ICR The Institute of Cancer Research

Creating new biomarker tests to guide cancer treatment

Position Statement from

The Institute of Cancer Research, London

Summary

The Institute of Cancer Research (ICR) believes that testing for biomarkers that tell us important information about cancers is essential to advance precision medicine for cancer. We believe that new precision medicines need to be accompanied by biomarker tests to target them at the patients who will most benefit. We need more research to identify biomarkers, and to support this with better national infrastructure to allow scientists access to tissue samples and patient data. All cancer clinical trials should be collecting exploratory biomarker data to make it easier to identify biomarkers.

We believe that the regulation of biomarker tests must be proportionate, and reflect their different uses and the associated risks. Tests conducted in clinical trials at an exploratory stage to identify new biomarkers, and which have no immediate impact on decisions about patient treatment, should not need the same level of regulatory rigour as tests which directly determine a patient's treatment. We believe that current guidance and training on the regulation of biomarker tests is too vague, and that as a result researchers, companies and regulatory inspectors are sometimes being too risk averse.

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Background information

Cancer research has increasingly focused on using our knowledge of the genetics and biology of the disease to deliver new forms of precision medicine. To target medicines in this way, we first need to gain detailed information about the patient and their cancer, which requires the identification and use of biomarkers. This catch-all term describes measurable indicators that could help us detect early signs of cancer in patients who have not been diagnosed yet, identify the type of cancer a patient has and how aggressive it is likely to be, or make judgements about how a patient is responding or is likely to respond to treatment.

Biomarkers are increasingly critical in drug evaluation and licencing decisions. Researchers are now using biomarkers to personalise treatment by targeting drugs at highly specific populations of patients. Testing for biomarkers can guide the use of precision medicines, by selecting patients for whom treatment is most likely to work, and monitoring them for their continued response. Biomarker tests can also help confirm that new therapies are reaching their intended target and having the anticipated effect.

Exploratory research will often test for genes or molecular changes to see whether these can give important information about patients and how they are responding to treatment. This research often uses patient samples and analysis from clinical trials, requiring new and evolving approaches to trial design. The information from these studies, when properly validated, can lead to the development of new biomarkers to help diagnose cancer patients, assess prognosis, or guide or monitor treatment.

Diagnostic tests are regulated to high standards to ensure that their use in research and clinical practice is safe and robust. In the UK, the responsibility for regulating these tests falls under the jurisdiction of the Medicines and Healthcare Products Regulatory Agency (MHRA). However, current regulations are in flux because of changes brought about by Brexit, and new UK-specific legislation from the Medicines and Medical Devices Act 2021. This means that the rules about how these tests can be used in research could change dramatically over the next few years. Concern has arisen due to mixed messages being received concerning future regulations. Generally, the Government and regulatory bodies have signalled a desire to streamline regulation however there have also been suggestions for tightening biomarker test validation. We do not want to see it become more difficult and bureaucratic for researchers to assess the potential of new biomarkers in exploratory research, or to design innovative new biomarker tests for use in the NHS.

The UK currently operates under the Medical Devices (Amendment etc.) (EU Exit) Regulations 2019 and 2020, which are drawn from the EU-wide Medical Devices Regulations 2002.[1,2] The 2019 Amendment regulations do not require a CE or

[1] The Medical Devices (Amendment etc.) (EU Exit) Regulations 2019 (legislation.gov.uk)
[2] The Medical Devices (Amendment etc.) (EU Exit) Regulations 2020 (legislation.gov.uk)

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UKCA mark for in vitro diagnostic tests that are used in clinical studies or manufactured and used only within a health institution. CE marking declares that a product complies with relevant EU regulatory requirements. UKCA marking replaced CE in January 2022 following the UK exit from the EU. Therefore, products previously requiring CE marking need to have a UKCA mark from June 2023 to be sold and used in the UK. Though the Medicines and Medical Devices Act 2021 is now in place which should provide the legislative powers to support new regulations, no new regulations are in place.

The MHRA has indicated to the research community that all diagnostic tests used in clinical trials, from tests for exploratory biomarkers in early-stage trials through to commercial biomarkers and companion diagnostics used in later-stage trials, must be assessed according to Good Clinical Practice (GCP) laboratory standards. Previously, GCP has not been applied to exploratory biomarkers since these do not have an immediate impact on decisions over a patient's treatment.

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Key ICR positions on creating new biomarker tests to guide cancer treatment

- We believe that every new cancer drug should include a biomarker strategy to help target treatment at those patients who will benefit most. Use of biomarkers holds the key to advancing precision medicine by optimising treatment for individual patients and for the NHS. Biomarker tests allow new drugs to be evaluated in smaller, smarter and cheaper clinical trials, and make it easier and faster to demonstrate that a new treatment is cost-effective. Biomarkers can also spare patients who are unlikely to benefit from the side effects of treatment. We need to discover and employ more precision biomarkers which can identify the patients who will benefit from a new treatment.

- We should be taking into account the need to discover and improve biomarkers right from the start of a treatment's discovery and through clinical development. The ICR believes clinical trials of new cancer treatments should be designed with the discovery of biomarkers in mind, and that all trials should collect data that can be used to maximise the discovery and validation of biomarkers.

- We need to incentivise companies and academic institutions to develop biomarker tests alongside new drugs and technologies, so that patients who are most likely to benefit from a drug are treated with it. We must build confidence among companies that healthcare systems will pay for effective cancer treatments and their associated biomarkers, to encourage them to work on precision medicine drug projects, especially given that targeting drugs at smaller populations can reduce the profits for companies.

- We need to highlight the economic benefits for pharmaceutical companies and healthcare systems of including biomarker identification in the drug discovery process. Not only will the creation of a companion diagnostic make a treatment more precise, but it increases the likelihood that it can be demonstrated as cost-effective and approved for use, since its use will be targeted precisely at those patients who will benefit most.

- We believe that investment into the discovery and development of biomarkers as companion diagnostics makes strong economic sense – especially compared with the costs of a drug trial that may fail to show clinical benefit or cost-effectiveness because of insufficient tailoring for patients. NICE currently factors in the additional cost of a companion biomarker test during the appraisal process, and we believe this can act as a disincentive for pharmaceutical companies in bringing forward a new treatment with a companion diagnostic as it can make the drug appear less cost-effective.

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- The Government needs to invest in better national infrastructure to support research into new biomarkers by making it easier to collect and access patient data and clinical samples. The UK needs to invest in dedicated tissue collection infrastructure, and in biobanks linking tissue samples, genomic data and data from trials to high-quality outcome data – such as patient survival time, response to therapy and adverse effects.

- We need to ensure all patient data is entered in a standard format that is suitable for research. Clinicians often do not have the capacity to support tissue collection, meaning that samples may not be collected, improperly collected or stored, or their submission to laboratories delayed. This affects biomarker development across all cancers but is a particular problem in rare cancers such as children's cancers. Implementing the necessary data collection systems will incentivise companies to carry out clinical trials using biomarkers in the UK.

- The ICR believes that regulatory systems for clinical trials must be highly robust but also proportionate and should not act as a barrier to research and innovation. We support the MHRA's ambitions to create a world-class regulatory system, and we are committed to working with regulatory partners to ensure clinical research is safe and benefits patients. However, it is essential that the regulatory system keeps pace with advances in science and clinical trial methodologies and supports innovation in research.

- We believe it should be of the highest priority for the MHRA to develop new UK regulations for the use of in vitro testing based on the Medicines and Medical Devices Act 2021 and welcome the consultation of the future regulation of medical devices in the UK. We would like these regulations to clearly state that exploratory research – such as research to identify new biomarkers – is considered 'research only use'. It should be possible for healthcare institutions to use 'research use only' products – for example for exploratory research on clinical samples.

- The ICR would like to see a regulatory system which recognises the different ways in which biomarker tests are used in clinical trials, and takes a proportionate approach based on risk. We agree that biomarkers used to select patients for treatment or make decisions about how a treatment is used must be held to the highest regulatory standards given their direct impact on healthcare. But research into biomarkers at an early exploratory stage – when the expected outcomes of the research may be unclear and there is no immediate impact on decisions about patient treatments – should not need the same level of regulatory rigour, which risks constricting the scope of vital early-stage clinical research. We believe regulatory standards should support testing for biomarkers in early, discovery-driven

research, while also protecting patient safety and being especially robust in later-stage trials.

- The administrative burden from applying excessive, blanket regulatory standards across all biomarker research risks slowing down early-stage clinical trials and increasing costs. We fear that such regulations could severely hamper clinical research, impede advances in biomarker development and ultimately delay advances in patient care. Early-stage clinical trials for cancer already operate within a tight funding envelope and resources would have to be redirected to meet the administrative costs of increased regulatory standards. The risk is that as a consequence a companion diagnostic will not be developed alongside the treatment – and the consequent lack of targeting will make it more difficult to demonstrate clinical benefit and cost-effectiveness in later-stage trials.

- The ICR wants to ensure that biomarkers and tests discovered at the ICR are as widely used as possible to achieve maximum patient benefit. We believe research findings relating to biomarkers should be published and developed in ways that enable multiple parties to discover, validate and perform biomarker tests. At the ICR, we either non-exclusively license our biomarker discoveries to as many organisations as possible or make these discoveries freely available through publication with the aim of providing the greatest impact for patients.

- The ICR believes that regulatory compliance training – including for GCP requirements – should be better tailored towards the needs of different aspects and stages of research. We would like tailored courses to be provided for researchers conducting exploratory biomarker research, to ensure that they are confident in meeting regulatory expectations. At present, accredited training is primarily targeted at researchers working on commercial biomarkers and therefore not appropriate for early-stage research into new biomarkers. The ICR believes that quality assurance and the appropriate application of good scientific practice will be strengthened by tailoring training in this way.