nature portfolio

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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	Data were collected by using MACRO Electronic Data Capture (EDC) (Infermed, version 3)
Data analysis	Statistical analyses were performed by using R software, version 3.3.2 (R Project for Statistical Computing), and SAS software, version 9.4 (SAS Institute).

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 that support the findings of this study are not publicly available due to information that could compromise research participant consent. According to French/European regulations, any re-use of the data must be approved by the appropriate ethics committee. Each request for access to the dataset (including the images) will be granted upon request to the corresponding author (AI). Source data are available for this study.

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	The design was based on a single-arm phase 2 trial based accordign to the optimal two-stage Simon's design. o Hypotheses for non-progression at 6 months: - 15% non-progression rate (null hypothesis), - 40% acceptable non-progression rate (alternative hypothesis), o 5% 1-sided type I error rate, o 90% power, A total of 29 eligible and assessable subjects will be necessary, with 13 assessable subjects recruited to the first stage. o Stage 1: Following the inclusion of the first 13 assessable patients, if 2 or less patients are progression-free at 6 months (complete response, partial response or stable disease), the study will be terminated early. Otherwise, the second group of 16 subjects will be recruited. o Stage 2: If at the end of recruitment, 8 patients or more are progression-free at 6 months (out of the 29 eligible and evaluable patients), experimental treatment will be considered worthy of further testing in this disease (efficacy rate >=15%). In order to account for not evaluable patients (+/- 10%), 32 patients with sarcoma with immune signature will be recruited.
Data exclusions	As per protocol, 5 patients (out of the 35 included in the study) were excluded from the efficacy analysis due to major deviations to eligibility criteria. All patients were included in the safety analysis.
Replication	The data presented in the main figures using multiplexed immunofluorescence analysis represent multiple tumor specimens analyzed in one experimental run. This is typical for human tumor tissue studies where the same tissue area/exact cells cannot be analyzed more than once and replicates may introduce variations due to tissue heterogeneity or spatial variation.
Randomization	No randomization was performed as this was a single arm study.
Blinding	Efficacy endpoints were based on blinded central review of imaging collected for each patient.

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
☐	☒ Human research participants
☐	☒ Clinical data
☒	☐ Dual use research of concern

Methods

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

Antibodies

Antibodies used	The following antibodies were used: CD8 (C8/144B; Dako; Agilent Technologies), GzmA (EPR20161; Abcam, Cambridge, UK), CD4 (SP35; Ventana), Foxp3 (236A/E7, Abcam), CD56 (MRQ-42, Cell Marque), Mum1 (EP190, Cell Marque), CD20 (L26, Ventana), CD27 (EPR8569, Abcam), CD3 (2GV6; Ventana; Roche, Basel, Switzerland), COL1A1 (E8F4L; Cell Signaling Technology), IgG (polyclonal; Cell Marque Corp., Rocklin, CA, USA).
Validation	Each antibody was validated according to manufacturer's instructions.

Human research participants

Policy information about studies involving human research participants

Population characteristics	Main eligibility criteria included: diagnosis of soft-tissue sarcoma histologically confirmed by central review, Advanced non resectable / metastatic disease, TLS positive status assessed by central review, and confirmation of disease progression by central review with two radiological assessments identical (CT scans or MRI) obtained at less than 6 months interval within the 12 months before inclusion.
Recruitment	Patients were recruited between September 2018 and December 2019 in 7 centers of the French Sarcoma Group.
Ethics oversight	The PEMBROSARC study was approved by the Agence nationale de sécurité du médicament et des produits de santé (ANSM) and the Comité de Protection des Personnes (CPP) du Sud-Ouest et d'Outre-Mer III on 18/02/2015 and 17/12/2014 respectively.

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	NCT02406781
Study protocol	The srudy protocol is available online
Data collection	Patients were recruited between September 2018 and December 2019 in 7 centers of the French Sarcoma Group (list of investigational sites available in the protocol)
Outcomes	The primary endpoint was non-progression at 6 months defined as complete response, partial response or stable disease more than 24 weeks as defined as per RECIST evaluation criteria v1.1 (RECIST v1.1,).