## Effect of BIM expression on the prognostic value of PD-L1 in advanced non-small cell lung cancer patients treated with EGFR-TKIs

Chang-Yao Chu<sup>1#</sup>, Chien-Yu Lin<sup>2#</sup>, Chien-Chung Lin<sup>2, 3, 4#</sup>, Chien-Feng Li<sup>5-7</sup>, Shang-Yin Wu<sup>8</sup>, Jeng-Shiuan Tsai<sup>2</sup>, Szu-Chun Yang<sup>2</sup>, Chian-Wei Chen<sup>2</sup>, Chia-Yin Lin<sup>9</sup>, Chao-Chun Chang<sup>10</sup>, Yi-Ting Yen<sup>10</sup>, Yau-Lin Tseng<sup>10</sup>, Po-Lan Su<sup>2\*</sup>, and Wu-Chou Su<sup>3, 8, 11</sup>

Supplementary Table 1. Cox proportional hazards regression analysis of progression-

free survival among patients who received first-generation EGFR-TKI

		HR (95% CI)	P-value
Age (years)	> 65 years vs. < 65 years	1.12 (0.58–2.14)	0.745
Sex	Male vs. Female	1.31 (0.72–2.39)	0.375
Brain metastasis	Presence vs. Absence	3.12 (1.52–6.38)	0.002
EGFR mutation	Exon 19 deletion vs. Others	1.00 (0.50–1.99)	0.996
PD-L1 level	≥ 1% vs. < 1%	0.87 (0.46–1.63)	0.665
E-cadherin	Loss vs. preserved	1.37 (0.62–3.03)	0.433
MET	Presence vs. absence	1.40 (0.76–2.58)	0.282
p-STAT3	Presence vs. absence	0.64 (0.31–1.32)	0.226
р-АКТ	Presence vs. absence	1.15 (0.58–2.27)	0.694
BIM	Presence vs. absence	2.28 (0.93–5.58)	0.070

EGFR, epidermal growth factor receptor; TKI, tyrosine kinase inhibitor

Supplementary Table 2. Cox proportional hazards regression analysis of progression-

		HR (95% CI)	P-value
Age (years)	> 65 years vs. < 65 years	1.35 (0.49–3.70)	0.561
Sex	Male vs. Female	0.51 (0.22–1.21)	0.127
Brain metastasis	Presence vs. Absence	0.89 (0.36–2.18)	0.798
EGFR mutation	Exon 19 deletion vs. Others	0.78 (0.33–1.88)	0.580
PD-L1 level	≥ 1% vs. < 1%	1.07 (0.45–2.54)	0.877
E-cadherin	Loss vs. preserved	1.20 (0.35–4.08)	0.767
MET	Presence vs. absence	0.38 (0.15–0.99)	0.049
p-STAT3	Presence vs. absence	0.91 (0.41–2.06)	0.825
р-АКТ	Presence vs. absence	1.03 (0.41–2.57)	0.949
BIM	Presence vs. absence	13.73 (2.62–72.02)	0.002

free survival among patients who received second-generation EGFR-TKI

EGFR, epidermal growth factor receptor; TKI, tyrosine kinase inhibitor

	BIM wild-type (n = 32)	BIM deletion polymorphism (n = 4)
Positive BIM expression	27	4
Negative BIM expression	5	0

Supplementary Table 3. Association between BIM protein expression and genotyping



**Supplementary Figure 1.** Kaplan–Meier analysis of progression-free survival among patients who received first-generation EGFR-TKIs and had different expression levels of PD-L1 (A) and BIM (B).



**Supplementary Figure 2.** Kaplan–Meier analysis of progression-free survival among patients who received second-generation EGFR-TKIs and had different expression levels of PD-L1 (A) and BIM (B).



**Supplementary Figure 3.** The original blots of HCC827 cells with transfection of siRNA targeting PD-L1 and BIM.



Genotyping W W W W W D W W W: Wild type D: Deletion polymorphism (Heterozygous) U: Unsatisfactory DNA quality W W W W W D W W Wild type allele: 362bp Deletion allele: 284bp

**Supplementary Figure 4.** Agarose gel images of the PCR products from wild type and BIM deletion alleles. The left side gels analyze the PCR product with wild-type primer, whereas the right side gels analyzed the PCR product with deletion primer.



**Supplementary Figure 4 (cont.).** Agarose gel images of the PCR products from wild type and BIM deletion alleles. The left side gels analyze the PCR product with wild-type primer, whereas the right side gels analyzed the PCR product with deletion primer.