Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

than likely, the success of surufatinib is attributable to both its novel mechanism of action and favourable business decisions around its development. In addition, we do not yet know how surufatinib will fit into the complex treatment algorithm for NETs. Evidence regarding sequence of therapies is a crucial need in the field, although might be impractical to study in prospective clinical trials. We also need to study mechanisms of resistance to tyrosine kinase inhibitors, develop and validate predictive biomarkers, understand reasons for heterogeneity in objective response, and identify better quantitative radiological response criteria in the setting of angiogenesis inhibition. Last, but not least, we must also keep patients with NETs at the core of how we think about optimal treatment strategies. Given the chronicity of well differentiated NETs, these patients will experience an accumulation of toxicities over years that include non-trivial drug side-effects, particularly with tyrosine kinase inhibitors.

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A roadmap for the early detection and diagnosis of cancer

If we are to beat cancer, early detection and diagnosis are arguably the most effective means we have at our disposal. Progress during the past 40 years has transformed the prospects of people diagnosed with cancer in the UK, with survival doubling since the 1970s.[1] However, further improvements are still greatly needed, because cancer remains the leading cause of death in the UK,[2] with a stark projection of rising incidence to more than half a million cases per year by 2035.[3] Patients diagnosed with cancer at an early stage have the best chance of curative treatment and long-term survival; for example, 57% of people with lung cancer survive their disease for 5 years or more when diagnosed at stage I compared with only 3% of those diagnosed at stage IV.[4] Despite cancer screening programmes, improved awareness, and more streamlined diagnostic pathways, only 54% of patients with cancer in England had their cancer detected at stage I or II in 2018.[5] With lower survival rates in the UK than in similar countries, such as Australia, Canada, or Norway,[6,7] and notable inequalities in survival across the UK,[8,9] there is a pressing need to see a paradigm shift in our ability to accurately detect and diagnose cancer at an early stage.

Beyond the clear potential for health benefit, the UK has the capacity to be a world leader in developing a thriving early detection and diagnosis industry, capitalising on its excellent science base and vast National Health Service (NHS) and data infrastructure, and attracting global investment. This potential for health and wealth benefit is recognised by UK's national governments, with ambitious targets set in NHS England's Long Term Plan (ie, a commitment to detect 75% of cancers at stage I and II by 2028) and the Scottish Government's Beating Cancer strategy,[10] and investments to support progress in early detection and diagnosis (eg, the Accelerating Detection of Disease


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For more on **NHS England's Long Term Plan for cancer** see https://www.england.nhs.uk/cancer/strategy/

For more on the **Accelerating Detection of Disease challenge** see https://www.ukri.org/innovation/industrial-strategy-challenge-fund/accelerating-detection-of-disease

For the **Early Detection and Diagnosis Roadmap** see https://www.cancerresearchuk.org/funding-for-researchers/research-opportunities-in-early-detection-and-diagnosis/early-detection-and-diagnosis-roadmap

For more on the **National Artificial Intelligence Diagnostics Lab** see https://www.digitalhealth.net/2019/08/government-250-million-artificial-intelligence-lab-diagnostics/

For more on the **Data to Early Diagnosis initiative** see https://www.ukri.org/innovation/industrial-strategy-challenge-fund/from-data-to-early-diagnosis-and-precision-medicine/

***Panel:* Key themes for action to deliver the roadmap**

- Understanding risk and prognosis, from biology to technology
- Biomedical data science and systems
- Incentivising and supporting development and commercialisation
- Health-care system innovation and supporting adoption

challenge, the National Artificial Intelligence Diagnostics Lab, and the Data to Early Diagnosis initiative).

The true potential of early detection and diagnosis remains largely unexploited globally due to many historical challenges. Early detection research is a comparatively new and fragmented field with substantial barriers to achieving validation because of, for example, complex and unclear biology, a paucity of availability of quality samples, and insufficient funding for translation. Furthermore, corporate investment is scant because of the high cost of research and development (eg, the requirement for expensive long-term studies to show beneficial effects on mortality), the low price point of diagnostics, undervaluing and underprioritisation of early detection and diagnosis by the health-care system, and complicated navigation of unclear regulatory and approval pathways.

The multidisciplinary and multisectoral network needed for development and delivery of early detection and diagnosis is complex and fragmented, spanning academic research, industry, research funders, regulators, investors, health-care professionals, NHS decision makers, government, and—crucially—patients and the public. A holistic vision, integrating this whole network end-to-end from discovery science to implementation, has been absent so far. Without such a vision, progress has been slow.

To unite the fragmented efforts of the early detection and diagnosis network, and to establish a pathway for early detection and diagnosis in the UK, Cancer Research UK consulted extensively with more than 100 expert stakeholders across a broad range of sectors to develop a roadmap for early detection and diagnosis of cancer. The roadmap presents a shared vision, from discovery to implementation, for a long-term future in which early detection and diagnosis of all cancers is a routine reality. It highlights current challenges that are impeding progress and makes a series of tangible recommendations for research, development, health system delivery, and government policy on how to overcome these challenges and realise the shared vision (panel). The recommendations are for collaborative efforts across an interlinked network, building in a stepwise manner to deliver a huge shift in early detection and diagnosis. Underlying every recommendation is a mandate to ensure early detection and diagnosis is delivered ethically, equitably, and transparently throughout the UK, with extensive involvement with patients and the public to reduce health inequalities.

Although this roadmap for early detection and diagnosis focuses on cancer, the future of health care lies not only in the effective treatment of symptomatic disease but also in health maintenance—ie, a holistic, proactive approach to understanding disease risk, early detection of deviations away from health, and intervening appropriately, whatever the disease. Cancer acts as an example to establish technologies and approaches that will deliver benefit across a range of disease areas, incorporating disease prevention via interception of predisease, further underscoring the need for partnerships across the health network. With emerging technological capabilities and increased urgency in the post-COVID-19 era, an unprecedented opportunity exists to transform health outcomes.

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How current assay approval policies are leading to unintended imprecision medicine

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Pathologists are responsible for selecting the assays for the optimal identification of patients for targeted therapy. The current paradigm of regulatory assay approval is that when a clinical trial involving a drug and a biomarker, using a specific assay to identify patients that might respond to the drug, meets its endpoint, the assay is approved concomitantly as a companion diagnostic. Private health insurance bodies or public health systems then decide on reimbursement of the assay when they decide on the reimbursement of the drug. Use of US Food and Drug Administration (FDA)-approved assays is obligatory in some countries, like the USA and Japan, to gain access to the drug. In the EU, the use of an FDA-approved assay is not mandatory to gain access to the drug, as long as the laboratory-developed test or assay that is used is validated.

Thresholds for defining a positive biomarker in a clinical trial, and what constitutes a positive biomarker, are not standardised. Moreover, companion assays are co-developed with a drug, as determined by the pharmaceutical company in collaboration with the company contracted to produce the assay, without regard to the other assays being developed for the same biomarker. For example, PD-L1 assay kits are approved by the FDA in 15 different cancer types but the PD-L1 staining patterns, scoring methods, and positivity thresholds are different in almost all of these cancer types. Moreover, the various assays and scoring systems are not equivalent, despite being matched to the same specific drug. There are at least five non-equivalent assays for PD-L1, each with its own scoring system and tumour site indications.

Absence of assay standardisation is an emerging issue for triple-negative breast cancer. In 2019, considering the results of the IMpassion130 trial, the FDA approved the Ventana PD-L1 (SP142) assay (Ventana Medical Systems, Tucson, AZ, USA) and cut-point (1% of tumour-infiltrating immune cells) to assess PD-L1 in patients with triple-negative breast cancer treated with atezolizumab.[1] However, following the Keynote 355 breast cancer trial,[2] the results of which were publicised in 2020, investigating pembrolizumab in the same patient population, the FDA is likely to approve the PD-L1 IHC 22C3 pharmDx assay (Agilent Technologies, Carpinteria, CA, USA) and its combined positivity score-scoring system to assess PD-L1. Using more than one assay for the same biomarker is problematic because the assays have different positive prevalence rates. In the IMpassion130 trial, 46% of patients with triple-negative breast cancer were deemed to be positive using the Ventana PD-L1 (SP142) assay; when using other assays (eg, the PD-L1 IHC 22C3 pharmDx assay) in the same patients, the PD-L1 positive prevalence increased to nearly 80%.[3] The cause of these inconsistencies is multifactorial and includes reproducibility issues and variable antibody and assay sensitivity, even when different assays use the same antibody.[4–6] One issue is the balance of risk, costs, and benefit. If treatment recommendations differ depending on the assay that is used, it is difficult for health-care providers to reliably analyse the cost-effectiveness for reimbursement of that particular treatment. Costs are arguably even more important in low-income and middle-income countries. Some private insurance companies or governments insist on the use of FDA-approved assays,