

Supplementary materials

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Table S1. Checklist of the PRISMA extension for network meta-analysis

Section and Topic	Item#	Checklist item*	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: • Background: main objectives; • Methods: data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods, such as network meta-analysis. • Results: number of studies and participants identified; summary estimates with corresponding confidence/credible intervals; treatment rankings may also be discussed. Authors may choose to summarize pairwise comparisons against a chosen treatment included in their analyses for brevity. • Discussion/Conclusions: limitations; conclusions and implications of findings. • Other: primary source of funding; systematic review registration number with registry name.	1-2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known, including mention of why a network meta-analysis has been conducted.	2
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	3
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. Clearly describe eligible treatments included in the treatment network, and note whether any have been clustered or merged into the same node (with justification).	3-4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Table S2
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	4
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding , PICOS, funding sources) and any assumptions and simplifications made.	4

Geometry of the network	S1	Describe methods used to explore the geometry of the treatment network under study and potential biases related to it. This should include how the evidence base has been graphically summarized for presentation, and what characteristics were compiled and used to describe the evidence base to readers.	4-5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means). Also describe the use of additional summary measures assessed, such as treatment rankings and surface under the cumulative ranking curve (SUCRA) values, as well as modified approaches used to present summary findings from meta-analyses.	4-5
Synthesis of results	14	Describe the methods of handling data and combining results of studies for each network meta-analysis. This should include, but not be limited to: • Handling of multi-arm trials; • Selection of variance structure; • Selection of prior distributions in Bayesian analyses; and • Assessment of model fit.	4-5
Assessment of Inconsistency	S2	Describe the statistical methods used to evaluate the agreement of direct and indirect evidence in the treatment network(s) studied. Describe efforts taken to address its presence when found.	4-5
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	4-5
Additional analyses	16	Describe methods of additional analyses, if done, indicating which were prespecified. This may include, but not be limited to the following: • Sensitivity or subgroup analyses; • Meta-regression analyses; • Alternative formulations of the treatment network; and • Use of alternative prior distributions for Bayesian analyses (if applicable).	4-5
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	5
Presentation of network structure	S3	Provide a network graph of the included studies to enable visualization of the geometry of the treatment network.	5
Summary of network geometry	S4	Provide a brief overview of characteristics of the treatment network. This may include commentary on the abundance of trials and randomized patients for the different interventions and pairwise comparisons in the network, gaps of evidence in the treatment network, and potential biases reflected by the network structure.	5
Study selection	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	5
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment.	Figure S1

Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study:1) simple summary data for each intervention group, and 2) effect estimates and confidence/credible intervals. Modified approaches may be needed to deal with information from larger networks.	5-9
Synthesis of results	21	Present results of each meta-analysis done, including confidence/credible intervals. In larger networks, authors may focus on comparisons versus a particular comparator (e.g. placebo or standard care), with full findings presented in an appendix. League tables and forest plots may be considered to summarize pairwise comparisons. If additional summary measures were	5-9
Exploration for inconsistency	S5	Describe results from investigations of inconsistency. This may include such information as measures of model fit to compare consistency and inconsistency models, P values from statistical tests, or summary of inconsistency estimates from different parts of the treatment network.	9
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies.	9
Additional analyses	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses meta-regression, alternative network geometries studied, alternative choice of prior distributions for Bayesian analyses, and so forth.	7-9
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	9-10
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). Comment on the validity of the assumptions, such as transitivity and consistency. Comment on any concerns regarding network geometry (e.g., avoidance of certain comparisons).	11
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	12
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1

PICOS = population, intervention, comparators, outcomes, study design.

*Text in *italics* indicates wording specific to reporting of network meta-analyses that has been added to guidance from the PRISMA statement

Table S2. Literature Search Criteria

1. Search strategy on PubMed

#1 Search: "Carcinoma, Non-Small-Cell Lung"[Mesh] 72329

#2 Search: (((((((((Carcinoma, Non Small Cell Lung[Title/Abstract]) OR (Carcinomas, Non-Small-Cell Lung[Title/Abstract])) OR (Lung Carcinoma, Non-Small-Cell[Title/Abstract])) OR (Lung Carcinomas, Non-Small-Cell[Title/Abstract])) OR (Non-Small-Cell Lung Carcinomas[Title/Abstract])) OR (Non-Small-Cell Lung Carcinoma[Title/Abstract])) OR (Non Small Cell Lung Carcinoma[Title/Abstract])) OR (Carcinoma, Non-Small Cell Lung[Title/Abstract])) OR (Non-Small Cell Lung Carcinoma[Title/Abstract])) OR (Non-Small Cell Lung Cancer[Title/Abstract])) OR (Non-small Cell Lung Cancer[Title/Abstract]) **86444**

#3 #1 0R #2 100790

#4 Search: (epidermal growth factor receptor[Title/Abstract]) OR (EGFR[Title/Abstract]) 105938

#5 Search: (((((((((((("Randomized Controlled Trials as Topic"[Mesh]) OR (Randomized Controlled Trial[Publication Type])) OR (Controlled Clinical Trials, Randomized[Publication Type])) OR (Trials, Randomized Clinical[Publication Type])) OR (Clinical Trials, Randomized[Publication Type])) OR (Randomized[Title/Abstract])) OR (Randomised[Title/Abstract])) OR (RCT[Title/Abstract])) OR (RCTs[Title/Abstract])) OR (control group[Title/Abstract])) OR (control groups[Title/Abstract])) OR (double-blind method[MeSH])) OR (double blind[Title/Abstract])) OR (placebo*[Title/Abstract]) **1640051**

#6

((N-(3-Chloro-4-fluorophenyl)-7-methoxy-6-(3-(4-morpholinyl)propoxy)-4-quinazolinamide[Title/Abstract])) OR (Iressa[Title/Abstract])) OR (ZD1839[Title/Abstract])) OR (ZD 1839[Title/Abstract])) OR (Hydrochloride, Erlotinib[Title/Abstract])) OR (Erlotinib HCl[Title/Abstract])) OR (HCl, Erlotinib[Title/Abstract])) OR (OSI-774[Title/Abstract])) OR (OSI 774[Title/Abstract])) OR (OSI774[Title/Abstract])) OR (CP 358774[Title/Abstract])) OR (358774, CP[Title/Abstract])) OR (CP 358,774[Title/Abstract])) OR (358,774, CP[Title/Abstract])) OR (CP-358,774[Title/Abstract])) OR (CP358,774[Title/Abstract])) OR (CP-358774[Title/Abstract])) OR (CP358774[Title/Abstract])) OR (11C-erlotinib[Title/Abstract])) OR (11C erlotinib[Title/Abstract])) OR (Erlotinib[Title/Abstract])) OR (N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)quinazolin-4-amine[Title/Abstract])) OR (Tarceva[Title/Abstract])) OR (4-((3-ethynylphenyl)amino)-6,7-benzo-12-crown-4-quinazoline[Title/Abstract])) OR ((2E)-N-(4-(3-Chloro-4-fluoroanilino)-7-(((3S)-oxolan-3-yl)oxy)quinoxazolin-6-yl)-4-(dimethylamino)but-2-enamide[Title/Abstract])) OR (BIBW-2992-MA2[Title/Abstract])) OR (BIBW 2992 MA2[Title/Abstract])) OR (BIBW-2992MA2[Title/Abstract])) OR (BIBW2992 MA2[Title/Abstract])) OR (Afatinib Maleate[Title/Abstract])) OR (BIBW 2992[Title/Abstract])) OR (BIBW2992[Title/Abstract])) OR (BIBW-2992[Title/Abstract])) OR (Gilotrif[Title/Abstract])) OR (Afatinib Dimaleate[Title/Abstract])) OR (Vizimpro[Title/Abstract])) OR (N-(4-(3-chloro-4-fluoroanilino)-7-methoxy-6-quinazoliny)-4-(1-piperidinyl)-2-butenamide[Title/ Abstract])) OR (PF 00299804[Title/Abstract])) OR (PF00299804[Title/Abstract])) OR (PF-00299804[Title/Abstract])) OR (N-(2-((2-(dimethylamino)ethyl)methylamino)-4-methoxy-5-((4-(1-methyl-1H-indol-3-yl)-2-pyri

midinyl)amino)phenyl)-2-propenamide[Title/Abstract])) OR (mereletinib[Title/Abstract])) OR (osimertinib mesylate[Title/Abstract])) OR (osimertinib mesilate[Title/Abstract])) OR (mereletinib mesilate[Title/Abstract])) OR (N-(2-((2-(dimethylamino[Title/Abstract])ethyl)methylamino)-4-methoxy-5-((4-(1-methyl-1H-indol-3-yl)-2-pyrimidinyl)amino)phenyl)-2-propenamide methanesulfonate (1:1))) OR (AZD9291 mesylate[Title/Abstract])) OR (mereletinib mesylate[Title/Abstract])) OR (AZD-9291 mesylate[Title/Abstract])) OR (AZD9291[Title/Abstract])) OR (AZD-9291[Title/Abstract])) OR (Tagrisso[Title/Abstract])) OR (almonertinib[Title/Abstract])) OR (N-(5-((4-(1-cyclopropylindol-3-yl)pyrimidin-2-yl)amino)-2-(2-(dimethylamino)ethyl-methylamino)-4-methoxyphenyl)prop-2-enamide[Title/Abstract])) OR (HS-10296[Title/Abstract])) OR (N-(2-(2-(dimethylamino)ethyl-methylamino)-5-((4-(1-methylindol-3-yl)pyrimidin-2-yl)amino)-6-(2,2,2-trifluoroethoxy)pyridin-3-yl)prop-2-enamide[Title/Abstract])) OR (AST2818[Title/Abstract])) OR (furmonertinib mesylate[Title/Abstract])) OR (furmonertinib[Title/Abstract])) OR (Ivesa[Title/Abstract])) OR (Befotertinib[Title/Abstract])) OR (amivantamab[Title/Abstract])) OR (JNJ-61186372[Title/Abstract])) OR (JNJ 61186372[Title/Abstract])) OR (CNTO-4424[Title/Abstract])) OR (Rybrevant[Title/Abstract])) OR (N-(5-((4-(4-((Dimethylamino)methyl)-3-phenyl-1H-pyrazol-1-yl)-2-pyrimidinyl)amino)-4-methoxy-2-(4-morpholinyl)phenyl)acrylamide[Title/Abstract])) OR (2-Propenamide, N-(5-((4-(4-((dimethylamino)methyl)-3-phenyl-1H-pyrazol-1-yl)-2-pyrimidinyl)amino)-4-methoxy-2-(4-morpholinyl)phenyl)-[Title/Abstract])) OR (Leclaza[Title/Abstract])) OR (((((((("Gefitinib"[Mesh]) OR "Erlotinib Hydrochloride"[Mesh]) OR "icotinib" [Supplementary Concept]) OR "Afatinib"[Mesh]) OR "dacomitinib" [Supplementary Concept]) OR "osimertinib" [Supplementary Concept]) OR "aumolertinib" [Supplementary Concept]) OR "aflutinib" [Supplementary Concept]) OR "amivantamab-vmjw" [Supplementary Concept]) OR "lazertinib" [Supplementary Concept])

14524

#7 #3 AND #4 AND #5 AND #6 Filters: Publication date from 0001/01/01-2023/11/03 **863**

2. Search strategy on Cochrane library

#1 MeSH descriptor: [Carcinoma, Non-Small-Cell Lung] explode all trees **5892**

#2 (Carcinoma, Non Small Cell Lung OR Carcinomas, Non-Small-Cell Lung OR Lung Carcinoma, Non-Small-Cell OR Lung Carcinomas, Non-Small-Cell OR Non-Small-Cell Lung Carcinomas OR Non-Small-Cell Lung Carcinoma OR Non Small Cell Lung Carcinoma OR Carcinoma, Non-Small Cell Lung OR Non-Small Cell Lung Carcinoma OR Non-Small Cell Lung Cancer OR Nonsmall Cell Lung Cancer):ti,ab,kw **16329**

#3 #1 OR #2 **16329**

#4 (epidermal growth factor receptor OR EGFR):ti,ab,kw **16365**

#5 MeSH descriptor: [Randomized Controlled Trial] explode all trees **25729**

#6 (Randomized OR Randomised OR RCT OR RCTs OR control group OR control groups OR double blind OR placebo*):ti,ab,kw **1534085**

#7 #5 OR #6 **1534085**

#8 MeSH descriptor: [Gefitinib] explode all trees **378**

#9 MeSH descriptor: [Erlotinib Hydrochloride] explode all trees **649**

#10 MeSH descriptor: [Afatinib] explode all trees **90**

#11 (Gefitinib OR Iressa OR ZD1839 OR ZD 1839 OR Erlotinib Hydrochloride OR Hydrochloride, Erlotinib OR Erlotinib HCl OR HCl, Erlotinib OR OSI-774 OR OSI 774 OR OSI774 OR CP 358774 OR 358774, CP OR CP 358,774 OR 358,774, CP OR CP-358,774 OR CP358,774 OR CP-358774 OR CP358774 OR 11C-erlotinib OR 11C erlotinib OR Erlotinib OR Tarceva OR icotinib OR Afatinib OR BIBW 2992 MA2 OR BIBW-2992MA2 OR BIBW 2992MA2 OR BIBW2992 MA2 OR Afatinib Maleate OR BIBW 2992 OR BIBW2992 OR BIBW-2992 OR Gilotrif OR Afatinib Dimaleate OR dacomitinib OR Vizimpro OR PF 00299804 OR PF00299804 OR PF-00299804 OR osimertinib OR mereletinib OR osimertinib mesylate OR osimertinib mesilate OR mereletinib mesilate OR AZD9291 mesylate OR mereletinib mesylate OR AZD-9291 mesylate OR AZD9291 OR AZD-9291 OR Tagrisso OR aumolertinib OR almonertinib OR HS-10296 OR aflutinib OR AST2818 OR furmonertinib mesylate OR furmonertinib OR Ivesa OR Befotertinib OR amivantamab-vmjw OR amivantamab OR JNJ-61186372 OR JNJ 61186372 OR CNTO-4424 OR Rybrevant OR lazertinib OR Leclaza):ti,ab,kw **3447**

#12 #8 OR #9 OR #10 OR #11 **3447**

#13 #3 AND #4 AND #7 AND #12 with Cochrane Library publication date from Jan 0001 to November 2023 **1391**

3. Search strategy on Embase

#1 'non small cell lung cancer'/exp **218447**

#2 'carcinoma, non small cell lung':ti,ab,kw OR 'carcinomas, non-small-cell lung':ti,ab,kw OR 'lung carcinoma, non-small-cell':ti,ab,kw OR 'lung carcinomas, non-small-cell':ti,ab,kw OR 'non-small-cell lung carcinomas':ti,ab,kw OR 'non-small-cell lung carcinoma':ti,ab,kw OR 'non small cell lung carcinoma':ti,ab,kw OR 'carcinoma, non-small cell lung':ti,ab,kw OR 'non-small cell lung carcinoma':ti,ab,kw OR 'non-small cell lung cancer':ti,ab,kw OR 'nonsmall cell lung cancer':ti,ab,kw **136052**

#3 #1 OR #2 **230615**

#4 'epidermal growth factor receptor':ti,ab,kw OR 'EGFR':ti,ab,kw **187414**

#5 'randomized controlled trial'/exp OR 'controlled trial, randomized':ti,ab,kw OR randomised:ti,ab,kw OR 'randomised controlled study':ti,ab,kw OR 'randomised controlled trial':ti,ab,kw OR 'randomized controlled study':ti,ab,kw OR 'trial, randomized controlled':ti,ab,kw OR rct:ti,ab,kw OR rcts:ti,ab,kw OR 'control group':ti,ab,kw OR 'control groups':ti,ab,kw OR 'controlled clinical trial':ti,ab,kw OR 'crossover procedure':ti,ab,kw OR 'cross over study':ti,ab,kw OR 'cross over studies':ti,ab,kw OR 'double blind procedure':ti,ab,kw OR 'double blind':ti,ab,kw OR placebo:ti,ab,kw OR placebo*:ti,ab,kw OR volunteer*:ti,ab,kw OR single*:ti,ab,kw OR double*:ti,ab,kw **5027004**

#6 'iressa':ti,ab,kw OR 'zd1839':ti,ab,kw OR 'zd 1839':ti,ab,kw OR 'hydrochloride, erlotinib':ti,ab,kw OR 'erlotinib hcl':ti,ab,kw OR 'hcl, erlotinib':ti,ab,kw OR 'osi-774':ti,ab,kw OR 'osi 774':ti,ab,kw OR 'osi774':ti,ab,kw OR 'cp 358774':ti,ab,kw OR '358774, cp':ti,ab,kw OR 'cp-358,774':ti,ab,kw OR 'cp358,774':ti,ab,kw OR 'cp-358774':ti,ab,kw OR 'cp358774':ti,ab,kw OR '11c-erlotinib':ti,ab,kw OR '11c erlotinib':ti,ab,kw OR 'erlotinib':ti,ab,kw OR 'tarceva':ti,ab,kw OR 'bibw-2992-ma2':ti,ab,kw OR 'bibw 2992 ma2':ti,ab,kw OR 'bibw-2992ma2':ti,ab,kw OR 'bibw 2992ma2':ti,ab,kw OR 'bibw2992 ma2':ti,ab,kw OR 'afatinib maleate':ti,ab,kw OR 'bibw 2992':ti,ab,kw OR 'bibw2992':ti,ab,kw OR

'bibw-2992':ti,ab,kw OR 'gilotrif':ti,ab,kw OR 'afatinib dimaleate':ti,ab,kw OR 'vizimpro':ti,ab,kw
OR 'pf 00299804':ti,ab,kw OR 'pf00299804':ti,ab,kw OR 'pf-00299804':ti,ab,kw OR 'or
mereletinib':ti,ab,kw OR 'osimertinib mesylate':ti,ab,kw OR 'osimertinib mesilate':ti,ab,kw OR
'mereletinib mesilate':ti,ab,kw OR 'azd9291 mesylate':ti,ab,kw OR 'mereletinib mesylate':ti,ab,kw
OR 'azd-9291 mesylate':ti,ab,kw OR 'azd9291':ti,ab,kw OR 'azd-9291':ti,ab,kw OR
'tagrisso':ti,ab,kw OR 'almonertinib':ti,ab,kw OR 'hs-10296':ti,ab,kw OR 'ast2818':ti,ab,kw OR
'furmonertinib mesylate':ti,ab,kw OR 'furmonertinib':ti,ab,kw OR 'ivesa':ti,ab,kw OR
'befotertinib':ti,ab,kw OR 'amivantamab':ti,ab,kw OR 'jnj-61186372':ti,ab,kw OR 'jnj
61186372':ti,ab,kw OR 'cnto-4424':ti,ab,kw OR 'rybrevant':ti,ab,kw OR 'leclaza':ti,ab,kw OR
'gefitinib':ti,ab,kw OR 'erlotinib hydrochloride':ti,ab,kw OR 'icotinib':ti,ab,kw OR
'afatinib':ti,ab,kw OR 'dacomitinib':ti,ab,kw OR 'osimertinib':ti,ab,kw OR 'aumolertinib':ti,ab,kw
OR 'aflutinib':ti,ab,kw OR 'amivantamab-vmjw':ti,ab,kw OR 'lazertinib':ti,ab,kw **29100**
#7 #3 AND #4 AND #5 AND #6 AND [1-1-0001]/sd NOT [3-11-2023]/sd **3559**

Table S3. Comparisons of the Fit of Consistency and Inconsistency Models Using Deviance Information Criteria (DIC).

		Model		
		Consistency Fixed	Consistency Random	Inconsistency
Overall	Progression-free survival	117.25462	71.32317	71.88841
	Overall survival	46.87692	48.35877	51.47585
	Objective response rate	129.95835	130.55742	132.98995
	Grade ≥ 3 adverse events	135.78081	114.96709	115.50497
19DEL	Progression-free survival	59.29309	57.46160	58.85661
	Overall survival	22.230762	22.99249	24.30008
21L858R	Progression-free survival	43.92971	45.75006	47.93766
	Overall survival	17.550517	19.369055	21.90787
Male	Progression-free survival	55.74423	53.56414	55.31173
	Overall survival	18.93698	20.494586	22.98396
Female	Progression-free survival	51.10772	52.28284	54.52578
	Overall survival	18.100692	19.912399	22.96778
Non-smoker	Progression-free survival	49.40125	49.81073	51.34984
	Overall survival	20.948865	21.918355	23.18855
Smoker	Progression-free survival	49.87774	48.4234	49.19522
	Overall survival	22.108227	22.91288	24.21918
Age ≥ 65	Progression-free survival	35.18749	36.9464	38.82459
	Overall survival	20.332206	18.640077	17.972138
Age < 65	Progression-free survival	47.50645	42.2619	42.35136
	Overall survival	16.207862	16.868937	17.962848
ECOG PS=0	Progression-free survival	38.47077	39.6923	40.95593
	Overall survival	13.928017	14.268717	14.422088
ECOG PS=1	Progression-free survival	35.04032	36.60361	38.64442
	Overall survival	15.416627	15.497311	15.592
Brain metastasis	Progression-free survival	26.83905	27.83538	27.91802
	Overall survival	7.962705	7.944573	8.096517
Brain no-metastasis	Progression-free survival	28.14355	29.18085	29.05254
	Overall survival	8.015301	7.966503	7.957769
Asian	Progression-free survival	67.57981	60.34636	61.83232
	Overall survival	36.06461	37.34598	41.52915
Non-asian	Progression-free survival	20.320857	21.34451	21.33662
	Overall survival	14.62526	14.02081	14.050241
The sensitive analysis by excluding phase II trials				
Overall	Progression-free survival	51.73777	49.46144	50.04028
	Overall survival	37.32662	37.99987	39.31869
	Objective response rate	96.41661	96.36098	97.4976
	Grade ≥ 3 adverse events	111.98343	91.78137	92.12087

19DEL	Progression-free survival	41.49552	41.85155	42.34242
	Overall survival	18.16787	18.654994	19.606746
21L858R	Progression-free survival	35.28282	36.96944	37.8075
	Overall survival	14.237032	15.871157	17.322959

Table S4. Node-splitting Analysis of Inconsistency.

Nodes	Direct effect	Indirect effect	Overall	P
Progression-free survival				
F_TKI vs AFA	1.4 (0.48, 3.9)	1.0 (0.43, 2.3)	1.1 (0.60, 2.1)	0.62695
PB vs AFA	1.7 (0.62, 4.8)	3.0 (1.1, 8.6)	2.3 (1.1, 4.6)	0.41488
PB vs F_TKI	2.1 (0.97, 4.7)	1.3 (0.35, 4.8)	2.0 (1.1, 3.7)	0.49855
PF vs F_TKI	2.8 (1.8, 4.4)	3.3 (0.87, 13.)	2.9 (1.9, 4.3)	0.80619
PB vs GEF_PB	6.2 (2., 20.)	2.7 (1.0, 7.4)	4. (1.9, 8.2)	0.25857
Overall survival				
F_TKI vs AFA	1.2 (0.82, 1.7)	1.1 (0.81, 1.5)	1.1 (0.90, 1.4)	0.77444
PB vs AFA	1.1 (0.79, 1.6)	1.2 (0.82, 1.8)	1.2 (0.91, 1.5)	0.77286
PF vs AFA	1.1 (0.75, 1.5)	1.1 (0.78, 1.5)	1.1 (0.86, 1.4)	0.93348
PB vs F_TKI	1.0 (0.73, 1.4)	1.0 (0.63, 1.6)	1.0 (0.82, 1.3)	0.96255
PF vs F_TKI	0.97 (0.81, 1.2)	0.96 (0.61, 1.5)	0.96 (0.83, 1.1)	0.98651
PB vs GEF_PB	2.2 (1.1, 4.4)	1.5 (1.0, 2.2)	1.6 (1.2, 2.2)	0.33044
Objective response rate				
F_TKI vs AFA	0.54 (0.28, 1.1)	0.76 (0.42, 1.4)	0.65 (0.43, 1.0)	0.42115
PB vs AFA	0.23 (0.11, 0.45)	0.16 (0.075, 0.32)	0.19 (0.11, 0.32)	0.448875
PF vs AFA	0.14 (0.071, 0.30)	0.13 (0.069, 0.25)	0.14 (0.088, 0.22)	0.857275
PB vs F_TKI	0.26 (0.14, 0.47)	0.38 (0.15, 0.91)	0.29 (0.18, 0.46)	0.49315
PF vs F_TKI	0.21 (0.15, 0.29)	0.23 (0.091, 0.55)	0.21 (0.15, 0.28)	0.874575
PB vs GEF_PB	0.095 (0.028, 0.29)	0.13 (0.064, 0.26)	0.12 (0.065, 0.21)	0.66295
Grade ≥ 3 adverse events				
F_TKI vs AFA	0.83 (0.20, 3.4)	0.51 (0.15, 1.8)	0.64 (0.26, 1.5)	0.57115
PB vs AFA	0.90 (0.24, 3.3)	2.5 (0.45, 14.)	1.3 (0.46, 3.8)	0.31265
PF vs AFA	2.7 (0.63, 11.)	2.2 (0.57, 8.6)	2.4 (0.98, 6.0)	0.82375
PB vs F_TKI	3.2 (0.79, 13.)	1.2 (0.22, 6.)	2.1 (0.72, 6.1)	0.3106
PF vs F_TKI	3.7 (2., 7.2)	4.6 (0.75, 29.)	3.8 (2.2, 6.8)	0.807725
Progression-free survival for exon 19 deletion subpopulation				
F_TKI vs AFA	1.3 (0.66, 2.6)	1.7 (0.89, 3.3)	1.5 (0.96, 2.4)	0.5112
PB vs AFA	3.6 (1.7, 7.4)	2.0 (0.81, 5.)	2.9 (1.6, 5.)	0.28539
PF vs AFA	5.0 (2.3, 11.)	5.4 (2.8, 12.)	5.2 (3.3, 8.7)	0.86699
PB vs F_TKI	1.5 (0.71, 3.1)	2.6 (1.1, 6.4)	1.9 (1.1, 3.3)	0.28194
PF vs F_TKI	3.5 (2.5, 5.2)	3.2 (1.2, 8.6)	3.5 (2.5, 4.9)	0.86283
Progression-free survival for Leu858Arg subpopulation				
F_TKI vs AFA	1.4 (0.87, 2.3)	1.2 (0.73, 2.)	1.3 (0.93, 1.8)	0.63727
PB vs AFA	1.4 (0.80, 2.4)	2.3 (1.2, 4.3)	1.7 (1.1, 2.6)	0.22725
PF vs AFA	3.1 (1.8, 5.6)	2.6 (1.6, 4.3)	2.8 (1.9, 4.0)	0.59256
PB vs F_TKI	1.6 (0.91, 2.7)	0.95 (0.49, 1.8)	1.3 (0.84, 1.9)	0.23566
PF vs F_TKI	2.1 (1.6, 2.8)	2.5 (1.2, 5.2)	2.1 (1.6, 2.8)	0.61758
Overall survival for exon 19 deletion subpopulation				
F_TKI vs AFA	1.2 (0.62, 2.3)	1.7 (0.93, 3.2)	1.4 (0.95, 2.2)	0.35959

PB vs AFA	1.8 (0.89, 3.8)	1.7 (0.69, 4.3)	1.8 (1.1, 3.0)	0.86515
PF vs AFA	1.6 (0.79, 3.1)	1.1 (0.55, 2.2)	1.3 (0.83, 2.1)	0.39402
PB vs F_TKI	1.2 (0.58, 2.5)	1.3 (0.52, 3.2)	1.2 (0.74, 2.1)	0.88326
PF vs F_TKI	0.84 (0.55, 1.3)	1.2 (0.51, 2.8)	0.92 (0.62, 1.3)	0.37903
Overall survival for Leu858Arg subpopulation				
F_TKI vs AFA	1.1 (0.63, 1.9)	0.85 (0.50, 1.4)	0.96 (0.67, 1.4)	0.46924
PB vs AFA	0.77 (0.41, 1.5)	0.87 (0.41, 1.9)	0.81 (0.52, 1.3)	0.78677
PF vs AFA	0.82 (0.46, 1.4)	1.0 (0.56, 1.8)	0.91 (0.61, 1.3)	0.59185
PB vs F_TKI	0.87 (0.48, 1.6)	0.77 (0.36, 1.7)	0.83 (0.54, 1.3)	0.77989
PF vs F_TKI	0.98 (0.67, 1.4)	0.80 (0.38, 1.7)	0.94 (0.68, 1.3)	0.57831
Progression-free survival for age < 65				
F_TKI vs AFA	1.5 (0.32, 6.6)	0.96 (0.15, 6.3)	1.3 (0.47, 3.3)	0.60422
PF vs AFA	3.3 (0.75, 15.)	5.1 (0.79, 32.)	3.9 (1.5, 10.)	0.59987
PF vs F_TKI	3.5 (1.2, 10.)	2.3 (0.28, 18.)	3.1 (1.4, 7.1)	0.59828
Progression-free survival for age ≥ 65				
F_TKI vs AFA	1.2 (0.47, 3.)	1.5 (0.35, 5.8)	1.2 (0.67, 2.3)	0.74446
PF vs AFA	6.4 (2.0, 20.)	4.9 (1.6, 16.)	5.4 (2.8, 11.)	0.71654
PF vs F_TKI	4.2 (2.1, 9.3)	5.3 (1.2, 23.)	4.4 (2.5, 8.1)	0.72496
Overall survival for age < 65				
F_TKI vs AFA	1.5 (0.83, 2.8)	1.3 (0.55, 3.1)	1.4 (0.90, 2.3)	0.73827
PF vs AFA	1.1 (0.64, 2.1)	1.3 (0.55, 3.2)	1.2 (0.76, 1.9)	0.73332
PF vs F_TKI	0.89 (0.47, 1.7)	0.76 (0.33, 1.8)	0.83 (0.52, 1.3)	0.74127
Overall survival for age ≥ 65				
F_TKI vs AFA	0.82 (0.39, 1.7)	2.5 (0.69, 9.1)	1.0 (0.55, 2.2)	0.12753
PF vs AFA	1.7 (0.71, 3.9)	0.54 (0.16, 1.8)	1.1 (0.55, 2.4)	0.12108
PF vs F_TKI	0.66 (0.25, 1.7)	2.0 (0.66, 6.2)	1.1 (0.49, 2.3)	0.12757
Progression-free survival for Asian				
F_TKI vs AFA	1.3 (0.66, 2.6)	1.1 (0.60, 1.8)	1.2 (0.77, 1.7)	0.58561
PB vs AFA	1.9 (0.96, 3.6)	2.9 (1.5, 5.7)	2.3 (1.5, 3.7)	0.29116
PF vs AFA	3.6 (1.8, 7.1)	3.0 (1.6, 5.7)	3.3 (2.1, 5.0)	0.69526
PB vs F_TKI	2.0 (1.3, 3.4)	1.4 (0.64, 3.2)	2. (1.4, 3.0)	0.3976
PF vs F_TKI	2.8 (2.1, 3.9)	3.2 (1.4, 7.9)	2.8 (2.2, 3.8)	0.69625
PB vs GEF_PB	6.3 (3., 13.)	2.8 (1.6, 4.9)	3.9 (2.5, 6.4)	0.08634
Overall survival for Asian				
F_TKI vs AFA	1.1 (0.69, 1.6)	1.1 (0.80, 1.6)	1.1 (0.85, 1.4)	0.81891
PB vs AFA	1.2 (0.79, 1.9)	1.2 (0.76, 1.8)	1.2 (0.89, 1.6)	0.85008
PF vs AFA	1.1 (0.74, 1.6)	1.1 (0.71, 1.6)	1.1 (0.82, 1.4)	0.94824
PB vs F_TKI	1.0 (0.73, 1.4)	1.1 (0.65, 1.9)	1.1 (0.84, 1.4)	0.7331
PF vs F_TKI	0.97 (0.80, 1.2)	0.99 (0.60, 1.7)	0.97 (0.82, 1.2)	0.91949
Progression-free survival for ECOG PS=0				
F_TKI vs AFA	1.1 (0.38, 3.3)	1.2 (0.22, 6.2)	1.1 (0.53, 2.5)	0.95736

PF vs AFA	4.6 (1.5, 14.)	4.4 (0.87, 22.)	4.5 (2.0, 9.9)	0.9445
PF vs F_TKI	3.9 (1.1, 13.)	4.1 (0.84, 20.)	3.9 (1.7, 9.0)	0.95508
Progression-free survival for ECOG PS=1				
F_TKI vs AFA	1.4 (0.73, 2.8)	1.3 (0.45, 3.6)	1.4 (0.87, 2.2)	0.84835
PF vs AFA	3.4 (1.7, 6.9)	3.8 (1.4, 10.)	3.6 (2.2, 5.7)	0.84096
PF vs F_TKI	2.7 (1.2, 5.9)	2.4 (0.92, 6.5)	2.6 (1.6, 4.3)	0.84223
Progression-free survival for male				
F_TKI vs AFA	1.1 (0.49, 2.7)	1.2 (0.53, 2.8)	1.2 (0.68, 2.0)	0.91081
PB vs AFA	1.6 (0.67, 4.)	1.4 (0.44, 4.5)	1.6 (0.80, 3.0)	0.82814
PF vs AFA	2.8 (1.1, 7.)	2.9 (1.2, 7.)	2.8 (1.6, 5.1)	0.94109
PB vs F_TKI	1.2 (0.47, 3.3)	1.4 (0.48, 4.4)	1.3 (0.68, 2.6)	0.82486
PF vs F_TKI	2.5 (1.5, 4.0)	2.3 (0.73, 7.4)	2.4 (1.6, 3.8)	0.94435
Progression-free survival for female				
F_TKI vs AFA	1.5 (0.91, 2.6)	1.2 (0.71, 1.9)	1.3 (0.95, 1.9)	0.41683
PB vs AFA	1.9 (1.1, 3.2)	2.4 (1.1, 4.7)	2.0 (1.3, 3.0)	0.54756
PF vs AFA	4.2 (2.3, 7.4)	4.7 (2.7, 8.5)	4.4 (3.1, 6.5)	0.72213
PB vs F_TKI	1.7 (0.94, 2.9)	1.3 (0.67, 2.6)	1.5 (1.0, 2.3)	0.54784
PF vs F_TKI	3.4 (2.5, 4.8)	3. (1.4, 6.2)	3.3 (2.5, 4.4)	0.71256
Overall survival for male				
F_TKI vs AFA	1.3 (0.64, 2.5)	1.5 (0.77, 2.8)	1.4 (0.88, 2.1)	0.70484
PB vs AFA	1.4 (0.67, 2.8)	1.7 (0.68, 4.2)	1.5 (0.88, 2.5)	0.68535
PF vs AFA	1.4 (0.74, 2.8)	1.0 (0.50, 2.0)	1.2 (0.76, 1.9)	0.43424
PB vs F_TKI	1.2 (0.56, 2.5)	0.98 (0.40, 2.3)	1.1 (0.64, 1.9)	0.69839
PF vs F_TKI	0.83 (0.53, 1.3)	1.2 (0.50, 2.7)	0.90 (0.60, 1.3)	0.44095
Overall survival for female				
F_TKI vs AFA	1.1 (0.69, 1.9)	1.2 (0.79, 2.)	1.2 (0.88, 1.6)	0.75654
PB vs AFA	1.3 (0.74, 2.1)	1.1 (0.59, 2.1)	1.2 (0.83, 1.8)	0.76091
PF vs AFA	1.1 (0.69, 1.9)	1.1 (0.66, 1.9)	1.1 (0.81, 1.6)	0.94844
PB vs F_TKI	0.96 (0.58, 1.6)	1.1 (0.57, 2.1)	1.0 (0.69, 1.5)	0.75849
PF vs F_TKI	0.94 (0.67, 1.3)	0.95 (0.50, 1.8)	0.94 (0.71, 1.2)	0.97077
Progression-free survival for smoker				
F_TKI vs AFA	2.1 (0.80, 5.4)	0.81 (0.32, 2.1)	1.3 (0.63, 2.6)	0.13579
PB vs AFA	0.95 (0.32, 2.9)	1.9 (0.44, 7.8)	1.2 (0.52, 2.9)	0.40097
PF vs AFA	2.2 (0.68, 7.)	4.0 (1.4, 12.)	3.1 (1.4, 6.4)	0.40025
PB vs F_TKI	1.3 (0.38, 4.2)	0.64 (0.17, 2.6)	0.93 (0.40, 2.3)	0.41217
PF vs F_TKI	2.6 (1.4, 4.8)	1.4 (0.32, 6.3)	2.3 (1.4, 4.1)	0.40391
Progression-free survival for non-smoker				
F_TKI vs AFA	1.3 (0.59, 2.6)	1.2 (0.61, 2.4)	1.2 (0.81, 1.9)	0.9598
PB vs AFA	2.1 (1.0, 4.5)	2. (0.76, 5.)	2.1 (1.2, 3.4)	0.86866
PF vs AFA	4.1 (1.9, 9.1)	4.5 (2.2, 9.8)	4.3 (2.8, 6.9)	0.83697
PB vs F_TKI	1.6 (0.76, 3.4)	1.7 (0.70, 4.5)	1.7 (1.0, 2.7)	0.86567

PF vs F_TKI	3.6 (2.4, 5.5)	3.3 (1.2, 8.6)	3.5 (2.6, 4.9)	0.83721
Overall survival for smoker				
F_TKI vs AFA	1.6 (0.64, 3.9)	0.83 (0.35, 2.)	1.2 (0.60, 2.1)	0.25972
PB vs AFA	1.1 (0.39, 3.0)	1.5 (0.39, 5.2)	1.2 (0.58, 2.6)	0.68945
PF vs AFA	0.77 (0.28, 2.2)	1.3 (0.50, 3.6)	1.0 (0.52, 2.1)	0.3936
PB vs F_TKI	1.2 (0.42, 3.4)	0.91 (0.25, 3.4)	1.1 (0.52, 2.3)	0.69913
PF vs F_TKI	1.0 (0.56, 1.8)	0.58 (0.16, 2.2)	0.91 (0.55, 1.5)	0.39485
Overall survival for non-smoker				
F_TKI vs AFA	1.1 (0.68, 1.7)	1.5 (0.98, 2.3)	1.3 (0.94, 1.8)	0.27187
PB vs AFA	1.3 (0.77, 2.3)	1.3 (0.69, 2.6)	1.3 (0.90, 2.)	0.97571
PF vs AFA	1.4 (0.89, 2.2)	0.97 (0.60, 1.6)	1.2 (0.85, 1.7)	0.24844
PB vs F_TKI	1.0 (0.61, 1.7)	1.0 (0.53, 2.)	1.0 (0.70, 1.5)	0.9834
PF vs F_TKI	0.85 (0.62, 1.2)	1.2 (0.67, 2.2)	0.92 (0.69, 1.2)	0.25182

Significant values ($P \leq 0.05$) are underlined, indicating a significant inconsistency between the direct effect and indirect effects.

(AUM=aumolertinib; OSI=osimertinib; DAC=dacomitinib; AFA=afatinib; ERL=erlotinib; GEF=gefitinib; ICO=icotinib; F-TKIs=(GEF, ERL, ICO); BEV=bevacizumab; CET=cetuximab; APA=apatinib; BEV=bevacizumab; RAM=ramucirumab; GEF+P=gefitinib plus pemetrexed; PB=pemetrexed based chemotherapy; PF=pemetrexed free chemotherapy)

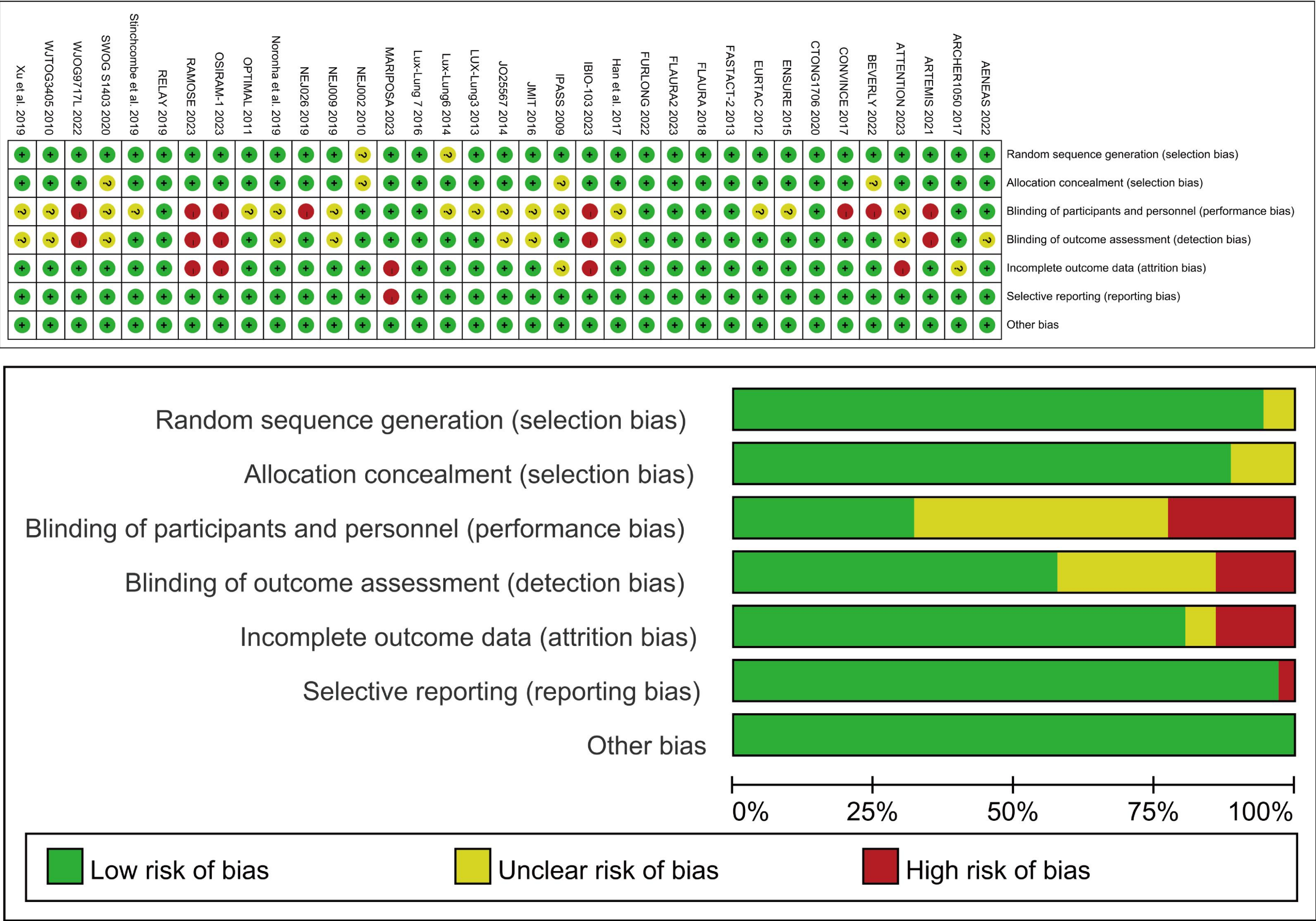


Figure S1. Summary of Results from Bias Risk Assessment of Studies Using the Cochrane Risk of Bias Tool.

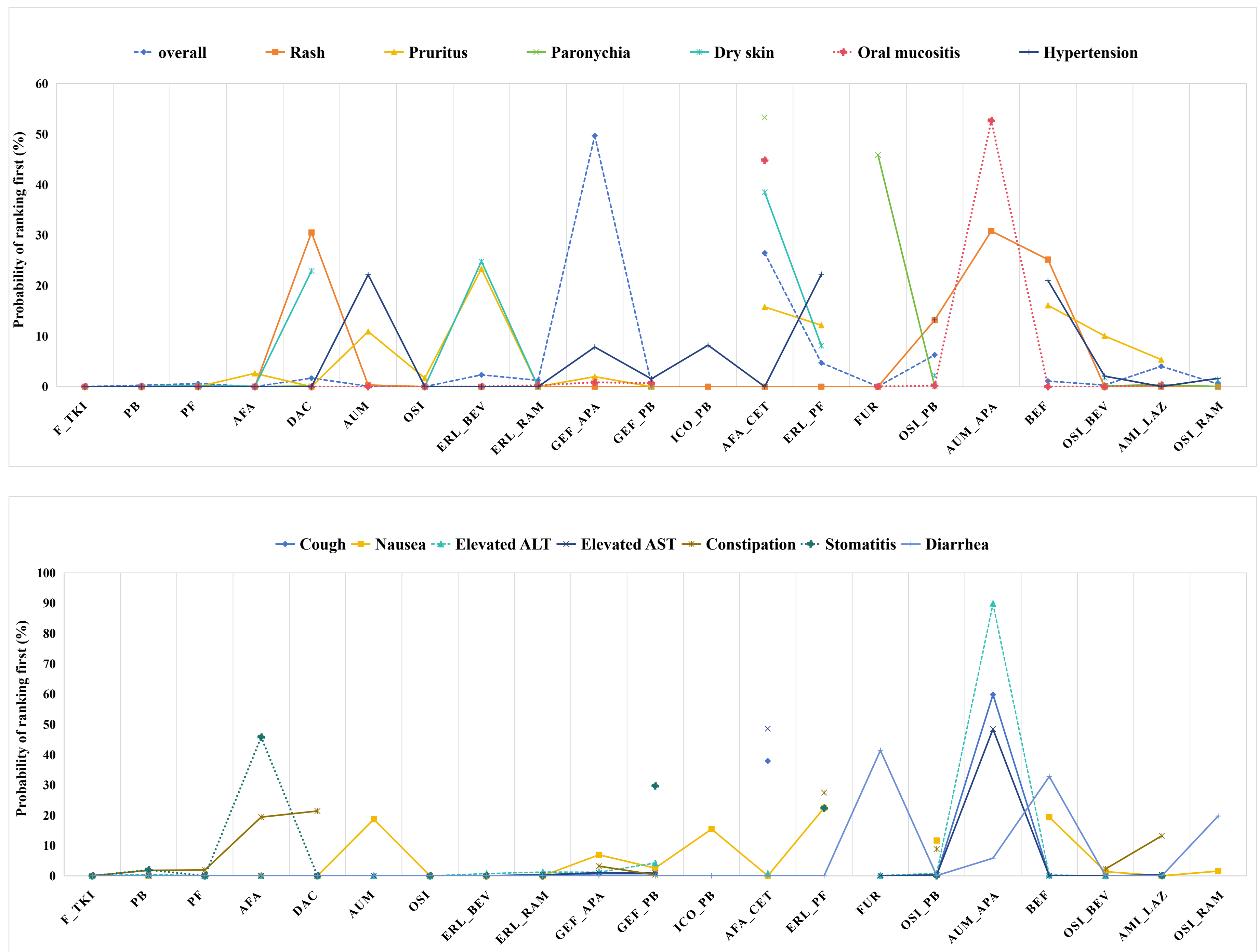


Figure S2. Relative toxicity of treatments on commonly reported specific grade 3 or higher adverse events for EGFR-TKIs.

		No. of studies	Sample size	PB	PF	F_TKI	AFA	DAC	AUM	OSI	FUR	BEF	GEF_APA	GEF_PB	ERL_BEV	ERL_RAM	ERL_PF	ICO_PB	AFA_CET	OSI_PB	OSI_BEV	OSI_RAM	AUM_APA	AMI_LAZ
Diarrhea	rash	34	10714	2.08	0.78	2.36	11.64	8.81	1.14	1.04	2.25	0.00	8.92	6.20	4.50	7.24	1.33	2.22	15.38	2.90	0.00	4.61	0.00	1.90
	Anemia	34	10637	0.69	0.72	4.84	12.48	4.41	0.00	0.87	0.00	1.10	3.82	5.08	19.06	0.90	5.31	3.33	26.92	0.36	0.00	1.97	2.08	14.96
	Fatigue	28	9293	2.78	9.98	1.07	0.54	0.88	0.93	1.29	0.56	2.20	NA	14.40	2.01	NA	11.50	0.00	1.28	19.93	1.64	3.23	NA	4.04
	Nausea	25	6871	12.50	3.04	1.09	1.96	2.20	NA	0.50	NA	0.00	1.27	5.00	2.54	NA	0.44	1.11	1.28	2.90	NA	3.23	NA	NA
	Neutropenia	24	8601	23.26	2.08	0.43	0.98	1.32	0.47	0.09	NA	0.55	0.64	0.60	0.32	0.90	0.44	4.44	2.56	1.45	0.00	0.00	NA	0.95
	Pruritus	23	6826	13.89	50.18	1.20	0.48	NA	1.52	2.02	0.56	NA	NA	17.80	0.00	NA	28.76	NA	NA	13.41	1.64	10.17	2.08	NA
	Paronychia	20	7774	0.40	0.11	0.44	0.42	0.44	0.00	0.26	NA	0.00	0.00	0.00	0.64	0.90	0.00	NA	3.85	NA	0.00	NA	NA	0.48
	Thrombocytopenia	20	7246	0.00	0.00	0.95	4.07	7.49	NA	0.70	0.56	NA	NA	0.00	0.64	4.07	NA	NA	5.13	0.72	6.56	1.97	NA	10.93
	Elevated ALT	20	5097	0.00	11.84	0.13	0.42	NA	1.52	1.13	1.12	8.79	4.46	9.89	NA	NA	14.16	0.00	NA	6.88	0.00	0.00	8.33	NA
	Leukopenia	19	6321	0.73	2.20	7.97	1.54	0.88	2.27	1.25	1.12	1.10	11.46	15.87	3.38	8.60	NA	NA	1.28	1.45	0.00	NA	2.08	4.99
	Vomiting	19	6249	5.90	26.43	0.79	0.72	NA	1.89	1.49	0.00	2.75	1.27	17.14	0.64	NA	7.08	12.22	1.28	3.26	1.64	NA	2.08	NA
	Decreased appetite	18	6928	17.34	4.22	0.46	1.43	0.88	0.00	0.00	NA	0.00	3.18	1.69	0.32	NA	1.33	0.00	NA	1.09	NA	NA	NA	NA
	Elevated AST	18	6645	14.11	2.08	1.12	1.75	3.08	0.93	1.32	NA	0.00	2.55	NA	1.60	2.71	0.44	0.00	NA	2.90	NA	NA	NA	0.95
	Stomatitis	18	6166	0.00	1.49	5.04	0.31	0.00	1.14	0.77	1.12	0.00	7.64	5.56	2.11	4.98	NA	NA	1.28	0.36	0.00	NA	2.08	3.09
	Dry skin	17	7058	0.90	0.09	0.49	6.37	3.52	NA	0.41	NA	NA	NA	2.03	0.87	1.81	0.00	NA	NA	0.36	NA	NA	NA	0.95
	constipation	17	6051	0.00	0.00	0.42	0.21	1.32	NA	0.15	NA	NA	NA	0.34	0.96	0.45	0.00	NA	3.85	0.00	0.00	0.00	NA	NA
	Hypertension	16	6453	0.00	0.09	0.05	0.00	0.00	NA	0.00	NA	NA	0.00	0.00	0.00	NA	0.00	NA	NA	0.36	0.00	NA	NA	0.00
	Hypokalemia	13	3264	NA	NA	6.46	NA	1.32	3.41	3.70	NA	NA	46.50	26.22	30.84	23.53	NA	NA	NA	NA	NA	19.74	6.25	NA
	Proteinuria	11	3339	3.65	7.96	1.34	2.27	4.85	1.87	NA	NA	NA	0.00	7.93	0.86	NA	NA	NA	5.13	NA	NA	NA	NA	NA
	Cough	11	2394	NA	NA	0.29	NA	NA	0.00	0.82	NA	0.00	17.83	NA	7.49	2.71	NA	NA	NA	NA	3.28	6.78	2.08	NA
	Blood bilirubin increased	10	3954	2.19	0.00	0.40	NA	0.00	NA	0.00	NA	NA	0.00	NA	0.00	0.45	0.00	NA	NA	NA	NA	0.00	NA	0.00
	Oral mucositis	10	3021	NA	NA	0.53	NA	NA	NA	NA	0.56	0.00	1.91	0.00	0.86	1.36	NA	1.11	NA	NA	NA	NA	NA	NA
	Pneumonitis	10	2648	NA	NA	0.18	4.71	0.00	0.00	0.82	0.00	0.55	NA	NA	2.11	NA	NA	0.00	7.69	NA	1.64	1.69	NA	NA
	Dyspnea	8	1701	NA	0.37	0.61	0.41	NA	0.00	1.64	NA	NA	NA	NA	NA	NA	NA	NA	2.56	NA	1.64	1.69	NA	NA
	Anorexia	7	2126	0.73	0.45	1.42	NA	2.20	NA	0.62	NA	NA	NA	NA	3.25	NA	0.44	NA	NA	NA	NA	0.00	NA	NA
	Chest pain	6	2077	0.00	2.72	2.34	NA	NA	NA	2.83	NA	NA	NA	0.95	1.25	NA	NA	NA	NA	NA	0.00	0.00	NA	NA
	Hyponatraemia	6	2015	0.73	0.45	0.13	NA	0.00	NA	NA	NA	0.00	NA	NA	0.42	NA	0.88	NA	NA	NA	NA	NA	NA	NA
	Back pain	6	1635	NA	3.54	6.28	1.26	NA	NA	0.00	NA	NA	NA	11.98	4.22	NA	NA	NA	NA	NA	NA	1.08	NA	NA
	Dermatitis acneiform	6	1617	0.00	NA	0.59	NA	0.00	NA	0.00	NA	NA	0.64	NA	0.64	NA	NA	NA	NA	NA	0.00	2.15	NA	NA
	Febrile neutropenia	5	2385	NA	0.00	4.09	NA	13.66	NA	0.00	NA	NA	NA	1.59	NA	14.93	0.88	NA	NA	NA	NA	NA	NA	8.08
	Hand-foot syndrome	4	1922	NA	2.98	0.10	NA	NA	NA	NA	NA	NA	NA	10.98	0.00	NA	NA	NA	NA	NA	NA	NA	NA	NA
	ILD	3	1081	NA	NA	0.00	0.63	0.88	NA	NA	NA	NA	3.18	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
		3	844	NA	NA	1.54	0.00	NA	NA	NA	NA	NA	NA	0.69	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Figure S3. Frequency toxicity profile in relation to the incidence (%) of each specific grade 3 or higher adverse events based on the population of each treatment we included. (NA=not available)

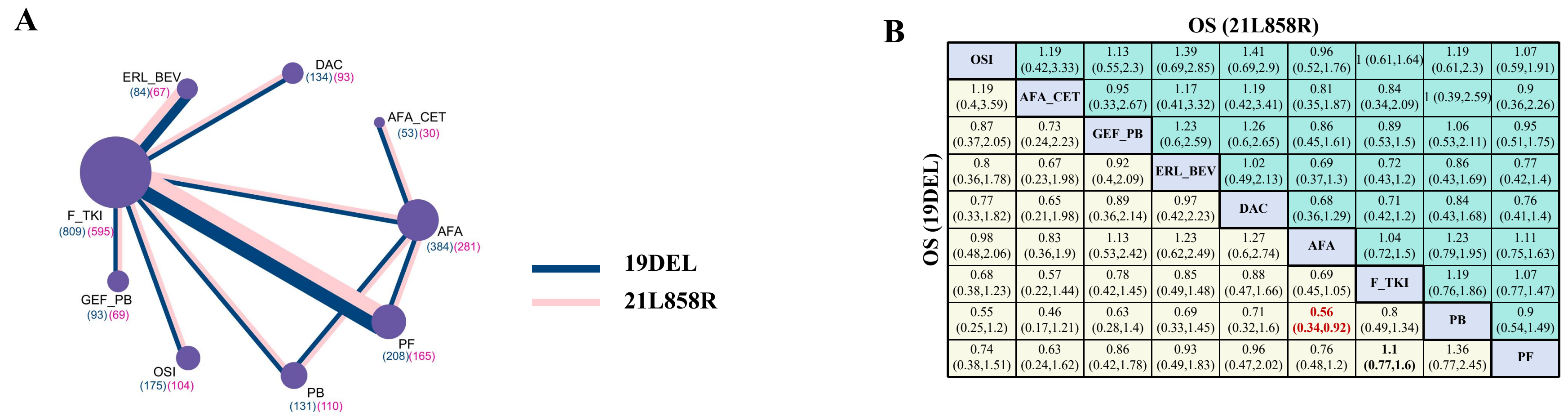


Figure S4. Network meta-analysis of comparisons of OS in EGFR mutated NSCLC based on EGFR mutation subtypes. **(A)** Network diagrams of comparisons on OS for patients with 19DEL and 21L858R. Each circular node represents a type of regimen and each line represents a type of head-to-head comparison. The size of the node and the thickness of the line are weighted according to the number of trials evaluating each regimen and direct comparison, respectively. The total number of patients in each regimen was shown in brackets. **(B)** Pooled HR (95% CI) for OS of patients with 19DEL (lower triangle) and 21L858R (upper triangle). Result in each cell is presented as HR (95% CI) for the comparison of row-defining regimen versus column-defining regimen. HR < 1 favor row-defining regimen. Significant results were bolded and highlighted in red.

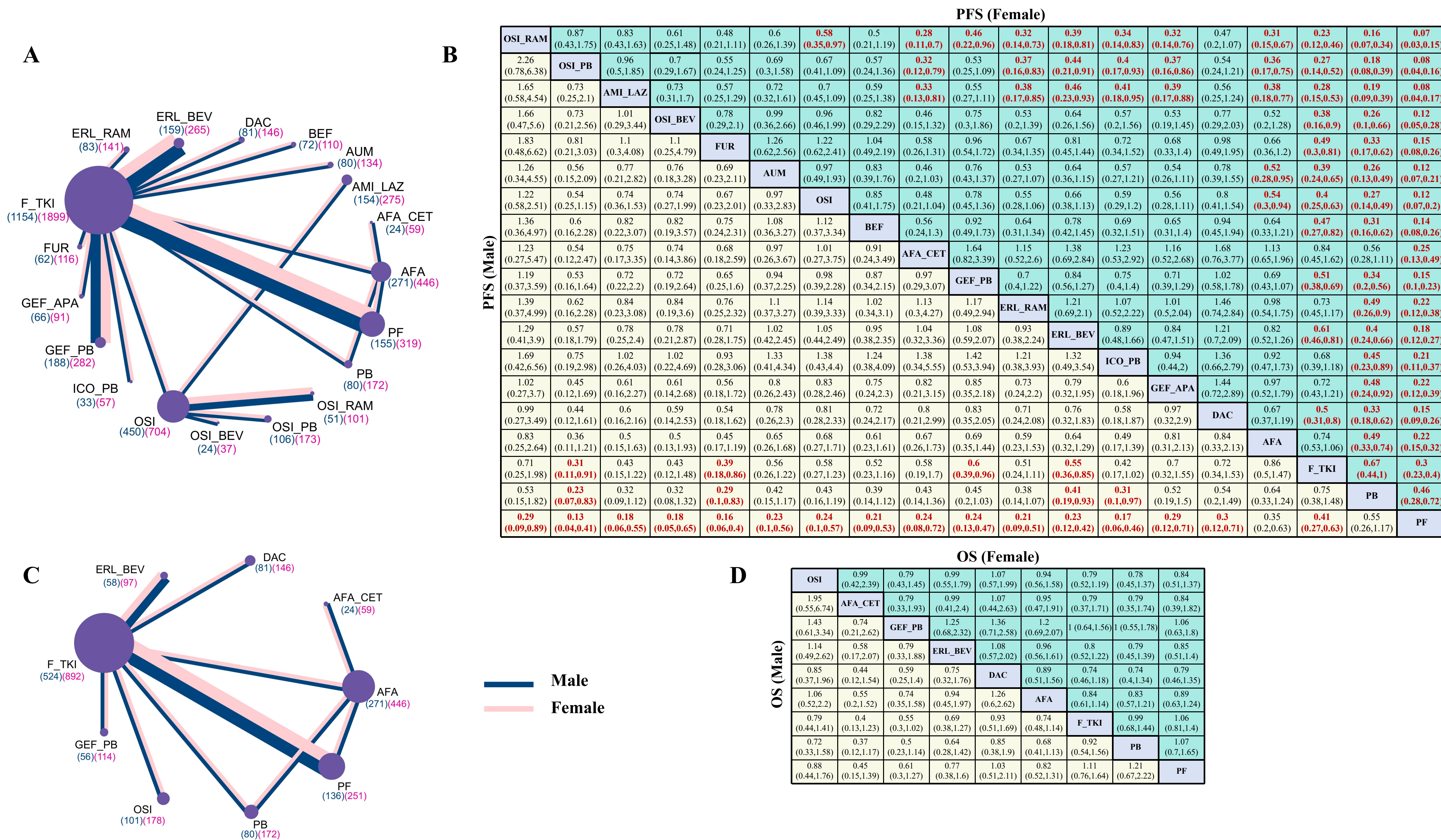


Figure S5. Network meta-analysis of comparisons of PFS and OS in EGFR mutated NSCLC based on sex. **(A and C)** Network diagrams of comparisons on PFS **(A)** and OS **(C)** for the male and female. Each circular node represents a type of regimen and each line represents a type of head-to-head comparison. The size of the node and the thickness of the line are weighted according to the number of trials evaluating each regimen and direct comparison, respectively. The total number of patients in each regimen was shown in brackets. **(B and D)** Pooled HR (95% CI) for PFS **(B)** and OS **(D)** of the male (lower triangle) and the female (upper triangle). Result in each cell is presented as HR (95% CI) for the comparison of row-defining regimen versus column-defining regimen. HR < 1 favor row-defining regimen. Significant results were bolded and highlighted in red.

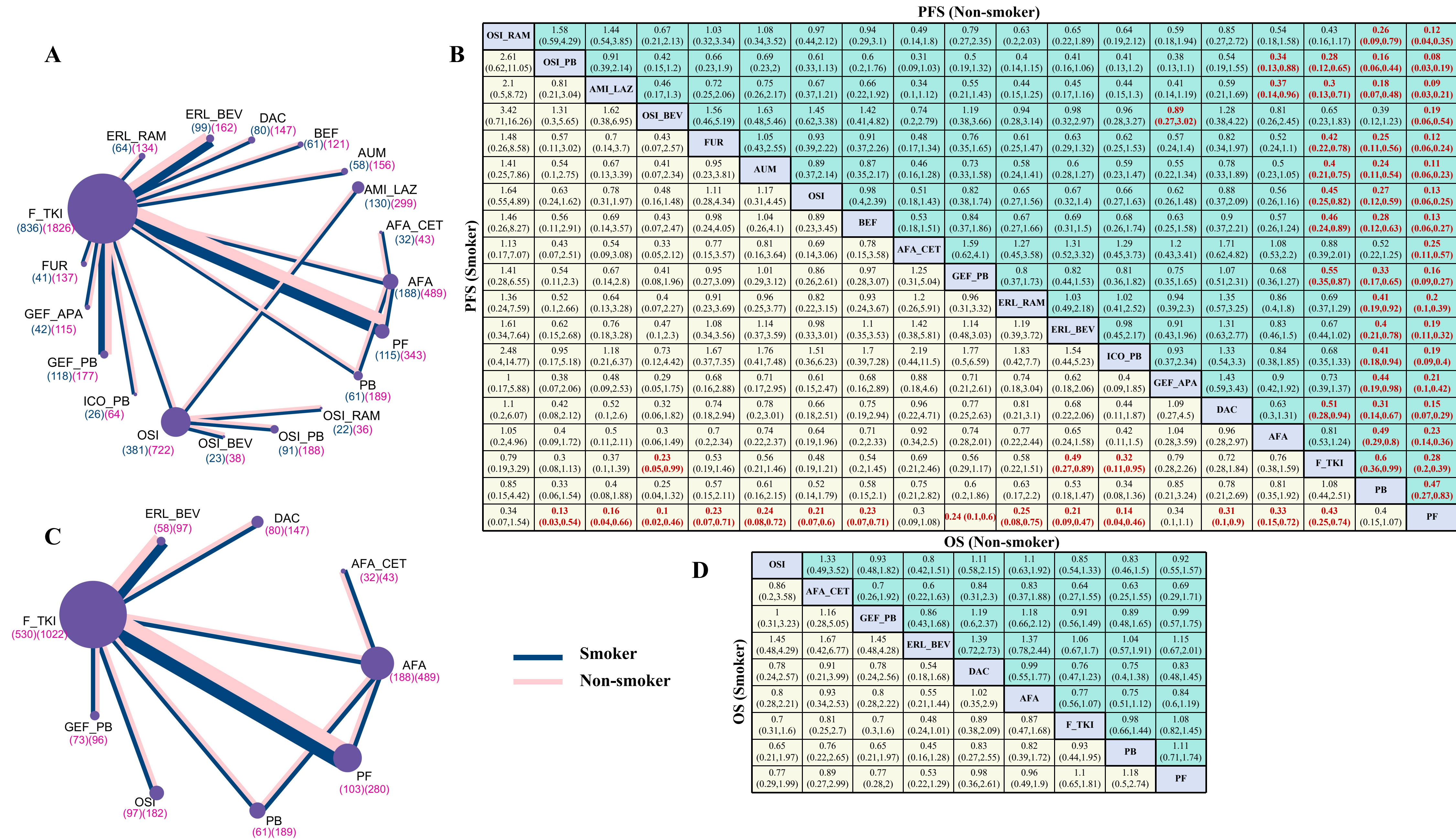
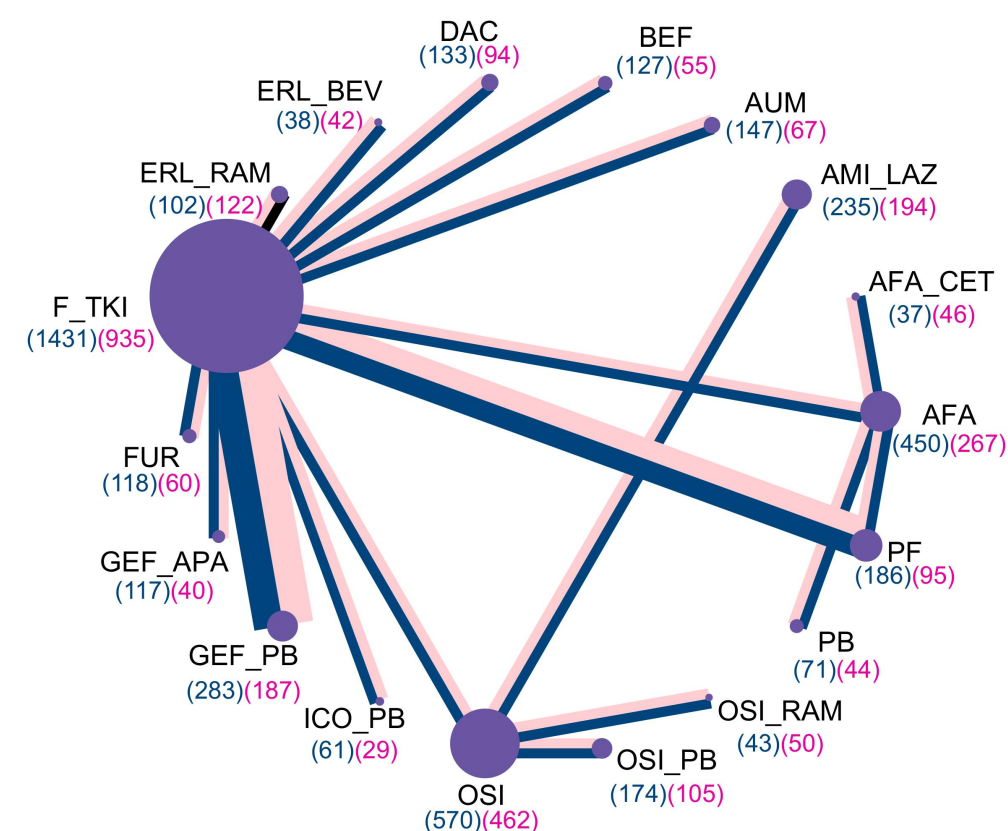
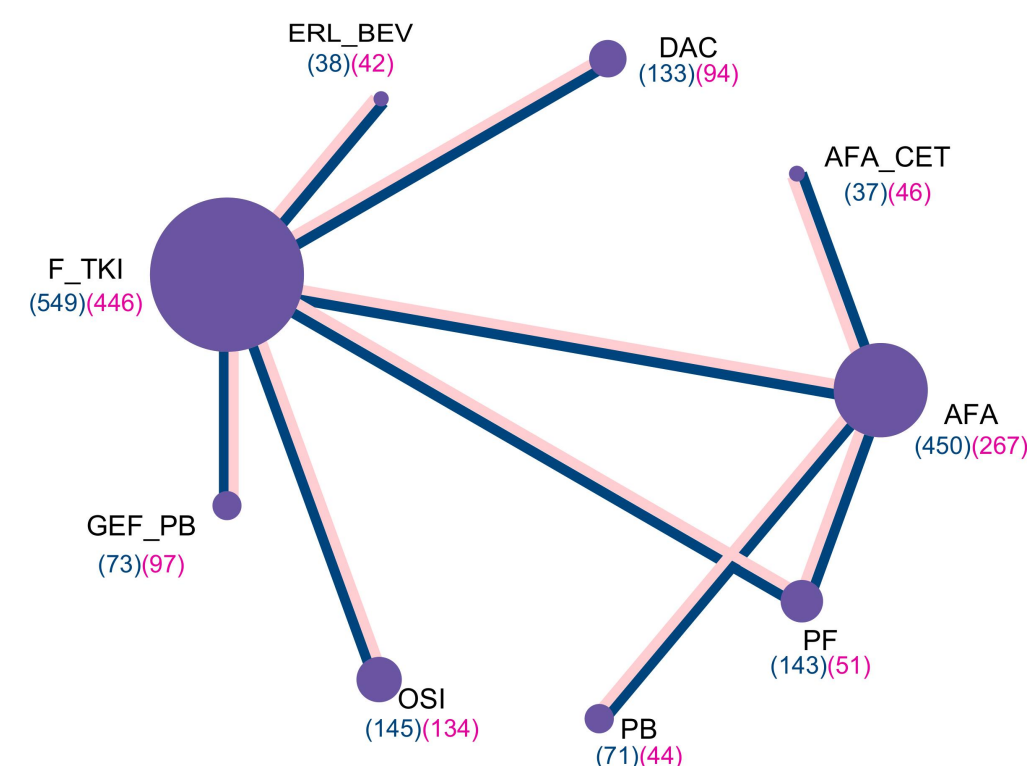


Figure S6. Network meta-analysis of comparisons of PFS and OS in EGFR mutated NSCLC based on smoking history. **(A and C)** Network diagrams of comparisons on PFS **(A)** and OS **(C)** for the smoker and non-smoker. Each circular node represents a type of regimen and each line represents a type of head-to-head comparison. The size of the node and the thickness of the line are weighted according to the number of trials evaluating each regimen and direct comparison, respectively. The total number of patients in each regimen was shown in brackets. **(B and D)** Pooled HR (95% CI) for PFS **(B)** and OS **(D)** of the smoker (lower triangle) and the non-smoker (upper triangle). Result in each cell is presented as HR (95% CI) for the comparison of row-defining regimen versus column-defining regimen. HR < 1 favor row-defining regimen. Significant results were bolded and highlighted in red.

A



C



B

PFS (Age < 65)

PFS (Age ≥ 65)																	
OSI_RAM	0.81 (0.26,2.55)	0.52 (0.17,1.62)	0.4 (0.1,1.52)	0.5 (0.13,1.95)	0.55 (0.22,1.41)	0.34 (0.08,1.39)	0.38 (0.09,1.67)	0.45 (0.13,1.49)	0.35 (0.09,1.33)	0.4 (0.1,1.51)	0.94 (0.23,3.8)	0.3 (0.07,1.25)	0.39 (0.1,1.47)	0.33 (0.09,1.2)	0.27 (0.09,0.84)	0.21 (0.05,0.94)	0.06 (0.02,0.21)
0.95 (0.15,5.98)	OSI_PB	0.64 (0.25,1.65)	0.49 (0.15,1.61)	0.62 (0.19,2.06)	0.68 (0.35,1.34)	0.42 (0.12,1.46)	0.46 (0.12,1.78)	0.55 (0.19,1.55)	0.43 (0.14,1.4)	0.49 (0.15,1.61)	1.15 (0.33,4.02)	0.37 (0.1,1.31)	0.49 (0.15,1.56)	0.41 (0.14,1.26)	0.33 (0.13,0.86)	0.26 (0.07,1.01)	0.08 (0.02,0.22)
1.12 (0.18,7.01)	1.18 (0.21,6.65)	AMI_LAZ	0.76 (0.23,2.46)	0.96 (0.29,3.14)	1.06 (0.55,2.03)	0.65 (0.19,2.23)	0.72 (0.22,2.73)	0.86 (0.31,2.35)	0.67 (0.22,2.12)	0.76 (0.24,2.47)	1.79 (0.52,6.13)	0.58 (0.17,2.01)	0.75 (0.24,2.39)	0.64 (0.22,1.93)	0.52 (0.21,1.32)	0.41 (0.11,1.54)	0.12 (0.04,0.34)
0.69 (0.07,6.2)	0.72 (0.09,6.09)	0.61 (0.07,5.07)	FUR	1.26 (0.45,3.58)	1.39 (0.52,3.73)	0.86 (0.29,2.59)	0.95 (0.29,3.17)	1.13 (0.48,2.62)	0.88 (0.33,2.41)	1 (0.36,2.81)	2.36 (0.78,7.02)	0.76 (0.25,2.32)	0.99 (0.37,2.69)	0.83 (0.33,2.15)	0.68 (0.33,1.43)	0.54 (0.16,1.79)	0.15 (0.06,0.38)
0.56 (0.06,5.07)	0.59 (0.07,4.92)	0.5 (0.06,4.15)	0.82 (0.14,4.66)	AUM	1.11 (0.41,2.95)	0.68 (0.23,2.04)	0.75 (0.23,2.5)	0.9 (0.38,2.06)	0.7 (0.26,1.9)	0.79 (0.28,2.23)	1.87 (0.62,5.62)	0.6 (0.2,1.83)	0.78 (0.29,2.12)	0.66 (0.26,1.7)	0.54 (0.26,1.13)	0.42 (0.13,1.42)	0.12 (0.05,0.31)
0.56 (0.14,2.22)	0.59 (0.17,2.02)	0.5 (0.15,1.7)	0.82 (0.14,4.69)	1 (0.18,5.68)	OSI	0.62 (0.22,1.76)	0.68 (0.22,2.17)	0.81 (0.37,1.76)	0.64 (0.25,1.64)	0.72 (0.27,1.91)	1.69 (0.59,4.85)	0.54 (0.19,1.58)	0.71 (0.28,1.83)	0.6 (0.25,1.47)	0.49 (0.25,0.95)	0.38 (0.12,1.23)	0.11 (0.05,0.26)
0.59 (0.06,5.36)	0.62 (0.07,5.21)	0.52 (0.06,4.43)	0.86 (0.15,4.95)	1.05 (0.18,5.98)	1.05 (0.18,5.97)	BEF	1.1 (0.32,3.86)	1.32 (0.52,3.26)	1.03 (0.36,2.95)	1.16 (0.39,3.46)	2.75 (0.85,8.66)	0.89 (0.27,2.87)	1.16 (0.4,3.29)	0.97 (0.36,2.66)	0.8 (0.35,1.79)	0.62 (0.18,2.18)	0.18 (0.07,0.48)
0.24 (0.02,2.82)	0.26 (0.02,2.73)	0.22 (0.02,2.3)	0.36 (0.05,2.72)	0.44 (0.06,3.27)	0.44 (0.06,3.31)	0.42 (0.05,3.17)	AFA_CET	1.19 (0.42,3.26)	0.94 (0.29,2.92)	1.05 (0.32,3.43)	2.49 (0.7,8.56)	0.8 (0.22,2.8)	1.05 (0.32,3.26)	0.88 (0.42,1.85)	0.72 (0.28,1.82)	0.56 (0.2,1.62)	0.16 (0.06,0.43)
0.5 (0.07,3.55)	0.53 (0.08,3.4)	0.45 (0.07,2.85)	0.73 (0.17,3.02)	0.89 (0.21,3.67)	0.89 (0.21,3.63)	0.85 (0.2,3.51)	2.04 (0.35,11.76)	GEF_PB	0.78 (0.36,1.75)	0.88 (0.38,2.07)	2.09 (0.83,5.29)	0.67 (0.26,1.74)	0.87 (0.4,1.96)	0.74 (0.37,1.56)	0.6 (0.4,0.93)	0.47 (0.17,1.36)	0.14 (0.07,0.27)
0.47 (0.05,4.25)	0.49 (0.06,4.12)	0.42 (0.05,3.43)	0.68 (0.12,3.87)	0.83 (0.15,4.71)	0.83 (0.14,4.67)	0.79 (0.14,4.57)	1.9 (0.25,14.34)	0.93 (0.22,3.89)	ERL_RAM	1.13 (0.42,3.02)	2.67 (0.92,7.62)	0.86 (0.29,2.5)	1.12 (0.43,2.87)	0.94 (0.39,2.32)	0.77 (0.39,1.5)	0.6 (0.19,1.95)	0.17 (0.07,0.41)
0.43 (0.05,4.18)	0.45 (0.05,4.01)	0.39 (0.04,3.36)	0.63 (0.1,3.8)	0.77 (0.13,4.63)	0.77 (0.13,4.65)	0.73 (0.12,4.42)	1.76 (0.22,14.09)	0.86 (0.19,3.9)	0.93 (0.15,5.65)	ERL_BEV	2.37 (0.78,7.03)	0.76 (0.25,2.3)	0.99 (0.37,2.66)	0.84 (0.33,2.15)	0.68 (0.33,1.41)	0.54 (0.16,1.78)	0.15 (0.06,0.38)
0.29 (0.03,2.67)	0.31 (0.04,2.56)	0.26 (0.03,2.17)	0.42 (0.07,2.45)	0.52 (0.09,2.96)	0.52 (0.09,2.96)	0.49 (0.08,2.85)	1.18 (0.15,9.13)	0.58 (0.14,2.48)	0.63 (0.11,3.59)	0.67 (0.11,4.09)	ICO_PB	0.32 (0.1,1.05)	0.42 (0.15,1.22)	0.35 (0.13,0.98)	0.29 (0.13,0.66)	0.23 (0.07,0.81)	0.07 (0.02,0.18)
0.37 (0.04,3.38)	0.39 (0.05,3.24)	0.33 (0.04,2.75)	0.54 (0.09,3.1)	0.66 (0.11,3.75)	0.66 (0.11,3.75)	0.63 (0.11,3.65)	1.5 (0.2,11.5)	0.73 (0.18,3.13)	0.79 (0.14,4.58)	0.85 (0.14,5.21)	1.27 (0.22,7.39)	GEF_APA	1.31 (0.45,3.83)	1.1 (0.4,3.11)	0.9 (0.39,2.11)	0.71 (0.2,2.53)	0.2 (0.07,0.56)
0.48 (0.05,4.41)	0.51 (0.06,4.25)	0.43 (0.05,3.6)	0.71 (0.12,4.04)	0.86 (0.15,4.87)	0.86 (0.15,4.89)	0.82 (0.14,4.72)	1.97 (0.26,15.06)	0.97 (0.24,4.02)	1.04 (0.18,5.93)	1.12 (0.19,6.78)	1.67 (0.29,9.6)	1.32 (0.23,7.54)	DAC	0.84 (0.35,2.09)	0.69 (0.35,1.36)	0.54 (0.17,1.75)	0.16 (0.06,0.37)
0.31 (0.04,2.44)	0.33 (0.05,2.37)	0.28 (0.04,1.98)	0.45 (0.09,2.16)	0.55 (0.12,2.6)	0.55 (0.12,2.59)	0.53 (0.11,2.5)	1.26 (0.34,4.62)	0.62 (0.19,2.07)	0.66 (0.14,3.18)	0.72 (0.14,3.63)	1.06 (0.22,5.17)	0.84 (0.17,4.03)	0.64 (0.13,3.02)	AFA	0.82 (0.45,1.45)	0.64 (0.3,1.35)	0.19 (0.09,0.36)
0.25 (0.04,1.54)	0.26 (0.05,1.48)	0.22 (0.04,1.24)	0.36 (0.11,1.24)	0.44 (0.13,1.5)	0.44 (0.13,1.5)	0.42 (0.12,1.45)	1.01 (0.2,5.05)	0.49 (0.24,1.02)	0.53 (0.16,1.83)	0.57 (0.15,2.13)	0.85 (0.25,2.96)	0.67 (0.19,2.32)	0.51 (0.15,1.74)	0.8 (0.31,2.1)	F_TKI	0.78 (0.31,2.04)	0.23 (0.13,0.39)
0.16 (0.01,1.82)	0.17 (0.02,1.77)	0.15 (0.01,1.49)	0.24 (0.03,1.77)	0.29 (0.04,2.13)	0.29 (0.04,2.11)	0.28 (0.04,2.04)	0.67 (0.11,4.03)	0.33 (0.06,1.86)	0.35 (0.05,2.61)	0.38 (0.05,2.91)	0.56 (0.08,4.21)	0.45 (0.06,3.26)	0.34 (0.05,2.46)	0.53 (0.15,1.83)	0.66 (0.14,3.18)	PB	0.29 (0.1,0.76)
0.08 (0.01,0.58)	0.08 (0.01,0.56)	0.07 (0.01,0.47)	0.12 (0.03,0.5)	0.14 (0.03,0.6)	0.14 (0.03,0.6)	0.13 (0.03,0.58)	0.32 (0.06,1.61)	0.16 (0.05,0.46)	0.17 (0.04,0.74)	0.18 (0.04,0.85)	0.27 (0.06,1.19)	0.21 (0.05,0.93)	0.16 (0.04,0.7)	0.26 (0.1,0.66)	0.32 (0.14,0.71)	0.48 (0.1,2.31)	PF

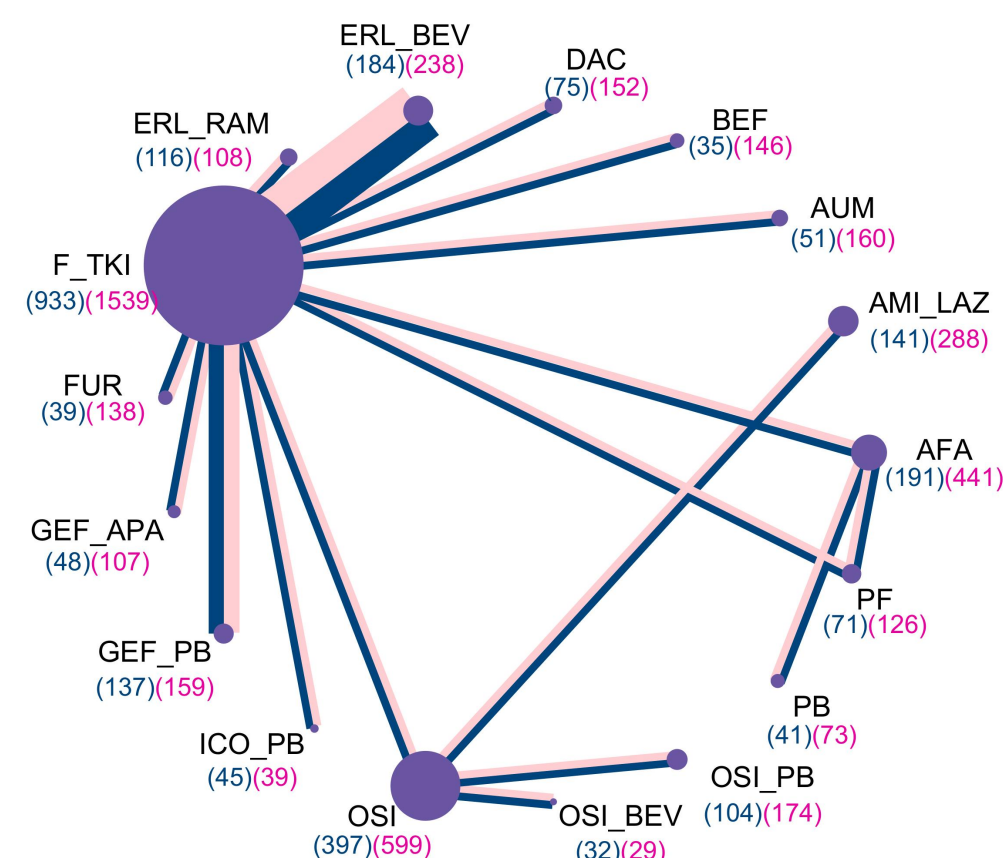
D

OS (Age < 65)

OS (Age ≥ 65)								
OSI	1.42 (0.36,6.17)	0.97 (0.33,2.84)	1.3 (0.41,4.13)	0.91 (0.3,2.74)	0.91 (0.34,2.65)	0.87 (0.41,1.87)	0.66 (0.18,2.62)	0.79 (0.28,2.45)
0.97 (0.31,3.04)	AFA_CET	0.68 (0.16,2.7)	0.91 (0.2,3.88)	0.64 (0.14,2.61)	0.64 (0.24,1.74)	0.61 (0.18,1.97)	0.47 (0.13,1.73)	0.56 (0.16,1.93)
0.98 (0.45,2.18)	1.02 (0.31,3.25)	GEF_PB	1.34 (0.42,4.25)	0.94 (0.31,2.83)	0.94 (0.36,2.73)	0.9 (0.42,1.93)	0.69 (0.19,2.7)	0.82 (0.29,2.52)
1.09 (0.4,3.0)	1.12 (0.29,4.28)	1.1 (0.39,3.13)	ERL_BEV	0.7 (0.21,2.28)	0.7 (0.24,2.21)	0.67 (0.28,1.61)	0.51 (0.13,2.15)	0.61 (0.2,2.04)
1 (0.47,2.17)	1.04 (0.33,3.27)	1.02 (0.45,2.27)	0.92 (0.33,2.57)	DAC	1 (0.37,3.0)	0.96 (0.43,2.14)	0.73 (0.2,2.95)	0.87 (0.3,2.76)
1.04 (0.51,2.1)	1.07 (0.43,2.63)	1.05 (0.5,2.22)	0.95 (0.36,2.54)	1.04 (0.5,2.13)	AFA	0.96 (0.46,1.81)	0.73 (0.31,1.7)	0.87 (0.42,1.81)
0.72 (0.42,1.23)	0.75 (0.27,2.04)	0.73 (0.41,1.3)	0.66 (0.28,1.58)	0.72 (0.41,1.25)	0.69 (0.44,1.1)	F_TKI	0.76 (0.27,2.36)	0.91 (0.44,2.05)
0.85 (0.34,2.1)	0.88 (0.3,2.52)	0.86 (0.34,2.2)	0.78 (0.25,2.43)	0.85 (0.34,2.12)	0.82 (0.46,1.45)	1.18 (0.56,2.46)	PB	1.19 (0.39,3.64)
0.87 (0.42,1.76)	0.89 (0.33,2.42)	0.88 (0.41,1.85)	0.79 (0.29,2.13)	0.86 (0.41,1.78)	0.83 (0.53,1.3)	1.2 (0.74,1.92)	1.02 (0.49,2.11)	PF

Figure S7. Network meta-analysis of comparisons of PFS and OS in EGFR mutated NSCLC based on age history. **(A and C)** Network diagrams of comparisons on PFS **(A)** and OS **(C)** for the age < 65 and the age ≥ 65. Each circular node represents a type of regimen and each line represents a type of head-to-head comparison. The size of the node and the thickness of the line are weighted according to the number of trials evaluating each regimen and direct comparison, respectively. The total number of patients in each regimen was shown in brackets. **(B and D)** Pooled HR (95% CI) for PFS **(B)** and OS **(D)** of the age < 65 (lower triangle) and the age ≥ 65 (upper triangle). Result in each cell is presented as HR (95% CI) for the comparison of row-defining regimen versus column-defining regimen. HR < 1 favor row-defining regimen. Significant results were bolded and highlighted in red.

A

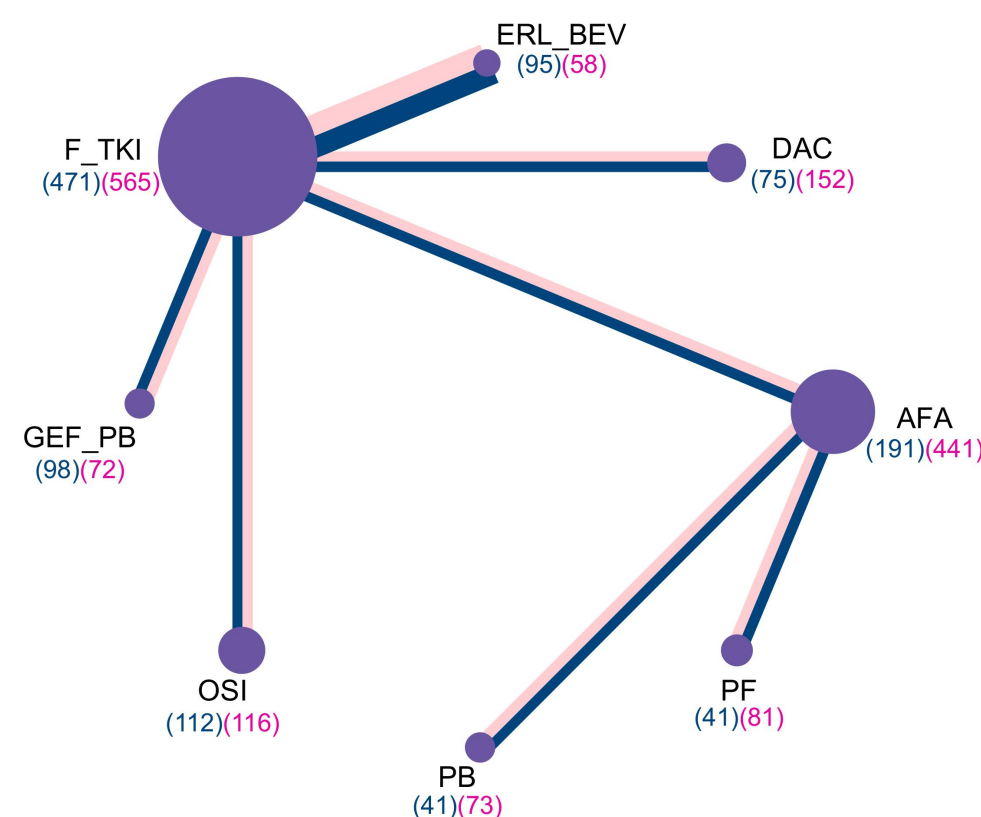


B

PFS (ECOG PS=0)

PFS (ECOG PS=1)																
OSI_PB	0.8 (0.39,1.67)	0.64 (0.25,1.68)	0.54 (0.22,1.34)	0.53 (0.21,1.31)	0.53 (0.31,0.9)	0.5 (0.2,1.25)	0.48 (0.2,1.1)	0.39 (0.16,0.99)	0.44 (0.2,0.99)	0.55 (0.2,1.5)	0.4 (0.16,1.02)	0.47 (0.19,1.17)	0.36 (0.15,0.87)	0.26 (0.13,0.56)	0.23 (0.08,0.64)	0.1 (0.04,0.25)
1 (0.31,3.22)	AMI_LAZ	0.8 (0.31,2.05)	0.68 (0.28,1.64)	0.66 (0.27,1.61)	0.66 (0.4,1.09)	0.62 (0.25,1.54)	0.6 (0.26,1.35)	0.49 (0.2,1.21)	0.55 (0.25,1.21)	0.69 (0.26,1.83)	0.5 (0.2,1.24)	0.59 (0.24,1.42)	0.46 (0.19,1.05)	0.33 (0.16,0.68)	0.29 (0.1,0.79)	0.13 (0.05,0.31)
0.87 (0.24,3.16)	0.87 (0.24,3.11)	OSI_BEV	0.84 (0.28,2.49)	0.82 (0.28,2.46)	0.82 (0.37,1.83)	0.78 (0.26,2.34)	0.74 (0.26,2.09)	0.61 (0.21,1.83)	0.68 (0.25,1.88)	0.86 (0.27,2.76)	0.62 (0.21,1.87)	0.73 (0.25,2.15)	0.57 (0.2,1.62)	0.41 (0.16,1.07)	0.36 (0.11,1.18)	0.16 (0.05,0.47)
0.93 (0.21,4.25)	0.93 (0.21,4.21)	1.07 (0.21,5.37)	FUR	0.98 (0.46,2.06)	0.98 (0.47,2.06)	0.92 (0.43,1.98)	0.88 (0.45,1.71)	0.73 (0.34,1.56)	0.81 (0.44,1.52)	1.02 (0.44,2.39)	0.74 (0.34,1.61)	0.87 (0.42,1.83)	0.67 (0.33,1.35)	0.49 (0.29,0.84)	0.43 (0.17,1.05)	0.19 (0.09,0.4)
0.83 (0.19,3.68)	0.83 (0.19,3.63)	0.95 (0.2,4.59)	0.9 (0.24,3.35)	AUM	1 (0.48,2.1)	0.94 (0.44,2.02)	0.9 (0.46,1.74)	0.75 (0.35,1.58)	0.83 (0.45,1.55)	1.05 (0.45,2.43)	0.76 (0.35,1.63)	0.89 (0.43,1.86)	0.69 (0.34,1.37)	0.5 (0.3,0.85)	0.44 (0.18,1.06)	0.2 (0.09,0.4)
0.79 (0.35,1.82)	0.79 (0.35,1.79)	0.91 (0.34,2.45)	0.85 (0.24,3)	0.95 (0.28,3.19)	OSI	0.94 (0.44,2.01)	0.9 (0.46,1.72)	0.75 (0.35,1.57)	0.83 (0.45,1.53)	1.04 (0.45,2.42)	0.76 (0.35,1.62)	0.89 (0.43,1.85)	0.69 (0.34,1.36)	0.5 (0.3,0.84)	0.44 (0.18,1.05)	0.19 (0.09,0.4)
0.79 (0.17,3.72)	0.79 (0.17,3.67)	0.91 (0.18,4.65)	0.85 (0.21,3.46)	0.95 (0.24,3.69)	1 (0.27,3.71)	BEF	0.96 (0.48,1.88)	0.79 (0.36,1.71)	0.88 (0.47,1.69)	1.11 (0.47,2.63)	0.81 (0.37,1.76)	0.95 (0.45,2.02)	0.73 (0.35,1.49)	0.53 (0.31,0.93)	0.46 (0.18,1.14)	0.21 (0.1,0.43)
0.58 (0.15,2.06)	0.57 (0.15,2.05)	0.66 (0.15,2.64)	0.62 (0.19,1.87)	0.69 (0.22,1.96)	0.73 (0.25,1.94)	0.72 (0.21,2.28)	GEF_PB	0.83 (0.42,1.64)	0.92 (0.55,1.58)	1.16 (0.53,2.55)	0.84 (0.43,1.7)	0.99 (0.52,1.93)	0.77 (0.42,1.42)	0.56 (0.37,0.84)	0.48 (0.21,1.12)	0.22 (0.11,0.42)
0.53 (0.13,2.22)	0.53 (0.13,2.22)	0.61 (0.13,2.81)	0.57 (0.16,2.02)	0.64 (0.19,2.15)	0.67 (0.21,2.16)	0.67 (0.18,2.48)	0.92 (0.35,2.7)	ERL_RAM	1.11 (0.6,2.1)	1.4 (0.6,3.28)	1.02 (0.47,2.22)	1.19 (0.57,2.52)	0.92 (0.45,1.86)	0.67 (0.39,1.15)	0.58 (0.23,1.44)	0.26 (0.12,0.54)
0.56 (0.17,2.12)	0.56 (0.17,2.1)	0.65 (0.17,2.68)	0.61 (0.22,1.86)	0.68 (0.26,1.96)	0.71 (0.3,1.95)	0.71 (0.24,2.28)	0.98 (0.5,2.36)	1.06 (0.44,2.9)	ERL_BEV	1.26 (0.6,2.63)	0.92 (0.48,1.74)	1.08 (0.58,1.96)	0.83 (0.47,1.44)	0.6 (0.43,0.83)	0.52 (0.23,1.16)	0.24 (0.13,0.43)
0.48 (0.11,2.03)	0.47 (0.11,2.02)	0.55 (0.12,2.55)	0.51 (0.14,1.86)	0.57 (0.16,1.98)	0.6 (0.18,1.99)	0.6 (0.16,2.28)	0.83 (0.3,2.5)	0.9 (0.27,2.97)	0.84 (0.3,2.13)	ICO_PB	0.73 (0.3,1.74)	0.85 (0.37,1.98)	0.66 (0.29,1.47)	0.48 (0.25,0.93)	0.42 (0.15,1.11)	0.19 (0.08,0.43)
0.4 (0.09,1.7)	0.39 (0.09,1.68)	0.45 (0.1,2.15)	0.43 (0.11,1.56)	0.48 (0.14,1.65)	0.5 (0.15,1.66)	0.5 (0.13,1.89)	0.69 (0.25,2.07)	0.75 (0.22,2.46)	0.7 (0.24,1.77)	0.83 (0.24,2.87)	GEF_APA	1.18 (0.55,2.52)	0.91 (0.44,1.86)	0.66 (0.38,1.15)	0.57 (0.23,1.43)	0.26 (0.12,0.54)
0.48 (0.11,2.03)	0.47 (0.11,1.99)	0.54 (0.12,2.54)	0.51 (0.14,1.84)	0.57 (0.17,1.95)	0.6 (0.18,1.96)	0.6 (0.16,2.24)	0.83 (0.3,2.47)	0.89 (0.28,2.91)	0.84 (0.3,2.08)	1 (0.3,3.38)	1.2 (0.36,4.07)	DAC	0.77 (0.39,1.52)	0.56 (0.34,0.94)	0.49 (0.2,1.18)	0.22 (0.11,0.45)
0.35 (0.09,1.41)	0.35 (0.09,1.39)	0.4 (0.09,1.77)	0.38 (0.11,1.27)	0.42 (0.13,1.35)	0.44 (0.15,1.35)	0.45 (0.13,1.56)	0.61 (0.24,1.67)	0.66 (0.22,2.01)	0.62 (0.24,1.42)	0.74 (0.24,2.34)	0.89 (0.28,2.8)	0.74 (0.24,2.28)	AFA	0.73 (0.46,1.15)	0.63 (0.36,1.12)	0.28 (0.17,0.45)
0.31 (0.1,1)	0.31 (0.1,0.98)	0.35 (0.1,1.28)	0.33 (0.13,0.87)	0.37 (0.15,0.9)	0.39 (0.17,0.89)	0.39 (0.14,1.08)	0.54 (0.3,1.04)	0.58 (0.25,1.33)	0.55 (0.32,0.83)	0.65 (0.27,1.55)	0.78 (0.33,1.88)	0.65 (0.28,1.51)	0.88 (0.42,1.85)	F_TKI	0.87 (0.42,1.79)	0.39 (0.23,0.64)
0.18 (0.03,0.91)	0.18 (0.03,0.9)	0.2 (0.04,1.13)	0.19 (0.04,0.84)	0.21 (0.05,0.9)	0.22 (0.05,0.91)	0.22 (0.05,1.03)	0.31 (0.09,1.17)	0.33 (0.08,1.36)	0.31 (0.09,1.02)	0.37 (0.09,1.56)	0.44 (0.11,1.88)	0.37 (0.09,1.53)	0.5 (0.21,1.21)	0.57 (0.18,1.8)	PB	0.45 (0.21,0.94)
0.08 (0.02,0.33)	0.08 (0.02,0.32)	0.09 (0.02,0.41)	0.08 (0.02,0.3)	0.09 (0.03,0.32)	0.1 (0.03,0.32)	0.1 (0.03,0.37)	0.14 (0.05,0.39)	0.15 (0.05,0.47)	0.14 (0.05,0.34)	0.16 (0.05,0.55)	0.2 (0.06,0.66)	0.16 (0.05,0.53)	0.22 (0.1,0.49)	0.25 (0.11,0.58)	0.44 (0.14,1.45)	PF

C



D

OS (ECOG PS=0)

OS (ECOG PS=1)							
OSI	1.4 (0.39,5.02)	1.01 (0.33,3.3)	0.98 (0.27,3.47)	0.93 (0.26,3.34)	0.7 (0.29,1.7)	0.66 (0.14,3.2)	0.77 (0.16,3.7)
1.12 (0.57,2.21)	GEF_PB	0.72 (0.23,2.43)	0.7 (0.19,2.52)	0.67 (0.18,2.42)	0.5 (0.2,1.26)	0.47 (0.1,2.32)	0.55 (0.12,2.7)
1.18 (0.59,2.36)	1.06 (0.54,2.05)	ERL_BEV	0.96 (0.29,2.98)	0.92 (0.28,2.87)	0.69 (0.32,1.41)	0.65 (0.15,2.81)	0.76 (0.17,3.25)
0.8 (0.36,1.77)	0.71 (0.33,1.55)	0.68 (0.31,1.48)	DAC	0.95 (0.27,3.42)	0.72 (0.29,1.77)	0.68 (0.14,3.31)	0.79 (0.17,3.83)
0.7 (0.33,1.51)	0.63 (0.3,1.32)	0.59 (0.28,1.27)	0.88 (0.37,2.08)	AFA	0.75 (0.3,1.85)	0.71 (0.29,1.78)	0.83 (0.34,2.07)
0.93 (0.57,1.53)	0.83 (0.52,1.32)	0.78 (0.49,1.27)	1.16 (0.63,2.18)	1.32 (0.74,2.38)	F_TKI	0.94 (0.26,3.45)	1.1 (0.31,4.01)
0.68 (0.25,1.83)	0.6 (0.22,1.61)	0.57 (0.21,1.55)	0.84 (0.29,2.48)	0.96 (0.5,1.84)	0.72 (0.3,1.73)	PB	1.17 (0.32,4.25)
0.58 (0.22,1.55)	0.51 (0.2,1.35)	0.49 (0.19,1.29)	0.72 (0.25,2.08)	0.82 (0.44,1.52)	0.62 (0.27,1.45)	0.86 (0.35,2.09)	PF

— PS = 0
— PS = 1

Figure S8. Network meta-analysis of comparisons of PFS and OS in EGFR mutated NSCLC based on ECOG PS. **(A and C)** Network diagrams of comparisons on PFS **(A)** and OS **(C)** for the PS = 0 and the PS = 1. Each circular node represents a type of regimen and each line represents a type of head-to-head comparison. The size of the node and the thickness of the line are weighted according to the number of trials evaluating each regimen and direct comparison, respectively. The total number of patients in each regimen was shown in brackets. **(B and D)** Pooled HR (95% CI) for PFS **(B)** and OS **(D)** of the PS = 0 (lower triangle) and the PS = 1 (upper triangle). Result in each cell is presented as HR (95% CI) for the comparison of row-defining regimen versus column-defining regimen. HR < 1 favor row-defining regimen. Significant results were bolded and highlighted in red.

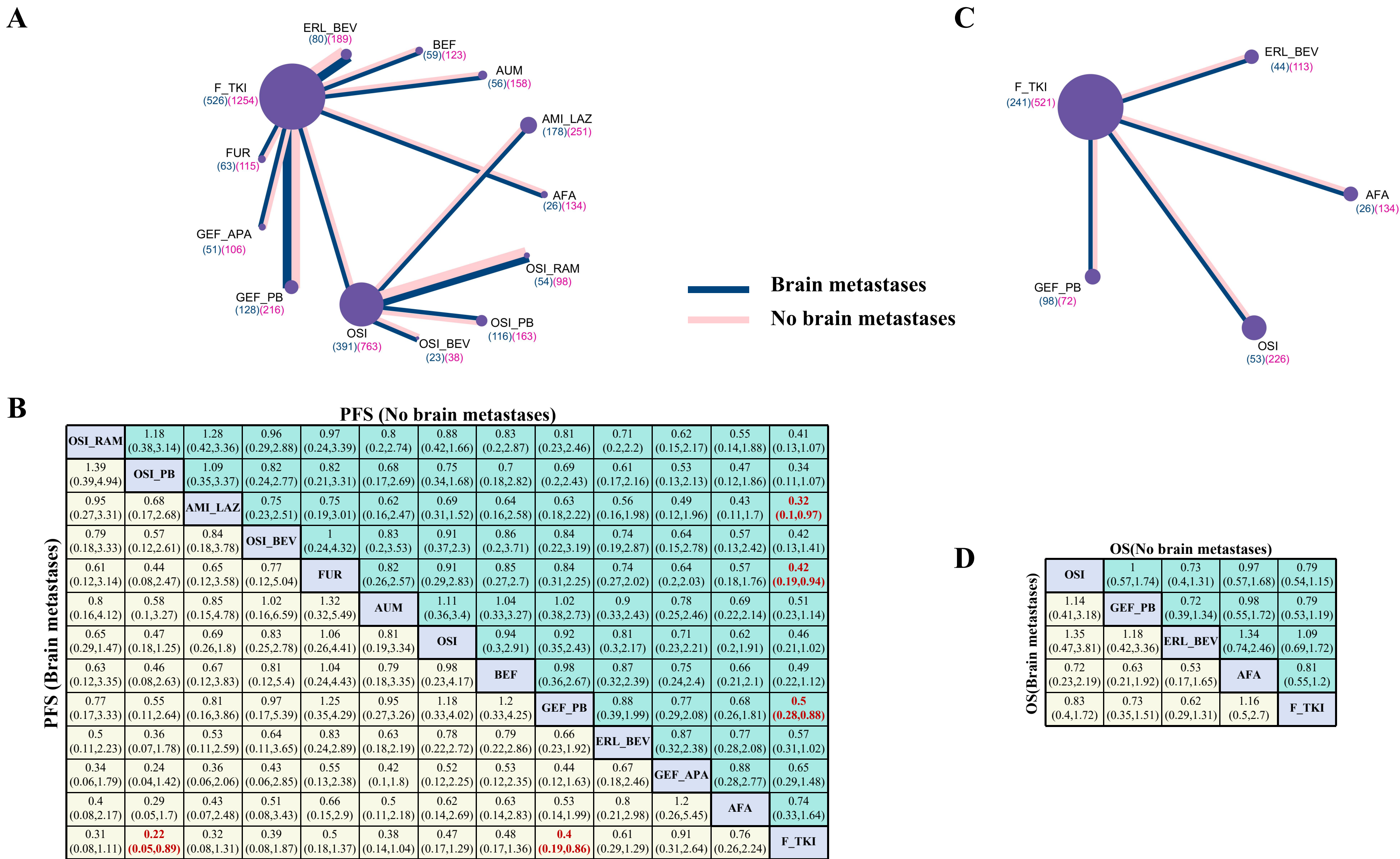


Figure S9. Network meta-analysis of comparisons of PFS and OS in EGFR mutated NSCLC based on the status of brain metastases. (**A and C**) Network diagrams of comparisons on PFS (**A**) and OS (**C**) for the brain metastases and the no brain metastases. Each circular node represents a type of regimen and each line represents a type of head-to-head comparison. The size of the node and the thickness of the line are weighted according to the number of trials evaluating each regimen and direct comparison, respectively. The total number of patients in each regimen was shown in brackets. (**B and D**) Pooled HR (95% CI) for PFS (**B**) and OS (**D**) of the brain metastases (lower triangle) and the no brain metastases (upper triangle). Result in each cell is presented as HR (95% CI) for the comparison of row-defining regimen versus column-defining regimen. HR < 1 favor row-defining regimen. Significant results were bolded and highlighted in red.

A

Network diagram showing the relationship between F_TKI (2898) and other genes. The nodes are purple circles, and the edges are black lines. The genes and their interaction counts are:

- F_TKI (2898)
- ERL_BEV (346)
- DAC (170)
- BEF (182)
- AUM_APA (48)
- AUM (264)
- AMI_LAZ (250)
- AFA (501)
- PF (675)
- PB (260)
- OSI_RAM (59)
- OSI_BEV (61)
- OSI_PB (71)
- OSI (616)
- ICO_PB (90)
- GEF_PB (513)
- GEF_APA (157)
- FUR (178)
- ERL_RAM (166)
- ERL_PF (49)

B

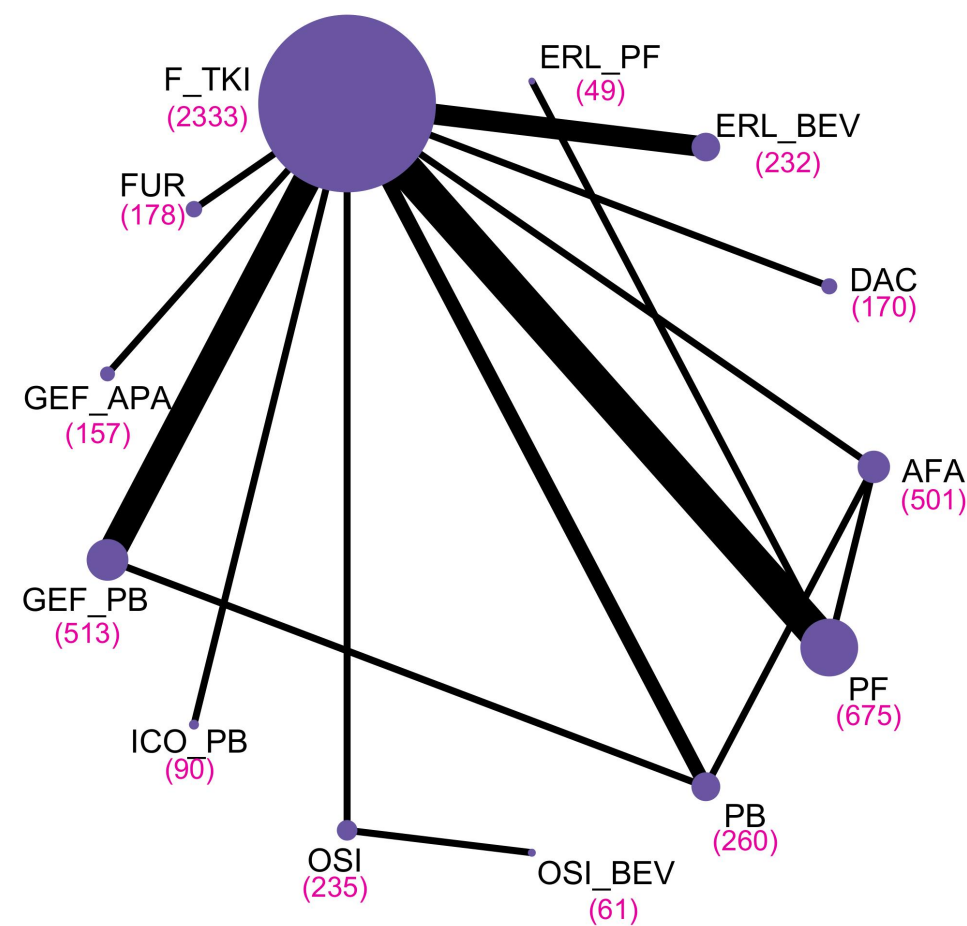
Network diagram showing the relationship between F_TKI (490) and other genes. The nodes are purple circles, and the edges are black lines. The genes and their interaction counts are:

- F_TKI (490)
- ERL_BEV (123)
- DAC (57)
- AMI_LAZ (117)
- AFA (131)
- PF (87)
- PB (32)
- OSI_RAM (93)
- OSI_PB (101)
- OSI (430)
- ERL_RAM (58)

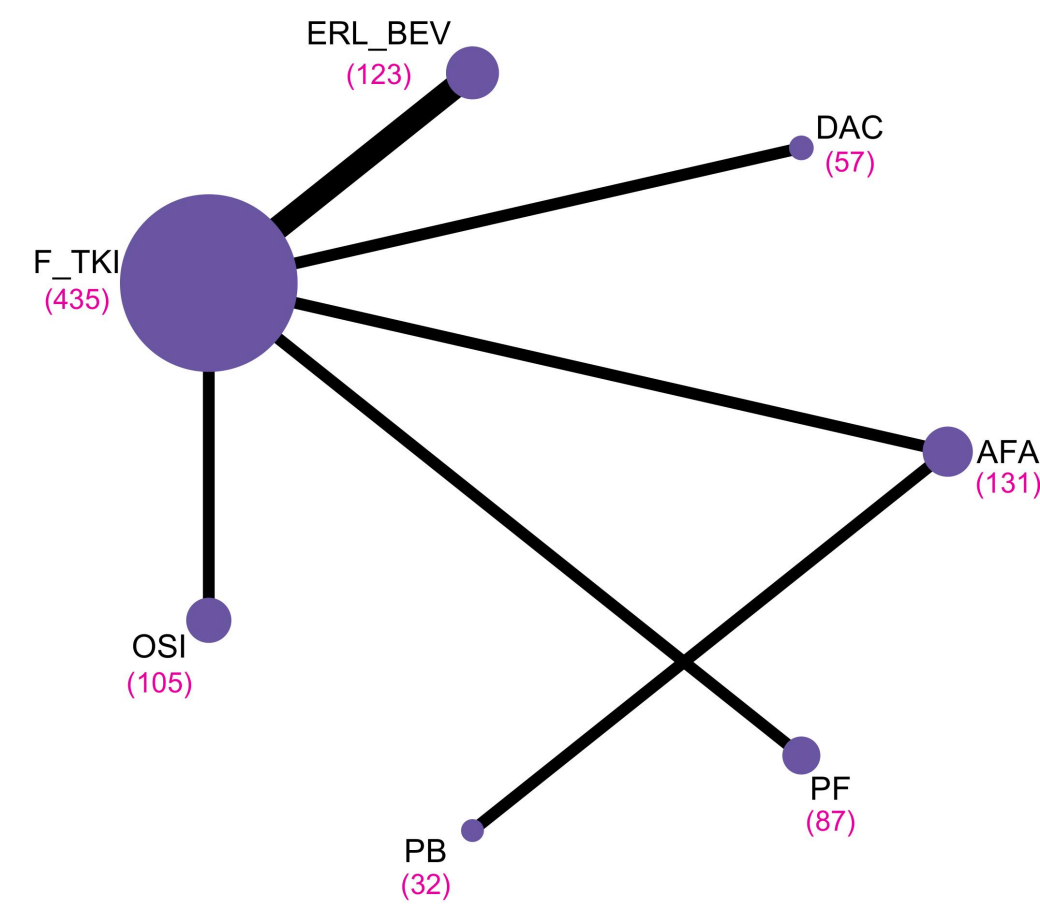
PFS (Asian)	PFS (Non-Asian)																			
	OSI_RAM	1 (0.19,5.25)	0.73 (0.14,3.8)					0.55 (0.17,1.82)			0.31 (0.04,2.37)	0.26 (0.04,1.62)				0.21 (0.03,1.61)	0.26 (0.03,1.95)	0.19 (0.04,0.99)	0.18 (0.02,1.84)	0.07 (0.01,0.52)
	0.11 (0.04,0.31)	OSI_PB	0.73 (0.15,3.7)					0.55 (0.17,1.75)			0.31 (0.04,2.31)	0.26 (0.04,1.56)				0.21 (0.03,1.56)	0.26 (0.04,1.89)	0.19 (0.04,0.95)	0.18 (0.02,1.8)	0.07 (0.01,0.52)
	0.08 (0.03,0.2)	0.73 (0.28,1.89)	AMI_LAZ					0.75 (0.24,2.32)			0.42 (0.06,3.08)	0.35 (0.06,2.1)				0.29 (0.04,2.12)	0.35 (0.05,2.55)	0.26 (0.05,1.28)	0.24 (0.02,2.43)	0.09 (0.01,0.69)
	0.08 (0.02,0.35)	0.74 (0.17,3.2)	1.02 (0.25,4.13)	AUM_APA																
	0.06 (0.02,0.17)	0.57 (0.2,1.6)	0.78 (0.3,2.0)	0.76 (0.18,3.23)	OSI_BEV															
	0.07 (0.02,0.21)	0.61 (0.2,1.9)	0.84 (0.29,2.42)	0.82 (0.23,2.87)	1.08 (0.35,3.35)	FUR														
	0.06 (0.02,0.2)	0.58 (0.19,1.82)	0.8 (0.28,2.31)	0.78 (0.31,1.96)	1.03 (0.33,3.19)	0.96 (0.4,2.27)	AUM													
	0.05 (0.03,0.11)	0.49 (0.23,1.02)	0.67 (0.36,1.23)	0.66 (0.19,2.3)	0.86 (0.42,1.79)	0.8 (0.34,1.91)	0.84 (0.35,1.99)	OSI			0.56 (0.11,2.91)	0.47 (0.11,1.87)				0.38 (0.07,1.97)	0.47 (0.09,2.39)	0.34 (0.11,1.07)	0.32 (0.04,2.4)	0.13 (0.02,0.65)
	0.06 (0.02,0.19)	0.55 (0.17,1.73)	0.75 (0.26,2.2)	0.74 (0.21,2.61)	0.97 (0.31,3.05)	0.9 (0.37,2.18)	0.94 (0.39,2.26)	1.12 (0.46,2.71)	BEF											
	0.06 (0.02,0.16)	0.52 (0.19,1.45)	0.72 (0.29,1.82)	0.7 (0.22,2.22)	0.93 (0.34,2.55)	0.86 (0.43,1.73)	0.9 (0.45,1.81)	1.07 (0.54,2.16)	0.95 (0.47,1.97)	GEF_PB										
	0.05 (0.02,0.14)	0.42 (0.13,1.31)	0.57 (0.21,1.66)	0.56 (0.16,1.96)	0.74 (0.24,2.3)	0.69 (0.29,1.64)	0.72 (0.3,1.7)	0.86 (0.36,2.04)	0.76 (0.32,1.86)	0.8 (0.4,1.59)	ERL_RAM	0.84 (0.19,3.47)				0.69 (0.13,3.59)	0.85 (0.16,4.43)	0.61 (0.19,1.98)	0.58 (0.07,4.41)	0.23 (0.04,1.19)
	0.05 (0.02,0.15)	0.48 (0.17,1.35)	0.66 (0.26,1.69)	0.65 (0.2,2.06)	0.85 (0.31,2.37)	0.79 (0.38,1.62)	0.83 (0.4,1.69)	0.99 (0.48,2.03)	0.88 (0.42,1.84)	0.92 (0.56,1.5)	1.15 (0.56,2.36)	ERL_BEV				0.82 (0.2,3.46)	1.01 (0.25,4.23)	0.73 (0.33,1.68)	0.69 (0.11,4.44)	0.27 (0.07,1.14)
	0.04 (0.01,0.14)	0.38 (0.11,1.28)	0.52 (0.16,1.62)	0.51 (0.13,1.9)	0.68 (0.2,2.24)	0.63 (0.23,1.64)	0.65 (0.24,1.7)	0.78 (0.29,2.03)	0.7 (0.26,1.85)	0.73 (0.31,1.62)	0.91 (0.34,2.38)	0.79 (0.33,1.82)	ERL_PF							
	0.05 (0.02,0.16)	0.46 (0.14,1.45)	0.62 (0.21,1.84)	0.61 (0.17,2.18)	0.8 (0.25,2.55)	0.75 (0.31,1.82)	0.78 (0.32,1.9)	0.93 (0.38,2.28)	0.83 (0.33,2.06)	0.87 (0.42,1.79)	1.09 (0.44,2.67)	0.95 (0.45,2)	0.95 (0.45,3.29)	ICO_PB						
	0.04 (0.01,0.13)	0.38 (0.12,1.18)	0.52 (0.18,1.5)	0.51 (0.14,1.78)	0.67 (0.21,2.07)	0.62 (0.26,1.48)	0.65 (0.27,1.55)	0.77 (0.32,1.85)	0.69 (0.28,1.68)	0.72 (0.36,1.44)	0.9 (0.38,2.16)	0.78 (0.38,1.62)	0.99 (0.38,2.68)	0.83 (0.34,2.04)	GEF_APA					
	0.06 (0.02,0.18)	0.53 (0.17,1.64)	0.72 (0.25,2.09)	0.71 (0.2,2.47)	0.93 (0.3,2.89)	0.86 (0.36,2.06)	0.9 (0.38,2.13)	1.08 (0.45,2.56)	0.96 (0.4,2.33)	1.01 (0.5,1.99)	1.26 (0.53,2.99)	1.09 (0.53								

27

A



B



C

OS (Non-Asian)													
OSI_BEV													
1.04 (0.43,2.55)	FUR												
0.97 (0.49,1.95)	0.94 (0.53,1.66)	OSI		0.59 (0.19,1.64)				0.75 (0.22,2.6)	0.69 (0.21,2.33)	0.54 (0.23,1.26)	0.47 (0.1,2.2)	0.56 (0.16,1.93)	
1.47 (0.66,3.38)	1.42 (0.88,2.36)	1.51 (1,2.36)	GEF_PB										
1.07 (0.47,2.44)	1.03 (0.63,1.7)	1.1 (0.71,1.71)	0.73 (0.51,1)	ERL_BEV				1.28 (0.43,4.1)	1.18 (0.42,3.65)	0.92 (0.5,1.86)	0.81 (0.2,3.55)	0.96 (0.33,3.03)	
2.1 (0.77,5.76)	2.03 (0.93,4.38)	2.16 (1.04,4.5)	1.43 (0.72,2.76)	1.97 (1,3.88)	ERL_PF								
1.19 (0.48,2.99)	1.15 (0.61,2.2)	1.23 (0.68,2.24)	0.81 (0.48,1.37)	1.13 (0.66,1.92)	0.57 (0.26,1.26)	ICO_PB							
0.88 (0.35,2.24)	0.85 (0.45,1.64)	0.91 (0.49,1.66)	0.6 (0.35,1.02)	0.83 (0.48,1.43)	0.42 (0.19,0.93)	0.74 (0.38,1.44)	GEF_APA						
1.2 (0.5,2.89)	1.16 (0.65,2.08)	1.23 (0.72,2.11)	0.82 (0.51,1.27)	1.13 (0.71,1.78)	0.57 (0.27,1.2)	1 (0.54,1.84)	1.35 (0.73,2.51)	DAC	0.93 (0.26,3.26)	0.72 (0.29,1.8)	0.63 (0.13,3.01)	0.75 (0.21,2.7)	
1.06 (0.47,2.43)	1.03 (0.62,1.7)	1.09 (0.7,1.71)	0.72 (0.51,1)	1 (0.7,1.42)	0.51 (0.26,0.98)	0.89 (0.52,1.52)	1.2 (0.7,2.07)	0.89 (0.56,1.41)	AFA	0.78 (0.33,1.85)	0.68 (0.27,1.74)	0.81 (0.23,2.8)	
0.97 (0.45,2.13)	0.94 (0.61,1.46)	1 (0.69,1.45)	0.66 (0.52,0.82)	0.91 (0.71,1.17)	0.46 (0.25,0.87)	0.81 (0.51,1.3)	1.1 (0.68,1.78)	0.81 (0.55,1.2)	0.91 (0.71,1.17)	F_TKI	0.87 (0.24,3.13)	1.04 (0.42,2.53)	
0.9 (0.4,2.05)	0.86 (0.52,1.44)	0.92 (0.59,1.44)	0.61 (0.43,0.83)	0.84 (0.59,1.2)	0.43 (0.22,0.84)	0.75 (0.44,1.27)	1.01 (0.59,1.75)	0.75 (0.47,1.2)	0.84 (0.62,1.14)	0.92 (0.71,1.2)	PB	1.19 (0.25,5.64)	
1 (0.45,2.24)	0.97 (0.61,1.55)	1.03 (0.69,1.54)	0.68 (0.51,0.89)	0.94 (0.7,1.27)	0.48 (0.26,0.88)	0.84 (0.51,1.37)	1.13 (0.68,1.88)	0.84 (0.55,1.28)	0.94 (0.73,1.22)	1.03 (0.87,1.22)	1.12 (0.83,1.51)	PF	

Figure S11. Network meta-analysis of comparisons of OS in EGFR mutated NSCLC based on the ethnicity. **(A-B)** Network diagrams of comparisons on OS for the Asian **(A)** and the non-Asian **(B)**. Each circular node represents a type of regimen and each line represents a type of head-to-head comparison. The size of the node and the thickness of the line are weighted according to the number of trials evaluating each regimen and direct comparison, respectively. The total number of patients in each regimen was shown in brackets. **(C)** Pooled HR (95% CI) for OS of the Asian (lower triangle) and the non-Asian (upper triangle). Result in each cell is presented as HR (95% CI) for the comparison of row-defining regimen versus column-defining regimen. HR < 1 favor row-defining regimen. Significant results were bolded and highlighted in red.

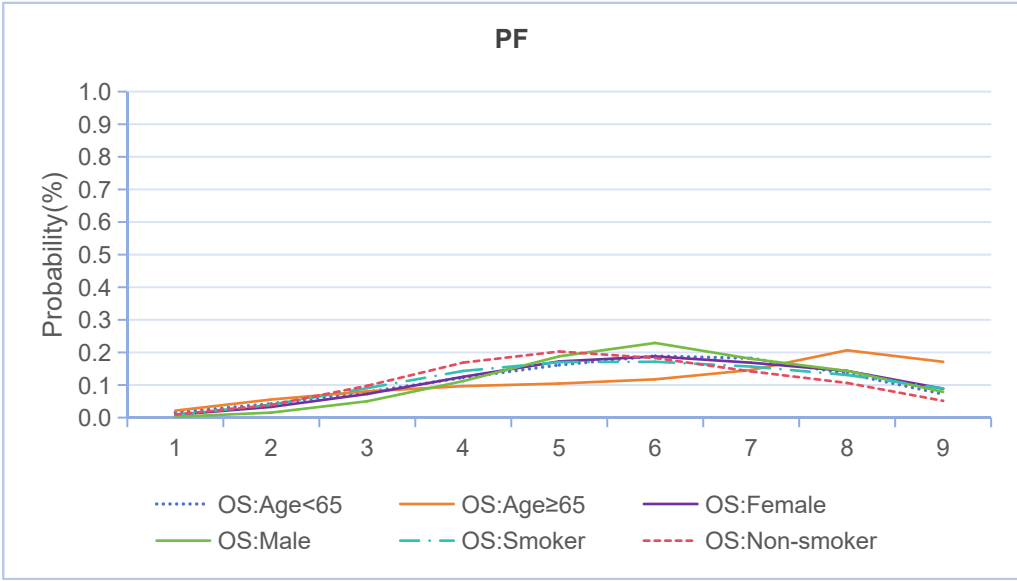
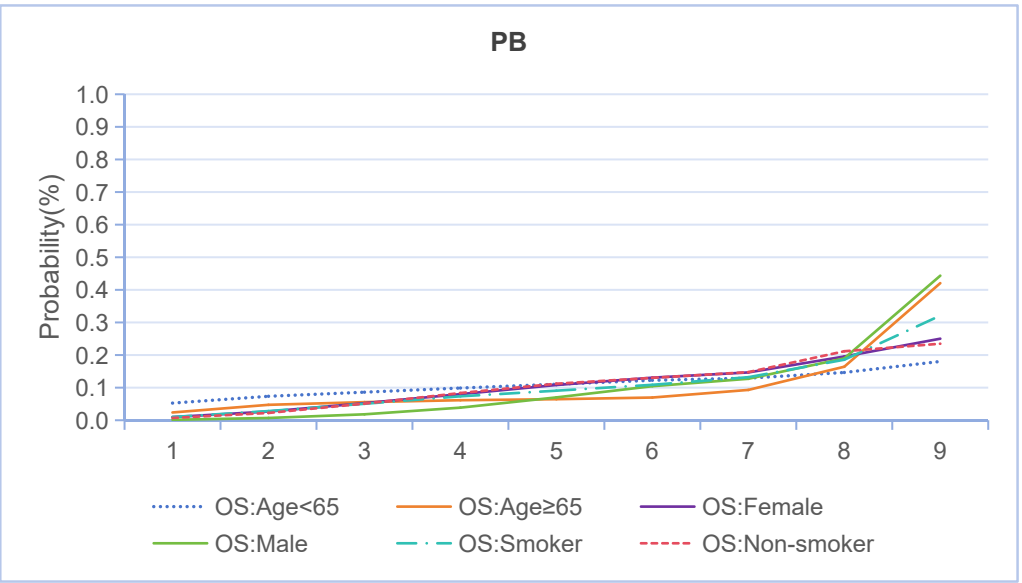
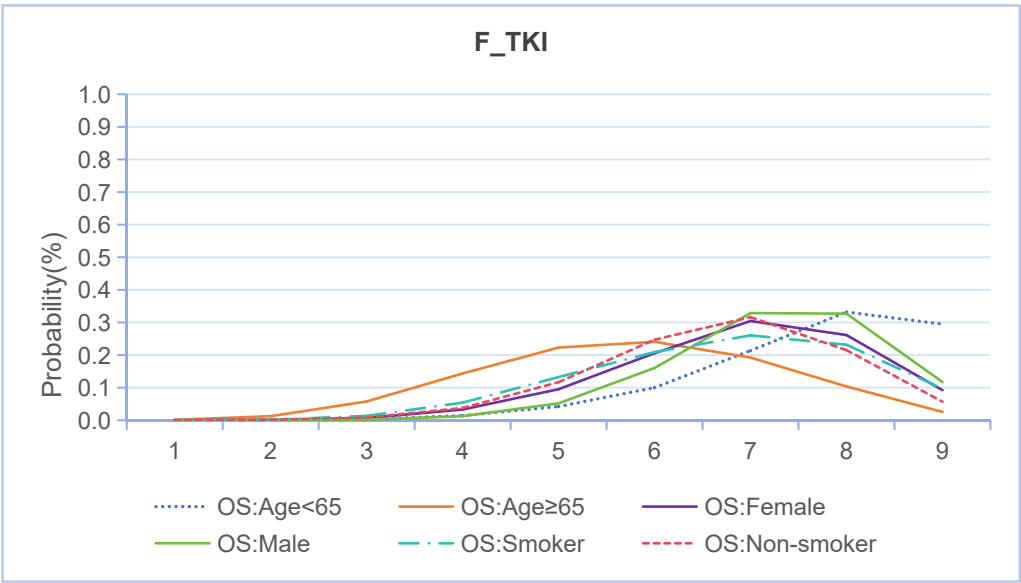
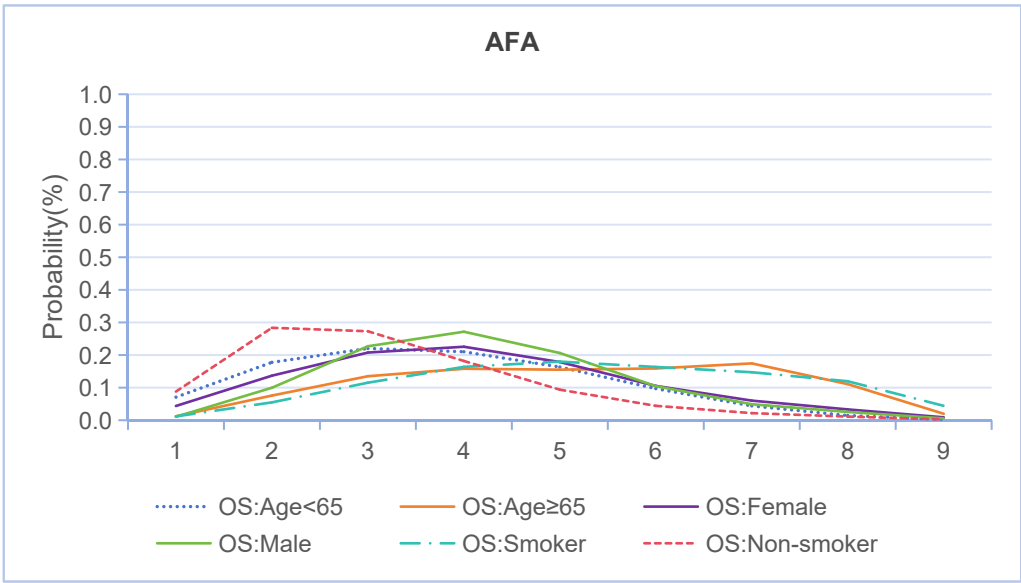
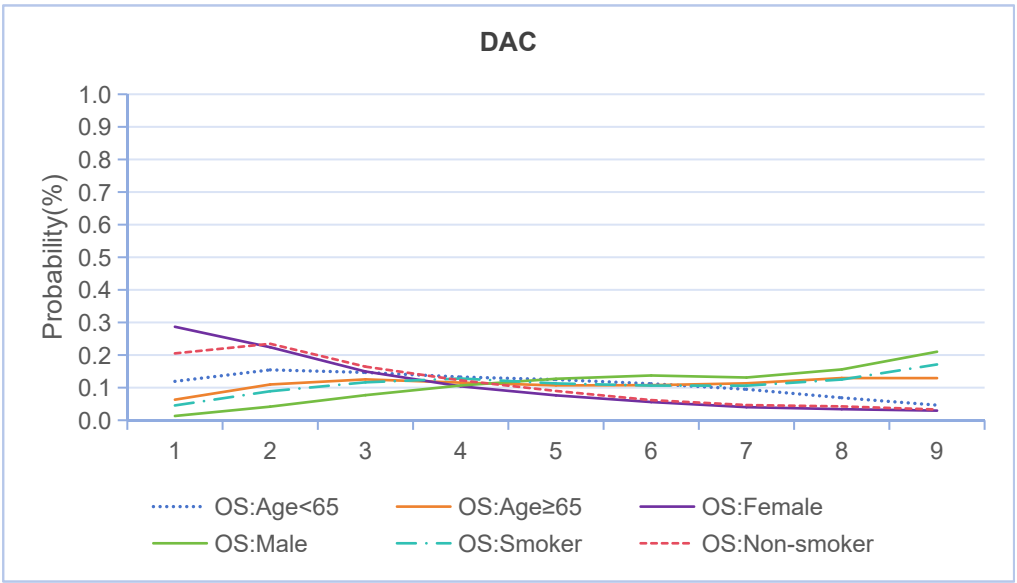
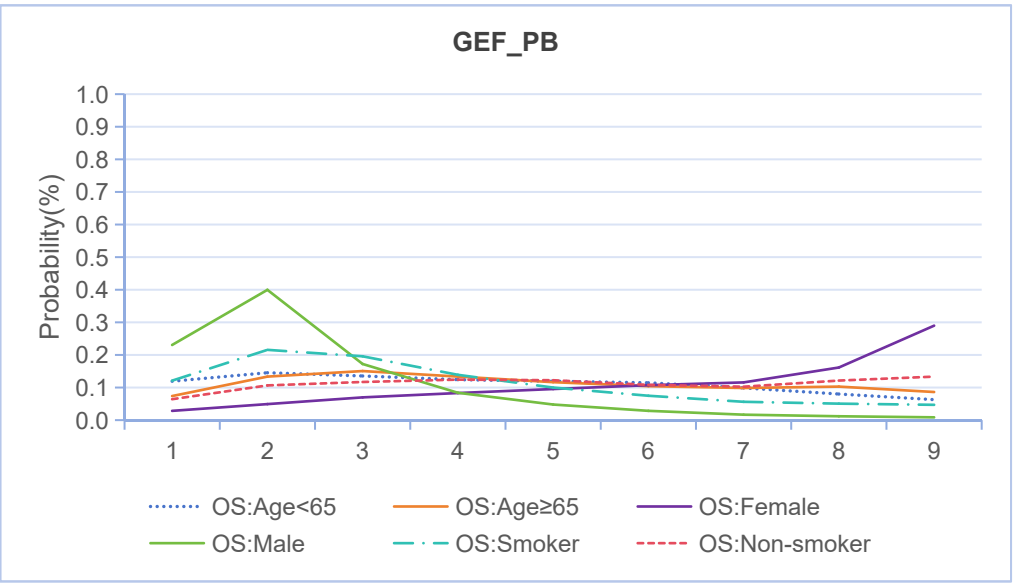
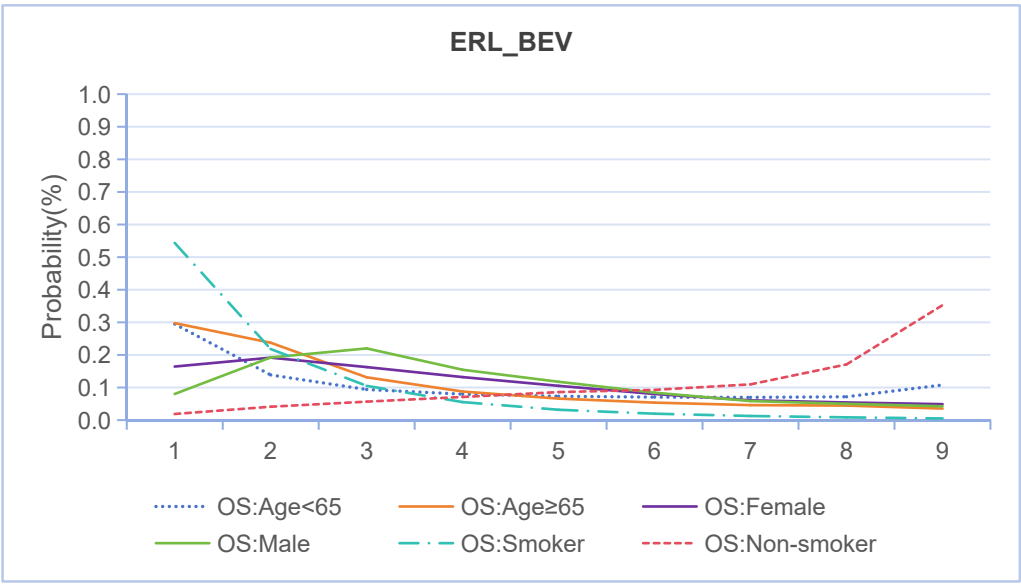
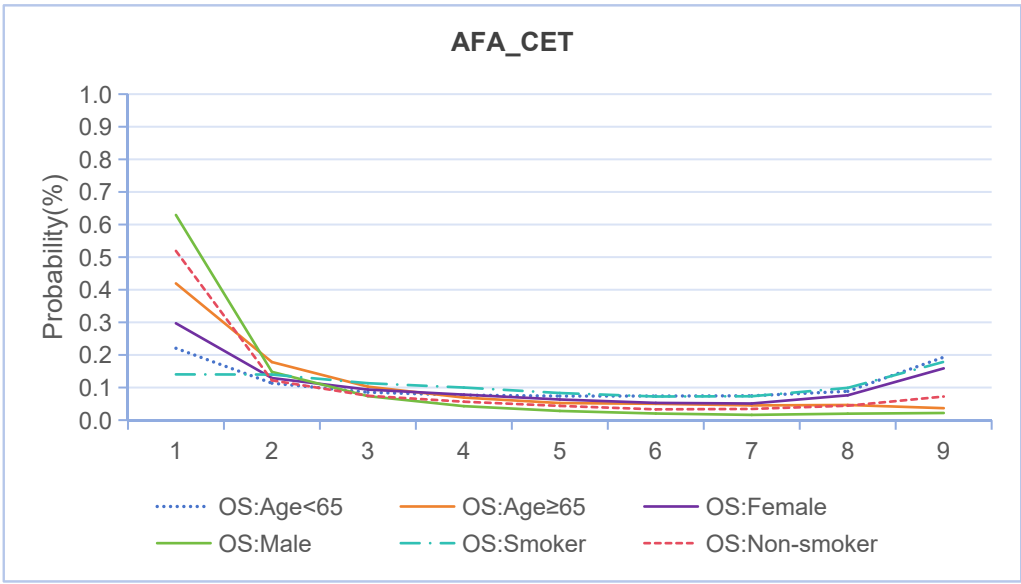
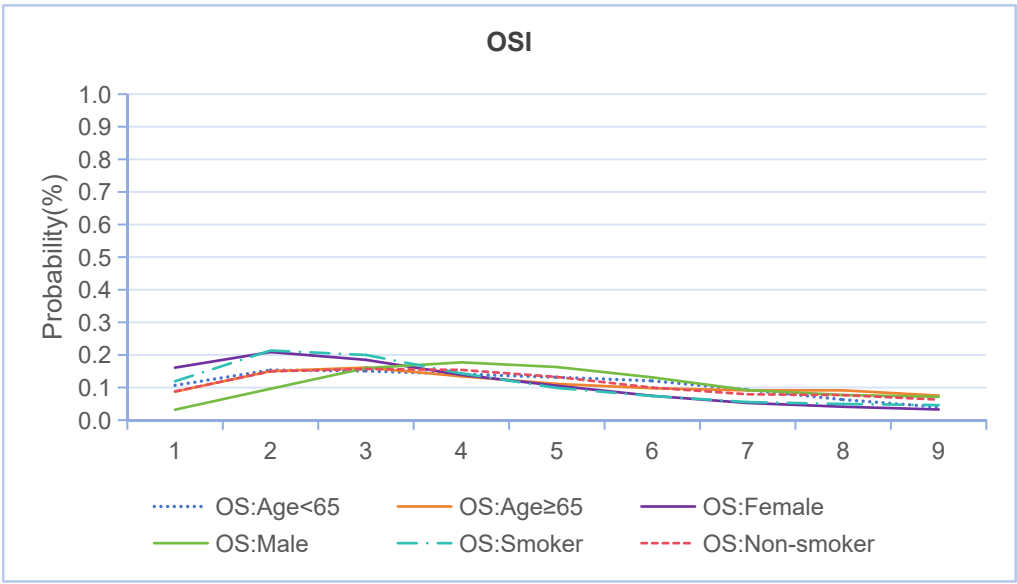
A



B



C



D



E

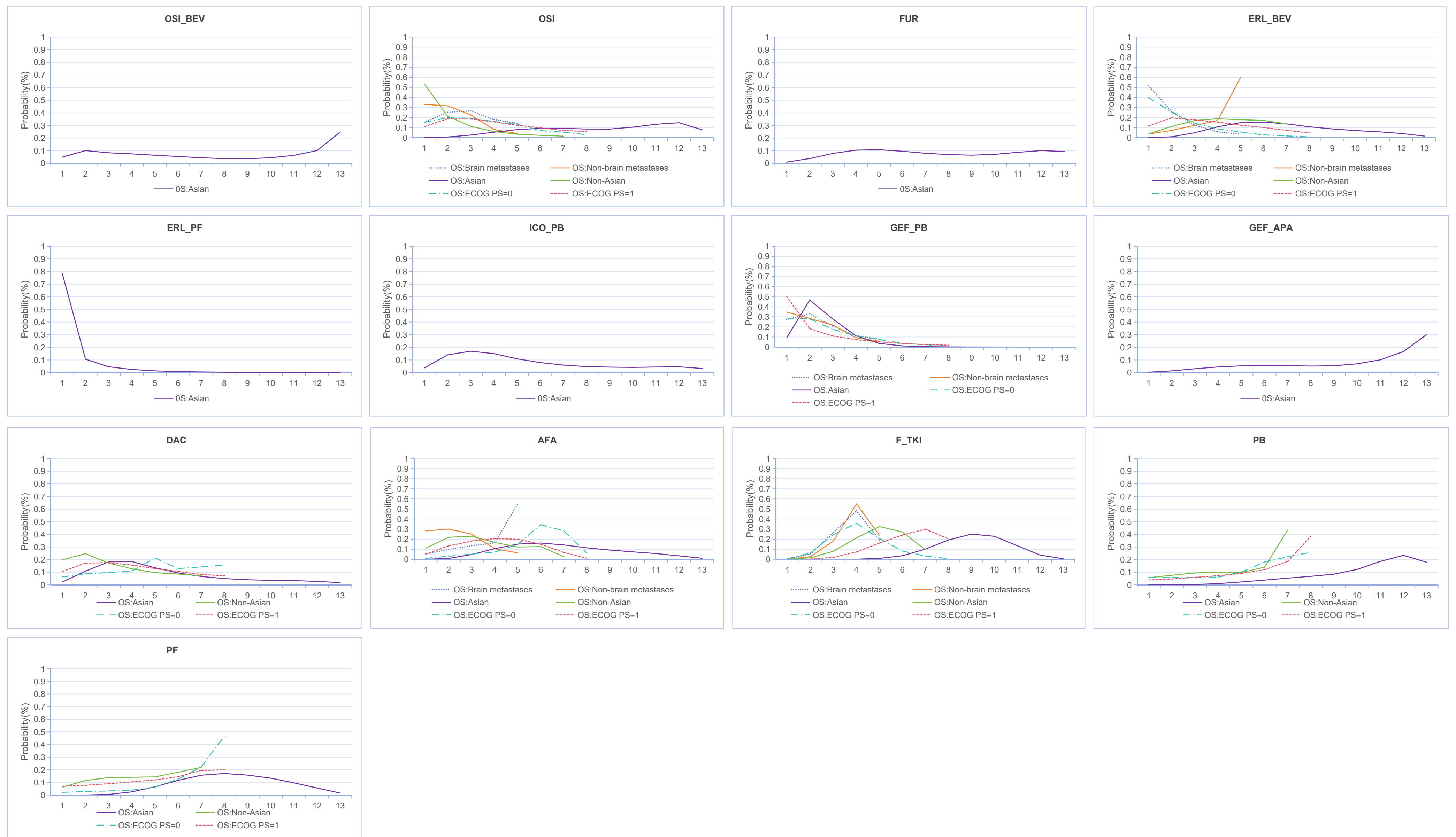


Figure S12. Bayesian ranking profiles of comparable treatments on PFS and for patients with advanced EGFR mutated NSCLC based on clinicopathological characteristics.

A

	Mutation subtype				Sex		Smoking		Age		ECOG		Brain metastasis		Ethnicity		Sensitivity analysis					
	PFS	ORR	≥3AEs	19DEL	21L858R	Male	Female	Yes	No	<65	≥65	PS=0	PS=1	Yes	No	Asian	Non-asian	PFS	ORR	≥3AEs	19DEL	21L858R
OSI_RAM	99	41	29	75	82	41	94	36	69	80	90			73	65	100	88					
OSI_PB	78	77	63	88	93	86	90	82	92	80	86	81	95	88	77	86	88	91	75	61	90	94
AMI_LAZ	74	55	58	85	84	71	88	73	89	85	65	81	87	71	82	75	79	87	54	56	87	85
AUM_APA	68	64														73		77	63			
OSI_BEV	65	34	23	84	47	69	71	88	45			73	72	58	61	60						
FUR	63	59	12	76	62	77	60	56	74	71	49	77	65	48	64	67		70	58	12	78	65
AUM	61	39	26	70	52	56	74	53	77	62	64	73	63	64	49	64		67	40	25	72	56
OSI	61	49	12	63	66	52	71	61	69	61	71	70	62	48	55	50	68	68	49	12	65	69
GEF_PB	58	88	64	52	61	52	57	54	57	58	58	53	54	61	50	57		62	89	60	59	66
BEF	58	41	51	66	48	61	62	56	68	64	39	70	58	50	52	60		63	41	49	67	52
ERL_RAM	49	40	52	38	49	62	32	51	41	54	40	48	37			41	51	48	40	51	38	53
ICO_PB	49	75		37	58	72	37	80	42	33	90	42	65			47						
DAC	49	45	56	49	47	39	58	39	62	55	48	42	53			57	33	48	45	55	49	52
ERL_BEV	46	58	77	44	52	58	44	62	43	50	49	52	45	36	39	50	43	46	63	68	37	59
ERL_PF	41	99	66													36		38	97	66		
GEF_APA	40	46	92	37	36	42	33	35	38	43	32	33	39	18	30	35		36	46	91	37	41
AFA_CET	32	42	84	28	61	54	26	42	29	28	46											
AFA	29	64	39	36	30	28	31	36	31	35	36	27	31	26	21	22	44	26	53	46	47	32
F_TKI	21	30	22	15	13	18	14	18	17	22	20	18	12	10	5	15	25	16	31	20	16	17
PB	6	5	50	6	7	11	6	26	7	16	16	10	12			5	27	7	6	53	8	9
PF	1	1	75	0	0	1	0	1	0	2	0	1	0			0	4	0	1	76	0	0

B

	Mutation subtype				Sex		Smoking		Age		ECOG		Brain metastasis		Ethnicity		Sensitivity analysis					
	OS	ORR	≥3AEs	19DEL	21L858R	Male	Female	Yes	No	<65	≥65	PS=0	PS=1	Yes	No	Asian	Non-asian	OS	ORR	≥3AEs	19DEL	21L858R
OSI_RAM		41	29																			
OSI_PB	66	77	63															66	75	61		
AMI_LAZ	78	55	58															78	54	56		
AUM_APA		64																	63			
OSI_BEV	56	34	23													42						
FUR	34	59	12													45		36	58	12		
AUM		39	26																40	25		
OSI	55	49	12	72	35	51	67	64	57	58	55	64	59	52	70	35	83	55	49	12	72	38
GEF_PB	79	88	64	58	50	80	31	64	47	56	52	76	82	65	69	87		79	89	60	59	53
BEF		41	51																41	49		
ERL_RAM	49	40	52															51	40	51		
ICO_PB	52	75														62						
DAC	62	45	56	45	76	34	73	43	70	58	46	42	57			64	63	62	45	55	46	76
ERL_BEV	39	58	77	48	74	62	64	88	27	63	73	81	60	79	20	50	43	43	63	68	42	83
ERL_PF	92	99	66													96		92	97	66		
GEF_APA	19	46	92													26		20	46	91		
AFA_CET	62	42	84	79	54	87	60	51	77	53	76											
AFA	41	64	39	73	27	60	61	45	72	65	47	32	55	24	66	50	59	41	53	46	85	19
F_TKI	21	30	22	26	31	22	26	28	29	16	41	56	24	30	25	32	33	23	31	20	29	36
PB	17	5	50	10	59	18	29	26	29	40	25	31	26			21	29	23	6	53	19	54
PF	28	1	75	40	44	37	39	41	44	40	35	19	38			39	40	30	1	76	49	41

Figure S13. Bayesian ranking profiles of comparable treatments on efficacy and safety for patients with advanced EGFR mutated NSCLC. **(A)** Number (percentage of surface under the cumulative ranking curve (SUCRA)) in each cell indicates the probability of each treatment being ranked from first (high value) to last (low value) on overall PFS, ORR, ≥3AEs, and PFS for subgroups. **(B)** Number (percentage of SUCRA) in each cell indicates the probability of each treatment being ranked from first (high value) to last (low value) on overall OS, ORR, ≥3AEs, and OS for subgroups.

A

OS

PFS

OSI_PB	1.12 (0.61,2.05)		0.77 (0.36,1.62)		0.9 (0.58,1.4)		1.09 (0.58,2.17)	0.87 (0.39,1.92)	0.81 (0.43,1.55)	1.54 (0.64,3.72)	0.65 (0.3,1.42)	0.95 (0.46,1.92)	0.8 (0.4,1.58)	0.72 (0.4,1.29)	0.7 (0.35,1.38)	0.74 (0.4,1.37)
0.89 (0.4,1.96)	AMI_LAZ		0.68 (0.32,1.42)		0.8 (0.53,1.2)		0.97 (0.53,1.89)	0.78 (0.36,1.67)	0.72 (0.39,1.34)	1.37 (0.58,3.25)	0.58 (0.27,1.24)	0.84 (0.42,1.67)	0.71 (0.37,1.37)	0.64 (0.37,1.12)	0.62 (0.32,1.2)	0.66 (0.37,1.19)
0.77 (0.21,2.91)	0.87 (0.23,3.25)	AUM_APA														
0.63 (0.24,1.7)	0.71 (0.27,1.9)	0.82 (0.25,2.72)	FUR		1.17 (0.64,2.17)		1.43 (0.83,2.58)	1.14 (0.56,2.34)	1.06 (0.61,1.85)	2.02 (0.89,4.57)	0.85 (0.42,1.72)	1.24 (0.66,2.31)	1.04 (0.58,1.9)	0.94 (0.58,1.52)	0.91 (0.51,1.66)	0.97 (0.58,1.62)
0.61 (0.23,1.63)	0.68 (0.26,1.81)	0.79 (0.32,1.92)	0.96 (0.42,2.16)	AUM												
0.62 (0.35,1.1)	0.7 (0.4,1.21)	0.8 (0.24,2.65)	0.98 (0.44,2.2)	1.02 (0.46,2.28)	OSI		1.22 (0.77,2.04)	0.97 (0.5,1.86)	0.9 (0.57,1.44)	1.72 (0.8,3.68)	0.73 (0.38,1.37)	1.05 (0.6,1.83)	0.89 (0.53,1.49)	0.8 (0.55,1.17)	0.78 (0.46,1.31)	0.83 (0.54,1.26)
0.57 (0.21,1.56)	0.64 (0.24,1.73)	0.74 (0.22,2.49)	0.9 (0.39,2.06)	0.94 (0.41,2.15)	0.92 (0.4,2.09)	BEF										
0.56 (0.23,1.37)	0.63 (0.26,1.53)	0.72 (0.23,2.25)	0.88 (0.44,1.79)	0.92 (0.46,1.86)	0.9 (0.45,1.8)	0.98 (0.48,2.02)	GEF_PB	0.79 (0.42,1.45)	0.74 (0.48,1.1)	1.41 (0.67,2.88)	0.6 (0.32,1.07)	0.87 (0.51,1.4)	0.73 (0.44,1.14)	0.66 (0.47,0.87)	0.64 (0.39,1)	0.68 (0.46,0.95)
0.47 (0.18,1.26)	0.53 (0.2,1.41)	0.61 (0.18,2.03)	0.75 (0.33,1.69)	0.78 (0.35,1.75)	0.76 (0.34,1.7)	0.83 (0.36,1.9)	0.85 (0.42,1.7)	ERL_RAM	0.93 (0.51,1.72)	1.77 (0.76,4.2)	0.75 (0.36,1.58)	1.09 (0.55,2.14)	0.92 (0.48,1.75)	0.83 (0.48,1.42)	0.8 (0.42,1.54)	0.85 (0.48,1.51)
0.46 (0.19,1.1)	0.52 (0.22,1.22)	0.6 (0.2,1.81)	0.73 (0.37,1.43)	0.76 (0.39,1.48)	0.74 (0.38,1.43)	0.81 (0.4,1.62)	0.83 (0.48,1.4)	0.98 (0.5,1.89)	ERL_BEV	1.9 (0.93,3.88)	0.81 (0.45,1.44)	1.17 (0.71,1.89)	0.98 (0.63,1.54)	0.89 (0.67,1.16)	0.86 (0.55,1.34)	0.92 (0.66,1.27)
0.4 (0.14,1.16)	0.45 (0.15,1.29)	0.52 (0.14,1.86)	0.64 (0.25,1.57)	0.66 (0.26,1.63)	0.65 (0.26,1.59)	0.71 (0.27,1.78)	0.72 (0.31,1.61)	0.85 (0.34,2.08)	0.87 (0.39,1.92)	ERL_PF	0.42 (0.18,0.98)	0.61 (0.28,1.33)	0.52 (0.25,1.06)	0.47 (0.24,0.9)	0.45 (0.22,0.94)	0.48 (0.25,0.91)
0.39 (0.15,1.07)	0.44 (0.17,1.18)	0.51 (0.15,1.7)	0.62 (0.27,1.41)	0.65 (0.29,1.47)	0.63 (0.28,1.43)	0.69 (0.3,1.59)	0.7 (0.35,1.43)	0.83 (0.37,1.88)	0.85 (0.43,1.69)	0.98 (0.39,2.49)	GEF_APA	1.45 (0.75,2.79)	1.22 (0.65,2.29)	1.1 (0.66,1.85)	1.07 (0.58,2)	1.14 (0.66,1.98)
0.47 (0.18,1.26)	0.53 (0.2,1.4)	0.61 (0.19,2.02)	0.75 (0.33,1.67)	0.78 (0.35,1.74)	0.76 (0.34,1.69)	0.83 (0.36,1.89)	0.85 (0.42,1.69)	1 (0.45,2.22)	1.02 (0.53,2)	1.17 (0.48,2.95)	1.2 (0.54,2.71)	DAC	0.84 (0.49,1.45)	0.76 (0.51,1.14)	0.74 (0.43,1.27)	0.78 (0.5,1.23)
0.34 (0.13,0.86)	0.38 (0.15,0.96)	0.43 (0.13,1.41)	0.53 (0.24,1.14)	0.55 (0.25,1.19)	0.54 (0.25,1.15)	0.59 (0.26,1.3)	0.6 (0.31,1.15)	0.71 (0.33,1.52)	0.73 (0.39,1.36)	0.83 (0.36,1.93)	0.85 (0.39,1.84)	0.71 (0.33,1.52)	AFA	0.9 (0.63,1.29)	0.88 (0.62,1.24)	0.93 (0.66,1.31)
0.28 (0.13,0.63)	0.32 (0.14,0.69)	0.36 (0.13,1.04)	0.44 (0.25,0.79)	0.46 (0.26,0.82)	0.45 (0.26,0.79)	0.49 (0.27,0.89)	0.5 (0.33,0.75)	0.59 (0.33,1.04)	0.6 (0.43,0.86)	0.69 (0.34,1.44)	0.71 (0.4,1.27)	0.59 (0.34,1.04)	0.83 (0.5,1.41)	F_TKI	0.97 (0.69,1.38)	1.03 (0.86,1.24)
0.18 (0.07,0.47)	0.21 (0.08,0.52)	0.24 (0.07,0.76)	0.29 (0.13,0.62)	0.3 (0.14,0.64)	0.3 (0.14,0.62)	0.32 (0.15,0.7)	0.33 (0.17,0.62)	0.39 (0.18,0.82)	0.4 (0.21,0.73)	0.45 (0.2,1.07)	0.47 (0.21,1)	0.39 (0.18,0.82)	0.55 (0.33,0.89)	0.66 (0.39,1.08)	PB	1.06 (0.74,1.53)
0.1 (0.04,0.23)	0.11 (0.05,0.26)	0.13 (0.04,0.38)	0.16 (0.08,0.29)	0.17 (0.09,0.3)	0.16 (0.09,0.3)	0.18 (0.09,0.34)	0.18 (0.11,0.29)	0.21 (0.11,0.39)	0.22 (0.14,0.33)	0.25 (0.13,0.49)	0.26 (0.13,0.48)	0.21 (0.11,0.39)	0.3 (0.18,0.49)	0.36 (0.28,0.46)	0.55 (0.32,0.93)	PF

B

ORR

≥3AEs																
OSI_PB	1.17 (0.14,9.89)		5.13 (0.36,73.53)	2.87 (0.21,39.28)	4.71 (1.04,21.31)	1.41 (0.1,19.46)	1.06 (0.1,11.58)	1.34 (0.1,18.36)	0.88 (0.09,8.94)	0.88 (0.06,12.94)	0.33 (0.02,4.61)	1.21 (0.09,16.59)	1.52 (0.12,18.52)	2.96 (0.35,24.85)	1.28 (0.1,15.29)	0.74 (0.08,6.88)
1.49 (0.5,4.39)	AMI_LAZ		4.39 (0.31,62.04)	2.46 (0.18,33.46)	4.04 (0.9,18.07)	1.21 (0.09,16.25)	0.91 (0.08,9.83)	1.15 (0.08,15.64)	0.76 (0.08,7.67)	0.75 (0.05,11.07)	0.29 (0.02,3.93)	1.03 (0.08,14.12)	1.3 (0.1,15.72)	2.53 (0.31,21.19)	1.1 (0.09,13.02)	0.64 (0.07,5.87)
1.22 (0.22,6.77)	0.82 (0.15,4.48)	AUM_APA														
1.4 (0.34,5.65)	0.94 (0.23,3.81)	1.14 (0.23,5.64)	FUR	0.56 (0.06,5.02)	0.92 (0.1,8.14)	0.27 (0.03,2.47)	0.21 (0.03,1.4)	0.26 (0.03,2.35)	0.17 (0.03,1.07)	0.17 (0.02,1.67)	0.06 (0.01,0.6)	0.24 (0.03,2.09)	0.3 (0.04,2.33)	0.58 (0.12,2.8)	0.25 (0.03,1.91)	0.14 (0.03,0.8)
1.87 (0.49,7.19)	1.25 (0.33,4.79)	1.53 (0.53,4.55)	1.34 (0.41,4.42)	AUM	1.65 (0.19,13.93)	0.49 (0.06,4.26)	0.37 (0.06,2.42)	0.47 (0.05,4)	0.31 (0.05,1.82)	0.31 (0.03,2.9)	0.12 (0.01,1.04)	0.42 (0.05,3.6)	0.53 (0.07,3.98)	1.03 (0.22,4.71)	0.45 (0.06,3.27)	0.26 (0.05,1.36)
1.61 (0.74,3.48)	1.08 (0.5,2.31)	1.32 (0.29,6.11)	1.15 (0.36,3.74)	0.86 (0.29,2.58)	OSI	0.3 (0.04,2.55)	0.22 (0.04,1.44)	0.28 (0.03,2.4)	0.19 (0.03,1.09)	0.19 (0.02,1.72)	0.07 (0.01,0.61)	0.26 (0.03,2.17)	0.32 (0.04,2.37)	0.63 (0.14,2.82)	0.27 (0.04,1.96)	0.16 (0.03,0.81)
1.83 (0.48,7)	1.23 (0.32,4.68)	1.5 (0.33,7.04)	1.31 (0.4,4.33)	0.98 (0.32,2.96)	1.14 (0.38,3.42)	BEF	0.75 (0.12,4.94)	0.95 (0.11,8.2)	0.63 (0.11,3.72)	0.62 (0.06,5.9)	0.24 (0.03,2.11)	0.86 (0.1,7.34)	1.08 (0.14,8.15)	2.1 (0.45,9.68)	0.91 (0.12,6.67)	0.53 (0.1,2.78)
0.71 (0.21,2.44)	0.48 (0.14,1.63)	0.58 (0.14,2.51)	0.51 (0.18,1.49)	0.38 (0.14,1)	0.44 (0.17,1.16)	0.39 (0.15,1.03)	GEF_PB	1.26 (0.19,8.18)	0.84 (0.2,3.43)	0.83 (0.11,5.95)	0.31 (0.05,2.13)	1.14 (0.17,7.29)	1.44 (0.25,7.92)	2.79 (0.94,8.29)	1.21 (0.21,6.47)	0.7 (0.19,2.5)
1.87 (0.48,7.17)	1.26 (0.33,4.8)	1.53 (0.33,7.21)	1.34 (0.41,4.41)	1 (0.33,3.04)	1.16 (0.39,3.49)	1.02 (0.34,3.1)	2.63 (0.99,6.96)	ERL_RAM	0.66 (0.11,3.88)	0.66 (0.07,6.16)	0.25 (0.03,2.21)	0.9 (0.11,7.66)	1.14 (0.15,8.45)	2.21 (0.48,10.11)	0.96 (0.13,6.96)	0.56 (0.1,2.91)
1.32 (0.39,4.4)	0.89 (0.27,2.93)	1.08 (0.26,4.5)	0.95 (0.34,2.64)	0.71 (0.28,1.8)	0.82 (0.32,2.07)	0.72 (0.28,1.84)	1.86 (0.85,4.01)	0.71 (0.28,1.8)	ERL_BEV	0.99 (0.15,6.53)	0.38 (0.06,2.3)	1.36 (0.23,7.93)	1.72 (0.33,8.56)	3.34 (1.35,8.32)	1.45 (0.29,6.97)	0.84 (0.27,2.59)
0.3 (0.05,1.65)	0.2 (0.03,1.1)	0.24 (0.04,1.61)	0.22 (0.04,1.05)	0.16 (0.03,0.74)	0.19 (0.04,0.85)	0.16 (0.03,0.76)	0.42 (0.09,1.77)	0.16 (0.03,0.74)	0.23 (0.05,0.92)	ERL_PF	0.38 (0.04,3.71)	1.37 (0.15,12.97)	1.73 (0.24,12.44)	3.36 (0.65,17.77)	1.46 (0.19,10.97)	0.84 (0.19,3.84)
1.71 (0.43,6.7)	1.15 (0.29,4.48)	1.4 (0.29,6.72)	1.22 (0.36,4.14)	0.91 (0.29,2.85)	1.06 (0.34,3.28)	0.93 (0.3,2.92)	2.4 (0.87,6.54)	0.91 (0.29,2.85)	1.29 (0.49,3.44)	5.7 (1.2,28.91)	GEF_APA	3.63 (0.41,31.84)	4.56 (0.57,35.3)	8.87 (1.87,42.38)	3.85 (0.49,29.01)	2.23 (0.4,12.21)
1.72 (0.45,6.59)	1.16 (0.31,4.39)	1.41 (0.31,6.63)	1.23 (0.38,4.04)	0.92 (0.31,2.79)	1.07 (0.36,3.2)	0.94 (0.31,2.84)	2.42 (0.92,6.39)	0.92 (0.31,2.78)	1.3 (0.52,3.33)	5.72 (1.26,28.8)	1.01 (0.33,3.15)	DAC	1.26 (0.16,9.44)	2.45 (0.54,11.24)	1.06 (0.14,7.78)	0.61 (0.12,3.22)
1.53 (0.42,5.67)	1.02 (0.28,3.76)	1.25 (0.28,5.69)	1.09 (0.35,3.47)	0.82 (0.28,2.37)	0.95 (0.33,2.74)	0.83 (0.29,2.43)	2.15 (0.87,5.38)	0.82 (0.28,2.37)	1.16 (0.48,2.81)	5.08 (1.22,23.42)	0.9 (0.3,2.69)	0.89 (0.31,2.54)	AFA	1.94 (0.52,7.62)	0.84 (0.23,3.01)	0.49 (0.14,1.77)
2.05 (0.69,6.1)	1.38 (0.47,4.06)	1.68 (0.45,6.35)	1.46 (0.61,3.6)	1.09 (0.5,2.4)	1.28 (0.59,2.75)	1.12 (0.51,2.46)	2.88 (1.62,5.13)	1.09 (0.5,2.41)	1.55 (0.93,2.61)	6.77 (1.84,28.22)	1.2 (0.53,2.76)	1.19 (0.55,2.57)	1.34 (0.65,2.72)	F_TKI	0.43 (0.11,1.57)	0.25 (0.13,0.49)
7.16 (1.98,25.96)	4.8 (1.34,17.34)	5.87 (1.32,26.04)	5.11 (1.69,15.86)	3.83 (1.35,10.84)	4.46 (1.6,12.45)	3.9 (1.38,11.14)	10.06 (4.14,24.58)	3.84 (1.36,10.84)	5.41 (2.33,12.77)	23.77 (5.61,111.25)	4.19 (1.45,12.28)	4.16 (1.49,11.65)	4.68 (2.36,9.27)	3.5 (1.78,6.91)	PB	0.58 (0.15,2.3)
9.92 (3.19,31.84)	6.66 (2.17,21.22)	8.15 (2.1,32.7)	7.09 (2.78,19.05)	5.31 (2.28,12.79)	6.17 (2.69,14.69)	5.4 (2.33,13.07)	13.96 (7.19,27.97)	5.31 (2.28,12.82)	7.5 (4.09,14.33)	32.88 (9.51,131.61)	5.81 (2.4,14.72)	5.76 (2.5,13.73)	6.49 (3.33,13.04)	4.85 (3.44,7.04)	1.39 (0.69,2.85)	PF

C

PFS (19DEL)

PFS (21L858R)														
OSI_PB	0.81 (0.4,1.64)	0.59 (0.24,1.46)	0.53 (0.21,1.34)	0.63 (0.37,1.06)	0.51 (0.19,1.36)	0.59 (0.26,1.36)	0.52 (0.21,1.27)	0.55 (0.24,1.24)	0.45 (0.18,1.12)	0.51 (0.21,1.25)	0.39 (0.16,0.96)	0.32 (0.15,0.67)	0.24 (0.1,0.59)	0.15 (0.07,0.32)
0.92 (0.37,2.27)	AMI_LAZ	0.73 (0.31,1.77)	0.66 (0.27,1.61)	0.78 (0.48,1.25)	0.63 (0.24,1.64)	0.73 (0.33,1.63)	0.64 (0.27,1.53)	0.68 (0.31,1.48)	0.55 (0.22,1.35)	0.63 (0.26,1.5)	0.48 (0.2,1.16)	0.4 (0.2,0.8)	0.3 (0.13,0.71)	0.18 (0.09,0.39)
0.73 (0.23,2.3)	0.8 (0.26,2.47)	FUR	0.9 (0.42,1.94)	1.06 (0.51,2.22)	0.86 (0.37,2)	1 (0.52,1.93)	0.88 (0.42,1.83)	0.93 (0.48,1.76)	0.75 (0.34,1.63)	0.86 (0.41,1.81)	0.65 (0.31,1.39)	0.54 (0.32,0.92)	0.41 (0.19,0.86)	0.25 (0.14,0.46)
0.66 (0.22,2.03)	0.71 (0.24,2.17)	0.9 (0.35,2.33)	AUM	1.18 (0.55,2.5)	0.96 (0.4,2.24)	1.11 (0.56,2.18)	0.97 (0.45,2.06)	1.03 (0.53,2)	0.83 (0.38,1.82)	0.96 (0.45,2.06)	0.72 (0.33,1.57)	0.6 (0.34,1.05)	0.45 (0.21,0.96)	0.28 (0.15,0.52)
0.6 (0.31,1.15)	0.65 (0.35,1.21)	0.82 (0.32,2.08)	0.91 (0.36,2.26)	OSI	0.81 (0.35,1.86)	0.94 (0.5,1.78)	0.82 (0.4,1.7)	0.88 (0.46,1.62)	0.71 (0.33,1.51)	0.81 (0.39,1.68)	0.61 (0.29,1.3)	0.51 (0.31,0.85)	0.38 (0.19,0.79)	0.23 (0.13,0.42)
0.61 (0.2,1.92)	0.67 (0.22,2.05)	0.83 (0.32,2.19)	0.93 (0.36,2.38)	1.02 (0.4,2.6)	BEF	1.17 (0.54,2.52)	1.02 (0.44,2.34)	1.08 (0.51,2.3)	0.87 (0.37,2.08)	1 (0.43,2.32)	0.76 (0.32,1.79)	0.63 (0.33,1.22)	0.48 (0.21,1.1)	0.29 (0.14,0.6)
0.54 (0.19,1.49)	0.58 (0.21,1.59)	0.73 (0.31,1.68)	0.81 (0.36,1.81)	0.89 (0.41,1.97)	0.87 (0.39,1.99)	GEF_PB	0.87 (0.46,1.66)	0.93 (0.54,1.57)	0.75 (0.38,1.48)	0.86 (0.45,1.64)	0.65 (0.34,1.27)	0.54 (0.37,0.8)	0.41 (0.22,0.78)	0.25 (0.15,0.4)
0.4 (0.13,1.21)	0.43 (0.14,1.31)	0.54 (0.21,1.39)	0.6 (0.24,1.51)	0.66 (0.27,1.65)	0.65 (0.25,1.66)	0.74 (0.33,1.64)	ERL_RAM	1.06 (0.56,1.99)	0.86 (0.4,1.84)	0.99 (0.47,2.04)	0.75 (0.36,1.57)	0.62 (0.37,1.03)	0.47 (0.23,0.96)	0.29 (0.16,0.51)
0.4 (0.15,1.08)	0.43 (0.16,1.15)	0.54 (0.24,1.21)	0.6 (0.28,1.3)	0.66 (0.31,1.42)	0.65 (0.29,1.44)	0.74 (0.4,1.38)	1 (0.46,2.17)	ERL_BEV	0.81 (0.41,1.59)	0.93 (0.5,1.75)	0.7 (0.37,1.37)	0.58 (0.41,0.85)	0.44 (0.24,0.83)	0.27 (0.17,0.43)
0.38 (0.12,1.2)	0.42 (0.14,1.28)	0.52 (0.2,1.38)	0.58 (0.23,1.5)	0.64 (0.25,1.63)	0.63 (0.24,1.65)	0.72 (0.31,1.63)	0.97 (0.38,2.49)	0.97 (0.44,2.15)	GEF_APA	1.15 (0.53,2.48)	0.87 (0.4,1.89)	0.72 (0.41,1.27)	0.54 (0.26,1.16)	0.33 (0.18,0.62)
0.47 (0.15,1.43)	0.51 (0.17,1.53)	0.64 (0.25,1.65)	0.71 (0.28,1.78)	0.78 (0.32,1.94)	0.76 (0.3,1.95)	0.87 (0.4,1.93)	1.18 (0.47,2.96)	1.18 (0.55,2.54)	1.22 (0.48,3.13)	DAC	0.76 (0.36,1.6)	0.63 (0.37,1.06)	0.47 (0.23,0.97)	0.29 (0.16,0.52)
0.45 (0.15,1.34)	0.49 (0.16,1.42)	0.62 (0.24,1.53)	0.68 (0.27,1.64)	0.75 (0.3,1.8)	0.74 (0.29,1.82)	0.84 (0.38,1.79)	1.14 (0.45,2.76)	1.14 (0.52,2.37)	1.18 (0.46,2.91)	0.96 (0.38,2.31)	AFA	0.83 (0.48,1.42)	0.63 (0.38,1.03)	0.38 (0.23,0.64)
0.26 (0.1,0.64)	0.28 (0.11,0.68)	0.35 (0.17,0.7)	0.39 (0.2,0.75)	0.43 (0.23,0.81)	0.42 (0.21,0.83)	0.48 (0.3,0.76)	0.65 (0.34,1.25)	0.65 (0.43,0.98)	0.67 (0.34,1.33)	0.55 (0.29,1.05)	0.57 (0.31,1.1)	F_TKI	0.75 (0.45,1.25)	0.46 (0.34,0.61)
0.15 (0.05,0.43)	0.16 (0.05,0.46)	0.2 (0.08,0.5)	0.22 (0.09,0.53)	0.24 (0.1,0.58)	0.24 (0.1,0.59)	0.27 (0.13,0.58)	0.37 (0.15,0.89)	0.37 (0.18,0.76)	0.38 (0.15,0.94)	0.31 (0.13,0.75)	0.33 (0.18,0.6)	0.57 (0.31,1.03)	PB	0.61 (0.36,1.04)
0.08 (0.03,0.2)	0.08 (0.03,0.21)	0.11 (0.05,0.22)	0.12 (0.05,0.23)	0.13 (0.06,0.25)	0.13 (0.06,0.26)	0.14 (0.08,0.25)	0.19 (0.09,0.39)	0.19 (0.11,0.32)	0.2 (0.09,0.41)	0.17 (0.08,0.33)	0.17 (0.09,0.31)	0.3 (0.21,0.41)	0.53 (0.27,0.97)	PF

D

OS (19DEL)

OS (21L858R)								
OSI	1.13 (0.51,2.48)	1.69 (0.64,4.48)	1.42 (0.64,3.14)	0.85 (0.39,1.83)	1 (0.58,1.73)	1.13 (0.53,2.37)	1.02 (0.53,1.97)	
0.87 (0.33,2.35)	GEF_PB	1.5 (0.56,4.03)	1.26 (0.56,2.82)	0.75 (0.35,1.66)	0.89 (0.5,1.57)	1 (0.47,2.14)	0.91 (0.46,1.78)	
0.73 (0.25,2.21)	0.84 (0.28,2.55)	ERL_BEV	0.83 (0.31,2.28)	0.5 (0.19,1.35)	0.59 (0.26,1.34)	0.66 (0.25,1.76)	0.6 (0.25,1.48)	
0.77 (0.29,2.09)	0.89 (0.32,2.44)	1.06 (0.35,3.22)	DAC	0.6 (0.27,1.33)	0.71 (0.4,1.25)	0.79 (0.37,1.71)	0.72 (0.37,1.43)	
1.17 (0.45,3.04)	1.34 (0.51,3.55)	1.6 (0.54,4.71)	1.51 (0.57,4.03)	AFA	1.18 (0.68,2.03)	1.32 (0.78,2.24)	1.21 (0.73,1.98)	
0.68 (0.34,1.36)	0.78 (0.38,1.59)	0.93 (0.39,2.19)	0.88 (0.43,1.81)	0.58 (0.3,1.12)	F_TKI	1.13 (0.67,1.87)	1.02 (0.71,1.47)	
0.6 (0.24,1.51)	0.69 (0.27,1.76)	0.82 (0.29,2.34)	0.77 (0.3,2)	0.51 (0.28,0.94)	0.88 (0.47,1.63)	PB	0.91 (0.52,1.59)	
0.79 (0.35,1.78)	0.9 (0.4,2.09)	1.08 (0.42,2.81)	1.02 (0.45,2.37)	0.67 (0.37,1.25)	1.16 (0.76,1.79)	1.32 (0.68,2.57)	PF	

Figure S14. Network meta-analysis of the sensitive analysis excluding phase II Trials. **(A)** Pooled hazard ratios (95% credible intervals) for progression-free survival (PFS) (lower triangle) and overall survival(OS) (upper triangle). The result in each cell is presented as hazard ratio (95% credible interval) for the comparison of row-defining treatment versus column-defining treatment. Hazard ratio <1 favors row-defining treatment. Significant results are in red. **(B)** Pooled odds ratios (95% credible intervals) for objective response rate (ORR) (lower triangle) and grade 3 or higher adverse events (≥3AEs) (upper triangle). **(C)** Pooled hazard ratios (95% credible intervals) for PFS of exon 19 deletion (lower triangle) and Leu858Arg (upper triangle) subpopulations. **(D)** Pooled hazard ratios (95% credible interval) for OS of exon 19 deletion (lower triangle) and Leu858Arg (upper triangle) subpopulations.

PFS

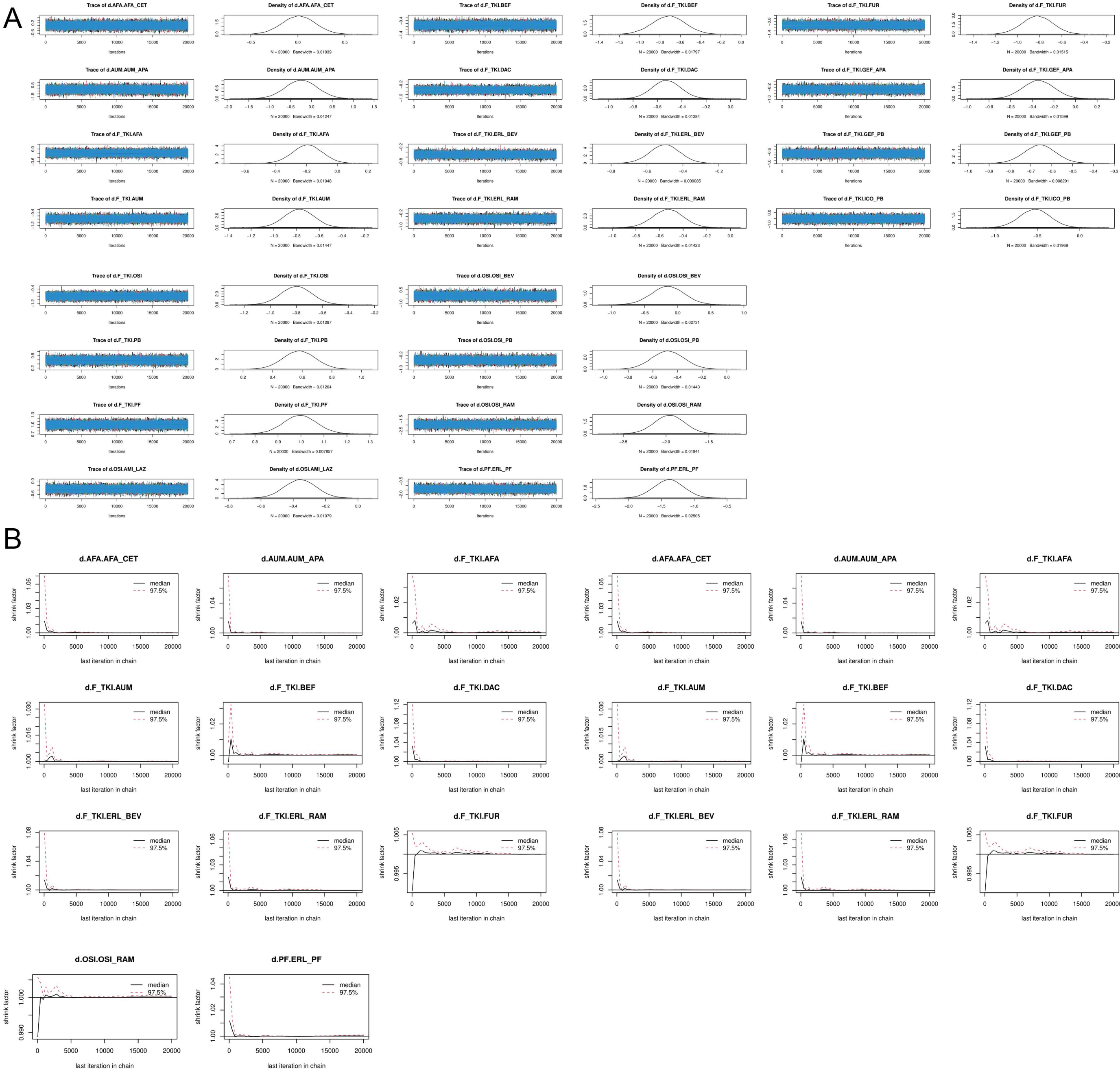


Figure S15. Convergence of the Four Chains Established by Inspection of the Trace Plot and the Brooks-Gelman-Rubin Diagnostic for progression-free survival in overall analysis.

OS

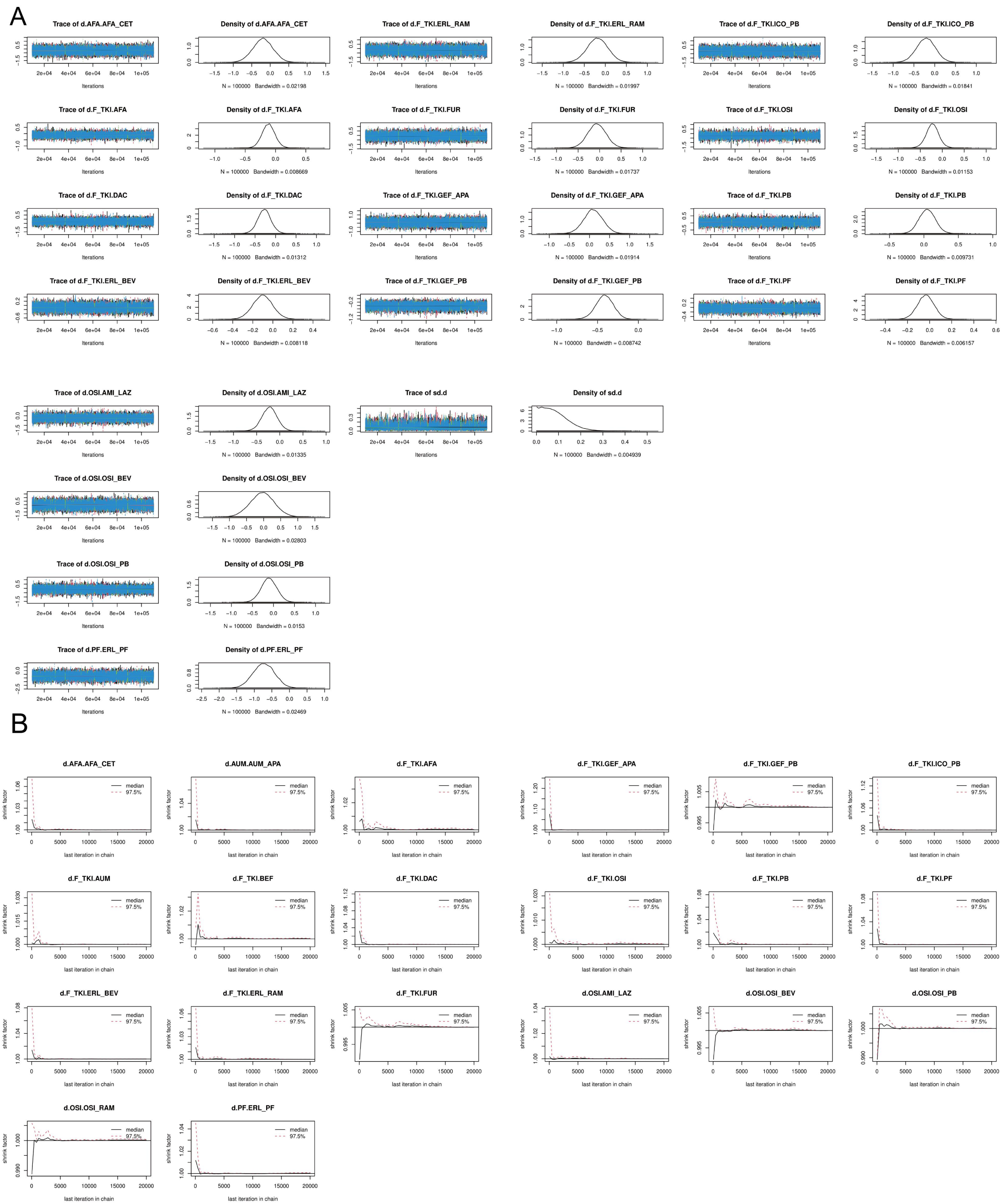
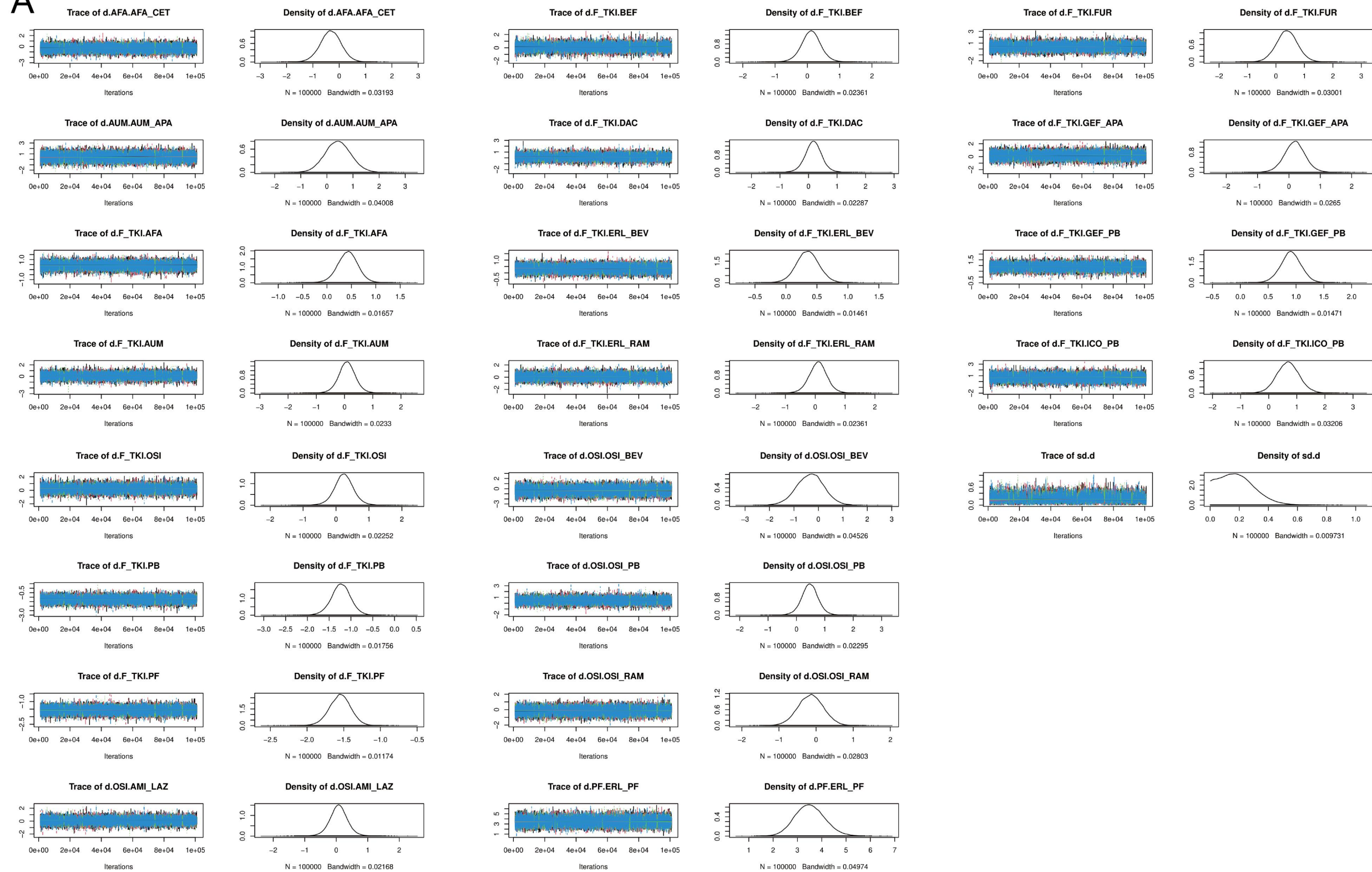


Figure S16.Convergence of the Four Chains Established by Inspection of the Trace Plot and the Brooks-Gelman-Rubin Diagnostic for overall survival in overall analysis.

ORR

A



B

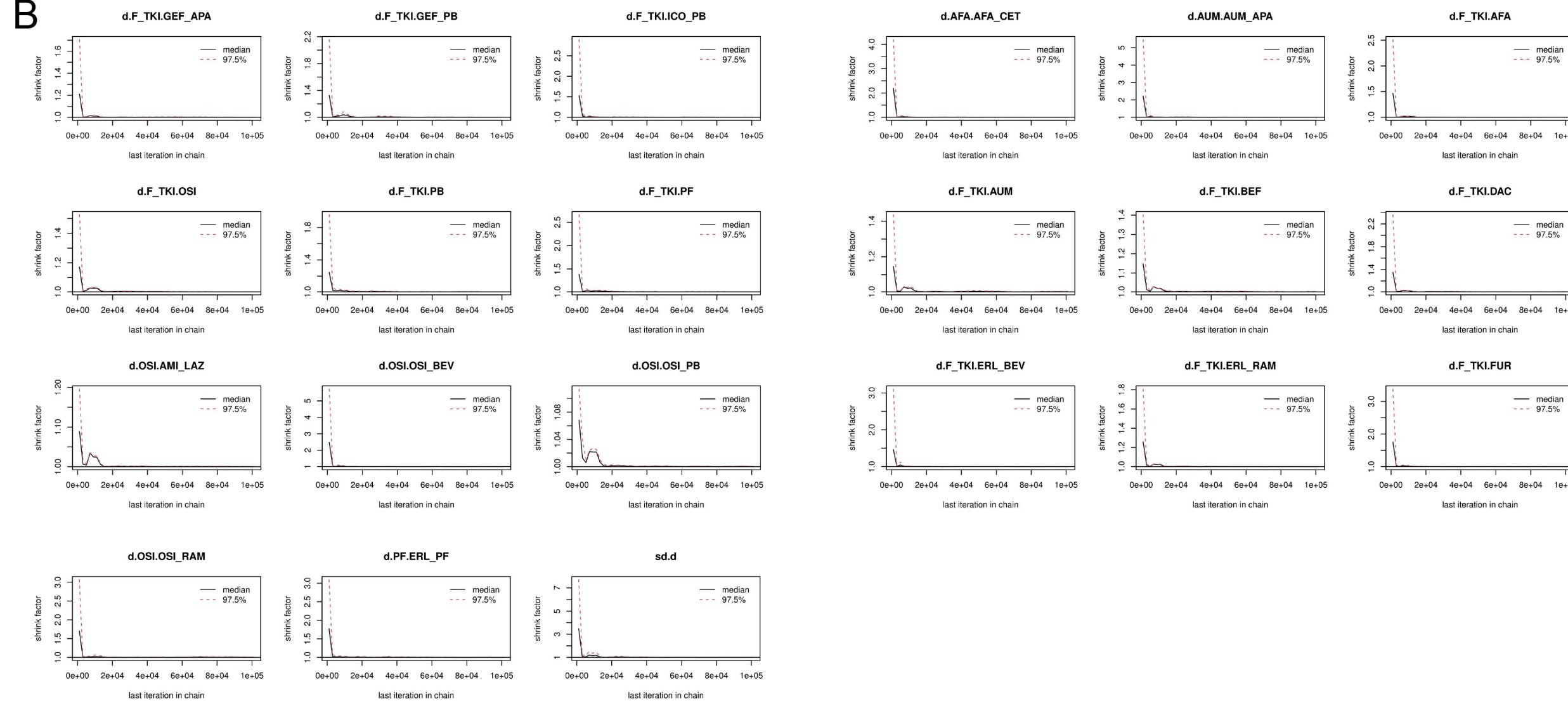


Figure S17.Convergence of the Four Chains Established by Inspection of the Trace Plot and the Brooks-Gelman-Rubin Diagnostic for objective response rate.

$\geq 3AEs$



Figure S18.Convergence of the Four Chains Established by Inspection of the Trace Plot and the Brooks-Gelman-Rubin Diagnostic for grade 3 or higher adverse events.

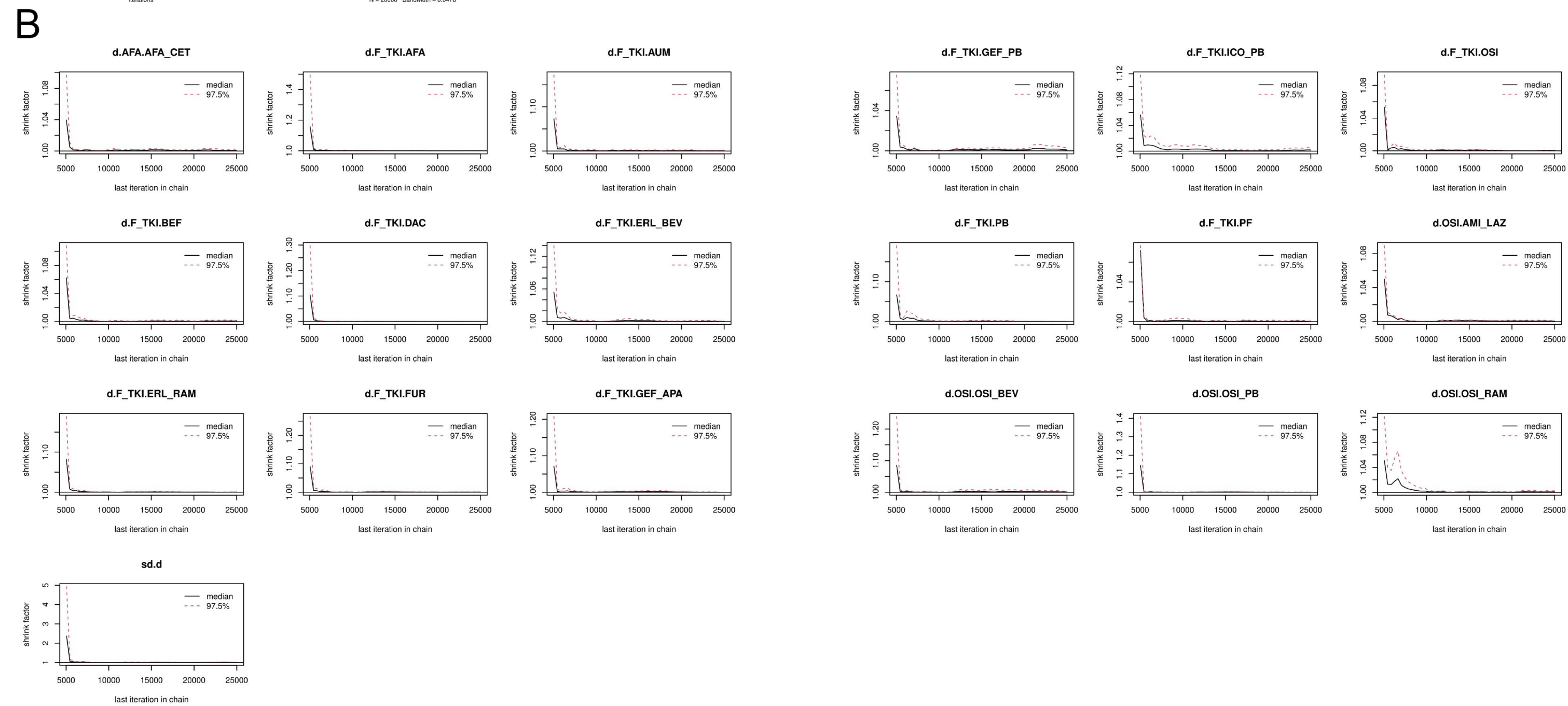
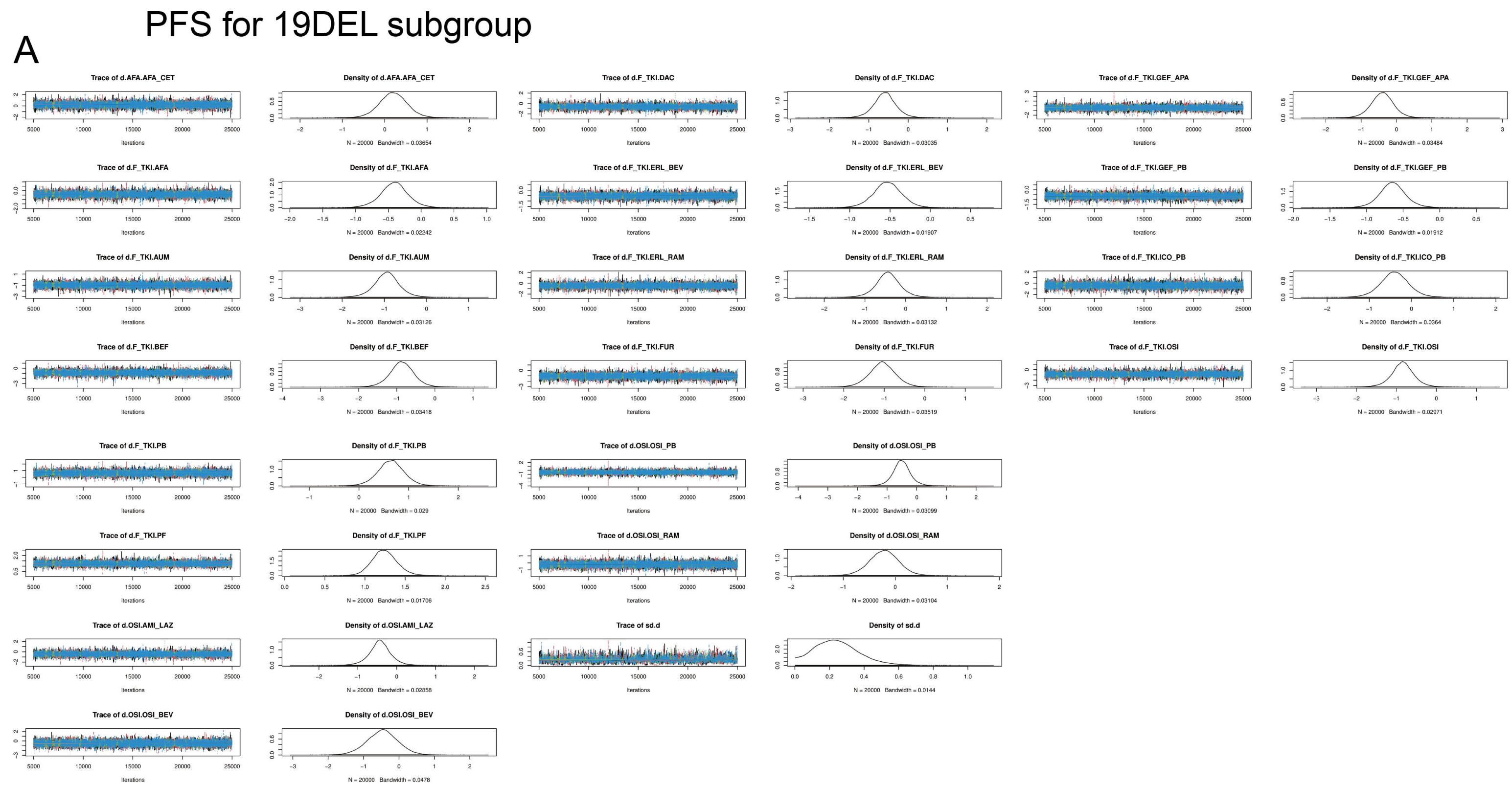
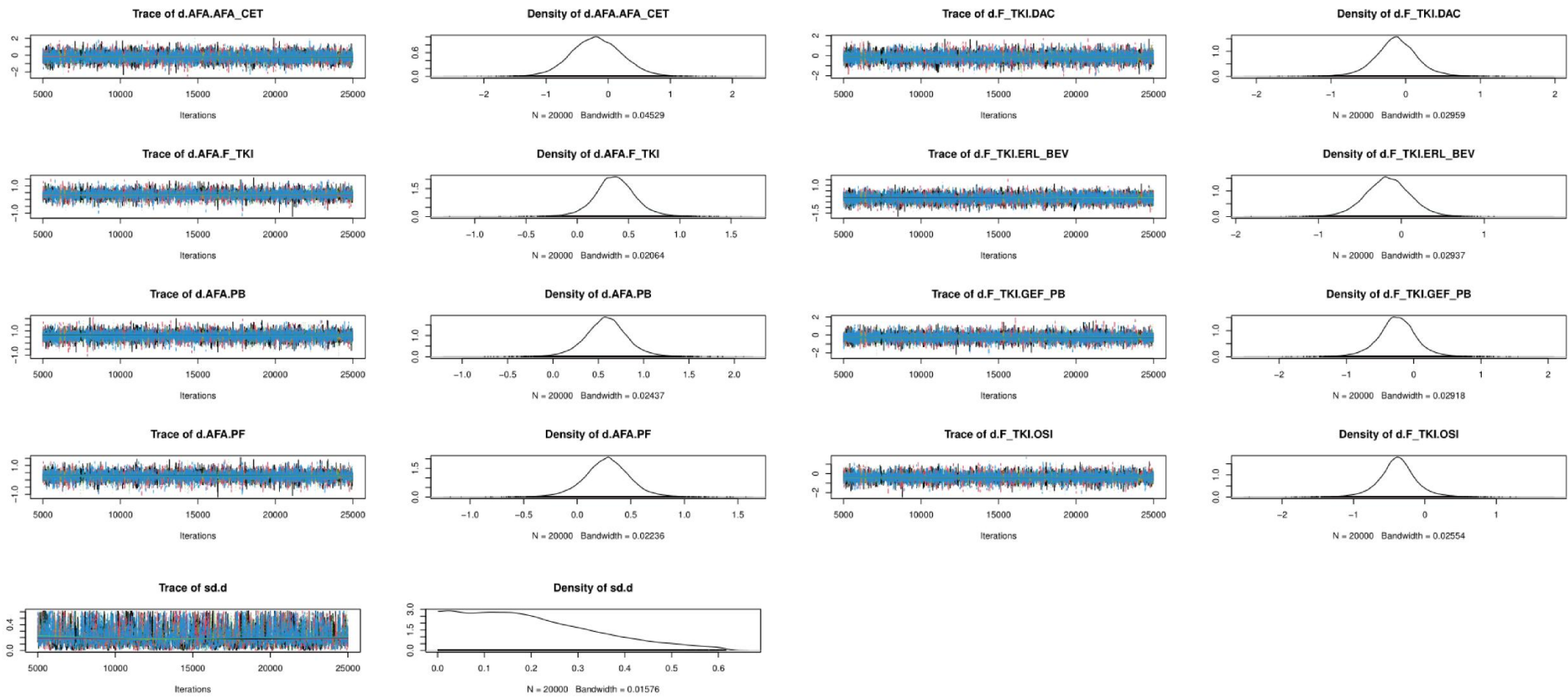


Figure S19.Convergence of the Four Chains Established by Inspection of the Trace Plot and the Brooks-Gelman-Rubin Diagnostic for progression-free survival in 19DEL subgroup.

OS for 19DEL subgroup

A



B

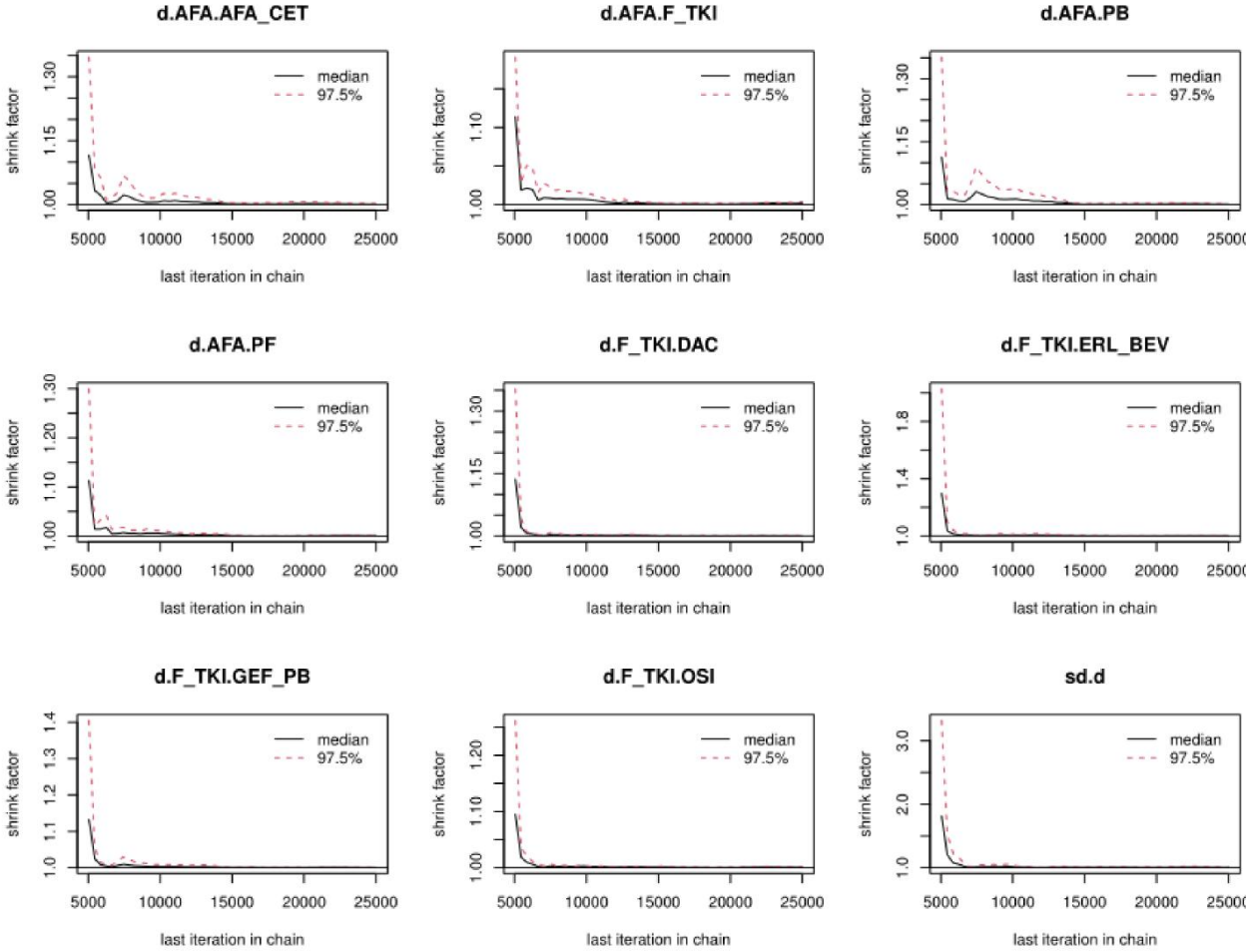


Figure S20.Convergence of the Four Chains Established by Inspection of the Trace Plot and the Brooks-Gelman-Rubin Diagnostic for overall survival in 19DEL subgroup.

A

PFS for 21L858R subgroup

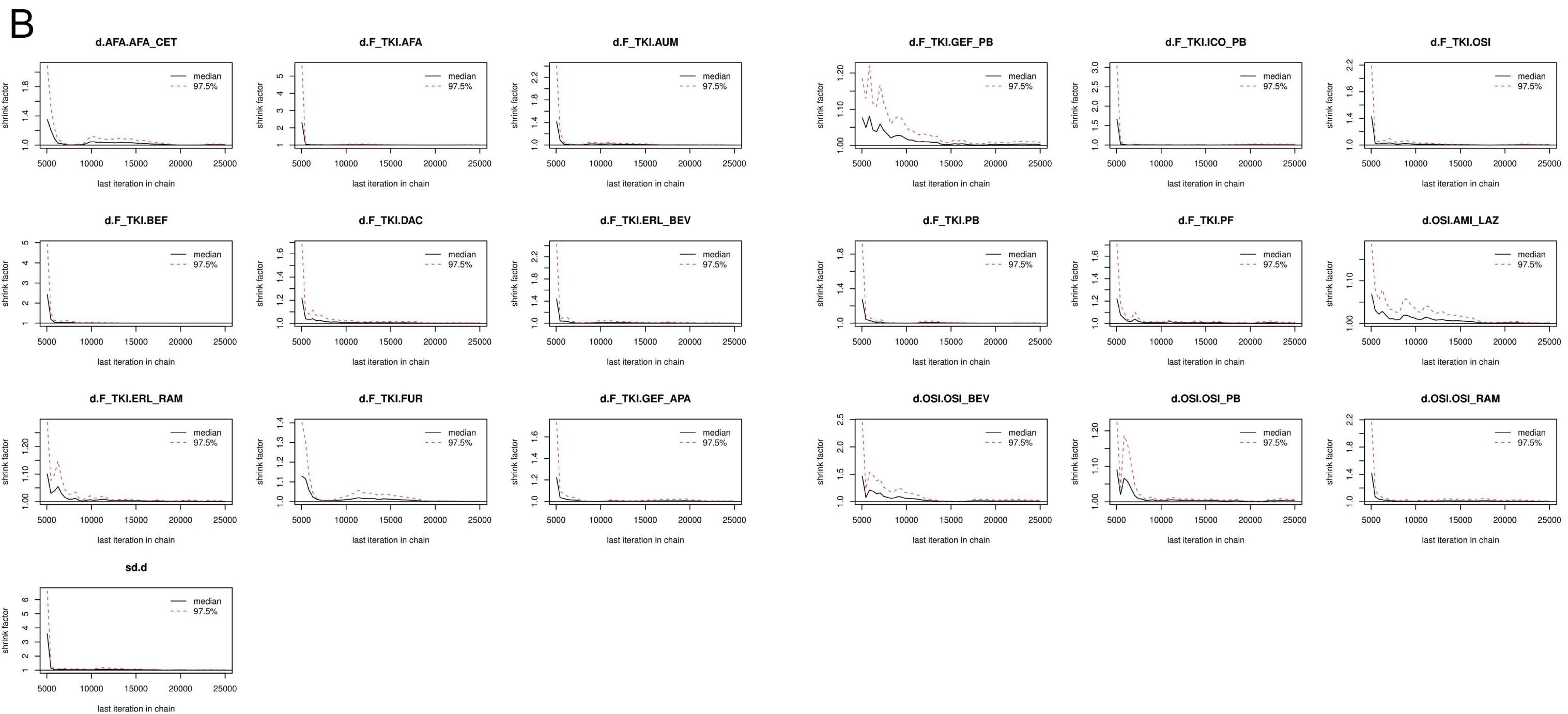
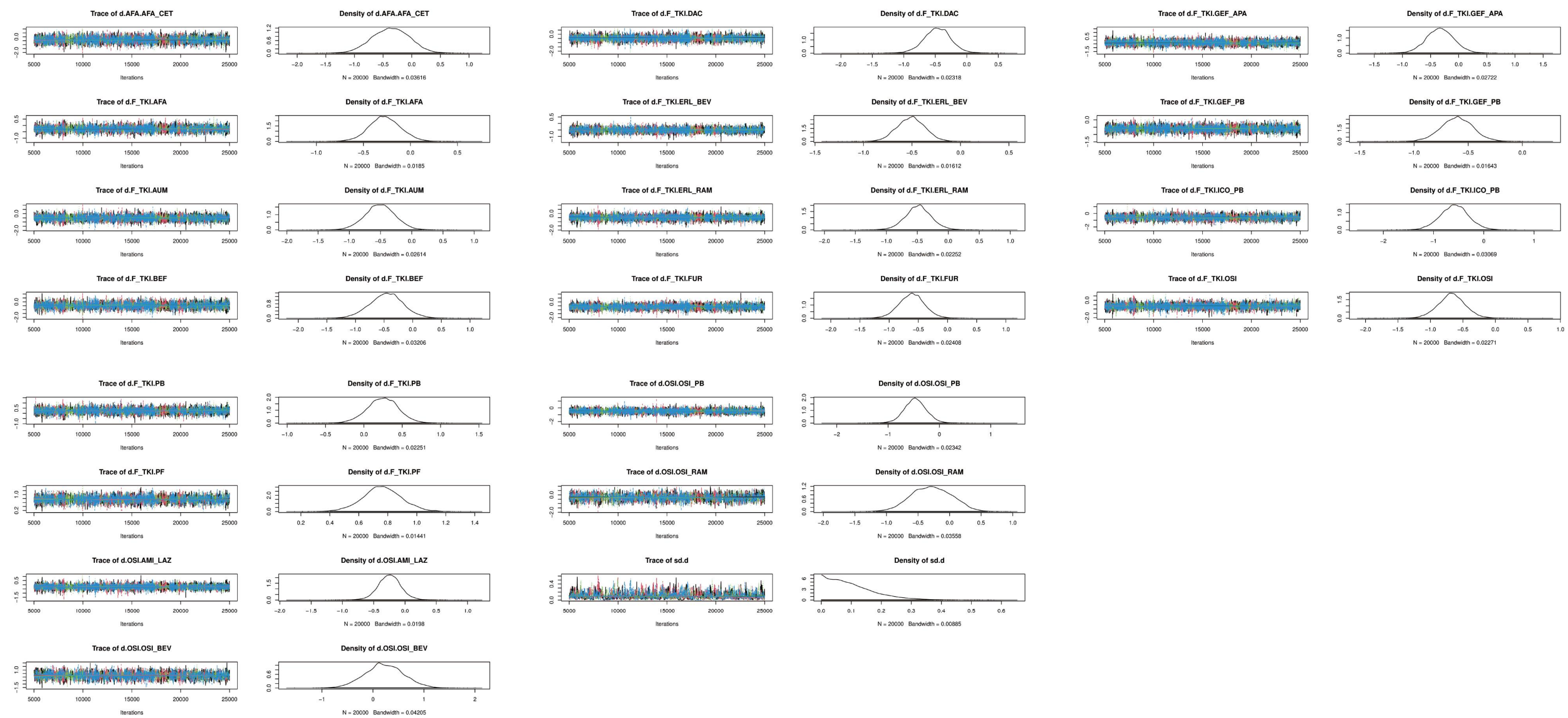


Figure S21. Convergence of the Four Chains Established by Inspection of the Trace Plot and the Brooks-Gelman-Rubin Diagnostic for progression-free survival in 21L858R subgroup.

OS for 21L858R subgroup

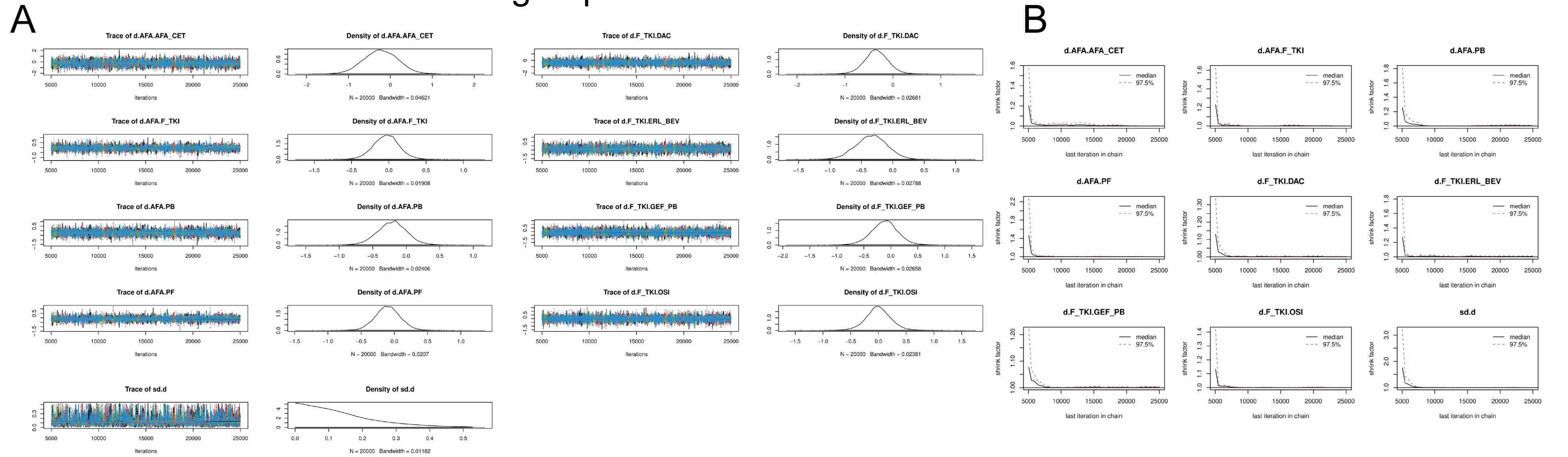


Figure S22. Convergence of the Four Chains Established by Inspection of the Trace Plot and the Brooks-Gelman-Rubin Diagnostic for overall survival in 21L858R subgroup.

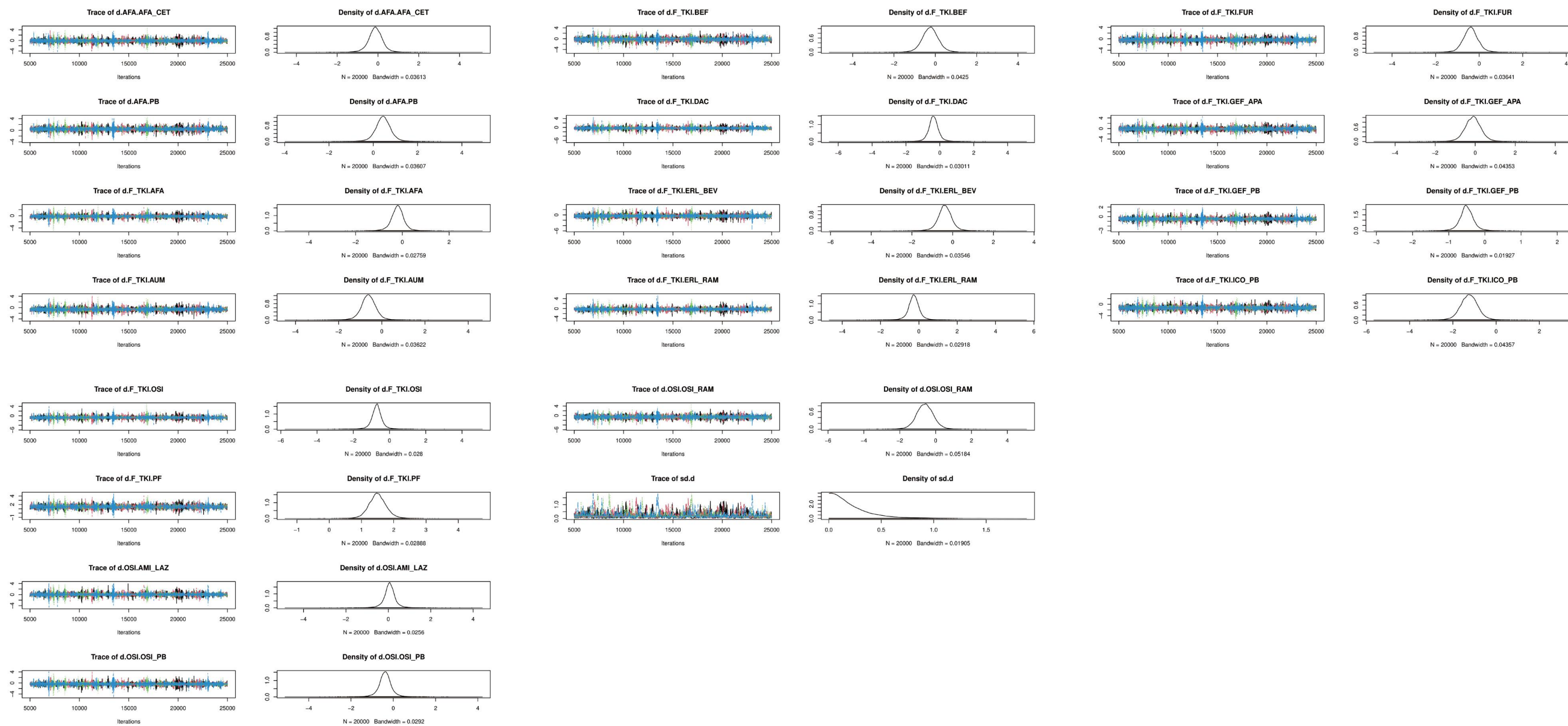
PFS for age < 65



Figure S23. Convergence of the Four Chains Established by Inspection of the Trace Plot and the Brooks-Gelman-Rubin Diagnostic for progression-free survival in age < 65 subgroup.

PFS for age ≥ 65

A



B

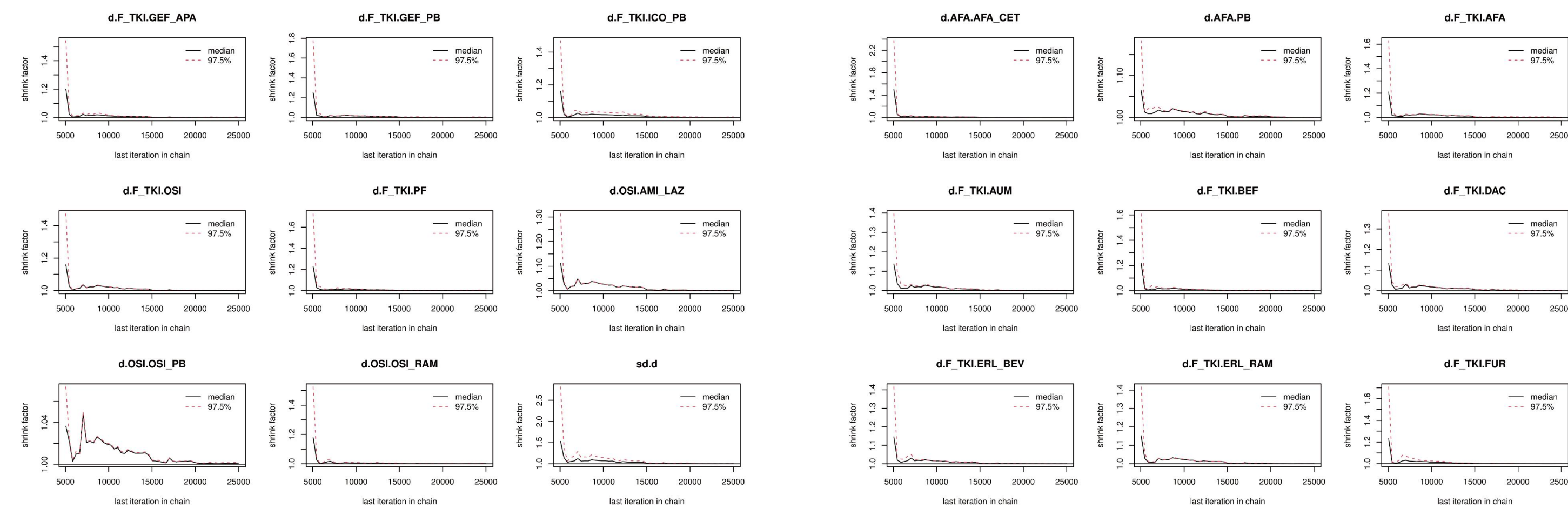
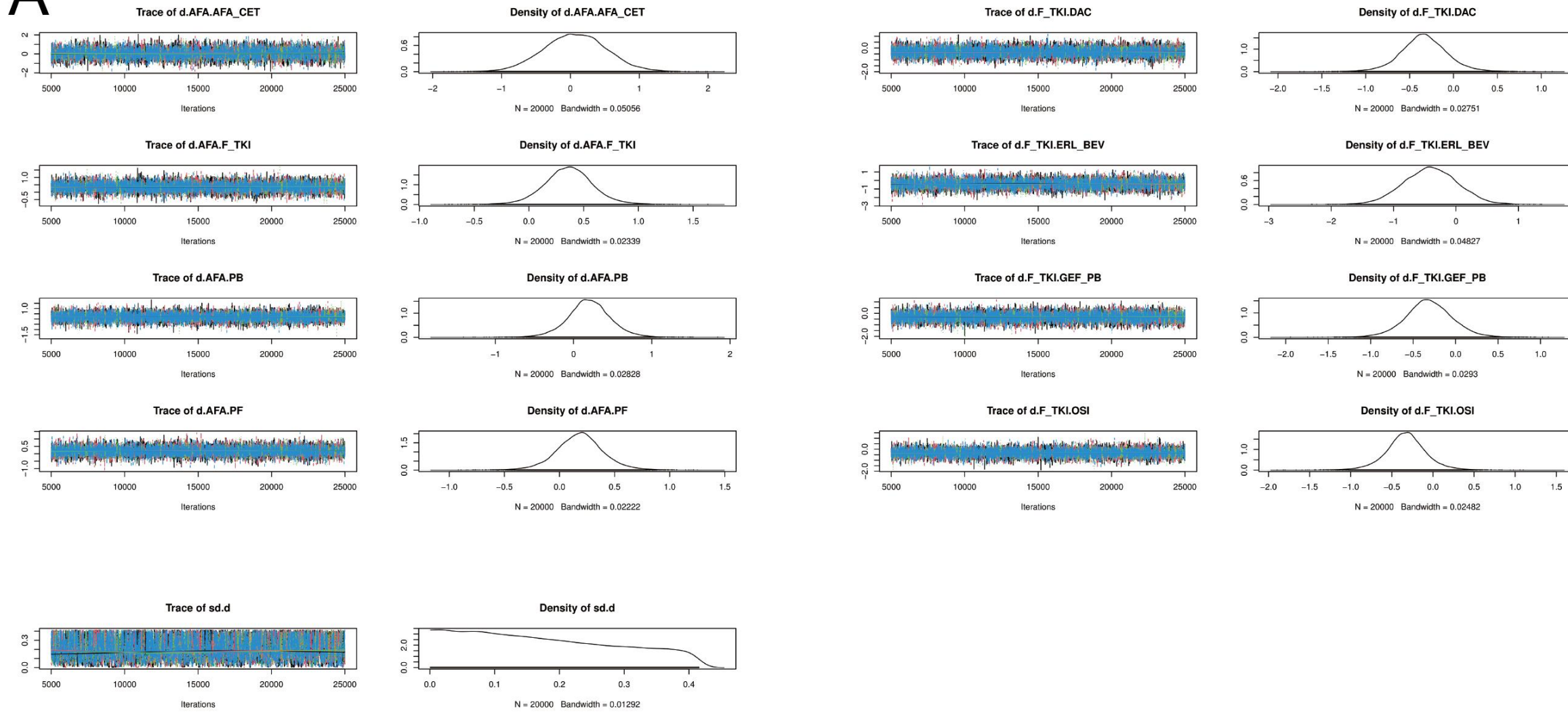


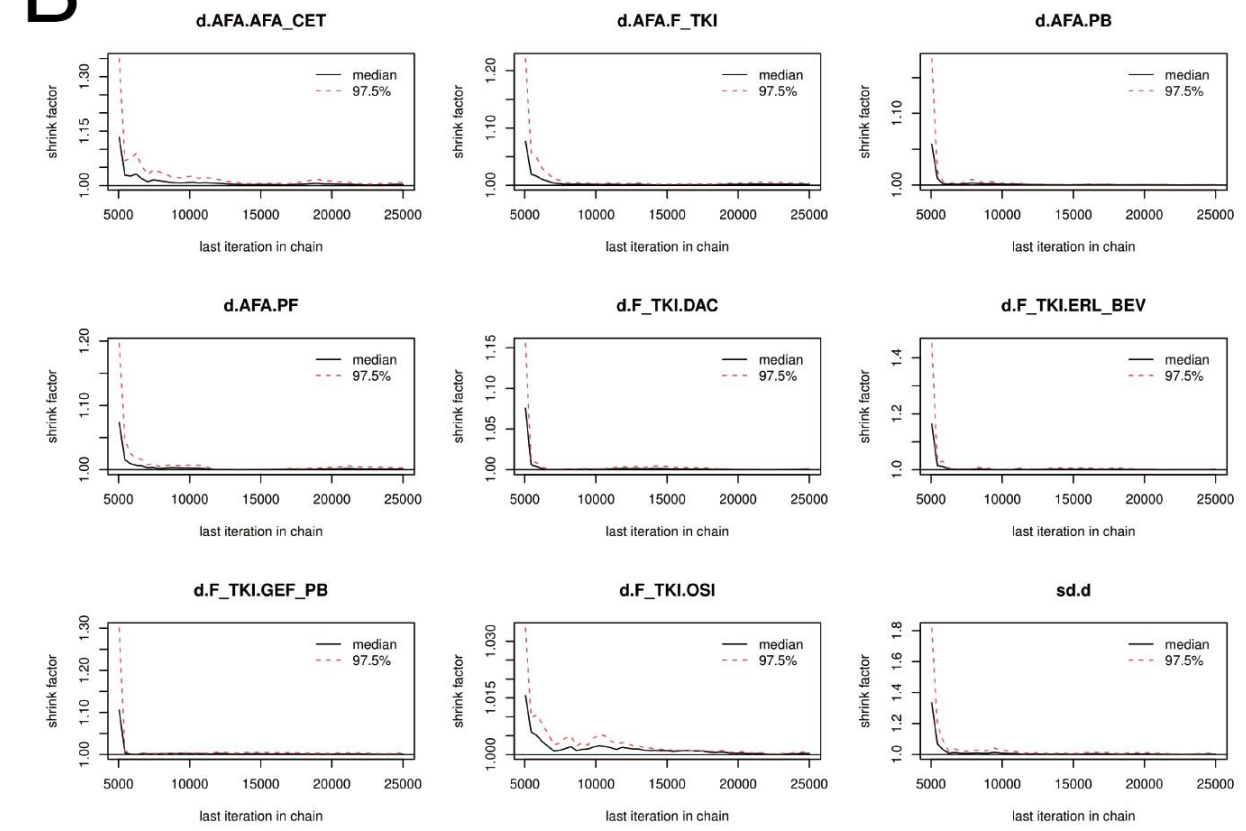
Figure S24. Convergence of the Four Chains Established by Inspection of the Trace Plot and the Brooks-Gelman-Rubin Diagnostic for progression-free survival in age ≥ 65 subgroup.

OS for age < 65

A

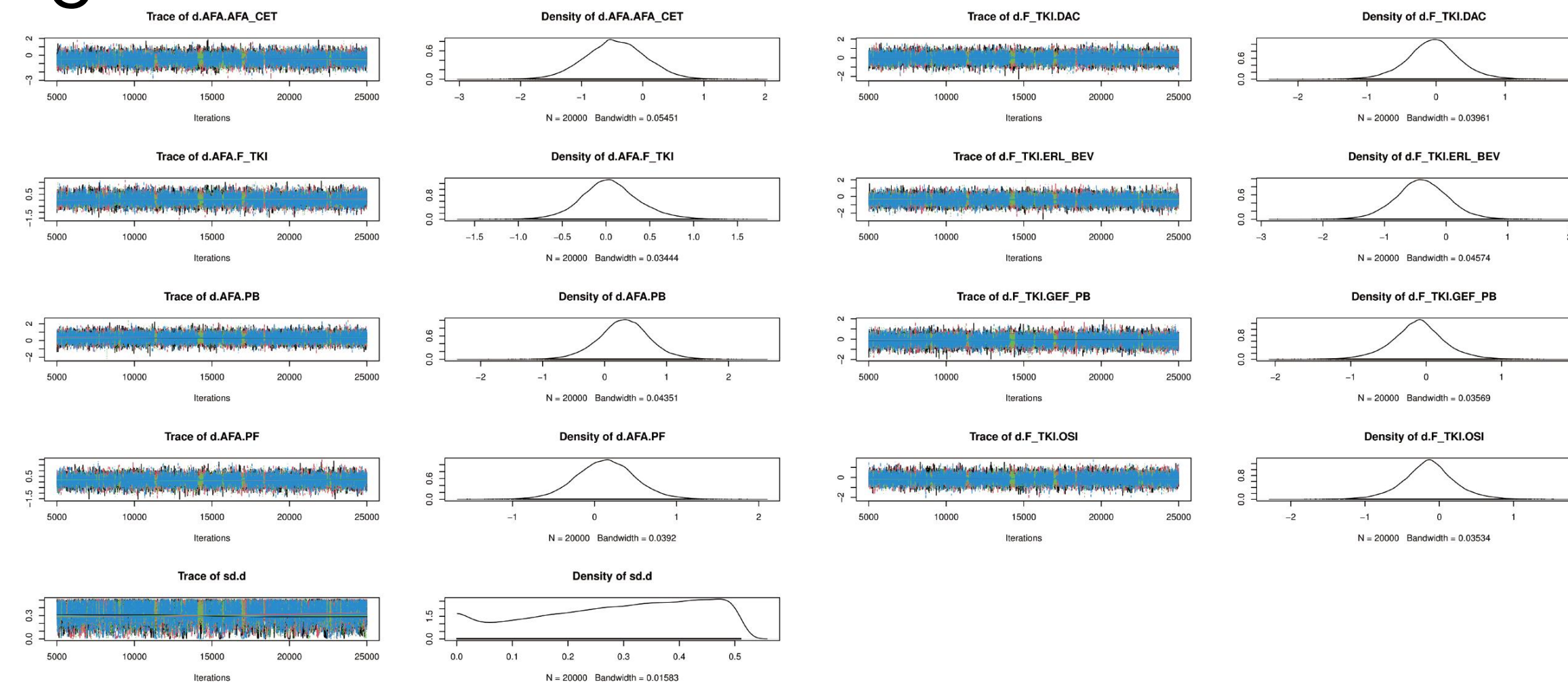


B



Overall survival for age ≥ 65

C



D

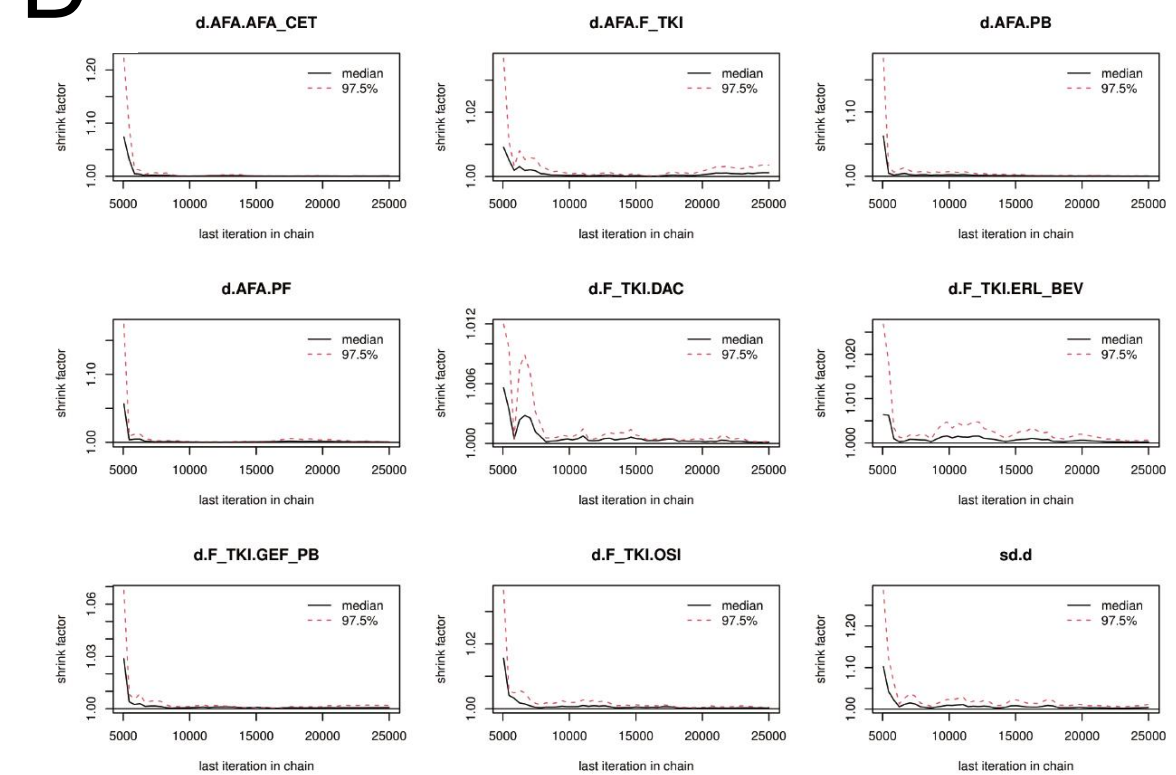


Figure S25. Convergence of the Four Chains Established by Inspection of the Trace Plot and the Brooks-Gelman-Rubin Diagnostic for overall survival in age < 65 and age ≥ 65 subgroups.

PFS for male subgroup



PFS for female subgroup

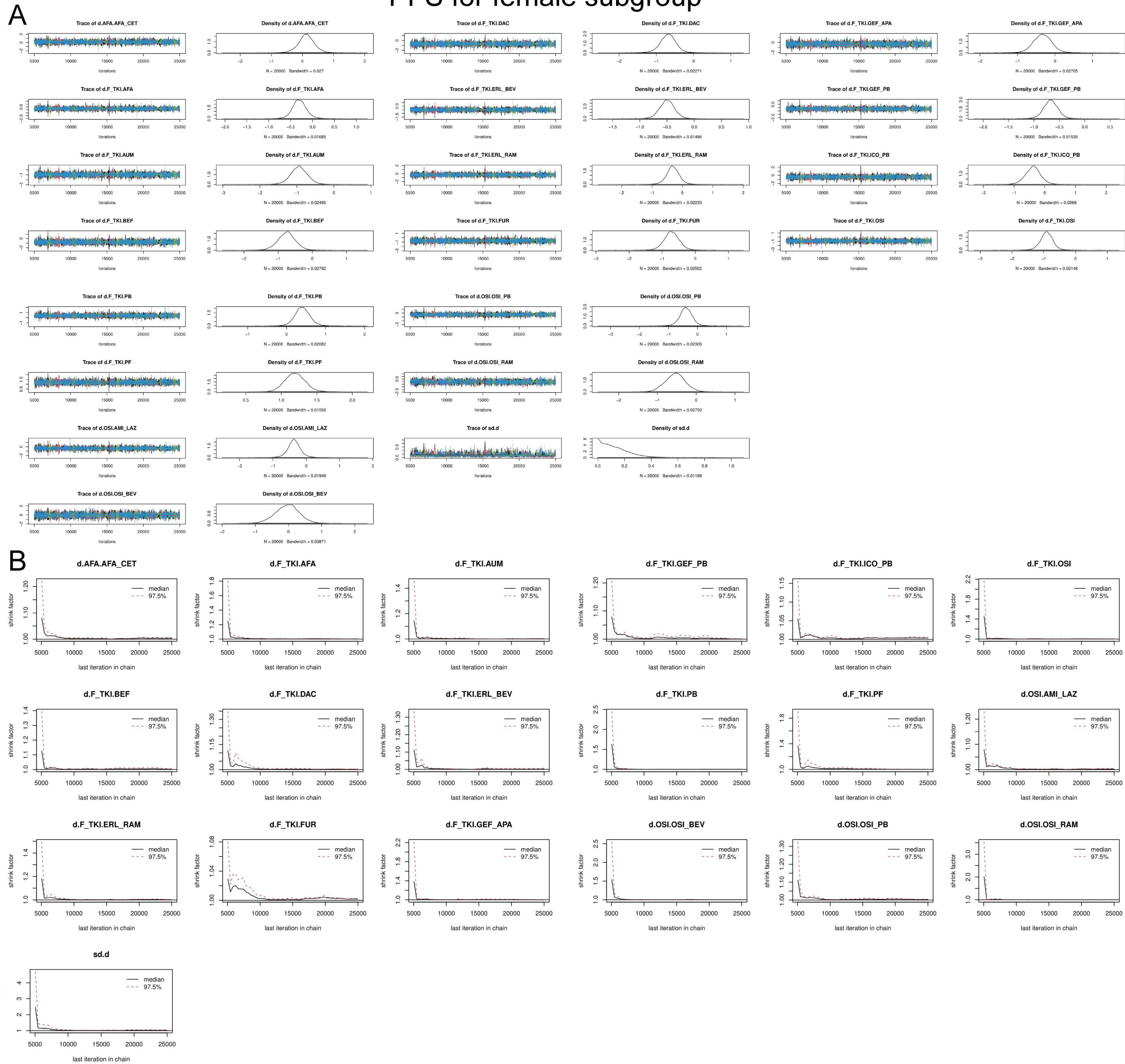
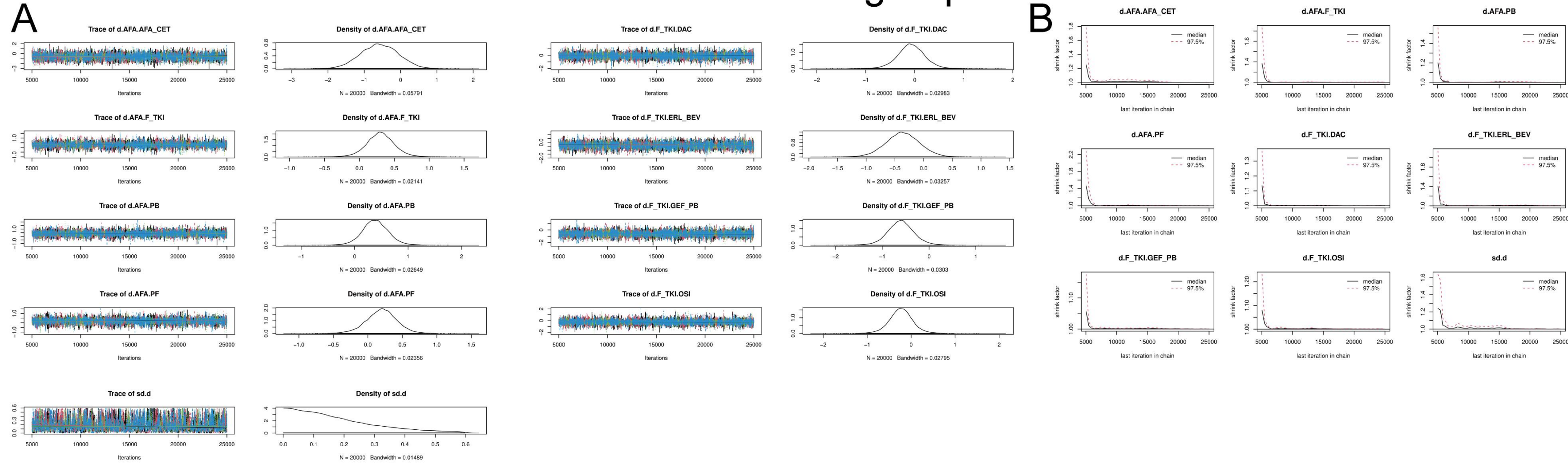


Figure S27. Convergence of the Four Chains Established by Inspection of the Trace Plot and the Brooks-Gelman-Rubin Diagnostic for progression-free survival in female subgroup.

OS for male subgroup



OS for female subgroup

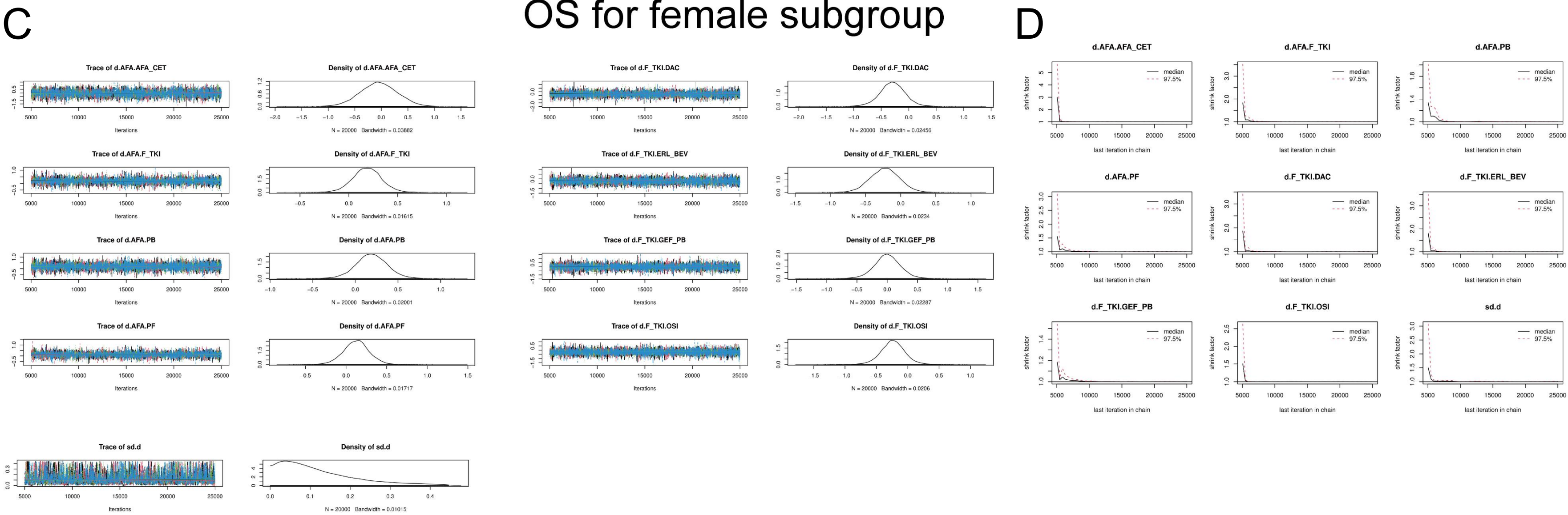


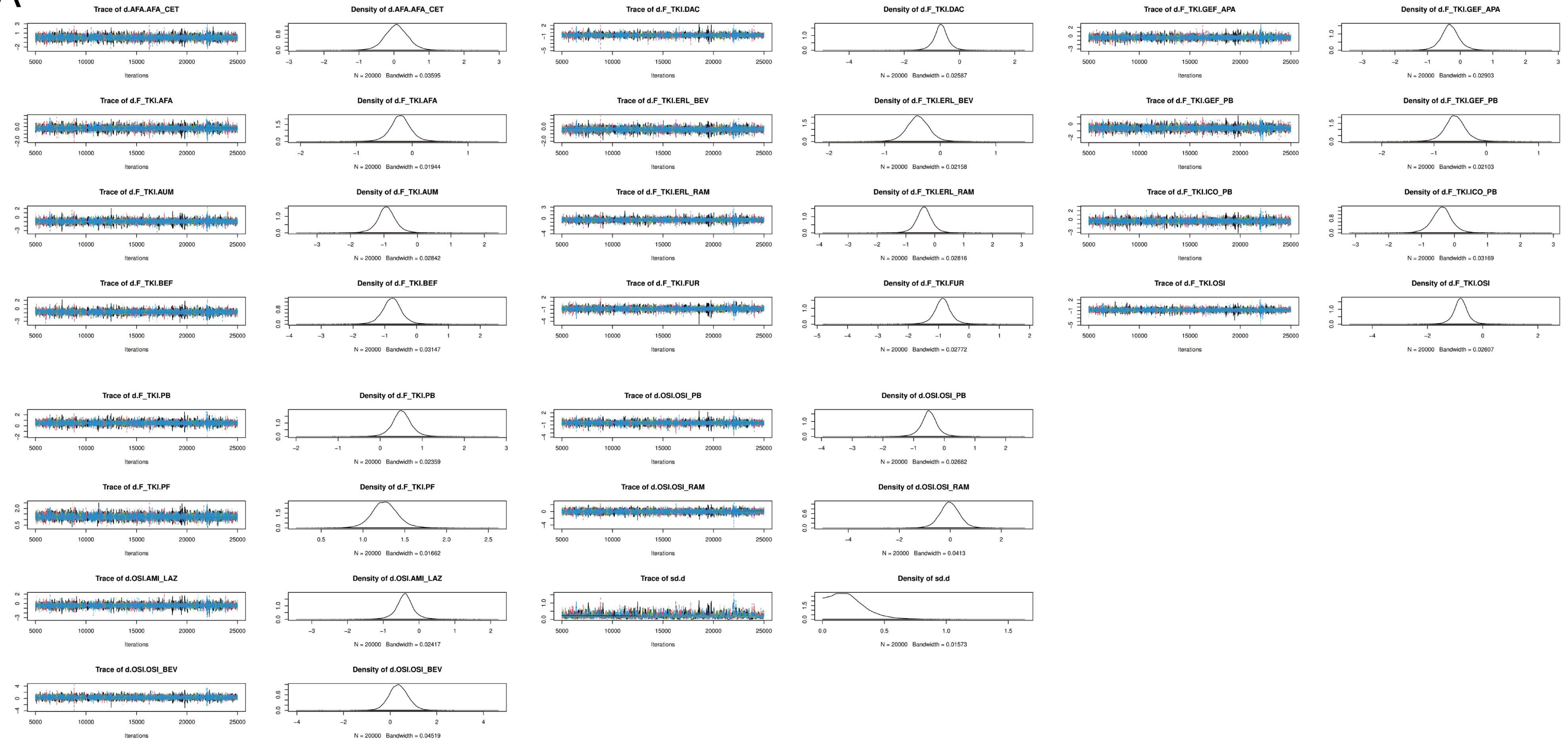
Figure S28. Convergence of the Four Chains Established by Inspection of the Trace Plot and the Brooks-Gelman-Rubin Diagnostic for overall survival in male and female subgroups.

PFS for smoker



PFS for non-smoker

A



B

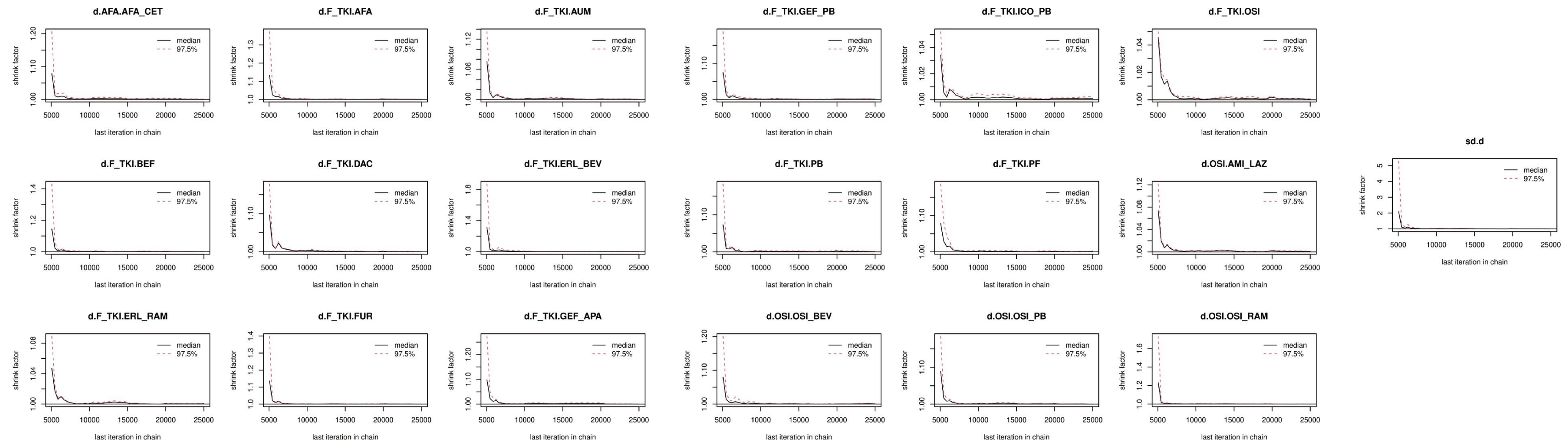
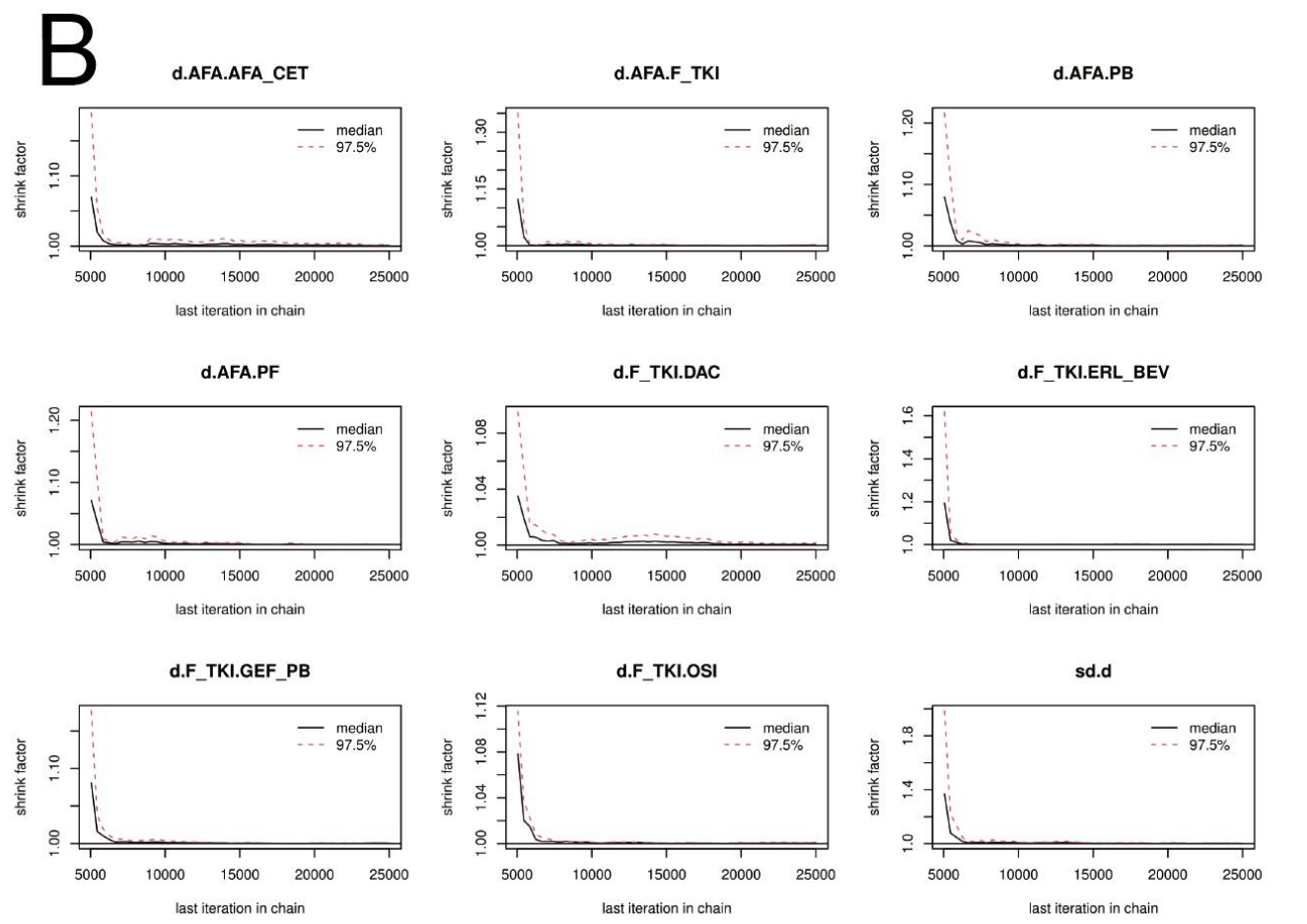
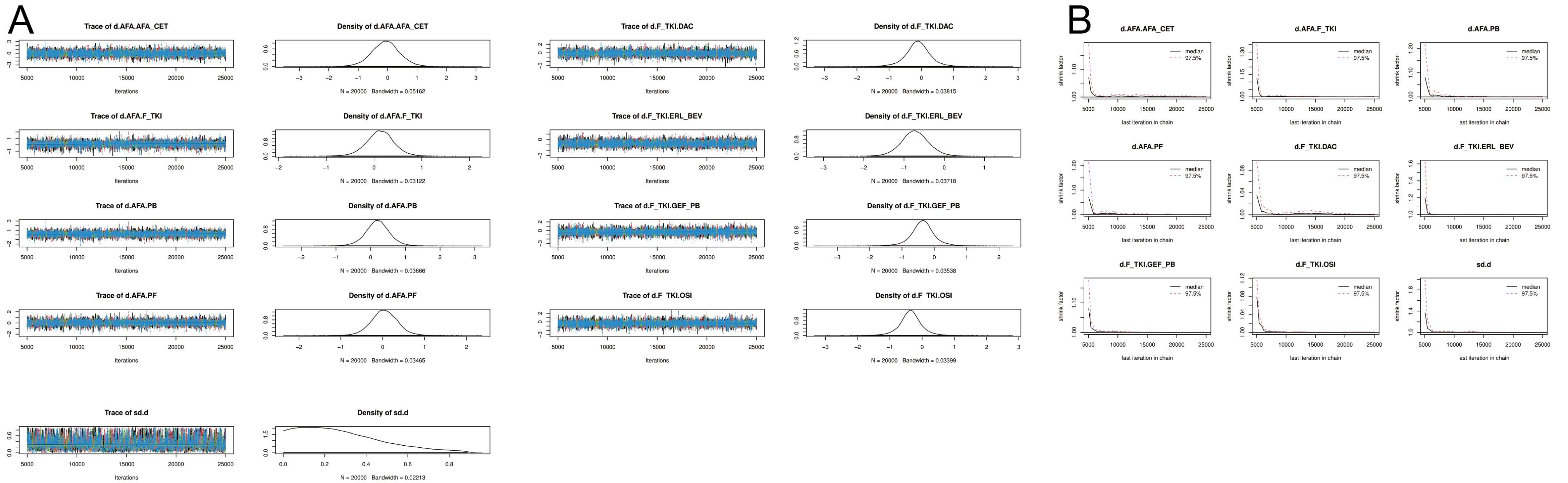


Figure S30. Convergence of the Four Chains Established by Inspection of the Trace Plot and the Brooks-Gelman-Rubin Diagnostic for progression-free survival in non-smoker subgroup.

OS for smoker



OS for non-smoker

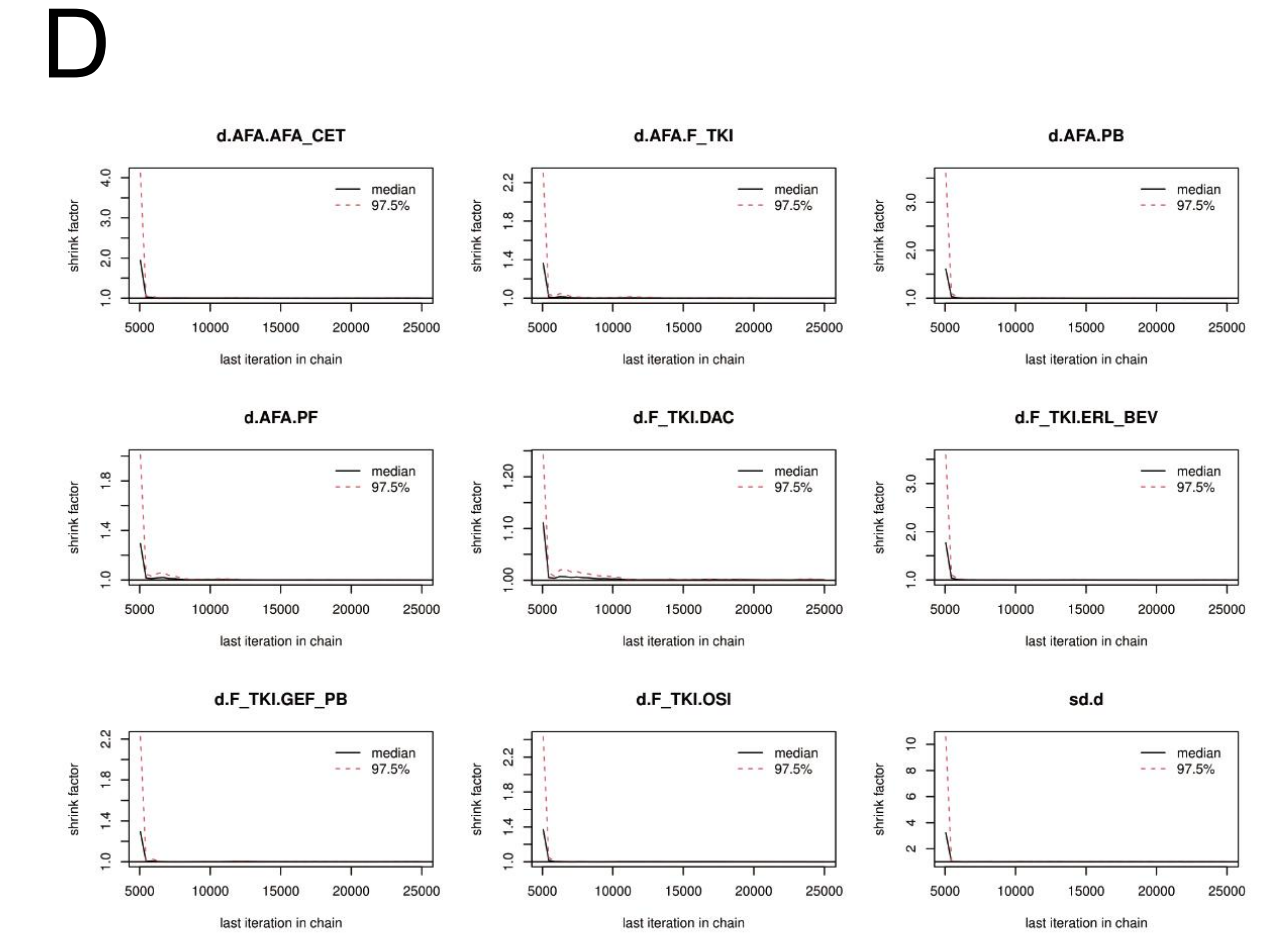
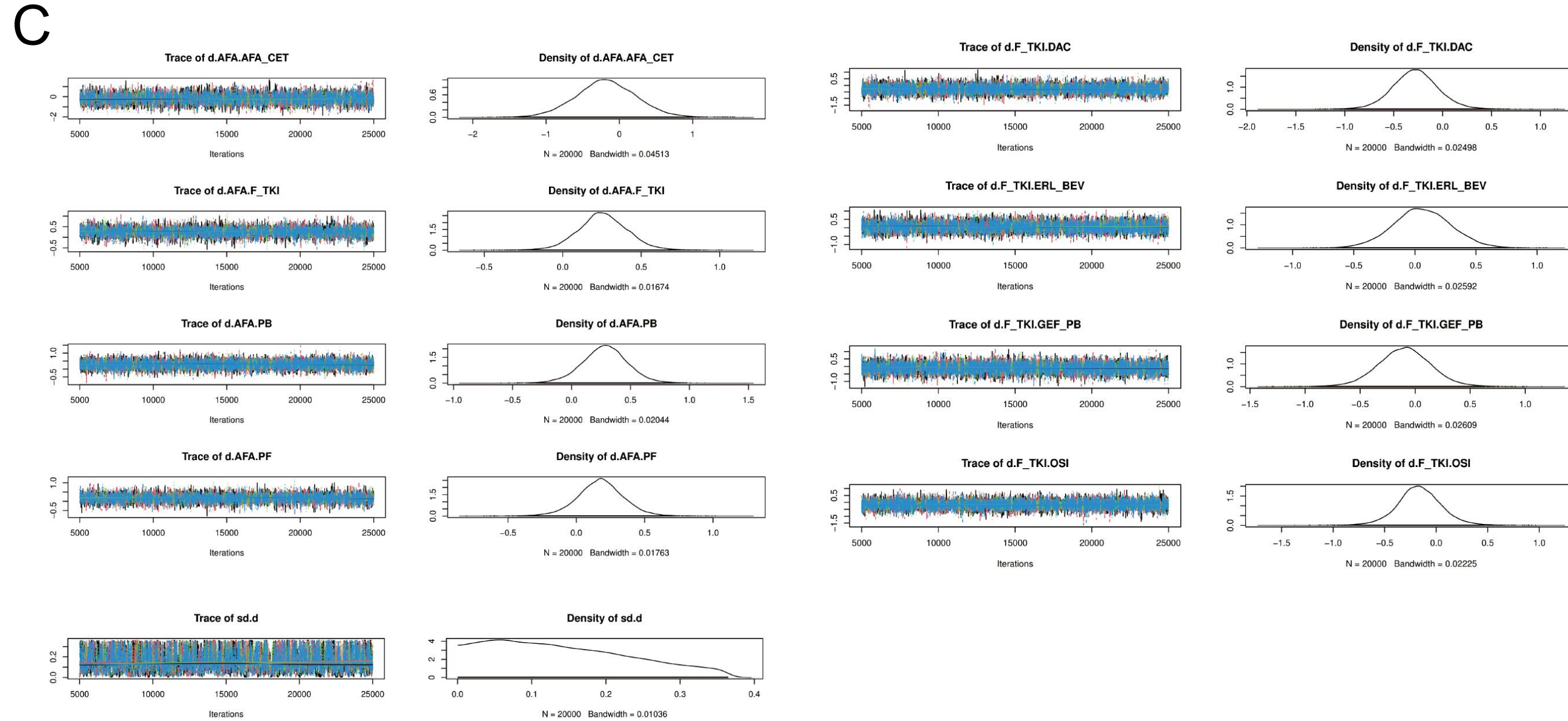


Figure S31. Convergence of the Four Chains Established by Inspection of the Trace Plot and the Brooks-Gelman-Rubin Diagnostic for overall survival in smoker and non-smoker subgroups.

PFS for brain metastasis

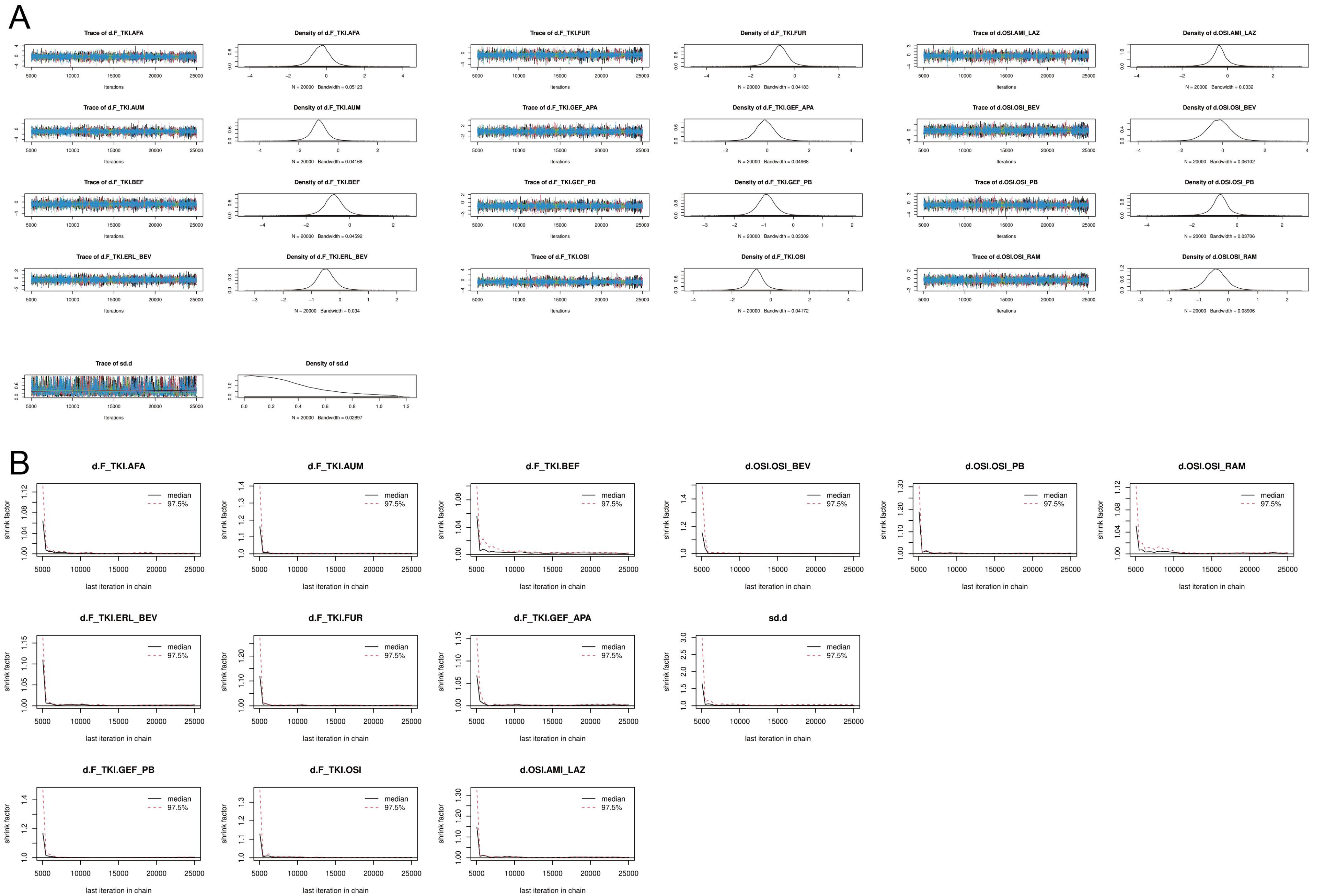
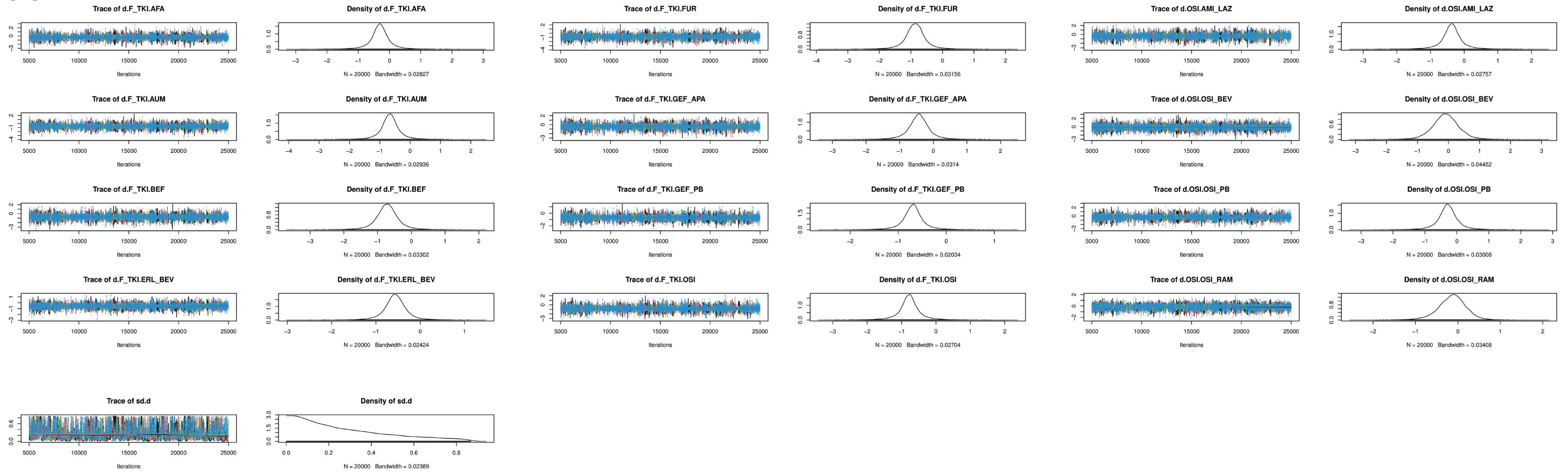


Figure S32. Convergence of the Four Chains Established by Inspection of the Trace Plot and the Brooks-Gelman-Rubin Diagnostic for progression-free survival in brain metastasis subgroup.

PFS for without brain metastases

A



B

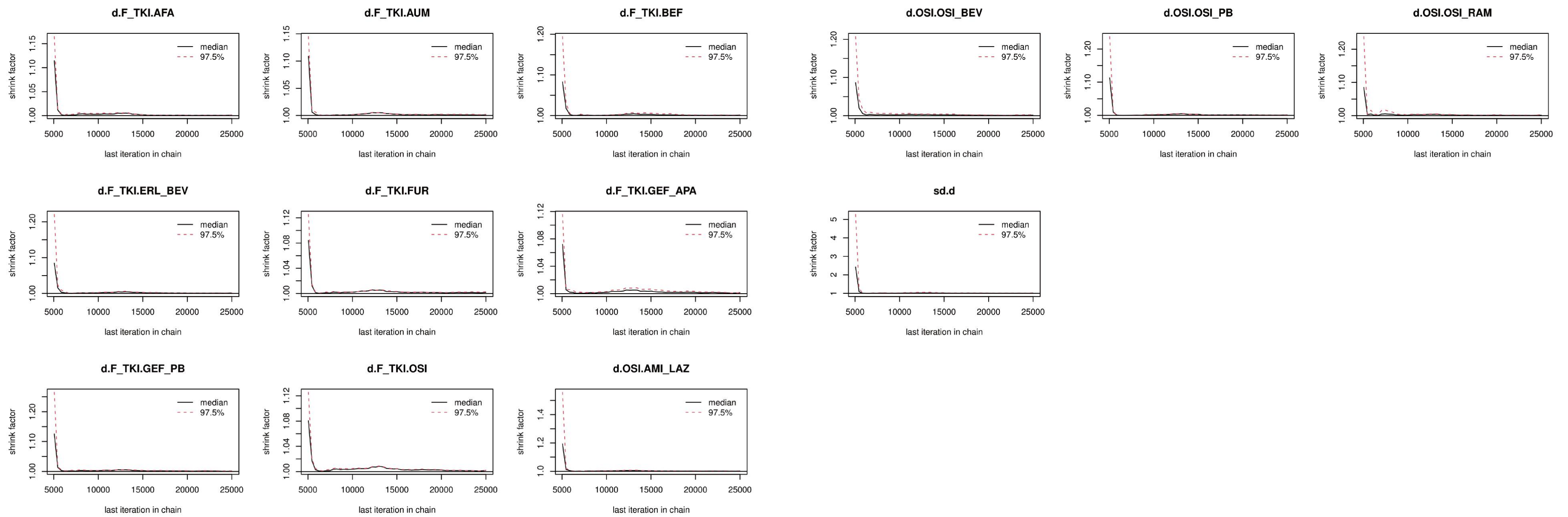
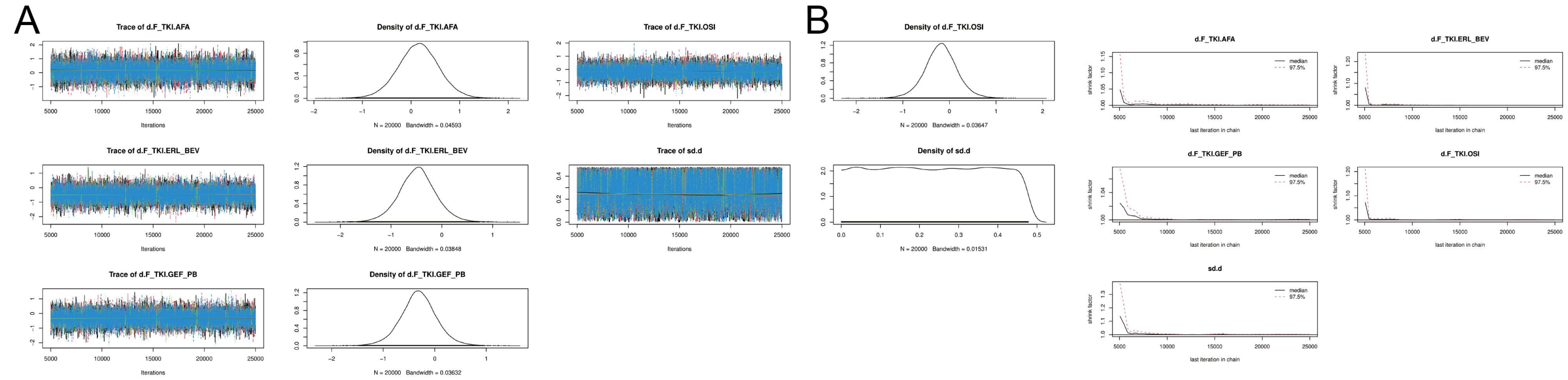


Figure S33. Convergence of the Four Chains Established by Inspection of the Trace Plot and the Brooks-Gelman-Rubin Diagnostic for progression-free survival in no brain metastasis subgroup.

OS for brain metastases



OS for without brain metastases

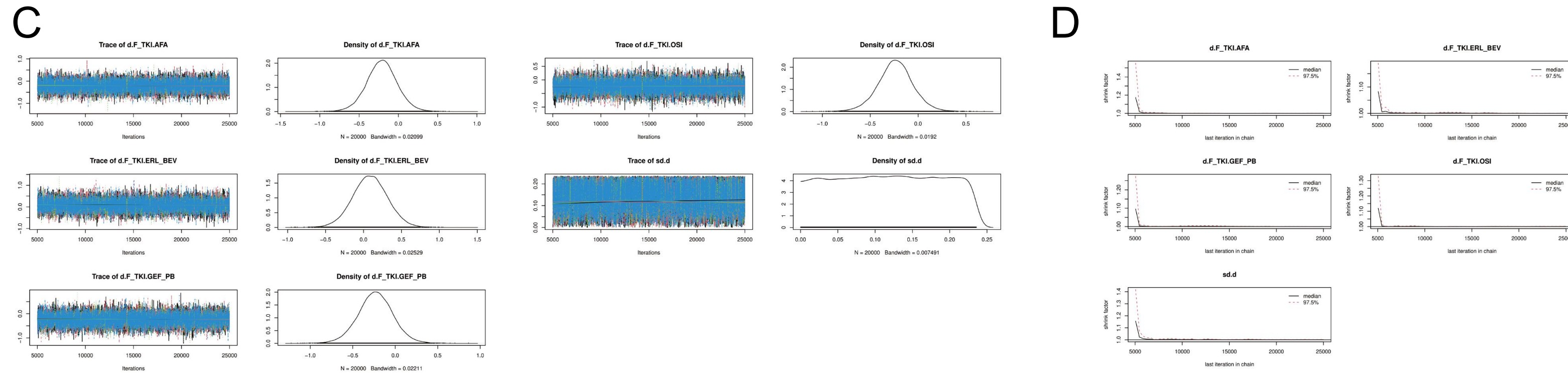


Figure S34. Convergence of the Four Chains Established by Inspection of the Trace Plot and the Brooks-Gelman-Rubin Diagnostic for overall survival in brain metastasis and no brain metastasis subgroups.

PFS for Asian

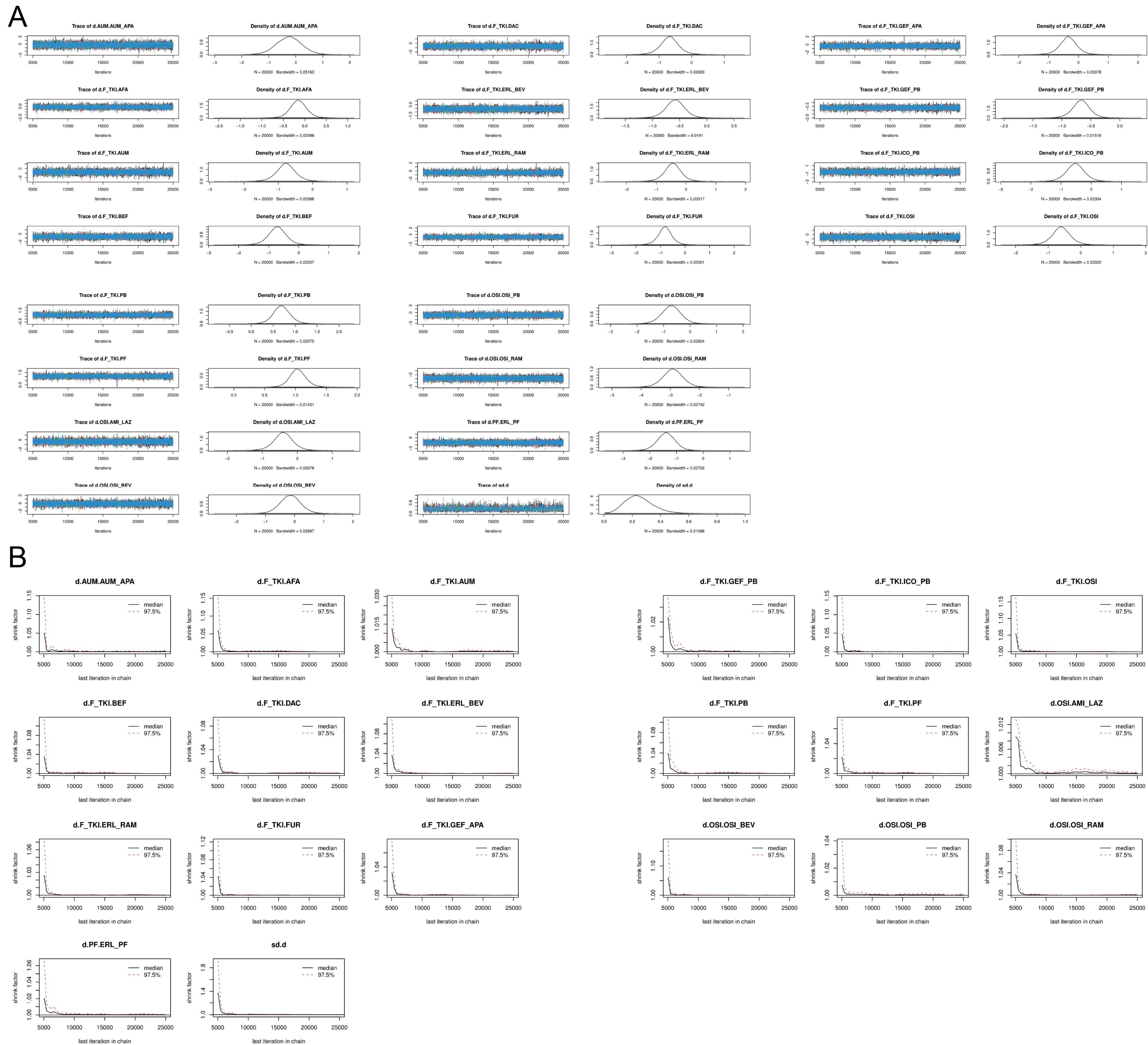


Figure S35. Convergence of the Four Chains Established by Inspection of the Trace Plot and the Brooks-Gelman-Rubin Diagnostic for progression-free survival in Asian subgroup.

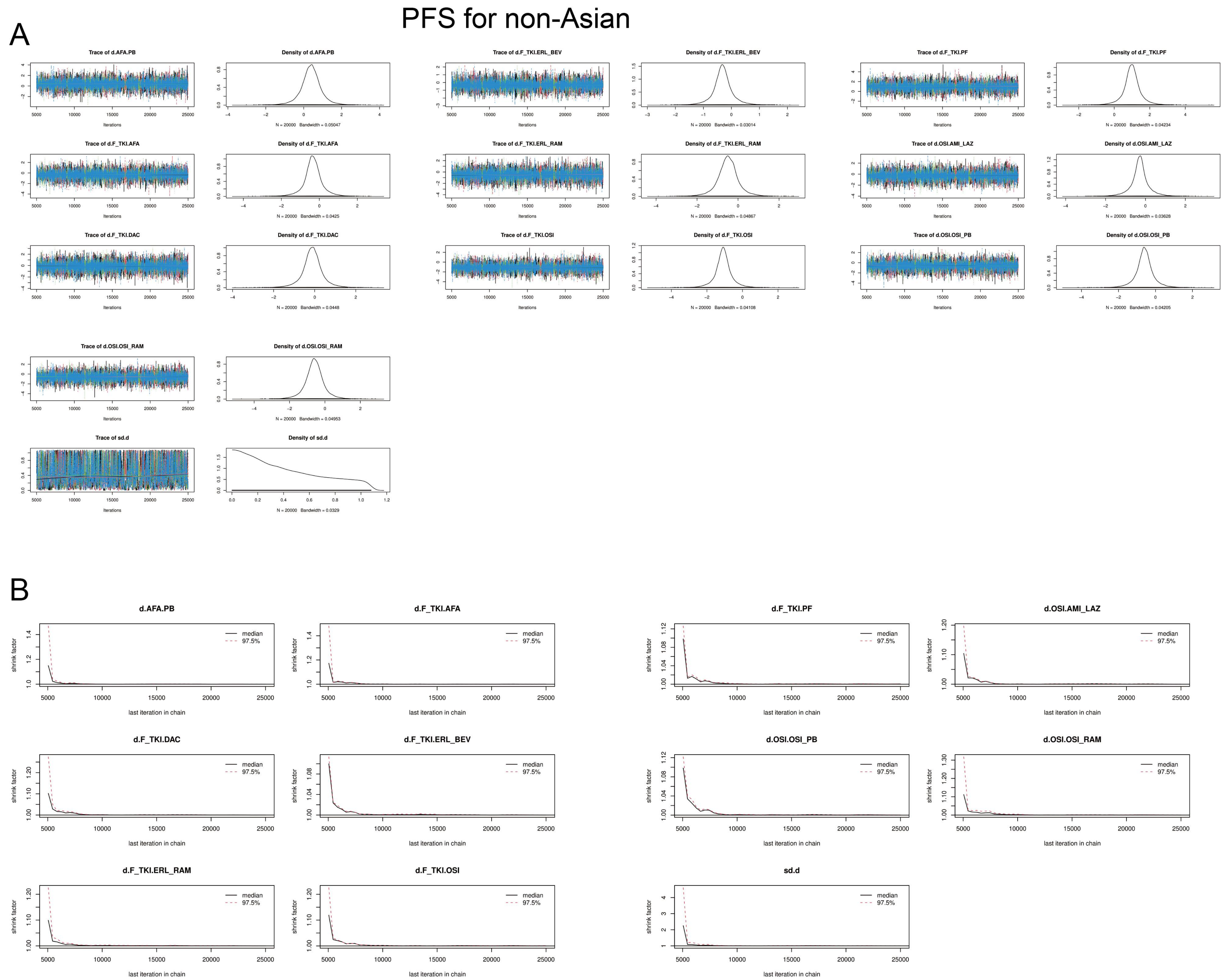
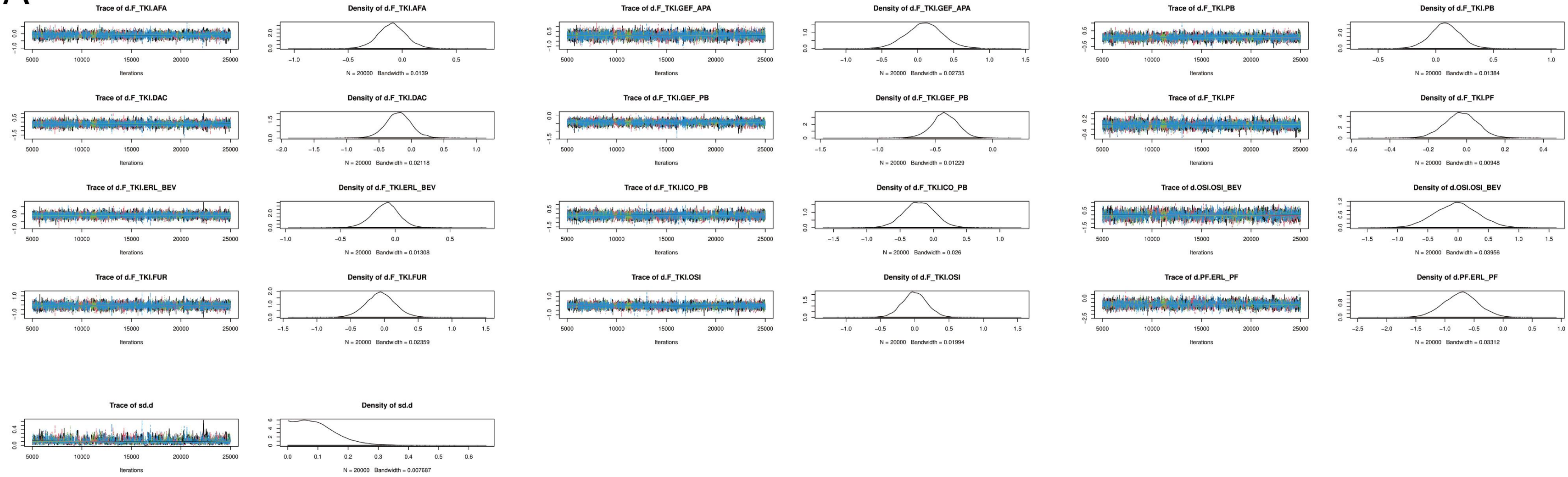


Figure S36. Convergence of the Four Chains Established by Inspection of the Trace Plot and the Brooks-Gelman-Rubin Diagnostic for progression-free survival in non-Asian subgroup.

OS for Asian

A



B

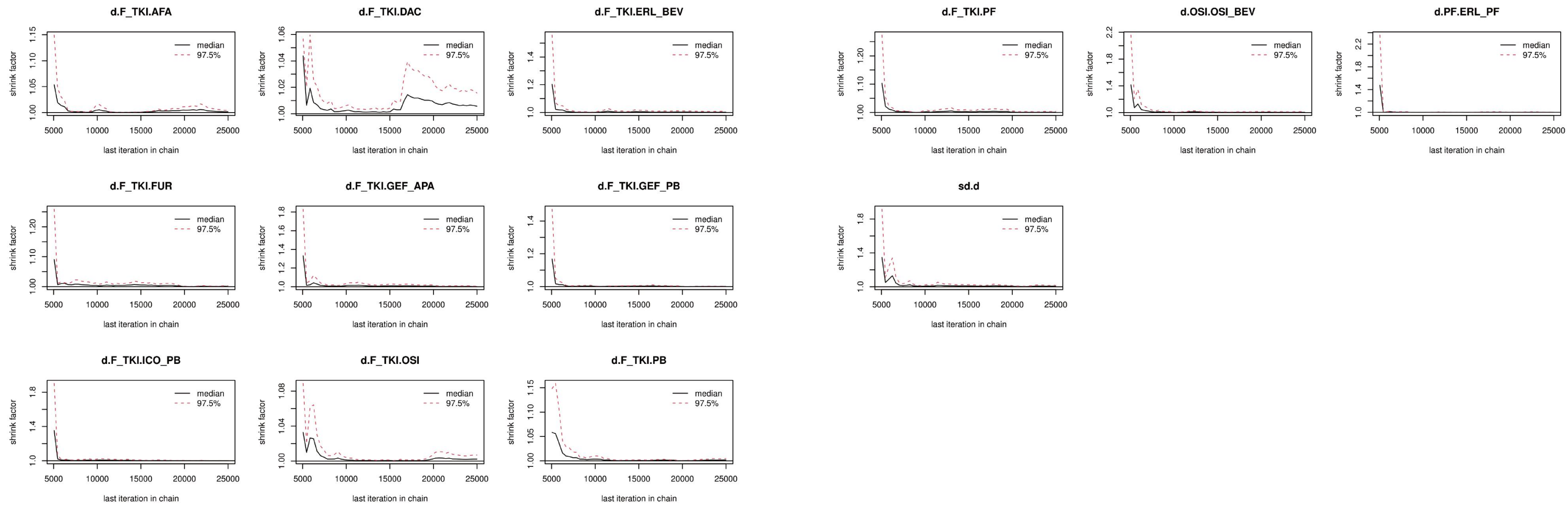


Figure S37. Convergence of the Four Chains Established by Inspection of the Trace Plot and the Brooks-Gelman-Rubin Diagnostic for overall survival in Asian subgroup.

OS for non-Asian

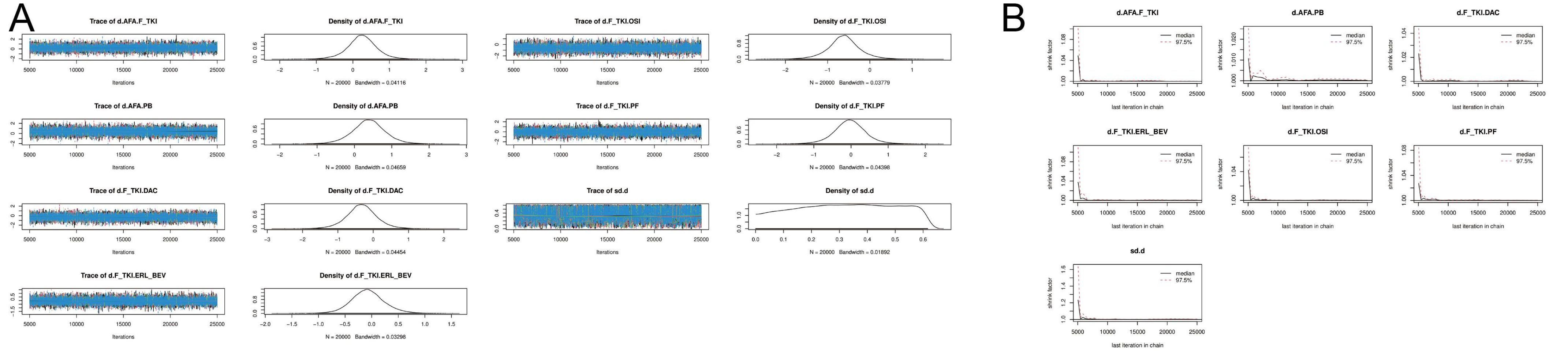


Figure S38. Convergence of the Four Chains Established by Inspection of the Trace Plot and the Brooks-Gelman-Rubin Diagnostic for overall survival in non-Asian subgroup.

PFS for PS=0 subgroup

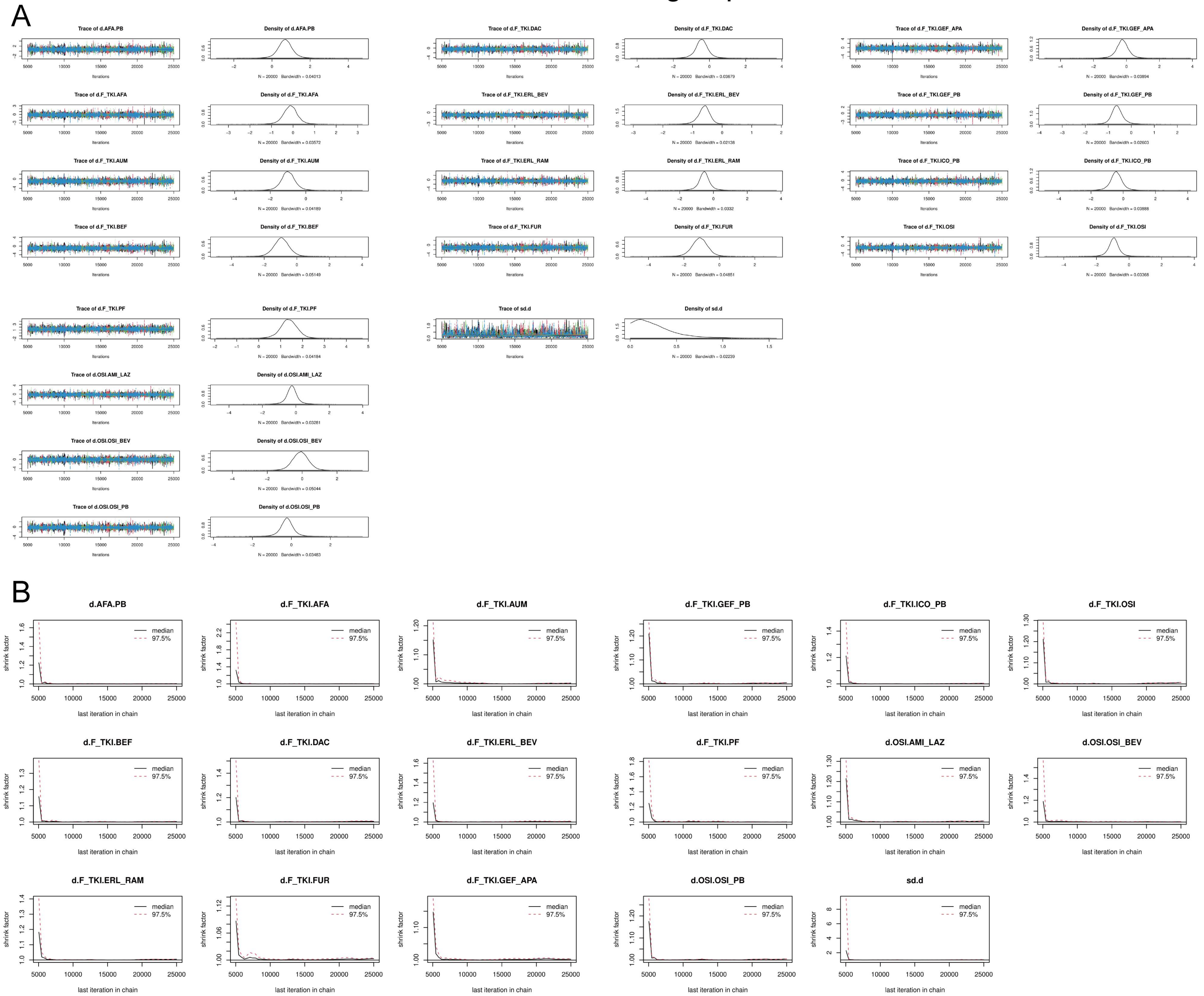
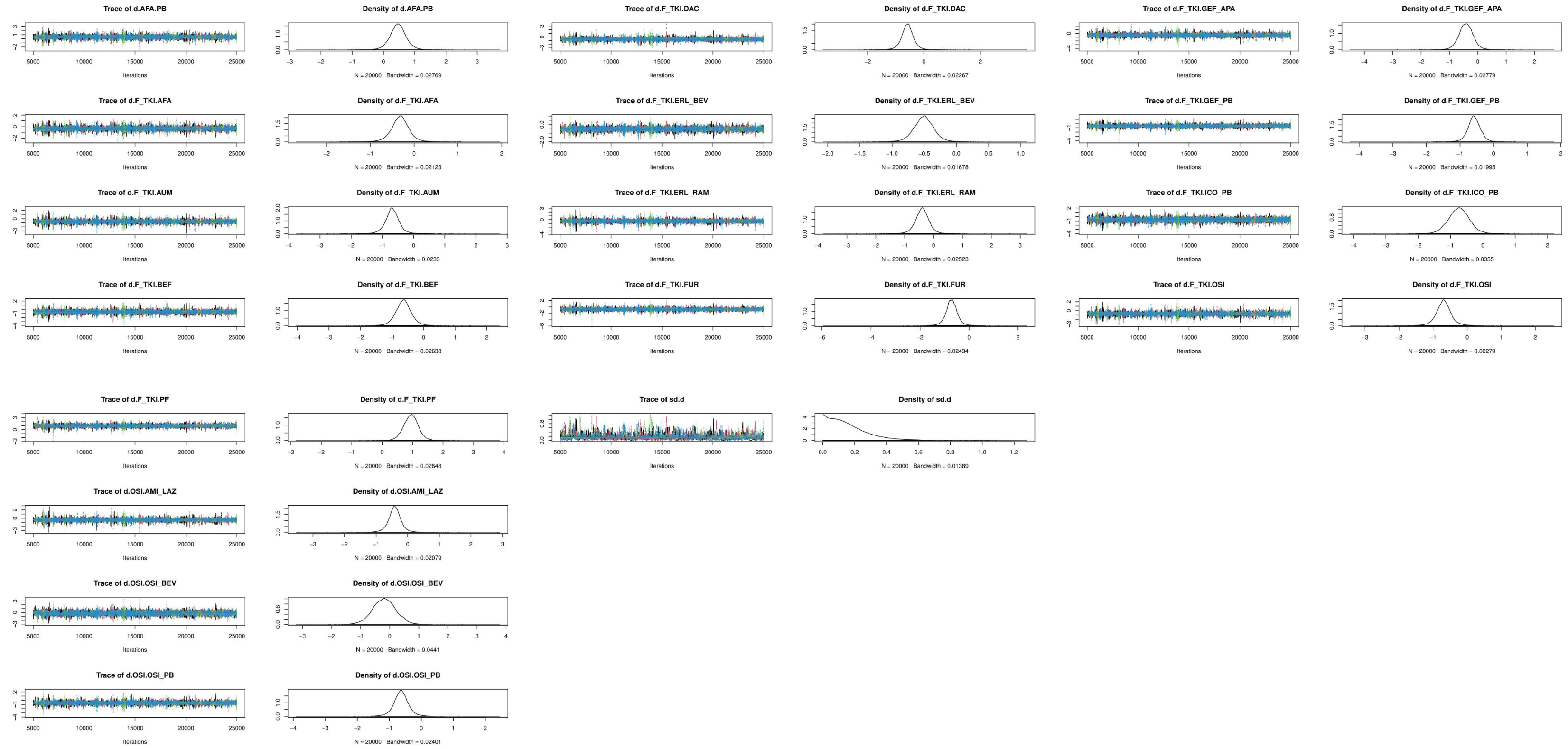


Figure S39. Convergence of the Four Chains Established by Inspection of the Trace Plot and the Brooks-Gelman-Rubin Diagnostic for progression-free survival in PS = 0 subgroup.

PFS for PS=1 subgroup

A



B

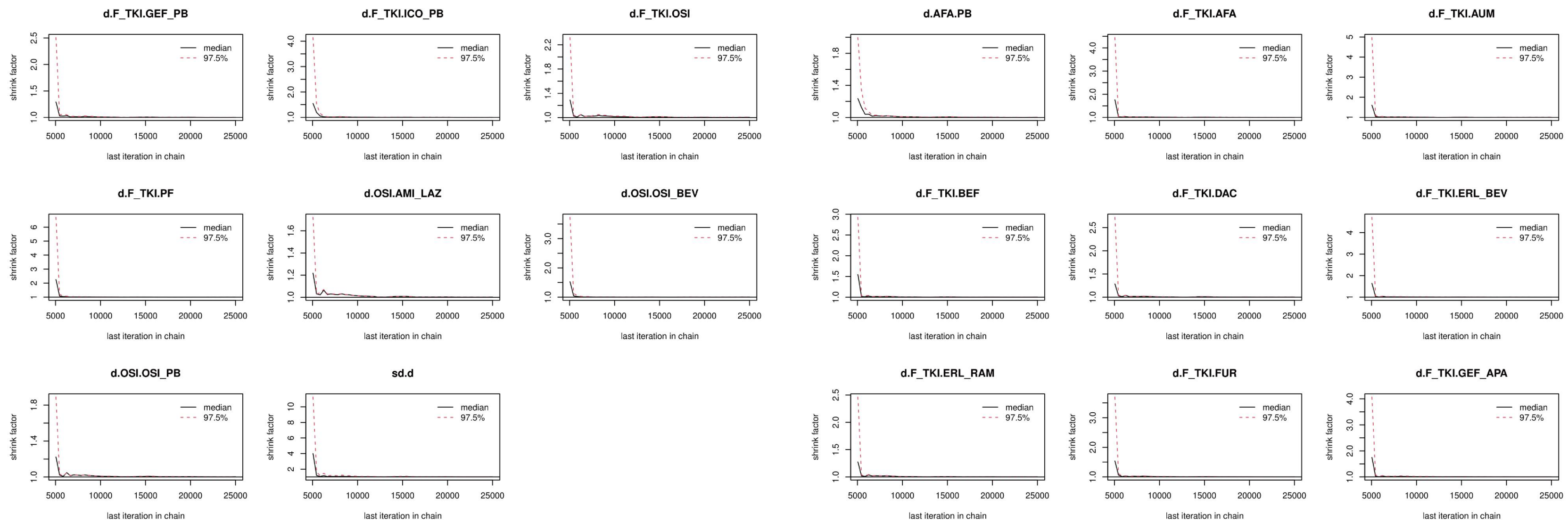
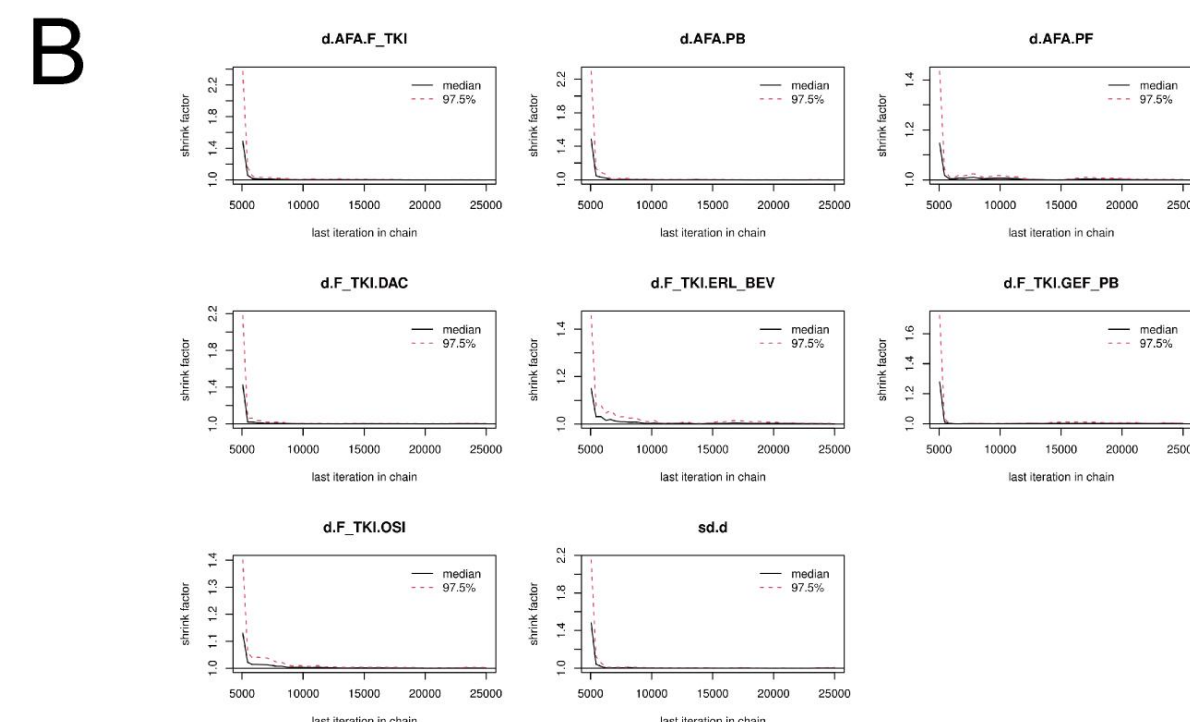
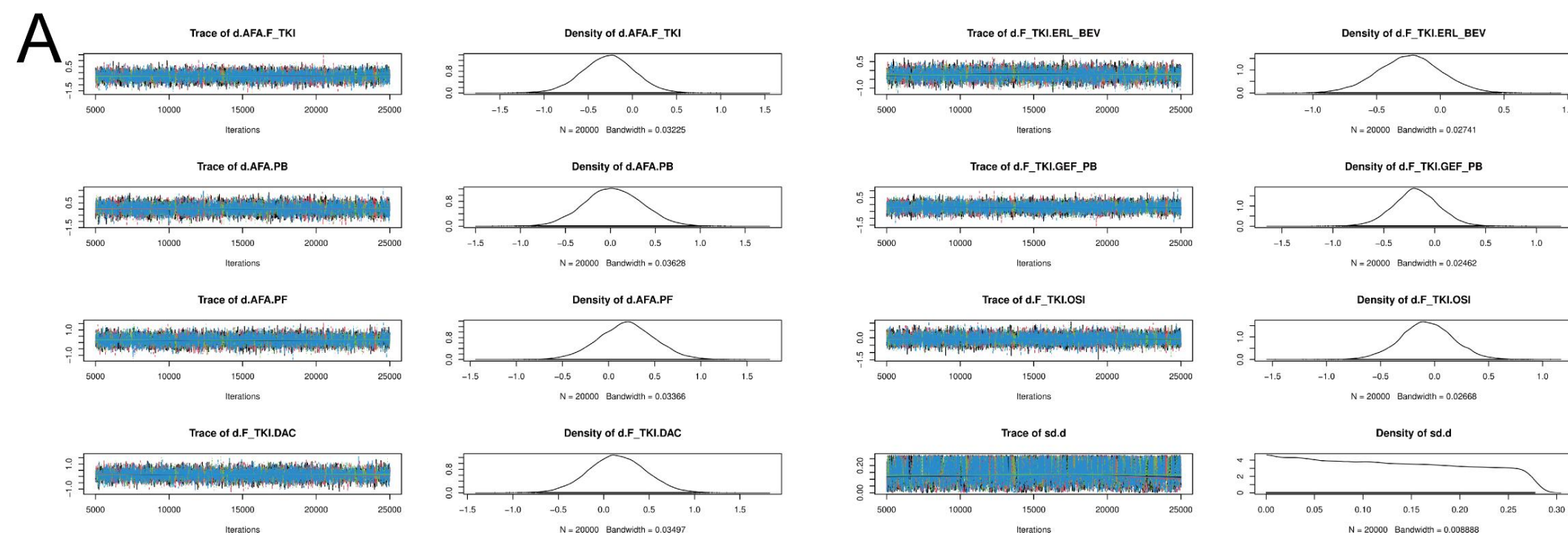


Figure S40. Convergence of the Four Chains Established by Inspection of the Trace Plot and the Brooks-Gelman-Rubin Diagnostic for progression-free survival in PS = 1 subgroup.

OS for PS=0 subgroup



OS for PS=1 subgroup

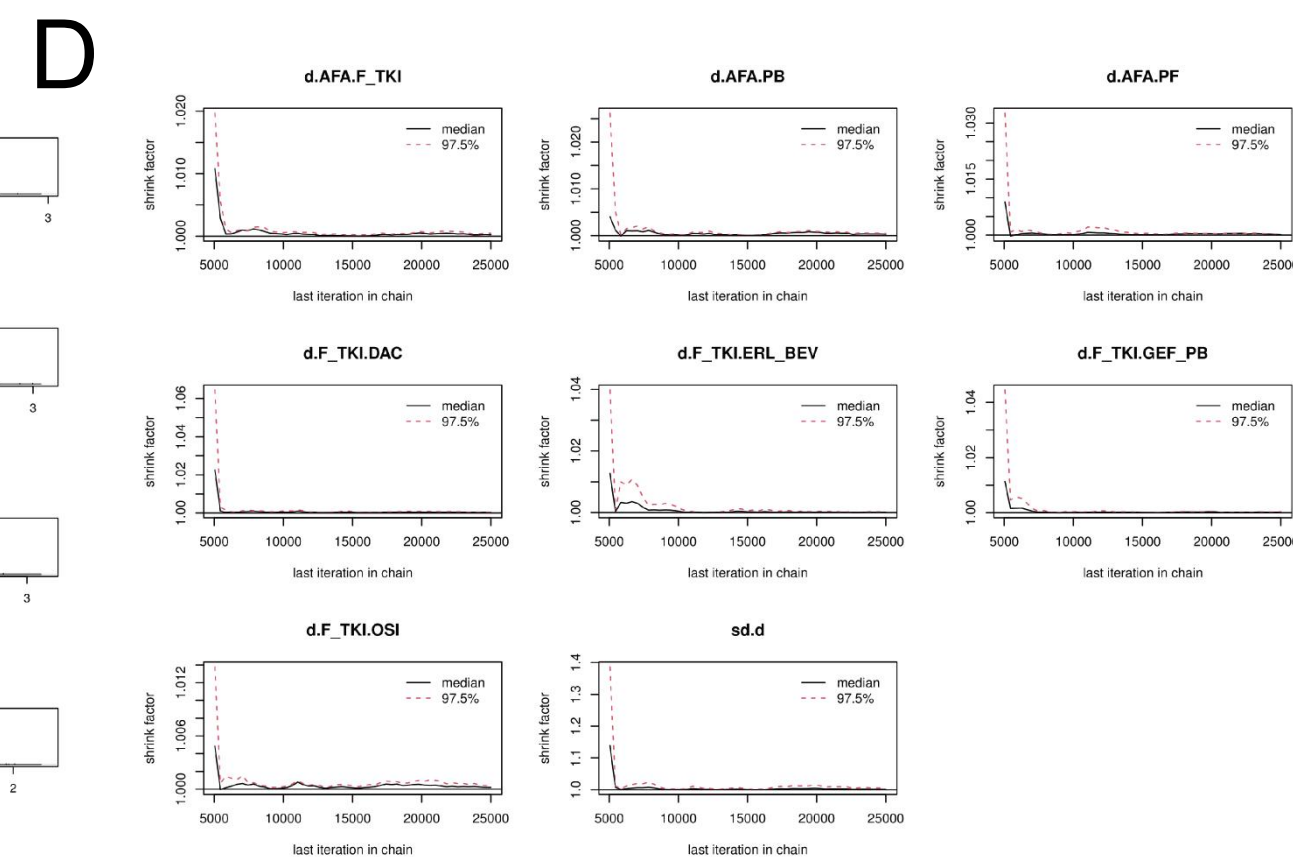
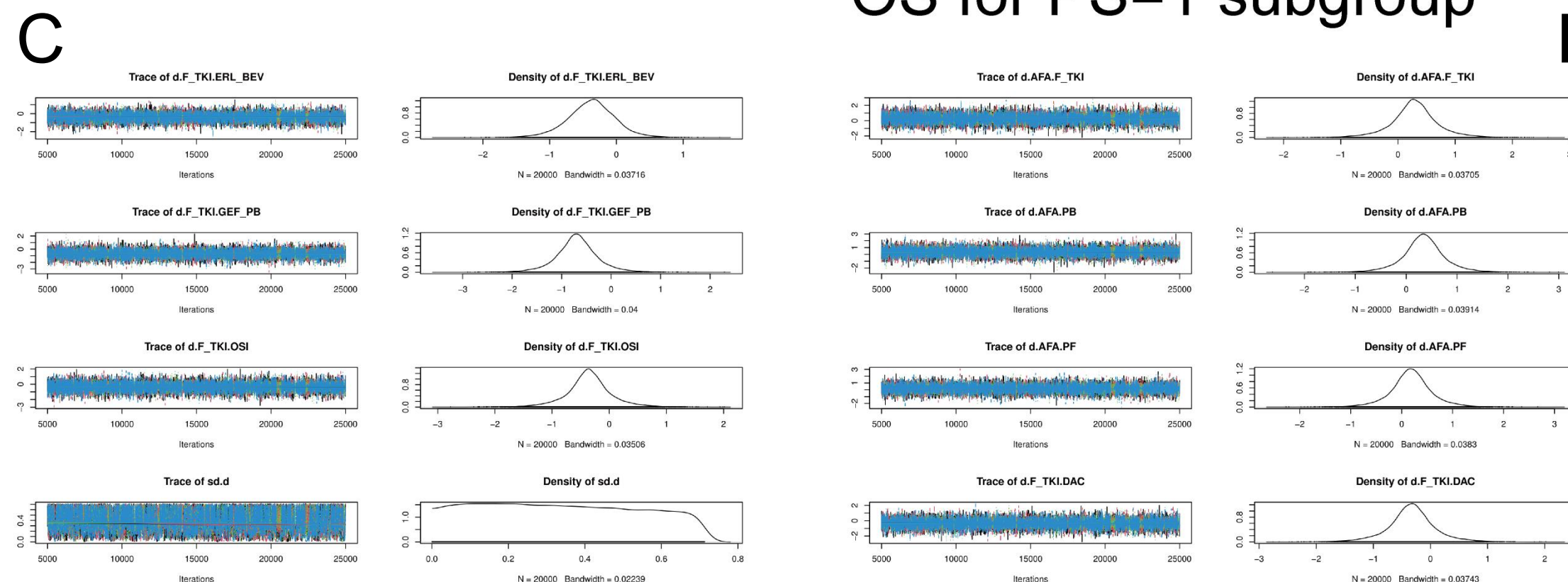


Figure S41. Convergence of the Four Chains Established by Inspection of the Trace Plot and the Brooks-Gelman-Rubin Diagnostic for overall survival in PS = 0 and PS = 1 subgroup.

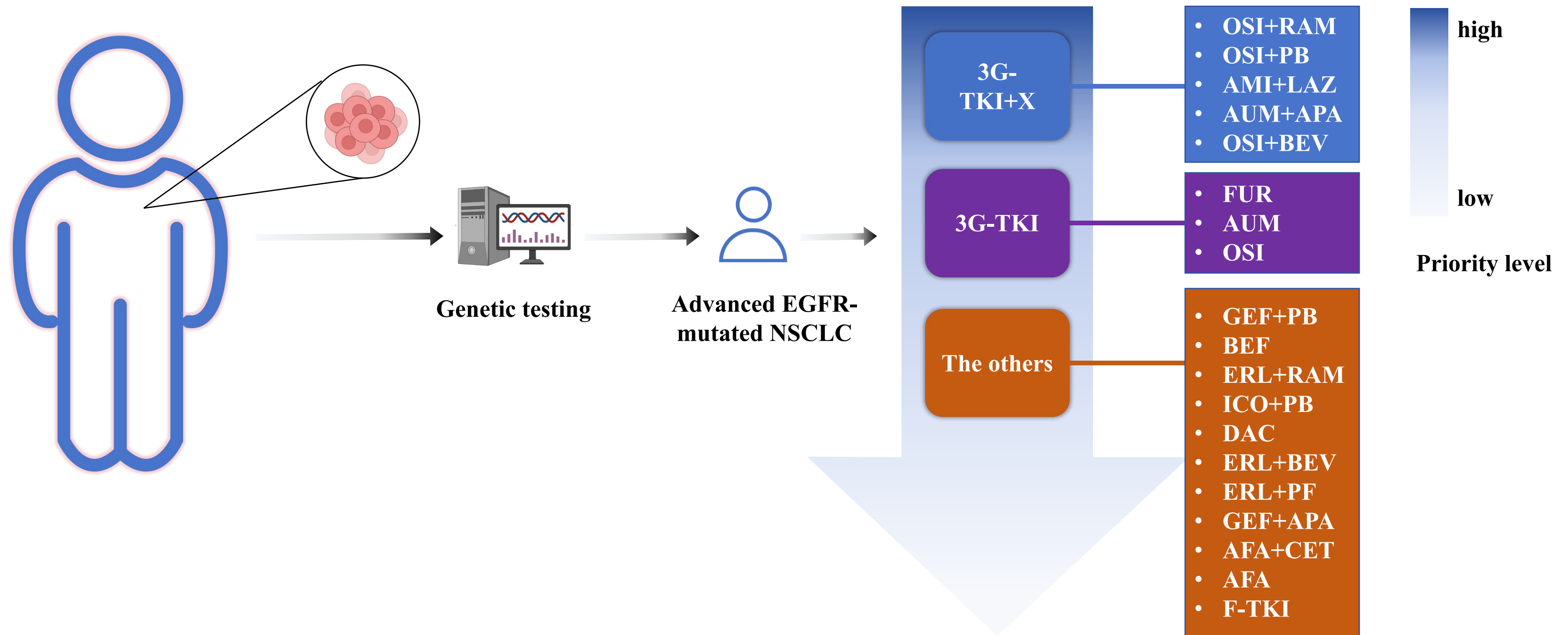


Figure S42. A prioritization scheme for treatment options as a guiding tool for the patient management pathway.

3G-TKI: third-generation TKI; OSI+RAM: osimertinib+ramucirumab; OSI+PB: osimertinib+pemetrexed based chemotherapy; OSI+BEV: osimertinib+bevacizumab; AMI+LAZ: amivantamab+lazertinib; AUM+APA: aumolertinib+apatinib; FUR: furmonertinib; AUM: aumolertinib; OSI: osimertinib; GEF+PB: gefitinib+pemetrexed based chemotherapy; BEF: befotertinib; ERL+RAM: erlotinib+ramucirumab; ICO+PB: icotinib+pemetrexed based chemotherapy; DAC: dacomitinib; ERL+BEV: erlotinib+bevacizumab; ERL+PF:erlotinib+pemetrexed free chemotherapy; GEF+APA: gefitinib+apatinib; AFA+CET: afatinib+cetuximab; AFA: afatinib; F-TKI: first-generation TKI.