**Background**

- RET (REarranged during Transfection) gene fusions occur in 1-2% non-small-cell lung cancers (NSCLCs).
- Timely and accurate detection screening methods are needed to identify patients likely to benefit from RET-targeted therapy.
- Fluorescence In Situ Hybridization (FISH) is commonly used for RET gene rearrangements detection.

**Aim of the study**

- To perform an up-to-date comprehensive review of publications in which RET rearrangement testing was performed by FISH and compare the methods used by the various laboratories with our own data.

**Methods**

- An electronic systematic literature search for publications from 2000 to 2021 reporting RET rearrangement testing.
- Comparison of the findings with the molecular results obtained from 2013 to 2021 at the Grenoble University Hospital.
- 784 *EGFR*, *KRAS*, *ALK* and *ROS1*-negative NSCLC samples were tested by RET breakapart FISH (Zytovision).
- FISH positivity threshold used: ≥15% of tumor cells showing separated 5’ and 3’ signals and/or isolated 3’ signals.
- All FISH-positive samples underwent a confirmatory RNA-sequencing analysis (ThermoFisher and/or ArcherDx RNA fusion commercial panels).

**Results**

- 170 publications reporting RET rearrangement testing were identified.
- 82 publications reported using RET FISH, 51 in lung cancer.

**Conclusion**

Based on our results and those reported in the literature:

- RET FISH is a sensitive technique, but the specificity is lowered by false-positive results, requiring a confirmatory technique for FISH-positive samples, especially those with 3’ isolated signals.
- The ≥15% positivity threshold, the most largely used in the literature, was adequate for the use of FISH as a RET rearrangement pre-screening tool with the probe used.

References:


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