Analytical performance of Vistara non-invasive prenatal screen for single nucleotide variants (SNVs)

Vistara screens for SNVs in 30 genes which can result in clinically significant and life-altering disorders. Screened conditions are not covered by traditional NIPTs or carrier screening.

Spike-in DNA samples

Artificial spike-in DNA samples were created by mixing genomic DNA from 13 affected individuals with maternal DNA. Fetal fractions ranged from 2.5 to 10%. The pathogenic variant of interest was identified in all created spike-in DNA samples.

Pregnancy plasma samples

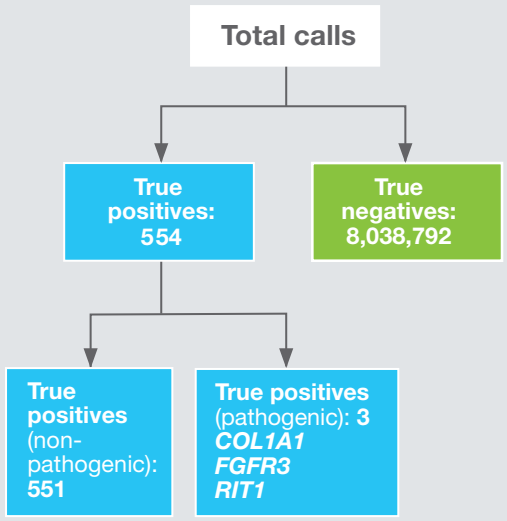
- 76 pregnant plasmas with paternal DNA samples
- 10 – 40 weeks gestational age range
- 4.5 – 30% fetal fraction range

Analysis compared cell-free fetal DNA (cffDNA) sequences with maternal DNA sequences and paternal DNA sequences.

This analytical validation involved the analysis of >8 million DNA base pairs across the 30 genes screened by Vistara.

All positive variants were confirmed by a secondary sequencing analysis.

Analysis of 30 genes from 76 pregnancies



True positives = Inherited paternal changes or *de novo* changes detected in cffDNA

True negatives = Homozygous parental reference DNA sequences also detected in cffDNA

Analytical validation results

Sensitivity: >99% (554/554)

Specificity: >99% (8,038,792/8,038,792)

- Correctly detected 3 affected cases and classified them as pathogenic/likely pathogenic (*COL1A1* , *FGFR3* , *RIT1*)
- Pathogenic *de novo* variants were confirmed by analysis of invasive or postnatal specimens
- Zero false negatives and zero false positives across >8 million base pairs

The analytical positive predictive value (PPV) for this test is >99% and the analytical negative predictive value (NPV) is >99%. The clinical PPV and NPV cannot be determined from this validation as they are dependent on additional factors, including specific disorder incidence rates.

Greater than 97% of variants are detected through next-generation sequencing.

Detection rates for pathogenic changes in genes screened by Vistara are dependent upon test performance and the proportion of pathogenic changes covered by Vistara.

vistara
SINGLE-GENE NIPT