vistara
SINGLE-GENE NIPT

cfDNA screening for skeletal, cardiac, and neurological disorders

- **Noonan syndrome**
- **Achondroplasia**
- **Osteogenesis imperfecta**
- **Rett syndrome**
- **And 21 other conditions across 30 genes**

Conditions screened by Vistara have a combined incidence of **1 in 600** higher than that of Down syndrome[1,2,3]

Vistara identifies risk for single-gene disorders that may have otherwise gone undetected prenatally

- Ultrasound findings are not a reliable indicator
- Conditions are not detected with standard microarray analysis
- Family history is typically not a good indicator of risk
- Early identification of these conditions is clinically actionable

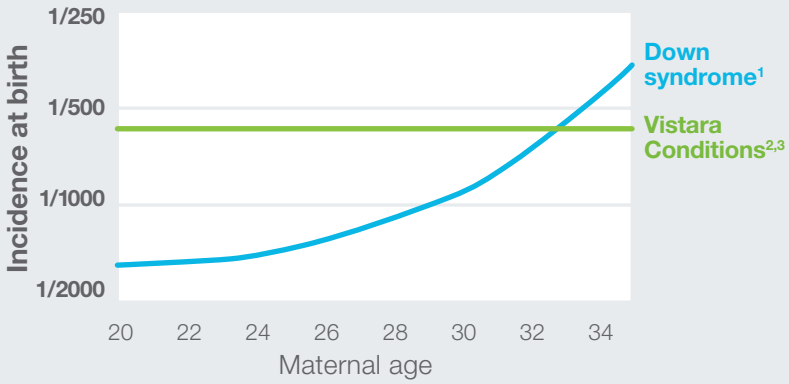
natera®
Conceive. Deliver.

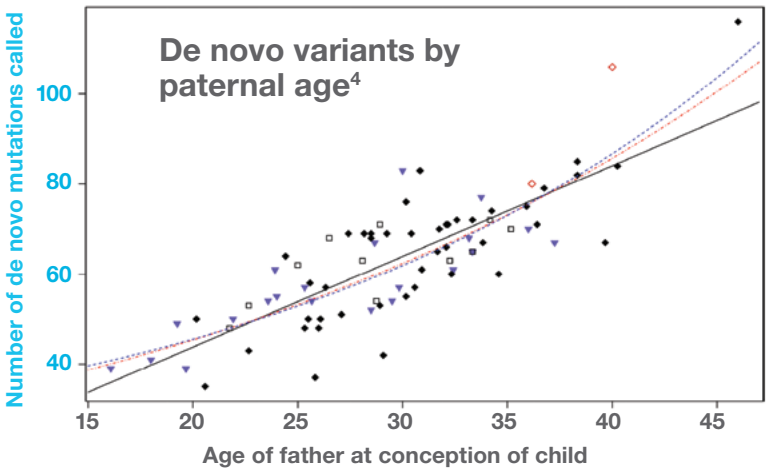
Screen non-invasively for Noonan syndrome, osteogenesis imperfecta, Rett syndrome, and other serious genetic conditions caused by single-gene mutations across 30 genes

Conditions screened by Vistara have a combined incidence of 1 in 600 – higher than that of Down syndrome

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

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





The single-gene disorders screened by Vistara are usually not inherited or related to family history

- Typically caused by new, or "de novo," genetic changes (variants)
- May occur more frequently as the age of the father increases[5]
- Are not related to the age of the mother
- Are autosomal or X-linked dominant – if the variant is present, the child is expected to be affected by the condition and experience related symptoms

Consider Vistara for the following indications:

Advanced paternal age

Women who want to know "everything"

Ultrasound anomalies, such as shortened long bones and increased NT

Adjunct to CVS and amniocentesis

"We have been offering Vistara when the father of the pregnancy is age 40 or over, and also when a couple opts to pursue CVS or amniocentesis. Our thought is that if a couple wants as much information as possible, then Vistara is a reasonable screen to offer."

– Dr. Sheri Hamersley, M.D., Maternal-Fetal Medicine Associates of Maryland

Vistara results may help direct prenatal and neonatal care

Vistara results will show whether a pathogenic or likely pathogenic single-gene variant has been identified

Result:
SCREEN POSITIVE

Genetic counseling and confirmatory diagnostic testing are recommended.

Diagnostic samples must be sent to a laboratory that provides testing for the genetic variant identified.

Result:
SCREEN NEGATIVE

No pathogenic or likely-pathogenic variants were identified in the 30 genes screened.

Vistara is not a diagnostic test and does not provide a definitive diagnosis of any conditions screened.

Demonstrated accuracy in validation studies, with no known false positives in commercial experience

Analytical validation[6]

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

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
- No false negatives and no false positives across >8 million base pairs in validation

Commercial experience in 2017[7]

No known false positives across 23 fetal screen-positive cases

- Four fetal diagnostic confirmations
- Nineteen positives with consistent ultrasound findings or paternal family history

Skeletal disorders *COL1A1, COL1A2, FGFR3*	**13 positives**
Noonan syndrome *PTPN11, RIT1, KRAS*	**5 positives**
Syndromic disorders *JAG1, TSC2, NIPBL*	**3 positives**
Craniosynostosis syndromes *FGFR2*	**2 positives**

Prenatal screening with Vistara can lead to improved delivery management and targeted neonatal care

Disorder	Clinical actions
Osteogenesis imperfecta	• Labor and delivery management to avoid fractures • Neonatal care • Early recognition and treatment of fractures
Achondroplasia	• Labor and delivery management • Monitor for spinal stenosis • Early sleep studies to reduce risk of SIDS
Noonan syndrome	• Fetal echocardiogram • Labor and delivery management • Early assessment for learning differences
Craniosynostosis	• Fetal MRI • Avoid instrumented delivery • Corrective surgery • Early medical and behavioral interventions

Provider

- **Proactive billing outreach and price transparency**
- **Complimentary mobile phlebotomy services and in-office phlebotomist for our testing***
- **Support from board-certified genetic counselors**
- **Provider portal to help you manage testing**

Patients

- **Patient portal and educational resources**
- **Convenient mobile phlebotomy services***
- **Complimentary pre- and post-test genetic information sessions**
- **Flexible payment plans**

**Where permitted by state law*

References

1. Snijders et al. Ultrasound Obstet Gynecol. 1999 Mar; 13(3):167–70.
2. GeneReviews. www.ncbi.nlm.nih.gov/books/NBK1116.
3. Genetics Home Reference. www.ghr.nlm.nih.gov.
4. Kong et al. Nature. 2012 Aug; 488(7412): 471–5.
5. American College of Medical Genetics (ACMG), Practice Guideline, June 2008.
6. Vistara validation white paper, 2017.
7. Commercial data, Natera, 2017.

natera®
Conceive. Deliver.

201 Industrial Road, Suite 410 | San Carlos, CA 94070 | www.natera.com | 1-650-249-9090 | Fax 1-650-730-2272

VTR_MD_BR_2018_02_14_NAT-801518