Report of Survival Analysis

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Date: 3/27/2021

***Statistical analysis***

A total of 117 subjects were included in the study. For each subject, the DNA Lib ID, Diagnosis, Variants, PFS, OS and Primary vs. Metastasis were recorded. One datapoint was considered to be censored when the PFS/OS was not filled. The PFS/OS was calculated by subtracting Date of Diagnosis from Date of Last Contact.

*Descriptive analysis*: The patients’ characteristics are summarized and compared between variants and non-variants. The diagnosis is presented with total number (column percentage) and compared with Fisher’s exact test. The metastasis status is treated as categorical variable and compared with chi-square test.

*Survival analysis:* Time of OS is calculated as the time from study enrollment to death or last contact. Time of PFS is calculated as the time from study enrollment to disease progression date, death date, or last contact whichever comes first. The survivor functions for PFS or OS are estimated by the method of Kaplan and Meier (Kalbfleisch JD and Prentice RL. The statistical analysis of failure time data. John Wiley and Sons, New York, 1980). The log-rank test will be used to test the difference in the overall PFS or OS between different groups stratified by the factors (variants, metastasis status and diagnosis).

COX models (Cox, D. R. Regression Models and Life Tables. Journal of the Royal Statistical Society Series 1972 B 34 (2): 187–220) are also employed to estimate the adjusted effect of variants, diagnosis and metastasis status on PFS or OS after adjustment for all other factors.

The SAS statistical package (SAS Institute, Inc., Cary, North Carolina) is used for all data managements and analyses.

***Results***

*Patient characteristics:* Diagnosis and metastasis of all patients are summarized in Table 1. Due to small sample size, Fisher’s exact test is used to examine the independence between variants and non-variants in each diagnosis category. The p-value is 0.0003, and this implies that distribution in variants and non-variants are not independent in each diagnosis category.

*PFS and OS with variants, diagnosis and metastasis status:* The stratified Kaplan-Meier curves of PFS and OS with variants, diagnosis and metastasis status are presented in Figure 1 – 6 respectively. Log-rank tests are performed to detect differences between PFS/OS in each stratum.

From the result of Log-rank tests, survival probabilities are significantly different in variants and non-variants. Also, survival probabilities (PFS and OS) are significantly different in metastasis, primary and recurrence groups. However, there is no significant difference of survival probabilities among diagnosis groups.

*Cox model of PFS and OS with variants, diagnosis and metastasis status:*

1. Metastasis status: the PFS is significantly associated with whether the metastasis status is primary or not (p = 0.0174), adjusting for all the other covariates. the OS is significantly associated with whether the metastasis status is primary or not (p = 0.0124), adjusting for all the other covariates.
2. Diagnosis: The PFS is significantly associated with cervical SCC (p = 0.0152), GIST (P = 0.0065), oncocytic RCC (p = 0.0370), adjusting for all the other covariates respectively. The OS is significantly associated with cervical SCC (p = 0.0179), GIST (P = 0.0071), oncocytic RCC (p = 0.0225), Breast Adeno (p = 0.0443), Lung SCC (p = 0.0290), Lung Small Cell Carcinnoma (p = 0.0457), Pancreatic Adeno (0.0295), adjusting for all the other covariates respectively.
3. Variants: There is no significant association between PFS and variants, adjusting for all the other covariates. However, the OS is significantly associated with variants (p = 0.0388).

Table 1. Characteristics of Patients

|  |  |  |  |
| --- | --- | --- | --- |
|  | Variant = No  (N = 54) | Variant = Yes  (N = 63) | p-value |
| Diagnosis |  |  | 0.0003\* |
| Breast Adeno | 2  (4%) | 4  (6%) |  |
| Carcinoma fo Unknown Origin | 5  (9%) | 0  (0%) |  |
| Cervical Adeno | 1  (2%) | 0  (0%) |  |
| Cervical SCC | 0  (0%) | 2  (2%) |  |
| Cholangiocarcinoma | 2  (4%) | 0  (0%) |  |
| Conjunctival SCC | 0  (0%) | 1  (2%) |  |
| Duodenal Neuroendocrine Tumor | 1  (2%) | 0  (0%) |  |
| EBV associated nasopharyngeal carc | 1  (2%) | 0  (0%) |  |
| Endometrial Adeno | 1  (2%) | 7  (11%) |  |
| Face SCC | 0  (0%) | 1  (2%) |  |
| GIST | 0  (0%) | 6  (10%) |  |
| Gastric Adeno | 1  (2%) | 1  (2%) |  |
| Head & Neck SCC | 0  (0%) | 1  (2%) |  |
| HiGSOvCa | 4  (7%) | 5  (8%) |  |
| LG Apendiceal Muc Tumor | 1  (2%) | 0  (0%) |  |
| LGSOvCa | 0  (0%) | 1  (2%) |  |
| Larynx SCC | 0  (0%) | 1  (2%) |  |
| Left Frontal Sinus SCC | 0  (0%) | 1  (2%) |  |
| Lung Adeno | 9  (17%) | 18  (29%) |  |
| Lung SCC | 3  (6%) | 5  (8%) |  |
| Lung Small Cell Carcinoma | 6  (11%) | 0  (0%) |  |
| Malignant Mesothelioma | 1  (2%) | 0  (0%) |  |
| Melanoma | 1  (2%) | 1  (2%) |  |
| Metastatic HNSCC | 1  (2%) | 0  (0%) |  |
| Metastatic RCC | 1  (2%) | 0  (0%) |  |
| Neuroendocrine Tumor | 1  (2%) | 0  (0%) |  |
| Oncocytic RCC | 7  (13%) | 2  (4%) |  |
| Pancreatic Adeno | 0  (0%) | 1  (2%) |  |
| Pancreatic Neuroendocrine Tumor | 0  (0%) | 1  (2%) |  |
| Pap Thyroid Carcinoma | 0  (0%) | 1  (2%) |  |
| Papillary Thyroid Carcinoma | 1  (2%) | 0  (0%) |  |
| Poorly Diff Carcinoma | 2  (4%) | 1  (2%) |  |
| Poorly Diff Lung Carcinoma | 0  (0%) | 1  (2%) |  |
| Salivary Gland High Grade | 0  (0%) | 1  (2%) |  |
| Tongue/Tonsil SCC | 0  (0%) | 1  (2%) |  |
| Urothelial Carcinoma | 1  (2%) | 0  (0%) |  |
| Prim vs. Met |  |  | 0.2312\*\* |
| Metastasis | 22  (41%) | 31  (49%) |  |
| Primary | 21  (39%) | 26  (41%) |  |
| Recurrence | 11  (20%) | 6  (10%) |  |

\*: Fisher’s exact test

\*\*: Chi-square test

Figure 1. The PFS by Variants with log-rank test result

Chart, line chart

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Figure 2. The OS by Variants with log-rank test result

Chart, line chart

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Figure 3. The PFS by Diagnosis with log-rank test result

Chart

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Figure 4. The OS by Diagnosis with log-rank test result

Chart, histogram

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Figure 5. The PFS by Metastasis status with log-rank test result

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Figure 6. The OS by Metastasis with log-rank test result

Chart, box and whisker chart

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