SUPPLEMENTARY

Comparative Efficacy of Targeted Therapies in Patients with Non-Small Cell Lung Cancer: A Network Meta-Analysis of Clinical Trial

Figure S1. Flow diagram for selection of relevant studies

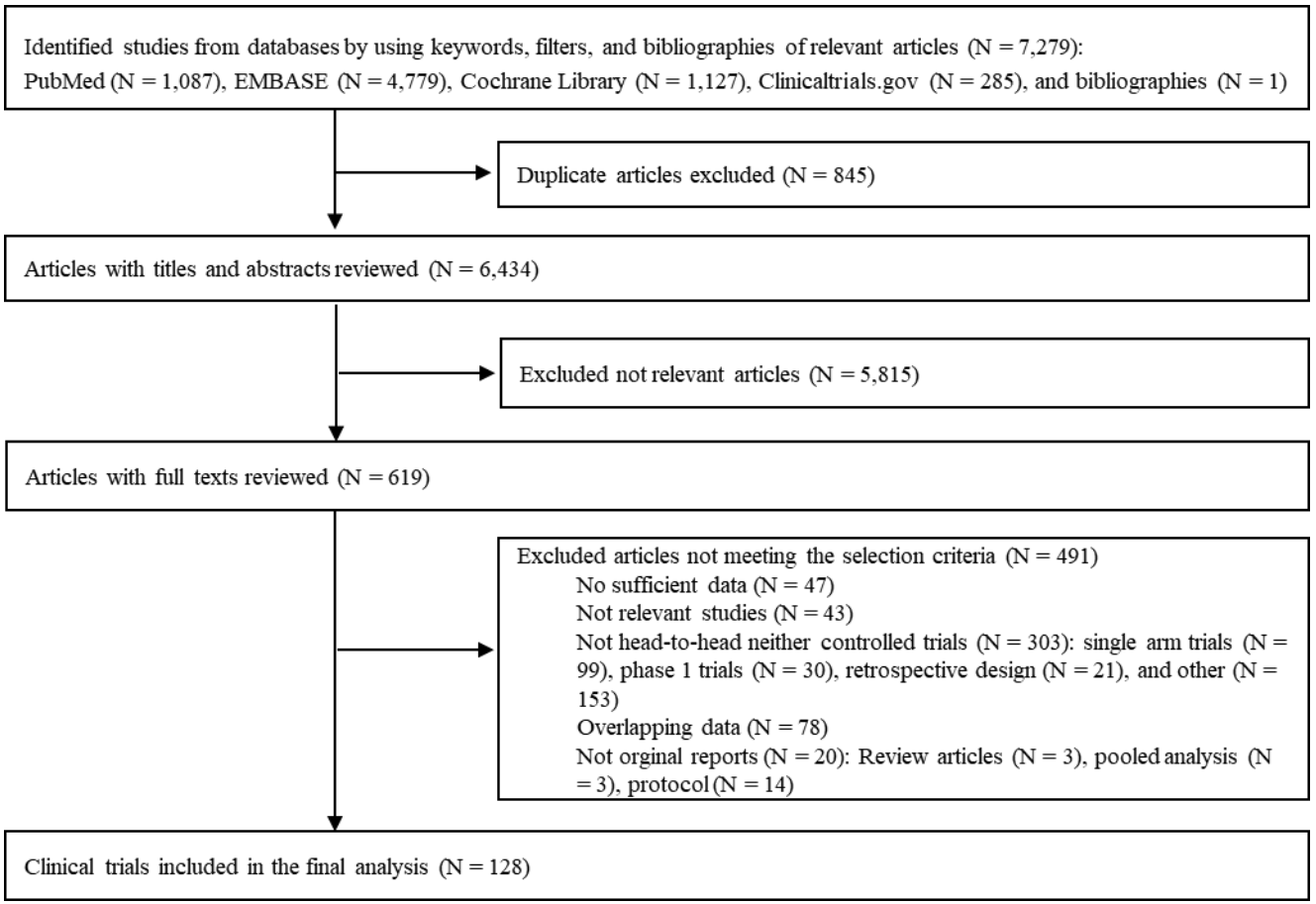
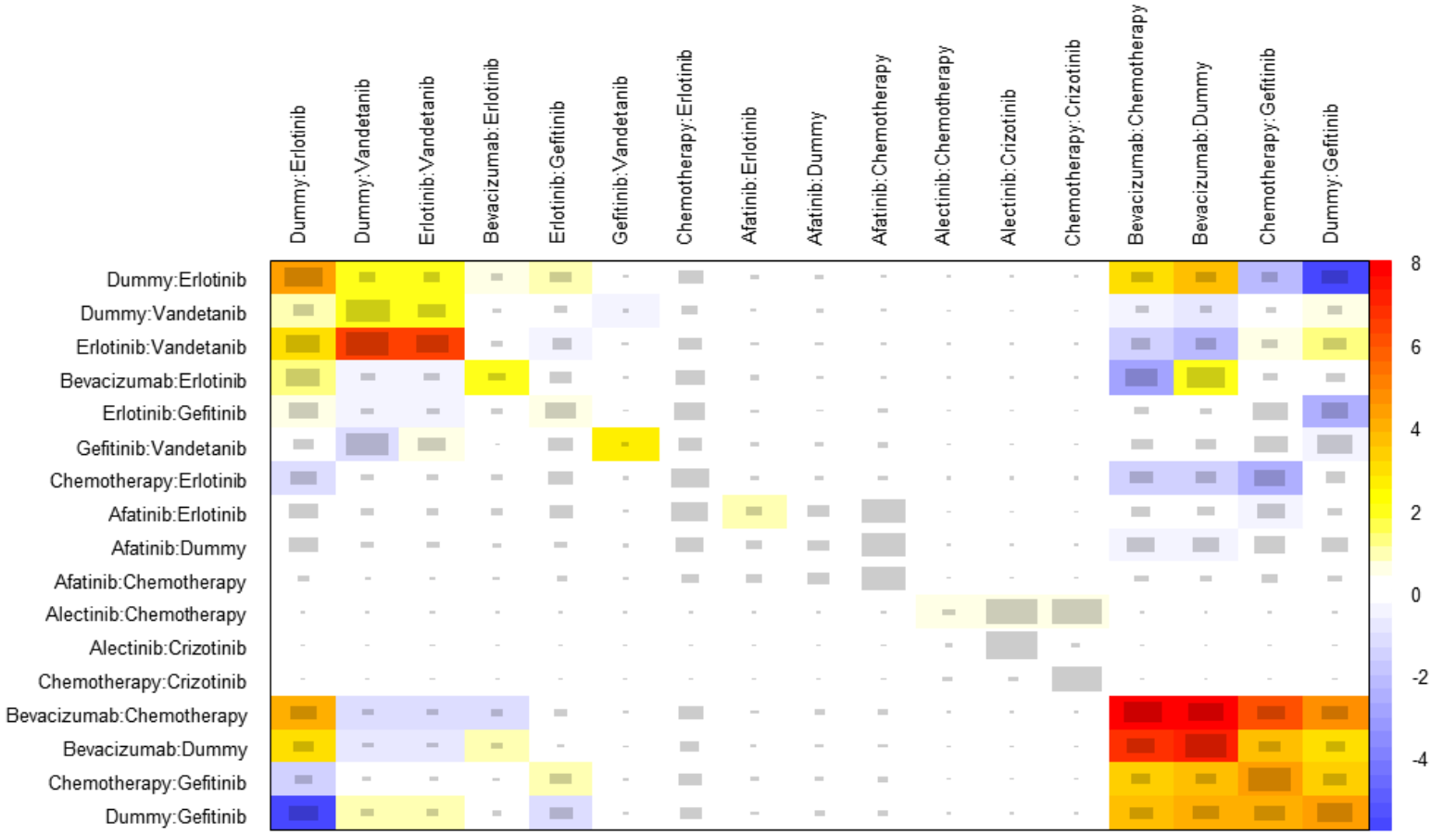
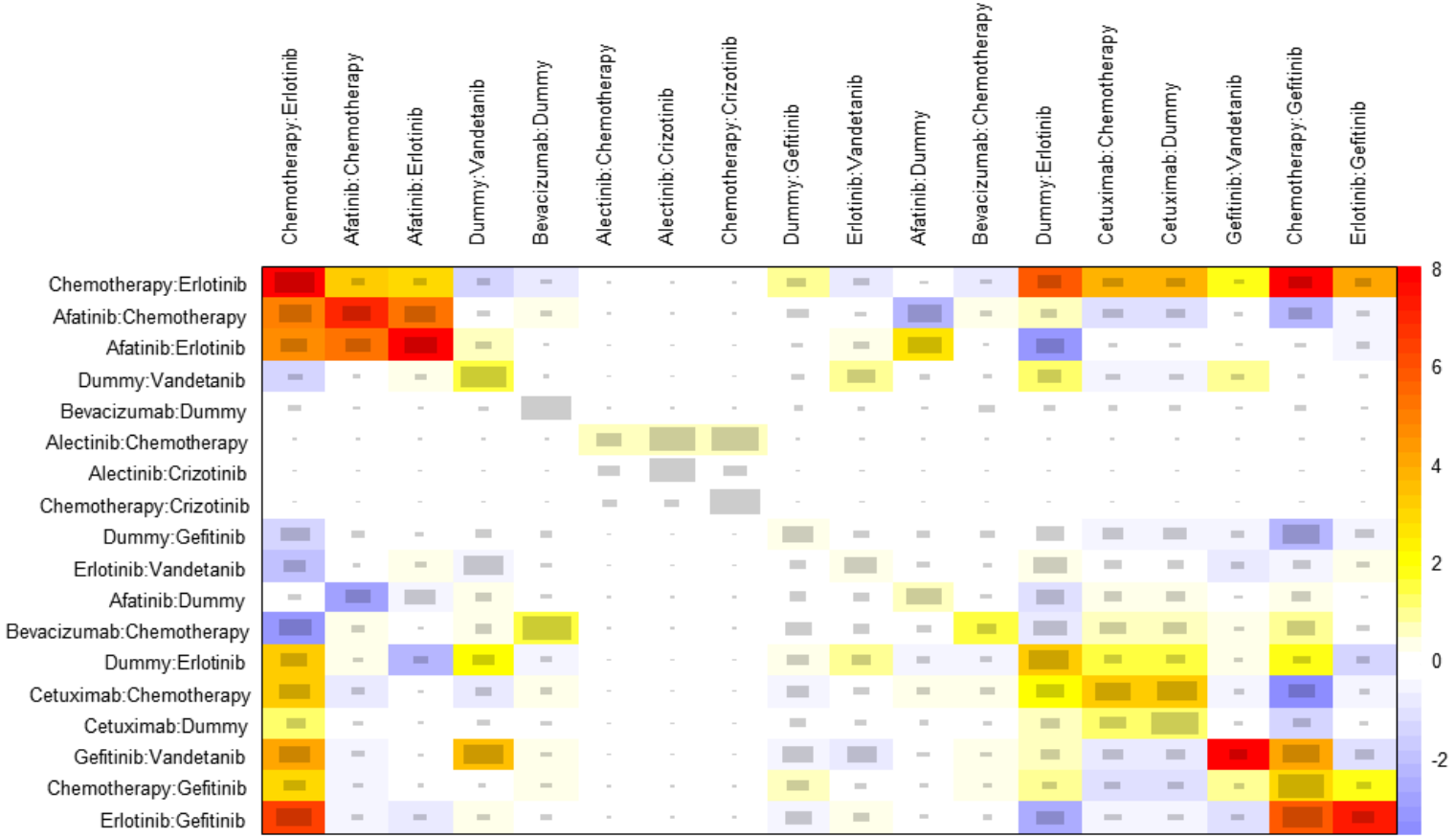


Figure S2. Inconsistency-detecting heat map between direct and indirect comparisons for overall response rate in the frequentist approach



The gray square represents the contribution of the direct estimate of the column-defining comparison to the network estimate in the row. The colors on the diagonal display the inconsistency contribution of the corresponding comparison. The colors on the off-diagonal are related to the change in inconsistency between direct and indirect estimate in a network estimate in the row after relaxing the consistency assumption for the effect of one comparison in the column.

Figure S3. Inconsistency-detecting heat map between direct and indirect comparisons for progression-free survival in the frequentist approach



The gray square represents the contribution of the direct estimate of the column-defining comparison to the network estimate in the row. The colors on the diagonal display the inconsistency contribution of the corresponding comparison. The colors on the off-diagonal are related to the change in inconsistency between direct and indirect estimate in a network estimate in the row after relaxing the consistency assumption for the effect of one comparison in the column.

Figure S4. Node-splitting analysis of inconsistency for the comparison of overall response rate in the Bayesian approach

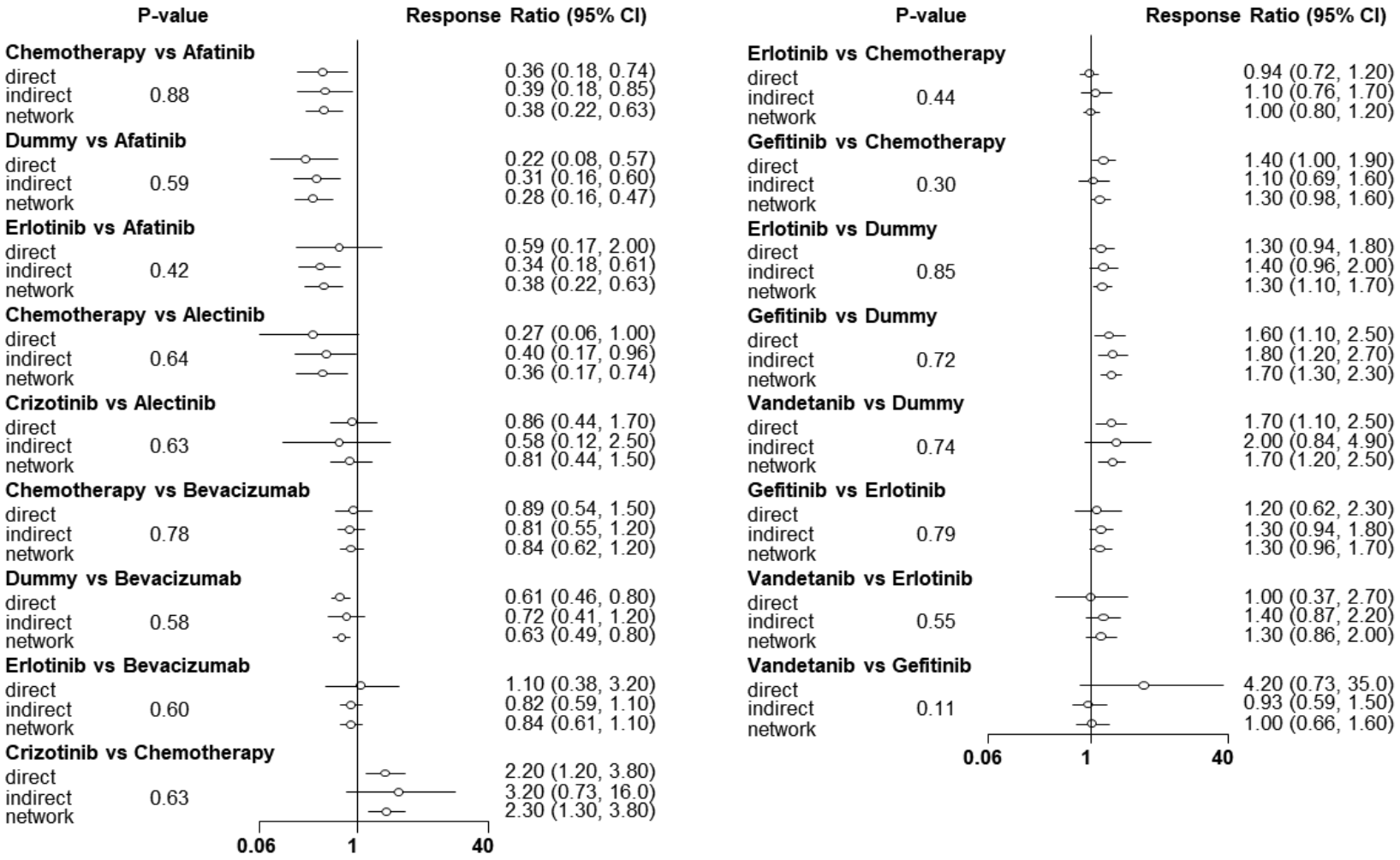


Figure S5. Node-splitting analysis of inconsistency for the comparison of progression-free survival in the Bayesian approach

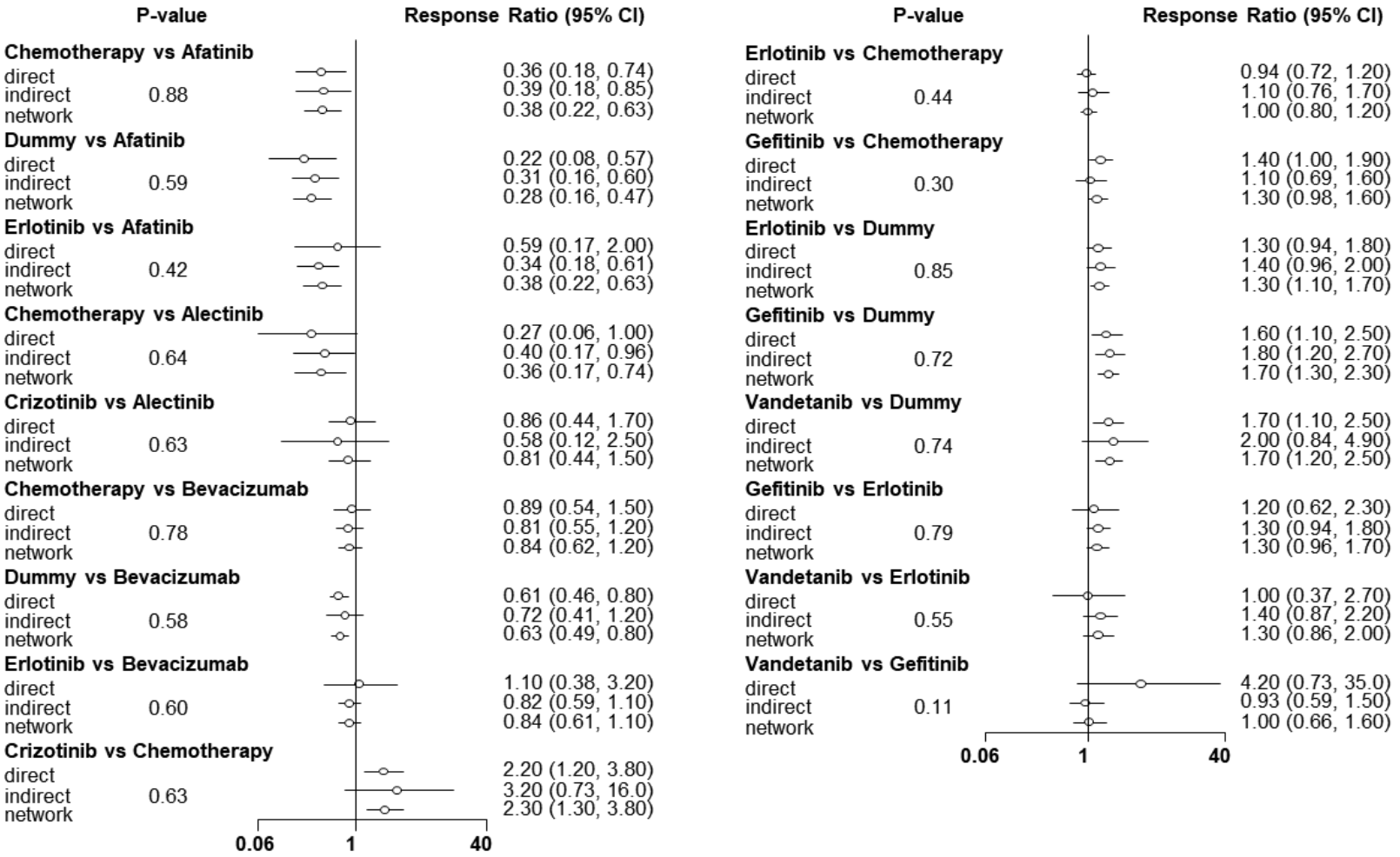
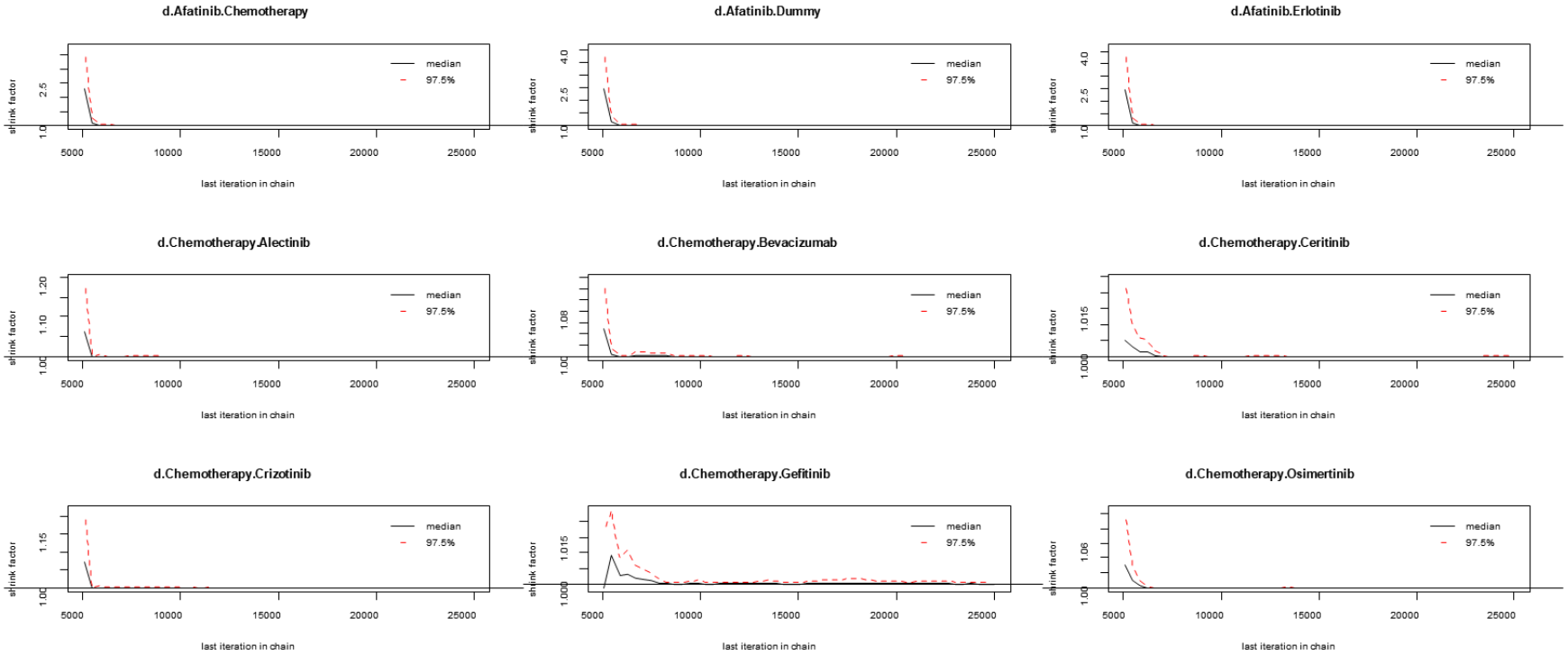
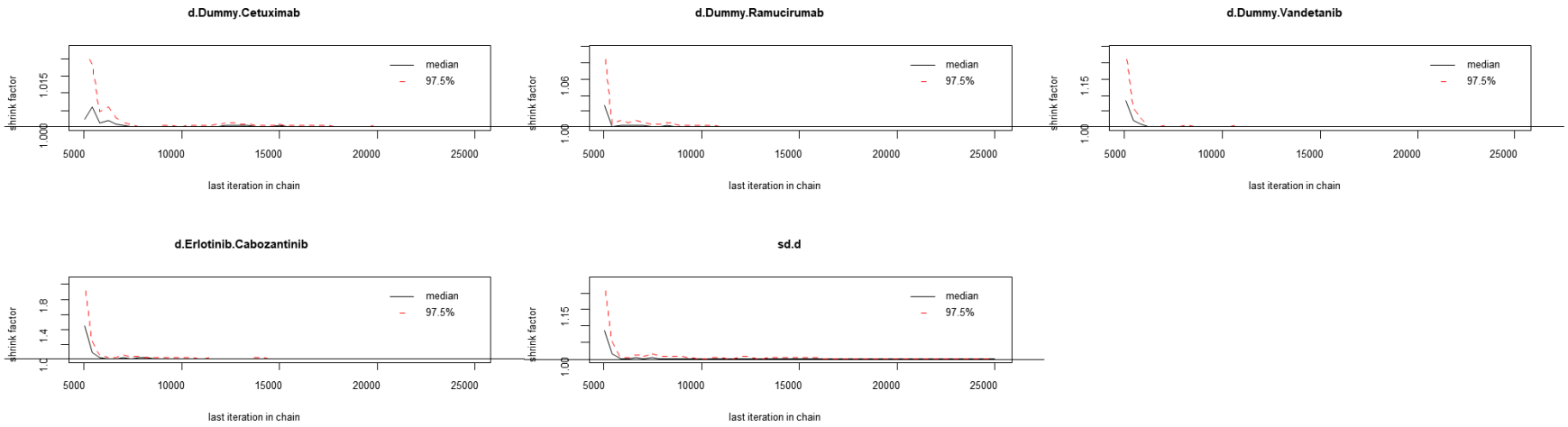


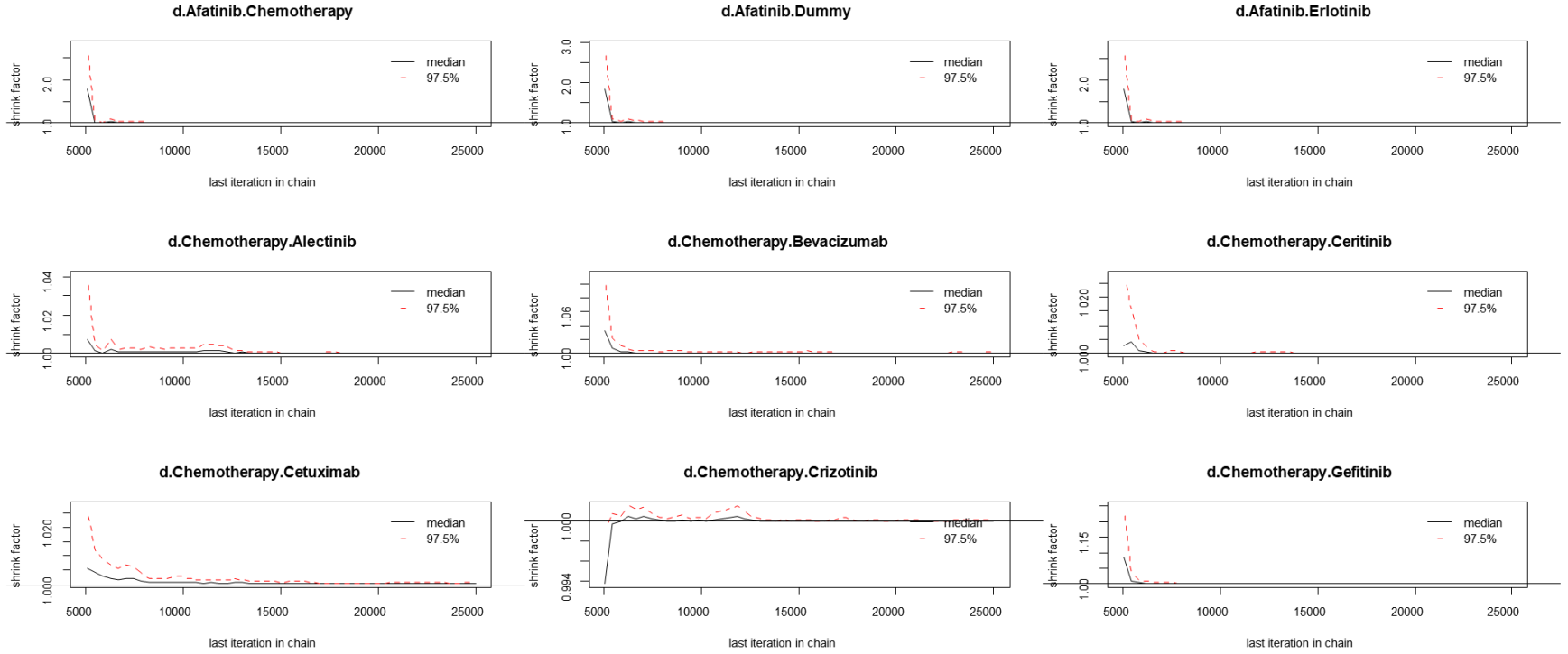
Figure S6. Convergence diagnostics for the comparison of overall response rate

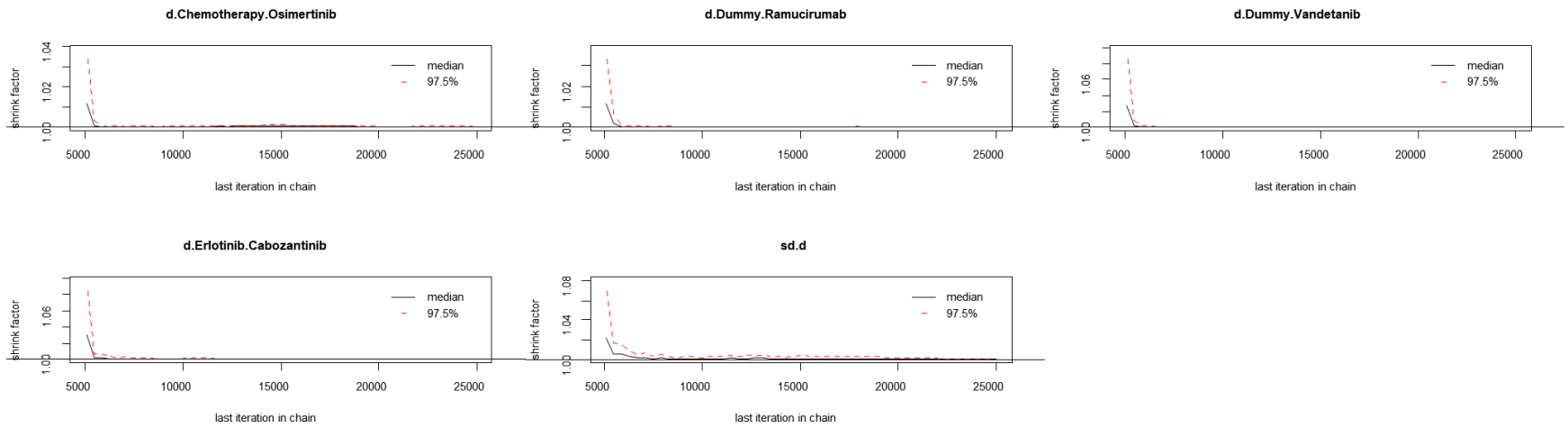




The Gelman diagram gives the scale reduction factors for each parameter. A factor of 1 means that between chain variance and within chain variance are equal, larger values mean that there is still a notable difference between chains.

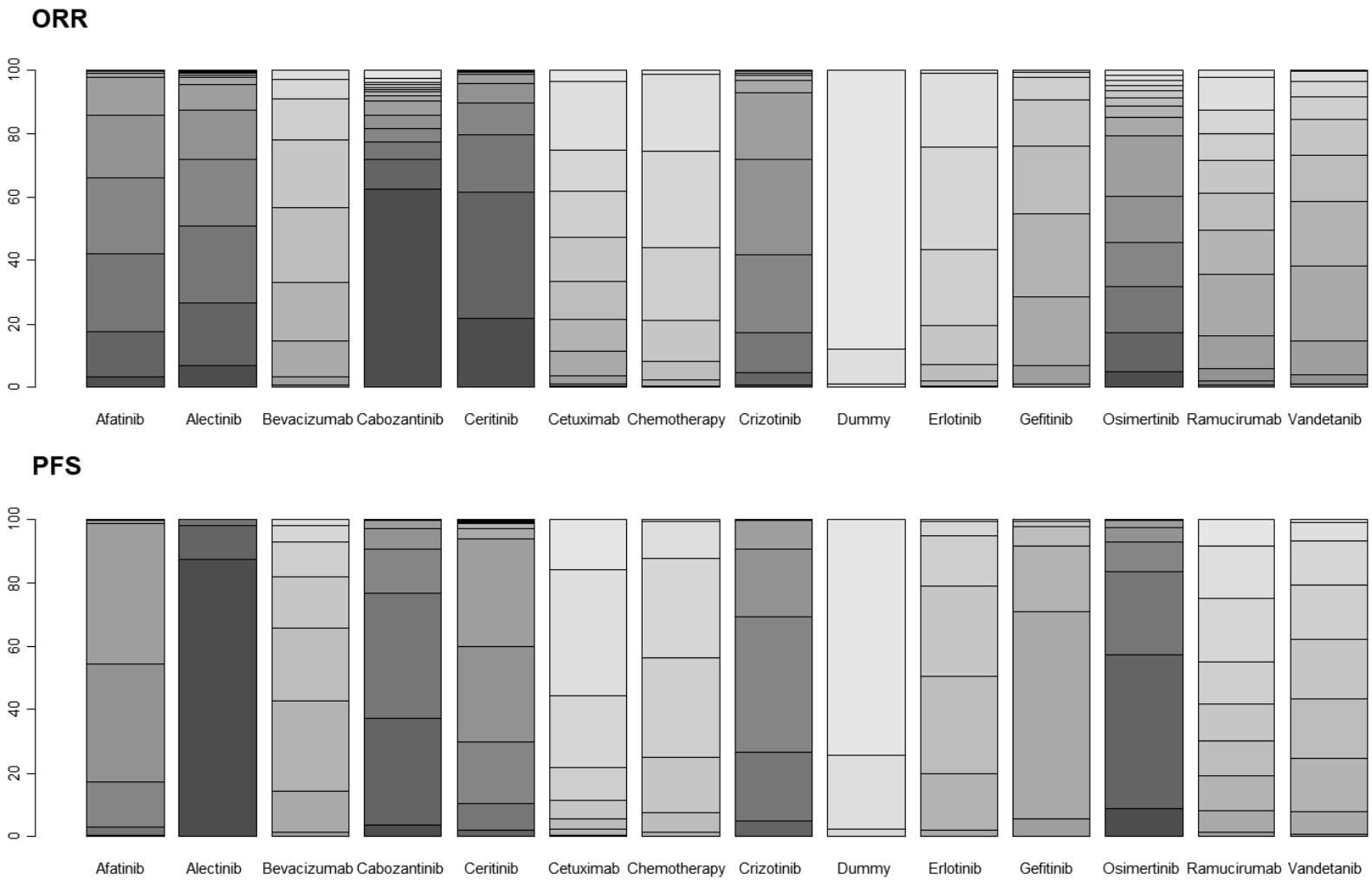
Figure S7. Convergence diagnostics for the comparison of progression-free survival





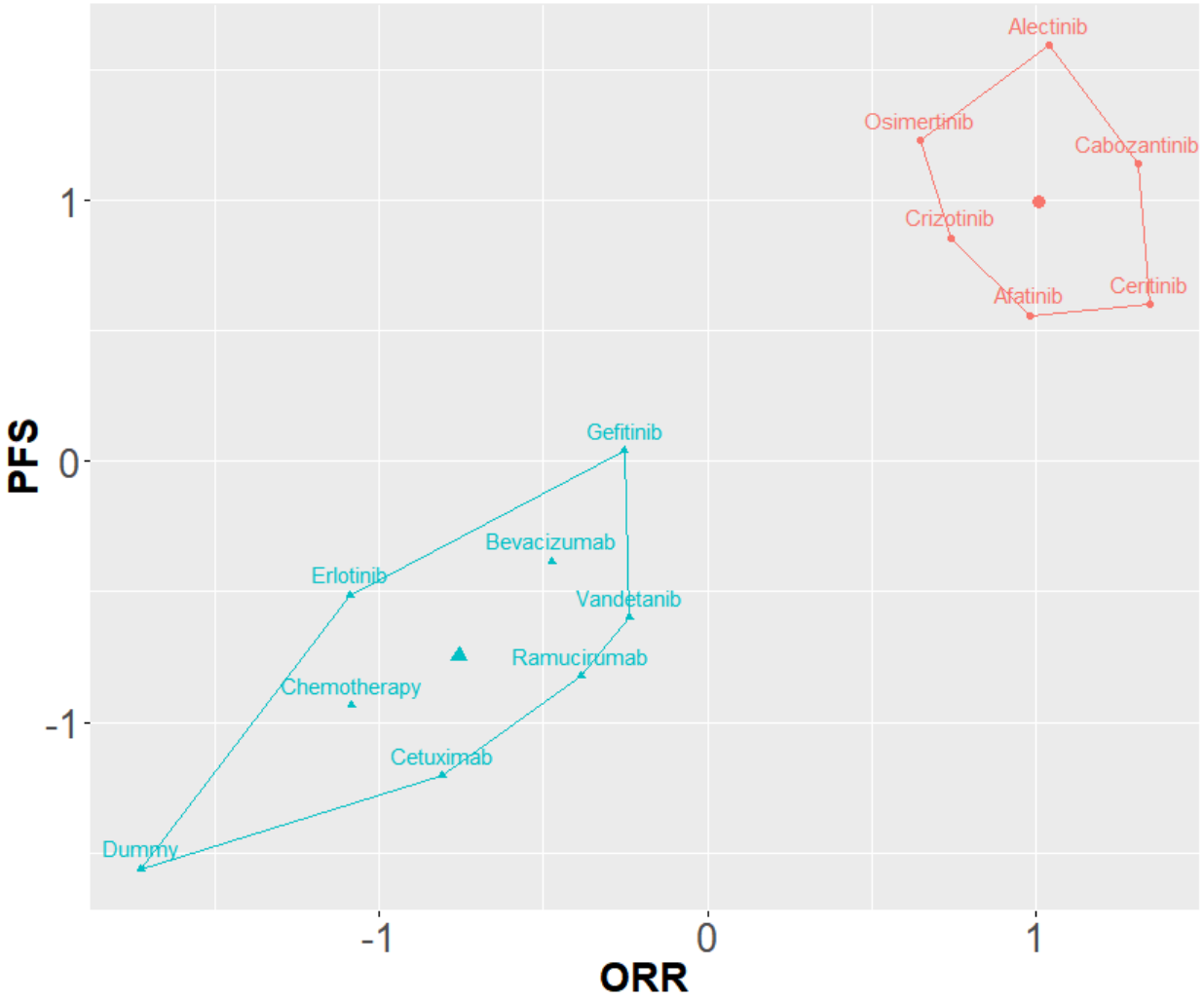
The Gelman diagram gives the scale reduction factors for each parameter. A factor of 1 means that between chain variance and within chain variance are equal, larger values mean that there is still a notable difference between chains.

Figure S8. Treatment ranking plots according to overall response rate and progression-free survival



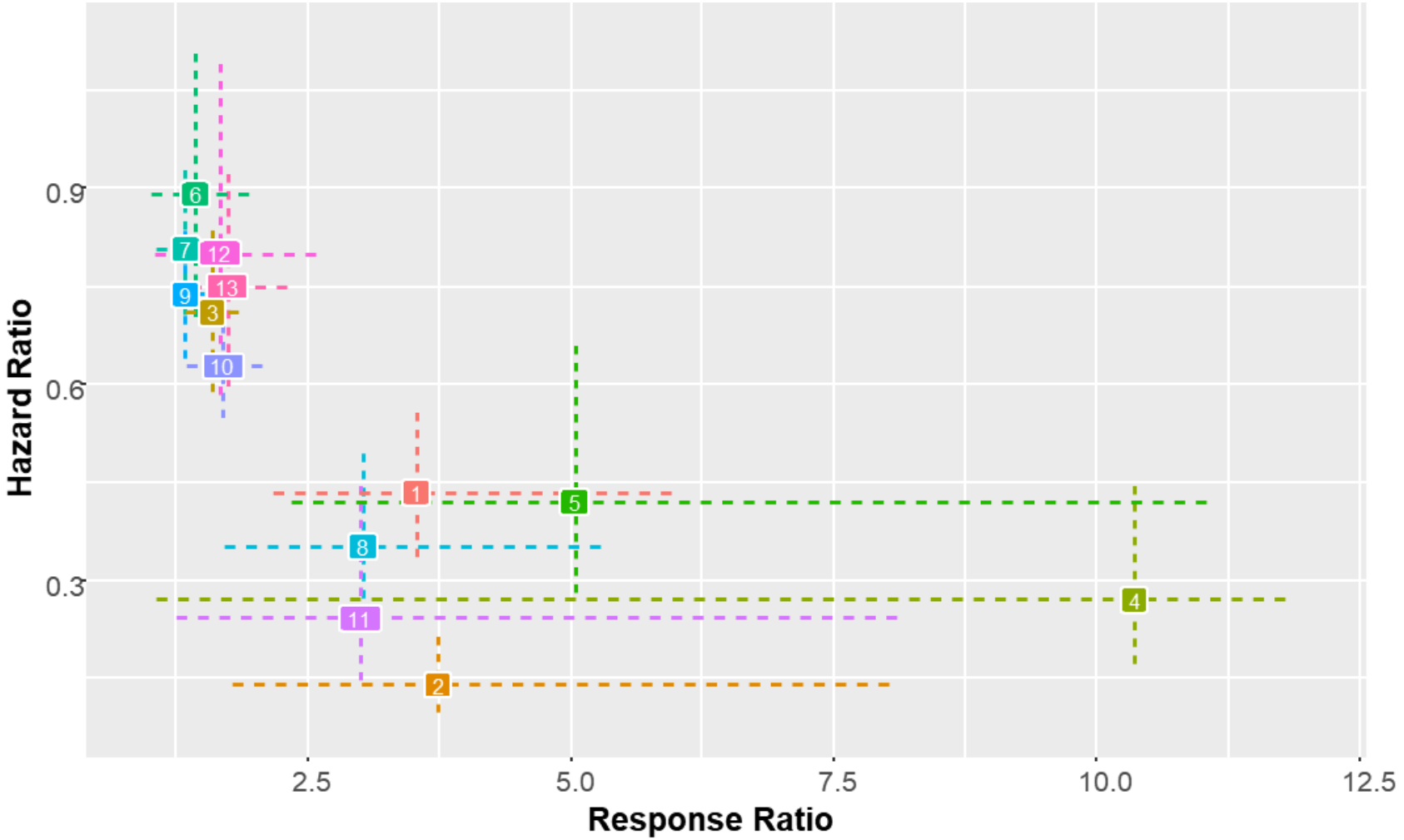
The treatment ranking was based on their probabilities in terms of both overall response rate (ORR) and progression-free survival (PFS) outcomes. In the plot, each vertical bar indicates probabilities that a specific treatment has different ranks. Darker area represents probabilities of having a higher rank. Thus, black area shows the probabilities of having the best treatment.

Figure S9. Cluster ranking plot based on SUCRA values of the overall response rate and progression-free survival of treatments



Correlation coefficient = 0.91

Figure S10. Two-dimensional graphs for response ratio and hazard ratio compared to dummy group



1, Afatinb; 2, Alectinib; 3; Bevacizumab; 4, Cabozantinib; 5, Ceritinib; 6, Cetuximab; 7, Chemotherapy; 8, Crizotinib; 9, Erlotinib; 10, Gefetinib; 11, Osimertinib; 12, Ramucizumab; 13, Vandetanib

Table S1. General characteristics of the studies included in the final analysis

Study	Period, country	Arm 1				Arm 2				HR (95% CI)
		Regimen	No.	ORR (%)	Median PFS (months)	Regimen	No.	ORR (%)	Median PFS (months)	
Johnson 2004	North America	Bevacizumab + Carboplatin + Paclitaxel	35	31.4	7.4	Carboplatin + Paclitaxel	32	18.8	4.2	-
Cufer 2005 (SIGN)	10/2003-06/2004 (12 countries)	Gefitinib	68	-	3	Docetaxel	73	-	3.4	0.94 (0.64-1.39)
Arnold 2007 (BR.20)	05/2003-03/2006 (Canada)	Vandetanib	53	-	2.7	Placebo	54	-	2.8	1.01 (0.64-1.59) [b]
Butts 2007	US, Canada	Gemcitabine + Cisplatin/ Carboplatin + Cetuximab	65	27.7	5.09	Gemcitabine + Cisplatin/ Carboplatin	66	18.2	4.21	-
Gatzemei 2007 (TALENT)	11/2001-09/2002 (27 countries)	Erlotinib + Gemcitabine	580	31.6	-	Placebo + Gemcitabine	579	39.9	-	-
Herbst 2007	10/2004-11/2005	Bevacizumab + Docetaxel/ Pemetrexed	40	12.5	4.8 [a]	Placebo + Docetaxel/ Pemetrexed	41	12.2	3 [a]	-
Heymach 2007	05/2003-07/2004 (3 countries)	Vandetanib + Docetaxel	44	18.2	3.97 [a]	Placebo + Docetaxel	41	12.2	2.8 [a]	0.83 (0.50-1.36)
Crino 2008 (INVITE)	07/2004-12/2005 (10 countries)	Gefitinib	97	3.1	2.7	Vinorelbine	99	5.1	2.9	1.19 (0.85-1.65)
Kelly 2008 (SWOG 0023)	06/2001-04/2005	Placebo	125	72.0	11.7	Gefitinib	118	68.6	8.3	0.80 (0.58-1.10)
Kim 2008 (INTEREST)	02/2004-03/2007 (24 countries)	Gefitinib	723	9.1	2.2	Docetaxel	710	7.6	2.7	1.04 (0.93-1.18)
Lilenbaum 2008	-	Erlotinib	52	3.8	1.91	Carboplatin/ Paclitaxel	51	11.8	3.52	1.45 (0.98-2.15)
Maruyama 2008 (V-15-32)	09/2003-01/2006 (Japan)	Gefitinib	245	22.4	2	Docetaxel	244	12.7	2	0.81 (0.65-1.02)
Rrosell 2008	02/2002-05/2003	Cetuximab + Cisplatin/ Vinorelbine	43	34.9	5	Cisplatin/ Vinorelbine	43	27.9	4.6	0.71 (0.4-1.2)
Goss 2009	09/2004-12/2006 (5 countries)	Gefitinib	100	6.0	1.43	Placebo	101	1.0	1.37	0.82 (0.60-1.12)

Study	Period, country	Arm 1				Arm 2				HR (95% CI)
		Regimen	No.	ORR (%)	Median PFS (months)	Regimen	No.	ORR (%)	Median PFS (months)	
Mok 2009	06/2006-04/1007 (7 countries)	Gemcitabine + Cisplatin/ Carboplatin + Erlotinib	76	35.5	6.86	Gemcitabine + Cisplatin/ Carboplatin + Placebo	78	24.4	5.46	0.47 (0.33-0.68)
Natale 2009	05/2003-08/2004 (6 countries)	Vandetanib	83	8.4	2.6	Gefitinib	85	1.2	1.9	0.69 (0.50-0.96)
Reck 2009 (AVAiL)	02/2005-08/2006 (20 countries)	Bevacizumab + Cisplatin + Gemcitabine	351	30.5	6.5 [a]	Cisplatin + Gemcitabine	347	20.2	6.1 [a]	0.82 (0.68-0.98)
Hong 2010	09/2005-08/2008 (Korea)	Gefitinib	20	26.3	3.5 [a]	Erlotinib	17	11.8	4.4 [a]	-
Lee 2010	09/2005-09/2006 (Korea)	Gefitinib	82	28.0	3.3	Docetaxel	79	7.6	3.4	0.73 (0.50-1.07) [b]
Lynch 2010 (BMS099)	01/2005-11/2006 (US)	Cetuximab + Paclitaxel/ Docetabaxel + Carboplatin	325	25.7	4.4	Paclitaxel/ Docetaxel + Carboplatin	320	16.9	4.24	0.90 (0.76-1.07)
Maemondo 2010	03/2006-05/2009 (Japan)	Gefitinib	114	73.7	10.8	Carboplatin + Paclitaxel	114	30.7	5.4	0.30 (0.22-0.41)
Mitsudomi 2010 (WJTOG 3405)	03/2006-06/2009 (Japan)	Gefitinib	86	61.6	9.2	Cisplatin + Docetaxel	86	32.6	6.3	0.49 (0.34-0.71)
Morere 2010 (IFCT-0301)	12/2004-06/2007	Docetaxel	41	7.3	2 [a]	Gefitinib	43	0.0	1.9 [a]	0.67 (0.43-1.05)
Takeda 2010 (WJTOG 0203)	03/2003-05/2005 (Japan)	Chemotherapy -> Gefitinib	298	34.2	4.6	Chemotherapy -> Chemotherapy	297	29.3	4.3	0.68 (0.57-0.80)
Brahmer 2011 (ECOG 4599)	08/2002-09/2006 (US)	Paclitaxel + Carboplatin + Bevacizumab	191	28.8	6.3	Paclitaxel + Carboplatin	230	15.7	4.3	0.64 (0.53-0.78)
			190	41.1	6.2		162	20.4	5.3	0.71 (0.57-0.88)
De Boer 2011	01/2007-03/2008	Vandetanib + Pemetrexed	256	19.1	4.11	Placebo + Pemetrexed	278	7.9	2.78	0.86 (0.71-1.04)b
GaAfatinibr 2011 (NCT00091156)	05/2004-07/2008 (5 countries)	Gefitinib	86	11.6	4.1	Placebo	87	1.1	2.9	0.61 (0.45-0.83)
Chen 2012	02/2007-07/2008	Erlotinib	57	22.8	4.57	Vinorelbine	56	8.9	2.53	0.64

Study	Period, country	Arm 1				Arm 2				HR (95% CI)
		Regimen	No.	ORR (%)	Median PFS (months)	Regimen	No.	ORR (%)	Median PFS (months)	
	(Taiwan)									(0.43-0.96)
Kelly 2012	01/2008-07/2009 (6 countries)	Pralatrexate	100	2.0	3.4	Erlotinib	101	6.9	2.8	0.91 (0.63-1.32)
Kim 2012	08/2007-10/2008	Gefitinib	48	47.9	4.9	Erlotinib	48	39.6	3.1	-
Lee 2012 (TOPICAL)	04/2005-04/2009 (UK)	Erlotinib	350	4.3	2.8	Placebo	320	2.2	2.6	0.80 (0.68-0.93)
Niho 2012 (JO19907)	04/2007-03/2008	Carboplatin/ Paclitaxel + Bevacizumab	121	60.7	6.9	Carboplatin/ Paclitaxel	59	31.0	5.9	0.61 (0.42-0.89)
Perol 2012	07/2006-06/2009	Chemotherapy -> Erlotinib	155	52.3	2.9 [a]	Chemotherapy	155	51.0	1.9 [a]	0.69 (0.54-0.88)
Rosell 2012 (EURTAC)	02/2007-01/2011	Erlotinib	86	58.1	9.7	Chemotherapy	87	14.9	5.2	0.37 (0.25-0.54)
Spigel 2012	-	Ixabepilone/ Carboplatin	42	28.6	5.3	Ixabepilone/ Carboplatin + Bevacizumab	40	50.0	6.7	-
Sun 2012 (KCSG-LU08-01)	07/2008-06/2010 (Korea)	Gefitinib	68	58.8	9	Pemetrexed	67	22.4	3	0.53 (0.36-0.80)
Boutsikou 2013	-	Erlotinib + Chemotherapy	52	44.2	-	Bevacizumab + Chemotherapy	56	39.3	-	-
Bylicki 2013 (IFCT-GFPC 05-02)	07/2006-06/2009 (France)	Erlotinib	116	-	4.2	Cisplatin + Gemcitabine	130	-	3.9	0.83 (0.64-1.09)
Dai 2013	01/2010-08/2012 (China)	Gefitinib	23	17.4	4.4	Pemetrexed	23	13.0	3.1	-
Fiala 2013	2008-2011 (Czech Republic)	Chemotherapy	150	18.2	-	Erlotinib	129	7.6	-	-
Garassino 2013 (TAILOR)	10/2007-03/2012 (Italy)	Docetaxel	110	13.6	2.9	Erlotinib	112	2.7	2.4	0.71 (0.53-0.95)
Gregorc 2013 (PROSE)	-	Erlotinib	134	-	2.5	Chemotherapy	129	-	4.8	1.26 (0.94-1.69)

Study	Period, country	Arm 1				Arm 2				HR (95% CI)
		Regimen	No.	ORR (%)	Median PFS (months)	Regimen	No.	ORR (%)	Median PFS (months)	
				-	1.7			-	2.8	1.51 (0.96-2.38)
Inoue 2013 (NEJ002)	-	Gefitinib	114	-	10.8	Carboplatin/ Paclitaxel	114	-	5.4	0.33 (0.24-0.44)
Lee 2013	11/2007-07/2010 (8 countries)	Erlotinib	82	29.3	3.8 [a]	Pemetrexed	80	10.0	4.4 [a]	0.99 (0.70-1.40)
Wang 2013	08/2008-09/2011	Pemetrexed + Carboplatin + Gefitinib	30	-	39.8	Pemetrexed + Carboplatin	30	-	27	0.37 (0.16-0.85)
Auliac 2014 (GFPC 10.02)	06/2011-02/2013	Erlotinib + Docetaxel	73	4.1	2.2	Docetaxel	74	1.4	2.5	-
Gridelli 2014	10/2008-12/2011 (Italy)	Vandetanib + Gemcitabine	61	14.8	6.1	Placebo + Gemcitabine	63	12.7	5.63	-
Heigener 2014	06/2006-08/2008 (Germany)	Erlotinib	144	7.6	2.4	Carboplatin + Vinorelbine	140	28.6	4.6	1.6 (1.22-2.09)
Kawaguchi2014 (DELTA)	08/2009-07/2012 (Japan)	Erlotinib	150	17.0	2.2	Docetaxel	151	17.9	3.2	1.22 (0.97-1.55)
Seto 2014 (JO25567)	02/2011-03/2012	Bevacizumab +Erlotinib	77	69.3	16	Erlotinib	77	63.6	9.7	0.54 (0.36-0.79)
Choi 2015	04/2010-12/2011 (Korea)	Gefitinib + Paclitaxel + Carboplatin	44	40.9	4.1	Paclitaxel + Carboplatin	46	39.1	4.1	0.94 (0.61-1.45)
Doebele 2015	10/2010-10/2011	Ramucirumab + Pemetrexed + Carboplatin/ Cisplatin	69	49.3	7.2	Pemetrexed + Carboplatin/ Cisplatin	71	38.0	5.6	0.75 (0.52-1.09) [b]
Halmos 2015	2008-2012	Erlotinib	22	13.6	5.5	Pemetrexed/ Docetaxel	24	16.7	4.4	-
Michael 2015 (GATE)	06/2009-09/2011 (Australia)	Gemcitabine	28	7.1	1.9	Erlotinib + Gemcitabine	26	3.8	2.4	1.3 (0.63-2.68)
Neal 2015 (E1512)	-	Carboplatin	39	-	3.9 [a]	Erlotinib	39	-	1.9 [a]	0.33 (0.18-0.61)bc
Pujol 2015 (IFCT-0802)	09/2009-10/2011 (French)	Bevacizumab	37	91.9	5.3	Chemotherapy	37	83.8	5.5	1.05 (0.67-1.67)
Seto 2015 (WJOG 5910L)	Japan	Bevacizumab + Docetaxel	50	-	4.4	Docetaxel	50	-	3.4	0.71 (0.47-1.09)

Study	Period, country	Arm 1				Arm 2				HR (95% CI)
		Regimen	No.	ORR (%)	Median PFS (months)	Regimen	No.	ORR (%)	Median PFS (months)	
Thomas 2015 (INNOVATIONS)	11/2007-08/2009 (Germany)	Erlotinib + Bevacizumab	111	11.7	3.5	Cisplatin + Gemcitabine + Bevacizumab	113	36.3	6.9	1.85 (1.39-2.45)
Wang 2015	01/2010-08/2013 (China)	Gefitinib	37	54.1	-	Chemotherapy	34	47.1	-	-
Karayama 2016	Japan	Bevacizumab + Pemetrexed	45	-	11.5	Pemetrexed	35	-	7.3	0.73 (0.44-1.19)
Kim 2016 (NCT01783834)	02/2008-06/2014 (Korea)	Pemetrexed	47	17.8	2	Gefitinib	48	8.7	2	-
Lee 2016 (NCT01502202)	06/2012-12/2014 (Korea)	Gefitinib	39	79.5	12.8	Placebo	37	54.1	7	0.51 (0.33-0.81) [b]
Urata 2016	-	Gefitinib	280	46.1	6.5	Erlotinib	279	44.1	7.5	1.13 (0.94-1.4)
Gautschi 2017	-	Bevacizumab + Pemetrexed	77	62.3	6.9	Pemetrexed	52	44.2	5.6	0.7 (0.5-1.0)
Herbst 2017 (NCT00946712)	-	Cetuximab	656	-	4.6	Chemotherapy	657	-	4.5	0.99 (0.88-1.10)
Hida 2017 (J-ALEX)	11/2013-08/2015 (Japan)	Alectinib	103	85.4	NA	Crizotinib	104	70.2	10.2	0.34 (0.17-0.71)
Prabhash 2017	India	Gefitinib	-	-	8.43	Pemetrexed + Cisplatin/ Carboplatin	-	-	5.6	0.66 (0.51-0.85)
Saruwatari 2017	01/2010-03/2016 (Japan)	Erlotinib	13	84.6	10.2	Gefitinib	10	60.0	7.2	-
Spigel 2017	-	Erlotinib + Sorafenib	24	8.3	3.1	Sorafenib	28	3.6	1.9	-
Wakelee 2017 (GO27821)	-	Bevacizumab + Onartuzumab + Paclitaxel	69	49.3	5	Pemetrexed + Onartuzumab + Paclitaxel	59	27.1	4.8	-
		Bevacizumab + Placebo + Paclitaxel	70	42.9	6.8	Pemetrexed + Placebo + Paclitaxel	61	36.1	6.9	-
Wakelee 2017 (NCT00596648)	-	Erlotinib + Cabazantinib	15	6.7	3.9	Cabozantinib	13	0.0	1.9	-
Gupta 2018	11/2014-03/2017	Erlotinib	100	-	4.5	Pemetrexed	100	-	4.46	0.98 (0.71-1.37)

Study	Period, country	Arm 1				Arm 2				HR (95% CI)
		Regimen	No.	ORR (%)	Median PFS (months)	Regimen	No.	ORR (%)	Median PFS (months)	
Spigel 2018 (ToPPS)	06/2009-07/2014 (US)	Bevacizumab + Pemetrexed	63	30.5	4 [a]	Pemetrexed	48	14.6	2.8 [a]	-
NCT00741988	09/2008-09/2010 (US)	Ixabepilone + Carboplatin + Bevacizumab	40	50.0	6.7	Ixabepilone + Carboplatin	42	28.9	5.3	-
NCT00085839	02/2004-03/2007 (US)	Erlotinib	52	3.8	1.91	Paclitaxel + Carboplatin	51	11.8	3.52	1.45 (0.98-2.15)
NCT00892710	06/2009-07/2014 (US)	Pemetrexed + Bevacizumab	63	30.5	4	Pemetrexed	48	14.6	2.8	-
NCT00948675	09/2009-01/2013 (US)	Paclitaxel + Carboplatin + Bevacizumab	179	27.4	5.45	Pemetrexed + Carboplatin	182	23.6	4.44	-
NCT00095199 (Kim 2013)	01/2005-07/2011 (Canada, US)	Cetuximab + Pemetrexed	301	6.6	2.89	Pemetrexed	304	4.3	2.76	1.03 (0.87-1.21)
		Cetuximab + DoCetuximabaxel	167	7.8	2.37	Docetaxel	166	6.6	1.54	0.91 (0.73-1.13)
NCT00112294	12/2004-04/2007 (US)	Carboplatin + Cetuximab + Taxane	338	25.7	4.4	Carboplatin + Taxane	338	17.2	4.24	0.90 (0.76-1.07)
NCT00130728 (Herbst 2011)	06/2005-07/2008 (16 countries)	Bevacizumab + Erlotinib	319	11.9	3.4	Placebo + Erlotinib	317	6.0	1.7	0.62 (0.52-0.75)
NCT00148798 (Pirker 2009)	10/2004-07/2007 (28 countries)	Cetuximab + Chemotherapy	557	36.4	4.8	Chemotherapy	568	29.2	4.8	0.94 (0.83-1.08)
NCT00257608 (Kabbinavar 2014)	01/2006-11/2014 (17 countries)	Erlotinib + Bevacizumab	370	-	4.8	Placebo + Bevacizumab	373	-	3.7	0.71 (0.58-0.86)
NCT00283244 (Stinchcombe 2011)	03/2006-09/2014 (US)	Erlotinib + Gemcitabine	51	21.6	4.1	Gemcitabine	44	6.8	3.7	-
NCT00312377 (Herbst 2010)	05/2006-08/2008 (25 countries)	Vandetanib + Docetaxel	694	17.3	4.04	Placebo + Docetaxel	697	10.2	3.27	0.79 (0.71-0.88) [b]
NCT00322452 (Mok 2009)	03/2006-04/2008 (9 countries)	Gefitinib	609	43.0	5.7	Carboplatin/ Paclitaxel	608	32.2	5.8	0.74 (0.65-0.85)
NCT00364351	08/2006-09/2008	Vandetanib	623	12.0	11.3	Erlotinib	617	12.0	8.9	0.98

Study	Period, country	Arm 1				Arm 2				HR (95% CI)
		Regimen	No.	ORR (%)	Median PFS (months)	Regimen	No.	ORR (%)	Median PFS (months)	
	(22 countries)									(0.87-1.10)
NCT00373425 (Kelly 2015)	09/2006-04/2013 (19 countries)	Erlotinib	623	-	55	Placebo	350	-	56.2	0.94 (0.78-1.14)
NCT00404924 (ZD6474)	11/2006-10/2009 (22 countries)	Vandetanib + BSC	617	2.6	1.9	Placebo + BSC	307	0.7	1.8	-
NCT00409006	02/2007-08/2009 (China, Korea, Taiwan)	Gefitinib + Pemetrexed + Cisplatin	39	46.2	9.95	Pemetrexed + Cisplatin	31	35.5	6.83	0.53 (0.27-1.04)
NCT00418886 (ZEAL)	01/2007-09/2008 (21 countries)	Vandetanib + Pemetrexed	256	19.1	17.6	Placebo + Pemetrexed	278	7.9	11.9	0.86 (0.69-1.06)
NCT00447057 (Dittrich 2014)	03/2007-07/2010 (5 countries)	Erlotinib + Pemetrexed	60	17.1	3.19	Pemetrexed	70	10.8	2.89	0.63 (0.44-0.90)
NCT00518011	08/2007-02/2009 (Australia)	Gemcitabine	8	0.0	5.44	Erlotinib + Gemcitabine	7	5.7	5.69	1.84 (0.48-7.03)
NCT00531960 (Ciuleanu 2013)	01/2008-01/2010 (13 countries)	Erlotinib + Bevacizumab	63	27.0	5.5	Erlotinib + Chemotherapy	61	44.3	8.1	1.05 (0.70-1.59)
NCT00550173	11/2007-01/2012 (7 countries)	Erlotinib + Pemetrexed	76	44.7	7.4	Pemetrexed	80	10.0	4.4	0.58 (0.39-0.85)
NCT00556322 (Ciuleanu 2012)	03/2006-06/2012 (27 countries)	Erlotinib	203	7.9	6.3	Chemotherapy	221	6.3	8.6	1.19 (0.97-1.46)
NCT00556712 (Cappuzzo 2010)	01/2006-11/2010 (28 countries)	Erlotinib	437	11.9	12.3	Placebo	447	5.4	11.1	0.71 (0.62-0.82)
NCT00606502	01/2008-06/2009 (6 countries)	Erlotinib	101	7.1	2.8	Pralatrexate	100	2.1	3.4	-
NCT00609804	03/2008-05/2012 (US)	Erlotinib + Sorafenib	24	8.3	3.1	Sorafenib	28	3.6	1.9	-
NCT00656136 (Miller 2012)	04/2008-10/2013 (15 countries)	Afatinib + Best support care	390	7.4	3.29	Placebo + Best support care	195	0.5	1.08	0.38 (0.31-0.48)
NCT00660816	01/2008-04/2013 (US)	Erlotinib + Pemetrexed/ Docetaxel	22	16.7	4.4	Pemetrexed/ Docetaxel	24	13.3	5.5	-
NCT00687297 (Aisner 2013)	04/2008-01/2011	Placebo + Docetaxel + Carboplatin	82	18.3	4.2	Vandetanib + Docetaxel + Carboplatin	80	18.8	4.5	1.49 (1.07-2.07)

Study	Period, country	Arm 1				Arm 2				HR (95% CI)
		Regimen	No.	ORR (%)	Median PFS (months)	Regimen	No.	ORR (%)	Median PFS (months)	
NCT00753714 (ZELIG)	10/2008-04/2011 (Italy)	Vandetanib + Gemcitabine	61	14.8	6.1	Placebo + Gemcitabine	63	12.7	5.6	-
NCT00770588	09/2008-08/2009	Gefitinib	148	23.6	4.8	Placebo	148	0.7	2.6	0.42 (0.33-0.55)
NCT00777179	10/2008-01/2010 (Korea)	Vandetanib	75	18.7	2.7	Placebo	42	2.4	1.7	-
NCT00800202 (BRAIN)	04/2009-10/2012 (France)	Erlotinib + Bevacizumab	22	12.5	6.3	Bevacizumab + Paclitaxel + Carboplatin	60	62.7	6.7	-
NCT00883779	04/2009-12/2014 (7 countries)	Erlotinib	226	17.7	7.6	Placebo	225	43.1	6	0.57 (0.46-0.70)
NCT00932893 (Shaw 2016)	09/2009-03/2012 (22 countries)	Crizotinib	173	65.3	7.7	Pemetrexed/ Docetaxel	174	19.5	3	0.49 (0.37-0.64)
NCT00949650 (LUX-lung 6)	08/2009-02/2012 (25 countries)	Afatinib	230	56.5	11.17	Pemetrexed/ Cisplatin	115	22.6	6.9	0.58 (0.43-0.78)
NCT01085136 (LUX-Lung 5)	02/2010-10/2013 (24 countries)	Afatinib + Paclitaxel	134	32.1	5.55	Chemotherapy	68	13.2	2.89	0.61 (0.44-0.85)
NCT01121393 (LUX-lung 3)	04/2010-12/2013 (3 countries)	Afatinib	242	67.8	11.01	Gemcitabine/ Cisplatin	122	23.0	5.59	0.28 (0.20-0.39)
NCT01154140 (PROFILE 1014)	01/2011-11/2013 (31 countries)	Crizotinib	172	74.4	10.9	Chemotherapy	171	45.0	7	0.45 (0.35-0.60)
NCT01160744 (Thomas 2017)	09/2010-01/2014 (6 countries)	Ramucirumab + Gemcitabine + Carboplatin/ Cisplatin	71	46.5	5.6	Gemcitabine + Carboplatin/ Cisplatin	69	24.6	5.4	0.88 (0.60-1.29) [b]
NCT01168973 (Reck 2018)	12/2010-12/2013 (27 countries)	Ramucirumab + Docetaxel	628	29.9	4.5	Placebo + Docetaxel	625	13.6	3	0.76 (0.68-0.86)
NCT01196078	02/2007-12/2010 (Taiwan)	Erlotinib	57	22.8	6.66	Vinorelbine	56	8.9	3.87	-
NCT01342965 (ENSURE)	03/2011-07/2012 (China)	Erlotinib	110	68.2	11	Gemcitabine+Cisplatin	107	39.3	5.5	0.34 (0.22-0.51)
NCT01351415	06/2011-06/2016 (18 countries)	Bevacizumab + Erlotinib/ Docetaxel/ Pemetrexed	245	8.6	5.45	Erlotinib/ Docetaxel/ Pemetrexed	240	6.3	3.98	0.83 (0.68-1.02) [b]

Study	Period, country	Arm 1				Arm 2				HR (95% CI)
		Regimen	No.	ORR (%)	Median PFS (months)	Regimen	No.	ORR (%)	Median PFS (months)	
NCT01523587 (Felip 2017)	03/2012-08/2013 (23 countries)	Afatinib	335	4.8	2.43	Erlotinib	334	3.0	1.94	0.82 (0.68-1.00)
NCT01544179 (Soria 2015)	03/2012-05/2014 (12 countries)	Gefitinib	133	31.6	5.4	Placebo	132	34.1	5.4	0.86 (0.65-1.13)
NCT01565538 (Li 2014)	12/2008-05/2012 (China)	Erlotinib	61	19.7	4.1	Pemetrexed	62	8.1	3.9	0.92 (0.62-1.37)
NCT01639001 (Lu 2016)	09/2012-06/2015 (5 countries)	Crizotinib	104	87.5	11.1	Chemotherapy	103	45.6	6.8	0.40 (0.28-0.57)
NCT01703091 (Hosomi 2015)	12/2012-12/2014 (Japan)	Ramucirumab + Docetaxel	76	28.9	5.2	Placebo + Docetaxel	81	18.5	4.2	0.83 (0.59-1.16)
NCT01708954 (Neal 2016)	02/2013-08/2015 (US)	Cabozantinib	38	0.11	4.3	Erlotinib	38	0.03	1.8	0.39 (0.27-0.55)
NCT01828099 (Soria 2017)	07/2013-06/2016 (30 countries)	Ceritinib	189	72.5	16.6	Chemotherapy	187	26.7	8.1	0.55 (0.42-0.73)
NCT01828112 (Shaw2017)	06/2013-01/2016 (20 countries)	Ceritinib	115	39.1	5.4	Pemetrexed/Docetaxel	116	6.9	1.6	0.49 (0.36-0.67)
NCT01998919	08/2006-11/2011 (8 countries)	Erlotinib + Chemotherapy	76	36.8	30.4	Placebo + Chemotherapy	78	24.4	23.4	0.47 (0.33-0.68)
NCT02075840 (Peters 2017)	08/2014-01/2016 (29 countries)	Alectinib	152	82.9	-	Crizotinib	151	75.5	11.1	0.47 (0.34-0.65)
NCT02151981 (Mok 2017)	08/2014-04/2016 (18 countries)	Osimertinib	279	70.6	10.1	Chemotherapy	140	31.4	4.4	0.30 (0.23-0.41)
NCT02604342	11/2015-01/2017 (13 countries)	Alectinib	72	37.5	9.6	Pemetrexed/Docetaxel	35	11.4	1.4	0.15 (0.08-0.29)

ORR, overall response rate; PFS, progression-free survival; HR, hazard ratio; 95% CI, 95% confidence interval

[a] Recalculated median PFS as the formula: $\text{PFS (months)} = \text{PFS (weeks)} * \frac{7}{30}$

[b] Recalculated 95% CI from different levels of significant α as the formula: $(1-\alpha)\%\ \text{CI for HR} = \exp[\hat{\beta}]: \exp[\hat{\beta} \pm z_{1-\alpha/2} * \sqrt{\widehat{\text{Var}}(\hat{\beta})}$

Table S2. Test for heterogeneity

RR for ORR				HR for PFS			
Treatment 1	**Treatment 2**	**Pair-wise I^2 (%)**	**Consi-stency I^2 (%)**	**Treatment 1**	**Treatment 2**	**Pair-wise I^2 (%)**	**Consi-stency I^2 (%)**
Afatinib	Chemotherapy	0.00	0.00	Afatinib	Chemotherapy	90.18	87.65
Afatinib	Dummy	76.89	40.37	Afatinib	Dummy	85.15	66.23
Afatinib	Erlotinib	-	23.85	Afatinib	Erlotinib	-	91.74
Alectinib	Chemotherapy	-	0.00	Alectinib	Chemotherapy	-	0.00
Alectinib	Crizotinib	14.89	43.56	Alectinib	Crizotinib	0.00	0.00
Bevacizumab	Chemotherapy	68.89	61.26	Bevacizumab	Chemotherapy	0.00	0.00
Bevacizumab	Dummy	35.97	26.79	Bevacizumab	Dummy	14.37	11.74
Bevacizumab	Erlotinib	-	26.45	Cabozantinib	Erlotinib	0.00	0.00
Cabozantinib	Erlotinib	-	-	Ceritinib	Chemotherapy	0.00	0.00
Ceritinib	Chemotherapy	86.89	86.79	Cetuximab	Chemotherapy	-	70.69
Cetuximab	Dummy	0.00	0.00	Cetuximab	Dummy	0.00	0.00
Chemotherapy	Crizotinib	87.62	83.92	Chemotherapy	Crizotinib	0.00	0.00
Chemotherapy	Erlotinib	85.10	83.81	Chemotherapy	Erlotinib	85.27	87.00
Chemotherapy	Gefitinib	69.48	72.18	Chemotherapy	Gefitinib	90.87	89.56
Chemotherapy	Osimertinib	-	-	Chemotherapy	Osimertinib	-	-
Dummy	Erlotinib	86.67	86.26	Dummy	Erlotinib	68.06	63.54
Dummy	Gefitinib	90.03	89.89	Dummy	Gefitinib	80.03	78.90
Dummy	Ramucirumab	60.26	60.08	Dummy	Ramucirumab	0.00	0.00
Dummy	Vandetanib	31.91	23.34	Dummy	Vandetanib	0.00	29.46
Erlotinib	Gefitinib	0.00	37.39	Erlotinib	Gefitinib	-	89.04
Erlotinib	Vandetanib	-	68.08	Erlotinib	Vandetanib	-	0.00
Gefitinib	Vandetanib	-	65.41	Gefitinib	Vandetanib	-	91.53
Global I^2		78.18	77.64	Global I^2		78.33	78.72

Table S3. Direct pairwise comparative efficacy in the frequentist approach

HR for PFS (95% CI)															RR for ORR (95% CI)
	Afat						*2.72 (1.59-4.66)*		*3.28 (1.39-7.75)*	1.60 (0.57-4.47)					
		Alec					*3.28 (1.01-10.7)*	1.16 (0.71-1.88)							
			Beva				1.10 (0.74-1.63)		*1.59 (1.27-1.98)*	0.89 (0.39-2.00)					
				Cabo						4.00 (0.42-37.9)					
					Ceri		*3.52 (1.97-6.30)*								
						Cetu			*1.39 (1.02-1.91)*						
	0.41 (0.27-0.61)	*0.15 (0.07-0.33)*	1.05 (0.67-1.65)		*0.52 (0.35-0.77)*	0.99 (0.60-1.62)	Chem	*0.46 (0.31-0.70)*		0.96 (0.76-1.21)	*0.66 (0.51-0.84)*	*0.45 (0.22-0.92)*			
		0.42 (0.26-0.68)					*2.23 (1.61-3.09)*	Criz							
	0.47 (0.32-0.69)		*0.69 (0.58-0.83)*			0.91 (0.73-1.14)			Dum	*0.72 (0.55-0.96)*	0.75 (0.54-1.05)		*0.58 (0.39-0.86)*	*0.56 (0.40-0.79)*	
	0.82 (0.49-1.37)			*0.37 (0.23-0.59)*			0.98 (0.85-1.12)		*1.52 (1.28-1.82)*	Erlo	0.84 (0.51-1.40)			1.00 (0.47-2.09)	
							1.44 (1.23-1.68)		*1.46 (1.18-1.79)*	0.88 (0.53-1.48)	Gefi			0.14 (0.02-1.24)	
							3.33 (1.93-5.77)					Osim			
									1.25 (0.94-1.66)				Ramu		
									1.21 (0.96-1.53)	1.02 (0.62-1.67)	1.45 (0.81-2.58)			Vand	

Drugs are reported in alphabetical order. Data are RRs and HRs (95%CI) in the row-defining treatment compared with the column-defining treatment. For ORR, RRs higher than 1 are favour the row-defining treatment. For PFS, HRs lower than 1 are favour the row-defining treatment (the first drug in alphabetical order). Significant results are in italic and underscored. RR, response ratio; HR, hazard ratio; CI, confidence interval; ORR: overall response rate; PFS: progression-free survival. Afat, afatinib; Alec, alectinib; Beva, bevacizumab; Cabo, cabozantinib; Ceri, ceritinib; Cetu, cetuximab; Chem, chemotherapy; Criz, crizotinib; Dum, dummy; Erlo, erlotinib; Gefi, gefitinib; Osim, osimertinib; Ramu, ramucirumab; Vand, vandetanib.

Table S4. Comparative efficacy of targeted therapies for overall response rate in the network meta-analysis based on the frequentist approach

Afat	0.96 (0.47-1.94)	*2.03 (1.27-3.24)*	0.56 (0.06-5.57)	0.72 (0.35-1.49)	*2.18 (1.26-3.77)*	*2.55 (1.67-3.89)*	1.15 (0.64-2.05)	*3.05 (1.95-4.76)*	*2.25 (1.45-3.50)*	*1.90 (1.20-2.99)*	1.13 (0.49-2.62)	1.76 (0.97-3.21)	*1.72 (1.01-2.94)*
1.04 (0.52-2.11)	Alec	*2.12 (1.14-3.93)*	0.59 (0.06-6.02)	0.76 (0.34-1.70)	*2.28 (1.15-4.52)*	*2.66 (1.51-4.67)*	1.20 (0.76-1.89)	*3.18 (1.73-5.83)*	*2.35 (1.30-4.26)*	*1.98 (1.09-3.61)*	1.18 (0.47-2.96)	1.84 (0.89-3.80)	1.80 (0.92-3.52)
0.49 (0.31-0.79)	*0.47 (0.25-0.88)*	Beva	0.28 (0.03-2.67)	*0.36 (0.19-0.67)*	1.08 (0.74-1.56)	1.25 (0.98-1.61)	*0.57 (0.35-0.90)*	*1.50 (1.23-1.83)*	1.11 (0.86-1.43)	0.93 (0.71-1.23)	0.56 (0.26-1.20)	0.87 (0.56-1.35)	0.85 (0.59-1.22)
1.78 (0.18-17.6)	1.7 (0.17-17.42)	3.60 (0.37-34.64)	Cabo	1.28 (0.12-13.21)	3.88 (0.4-37.93)	4.52 (0.47-43.2)	2.04 (0.21-20.2)	5.41 (0.56-51.7)	4.00 (0.42-37.9)	3.37 (0.35-32.3)	2.01 (0.19-21.5)	3.13 (0.32-31.0)	3.06 (0.31-29.8)
1.38 (0.67-2.84)	1.32 (0.59-2.98)	*2.81 (1.49-5.29)*	0.78 (0.08-8.01)	Ceri	*3.02 (1.50-6.07)*	*3.52 (1.97-6.30)*	1.59 (0.78-3.21)	*4.21 (2.26-7.85)*	*3.11 (1.69-5.74)*	*2.62 (1.41-4.86)*	1.57 (0.62-3.97)	*2.44 (1.16-5.11)*	*2.38 (1.20-4.73)*
0.46 (0.27-0.79)	*0.44 (0.22-0.87)*	0.93 (0.64-1.35)	0.26 (0.03-2.52)	*0.33 (0.16-0.67)*	Cetu	1.17 (0.79-1.72)	*0.53 (0.30-0.91)*	*1.39 (1.02-1.91)*	1.03 (0.71-1.50)	0.87 (0.59-1.29)	0.52 (0.23-1.18)	0.81 (0.49-1.34)	0.79 (0.51-1.22)
0.39 (0.26-0.60)	*0.38 (0.21-0.66)*	0.80 (0.62-1.02)	0.22 (0.02-2.11)	*0.28 (0.16-0.51)*	0.86 (0.58-1.26)	Chem	*0.45 (0.30-0.67)*	1.20 (0.96-1.50)	0.89 (0.73-1.07)	*0.74 (0.61-0.91)*	*0.45 (0.22-0.92)*	0.69 (0.44-1.09)	*0.68 (0.47-0.98)*
0.87 (0.49-1.56)	0.83 (0.53-1.32)	*1.77 (1.11-2.83)*	0.49 (0.05-4.85)	0.63 (0.31-1.27)	*1.90 (1.09-3.31)*	*2.22 (1.49-3.30)*	Criz	*2.65 (1.68-4.18)*	*1.96 (1.27-3.04)*	*1.65 (1.06-2.58)*	0.99 (0.43-2.25)	1.54 (0.84-2.81)	1.50 (0.88-2.57)
0.33 (0.21-0.51)	*0.31 (0.17-0.58)*	*0.67 (0.55-0.81)*	0.19 (0.02-1.77)	*0.24 (0.13-0.44)*	*0.72 (0.52-0.98)*	0.84 (0.67-1.05)	*0.38 (0.24-0.59)*	Dum	*0.74 (0.60-0.91)*	*0.62 (0.49-0.79)*	*0.37 (0.17-0.79)*	*0.58 (0.39-0.86)*	*0.57 (0.42-0.77)*
0.44 (0.29-0.69)	*0.43 (0.23-0.77)*	0.90 (0.7-1.16)	0.25 (0.03-2.37)	*0.32 (0.17-0.59)*	0.97 (0.67-1.41)	1.13 (0.94-1.36)	*0.51 (0.33-0.79)*	*1.35 (1.10-1.66)*	Erlo	0.84 (0.67-1.06)	0.50 (0.24-1.06)	0.78 (0.50-1.22)	0.76 (0.54-1.08)
0.53 (0.33-0.83)	*0.51 (0.28-0.92)*	1.07 (0.81-1.41)	0.30 (0.03-2.85)	*0.38 (0.21-0.71)*	1.15 (0.78-1.71)	*1.34 (1.09-1.65)*	*0.61 (0.39-0.95)*	*1.61 (1.27-2.03)*	1.19 (0.94-1.50)	Gefi	0.60 (0.28-1.27)	0.93 (0.59-1.48)	0.91 (0.63-1.32)
0.88 (0.38-2.04)	0.85 (0.34-2.12)	1.79 (0.83-3.86)	0.50 (0.05-5.32)	0.64 (0.25-1.62)	1.93 (0.85-4.38)	*2.25 (1.09-4.64)*	1.01 (0.44-2.31)	*2.69 (1.26-5.74)*	1.99 (0.94-4.20)	1.67 (0.79-3.55)	Osim	1.56 (0.66-3.66)	1.52 (0.68-3.42)
0.57 (0.31-1.03)	0.54 (0.26-1.12)	1.15 (0.74-1.79)	0.32 (0.03-3.17)	*0.41 (0.20-0.86)*	1.24 (0.75-2.06)	1.44 (0.91-2.28)	0.65 (0.36-1.19)	*1.73 (1.16-2.57)*	1.28 (0.82-2.00)	1.08 (0.68-1.71)	0.64 (0.27-1.51)	Ramu	0.98 (0.59-1.62)
0.58 (0.34-0.99)	0.56 (0.28-1.09)	1.18 (0.82-1.69)	0.33 (0.03-3.18)	*0.42 (0.21-0.83)*	1.27 (0.82-1.97)	*1.48 (1.03-2.13)*	0.67 (0.39-1.14)	*1.77 (1.30-2.40)*	1.31 (0.92-1.85)	1.10 (0.76-1.60)	0.66 (0.29-1.48)	1.02 (0.62-1.69)	Vand

Drugs are reported in alphabetical order. Data in the right-upper triangle are RRs (95%CI) in the row-defining treatment compared with the column-defining treatment. RRs higher than 1 favor the row-defining treatment (the first drug in alphabetical order). RRs for the opposite comparison of ORR are in the left-lower triangle. Each comparison is shown twice in the table, once with drug A versus drug B and once with drug B versus drug A. Significant results are in italic and underscored. RR, response ratio; CI, confidence interval; ORR: overall response rate; Afat, afatinib; Alec, alectinib; Beva, bevacizumab; Cabo, cabozantinib; Ceri, ceritinib; Cetu, cetuximab; Chem, chemotherapy; Criz, crizotinib; Dum, dummy; Erlo, erlotinib; Gefi, gefitinib; Osim, osimertinib; Ramu, ramucirumab; Vand, vandetanib.

Table S5. Comparative efficacy of targeted therapies for progression-free survival in the network meta-analysis based on the frequentist approach

Afat	*3.10 1.82-5.27)*	*0.62 0.46-0.83)*	1.61 0.94-2.78)	1.04 0.65-1.67)	*0.49 0.35-0.68)*	*0.54 0.42-0.70)*	1.24 0.83-1.85)	*0.44 0.34-0.57)*	*0.59 0.46-0.77)*	*0.69 0.53-0.91)*	1.80 0.98-3.30)	*0.55 0.37-0.80)*	*0.58 0.42-0.80)*
0.32 0.19-0.55)	Alec	*0.20 0.12-0.33)*	0.52 0.27-1.03)	*0.34 0.18-0.62)*	*0.16 0.09-0.27)*	*0.17 0.11-0.28)*	0.40 0.26-0.61)	*0.14 0.09-0.23)*	*0.19 0.12-0.31)*	*0.22 0.14-0.36)*	0.58 0.28-1.20)	*0.18 0.10-0.31)*	*0.19 0.11-0.32)*
1.62 1.20-2.20)	*5.02 3.01-8.37)*	Beva	*2.62 1.56-4.40)*	*1.69 1.08-2.64)*	0.79 0.61-1.03)	0.88 0.71-1.08)	*2.01 1.39-2.92)*	*0.71 0.60-0.84)*	0.96 0.78-1.18)	1.13 0.91-1.40)	*2.93 1.63-5.26)*	0.89 0.64-1.24)	0.95 0.73-1.22)
0.62 0.36-1.06)	1.92 0.98-3.77)	*0.38 0.23-0.64)*	Cabo	0.64 0.34-1.21)	*0.30 0.18-0.52)*	*0.34 0.21-0.55)*	0.77 0.43-1.37)	*0.27 0.17-0.44)*	*0.37 0.23-0.59)*	*0.43 0.26-0.71)*	1.12 0.54-2.33)	*0.34 0.19-0.60)*	*0.36 0.21-0.61)*
0.96 0.60-1.54)	*2.98 1.62-5.49)*	*0.59 0.38-0.93)*	1.55 0.83-2.91)	Ceri	*0.47 0.30-0.74)*	*0.52 0.35-0.77)*	1.19 0.72-1.97)	*0.42 0.28-0.64)*	*0.57 0.38-0.86)*	0.67 0.44-1.01)	1.73 0.88-3.41)	*0.53 0.32-0.88)*	*0.56 0.35-0.89)*
2.04 1.48-2.82)	*6.33 3.76-10.7)*	1.26 0.97-1.63)	*3.30 1.94-5.60)*	*2.13 1.34-3.36)*	Cetu	1.11 0.88-1.40)	*2.54 1.72-3.73)*	0.89 0.73-1.09)	1.21 0.96-1.52)	*1.42 1.11-1.81)*	*3.69 2.03-6.69)*	1.12 0.79-1.59)	1.19 0.90-1.58)
1.85 1.43-2.39)	*5.72 3.59-9.12)*	1.14 0.93-1.40)	*2.98 1.83-4.87)*	*1.92 1.29-2.86)*	0.90 0.72-1.14)	Chem	*2.29 1.69-3.12)*	*0.81 0.70-0.93)*	1.09 0.97-1.23)	*1.28 1.13-1.46)*	*3.33 1.93-5.77)*	1.01 0.74-1.39)	1.08 0.85-1.36)
0.81 0.54-1.20)	*2.50 1.65-3.78)*	*0.50 0.34-0.72)*	1.30 0.73-2.32)	0.84 0.51-1.38)	*0.39 0.27-0.58)*	*0.44 0.32-0.59)*	Criz	*0.35 0.25-0.50)*	*0.48 0.34-0.66)*	*0.56 0.40-0.78)*	1.45 0.78-2.72)	*0.44 0.28-0.69)*	*0.47 0.32-0.69)*
2.29 1.77-2.96)	*7.08 4.34-11.5)*	*1.41 1.19-1.67)*	*3.69 2.25-6.05)*	*2.38 1.56-3.62)*	1.12 0.92-1.37)	*1.24 1.07-1.43)*	*2.84 2.02-3.98)*	Dum	*1.35 1.18-1.55)*	*1.59 1.37-1.84)*	*4.12 2.34-7.27)*	1.25 0.94-1.66)	*1.33 1.09-1.63)*
1.69 1.31-2.19)	*5.24 3.24-8.47)*	1.04 0.85-1.28)	*2.73 1.70-4.40)*	*1.76 1.16-2.66)*	0.83 0.66-1.05)	0.92 0.81-1.03)	*2.10 1.51-2.92)*	*0.74 0.65-0.85)*	Erlo	*1.18 1.01-1.37)*	*3.05 1.74-5.35)*	0.93 0.68-1.27)	0.99 0.79-1.23)
1.44 1.09-1.90)	*4.46 2.75-7.24)*	*0.89 0.72-1.10)*	*2.33 1.41-3.83)*	1.50 0.99-2.27)	*0.70 0.55-0.90)*	*0.78 0.68-0.89)*	*1.79 1.28-2.50)*	*0.63 0.54-0.73)*	*0.85 0.73-0.99)*	Gefi	*2.60 1.48-4.56)*	0.79 0.57-1.09)	0.84 0.67-1.06)
0.55 0.30-1.02)	1.72 0.84-3.52)	*0.34 0.19-0.61)*	0.90 0.43-1.87)	0.58 0.29-1.13)	*0.27 0.15-0.49)*	*0.30 0.17-0.52)*	0.69 0.37-1.29)	*0.24 0.14-0.43)*	*0.33 0.19-0.57)*	*0.39 0.22-0.68)*	Osim	*0.30 0.16-0.57)*	*0.32 0.18-0.59)*
1.82 1.24-2.68)	*5.65 3.21-9.93)*	1.12 0.81-1.56)	*2.94 1.66-5.21)*	*1.90 1.14-3.15)*	0.89 0.63-1.26)	0.99 0.72-1.36)	*2.26 1.45-3.52)*	0.80 0.60-1.06)	1.08 0.79-1.48)	1.27 0.92-1.74)	*3.29 1.75-6.20)*	Ramu	1.06 0.75-1.50)
1.71 1.25-2.36)	*5.31 3.15-8.94)*	1.06 0.82-1.37)	*2.77 1.64-4.68)*	*1.78 1.13-2.82)*	0.84 0.63-1.11)	0.93 0.74-1.17)	*2.13 1.45-3.13)*	*0.75 0.61-0.92)*	1.01 0.81-1.27)	1.19 0.94-1.50)	*3.09 1.71-5.61)*	0.94 0.66-1.33)	Vand

Drugs are reported in alphabetical order. Data in the right-upper triangle are HRs (95%CI) in the row-defining treatment compared with the column-defining treatment. HRs lower than 1 favour the row-defining treatment (the first drug in alphabetical order). HRs for the opposite comparison of PFS are in the left-lower triangle. Each comparison is shown twice in the table, once with drug A versus drug B and once with drug B versus drug A. Significant results are in italic and underscored. HR, hazard ratio; CI, confidence interval; PFS: progression-free survival. Afat, afatinib; Alec, alectinib; Beva, bevacizumab; Cabo, cabozantinib; Ceri, ceritinib; Cetu, cetuximab; Chem, chemotherapy; Criz, crizotinib; Dum, dummy; Erlo, erlotinib; Gefi, gefitinib; Osim, osimertinib; Ramu, ramucirumab; Vand, vandetanib.

Table S6. Treatment ranking probability based on overall response rate

Rank	[1]	[2]	[3]	[4]	[5]	[6]	[7]	[8]	[9]	[10]	[11]	[12]	[13]	[14]	SUCRA
Afatinib	3.40	14.21	24.69	23.67	19.88	11.92	1.54	0.39	0.17	0.07	0.04	0.01	0.01	0.00	77.82
Alectinib	6.87	19.81	24.12	21.02	15.64	8.11	2.07	0.91	0.60	0.40	0.23	0.11	0.10	0.03	79.52
Bevacizumab	0.00	0.00	0.01	0.07	0.46	2.91	11.01	18.85	23.54	21.20	12.93	6.02	2.98	0.02	36.52
Cabozantinib	62.53	9.42	5.48	4.35	4.24	4.35	1.65	1.11	0.85	0.81	0.71	0.81	1.20	2.47	87.18
Ceritinib	21.73	39.86	18.08	9.98	6.15	3.22	0.55	0.20	0.12	0.06	0.03	0.02	0.01	0.00	88.20
Cetuximab	0.00	0.01	0.04	0.19	0.73	2.84	7.55	10.23	11.97	13.81	14.33	13.18	21.48	3.63	27.07
Chemotherapy	0.00	0.00	0.00	0.00	0.00	0.04	0.39	1.93	5.76	12.96	23.12	30.43	24.12	1.24	19.20
Crizotinib	0.55	4.08	12.68	24.36	30.32	20.90	4.03	1.53	0.75	0.47	0.21	0.10	0.03	0.01	71.01
Dummy	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.08	0.97	11.10	87.83	1.02
Erlotinib	0.00	0.00	0.00	0.00	0.00	0.04	0.36	1.63	5.24	12.31	23.75	32.57	23.32	0.79	19.06
Gefitinib	0.00	0.00	0.02	0.14	0.92	5.90	21.77	25.85	21.75	14.38	7.08	1.69	0.49	0.00	42.77
Osimertinib	4.91	12.47	14.24	13.95	14.87	18.82	5.94	3.52	2.61	2.10	1.71	1.57	1.85	1.45	68.33
Ramucirumab	0.01	0.12	0.46	1.44	3.84	10.34	19.35	13.80	11.78	10.42	8.31	7.70	10.04	2.38	39.04
Vandetanib	0.00	0.02	0.18	0.83	2.95	10.61	23.79	20.05	14.86	10.99	7.48	4.82	3.28	0.14	43.26

Table S7. Treatment ranking probability based on progression-free survival

Rank	[1]	[2]	[3]	[4]	[5]	[6]	[7]	[8]	[9]	[10]	[11]	[12]	[13]	[14]	SUCRA
Afatinib	0.00	0.30	2.90	13.98	37.17	44.10	1.25	0.23	0.06	0.02	0.00	0.00	0.00	0.00	67.16
Alectinib	87.48	10.81	1.65	0.05	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	98.89
Bevacizumab	0.00	0.00	0.00	0.00	0.07	1.15	12.98	28.74	22.81	16.35	10.78	5.52	1.57	0.03	38.27
Cabozantinib	3.59	33.67	39.25	14.21	6.23	2.82	0.14	0.06	0.02	0.00	0.00	0.00	0.00	0.00	84.97
Ceritinib	0.03	1.96	8.31	19.51	30.25	33.60	3.36	1.40	0.68	0.39	0.25	0.16	0.07	0.04	68.42
Cetuximab	0.00	0.00	0.00	0.00	0.00	0.03	0.40	1.68	3.42	5.70	10.48	22.67	39.65	15.96	13.03
Chemotherapy	0.00	0.00	0.00	0.00	0.00	0.00	0.02	1.31	6.27	17.41	31.28	31.56	11.72	0.43	21.36
Crizotinib	0.00	5.00	21.46	42.85	21.54	8.87	0.21	0.05	0.02	0.01	0.00	0.00	0.00	0.00	76.25
Dummy	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.04	2.00	23.58	74.38	2.13
Erlotinib	0.00	0.00	0.00	0.00	0.00	0.05	1.96	17.84	30.48	28.68	15.93	4.40	0.66	0.00	34.27
Gefitinib	0.00	0.00	0.00	0.00	0.19	5.27	65.26	21.05	6.18	1.67	0.33	0.04	0.01	0.00	51.20
Osimertinib	8.89	48.27	26.42	9.40	4.38	2.27	0.19	0.08	0.04	0.02	0.02	0.01	0.00	0.00	87.63
Ramucirumab	0.00	0.00	0.00	0.00	0.12	1.08	7.10	10.70	11.26	11.25	13.61	19.87	16.53	8.46	24.77
Vandetanib	0.00	0.00	0.00	0.00	0.04	0.76	7.13	16.87	18.76	18.50	17.28	13.76	6.21	0.69	31.61

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