Diagnostic Yield and Utility of Clinical Exome Sequencing

1. Introduction

• Clinical exome sequencing (CES) is sequencing and analysis of the exons of only clinically-relevant genes compared to sequencing the exons of all 20,000 genes in whole exome sequencing (WES).

• CentoDx Plus™ is a customized CES test targeting ~6,700 genes with 100% coverage of the exons of >4000 genes.
  • It is the largest NGS panel covering genes within all disease specialties.
  • Boosted coverage of regions of clinical interest allows better and more uniform coverage compared to WES.
  • Due to good coverage and affordability, CES is suitable for patients and physicians in regions where high cost is a significant barrier to uptake of genetic testing and diagnosis.

2. Aim

To assess the clinical utility of CES (CentoDx Plus™) at CENTOGENE using diagnostic yield as a measure.

3. Methods

• CES was performed on 206 patients utilizing Illumina technology and custom probes for ~6,700 genes.
• Reported cases were analyzed to determine cases with diagnostic variants.

4. Results

• The diagnostic rate (confirmed diagnoses) of CES in this cohort was 53.4% (110 of 206 cases).
• If the additional 35.9% of cases (74/206) with relevant VUS findings are considered, the overall diagnostic rate is as high as 89.3%.

5. Conclusions

• The high diagnostic yield of CES is evident in this small cohort of samples.
• The higher yield compared to a WES is likely due to using the test to diagnose both – patients with known, suspected diagnoses (in lieu of sequential single gene testing or one or more NGS panels) and undiagnosed cases with unknown, complex phenotypes (instead of a WES).
• CES is a single, versatile test yielding a higher diagnostic rate and clinically useful result for a variety of diagnostic indications and needs.
• Due to the cost- and time-efficient nature, good coverage & high diagnostic rate, CES is a good alternative to sequential testing, NGS panels or even a WES.
• Especially in regions with economic barriers to genetic testing, CES should be considered a prime test of choice for patient undergoing genetic testing.

References


Disclosures

The lead author is an employee of CENTOGENE AG, Rostock, Germany. Co-authors are employees of the organizations as described above. The authors have no other conflicts of interest to declare.