NEW APPROACHES IN 1ST TRIMESTER SCREENING
Maternal serum placental growth factor (PlGF) measured in the first trimester of pregnancy has been shown to improve the performance of Down syndrome screening. PerkinElmer has now made available the first CE-marked PlGF assay for Down syndrome screening.

Including PlGF can almost halve the number of false positives

The addition of the PlGF marker to the Combined test (NT, PAPP-A and free β-hCG) makes it possible to achieve the same detection rate (DR) as that achieved with the Combined test alone, but for a significantly lower false positive rate (FPR). In fact, recent studies have shown that addition of PlGF at 11 - 13+6 weeks improved performance so much that false positives could be reduced by almost 50%.

In the example illustrated below, when working with a risk cut-off level of 1 in 200, the addition of PlGF will increase DR by about 3% and decrease FPR by about 10%. A preferred alternative might be to keep the DR at roughly the same level and lower the cut-off to 1 in 100, so that the FPR will then be reduced by 46% (Pandya et al. 2012).

ROC curve that shows how the addition of PlGF (blue curve) makes it possible to lower the risk cut-off level so as to achieve 46% fewer false positives. The green curve shows performance for the combined test without PlGF, based on results reported by Pandya et al. (2012)
By utilizing the performance benefits of PlGF, unnecessary fetal losses are avoided

The following scenario illustrates the important role of the PlGF marker in helping to reduce false positives.

If 100,000 women are undergoing screening, at a 1 in 700 prevalence of T21, we would expect to see 143 affected fetuses. Implementing PlGF as an additional test and changing the cut-off from 1 in 200 to 1 in 100 would reduce the number of invasive tests by 2,200. Assuming a procedural loss of 1 in 200, this is likely to prevent the loss of 11 unaffected babies. In this context the loss or gain of a percent in the DR is of lesser importance. The value of the additional marker is in helping to reduce false positives. Screening performance figures in the summary below are as reported by Pandya et al. (2012).

<table>
<thead>
<tr>
<th>Model of screening</th>
<th>Cut-off</th>
<th>Detection Rate (%)</th>
<th>Cases of T21 detected</th>
<th>False Positive Rate (%)</th>
<th>Number of invasive tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combined (NT, PAPP-A &amp; free β-hCG)</td>
<td>1/200</td>
<td>89</td>
<td>127/143</td>
<td>4.8</td>
<td>4,800</td>
</tr>
<tr>
<td>Combined + PlGF</td>
<td>1/100</td>
<td>88</td>
<td>126/143</td>
<td>2.6</td>
<td>2,600</td>
</tr>
</tbody>
</table>

Adopting PlGF can reduce costs, anxiety and procedural losses

The following example illustrates the impact of reducing the number of invasive tests by adding PlGF to a screening program:

In a program with 10,000 women screened yearly, the estimated number of invasive tests, based on the combined test performance demonstrated by Pandya et al. (see table above), would be 480. At an average cost of 750€/test, this equates to a cost of 360,000€.

The addition of PlGF would reduce the number of invasive tests to 260. At 12€/sample (average PlGF reagent price) this would result in an additional cost to the program of 120,000€. This would be offset by the reduction in invasive tests, with 260 tests at 195,000€ bringing the total cost of PlGF and invasive testing to 315,000€. The net annual saving to the program is then 45,000€.

The addition of PlGF therefore brings a considerable cost saving while also reducing the number of fetal losses, and a large amount of anxiety. Additionally, PlGF enables pre-eclampsia risk assessment with the same marker.

Benefit from NIPT using a PlGF contingent protocol

According to Cuckle et al. (2013), the cost of NIPT (non-invasive prenatal testing) needs to fall substantially before it can be routinely offered to all women. Based on modeling, it is suggested that NIPT implementation would be economically justifiable if offered as a contingent test to 10-20% of women found to be at moderate or high risk using conventional screening.

Now with the addition of PlGF to the Combined test, the improved screening performance makes it possible to achieve the needed high DR while keeping the number of samples that go forward for NIPT well within the 10-20% range.

<table>
<thead>
<tr>
<th>FPR (Combined)</th>
<th>FPR (Combined + PlGF)</th>
<th>DR</th>
</tr>
</thead>
<tbody>
<tr>
<td>22 - 24%</td>
<td>14 - 17%</td>
<td>95%</td>
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</table>

Modeling of detection rates and false positive rates achievable at 12 weeks for use in a NIPT contingent strategy.

Down syndrome risk calculation that includes PlGF is available in PerkinElmer’s latest data management - risk calculation informatics package, LifeCycle v 4.
Pre-eclampsia risk as part of your aneuploidy screening program

PIGF is recognized to be the most sensitive and specific first trimester biochemical marker for pre-eclampsia. The results obtained with the PerkinElmer PIGF assay are suitable for use directly in both T21 and pre-eclampsia risk calculations.

References

Maternal serum placental growth factor at 11-13 weeks in chromosomally abnormal pregnancies. Ultrasound Obstet Gynecol;33 382-386.

First trimester maternal serum placental growth factor in trisomy 21 pregnancies. Prenat Diagn 30;449-453.

Maternal Serum Placental Growth Factor in Prospective Screening for Aneuploidies at 8-13 Week’s Gestation. Fetal Diagn Ther 31, 87–93; (available online on the www.fetalmedicine.com website).


Donalson K. et al. (2013)

ORDERING INFORMATION

<table>
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<tr>
<th>Code</th>
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<tbody>
<tr>
<td>6007-0020002C</td>
<td>DELFIA Xpress PIGF kit</td>
</tr>
<tr>
<td>8055-201</td>
<td>DELFIA/AutoDELFIA PIGF kit</td>
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</table>

The PerkinElmer PIGF assay is available on both DELFIA Xpress and DELFIA/AutoDELFIA platforms.

PerkinElmer PIGF kits and LifeCycle v 4 are not available in the USA, China and Japan. The kits may also not be available in Canada, Latin-America countries and some Asian countries prior to registration notifications.

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