



Figure S1 Parametric distributions for treated with (A) PRL in the first-line therapy, (B) PRL in the second-line setting, (C) cisplatin plus pemetrexed followed by maintenance treatment with pemetrexed, (D) docetaxel, (E) best supportive care. BSC, best supportive care; PRL, pralsetinib.

Table S1 AIC and BIC statistics for alternate parametric survival distributions

Distribution	PRL 1st		PRL 2nd		Pemetrexed		Docetaxel		BSC	
	AIC	BIC	AIC	BIC	AIC	BIC	AIC	BIC	AIC	BIC
Exponential	232.2	234.5	545.1	548.0	1,291.2	1,295.0	278.9	280.9	247.3	249.2
Gamma	231.9	236.5	546.3	552.2	1,117.4	1,125.1	274.5	278.5	241.2	245.0
Gengamma	232.7	239.7	538.6	547.4	1,073.0	1,084.6	276.5	282.5	236.9	242.5
Gompertz	233.8	238.5	546.3	552.1	1,213.9	1,221.7	279.0	283.1	249.3	253.0
Weibull	232.3	236.9	546.8	552.6	1,150.0	1,157.8	275.2	279.2	244.6	248.4
Log-logistic	231.2	235.8	542.1	547.9	1,104.4	1,112.2	278.3	282.3	232.5	236.3
Log-normal	230.7	235.3	538.58	544.4	1,092.5	1,100.3	281.1	285.1	235.1	238.9

AIC, Akaike Information Criteria; BIC, Bayesian Information Criteria; PRL, pralsetinib; BSC, best supportive care.

Table S2 Background mortality rate

Age	Background mortality rate
26	0.000968
27	0.000994
28	0.001024
29	0.001058
30	0.001095
31	0.001132
32	0.001171
33	0.001213
34	0.00126
35	0.001319
36	0.001389
37	0.001467
38	0.00155
39	0.001639
40	0.001743
41	0.001864
42	0.002001
43	0.002159
44	0.002345
45	0.002547
46	0.002778
47	0.003059
48	0.003391
49	0.003753
50	0.004118
51	0.004484
52	0.004874
53	0.005302
54	0.005771
55	0.006274
56	0.006793
57	0.007321
58	0.007854
59	0.008403
60	0.008999
61	0.009652
62	0.010341
63	0.011056

Table S2 (continued)

Age	Background mortality rate
64	0.011804
65	0.012598
66	0.013484
67	0.014501
68	0.015701
69	0.017146
70	0.018855
71	0.020762
72	0.022816
73	0.02501
74	0.027353
75	0.029897
76	0.03287
77	0.036315
78	0.040253
79	0.044908
80	0.049974
81	0.055475
82	0.061509
83	0.068675
84	0.076701
85	0.085469
86	0.095935
87	0.107533
88	0.120347
89	0.134457
90	0.149939
91	0.166861
92	0.185276
93	0.205223
94	0.226719
95	0.24976
96	0.274312
97	0.300311
98	0.327661
99	0.356235
100+	1

Table S2 (continued)

Table S3 Model parameters and distributions

Variable	Baseline value (reference)	Range		Distribution
		Minimum	Maximum	
Lognormal PFS survival model with PRL 1st line	Meanlog =2.699; sdlog =1.213	–	–	–
Lognormal PFS survival model with PRL 2nd line	Meanlog =2.698; sdlog =1.305	–	–	–
Gengamma PFS survival model with pemetrexed + carboplatin followed by maintenance of pemetrexed	mu =1.825; sigma =0.500; Q=-0.853	–	–	–
Gamma PFS survival model with docetaxel	Shape =1.597; rate =0.350	–	–	–
Loglogistic PFS survival model with BSC	Shape =2.258; rate =4.731			
Grade ≥3 AEs incidence in PRL therapy				
Neutropenia	0.20 (10)	0.16	0.24	
Anemia	0.12 (10)	0.096	0.144	Beta
Hypertension	0.12 (10)	0.096	0.144	Beta
Increased blood creatine phosphokinase	0.06 (10)	0.048	0.072	Beta
Grade ≥3 AEs incidence in pemetrexed + cisplatin chemotherapy				
Anemia	0.04 (18)	0.032	0.048	Beta
Neutropenia	0.04 (18)	0.032	0.048	Beta
Fatigue	0.04 (18)	0.032	0.048	Beta
Grade ≥3 AEs incidence in docetaxel chemotherapy				
Neutropenia	0.455 (19)	0.364	0.546	Beta
Febrile neutropenia	0.073 (19)	0.0584	0.0876	Beta
Anemia	0.073 (19)	0.0584	0.0876	Beta
Asthenia	0.055 (19)	0.044	0.066	Beta
Utility				
Progression-free disease	0.71 (32)	0.568	0.852	Beta
Progressed disease after first-line	0.67 (32)	0.536	0.804	Beta
Progressed disease after second-line	0.59 (32)	0.472	0.708	Beta
Progressed disease after third/fourth-line	0.46 (32)	0.368	0.552	Beta
AEs disutility				
Anemia	0.073 (34)	0.0584	0.0876	Beta
Neutropenia	0.09 (33)	0.072	0.108	Beta
Hypertension	0.05 (35)	0.04	0.06	Beta
Febrile neutropenia	0.09 (33)	0.072	0.108	Beta
Fatigue	0.074 (33)	0.0592	0.0888	Beta
Asthenia	0.074 (33)	0.0592	0.0888	Beta
Drug cost, US\$				
PRL/100 mg	186.43 (24)	149.14	186.43	Fixed in PSA
Pemetrexed/10 mg	9.157 (25)	7.3256	10.9884	Gamma
Cisplatin/10 mg	1.687 (25)	1.3496	2.0244	Gamma
Docetaxel/1 mg	0.455 (25)	0.364	0.546	Gamma
AEs cost, US\$				
Anemia	23,184.11 (26)	18,547.288	27,820.932	Gamma
Neutropenia	19,660.72 (26)	15,728.576	23,592.864	Gamma
Hypertension	3,698.47 (26)	2,958.776	4,438.164	Gamma
Febrile neutropenia	19,660.72 (26)	15,728.576	23,592.864	Gamma
Administration cost per cycle	155.09 (15)	124.072	186.108	Gamma
Tumor imaging cost per cycle	249.48 (14)	199.584	299.376	Gamma
Laboratory testing cost per cycle	340.20 (14)	272.16	408.24	Gamma
End-of-life care cost in end-stage disease	10,187.64 (30)	8,150.112	12,225.168	Gamma
Physician visit cost per cycle	160.20 (14)	128.16	192.24	Gamma
Best supportive care per cycle	481.57 (43)	385.256	577.884	Gamma
Patients' weight, kg	70 (14)	56	84	Normal
Patients' body surface area, m ²	1.82 (15)	1.456	2.184	Normal
Discount rate (%)	3 (15)	0	5	Fixed in PSA

PRL, pralsetinib; PFS, progression-free survival; BSC, best supportive care; AEs, adverse events; PSA, probability sensitivity analyses.

Table S4 The median progression-free survival analysis observed in the clinical trials and estimated by the current cost-effectiveness model in RET fusion-positive NSCLC

Treatment	Median progression-free survival, months		
	Model	Clinical trials	Difference
PRL 1st line	12.99	13.0	0.01
PRL 2nd line	16.54	16.5	0
Pemetrexed	6.92	6.90	0.02
Docetaxel	3.90	3.90	0
BSC	4.63	4.60	0.03

PRL, pralsetinib; RET, rearranged during transfection; NSCLC, non-small cell lung cancer; BSC, best supportive care.

References

43. Cancer Genome Atlas Research Network; Analysis Working Group; Asan University; BC Cancer Agency; et al. Integrated genomic characterization of oesophageal carcinoma. *Nature* 2017;541:169-75.