nature portfolio

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Last updated by author(s): Nov 7, 2024

Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed	
☐	☒	The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒	A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒	The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☒	☐	A description of all covariates tested
☐	☒	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒	A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☒	☐	For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☒	☐	Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	Clinical and outcomes data were collected, and the first liquid biopsy drawn was collected for each patient. The Guardant Health genomic database was queried (2020-2023) for patients with breast or prostate cancer who had ctDNA NGS
Data analysis	Descriptive statistics were used to summarize baseline characteristics. Time to event analysis was caluclated by the inverse kaplan-meier method. Statistical analyses were performed using SPSS V.23 and all statistical tests used for comparison were 2-sided. For genomic analyses, Fisher's Exact test was utilized to statistically compare groups. Figures were generated using cBioPortal and Graph Pad Prism 9 software (* p-value <0.05, ** p-value ≤0.01, *** p-value ≤0.001, and **** p-value ≤ 0.0001).

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Human research participants

Policy information about studies involving human research participants and Sex and Gender in Research.

Reporting on sex and gender	Findings do not apply to sex which was used to define biologically patients included in the clinical cohort.
Population characteristics	Between 10/2020 and 12/2022, consecutive patients with metastatic breast (excluded triple negative), ovarian, pancreatic, and prostate cancer who received treatment with an ICI following a bTMB ⍰10 mutations per megabase (mut/Mb) detected by Guardant360, were included in this study. Given low attrition of patients with ovarian and pancreatic cancers, only breast and prostate cancer was included in the final analysis.
Recruitment	CLinical cohort included patients from all eleven participating sites. Guardant Health genomic databased included 13,992 samples who had ctDNA NGS as part of clinical care, around the country
Ethics oversight	UH IRB approved the protocol and study - (STUDY20230043)

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	this multi-institutional clinical cohort included 48 patients. The Guardant Health genomic database included 13,992 prostate/breast samples
Data exclusions	The Guardant Health genomic database was queried from 2020-2023. Clinical cohort included patients between 10/2020 and 12/2022
Replication	NA
Randomization	No randomization was done in this study
Blinding	No blinding was done in this study

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☐	☒ Clinical data
☒	☐ Dual use research of concern

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Clinical data

Policy information about clinical studies

All manuscripts should comply with the ICMJE guidelines for publication of clinical research and a completed CONSORT checklist must be included with all submissions.

Clinical trial registration	NA
Study protocol	protocol for the retrospective cohort was approved at UH. It can be provided upon request
Data collection	Clinical and outcomes data were collected, and the first liquid biopsy drawn was collected for each patient. The Guardant Health genomic database was queried (2020-2023) for patients with breast or prostate cancer who had ctDNA NGS
Outcomes	response rate, progression free survival, overall survival