Table 1. Combined analysis results of the two validated SNPs out of 42 selected SNPs* in both PLCO and HLCS datasets

SNP	Allele [a]	Gene	PLCO (n=1185)			HLCS (n=984)			Combined analysis			
			EAF	HR (95% CI) [b]	*P* [b]	EAF	HR (95% CI) [c]	*P* [c]	HR (95% CI) [d]	*P* [d]	P_{het} [e]	I^2
rs11606640	A/G	*ETS1*	0.15	0.82 (0.71-0.95)	0.006	0.17	0.73 (0.62-0.85)	7.20×10^{-5}	0.78 (0.70-0.86)	2.55×10^{-6}	0.275	16.09
rs62053220	G/C	*ZFHX3*	0.08	0.71 (0.58-0.86)	4.4×10^{-4}	0.08	0.73 (0.60-0.89)	0.002	0.73 (0.63-0.83)	2.54×10^{-6}	0.841	0

* See Supplemental Table 3 for all the 42 SNPs.

PLCO = Prostate, Lung, Colorectal and Ovarian cancer trial; HLCS = Harvard Lung Cancer Susceptibility study; SNPs = Single nucleotide polymorphisms; EAF = Effect allele frequency; HR = Hazards ratio; 95% CI = 95% Confidence interval.

[a] Effect/reference allele;

[b] Adjusted for age, sex, stage, histology, smoking status, chemotherapy, radiotherapy, surgery, PC1, PC2, PC3 and PC4;

[c] Adjusted for age, sex, stage, histology, smoking status, chemotherapy, radiotherapy, surgery, PC1, PC2 and PC3;

[d] in an additive model;

[e] *P* value for heterogeneity by Cochrane's Q test.

Table 2. Predictors of OS obtained from stepwise Cox regression analysis in the PLCO dataset

Variables [a]	Category	Frequency [b]	HR (95% CI)	*P*
Age	Continuous	1163	1.03 (1.02-1.05)	<0.001
Sex	Male	690	1.00	
	Female	473	0.80 (0.69-0.93)	0.003
Smoking status	Never	113	1.00	
	Current	413	1.68 (1.25-2.25)	0.001
	Former	637	1.65 (1.25-2.17)	<0.001
Histology	Adenocarcinoma	568	1.00	
	Squamous cell	281	1.15 (0.96-1.39)	0.137
	others	314	1.32 (1.11-1.56)	0.002
Tumor stage	I-IIIA	650	1.00	
	IIIB-IV	513	2.90 (2.38-3.52)	<0.001
Chemotherapy	No	632	1.00	
	Yes	531	0.58 (0.48-0.69)	<0.001
Radiotherapy	No	753	1.00	
	Yes	410	0.94 (0.79-1.10)	0.422
Surgery	No	629	1.00	
	Yes	534	0.21 (0.16-0.27)	<0.001
ETS1 rs11606640 G>A	GG/GA/AA	834/301/28	0.82 (0.71-0.95)	0.007
ZFHX3 rs62053220 C>G	CC/CG/GG	985/172/6	0.70 (0.58-0.85)	<0.001

OS = Overall survival; PLCO = Prostate, Lung, Colorectal and Ovarian cancer trial; HR = Hazards ratio; 95% CI = 95% Confidence interval.

[a] Stepwise analysis included age, sex, smoking status, tumor stage, tumor histology, chemotherapy, radiotherapy, surgery, top four principal components and all 42 SNPs (including *ETS1* rs11606640 and *ZFHX3* rs62053220 in an additive model);

[b] Ten observations missing of clinical variables (two of tumor stage and eight of chemotherapy/ radiotherapy/ surgery); Eight observations missing of *ETS1* rs11606640; Four observations missing of *ZFHX3* rs62053220; 1,163 patients remained for the stepwise analysis.

Table 3. Associations of the two validated SNPs in the c-Myb pathway with OS of NSCLC in the PLCO dataset

	OS Univariate analysis				OS Multivariate analysis [a]			
	Frequency				Frequency			
Genotype	**All**	**Death(%)**	**HR (95% CI)**	***P***	**All**	**Death(%)**	**HR (95% CI)**	***P***
***ETS1* rs11606640 G > A**								
	n=1177				**n=1167**			
GG	842	569 (67.6)	1.00		835	562 (67.3)	1.00	
GA	307	202 (65.8)	0.94 (0.80-1.11)	0.480	304	200 (65.8)	0.78 (0.66-0.92)	0.004
AA	28	21 (75.0)	1.07 (0.69-1.66)	0.753	28	21 (75.0)	0.87 (0.56-1.35)	0.530
Trend				0.689			0.83 (0.72-0.95)	0.008
GA+AA	335	223 (66.6)	0.96 (0.82-1.12)	0.560	332	221 (66.6)	0.79 (0.68-0.93)	0.004
Genotype missing [b]	8				8			
Phenotype missing [c]	N/A				10			
***ZFHX3* rs62053220 C > G**								
	n=1181				**n=1171**			
CC	1002	685 (68.4)	1.00		992	676 (68.2)	1.00	
CG	173	109 (63.0)	0.84 (0.69-1.03)	0.095	173	109 (63.0)	0.75 (0.61-0.92)	0.006
GG	6	2 (33.3)	0.38 (0.10-1.52)	0.170	6	2 (33.3)	0.20 (0.05-0.81)	0.025
Trend				0.039			0.71 (0.58-0.86)	<0.001
CG+GG	179	111 (62.0)	0.82 (0.67-1.01)	0.058	179	111 (62.0)	0.72 (0.59-0.88)	0.001
Genotype missing [b]	4				4			
Phenotype missing [c]	N/A				10			
NPG [a]								
	n=1173				**n=1163**			
0	717	492 (68.6)	1.00		710	485 (68.3)	1.00	
1	402	264 (65.7)	0.89 (0.77-1.04)	0.130	399	262 (65.7)	0.70 (0.60-0.81)	<0.001
2	54	34 (63.0)	0.86 (0.61-1.22)	0.394	54	34 (63.0)	0.71 (0.50-1.01)	0.060
Trend				0.111				<0.001
0	717	492 (68.6)	1.00		710	485 (68.3)	1.00	
1-2	456	298 (65.4)	0.89 (0.77-1.03)	0.103	453	296 (65.3)	0.70 (0.60-0.81)	<0.001
Genotype missing [c]	12				12			
Phenotype missing [d]	N/A				10			

SNPs = Single nucleotide polymorphisms; OS = Overall survival; NSCLC = Non-small cell lung cancer; PLCO = Prostate, Lung, Colorectal and Ovarian cancer trial; NPG = Number of protective genotypes; HR = Hazard ratio; 95%CI = 95%Confidence interval; N/A = Not applicable.

[a] Protective genotypes were *ETS1* rs11606640 GA+AA and *ZFHX3* rs62053220 CG+GG;

[b] Multivariate Cox hazards regression analyses were adjusted for age, sex, smoking, stage, histology, chemotherapy, radiotherapy, surgery, and top four principal components;

[c] Eight observations missing of *ETS1* rs11606640; Four observations missing of *ZFHX3* rs62053220;

[d] Two observations missing of tumor stage and eight observations missing of chemotherapy/radiotherapy/surgery in the PLCO dataset.