Non-invasive prenatal screen

Panorama: the next generation of NIPT

Screens for:

Singleton pregnancies
- Trisomies 21, 18, 13
- Monosomy X
- Triploidy
- Sex chromosome trisomies*
- 22q11.2 deletion syndrome (optional)
- Additional microdeletion syndromes (optional)
- Fetal sex (optional)

Twin pregnancies
- Zygosity
- Trisomies 21, 18, 13
- Fetal sex for each twin (optional)

If screening reveals monozygotic twins, Panorama can additionally screen for:
- Monosomy X
- Sex chromosome trisomies*
- 22q11.2 deletion syndrome (optional)

Egg donor or surrogate pregnancies (Singleton pregnancies only)
- Trisomies 21, 18, 13
- Fetal sex (optional)

*Reported when suspected
Panorama’s unique SNP-based technology enables more comprehensive screening with greater accuracy in validation\textsuperscript{1–16}

**Singleton pregnancies**
- Fewer false negatives and false positives\textsuperscript{1–12}
- Fetal sex accuracy\textsuperscript{1,2,3}
- Triploidy\textsuperscript{13,14}
- Complete molar pregnancy\textsuperscript{14}
- Vanishing twin\textsuperscript{14}
- Maternal contribution\textsuperscript{15}

**Twin pregnancies**
- Zygosity\textsuperscript{16}
- Individual fetal fractions for dizygotic twins\textsuperscript{16}
- Fetal sex for each twin\textsuperscript{16}
- Monosomy X, sex chromosome trisomies,* and 22q for monozygotic twins\textsuperscript{16}

*Reported when suspected

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Only Panorama distinguishes between maternal and fetal (placental) DNA

Panorama evaluates SNPs – the 1% of our DNA that makes us different from one another

Other NIPTs look at chromosome fragments of conserved DNA – the 99% of our DNA that makes us the same

Mother or baby?  
Mother or baby?
Panorama's SNP-based approach yields the highest commercially available sensitivity for the most common ~3Mb 22q11.2 deletion.

For small deletions like 22q11.2, Panorama's ability to evaluate unique DNA sequences within the region of interest enables better detection.

Panorama reduces both false negative rates (FNR) and false positive rates (FPR) compared to other NIPTs.

Panorama’s SNP-based technology results in the highest fetal sex accuracy of any NIPT in validation studies.

Other NIPTs may report incorrect gender for as many as 1 in 77 cases. A wrong call can lead to unnecessary clinical work-up and create anxiety for the patient.

Panorama's SNP-based approach yields the highest commercially available sensitivity for the most common ~3Mb 22q11.2 deletion.

For small deletions like 22q11.2, Panorama’s ability to evaluate unique DNA sequences within the region of interest enables better detection.

*Based on a validation study of 419 samples, in which Panorama correctly identified 9/10 samples that were positive for 22q11.2. Only the paternal allele is evaluated at fetal fractions < 6.5%.
Accurate fetal fraction measurement is essential for accurate results\textsuperscript{22}

**Panorama is the only NIPT that has always measured and reported fetal fraction**

Panorama’s SNP-based method is a gold standard in fetal fraction measurement

<table>
<thead>
<tr>
<th>Method of fetal fraction measurement</th>
<th>Panorama\textsuperscript{1,2,3}</th>
<th>Harmony\textsuperscript{4,23}</th>
<th>MaterniT21\textsuperscript{5,6,7,24}</th>
<th>Verifi\textsuperscript{10,11,12}</th>
<th>Illumina platforms</th>
</tr>
</thead>
<tbody>
<tr>
<td>SNPs</td>
<td>13,392</td>
<td>576</td>
<td>Distribution of short (&lt;150 bp) cfDNA</td>
<td>No data available on methodology or performance</td>
<td>No data available on methodology or performance</td>
</tr>
<tr>
<td>Combined false negative rate in validation studies (trisomies 21, 18, 13)</td>
<td>0.60%</td>
<td>1.33%</td>
<td>1.89%</td>
<td>2.40%</td>
<td>No published data</td>
</tr>
</tbody>
</table>

Counting methodologies’ ability to detect abnormalities decreases below 8\% fetal fraction, which may increase false negative results\textsuperscript{25,26}

Deeper sequencing on chromosomal regions of interest enables Panorama to maintain high-quality results at lower fetal fractions

Panorama’s proprietary algorithm incorporates fetal fraction measurement and reflexes samples with lower fetal fraction to a higher depth of read.
Panorama for twin pregnancies

Only Panorama reports zygosity, individual fetal fractions for dizygotic twins, and fetal sex for each twin\textsuperscript{16}

<table>
<thead>
<tr>
<th></th>
<th>Panorama\textsuperscript{16}</th>
<th>Harmony\textsuperscript{29,30}</th>
<th>MaterniT21\textsuperscript{31}</th>
<th>Verifi\textsuperscript{32}</th>
<th>Illumina platforms\textsuperscript{33,34,35,36}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zygosity</td>
<td>✓</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>×</td>
</tr>
<tr>
<td>Individual</td>
<td>✓</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>×</td>
</tr>
<tr>
<td>fetal fractions</td>
<td>✓</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>×</td>
</tr>
<tr>
<td>Fetal sex for each</td>
<td>✓</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>×</td>
</tr>
<tr>
<td>twin</td>
<td>Trisomies 21, 18, 13</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Monosomy X\textsuperscript{*}</td>
<td>✓</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>×</td>
</tr>
<tr>
<td>22q11.2 deletion</td>
<td>syndrome\textsuperscript{*}</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

\textsuperscript{*}Available for monozygotic twins only

\textbf{FINAL RESULTS SUMMARY: TWINS}

\textit{Result}

\textbf{LOW RISK}

\begin{itemize}
  \item Zygosity: Dizygotic
  \item Fetal Sex: Male, Female
  \item Fetal Fraction(s): 8.3%, 8.4%
\end{itemize}

Notes by the clinical reviewer, if any, will be shown here.

Panorama allows clinicians to align their ultrasound findings with early and accurate zygosity information

Chorionicity is the strongest predictor for pregnancy complications in twins.\textsuperscript{37} Studies have shown that up to 19\% of monochorionic pregnancies are incorrectly classified as dichorionic using ultrasound.\textsuperscript{38}

\begin{itemize}
  \item Monozygotic
    \begin{itemize}
      \item Higher risk for twin-twin transfusion syndrome (TTTS), birth defects, etc. if monochorionic
      \item Consider early MFM referral to confirm chorionicity
      \item Develop tailored care plan for pregnancy
    \end{itemize}
  \item Dizygotic
    \begin{itemize}
      \item All dizygotic pregnancies are dichorionic
      \item Low risk for TTTS
      \item Continue standard care for pregnancy
    \end{itemize}
\end{itemize}

Fetal fraction measurement and reporting in twins is important for reliable NIPT results

Fetal fraction is, on average, 30\% higher in twin pregnancies, but fetal fraction per twin is lower compared to singleton pregnancies.\textsuperscript{28}
5. Jones et al. Ultrasound Obstet Gynecol. Accepted manuscript. DOI: 10.1002/uog.18986

The tests described have been developed and their performance characteristics determined by the CLIA-certified laboratory performing the tests. These tests have not been cleared or approved by the U.S. Food and Drug Administration (FDA). Although FDA does not currently clear or approve laboratory–developed tests in the U.S., certification of the laboratory is required under CLIA to ensure the quality and validity of the tests. ©2018 Natera, Inc. All Rights Reserved. PAN_MD_BR_2018_02_12_NAT-801513