Enhanced detection of esr1 mutations in breast cancer: validation of the galeas upcr:esr1 kit on multiple commercially available reference standards.

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Abstract

Background

Mutations in the ESR1 gene are a significant cause of resistance to hormone therapy in estrogen receptor (ER)-positive breast cancer patients and occur in 10-50% of metastatic endocrine-therapy resistant cancers. Detecting these mutations through liquid biopsy testing can guide treatment towards more effective targeted therapies, as recommended by ESMO and ASCO guidelines. However, current ESR1 variant testing on cfDNA is mostly conducted using complex, time-consuming, and expensive sequencing technologies.

Objectives

To validate the Galeas uPCR:ESR1 kit developed by Nonacus using commercially available reference standards provided by SensID, ZeptoMetrix, and SeraCare; and thus confirming the kit's performance in detecting common ESR1 variants with high analytical sensitivity and specificity.

Methods

The Galeas uPCR:ESR1 kit uses proprietary qPCR technology developed at Nonacus to detect 11 of the most common ESR1 mutations, which account for over 90% of variants associated with endocrine therapy resistance. The analytical sensitivity of the kit is greater than 90% at limits of detection ranging from 0.04% to 0.33% variant allele frequency (VAF) across the 11 targets, with an analytical specificity of ≥98%.

Results

The technology was evaluated using ESR1 cfDNA reference material provided by SensID, which included the E380Q, D538G, Y537S, Y537N, S463P, Y537C, L536H, and L536R variants. At 15 ng input, all variants were detected at contrived VAFs of 1%, 0.3%, and 0.1%. Additionally, the kit’s performance was evaluated on the Zeptometrix ESR1 Control Kit, confirming that 10 out of 11 mutations could be detected down to 0.1% VAF, with only the S463P variant not detected at the lowest VAF tested. Further validation with SeraCare ctDNA ESR1 Mutation Mix AF1 reference material showed positive amplification for all tested VAFs (1%, 0.3%, and 0.1%), with HEX channel variants E380Q and S463P detected down to 0.1% VAF in all replicates.

Conclusions

The Galeas uPCR:ESR1 qPCR kit presents a simple yet powerful solution for the detection of ESR1 mutations linked with endocrine therapy resistance in breast cancer. This new technology offers a faster, accurate, and cost-effective alternative to existing sequencing methods, potentially improving treatment outcomes for breast cancer patients. The validation with SensID, ZeptoMetrix, and SeraCare reference standards further supports the kit's robustness and reliability.

Do you have any conflicts of interest?

Yes, I have a conflict of interest.

I am employed by Nonacus Ltd