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	The Medidata RAVE electronic data capture system was used to capture, manage, clean and report the trial data. No custom computer code or algorithms were used.
Data analysis	Tables were generated using SAS version 9.4. Figures were generated using R version 4.4.3. No custom computer code or algorithms were used.

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

For eligible studies, qualified researchers may request access to individual patient-level clinical data via the cross-industry request site https://vivli.org. Full details of Roche's approach to sharing individual patient-level clinical data via the Vivli site can be found at https://vivli.org/ourmember/roche. In summary, access requests

are assessed by an Independent Review Panel managed by Vivli. The panel considers the scientific merit of each application and compliance with patient consent and data-sharing policies, with the timeline for request approval (usually 2–5 months) influenced by the number of data contributors, the number of studies and the requestor's availability to respond to comments. Once approved, the data is anonymized and made available for a minimum of 12 months. For up-to-date details on Roche's Global Policy on the Sharing of Clinical Information and how to request access to related clinical study documents, see here: https://go.roche.com/data_sharing. Anonymized records for individual patients across more than one data source external to Roche cannot, and should not, be linked due to a potential increase in risk of patient re-identification.

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	Sex was based on self-reported demographics obtained at screening. No sex-based analyses were performed, as this was a first-in-human, Phase I study.
Reporting on race, ethnicity, or other socially relevant groupings	Race was based on self-reported demographics obtained at screening. No race-based analyses were performed, as this was a first-in-human, Phase I study.
Population characteristics	Among the 324 patients enrolled, median age was 65 years (range: 33 to 90), 55.6% were male and 75.9% were white (Table 2).
Recruitment	Between September 19, 2017 and July 18, 2023, 324 patients were enrolled into the cevostamab monotherapy cohorts at 17 centers in the United States, Canada, Spain, and Australia (Supplementary Data Table 1). Participants were identified for potential recruitment by the investigators using pre-screening enrolment logs and institutional databases.
Ethics oversight	The study was conducted in accordance with International Conference on Harmonization guidelines for Good Clinical Practice. The protocol was approved by the ethics committee at each participating center (Supplementary Data Table 1). Patients provided written informed consent and were not compensated.

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	Planned enrollment was approximately 180 patients in the dose-escalation stage and ≥30 patients per dosing regimen in the dose-expansion stage. Notably, 30 patients is a reasonable size to obtain an estimate of the response rate; with a sample size of 30 and an observed response rate of 20%, the 90% confidence interval (CI) or the true response rate is (8%, 32%) and the expected number of responses is 6. Thirty patients is also a reasonable size to obtain an estimate of the rate of Grade ≥2 cytokine release syndrome (CRS) events; with a sample size of 30 and an observed Grade ≥2 CRS rate of 27%, the 90% CI for the true Grade ≥2 CRS rate is (13%, 40%) and the expected number of Grade ≥2 CRS events is 8.
Data exclusions	The safety and efficacy of tocilizumab as premedication for the mitigation of cytokine release syndrome after cevostamab dosing was evaluated, but these data were not included in the current analysis and will be reported elsewhere. Data on cevostamab retreatment were also not included in the current analysis and will be reported elsewhere.
Replication	Not applicable. This was a first-in-human, Phase I study.
Randomization	Not applicable. This was a non-randomized, Phase 1 study.
Blinding	Not applicable. This was an open-label (non-blinded), Phase 1 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
☒	☐ Plants

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	NCT03275103
Study protocol	The study protocol was included in the submission package to inform the peer review. The study protocol has also been included as supporting information for online review.
Data collection	Between September 19, 2017 and July 18, 2023, 324 patients were enrolled into the cevostamab monotherapy cohorts at 17 centers in the United States, Canada, Spain, and Australia (Supplementary Data Table 1).
Outcomes	Primary objectives were to evaluate safety, including determination of the maximum-tolerated dose, and identify a recommended phase 2 dose and schedule. Secondary objectives were to evaluate pharmacokinetics, immunogenicity and activity. Activity endpoints were the rate of response and duration of response as determined by investigators according to International Myeloma Working Group criteria. Progression-free survival was assessed in a post-hoc analysis.

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.*

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	FcRH5 expression was assessed on myeloma cells collected at baseline by bone marrow aspiration. Samples were prepared and analysed by ICON plc.
Instrument	BD FACSCanto™ II Clinical Flow Cytometry System.
Software	Gating of the sample data was done using FCS Express Clinical Edition. The numerical outcome of the analysis was plotted using R.

Cell population abundance	No sorting was done.
Gating strategy	Singlet/WBC/CD45-/CD38+(CD138+ OR CD319+)/FcRH5+.

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