MT-RNR1

Pharmacogenetics to Avoid Loss of Hearing (PALOH) Summary

Article Title	Rapid Point-of-Care Genotyping to Avoid Aminoglycoside-Induced Ototoxicity in Neonatal Intensive Care
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Objective of Study

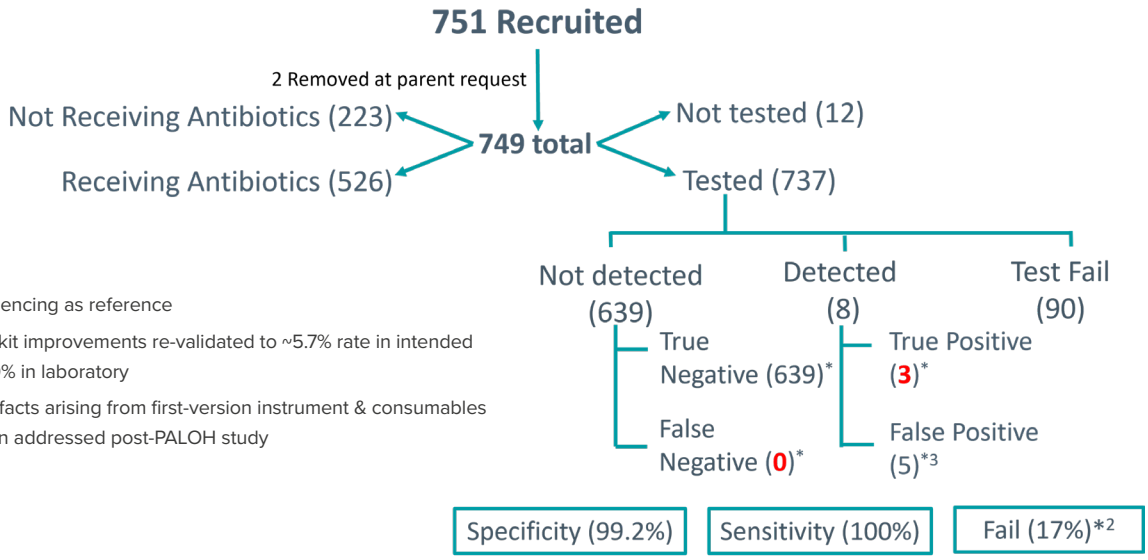
To develop a rapid point-of-care test for the MT-RNR1 m.1555A>G variant and implement in the acute neonatal setting to guide antibiotic prescribing and avoid antibiotic induced hearing loss without disrupting normal standard of care. The prospective implementation trial, also known as the PALOH Study, recruited neonates admitted to 2 large neonatal intensive care units in the UK, in 2020.

Key Takeaways

1. The PALOH study was published in JAMA Pediatrics in March 2022, with an accompanying editorial[1] describing the Genedrive® MT-RNR1 test as “entering a new era” and “an important step in the management of neonatal sepsis”.
2. Clinicians were able to successfully integrate the novel Genedrive® MT-RNR1 point-of-care test into the neonatal admission process without disrupting normal clinical practice.
3. Genotype was used to guide antibiotic prescription and avoid antibiotic induced hearing loss. This approach identified the m.1555A>G variant in a practice-changing time frame, and wide adoption could significantly reduce the burden of antibiotic induced hearing loss.
4. Three participants with the m.1555A>G variant were identified, all of whom avoided aminoglycoside antibiotics. Alternative cephalosporin-based treatments were used.
5. The test was able to genotype the m.1555A>G variant in 26 minutes. Median time to swab was 6 minutes.
6. The mean time to antibiotics was equivalent to previous practice (55.87 Vs 55.18 minutes)
7. There was a high degree of acceptability for this novel genetic testing approach from clinicians and parents.

1. De-Ann M. Pillers. JAMA Pediatr. 2022;176(5):448-449. doi:10.1001/jamapediatrics.2022.0184

Key Data



* Sanger sequencing as reference

*2 Post-study kit improvements re-validated to ~5.7% rate in intended setting/user, 0% in laboratory

*3 Due to artefacts arising from first-version instrument & consumables that have been addressed post-PALOH study

A total of 424 (80.6%) neonates were genotyped and prescribed antibiotics, including a total of 3 true positives. All results were confirmed using Sanger sequencing.

There were no false negative results.

Important Points

1. A total of 5 false positive results occurred early in the first month of the study.
2. Throughout the study data was collected to inform product modification by Genedrive to improve the final system performance. This included redesign of the assay cartridge lid to ensure complete insertion and reduce the test fail and false positive rate.
3. Post-study product enhancements have led to substantial improvement in assay analytical sensitivity, thereby addressing the test fail rate seen during the study. This included modifications to the assay buffer formulation to improve the analytical sensitivity. A new CE marked Genedrive® System was developed based on the feedback provided by the nurses during the study, which replaced the early Genedrive® instrument that was used.

PALOH Study Genedrive® Product

Post-Study Genedrive® Product

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