## Vistara non-invasive prenatal screen



Vistara identifies probability for conditions that may have otherwise gone undetected until after birth or into childhood. All conditions are inherited in an autosomal or X-linked dominant fashion, which means that if the mutation is present, the child will be affected by the condition and experience related symptoms.

| <b>Condition</b> <sup>1</sup><br>Gene(s)   | Clinical synopsis <sup>2,3</sup>   | Cases<br>caused by<br>de novo<br>mutations <sup>2,3</sup> | Ultrasound findings <sup>2,3</sup> |                 |                  | Clinical   | Detection         |
|--|--|---|------------------------------------|-----------------|------------------|--|-------------------|
|  |  |   | None                               | Third trimester | Non-<br>specific | actionability  | rate for<br>gene¹ |
| <b>Achondroplasia</b><br>FGFR3   | The most common form of skeletal dysplasia; may cause hydrocephalus, delayed motor milestones, and spinal stenosis   | 80%   |                                    | •               | •                | Labor and delivery<br>management, monitor for<br>spinal stenosis, early sleep<br>studies to reduce<br>risk of SIDS                   | >96%              |
| Alagille<br>syndrome<br>JAG1   | Affects multiple organ systems<br>and may cause growth problems,<br>congenital heart defects, and<br>vertebral differences   | 50% to 70%  | •                                  |                 |                  | Symptom-based treatment  | >86%              |
| Antley Bixler<br>syndrome<br>FGFR2   | A type of craniosynostosis; also causes<br>premature fusion of the arm bones,<br>blockage of the nasal passage, and<br>permanently flexed or extended joints   | more<br>severe<br>forms                                   |                                    | •               |                  | Fetal MRI, avoid<br>instrumented delivery,<br>corrective surgery, monitor for<br>hydrocephalus                                       | >96%              |
| Apert<br>syndrome<br>FGFR2   | A type of craniosynostosis; also causes abnormal formation of the fingers, toes, and vertebrae, and other organ anomalies  | more<br>severe<br>forms                                   |                                    | •               |                  | Fetal MRI, avoid<br>instrumented delivery,<br>corrective surgery, monitor for<br>hydrocephalus                                       | >96%              |
| Cardiofaciocu-<br>taneous syndrome<br>1,3,4<br>BRAF, MAP2K1,<br>MAP2K2                   | Causes abnormalities of the heart, face, skin, and hair; may cause developmental delays and intellectual disability  | majority  |                                    | •               | •                | Fetal echocardiogram   | >96%              |
| CATSHL syndrome<br>FGFR3   | Acronym stands for camptodactyly,<br>tall stature, scoliosis, and hearing<br>loss; may increase risk for<br>intellectual disability  | unknown   | •                                  |                 |                  | Early adoptionof sign<br>language and behavioral<br>intervention   | >96%              |
| CHARGE<br>syndrome<br>CHD7   | Acronym stands for coloboma, heart defects, atresia of the choanae, retardation of growth and development, genital abnormality, ear abnormalities; may cause hearing loss, developmental delays, and cleft lip and/or palate | majority  | •                                  | •               | •                | Early referral to<br>endocrinology, adoption<br>of sign language, and<br>behavioral intervention                                     | >91%              |
| Cornelia de Lange<br>syndrome 1,2,3,4,5<br>NIPBL, SMC1A,<br>SMC3, RAD21,<br>HDAC8        | Causes a range of physical, cognitive, and medical challenges  | 99%   | •                                  |                 | •                | Monitor for cardiac,<br>GI, and limb<br>comorbidities  | 53% to >96%       |
| Costello syndrome<br>HRAS  | Causes heart defects, intellectual disability, developmental delays, growth delays, and increased risk of malignant tumors   | majority  | •                                  |                 | •                | Nasogastric or<br>gastronomy feeding,<br>behavioral and<br>medical intervention  | >92%              |
| Crouzon<br>syndrome<br>FGFR2, FGFR3  | A type of craniosynostosis; also causes<br>hearing loss and dental problems in<br>some cases   | more<br>severe<br>forms                                   |                                    | •               |                  | Fetal MRI, avoid instru-<br>mented delivery, corrective<br>surgery, monitor for<br>hydrocephalus, early adoption<br>of sign language | >96%              |
| Ehlers-Danlos<br>syndrome, classic,<br>type VIIA, cardiac<br>valvular form, type<br>VIIB | Causes defects in connective tissue that can vary from mildly loose joints to life-threatening complications, such as aortic dissection  | 50%   | •                                  |                 |                  | Orthotic treatment, monitoring for vascular complications  | >92%              |
| Epileptic encepha-<br>lopathy, early<br>infantile, 2                                     | Causes seizures with secondary developmental delay   | majority  | •                                  |                 |                  | Monitor and treat seizures   | >84%              |

| <b>Condition</b> <sup>1</sup><br>Gene(s)  | Clinical synopsis <sup>2,3</sup>  | Cases<br>caused by<br>de novo<br>mutations <sup>2,3</sup> | Ultra | sound findi        | ngs <sup>2,3</sup> | Clinical<br>actionability   | Detection<br>rate for<br>gene <sup>1</sup> |
|---|---|---|-------|--------------------|--------------------|---|--|
|   |   |   | None  | Third<br>trimester | Non-<br>specific   |   |  |
| Hypochondro-<br>olasia<br>FGFR3   | Causes a mild form of dwarfism; may cause seizures with secondary developmental delay   | up to 80%   | •     |                    |                    | Monitor and treat seizures  | >96%                                       |
| ntellectual<br>disability<br>SYNGAP1  | Causes intellectual disability and developmental delays   | ~100%   | •     |                    |                    | Early behavioral interventions  | >86%                                       |
| Jackson Weiss<br>syndrome<br>FGFR2  | A type of craniosynostosis; also causes foot abnormalities  | more<br>severe<br>forms                                   |       | •                  |                    | Fetal MRI, avoid instrumented delivery, corrective surgery, monitor for hydrocephalus   | >96%                                       |
| Juvenile<br>myelomonocytic<br>eukemia (JMML)<br>PTPN11  | A rare pediatric blood cancer; five-<br>year survival is approximately 50%  | unknown   | •     |                    |                    | Monitor bloodwork<br>and medical<br>intervention  | >96%                                       |
| EEOPARD<br>syndrome 1,2<br>(Noonan syndrome<br>with multiple<br>entigines)<br>PTPN11, RAF1                                    | Similar to Noonan syndrome,<br>with notable brown skin spots<br>(lentigines); causes short stature,<br>heart defects, bleeding problems,<br>and, in some cases, mild<br>intellectual disabilities | unknown   | •     |                    | •                  | Fetal<br>echocardiogram   | >96%                                       |
| Muenke syndrome<br>FGFR3  | A type of craniosynostosis;<br>may cause hearing loss,<br>developmental delays, and<br>cleft lip and/or palate  | unknown   |       | •                  |                    | Fetal MRI, corrective surgery,<br>early adoption of sign language,<br>and behavioral intervention   | >96%                                       |
| Noonan syndrome<br>1,3,4,5,6,8,9<br>PTPN11, SOS1,<br>RAF1, RIT1, KRAS,<br>NRAS, SOS2,<br>SHOC2, BRAF,<br>MAP2K1, HRAS,<br>CBL | Causes short stature, heart defects, bleeding problems, and, in some cases, mild intellectual disabilities  | 25% to 70%  | •     | •                  | •                  | Fetal echocardiogram, labor<br>and delivery management, early<br>assessment for learning<br>differences   | >92% to<br>>96%                            |
| Osteogenesis<br>Imperfecta,<br>Itype I,II,III,IV<br>COL1A1, COL1A2  | Causes fragile bones that break easily, often without an identifiable cause   | more<br>severe<br>forms                                   | •     |                    |                    | Labor and delivery management,<br>neonatal care, early recognition<br>and treatment of fractures  | >92%                                       |
| Pfeiffer<br>syndrome<br>type 1,2,3<br>FGFR2   | A type of craniosynostosis; also causes hearing loss, intellectual disability, hand abnormalities, and may result in early death  | more<br>severe<br>forms                                   |       | •                  |                    | Fetal MRI, avoid instrumented<br>delivery, corrective surgery,<br>monitor for hydrocephalus, early<br>adoption of sign language, and<br>behavioral intervention | >96%                                       |
| Rett syndrome<br>MECP2  | Causes a rapid regression in language<br>and motor skills at 6 to 18 months of<br>age; autism, seizures, and long QT<br>syndrome are often present  | >99%  | •     |                    |                    | Evaluate for cardiac<br>risk, monitor and treat seizures,<br>early medical and behavioral<br>interventions  | >78%                                       |
| Sotos syndrome 1<br>NSD1  | Overgrowth syndrome; also causes developmental delays, intellectual disability, and behavioral problems   | >95%  |       | •                  |                    | Fetal echocardiogram, fetal<br>renal ultrasound, and early<br>behavioral intervention   | >47%                                       |
| Thanatophoric<br>dysplasia,<br>types I,II<br>FGFR3  | A severe skeletal disorder that typically results in stillbirth or neonatal death due to respiratory failure  | majority  |       |                    | •                  | Labor and delivery management   | >96%                                       |
| Tuberous sclerosis<br>1,2<br>TSC1, TSC2   | Causes benign tumor growth in many organ systems in the body that can be life-threatening; may also cause seizures and secondary developmental delays   | 66%   |       |                    |                    | Fetal echocardiogram, postnatal MRI, medical and behavioral interventions   | >91% to >96%                               |

= some types or cases

- References
  1. Validation data, Baylor. 2020.
  2. GeneReviews. https://www.ncbi.nlm.nih.gov/books/NBK1116/
  3. Genetics Home Reference. https://ghr.nlm.nih.gov/
- Vistara has been developed and its performance characteristics determined by the CLIA-certified laboratory performing the test. The test has not been cleared or approved by the US Food and Drug Administration (FDA). CAP accredited, ISO 13485 certified, and CLIA certified. © 2021 Natera, Inc. All Rights Reserved.