

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 (<i>n</i>) 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 <i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i>
☒	☐ 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>
☒	☐ 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 <i>d</i> , Pearson's <i>r</i>), 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 via an internet-based, controlled electronic data capture (EDC) system for further analysis.
Data analysis	All statistical analyses were performed using SAS (version 9.4).

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](#)

To protect the privacy of study participants and proprietary information, the sponsor shares anonymized individual patient data upon request or as required by law or regulation with qualified external researchers based on submitted curriculum vitae and reflecting non-conflict of interest. The data provided include demographic, efficacy, and safety information. Approval of such requests is at the sponsor's discretion and depends on the nature of the request, the merit of the research proposed, the availability of the data, and the intended use of the data. Data requests should be sent to mict@kelun.com. In response to the inquiry,

please be informed that the timeframe for responding to requests is approximately 2 weeks. The redacted version of the trial protocol and statistical analysis plan is in the supplementary documents.

Research involving human participants, their data, or biological material

Policy information about studies with [human participants or human data](#). See also policy information about [sex, gender \(identity/presentation\), and sexual orientation](#) and [race, ethnicity and racism](#).

Reporting on sex and gender	The sex of patients in the trial was self-reported. All 263 patients enrolled were female.
Reporting on race, ethnicity, or other socially relevant groupings	N/A
Population characteristics	Patients were randomly assigned to receive either sac-TMT (n = 130) or chemotherapy of the physician's choice (n = 133). Across both treatment groups, the median age of the enrolled patients was 51.0 years, and 90.5% of patients were aged less than 65 years. More than two-thirds of cases (68.4%) were confirmed as TNBC at initial diagnosis. All patients received taxanes as part of prior therapy. Additionally, most patients (92.8%) received prior anthracyclines, 25.9% of patients received programmed death-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitors, and 88.6% of patients received prior neoadjuvant or adjuvant therapy. Overall, 86.7% of patients presented with visceral metastases and 34.2% of patients presented with liver metastases. Almost half of the patients (47.5%) had received three or more previous chemotherapy regimens in metastatic setting. The baseline demographics and clinical characteristics were generally balanced between the treatment groups (Table 1).
Recruitment	Between 11 August 2022 and 26 April 2023, 396 patients were assessed for eligibility. A total of 263 patients with locally advanced, recurrent, or metastatic TNBC were enrolled across 49 sites in China. Patients were eligible for enrollment if they met the following criteria: histologically confirmed diagnosis of TNBC according to standard American Society of Clinical Oncology–College of American Pathologists criteria based on local lab assessment, and previous treatment with two or more systemic therapies (with at least one for metastatic disease and previous taxane therapy) for unresectable, locally advanced, or metastatic disease. For (neo)adjuvant chemotherapy, if progression occurred during treatment or within 12 months after treatment discontinuation, it would be considered one regimen for advanced setting. A full list of inclusion and exclusion criteria is available in the protocol and Supplementary Information (Supplementary Table S4). A potential bias may exist in the possible difficulty of recruiting patients from some remote areas of China, but this is unlikely to have a major impact on the results. Participants did not receive compensation for study participation; however, they were reimbursed for certain expenses (e.g., hotel rooms, transportation, tumor tissue biopsies).
Ethics oversight	The trial was approved by the research ethics committee of each participating institution. All participating patients read and signed an informed consent form. This trial was performed in accordance with Good Clinical Practice standards, the Declaration of Helsinki, and relevant laws and regulations.

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	The planned sample size was 254 patients. Sample size was calculated based on the primary endpoint of PFS per BICR. Under the assumption of a HR for PFS (sac-TMT versus chemotherapy) of 0.60 and the expected median PFS of 2 months for the chemotherapy group, 183 events of progression or death would provide approximately 93% power to detect a significant between-group difference in PFS, with a one-sided alpha of 0.025. Patients were enrolled in a 1:1 ratio over an anticipated 15-month recruitment period, considering a cumulative dropout rate of 10%.
Data exclusions	Efficacy analysis was performed in the intention-to-treat population, which included all patients who underwent randomization. All patients who received at least one dose of study treatment were included in the safety analysis. Only one patient assigned to receive chemotherapy received no study treatment and was included in the efficacy analysis but not in the safety analysis.
Replication	Not applicable as this was a clinical trial.
Randomization	Patients were stratified at randomization according to lines of prior therapy (2 or 3 vs >3) and presence of liver metastases (yes vs no). The records of the random allocation sequences were maintained by an independent, third-party, and unblinded statistician. The randomization of patients was carried out through an interactive response technology system. Patients were randomly assigned in a 1:1 ratio to receive sac-TMT or single-agent chemotherapy. Patients in the sac-TMT group received 5 mg/kg sac-TMT intravenously once every two weeks over a 28-day cycle. Patients in the chemotherapy group received one of the following four options at the physician's discretion: eribulin, given intravenously at 1.4 mg/m ² on days 1 and 8 of a 21-day cycle; capecitabine, given as oral tablets at 1000–1250 mg/m ² twice daily on days 1

through 14 of a 21-day cycle; gemcitabine, given intravenously at 1000 mg/m² on days 1 and 8 of a 21-day cycle; or vinorelbine, given intravenously at 25 mg/m² on days 1 and 8 of a 21-day cycle.

Blinding

This study was an open-label design.

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 |
| ☒ | ☐ Plants |

Methods

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

Antibodies

Antibodies used

Protein-level expression of TROP2 was assessed by immunohistochemistry using anti-TROP2 antibody (EPR20043 by Abcam) at a dilution of 1:3000.

Validation

Antibodies used in this study are all commercially available. Validation of each antibody for the species, application, relevant citations and antibody profiles are available online from the manufacturer's website.

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

NCT05347134

Study protocol

Study protocol is provided and submitted with the manuscript as the supplementary documents.

Data collection

Between 11 August 2022 and 26 April 2023, 396 patients were assessed for eligibility. A total of 263 patients with locally advanced, recurrent, or metastatic TNBC were enrolled across 49 sites in China.

Outcomes

The primary endpoint was PFS as assessed by BICR using Response Evaluation Criteria in Solid Tumors version 1.1. PFS was defined as the time from randomization to disease progression or death, whichever occurred first. The secondary endpoints included PFS by investigator assessment, OS, ORR, DCR, DOR, TTR, and safety. OS was defined as the time from randomization to death due to any cause. ORR was defined as the proportion of patients with complete response (CR) or partial response (PR) as the best overall response. DCR was defined as the proportion of patients with CR, PR, or stable disease (SD) as the best overall response. DOR was defined as the time from the date of the first response to progression or death, whichever occurred first. TTR was defined as the time from randomization to the first response (CR/PR).

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, mosaicism, off-target gene editing) were examined.