

The non-invasive prenatal test (NIPT) that screens for single-gene mutations in cell-free fetal (placental) DNA



Vistara has a combined analytical sensitivity of >99% and a combined analytical specificity of >99% in validation studies.¹

Vistara facilitates early diagnosis and helps direct appropriate prenatal care

Vistara identifies the risk for conditions that may have otherwise gone undetected until after birth or into childhood.

- Ultrasound findings are not a reliable indicator of these conditions.
- Other NIPTs do not offer screening for these conditions, and invasive testing does not guarantee a diagnosis.
- Patient or family history are typically not good indicators of risk for these conditions, which are commonly caused by de novo mutations.

Vistara's identification of screened single-gene disorders enables clinicians to more thoroughly evaluate a pregnancy, guide labor and delivery management, and channel patients to necessary specialists.

Conditions screened through Vistara have a combined incidence of 1 in 600, higher than that of Down syndrome^{2,3}

The conditions screened meet at least one of the following criteria:

- Cause cognitive disability
- Require surgical or medical intervention
- Affect quality of life

These conditions are usually not inherited or tied to patient or family history

The conditions screened by Vistara are commonly caused by de novo mutations. These conditions are inherited in an autosomal or X-linked dominant fashion, which means that, if the mutation is present, the child is expected to be affected by the condition and experience related symptoms. The de novo mutations that cause these conditions may occur more frequently as the age of the father increases.

Vistara screens for for severe conditions across 30 genes that affect the skeletal, cardiac, and neurological system

Key conditions:

Condition <i>Gene detected</i>	Clinical synopsis ^{2,3}	Clinical actionability	Inheritance pattern ^{2,3}	Detection rate ¹
Noonan syndrome <i>PTPN11, SOS1, RAF1, RIT1, KRAS, NRAS, SOS2, SHOC2, BRAF, MAP2K1, HRAS, CBL</i>	Causes short stature, cardiac defects, bleeding problems and mild intellectual disabilities in some cases	<ul style="list-style-type: none"> • Fetal echocardiogram • Delivery at tertiary care unit • Early assessment for learning differences 	Caused by de novo mutations in 25–70% of cases	>86% to >96%
Osteogenesis imperfecta (OI) type I, II, III, IV <i>COL1A1, COL1A2</i>	Causes extremely fragile bones that break easily, often without an identifiable cause	<ul style="list-style-type: none"> • Delivery at tertiary care center • Early recognition and treatment of fractures 	More severe forms are likely to be de novo	>92%
Craniosynostosis <i>FGFR2, FGFR3</i>	Causes a premature fusion of the cranial bones, in some cases, intellectual disabilities	<ul style="list-style-type: none"> • Fetal MRI • Avoid instrumented delivery • Corrective surgery • Monitor for hydrocephalus 	More severe forms are likely to be de novo	>96%
Achondroplasia <i>FGFR3</i>	The most common form of skeletal dysplasia	<ul style="list-style-type: none"> • Delivery at tertiary care unit • Monitor for spinal stenosis • Early sleep studies to reduce risk of SIDS 	Caused by a de novo mutation in 80% of cases	>96%
Rett syndrome <i>MECP2</i>	Causes a rapid regression in language and motor skills at 6 to 18 months of age; autism, seizures, and long QT syndrome are often present	<ul style="list-style-type: none"> • Early medical and behavioral interventions • Evaluate for cardiac risk • Monitor and treat seizures 	Caused by a de novo mutation in more than 99% of cases	>78%

Prenatal testing for these conditions can lead to improved delivery management, better neonatal care, and more comprehensive prenatal education for parents

Vistara can identify conditions that may have otherwise gone undetected

Ability to detect conditions with ultrasound

A substantial number have no ultrasound findings

When there is no indication of a condition prenatally, clinicians and their patients cannot prepare for the birth of an affected child.

Examples:

Osteogenesis imperfecta (OI)^{2,3}

- Causes extremely fragile bones
- Includes many subtypes that range in severity
- Milder forms often do not have ultrasound findings and may not be detected prenatally
- Early diagnosis can help inform labor and delivery management and neonatal care

Rett syndrome^{2,3}

- Causes a rapid regression in language and motor skills at 6 to 18 months of age
- Has no ultrasound findings and is rarely detected using microarray
- Often goes undiagnosed until childhood
- Affected children may benefit from early medical and behavioral interventions

Many have late-gestation ultrasound findings

Ultrasound abnormalities for these conditions may present in the third trimester, when confirmatory invasive testing can pose a risk of preterm birth.

Examples:

Craniosynostosis²

- Causes a premature fusion of the cranial bones
- May not be visible until the third trimester
- Affected pregnancies may benefit from targeted evaluations, like fetal MRIs, to characterize the condition prenatally

Achondroplasia²

- The most common form of skeletal dysplasia
- May not be visible until the third trimester
- Affected pregnancies may need to be monitored to inform labor and delivery management and neonatal care

Many have non-specific ultrasound findings

Non-specific ultrasound findings, such as increased nuchal translucencies (NT) and heart defects, are relatively common and have a variety of genetic and non-genetic causes.

Example:

Noonan syndrome^{2,3}

- Affects 1 in 1,000 to 1 in 2,500 births
- Causes short stature, cardiac defects, bleeding problems, and mild intellectual disabilities in some cases
- Has non-specific ultrasound findings and may not be suspected prenatally
- Often goes undiagnosed until childhood
- Early diagnosis can help inform labor and delivery management and direct early assessments for learning differences

Other NIPTs cannot detect these conditions

Other non-invasive prenatal screening options can only identify whole-chromosome aneuploidies and select microdeletions or duplications. Vistara identifies risk for single-gene mutations in the cell-free fetal DNA found in maternal blood.

These conditions are not routinely detected using standard karyotype, FISH, or microarray

Patients who elect to have invasive testing are not typically offered prenatal diagnosis for these conditions.

If ultrasound abnormalities are seen and diagnostic testing is offered, it can be difficult for clinicians to know which panels should be ordered, especially when ultrasound findings are non-specific.

Screening with Vistara may help direct prenatal and neonatal care



Early screening with Vistara enables patients to be referred to an MFM and other specialists for targeted evaluations, such as fetal echocardiograms, MRIs, and targeted anatomic surveys.

Pregnancies at increased risk for Noonan syndrome require comprehensive evaluation for associated birth defects, particularly cardiac malformations.⁴ Fetal echocardiogram findings can help determine whether surgical intervention is required immediately after birth and whether delivery should take place at a tertiary care unit.



Prenatal diagnosis of birth defects allows providers and patients to plan delivery in centers equipped to provide prompt evaluation and treatment.

Pregnancies affected by OI are at increased risk for pre-term delivery and breech presentation.⁵ Newborns with OI must be handled with extreme care at delivery to reduce the risk of bone fractures.

Infants with syndromic craniosynostosis require corrective surgeries and care by a craniofacial team. In addition, these infants are at risk for breathing problems, failure to thrive, and hydrocephalus.²



Learning about these complex genetic disorders before birth enables families to mobilize resources, ask questions, and anticipate future needs.

With a correct diagnosis, expectant parents have the opportunity to meet with pediatric surgeons or other sub-specialists to prepare for possible neonatal interventions. Early diagnosis enables families to establish care with specialists who can support their child's health and development.

References

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