

No association between *ECSIT* germline mutations and hemophagocytic lymphohistiocytosis in natural killer/T-cell lymphoma

Shin Yeu Ong,^{1*} Jing Quan Lim,^{2,3*} Nicholas Grigoropoulos,¹ Yurike Laurensia,² Dachuan Huang,^{2,3} Burton Kuan Hui Chia,² Daryl Cheah Ming Zhe,² Sahil Ajit Saraf,⁴ Chee Leong Cheng,⁴ Wen-Yu Chuang,⁵ Ming-Chung Kuo,⁶ Yi-Jiun Su,⁶ Colin Phipps,¹ Chandramouli Nagarajan,¹ Yuh Shan Lee,¹ Daryl Tan Chen Lung,¹ Lee-Yung Shih,⁶ Yeow Tee Goh,¹ Soon Thye Lim^{2,3#} and Choon Kiat Ong^{2,3,7#}

¹Department of Haematology, Singapore General Hospital, Singapore; ²National Cancer Center, Singapore; ³Duke-NUS Medical School, Singapore; ⁴Department of Pathology, Singapore General Hospital, Singapore; ⁵Department of Pathology, Chang Gung Memorial Hospital at Linkou and Chang Gung University, Taoyuan, Taiwan; ⁶Division of Hematology-Oncology, Chang Gung Memorial Hospital at Linkou, and Chang Gung University, Taoyuan, Taiwan and ⁷Genome Institute of Singapore, A*STAR, Singapore.

*SYO and JQL contributed equally as co-first authors.

#STL and CKO contributed equally as co-senior authors.

Correspondence: CHOON KIAT ONG - cmrock@nccs.com.sg

SOON THYE LIM - lim.soon.thye@singhealth.com.sg

doi:10.3324/haematol.2020.269209

Supplementary information

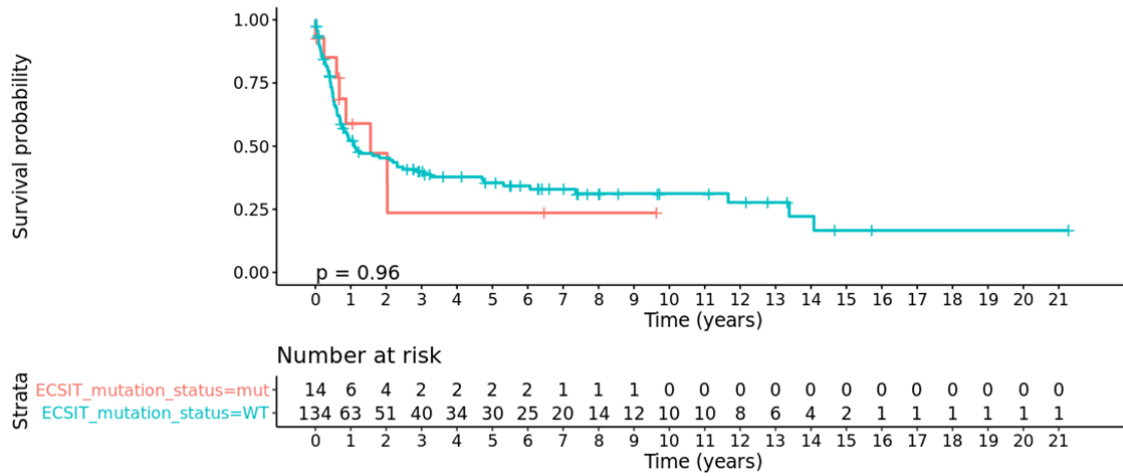
Supplementary Figure 1. Kaplan-Meier survival curves for all 149 patients from Singapore and Taiwan showing (A) Overall Survival (OS) and (B) Progression-Free Survival (PFS) according to ECSIT^{V140A} mutation status. ECSIT^{V140A} was not associated with survival (PFS, P=0.91; OS, P=0.96, log-rank)

Supplementary Table 1. Hemophagocytic lymphohistiocytosis (HLH) was not associated with ECSIT^{V140A} in the 64 patients from Singapore (OR=4.45, 95% CI [0.56, 35.17], P=0.18, Fisher's exact test).

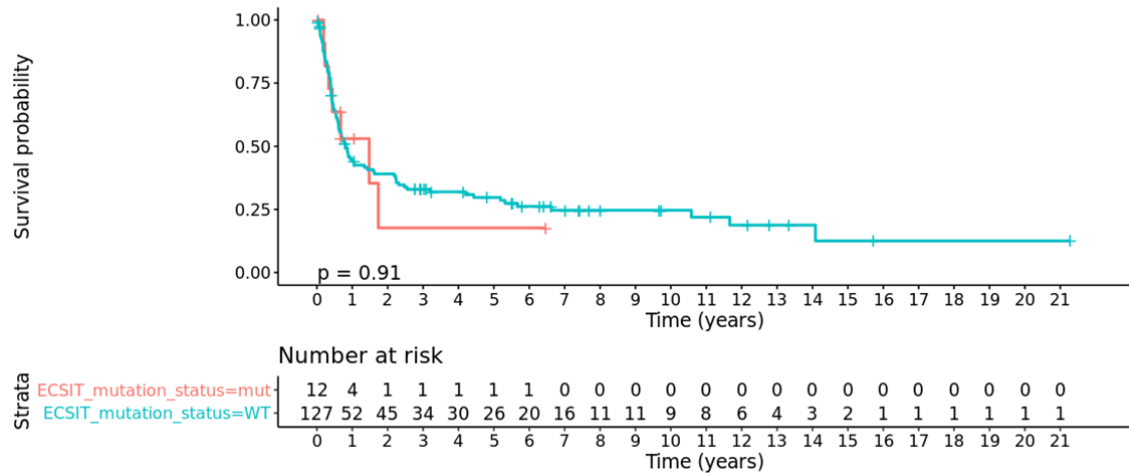
Supplementary Table 2. Hemophagocytic lymphohistiocytosis (HLH) was not associated with ECSIT^{V140A} in the 149 patients from Singapore and Taiwan (OR=1.48, 95% CI [0.38, 5.76], P≈1.0, Fisher's exact test).

Supplementary Table 3. Association between *ECSIT* mutation and clinical characteristics of NKTCL patients in Singapore and Taiwan

A



B



Supplementary Figure 1. Kaplan-Meier survival curves for all 149 patients from Singapore and Taiwan showing (A) Overall Survival (OS) and (B) Progression-Free Survival (PFS) according to ECSIT^{V140A} mutation status. ECSIT^{V140A} was not associated with survival (PFS, $P=0.91$; OS, $P=0.96$, log-rank)

Supplementary Table 1. Hemophagocytic lymphohistiocytosis (HLH) was not associated with ECSIT^{V140A} in the 64 patients from Singapore (OR=4.45, 95% CI [0.56, 35.17], $P=0.18$, Fisher's exact test).

Odds=4.45, 95% CI [0.56, 35.17]

P=0.18	ECSIT ^{MUT}	ECSIT ^{WT}
HLH	2	11
No HLH	2	49

Supplementary Table 2. Hemophagocytic lymphohistiocytosis (HLH) was not associated with ECSIT^{V140A} in the 149 patients from Singapore and Taiwan (OR=1.48, 95% CI [0.38, 5.76], $P\approx 1.0$, Fisher's exact test).

Odds=1.48, 95% CI [0.38, 5.76]

P=1	ECSIT ^{MUT}	ECSIT ^{WT}
HLH	3	21
No HLH	11	114

Supplementary Table 3. Association between *ECSIT* mutation and clinical characteristics of NKTCL patients in Singapore and Taiwan

Characteristic	<i>ECSIT</i> ^{WT}	<i>ECSIT</i> ^{MUT}	<i>P</i> value	Univariate OR
HLH, Y/N	21/114	3/11	1.0	1.48 [0.38, 5.76]
< 60 years, Y/N	10/4	42/49	0.0921	2.92 [0.85, 9.98]
Sex, M/F	7/7	93/42	0.230	0.45 [0.15, 1.37]
Stage I+II, Y/N	8/5	71/55	0.777	1.24 [0.38, 4.0]
ECOG 0-1, Y/N	9/3	102/15	1.0	0.44 [0.11, 1.82]
IPI 0-2, Y/N	6/6	80/38	0.220	0.48 [0.14, 1.57]

* OR, odds ratio; HLH, hemophagocytic lymphohistiocytosis; IPI, international prognostic index