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Supplementary information

Accelerating precision oncology by converging pragmatic trials and real-world evidence

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What components need to be funded to establish a European digital precision oncology research network?

The key challenge for the proposal for a digital precision oncology research network described in this article is to secure initial funding for several critical components.

The first component is the investment to integrate comprehensive genomic profiling (CGP) into routine care for all patients with metastatic cancers who are running out of standard treatment options. These tests drive the identification of potential biomarkers that could allow rational off-label use of existing drugs. Today, CGP is funded in some countries in Europe through traditional reimbursement. In contrast, in other PRIME-ROSE partner networks, CGP is supported through research grants or national research infrastructure, which is not sustainable in the long term. Getting CGP reimbursed today faces a catch-22: countries need real-world evidence to demonstrate the broader benefit of CGP to secure reimbursement, but nobody has the responsibility for collecting that evidence without reimbursement to allow its routine use.

The second component is the digital investment inside 50–100 hospitals (€25–50 million) to prepare large-scale cohorts with linked molecular data, to drive not only care-quality improvement and complex biomarker validation, but also support the new pragmatic trial designs that would significantly reduce the cost and risk in next-indication expansion for pharma companies and which includes real-world evidence control cohorts.

The third component is sustainable approaches to introduce drugs into use in healthcare, not only in trials where pharma companies provide drugs, but also beyond that when patients have individualized treatment following CGP and discussion in molecular tumour boards. Here, registries to collect data on off-label treatment and managed entry agreements, facilitating early introduction while evidence to support later health-technology assessments and pricing negotiations continue to be collected, may be a way forward.

A proposal for funding via a public–private partnership

To provide the funding needed, we propose a large-scale public–private partnership around this grand bargain — the pharmaceutical industry invests in the digital infrastructure to enable lower-cost next indication expansion and expanded sales, while national treasuries (not health systems) invest in the expansion of broad molecular testing through CGP to position Europe well for a pro-growth, pro-jobs future. This investment would also enable the coming revolution in artificial intelligence approaches that harness digital health data.

The economic benefits of broader, faster and cheaper next-indication expansion naturally accumulate towards industry sponsors, as they market drugs that could achieve greater sales revenues. We have re-analysed the data from the companion publication[1] to the original DRUP trial on indication expansion potential and the global oncology market to estimate the size of that potential benefit to the industry at around $55 billion in additional sales per annum from an initial investment of roughly $50 million. We propose that the industry drives this investment, so as to better make pragmatic decisions about site selection, technology norms and data standards.

#	Item	Value	Source/comment
1	Global oncology market 2023	$223 billion	IQVIA Institute for Human Data Science, Global oncology trends 2024: outlook to 2028, May 2024
2	Estimated % sales from targeted drugs	50%	Combination of market share estimates for immunotherapy, kinase inhibitor, antibodies and antibody–drug conjugates
3	Value of targeted oncology drug market in 2023	$112 billion	Calculation
4	% patients actionable by NGS from on-label drug options	18%	Priestley et al.[1]
5	% patients actionable by NGS from both on-label and off-label options	62%	Priestley et al.[1]
6	Label expansion ratio	3.4	Calculation: #5 divided by #4
7	Full annual potential market for targeted drugs	$384 billion	Calculation: #3 targeted oncology market (assumes sales are on-label) × #6 expansion ratio (assumes all mechanistically rational indication expansions successful)
8	Implied additional sales from expansion of indications for targeted drugs	$273 billion	Full potential targeted market (#7) minus today's targeted market (#3), by calculation
9	Estimated success rate for expansion of indications of approved oncology drugs	20%	Conservative expert judgement; values over 40% are reported in the literature
10	Risk-adjusted annual sales revenue from expansion of indications for targeted drugs	**$55 billion**	Calculation: #8 × #9

Fund molecular tests, digitization and early introduction of precision cancer medicines through growth economics (not health economics) until the evidence 'Catch-22' is solved

Traditional health economics is the art of allocating scarce health budgets in the face of evolving medical evidence and competing demands. In this context, decisions to prioritise simpler, cheaper tests with high evidence levels, and not more expensive tests with broader, but yet-to-be-proven benefits (such as CGP), or to stay away from new drugs being introduced are mathematically correct — within the zero-sum budgets of today's healthcare systems.

However, clinical research has economic benefits in terms of job creation, foreign direct investment, economic growth and increased tax receipts that are not captured in traditional health economics. Large-scale deployment of broad molecular testing is now critical in industry oncology trial location settings. Europe has lost trial share over the last decade to Asia and America, partly due to the lack of deployment of broad molecular testing at scale to open up trial access and partly due to strict policing of off-label use in a number of countries. There is a strong economic argument to be made to national treasuries to fund CGP tests as well as early introduction of drugs to drive economic growth, especially at this time of turmoil for the US research sector.

With routine deployment, we believe the linked molecular–clinical outcome data would soon demonstrate beneficial health-economic outcomes by reducing over-treatment in areas such as routine chemotherapy and radiotherapy, by enabling systematic identification of molecular cohorts with strong responses that can have lower treatment duration, so-called "precision de-escalation". Savings in those treatment budgets could then fund CGP tests via traditional health budgets.

References

1. Priestley, P. et al. Pan-cancer whole-genome analyses of metastatic solid tumours. *Nature* **575**, 210–216 (2019).