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► **To cite this version:**

E. Rassy, J.-M. Heard, F. Andre. The paradigm shift to precision oncology between political will and cultural acceptance. *ESMO Open*, 2023, 8 (5), pp.101622. 10.1016/j.esmooop.2023.101622 . inserm-04521235

**HAL Id: inserm-04521235**

<https://inserm.hal.science/inserm-04521235>

Submitted on 26 Mar 2024

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EDITORIAL



## The paradigm shift to precision oncology between political will and cultural acceptance

Since the beginning of the century, the field of oncology has experienced an unprecedented surge in therapeutic research and innovation. The rate of approvals for oncology indications has risen, primarily driven by approvals for targeted therapies, alongside an increase in the development of novel therapeutic approaches.<sup>1,2</sup> However, the disparity between the progress of research outcomes and the challenges in effectively implementing them raises significant concerns regarding the accessibility to innovative treatments.<sup>3</sup> Precision oncology, defined by the molecular profiling of patients and tumors, presents the opportunity to address this issue by enabling the delivery of personalized cancer treatments, tailored to each patient's specific needs, ensuring the right treatment, at the right dose, and at the right time.<sup>4,5</sup> Practically, a set of molecular tests is carried out at the time of cancer diagnosis and during follow-up, with the goal of predicting treatment sensitivity and assessing the risk of unfavorable cancer progression. When the molecular characteristics indicate a likelihood of favorable outcomes, the possibility of therapeutic de-escalation can be considered and evaluated in dedicated trials. Conversely, if there is a risk of poor response to standard treatments, innovative therapies in specialized settings are justified. Subsequently, a shared decision making between the oncologist and the patient can guide treatment choices, taking into account survival outcomes, quality of life considerations, and patient preferences.

Despite showcasing numerous benefits and substantial industrial potential, precision oncology has not been optimally developed in many countries. This was largely due to the absence of an industrial development model and political will, although the development of modern precision oncology should have been at the top of our collective agenda. This priority for advancing precision oncology is driven by two fundamental reasons. Firstly, precision oncology plays a pivotal role in enhancing patient care by tailoring treatments to individual needs and has demonstrated a positive impact on patient survival. Secondly, it helps conserve health care resources while promoting innovation in the field by expediting clinical research and providing better access to cutting-edge treatments.

To exemplify the impact of precision oncology in making treatment decisions and research development, several practical examples illustrate its potential benefits. Precision

oncology can assess the probability of unfavorable outcomes and help in avoiding overtreatment of cured patients, particularly those diagnosed with localized cancer. For example, the implementation of genomic tests in breast cancer has led to a reduction of ~20% in the utilization of chemotherapy treatments. By extending the development of similar tests to the five most prevalent localized cancers, chemotherapy could be spared for ~200 000 patients annually in Western countries. Moreover, this approach could potentially reduce the number of individuals undergoing national screening tests, as being explored by the European study MyPebs which evaluates the possibility of increasing mammography screening intervals for patients without traditional genetic risk factors for breast cancer.<sup>6</sup> In addition, precision oncology enables a more accurate determination of the most effective therapy for a specific patient at the time of diagnosis, potentially avoiding the need for multiple therapeutic sequences. Currently, a patient with localized hormone receptor-positive and human epidermal growth factor receptor 2-positive breast cancer may undergo two 6-month sequences of chemotherapy, followed by a year of trastuzumab, and up to 10 years of hormone therapy.<sup>7</sup> Precision oncology could identify patients who achieve a cure after the first therapeutic sequence without the need to pursue additional therapy. Precision oncology demonstrated impressive results in the recently reported NICHE-2 trial, which enrolled patients with mismatch repair-deficient colon cancer. This study showed that 67% of patients had a complete response to immunotherapy administered for only 8 weeks, alluding for the potential for curing these patients with an extremely short treatment duration of therapy.<sup>8</sup> It is estimated that around 10% of cancer patients have molecular abnormalities that render them highly sensitive to treatment, making them eligible for effective ultra-short treatments. From a research perspective, focusing on patients at high risk of unfavorable progression reduces the sample size of clinical trials, accelerates the availability of drugs, and reduces development costs.

This paradigm shift toward precision oncology necessitates a transformation in the cognitive framework of cancer research and medicine. It also entails addressing fundamental normative values, turning it into a matter of political will. Access to innovations in oncology raises questions of social justice and modern molecular oncology holds the potential to diminish social disparities in accessing optimal health care. The development of new technologies has led to substantial cost reductions and task automation. For

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example, the cost of complete genome sequencing has dropped significantly, currently amounting to around 200 euros, compared to over a thousand euros just 3 years ago. By widely adopting these cost-effective technologies, we can expand the number of patients benefiting from therapeutic innovations, particularly by identifying those with rare genomic abnormalities at the time of diagnosis. This model hinges on the extensive utilization of genomics and artificial intelligence-based diagnostics. When integrated within a renewed paradigm of systematic care, these approaches would offer all patients with fairer opportunities for treatment innovations.

However, for the complete implementation of precision oncology, we must establish reimbursement mechanisms and further develop this approach in both research and clinical practice. But as reducing inequalities in cancer care requires widespread access to diagnostic technologies, cost reductions in technology and reduced reliance on human expertise seem essential. Thus, the implementation of precision oncology is within reach but its execution requires a cultural shift and political will. The cultural change involves redefining cancers based not only on their organ of origin but also on their molecular characteristics. This shift applies to academic stakeholders and regulatory agencies responsible for drug approvals alike. The political will is essential to make a difference and significant impact in implanting precision oncology. Specifically, it entails establishing dedicated research structures, developing a market for molecular diagnostic tests, disseminating guidelines for oncologists, and creating reimbursement mechanisms and incentives. A remaining obstacle to the advancement of precision oncology in France is that high-throughput genomic sequencing of tumor genomes is currently only reimbursed through a temporary program scheduled for the following year after the test is conducted. Given that certain tests have the potential to reduce the need for expensive medications, we should explore the possibility of funding their integration into routine practice by allocating a percentage of the cost savings achieved.

We believe that the benefits of precision oncology call for a strategic approach to evolution. The promotion and widespread adoption of precision oncology practices go beyond mere technical and scientific choices that can revolutionize oncology and improve patients' lives; they are also strategic and political choices that require political will. The existing reimbursement schemes currently do not cover high-throughput genomic sequencing of tumor genomes, unlike other medical biological procedures covered by health insurance. Nevertheless, for the successful implementation of precision oncology, it becomes essential to establish sustainable financing models that support the integration of these tests into routine clinical practice. By explicitly acknowledging the value of precision oncology in reducing inequalities and improving access to innovation,

we can promote its widespread adoption and secure its long-term viability.

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Available online xxx

<https://doi.org/10.1016/j.esmooop.2023.101622>

## FUNDING

None declared.

## DISCLOSURE

ER: honoraria: Eli Lilly. Travel, accommodations, expenses: Pfizer, Roche, Mundipharma; grants: Gilead (institutional). FA: research funding: AstraZeneca (Inst), Novartis (Inst), Pfizer (Inst), Eli Lilly (Inst), Roche (Inst), Daiichi (Inst). Travel, accommodations, expenses: Novartis, Roche, GlaxoSmithKline, AstraZeneca. Ad boards or symposium compensated to the hospital: AstraZeneca, Lilly, Novartis, Pfizer, Daiichi-Sankyo, Relay Tx and Roche. Ad board compensated to the author: Lilly. JMH has declared no conflicts of interest.

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