PIGF with the Combined, Quadruple, serum Integrated and Integrated tests.

Maternal characteristics were included in the analysis of 532 Down syndrome pregnancies and 1,155 matched unaffected pregnancies.

Results

First trimester median PIGF was 15%, 28% and 39% lower in Down syndrome than unaffected pregnancies at 11, 12 and 13 completed weeks' gestation respectively (all $p<0.001$).

Second trimester median PIGF was 31% lower at 14 weeks ($p<0.001$), and the difference decreased (6% lower at 17 weeks).

At a 90% DR with first trimester markers measured at 13 weeks, adding PIGF

- decreased the FPR from 11.1 to 5.1% using the Combined test,
- decreased the FPR from 9.3% to 4.5% using the serum Integrated test,
- decreased the FPR from 3.4% to 1.5% using the Integrated test (or 1.5 to 1.4% with first trimester markers measured at 11 weeks).
- to the Quadruple test (measured at 15 weeks) decreased the FPR from 10.0% to 9.6% at a 90% DR.

KEY FACTS

- **First trimester PIGF measurements improve the performance of antenatal screening for Down syndrome using the Combined, serum Integrated and Integrated tests.**
- **Second trimester PIGF measurements are of limited value.**

Maternal serum placental growth factor in prospective screening for aneuploidies at 8-13 weeks' gestation

Pandya P, Wright D, Syngelaki A, Akolekar R, Nicolaides KH.
Fetal Diagn Ther 2012;31(2):87-93

Rationale

To investigate whether measurement of PlGF can improve the performance of first-trimester combined screening for trisomy 21 by fetal nuchal translucency thickness and serum free β-hCG and PAPP-A.

Patients/Methods

In singleton pregnancies attending for routine care, serum PlGF, free β-hCG and PAPP-A were measured at 8+0 - 13+6 weeks' gestation, and fetal NT was measured at 11+0 - 13+6 weeks. The population included 12,154 normal and 44 trisomy 21 pregnancies. The effect of adding PlGF on the performance of screening by the combined test was examined.

Results

In the trisomy 21 pregnancies the median multiple of the normal median PLGF, adjusted for gestational age, maternal weight, racial origin, smoking status and method of conception, was significantly reduced (0.6070, 95% CI 0.5543-0.6648), and this did not change significantly with gestational age.

Adding PlGF to combined testing with a risk cut-off of 1 in 100

- reduced the FPR from 2.7% (95% CI 2.5-3.0) to 2.6% (95% CI 2.4-2.8) and
- increased the detection rate from 85% (95% CI 75-93) to 88% (95% CI 78-95).

KEY FACTS

- **Inclusion of serum PlGF improves the performance of the first-trimester combined test in screening for trisomy 21.**
- **This study, based on the assessment of more than 11.000 pregnant women, is the largest to have investigated the value of measuring PlGF during routine first trimester screening for trisomy 21.**

First-trimester combined screening for trisomy 21 with different combinations of PlGF, free β-hCG and PAPP-A

Kagan KO, Hoopmann M, Abele H, Alkier R, Lüthgens K
Ultrasound Obstet Gynecol 2012 Nov;40(5):530-5

Rationale

To examine PlGF in euploid and trisomy 21 pregnancies at 11-13 weeks' gestation and to model the impact on first-trimester combined screening.

Patients/Methods

PlGF was measured in 509 (409 euploid and 100 trisomic) fetal serum samples derived from prospective first-trimester combined screening for trisomy 21 at 11-13 weeks' gestation. The serum samples were stored at -80°C, following the measurement of free β-hCG and PAPP-A levels, for median time spans of 0.9 and 4.1 years in the euploid and trisomy 21 pregnancies, respectively. The effect of additional PlGF measurement at the time of combined screening was investigated by simulating fetal NT measurements and MoM values for PAPP-A, free β-hCG and PlGF for 20,000 euploid and 20,000 trisomy 21 pregnancies. Patient-specific combined risks were calculated based on maternal age and fetal NT in addition to free β-hCG, PAPP-A and PlGF, PAPP-A and PlGF or free β-hCG and PlGF, and detection and false-positive rates were calculated.

Results

Median PlGF-MoM was 1.0 (95% CI, 0.96-1.04) in euploid fetuses and significantly lower, at 0.73 (95% CI, 0.70-0.76), in trisomy-21 fetuses ($p<0.0001$). There was no significant dependency between PlGF-MoM and either gestational age at the time of blood sampling ($r=0.087$, $p=0.392$) or sample storage time ($r=0.028$, $p=0.785$). Modeled detection and false-positive rates for first-trimester combined screening (based on maternal and gestational age, fetal NT and maternal serum biochemistry) without PlGF were 85% and 2.7% for a fixed risk cut-off of 1:100.

The addition of PlGF increased the detection rate to 87% and reduced the false-positive rate to 2.6%. Screening by maternal age and fetal NT in combination with PlGF and PAPP-A or in combination with PlGF and free β-hCG provided detection rates of 82% and 79%, with false-positive rates of 2.7% and 3.0%, respectively.

KEY FACTS

- **In pregnancies with trisomy 21 PlGF is reduced.**
- **The impact on the overall screening performance for trisomy 21 is low and does not justify the measurement of PlGF solely for trisomy 21 screening.**
- **However, as PlGF is measured with the aim of assessing the risk for pre-eclampsia, further improvement in screening for trisomy 21 can be considered as an added benefit.**

Improvements in antenatal screening for Down's syndrome

Wald NJ, Bestwick JP, Huttly WJ
J Med Screen 2013 Mar;20(1):7-14

Rationale

To estimate improvements to four antenatal screening tests for Down's syndrome

- First trimester Combined test
- Second trimester Quadruple test
- First and second trimester Integrated test
- Serum Integrated test

based on adding ductus venosus pulsatility index, fetal nasal bone examination and serum placental growth factor.

Patients/Methods

Statistical analysis of data from several sources modelled using the maternal age distribution of live births in England and Wales from 2006 to 2008. Monte Carlo simulation carried out to estimate the screening performance of tests with the addition of combinations of DVPI, NBE and PlGF.

Results

At a 95% DR, with first trimester markers measured at 11 completed weeks' gestation, the addition of DVPI, NBE and PlGF

- decreased the FPR of the Combined test from 16.1% to 3.0%,
- the addition of PlGF to the Quadruple test decreased the FPR from 15.7% to 15.3%,
- the addition of DVPI, NBE and PlGF to the Integrated test decreased the FPR from 4.1% to 0.6%
- the addition of PlGF to the Serum Integrated test decreased the FPR from 15.1% to 11.1%.

At a 90% detection rate, the reductions in the FPR were from 6.8% to 0.8%, 7.7% to 7.4%, 1.2% to 0.1% and 6.2% to 4.8%, respectively.

KEY FACTS

- **The addition of DVPI, NBE and PlGF to the Combined and Integrated tests significantly improves screening performance, reducing the FPRs by over 80%.**
- **The Integrated test with DVPI, NBE and PlGF is significantly better than the Combined test with DVPI, NBE and PlGF.**

Maternal serum placental growth factor and α-fetoprotein testing in first trimester screening for Down syndrome

Donalson K, Turner S, Morrison L, Liitti P, Nilsson C, Cuckle H.
Prenat Diagn 2013 May;33(5):457-61

Rationale

To evaluate the addition of first trimester maternal serum placental growth factor and α-fetoprotein to the combined test for Down syndrome and a serum only protocol of PlGF, AFP, free β-human chorionic gonadotropin and pregnancy-associated plasma protein-A.

Patients/Methods

Samples were from 92 Down syndrome cases with 552 matched controls. All women had a combined test at 11-14 weeks gestation. PlGF and AFP were measured and expressed in multiples of the gestation-specific median (MoM), adjusting for maternal weight and smoking status. Multivariate Gaussian modeling was used to predict detection and false-positive rates.

Results

The median PlGF level in the cases was 0.694 MoM and controls 1.000 MoM ($p \leq 0.0001$). The corresponding values for AFP were 0.764 MoM and 0.990 MoM ($p < 0.0001$).

Statistical modeling predicted that for a given false-positive rate, the addition of PlGF to the combined test increases the detection rate by 4-7%. For a given detection rate, the false-positive rate could be almost halved.

When both PlGF and AFP are used, the detection rate increase is 5-8%. A serum only protocol had a predicted detection rate of 71% for a false-positive rate of 5%.

KEY FACTS

Results suggest a substantial benefit of adding PlGF to the combined test.

First-trimester contingent screening for trisomy 21 by biomarkers and maternal blood cell-free DNA testing

Nicolaides KH, Wright D, Poon LC, Syngelaki A, Gil MM
Ultrasound Obstet Gynecol 2013 Jul;42(1):41-50

Rationale

To define risk cut-offs with corresponding detection rates and false-positive rates in screening for trisomy 21 using maternal age and combinations of first-trimester biomarkers in order to determine which women should undergo contingent maternal blood cell-free DNA testing.

Patients/Methods

From singleton pregnancies undergoing screening for aneuploidies at three UK hospitals between March 2006 and May 2012, we analyzed prospectively collected data on the following biomarkers: fetal nuchal translucency thickness and ductus venosus pulsatility index for veins at 11+0 to 13+6 weeks' gestation and serum free β-hCG, PAPP-A, PlGF and AFP at 8+0 to 13+6 weeks. Estimates of risk cut-offs, DRs and FPRs were derived for combinations of biomarkers and these were used to define the best strategy for contingent cfDNA testing.

Results

In first trimester screening the median MoMs for PlGF in the T21 group compared to unaffected pregnancies (MoM=1,002 IQ range 0,784-1,285) were reduced 0,667 (IQ range 0,524-0,843).

In contingent screening, detection of 98% of fetuses with trisomy 21 at an overall invasive testing rate <0.5% can be potentially achieved by offering cfDNA testing to about 36%, 21% and 11% of cases identified by first-line screening using the combined test alone, using the combined test with the addition of serum PlGF and AFP and using the combined test with the addition of PlGF, AFP and DV-PIV, respectively.

KEY FACTS

- **First trimester pregnancies affected by fetal T21 are associated with significantly lower PlGF levels compared to unaffected controls.**
- **Effective first-trimester screening for trisomy 21, with DR of 98% and invasive testing rate <0.5%, can be potentially achieved by contingent screening incorporating biomarkers and cfDNA testing.**

First-trimester Down syndrome screening using additional serum markers with and without nuchal translucency and cell-free DNA

Johnson J, Pastuck M, Metcalfe A, Connors G, Krause R, Wilson D, Cuckle H
Prenat Diagn 2013 Nov;33(11):1044-9

Rationale

To evaluate serum-only four-marker first trimester (1T-Quad) Down syndrome screening, alone or contingently to select 10-20% with highest risk for NT or cell-free DNA.

Patients/Methods

Stored maternal serum samples (-80°C) from 90 pregnancies with fetal Down syndrome and 1607 controls were retrieved and measured for PlGF, AFP, PAPP-A and free β-hCG.

Samples were from singleton pregnancies (9-13+6 weeks), and NT was measured between 11 and 13+6 weeks. Markers were expressed in MoM for gestation. Gaussian models were fitted to the distribution of log MoMs by using observed parameters, standardized maternal age distribution (mean 27, SD 5.5) and published cfDNA results.

Results

In the current first trimester screening approach the median MoMs for PlGF in the T21 group compared to unaffected pregnancies (MoM=1,027) were significantly reduced 0,673 (p<0,0001).

The addition of PlGF as a third serum marker (to Free β-hCG and PAPP-A) increased the detection rate by 5-8% (depending on the respective FPR).

The model-predicted detection rate for 1T-Quad was 74% [5% false-positive rate]. When used contingently to select for NT, the DR was 89% at 5%. When used to select for cfDNA, the DR was 91% (FPR<0.05%).

KEY FACTS

- **The 1T-Quad test can achieve a similar DR to a second-trimester Quad test. When used contingently to select for NT, the DR is similar to the combined test.**
- **Used contingently to select for cfDNA would achieve even higher detection.**

First-trimester screening for trisomies 21, 18 and 13 by ultrasound and biochemical testing

Wright D, Syngelaki A, Bradbury I, Akolekar R, Nicolaides KH
Fetal Diagn Ther 2014;35(2):118-26

Rationale

To examine the performance of screening for trisomies 21, 18 and 13 at 11-13 weeks' gestation using specific algorithms for these trisomies based on combinations of fetal NT, fetal heart rate, ductus venosus pulsatility index for veins, and serum Free β-hCG), PAPP-A, PlGF and AFP.

Patients/Methods

Model-based estimates of screening performance were produced for the distribution of maternal ages in England and Wales in 2011, and prospectively collected data on fetal NT, FHR, DV PIV, β-hCG, PAPP-A, PlGF and AFP from singleton pregnancies undergoing aneuploidy screening.

Results

In screening by NT, FHR, free β-hCG and PAPP-A, using specific algorithms for trisomy 21 and trisomies 18 and 13 at the risk cutoff of 1:100, the estimated detection rate (DR) was 87.0% for trisomy 21 and 91.8% for trisomies 18 and 13, at a false-positive rate (FPR) of 2.2%.

Addition of PLGF, AFP and DV PIV increased the DR to 93.3% for trisomy 21 and 95.4% for trisomies 18 and 13 and reduced the FPR to 1.3%.

KEY FACTS

Effective screening for trisomies can be achieved using specific algorithms based on NT, FHR, DV PIV, β-hCG, PAPP-A, PlGF and AFP.

Maternal Serum PlGF Isoforms 1 and 2 at 11-13 Weeks' Gestation in Normal and Pathological Pregnancies

Nucci M, Poon LC, Demirdjian G, Darbouret B, Nicolaides KH.
Fetal Diagn Ther 2014 Jan 23

Rationale

To compare the maternal serum concentration of PlGF-1 and PlGF-2 at 11-13 weeks' gestation in normal pregnancies and in those complicated by preeclampsia, delivery of small for gestational age neonates and fetal trisomies 21, 18 and 13.

Patients/Methods

Serum PlGF-1 and PlGF-2 were measured in 270 pathological pregnancies (PE, n = 80; SGA, n = 80; trisomy 21, n = 44; trisomy 18, n = 38; trisomy 13, n = 28) and 590 normal controls. The values were expressed as multiple of the median after adjustment for maternal characteristics and corrected for adverse pregnancy outcomes and the median MoM values in each pathological pregnancy were compared to the normal group.

Results

There were significant contributions to PlGF-1 and PlGF-2 from gestational age, smoking and racial origin. In addition, there were significant contributions to PlGF-1 from parity and method of conception.
The median MoM of PlGF-1 and PlGF-2 was significantly decreased in

- PE (0.783 and 0.916 MoM)
- SGA (0.891 and 0.851 MoM)
- trisomy 21 (0.609 and 0.749 MoM)
- trisomy 18 (0.529 and 0.730 MoM)
- trisomy 13 (0.373 and 0.699 MoM).

KEY FACTS

In pathological pregnancies, except SGA, the decrease in serum PlGF-1 at 11-13 weeks' gestation is more marked than the decrease in PlGF-2.

Glossary

ADAM12	A disintegrin and metalloprotease 12
AFP	Alpha fetoprotein
CI	Confidence interval
DR	Detection rate
DVPI	Ductus venosus pulsatility index
FHR	Fetal heart rate
FPR	False-positive rate
GA	Gestational age
MoM	Multiple of the median
NBE	Fetal nasal bone
NT	Nuchal translucency
PAPP-A	Pregnancy-associated plasma protein A
PE	Pre-eclampsia
PlGF	Placental growth factor
PP13	Placental protein 13
SGA	Small for gestational age
T21	Trisomy 21
β-hCG	Human chorionic gonadotropin

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Automated immunofluorescent assay for the quantitative determination of human Placental Growth Factor (PIGF) in human serum

- Excellent precision
- Very low detection limit: 3.6 pg/mL
- Best functional assay sensitivity (FAS): 6.7 pg/mL

► **Reliable detection of clinical values throughout pregnancy**

Clinical Interest

Screening for pre-eclampsia in first trimester of pregnancy in conjunction with other biological and clinical data to assess the risk of developing pre-eclampsia.

Screening for fetal chromosomal abnormalities in first trimester in conjunction with other biological and clinical findings for assessing the risk of fetal trisomy 21.

Aid in diagnosis and short-term prognosis of pre-eclampsia together with B·R·A·H·M·S sFlt-1 KRYPTOR and additional clinical data in pregnant women with suspicious pre-eclampsia

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Clinical Diagnostics

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