ICR The Institute of Cancer Research

Use of biomarkers in cancer research and treatment

Consensus statements – July 2022

Coordinated by The Institute of Cancer Research, London

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Introduction

We know more than ever about the genetic and molecular changes driving cancers and we are reaping the rewards through a range of exciting new targeted treatments and immunotherapies. We are in a new era of precision medicine which is transforming the effectiveness of cancer treatment as well as the ways in which drugs are developed and marketed.

However, to use precision medicines effectively, we first need to gain detailed information about a patient and their cancer. Biomarker tests, including genetic tests and gene expression profiles, protein expression tests and immunohistochemistry, are essential for the effective treatment of cancer. Biomarker tests can help identify the type of cancer a patient has and crucially inform on the suitability of a treatment and how a patient is likely to respond.

The ICR has been working with organisations from across the medical research sector to discuss how to encourage the development and use of biomarkers in cancer research. A group of 10 leading institutions, charities, stakeholder groups and life-science companies have now developed a new set of 13 consensus statements aiming to drive wider use of biomarkers and more effective use of precision medicine for cancer patients.

Our consensus statements call for an acceleration of research to identify new biomarkers for cancer, and for changes to regulations and funding to ensure biomarker tests and molecular profiling of cancers are used more routinely as part of NHS care.

Professor Kristian Helin

Chief Executive, The Institute of Cancer Research, London

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Recommendations

1. We want to see further increases in the number of precision medicines that are developed with a companion biomarker test, in order to direct treatment precisely at those patients who will most benefit. To achieve this we need to remove barriers to pharmaceutical and *in vitro* diagnostics companies developing a biomarker alongside a drug, and to provide new incentives for them to do so. Companies need more confidence that developing a biomarker alongside a new drug will facilitate the passage of a treatment into the NHS, rather than making it more difficult.

2. We need the regulation of biomarker tests in clinical trials to be fit for purpose. The level of regulation should be adapted depending on whether cancer biomarkers are being evaluated as part of exploratory research or whether they are shaping the management of patient care. The ways in which biomarker tests will be used in research and treatment should be taken into consideration when reviewing proposals for trials, and different levels of regulatory rigour should be applied depending on the circumstances. If the regulatory framework is overly restrictive, it has the potential to delay or restrict the establishment of innovative clinical trials involving the use of biomarkers, and so to stifle exploratory research and innovation.

3. We believe that the costs of developing biomarker tests currently outweigh the financial benefits of doing so – and that this is discouraging industry and academia from investing in biomarker research. We think the Government should encourage collaborations between public institutions and companies on biomarker research – as a means of helping to fund research that might otherwise not take place, and to share the risk between public and private sectors.

4. We believe that the UK's health technology assessment bodies, such as NICE, should take a more positive view of the

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use of companion biomarker tests alongside new drugs. Biomarkers are an important way of directing treatment to those cancer patients who will benefit most and therefore are likely to increase the cost-effectiveness of treatment. But drug appraisals tend to consider companion diagnostic tests as an additional cost, affecting the apparent cost-effectiveness of the drug, and so potentially acting as a disincentive for companies in bringing forward a new treatment with a companion diagnostic. We are also concerned that the current system places the burden of both proof and cost on the first company to introduce a biomarker test, with those coming later benefiting from established testing infrastructure, and not being expected to justify the costs of testing alongside those of their drug. That acts as a clear penalty to innovation. We would like to see the NHS explore the possibility of offering subsidies for companies that bring forward biomarker tests alongside new treatments.

5. We believe that cancer treatments should not be tied to one specific named biomarker test. There should be flexibility in the tests that are used, provided that tests are quality assured, as this encourages innovation and greater competition. The US Food and Drug Administration currently requires a specific named test to be provided with a treatment, but the European Medicines Agency and the UK's MHRA are more flexible and we believe they should continue to be so.

6. We should encourage the development of biomarker tests as early as possible during the discovery of a drug so that they can be refined, and robust evidence generated on their use ahead of evaluation. We need to encourage collaborative research and early engagement between drug discovery scientists, clinicians, industry and other stakeholders to identify unmet need and harness the use of biomarker tests for precision medicine. These interactions will help to ensure that biomarker tests are created alongside the discovery of new targeted medicines and can be taken into clinical practice as rapidly as possible.

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7. We believe retrospectively developing biomarkers and developing companion biomarker tests for drugs that already exist could improve and guide the use of existing cancer treatments.

8. We believe that all people with cancer should have their cancers molecularly profiled as standard within the NHS to identify mutations and help guide their treatment. We would like to see cancer molecular profiling offered both at the point of diagnosis and during treatment to monitor how the cancer is evolving. We see this as critical to ensure patients can access more personalised and effective treatments as part of standard care and by taking part in clinical trials.

9. We believe that cancers should be molecularly profiled using broad genomic panels to test for many different cancer mutations at once. We think the NHS should be using genomic panels as well as whole-genome sequencing since for the purpose of directing treatment they are likely to be more useful. Panels focus on a range of genes that are known to be involved in cancer, and so provide more easily actionable information. We think it is important that the panels used cover a large number of genes, to increase the chances of detecting important cancer mutations, and also to allow the identification of future biomarkers predicting response to treatment or other aspects of prognosis.

10. We need to ensure that the pathways to enabling access to new biomarker tests cover all forms of biomarkers and not just genomic tests. The National Genomic Test Directory has a clear route for genomic tests to be made available, but immunohistochemistry tests fall outside of its remit. We need a broader and more transparent directory of biomarker tests that includes all the non-genomic tests the NHS will provide alongside gene tests and provides clarity about how the use of these tests will be funded. There is currently wide variation in access to biomarker tests in different parts of the UK depending on local funding arrangements.

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11. We need to ensure that both patients and clinicians are more aware of the biomarker tests available to them and their benefits. We should describe them as ‘tests to guide treatment’ – as the word ‘biomarker’ is not widely understood. Clinicians should be encouraged to talk to patients about the benefits of biomarker testing at the point of cancer diagnosis, both as a means of enabling shared decision making and so patients and advocacy groups will value and campaign for access to tests in the same way as they do for cancer drugs. The NHS needs to provide clarity on who are the best people to have conversations with patients about biomarkers, how and when these conversations should take place, and what the follow-up procedures should be.

12. We need to understand the workforce challenges around the use of biomarkers so that these can be addressed. We know, for example, that there are issues with the levels of training currently provided for histopathologists, radiologists, haematologists and oncologists on the science, use and availability of biomarker tests. An analysis is needed of the workforce challenges the sector is currently facing, where bottlenecks are impeding the implementation of biomarker testing, and what new skillsets and training are required. We need training too, to support the use of new technologies, such as digital analysis of clinical data and use of AI, which have the potential to increase efficiency and ease the workload burden on staff.

13. We need to keep track of how the UK is doing on the use and implementation of biomarker testing by carrying out regular benchmarking against international comparators, comparing rate of uptake and the time it takes to access tests alongside new therapies. We should also be monitoring how biomarker tests are used and accessed across the UK to limit regional variation.

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