Letter to the Editor

Implosion of Grail's Galleri Cancer Screening Test?

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A recent prospective clinical trial using the Galleri Multi-Cancer Detection Test was temporarily put on hold, likely due to poor clinical performance (details were not made public), highlighting the need for its re-evaluation as a new and revolutionary cancer screening tool. In this correspondence we provide several questions that need to be answered by Grail before this technology is disseminated to the general public (although the test is marketed now).

Grail is a multi-billion-dollar biotechnology/diagnostic company, which developed a non-invasive blood test, claiming to detect 50 types of cancer at early and potentially curable stages. Since their first publication [1], we expressed concerns about the sensitivity and specificity of the test (now widely known as the Galleri test) and its suitability for population screening [2-4]. To their credit, Grail conducted large prospective studies [5] to demonstrate the test's clinical capability. The initial promising results, and Grail's anticipated financial success, prompted the next generation sequencing giant Illumina to purchase Grail for $8 billion (2021). Another collaboration of Grail with the UK National Health System (UK-NHS) includes a 3-year prospective trial conducted in parallel with the current standard of care. At the end of the first year, UK-NHS unexpectedly announced that the trial was put on hold, likely due to rather poor clinical performance (no details given) and until they analyze the first-year data which will be available by end of 2026 [6,7]. Legal and financial issues between the interested parties are currently not public [8]. The Grail case has some similarities to the Theranos story, which sent some executives to jail and led to company bankruptcy [9].

One reason that such unfortunate events are happening is the hype that is (intentionally) created around new technologies to make them more attractive to investors. Due to the unknown possible harms of the Galleri test [10], we suggest its withdrawal from the market, until its capabilities and shortcomings become clearer. For example, the ongoing trials will answer the critical question of better survival of those who are screened and the test's associated harms. After in-depth data analysis, Grail has the obligation to make their first-year results transparent, so that interested parties understand the benefits and harms of this screening. For more detailed discussion please see the cited literature [6,7,10].

A partial list of relevant questions related to the Grail-NHS Collaboration includes (these questions were also presented in a more detailed version of our manuscript) [10]: How

many Galleri tests generated equivocal (uninterpretable) results? In such cases, what recommendations are provided to the tested individuals, including money-back refunds? The test currently costs about $1,000. How many results were false positives and how were they confirmed? Were the confirmation tests invasive and produced any harm (including death) due to invasive confirmatory procedures? How many of the detected tumors were indolent? How many patients who developed cancer on follow-up initially had a negative test? Did screened individuals have stage migration from stage III-IV to lower stage? For how many patients was the tumor site correctly identified? Were there complications in trying to locate the tumor in the wrong organ? In patients who test negative at first screening, what explanation would be given to them if the subsequent biannual test discovers a late-stage cancer? Would the testing company be liable for delivering misleading information? We understand that the most fundamental question, "if screening extends overall or disease-specific survival", will require much longer follow-up.

Finally, these and other similar tests should ideally be identified early by regulatory agencies, to protect patients, investors, and other stakeholders from artificially created situations which, at least partially, are motivated by profit [6,7,10].

References

1. Aravanis AM, Lee M, Klausner RD. Next-Generation Sequencing of Circulating Tumor DNA for Early Cancer Detection. Cell. 2017;168(4):571-574.
2. Fiala C, Diamandis EP. Utility of circulating tumor DNA in cancer diagnostics with emphasis on early detection. BMC Med. 2018;16(1):166.
3. Fiala C, Diamandis EP. A multi-cancer detection test: focus on the positive predictive value. Annals of Oncology. 2020 ;31(9):1267–1268.
4. Fernandez-Uriarte A, Pons-Belda OD, Diamandis EP. Cancer Screening Companies Are Rapidly Proliferating: Are They Ready for Business? Cancer Epidemiol Biomarkers Prev. 2022;31(6):1146-1150.
5. Schrag D, Beer TM, McDonnell CH 3rd, Nadauld L, Dilaveri CA, Reid R, Marinac CR, Chung KC, Lopatin M, Fung ET, Klein EA. Blood-based tests for multicancer early detection (PATHFINDER): a prospective cohort study. Lancet. 2023;402(10409):1251-1260.
6. Robbins HA. Multicancer Early Detection Tests — Keeping a High Bar for Evidence of Benefit. New England Journal of Medicine. 2024 ;391(4):292–294.
7. McCartney M, Cohen D. Galleri promises to detect multiple cancers—but new evidence casts doubt on this much hyped blood test. BMJ. 2024 Aug 7;386:q1706.
8. Fiala C, Diamandis EP. Can a Broad Molecular Screen Based on Circulating Tumor DNA Aid in Early Cancer Detection? J Appl Lab Med. 2020 ;5(6):1372–1377.
9. Diamandis EP, Lackner KJ, Plebani M. Theranos revisited: the trial and lessons learned. Clinical Chemistry and Laboratory Medicine (CCLM). 2022 ;60(1):4–6.
10. Chatanaka MK, Yousef GM, Diamandis EP. The Unholy Grail of cancer screening: or is it just about the Benjamins? Clin Chem Lab Med. 2024 Sep 23. doi: 10.1515/cclm-2024-1013. Epub ahead of print. PMID: 39301604.