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	Genomic DNA was extracted from blood samples using the DNA Blood400 kit (Chemagic) and eluted in 50µL Elution Buffer (EB, Qiagen). DNA was sheered (Covaris LE220) and sequencing libraries were prepared using the TruSeq Nano DNA HT kit (Illumina Inc.). Libraries were sequenced at Human Longevity (San Diego, CA, USA). All sequencing data was checked for concordance with SNP fingerprint data collected before sequencing. 150bp paired-end whole-genome sequencing (WGS) data was generated to an average read depth of 30x using the HiSeq platform (Illumina X10, San Diego, CA, USA).
Data analysis	Reads were aligned using the functionally equivalent BAM (FEB) pipeline (bwa v0.7.15 and picard 2.18.7). Samples were joint genotyped using Sentieon GATK release 201911. ADMIXTURE v1.23 was used estimate ancestry in the 5 major populations using supervised mode. Statistical analyses were performed using the R programming language v3.6.1. Mixed effects cox models were constructed using the coxme R package v2.2. Standard Cox models were constructed using the survival R package v3.2. Fine mapping was performed using GCTA-COJO v1.92.4. Relatedness analysis was performed using SNPRelate v1.24. plink v1.90 and SeqArray v1.30.0 were used to manipulate genetic data and extract variants.

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

Summary statistics for the common variant GWAS are available for download here
https://my.locuszoom.org/gwas/74850/?token=594900c165994363972fd86bcdd8a4fa

Human research participants

Policy information about studies involving human research participants and Sex and Gender in Research.

Reporting on sex and gender	Sex and gender were not considered in study design
Population characteristics	This study was a meta-analysis of individual participant data from completed randomized controlled trials. Details on the population characteristics are provided in the original clinical trial study publications referenced in the supplementary information and in the main manuscript text of this study.
Recruitment	Details on patient recruitment are provided in the clinical trial protocols which were provided as supplementary materials in the original study publications.
Ethics oversight	We conducted a retrospective meta-analysis analysis of chemotherapy induced peripheral neuropathy (CIPN) events using individual participant data from previously completed randomized controlled trials. Detailed clinical trial results have been previously reported, and the clinical trial protocols have been provided as supplementary materials in the original study publications. All of the trials were sponsored by F. Hoffmann–La Roche/Genentech. The sponsor provided the study drugs and collaborated with the investigators across countries and study sites on the clinical trial and collection of the data. Each trial was conducted in accordance with the International Conference on Harmonization Good Clinical Practice guidelines and with the principles of the Declaration of Helsinki. An independent data monitoring committee reviewed safety data. All patients provided informed consent for the main study. A subset of patients signed an optional Research Biosample Repository (RBR) Informed Consent Form (ICF) and provided whole blood samples for genetic research. Ethics Committees (EC) and Institutional Review Boards (IRB) in each country and each study site for each clinical trial approved the clinical trial protocol, the main study ICF, and the RBR ICF. The EC and IRB for each clinical trial, country, and study site are provided as Supplementary Data.

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	We conducted our analysis of chemotherapy induced peripheral neuropathy events and the association between them and the germline genotypes of subjects using the entire safety evaluable population across the clinical trials we analyzed. Our analysis of germline genetic data was limited by the number of patients that provided informed consent for germline genetic data collection across the clinical trials we considered.
Data exclusions	Patients were excluded if they were not in the safety evaluable population of the clinical trials, if they did not provide informed consent for genetic data collection, their whole genome sequencing data failed quality control, or were not of European ancestry.
Replication	We conducted an individual participant data meta-analysis across clinical trial arms. All findings reported have statistically significant meta-analysis p-values indicating the findings are reproducible and that a consistent effect size is obtained across the trial arms. Within study effect sizes were examined to confirm no significant heterogeneity exists between within study effect sizes.
Randomization	Patient randomization was conducted as described in the original clinical trial study publications. All genetic association analyses included age, sex and 5 genotype eigenvectors to account for population stratification.

Blinding	Germline genetic data was collected on the basis of availability of informed consent. All germline genetic data was blinded to study allocation, safety events, and study outcomes.

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

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	This study used individual participant data from the following completed randomized clinical trials to perform a meta-analysis:
Study protocol	Study protocols are available in the original clinical trial study publications as referenced in the manuscript.
Data collection	Details on settings and places where the data were collected as well as the periods of time for recruitment and data collection including the investigators and their institutions and study sites are provided in the original clinical trial study publications.
Outcomes	This study was not a clinical trial. It was retrospective meta-analysis of individual participant data from previously completed, randomized controlled trials. As such, no pre-specification of outcomes was needed.