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 <u>Editorial Policies</u> and the <u>Editorial Policy Checklist</u>.

Statistics

Fora	all st	atistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.	
n/a	Confirmed		
	X	The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement	
\Box	X	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.	
X		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. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>	
X		For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings	
	X	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 <u>availability of computer code</u>		
Data collection	No software was used for data collection	
Data analysis	All statistical analyses were performed with SAS version 9.4 (SAS Institute Inc., 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 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

Patient baseline clinical data are available in Table 1 and within the text. The surgery protocol and radiotherapy protocol are available as Supplementary Note in the Supplementary information file. The individual de-identified participant data, Study Protocol, Statistical Analysis plan and the full image dataset are available by sending requests to the corresponding author Baorui Liu (baoruiliu@nju.edu.cn;) within 5 years after this paper's publication. The remaining data are available within the Article, Supplementary Information, or Source Data file. Source data are provided with this paper.

Research involving human participants, their data, or biological material

Policy information about studies with <u>human participants or human data</u>. See also policy information about <u>sex, gender (identity/presentation),</u> and sexual orientation and <u>race, ethnicity and racism</u>.

Reporting on sex and gender	Among 34 included patients, 28 patients (82.4%) were male and 6 (17.6%) were female, which was recorded according to their biological sex.
Reporting on race, ethnicity, or other socially relevant groupings	Not applicable.
Population characteristics	From July 20th 2019 to October 10th 2021, 42 patients were screened for eligibility, and 8 were excluded due to refusal to participate (n=4), peritoneal metastasis (n=3), and a history of severe rash (n=1). Finally, a total of 34 patients were enrolled, with a median age of 65.5 years (range, 58-68). Among them, 28 patients (82.4%) were male, and 26 (76.5%) had an ECOG PS score of 0. Thirty-one patients (91.2%) were diagnosed with gastric cancer, and 3 (8.8%) had GEJ cancer. Three (8.8%), 18 (52.9%), 7 (20.6%), and 6 (17.7%) cases were Bormann type I, II, III, and IV, respectively.
Recruitment	Treated-naïve patients aged over 18, with histologically or cytologically confirmed locally advanced G/GEJ cancers were recruited from three centers in China. We conducted patient recruitment in the inpatient wards/outpatient clinics of all study centres to screen for locally advanced
	In the screening process, we excluded patients with severe complications and comorbidities that might underestimate the toxicity of this neoadjuvant regimen.
Ethics oversight	This study was approved by the ethics committees of the Comprehensive Cancer Centre of Drum Tower Hospital (2019-093-02), Xuzhou Central Hospital and Huai'an First People's Hospital.

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.

Ecological, evolutionary & environmental sciences

- **x** Life sciences Behavioural & social sciences
 - For a reference copy of the document with all sections, see <u>nature.com/documents/nr-reporting-summary-flat.pdf</u>

Life sciences study design

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

Sample size	A Simon 2-stage design was employed. The null hypothesis in this study was 15% and the alternative hypothesis was 35%, with one-sided α of 0.05 and a power of 80%. In case one or more of the nine patients reached pCR in the first stage, another 25 patients would be enrolled in the second stage.
Data exclusions	No data were excluded from the analyses.
Replication	The interventions for eligible patients with sufficient details have been provided in the Methods section to allow replication. Regarding the reproduction of the figures, we double checked the reproduced figures to make sure the validity of the figures. We confirm that the attempts at replication are successful.
Randomization	The study was a single-arm phase 2 trial. So randomization was not applicable in this study.
Blinding	The study was a single-arm phase 2 trial without comparator, the blinding was not applicable in this study.

Behavioural & social sciences study design

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

Study description	Briefly describe the study type including whether data are quantitative, qualitative, or mixed-methods (e.g. qualitative cross-sectional, quantitative experimental, mixed-methods case study).
Research sample	State the research sample (e.g. Harvard university undergraduates, villagers in rural India) and provide relevant demographic information (e.g. age, sex) and indicate whether the sample is representative. Provide a rationale for the study sample chosen. For studies involving existing datasets, please describe the dataset and source.
Sampling strategy	Describe the sampling procedure (e.g. random, snowball, stratified, convenience). Describe the statistical methods that were used to predetermine sample size OR if no sample-size calculation was performed, describe how sample sizes were chosen and provide a

rationale for why these sample sizes are sufficient. For qualitative data, please indicate whether data saturation was considered, and what criteria were used to decide that no further sampling was needed. Data collection Provide details about the data collection procedure, including the instruments or devices used to record the data (e.g. pen and paper, computer, eve tracker, video or audio equipment) whether anyone was present besides the participant(s) and the researcher, and whether the researcher was blind to experimental condition and/or the study hypothesis during data collection. Timing Indicate the start and stop dates of data collection. If there is a gap between collection periods, state the dates for each sample cohort. If no data were excluded from the analyses, state so OR if data were excluded, provide the exact number of exclusions and the Data exclusions rationale behind them, indicating whether exclusion criteria were pre-established. State how many participants dropped out/declined participation and the reason(s) given OR provide response rate OR state that no Non-participation participants dropped out/declined participation. Randomization If participants were not allocated into experimental groups, state so OR describe how participants were allocated to groups, and if

Ecological, evolutionary & environmental sciences study design

allocation was not random, describe how covariates were controlled.

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

Study description	Briefly describe the study. For quantitative data include treatment factors and interactions, design structure (e.g. factorial, nested, hierarchical), nature and number of experimental units and replicates.
Research sample	Describe the research sample (e.g. a group of tagged Passer domesticus, all Stenocereus thurberi within Organ Pipe Cactus National Monument), and provide a rationale for the sample choice. When relevant, describe the organism taxa, source, sex, age range and any manipulations. State what population the sample is meant to represent when applicable. For studies involving existing datasets, describe the data and its source.
Sampling strategy	Note the sampling procedure. Describe the statistical methods that were used to predetermine sample size OR if no sample-size calculation was performed, describe how sample sizes were chosen and provide a rationale for why these sample sizes are sufficient.
Data collection	Describe the data collection procedure, including who recorded the data and how.
Timing and spatial scale	Indicate the start and stop dates of data collection, noting the frequency and periodicity of sampling and providing a rationale for these choices. If there is a gap between collection periods, state the dates for each sample cohort. Specify the spatial scale from which the data are taken
Data exclusions	If no data were excluded from the analyses, state so OR if data were excluded, describe the exclusions and the rationale behind them, indicating whether exclusion criteria were pre-established.
Reproducibility	Describe the measures taken to verify the reproducibility of experimental findings. For each experiment, note whether any attempts to repeat the experiment failed OR state that all attempts to repeat the experiment were successful.
Randomization	Describe how samples/organisms/participants were allocated into groups. If allocation was not random, describe how covariates were controlled. If this is not relevant to your study, explain why.
Blinding	Describe the extent of blinding used during data acquisition and analysis. If blinding was not possible, describe why OR explain why blinding was not relevant to your study.

Did the study involve field work?

Yes No

Field work, collection and transport

Field conditions	Describe the study conditions for field work, providing relevant parameters (e.g. temperature, rainfall).
Location	State the location of the sampling or experiment, providing relevant parameters (e.g. latitude and longitude, elevation, water depth).
Access & import/export	Describe the efforts you have made to access habitats and to collect and import/export your samples in a responsible manner and in compliance with local, national and international laws, noting any permits that were obtained (give the name of the issuing authority, the date of issue, and any identifying information).
Disturbance	Describe any disturbance caused by the study and how it was minimized.

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		Methods
n/a Involved in the study		n/a Involved in the study
	X Antibodies	X ChIP-seq
×	Eukaryotic cell lines	🗴 📃 Flow cytometry
×	Palaeontology and archaeology	🗙 🔲 MRI-based neuroimaging
×	Animals and other organisms	
	X Clinical data	
×	Dual use research of concern	
×	Plants	
	•	

Antibodies

Antibodies used	Primary antibodies used were raised against CD163 (Abcam, ab182422, 1:500), CD8 (Abcam, ab178089, 1:200), CD68 (Abcam, ab213363, 1:1000), CD20 (DAKO, L26, IR604, 1:1), CD3 (DAKO, A0452, 1:1), CD4 (Abcam, ab133616, 1:100), CD56 (Abcam, ab75813, 1:1000), and FoxP3 (Abcam, ab20034, 1:100) for panel 2.
Validation	The details of antibody used in this study were described in the manuscipt, supplementary material and aurthor checklist, please kindly review.

Eukaryotic cell lines

Policy information about <u>cell lines and Sex and Gender in Research</u>		
Cell line source(s)	State the source of each cell line used and the sex of all primary cell lines and cells derived from human participants or vertebrate models.	
Authentication	Describe the authentication procedures for each cell line used OR declare that none of the cell lines used were authenticated.	
Mycoplasma contamination	Confirm that all cell lines tested negative for mycoplasma contamination OR describe the results of the testing for mycoplasma contamination OR declare that the cell lines were not tested for mycoplasma contamination.	
Commonly misidentified lines (See <u>ICLAC</u> register)	Name any commonly misidentified cell lines used in the study and provide a rationale for their use.	

Palaeontology and Archaeology

Specimen provenance	Provide provenance information for specimens and describe permits that were obtained for the work (including the name of the issuing authority, the date of issue, and any identifying information). Permits should encompass collection and, where applicable, export.
Specimen deposition	Indicate where the specimens have been deposited to permit free access by other researchers.
Dating methods	If new dates are provided, describe how they were obtained (e.g. collection, storage, sample pretreatment and measurement), where they were obtained (i.e. lab name), the calibration program and the protocol for quality assurance OR state that no new dates are provided.
Tick this box to confi	rm that the raw and calibrated dates are available in the paper or in Supplementary Information.
Ethics oversight	Identify the organization(s) that approved or provided guidance on the study protocol, OR state that no ethical approval or guidance was required and explain why not.

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

Animals and other research organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research, and Sex and Gender in Research

Laboratory animals	For laboratory animals, report species, strain and age OR state that the study did not involve laboratory animals.
Wild animals	Provide details on animals observed in or captured in the field; report species and age where possible. Describe how animals were caught and transported and what happened to captive animals after the study (if killed, explain why and describe method; if released, say where and when) OR state that the study did not involve wild animals.
Reporting on sex	Indicate if findings apply to only one sex; describe whether sex was considered in study design, methods used for assigning sex. Provide data disaggregated for sex where this information has been collected in the source data as appropriate; provide overall numbers in this Reporting Summary. Please state if this information has not been collected. Report sex-based analyses where performed, justify reasons for lack of sex-based analysis.
Field-collected samples	For laboratory work with field-collected samples, describe all relevant parameters such as housing, maintenance, temperature, photoperiod and end-of-experiment protocol OR state that the study did not involve samples collected from the field.
Ethics oversight	Identify the organization(s) that approved or provided guidance on the study protocol, OR state that no ethical approval or guidance was required and explain why not.

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

Clinical data

Policy information about <u>clinical studies</u>

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

Clinical trial registration	ChiCTR1900024428
Study protocol	Wei, J. et al. Efficacy and Safety of Sintilimab in Combination with Concurrent Chemoradiotherapy for Locally Advanced Gastric or Gastroesophageal Junction (GEJ) Adenocarcinoma (SHARED): Study Protocol of a Prospective, Multi-Center, Single-Arm Phase 2 Trial. Cancer Manag Res. 14, 2007-2015 (2022).
Data collection	From July 20th 2019 to October 10th 2021, 42 patients were screened for eligibility, and a total of 34 patients were enrolled. At the cutoff date of April 8th, 2022, median follow-up times were 13.9 (range 1.0-20.9) months for disease-free survival (DFS) and 18.2 (range, 7.0-32.4) months for event-free survival (EFS) and OS. Patients were regularly admitted to hospital for assessment of efficacy and safety, and the data were collected and completed using CRF forms.
Outcomes	The primary endpoint was the pCR rate, i.e., the absence of viable residual tumor cells in the resected specimen. Secondary endpoints included major pathological response (MPR, i.e., residual tumor cells below 10% in the resected specimen), R0 resection rate (i.e., complete removal of the tumor with a tumor-free margin), DFS, EFS, and OS. DFS was defined as the time from surgery to postoperative recurrence or death from any cause, whichever occurred first. DFS was censored on the last tumor assessment date for patients still alive and without recurrence. EFS was the time from enrolment to recurrence or death from any cause. EFS was censored on the last tumor assessment date for patients still alive and without recurrence. S was the time from enrolment to recurrence. OS was the time from enrolment to death from any cause. OS was censored on the last date known to be alive for patients without documentation of death. Safety endpoints included TEAEs, TRAEs, irAEs, and surgical AEs (i.e., complications occurring during or within 30 days of surgery). Tumor assessments were evaluated per RECIST v1.1 by CT/magnetic resonance imaging (MRI) and endoscopic ultrasound (EUS) every six weeks preoperatively, every nine weeks postoperatively, and every three months after treatment completion until disease progression (up to two years) or new anticancer treatment initiation. Routine blood tests and blood biochemistry were reviewed weekly. Tumor biomarkers and thyroid function were reviewed preoperatively at weeks 3 and 8 of neoadjuvant therapy and postoperatively every 3 weeks. Adverse events (AEs) from the first dosing of the study regimen to 90 days after the last dosing were recorded and graded according to the National Cancer Institute's Common Terminology Criteria for Adverse Events (NCI CTCAE, version 4.03). Surgical complications were grading using Clavien-Dindo. Judgment and grading of the AEs were based on the time of occurrence of the AEs, clinical manifestations, and relevant test and examination results. If necessa

Dual use research of concern

Policy information about <u>dual use research of concern</u>

Hazards

Could the accidental, deliberate or reckless misuse of agents or technologies generated in the work, or the application of information presented in the manuscript, pose a threat to:

No	Yes
	Public health
	National security
	Crops and/or livestock
	Ecosystems
	Any other significant area

Experiments of concern

Does the work involve any of these experiments of concern:

No	Yes
	Demonstrate how to render a vaccine ineffective
	Confer resistance to therapeutically useful antibiotics or antiviral agents
	Enhance the virulence of a pathogen or render a nonpathogen virulent
	Increase transmissibility of a pathogen
	Alter the host range of a pathogen
	Enable evasion of diagnostic/detection modalities
	Enable the weaponization of a biological agent or toxin
	Any other potentially harmful combination of experiments and agents

Plants

Seed stocks	Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.
Novel plant genotypes	Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.
Authentication	Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosiacism, off-target gene editing) were examined.

ChIP-seq

Data deposition

Confirm that both raw and final processed data have been deposited in a public database such as GEO.

Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

Data access links May remain private before publication.	For "Initial submission" or "Revised version" documents, provide reviewer access links. For your "Final submission" document, provide a link to the deposited data.
Files in database submission	Provide a list of all files available in the database submission.
Genome browser session (e.g. <u>UCSC</u>)	Provide a link to an anonymized genome browser session for "Initial submission" and "Revised version" documents only, to enable peer review. Write "no longer applicable" for "Final submission" documents.

Methodology

Replicates	Describe the experimental replicates, specifying number, type and replicate agreement.	
Sequencing depth	Describe the sequencing depth for each experiment, providing the total number of reads, uniquely mapped reads, length of reads and whether they were paired- or single-end.	
Antibodies	Describe the antibodies used for the ChIP-seq experiments; as applicable, provide supplier name, catalog number, clone name, and lot number.	
Peak calling parameters	Specify the command line program and parameters used for read mapping and peak calling, including the ChIP, control and index files used.	

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Data quality

Software

Describe the methods used to ensure data quality in full detail, including how many peaks are at FDR 5% and above 5-fold enrichment.

Describe the software used to collect and analyze the ChIP-seq data. For custom code that has been deposited into a community repository, provide accession details.

Flow Cytometry

Plots

Confirm that:

The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).

The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).

All plots are contour plots with outliers or pseudocolor plots.

A numerical value for number of cells or percentage (with statistics) is provided.

Methodology

Sample preparation	Describe the sample preparation, detailing the biological source of the cells and any tissue processing steps used.
Instrument	Identify the instrument used for data collection, specifying make and model number.
Software	Describe the software used to collect and analyze the flow cytometry data. For custom code that has been deposited into a community repository, provide accession details.
Cell population abundance	Describe the abundance of the relevant cell populations within post-sort fractions, providing details on the purity of the samples and how it was determined.
Gating strategy	Describe the gating strategy used for all relevant experiments, specifying the preliminary FSC/SSC gates of the starting cell population, indicating where boundaries between "positive" and "negative" staining cell populations are defined.

Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.

Magnetic resonance imaging

Experimental design		
Design type	Indicate task or resting state; event-related or block design.	
Design specifications	Specify the number of blocks, trials or experimental units per session and/or subject, and specify the length of each trial or block (if trials are blocked) and interval between trials.	
Behavioral performance measure	State number and/or type of variables recorded (e.g. correct button press, response time) and what statistics were used to establish that the subjects were performing the task as expected (e.g. mean, range, and/or standard deviation across subjects).	
Acquisition		
Imaging type(s)	Specify: functional, structural, diffusion, perfusion.	
Field strength	Specify in Tesla	
Sequence & imaging parameters	Specify the pulse sequence type (gradient echo, spin echo, etc.), imaging type (EPI, spiral, etc.), field of view, matrix size, slice thickness, orientation and TE/TR/flip angle.	
Area of acquisition	State whether a whole brain scan was used OR define the area of acquisition, describing how the region was determined.	
Diffusion MRI Used	Not used	
Preprocessing		
	Provide detail on software version and revision number and on specific parameters (model/functions, brain extraction, segmentation, smoothing kernel size, etc.).	
	If data were normalized/standardized, describe the approach(es): specify linear or non-linear and define image types used for transformation OR indicate that data were not normalized and explain rationale for lack of normalization.	

Normalization template	Describe the template used for normalization/transformation, specifying subject space or group standardized space (e.g. original Talairach, MNI305, ICBM152) OR indicate that the data were not normalized.
Noise and artifact removal	Describe your procedure(s) for artifact and structured noise removal, specifying motion parameters, tissue signals and physiological signals (heart rate, respiration).
Volume censoring	Define your software and/or method and criteria for volume censoring, and state the extent of such censoring.

Statistical modeling & inference

statistical modeling a me		
Model type and settings	Specify type (mass univariate, multivariate, RSA, predictive, etc.) and describe essential details of the model at the first and second levels (e.g. fixed, random or mixed effects; drift or auto-correlation).	
Effect(s) tested	Define precise effect in terms of the task or stimulus conditions instead of psychological concepts and indicate whether ANOVA or factorial designs were used.	
Specify type of analysis:	Whole brain 🔲 ROI-based 🔲 Both	
Statistic type for inference	nce Specify voxel-wise or cluster-wise and report all relevant parameters for cluster-wise methods.	
(See <u>Eklund et al. 2016</u>)		
Correction	Describe the type of correction and how it is obtained for multiple comparisons (e.g. FWE, FDR, permutation or Monte Carlo).	
Models & analysis		
n/a Involved in the study		
Functional and/or effec	tive connectivity	
Graph analysis		
Multivariate modeling o	or predictive analysis	

· Functional and/or effective connectivity	Report the measures of dependence used and the model details (e.g. Pearson correlation, partial correlation, mutual information).
Graph analysis	Report the dependent variable and connectivity measure, specifying weighted graph or binarized graph, subject- or group-level, and the global and/or node summaries used (e.g. clustering coefficient, efficiency, etc.).
Multivariate modeling and predictive analysis	Specify independent variables, features extraction and dimension reduction, model, training and evaluation metrics.