

General information about positive NIPT results: Partial duplication (CNV \geq 7 Mb)

My patient's NIPT is positive for a partial duplication.

What does this mean?

Your patient's noninvasive prenatal testing (NIPT) result detected a partial duplication of 7 Mb or larger. See the report for details regarding the size and the region of the chromosome involved. NIPT is a screening test; false positives can occur. The actual chance for the pregnancy to have a partial duplication depends on many factors, including the patient's clinical and family history.

Next steps to consider: You should discuss the results and the potential clinical implications with your patient. Globally, professional medical societies recommend that all women with a positive screening result should have genetic counseling and a comprehensive ultrasound evaluation with an opportunity for diagnostic testing to confirm the results.^{1,2} Confirmation prior to birth can also help with pregnancy and neonatal management.

See below for information about partial duplications.

What is a partial duplication?

A partial duplication is a gain of part of a chromosome. It can be either interstitial (within a chromosome) or terminal (at the end of the chromosome), or due to an isochromosome (duplication of the whole arm). It results in a gain of genomic material for the region of the duplicated segment of the chromosome. Duplications of 7 Mb or larger are likely to be seen on karyotype analysis.

What are the features of a partial duplication?

The clinical significance is variable and is based on the size and location of the duplication, presence of additional deletions or duplications, and whether it is inherited from a phenotypically normal parent. In general, partial duplications that are 7 Mb or larger are likely to be associated with a clinical phenotype, which can include intellectual disability, structural anomalies, dysmorphic features, and possibly other medical issues. There are certain recurring duplications for which the clinical features are well described. Some examples of these include 9q duplication and 10q duplication. However, other duplications may not be associated with a specific syndrome. Some duplications may be inherited from a phenotypically normal parent and may not be of clinical significance. The exact phenotype will depend on the region of the chromosome involved. This will require a specific literature search to better understand the clinical significance. Confined placental mosaicism (CPM; when cells with partial duplications are present in the placenta, but not in the fetus) has been reported.

What is the prevalence of this condition?

Birth prevalence is approximately 1 to 2 per 10,000.³ Prevalence in NIPT is reported to be 0.12% to 0.16% (includes deletions and duplications). Positive predictive value (PPV) in one study was 32%.⁴

What testing could be considered?

Specialized genetic tests such as karyotyping, fluorescence *in situ* hybridization (FISH), quantitative polymerase chain reaction (qPCR), and microarray are available to confirm the presence of a partial duplication.

These confirmatory tests are generally performed on cells from chorionic villus sampling (CVS) or amniocentesis during pregnancy, on cord blood or peripheral blood sample after the baby is born, or on products of conception (POC) in the case of a miscarriage. The type of invasive procedure and diagnostic testing should take into account the underlying chromosome anomaly.^{5,6}

Ultrasound evaluation may be useful in aiding with a prenatal diagnosis of partial duplication, but a normal ultrasound cannot exclude this condition.

Special considerations

The presence of a maternal copy number variation (CNV) may lead to a positive NIPT result (causing a false positive fetal result). Some of these CNV are likely to be benign. Presence of partial duplication may be due to a balanced parental rearrangement; it may be appropriate to consider parental karyotyping.

Resources for partial duplication

ClinGen Clinical Genome Resource
clinicalgenome.org

Unique, The Rare Chromosome Disorder Support Group
rarechromo.org

References

- Rose NC, Kaimal AJ, Dugoff L, et al. *Screening for Fetal Chromosomal Abnormalities: ACOG Practice Bulletin, Number 226. Obstet Gynecol.* 2020;136(4):e48-e69.
- Benn P, Borrell A, Chiu RW, et al. *Position statement from the Chromosome Abnormality Screening Committee on behalf of the Board of the International Society for Prenatal Diagnosis. Prenat Diagn.* 2015;35(8):725-734.
- Wellesley D, Dolk H, Boyd PA, et al. *Rare chromosome abnormalities, prevalence and prenatal diagnosis rates from population-based congenital anomaly registers in Europe. Eur J Hum Genet.* 2012;20(5):521-526.
- van der Meij KRM, Sistermans EA, Macville MVE, et al. *TRIDENT-2: National Implementation of Genome-wide Non-invasive Prenatal Testing as a First-Tier Screening Test in the Netherlands. Am J Hum Genet.* 2019;105(6):1091-1101.
- Cherry AM, Akkari YM, Barr KM, et al. *Diagnostic cytogenetic testing following positive noninvasive prenatal screening results: a clinical laboratory practice resource of the American College of Medical Genetics and Genomics (ACMG). Genet Med.* 2017;19(8):845-850.
- Van Opstal D, Srebniak MI. *Cytogenetic confirmation of a positive NIPT result: evidence-based choice between chorionic villus sampling and amniocentesis depending on chromosome aberration. Expert Rev Mol Diagn.* 2016;16(5):513-520.

Additional resources

Gardner RJM, Amor DJ. *Gardner and Sutherland's Chromosome Abnormalities and Genetic Counseling.* 5th ed. Oxford University Press; 2018.

Jones KL, Jones MC, del Campo M. *Smith's Recognizable Patterns of Human Malformation.* 7th ed. W.B. Saunders Company; 2013.

Snyder MW, Simmons LE, Kitzman JO, et al. *Copy-number variation and false positive prenatal aneuploidy screening results. N Engl J Med.* 2015;372(17):1639-1645.