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Corresponding author(s): Alexander Drilon

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Reporting Summary

Nature Research 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 Research policies, see Authors & Referees 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	Data were collected in a database created with Oracle Clinical (Oracle).
Data analysis	Data were analyzed with the use of SAS statistical software, version 9.2 or later (SAS Institute, Cary, NC, USA).

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/reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research 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 list of figures that have associated raw data
- A description of any restrictions on data availability

Upon request, and subject to certain criteria, conditions and exceptions (see https://www.pfizer.com/science/clinical-trials/trial-data-and-results for more information), Pfizer will provide access to individual de-identified participant data from Pfizer-sponsored global interventional clinical studies conducted for medicines, vaccines and medical devices (1) for indications that have been approved in the US and/or EU or (2) in programs that have been terminated (i.e., development for all indications has been discontinued). Pfizer will also consider requests for the protocol, data dictionary, and statistical analysis plan. Data may be requested from Pfizer trials 24 months after study completion. The de-identified participant data will be made available to researchers whose proposals meet the research criteria and other conditions, and for which an exception does not apply, via a secure portal. To gain access, data requestors must enter into a data access agreement with Pfizer.

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	It was originally anticipated that 33 patients would need to be enrolled in the MET exon 14-altered NSCLC group. This would achieve a power of ≥90% to test the null hypothesis that the ORR of crizotinib would be ≤10%, versus the alternative hypothesis that the ORR would be >10% (one-sided alpha level of 0.05, single-stage design). For the alternative hypothesis, the target ORR was 30%. As of August 01, 2016, there were 11 objective responses (among 28 evaluable patients), which exceeded the 7 required to reject the null hypothesis. To permit a more accurate assessment of antitumor activity and safety, the sample size was expanded to 68, and later to 81 patients. The number of additional patients was not based on statistical considerations.
Data exclusions	No data exclusions
Replication	First report in human subjects- findings have not been replicated
Randomization	All patients with MET exon 14 advanced NSCLC enrolled in PROFILE 1001 were treated with crizotinib 250 mg BID, randomization was not applied.
Blinding	PROFILE 1001 is an ongoing single-arm phase I trial with an open-label design. Blinding is not standard practice in single arm phase 1 trials of oncologic therapies

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
☒	☐ Animals and other organisms
☐	☒ Human research participants
☐	☒ Clinical data

Methods

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

Human research participants

Policy information about studies involving human research participants

Population characteristics	Eligible patients had histologically confirmed NSCLC that harbored a MET exon 14-alteration (local molecular testing). Other eligibility criteria included an age of ≥18 years (≥20 years for Japanese patients), an Eastern Cooperative Oncology Group performance status of 0 to 1 (2 was allowed with sponsor approval), adequate organ function, and measurable disease (non-measurable disease was allowed with sponsor approval) per Response Evaluation Criteria in Solid Tumors (RECIST), version 1.0.
Recruitment	Patients were referred to Investigators from either the patients' local clinic or from other doctors within their institution. The investigators included the patients into the study if they met the criteria described in the population characteristics field above. No self-selection bias was likely.
Ethics oversight	The protocol (available with the full text of this article at Nature.com) was approved by the institutional review board or independent ethics committee at each site and complied with the International Ethical Guidelines for Biomedical Research Involving Human Subjects, Good Clinical Practice guidelines, the Declaration of Helsinki, and local laws. The institutions approving the study protocol were as follows: Peter MacCallum Cancer Centre, Human Research Ethics Committee, 305 Grattan St, Melbourne, VICTORIA 3000, AUSTRALIA; Kindai University Hospital Institutional Review Board, 377-2 Ohnohigashi, Osakasayama, OSAKA 589-8511, JAPAN; Hyogo Cancer Center Institutional Review Board, 13-70 Kitaoji-cho, Akashi, HYOGO 673-8558, JAPAN; Aichi cancer center central hospital Institutional Review Board, 1-1 Kanokoden Chikusa-ku, Nagoya, AICHI 464-8681, JAPAN; Office For Human Research Studies, Dana Farber Cancer Institute, 450 Brookline Ave, Boston, MA 02215,

UNITED STATES; Colorado Multiple Institutional Review Board, 13001 17th Place, Aurora, CO 80010, UNITED STATES; Memorial Sloan - Kettering Cancer Center IRB, 1275 York Ave, New York, NY 10065, UNITED STATES; University of California Irvine, 141 Innovation Office of Research Administration, Ste 250, Irvine, CA 92617-7600, UNITED STATES; Western Institutional Review Board, 1019 39th Ave SE, Ste 120, Puyallup, WA 98374, UNITED STATES; The University of North Carolina at Chapel Hill, Medical School Bldg 52, CB 7097 Office of Human Research Ethics, 105 Mason Farm Rd, Chapel Hill, NC 27599-7097, UNITED STATES. All patients provided written informed consent.

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

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	NCT00585195
Study protocol	Redacted versions of the full trial protocol, protocol amendment, and Statistical Action Plan have been submitted with the manuscript, and will be available on the journal website if accepted.
Data collection	Data collection took place at major medical centers in Australia, Japan and the United States. Patients with MET exon 14 alterations were eligible to enroll following Protocol Amendment 21 (April 07, 2015), which specified that these patients were allowed to enroll into the previously-specified "Enriched Other" cohort. The data cutoff date for inclusion in the present report was January 31, 2018.
Outcomes	Objective response was the primary end point. Duration of response, time to tumor response, progression-free survival, overall survival, and safety were additional end points. All of these endpoints were prespecified per the study procotol, and measurement on specification of each of these end points is included in the submitted protocol, protocol amendment and Statistical Action Plan.