DXRX
The Diagnostic Network

by

Diaceutics
Better Testing, Better Treatment

FGFR3 testing in bladder cancer

FAQs

Dr. Michael Hubank

Q1: Which molecular testing method is best suited for the detection of FGFR3 genetic alterations? Are there any challenges with false positives or false negatives using archival samples?

Archival samples can be very important in metastatic cases or when it's difficult to take another biopsy. In some cases, it's better to use new samples as they provide the exact description of the tumor state as it is now, which has its benefits. Since FGFR3 alterations can frequently be an early event, they are likely to be present in the archival material from the initial sample. If the test hasn't been done on the patient and only archival material is available, it's important to conduct the test on that material. There is a good chance that the FGFR3 mutation, if present, will be detected in the sample. The only exception would be if the material hasn't been fixed properly.

In terms of the best methodologies, we recommend using a large gene panel that comprehensively covers the full DNA and RNA sequences for FGFR2 and FGFR3. A sequencing-based approach is also recommended for its comprehensiveness, and it's important to perform both DNA and RNA tests to detect fusions and DNA point mutations.

Ideally, performing next-generation sequencing (NGS) on a gene panel, whether using DNA and RNA from archival samples or new ones, should not significantly affect the results if you want a comprehensive analysis. Only in cases where there isn't enough material or there's a pressing turnaround time (TAT), should you consider using other methodologies.

Q2: Are there any recommended non-invasive testing methods based on urine or blood for FGFR3 testing?

In the UK, we are looking to develop a lot more liquid biopsy-based testing. From a technical standpoint, it should work well, particularly from blood and in the case of bladder cancer, where urine testing has shown to be effective. However, the main issue currently is the lack of sufficient evidence to determine when and how to use liquid biopsies and their reliability. Tissue testing is currently the standard approach, and in order to replace it with liquid biopsies, we need to establish the evidence that the test is accurate, comprehensive, and can be implemented by healthcare facilities. We also need clinical evidence demonstrating the effectiveness of liquid biopsies for specific medical conditions.

While I believe that we will eventually transition to a liquid biopsy approach, we are not quite there yet. However, we may use it in certain situations. In fact, we are already using it or planning to use it as a standard practice in lung cancer cases where fast results are crucial. We don't intend to completely eliminate the histological pathway, but we do need rapid results. The urgency may not be as high for bladder cancer, but it is still a viable option.

Q3: What are the current testing gaps in bladder cancer and what are your recommendations to ensure eligible patients do not miss out on targeted therapies?

I believe that we are testing less than half of the actual number of cases in our region. This is due to several reasons. Firstly, there is a lack of awareness about the availability and effectiveness of testing among clinical professionals. Secondly, the pathways for testing are sometimes hard to navigate or not clearly defined. Even when pathways are in place, they might be inefficient, leading to delays in test results. It is crucial to increase awareness and communicate the value of testing to the community. Additionally, we need to address any problems in the testing pathways to ensure that patients receive the testing they need. It's important to spread the word about the benefits of targeted therapies and to continue improving testing processes for the benefit of the patients.

Another important aspect is to improve practices in PATH Labs so that the fixation methodologies are effective in order to avoid failures. There are several factors contributing to suboptimal testing. If we all work together on this, we can ensure that our patients truly benefit from these exciting new therapies.

Q4: Would you recommend testing all the patients for FGFR3 genetic alterations?

In England, coverage criteria include the requirement that test results are actionable. Pre-emptive testing may not be covered in the UK, but it might be in other regions. As someone involved in testing, I believe it's valuable in all circumstances, and it ultimately comes down to reimbursement.

It's important to consider if I would take action based on a specific genetic mutation found in a patient. If so, testing for that mutation is crucial. However, early testing may not align with the standard treatment pathway, raising questions about cost-effectiveness. Discussions with reimbursers are essential to determine funding for tests.

Q5: Testing for FGFR3 at diagnosis is recommended with newly collected samples. Do you recommend new sample collection at the metastatic setting or the use of archived tissue?

I generally recommend using archived tissue. Collecting new tissue can be difficult so I only recommend if there is a feasible pathway and if it is cost-effective. As said before, for FGFR3, the variant is likely to be present even in earliest stage. I don't want people to think that we need a fresh sample. Don't skip the test just because you don't have a fresh or poor sample. Always send the archival tissue for testing.

Q6: Do you have any suggestions for improving MDT collaboration for optimal testing and reporting? Can you tell us about your experience?

It's important to have the right blend of people at the MDT. I think the critical thing is that you need clinical scientists who can properly interpret the results. You need a pathologist, and obviously, you need an oncologist who knows the pathway. So, my recommendation is just to have the right people in the room. Have it done regularly so that the people who participate in the MDTs can learn and gain experience from doing so. That's certainly something we've benefited from hugely.

Q7: What percentage of bladder cancer is caused by FGFR3 mutations?

Up to 80% of stage Ta tumours have activating point mutations in FGFR3.