Prenatal Screening for 22q11.2 Deletion Using a Targeted Microarray-based Cell-free DNA (cfDNA) Test

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Study Population

Two part-study (analytical validation and clinical verification) of 1953 plasma samples, 122 of which had confirmed deletions.

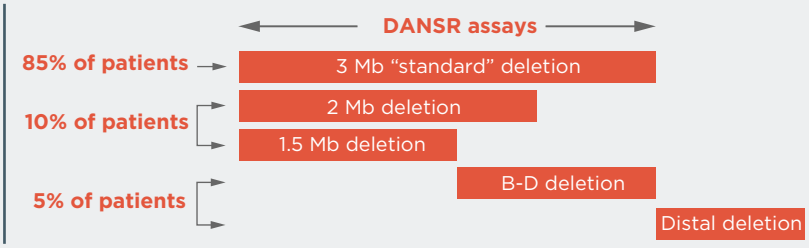
Fetal 22q11.2 deletions of 3 Mb and smaller were assessed.

Summary and Key Points

Purpose: To evaluate the performance of the Harmony® prenatal test, a targeted microarray based cfDNA test, in identifying pregnancies at increased risk for a 22q11.2 deletion.

Result: The Harmony® prenatal test is able to identify pregnancies at increased risk for 22q11.2 deletions of 3Mb and smaller while maintaining a low false positive rate.

Harmony prenatal test DANSR assays coverage



Results

Analytical validation: 92 out of 122 samples with confirmed deletions were identified as having a high probability of 22q11.2 deletion. 1606 out of 1614 presumed unaffected pregnancies were reported as having no evidence of deletion. Specificity of 99.5%.

Smallest size deletion detected: 1.96 Mb. No correlation observed between sensitivity and deletion size.

Clinical verification: 5 out of 7 samples with deletions were reported as having a high probability of deletion. No false positives in the 210 unaffected samples.

Conclusions

The Harmony® prenatal test identifies pregnancies at increased risk for 22q11.2 deletions of 3Mb and smaller with high specificity.

	Analytical validation	Clinical verification	Combined
Total samples (N)	1736	217	1953
22q11.2 (n/N)	92/122	5/7	97/129
No evidence of a deletion (n/N)	1606/1614*	210/210	1816/1824
Sensitivity %, (95% CI)	75.4 (67.1-82.2)	71.4 (35.9-91.8)	75.2 (67.1-81.8)
Specificity %, (95% CI)	99.5 (99.0-99.7)	100 (98.2-100)	99.6 (99.1-99.8)

*Estimations were made using samples with no known 22q11.2 deletion and were presumed to be unaffected. Actual specificity could be higher.

1. Sparks AB, Struble CA, Wang ET, Song K, Oliphant A: Noninvasive prenatal detection and selective analysis of cell-free DNA obtained from maternal blood: evaluation for trisomy 21 and trisomy 18. *Am J Obstet Gynecol* 2012;206:319.e1-9.
2. McDonald-McGinn DM, Tonnesen MK, Laufer-Cahana A, Finucane B, Driscoll DA, Emanuel BS, Zackai EH: Phenotype of the 22q11.2 deletion in individuals identified through an affected relative: cast a wide FISHing net. *Genet Med* 2001;3:23-29