A collaborative outcome study in uveal melanoma with the US National Cancer Institute's Surveillance, Epidemiology, and End Results Program Registries (NCI SEER): Performance of the 15-gene expression profile test in prospectively tested uveal melanoma patients (Analysis 1)

Katherina M Alsina, PhD[1], Sarah J Kurley, PhD[1], Christine N Bailey, MPH[1], **Kelli L Ahmed, PhD**[1], Valentina I Petkov, MD, MPH[2], Jason H Rogers, MSc[1], Kyle R Covington, PhD[1], and Robert W Cook, PhD[1]

[1]Castle Biosciences, Inc. Friendswood, Texas, USA [2]National Cancer Institute, Surveillance Research Program. Bethesda, Maryland, USA

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Background

- **Uveal melanoma** (**UM**) is a rare but aggressive intraocular cancer, with up to 50% of patients experiencing metastatic disease.[1,2]
- A commercially available **15-gene expression profile** (**15-GEP**) test is widely used across the US and western Canada and is recommended for metastatic risk stratification in UM by the National Comprehensive Cancer Network clinical guidelines.[3,4,5]
- A low-risk (Class 1A) test result has been found to be associated with lower metastatic rates than an intermediate-risk (Class 1B) or high-risk (Class 2) result.[6]
- The US **National Cancer Institute's Surveillance, Epidemiology, and End Results Program Registries** (**NCI SEER**) collects cancer incidence and survival data representing 48% of the US population, allowing retrospective outcome analysis of large, real-world cohorts.[7]

Objective

Here we report findings from an ongoing collaborative study conducted with the NCI SEER in an unselected cohort of uveal melanoma patients prospectively tested with the 15-GEP

Methods

- The NCI SEER registries conducted a linkage of all patients with UM (using a third-party honest broker, Information Management Services) to those tested with the 15-GEP and provided a deidentified dataset.
- The study included all linked cases diagnosed anytime in 2018 with survival outcome information and a 15-GEP test result. Only cases with primary uveal melanoma were included. Patients diagnosed with stage IV disease (evidence of distant metastasis) at initial presentation were excluded from analysis.
- Kaplan-Meier analysis with log-rank test was used to analyze **overall survival** (**OS**) and **melanoma-specific survival** (**MSS**). Univariate analysis hazard ratios and P values were calculated with a Cox proportional hazards regression model.

Results: Patient characteristics

- In this cohort of patients diagnosed in 2018 that were captured by the NCI SEER database (N=615), the linkage rate with the 15-GEP database was 41% (255/615 patients had 15-GEP test results).
- The cohort was comprised of majority (96.9%) white ethnicity and had a roughly balanced gender distribution of 56.1% male. The median age was 64 years (range, 20-92) (**Table 1**).
- There was a trend toward worsening AJCC T stage[8] with higher risk 15-GEP Class result similar to previous studies[3,9] that did not reach statistical significance in this cohort (**Table 1**).

Table 1. 15-GEP tested patient characteristics from the NCI SEER registries

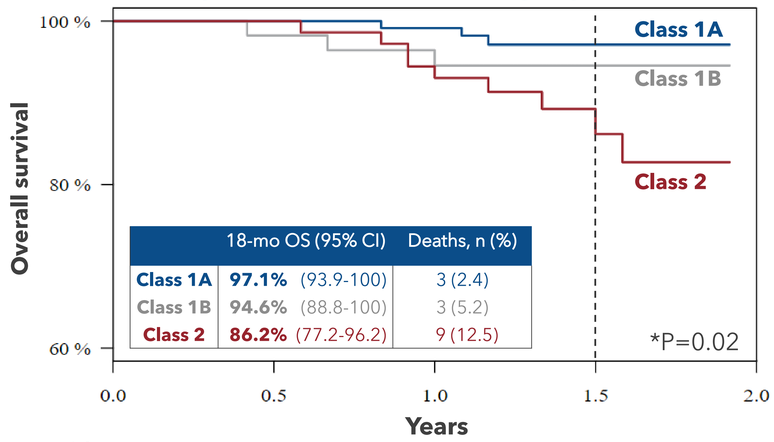
	Class 1A *n=125*	Class 1B *n=58*	Class 2 *n=72*	**Combined *n=255***	*P value*
Sex, male, n (%)	68 (54.4%)	34 (58.6%)	41 (56.9%)	**143 (56.1%)**	0.853 [X]
Age, years median (range)	62 (20-85)	61.5 (23-82)	67 (24-92)	**64 (20-92)**	0.01 [KW]
LBD#, mm median (range)	(*n=84*) 10.7 (0.1-20)	(*n=46*) 11.9 (1.1-22)	(*n=52*) 12.3 (0.9-22)	(***n=182***) **11.5 (0.1-22)**	0.319 [KW]
T stage[8], n# (%) 1 2 3 4	(*n=78*) 45 (57.7) 18 (23.1) 3 (3.9) 12 (15.4)	(*n=42*) 16 (38.1) 15 (35.7) 0 (0) 11 (26.2)	(*n=48*) 19 (39.6) 17 (35.4) 0 (0) 12 (25)	(***n=168***) **80 (47.6)** **50 (29.8)** **3 (1.8)** **35 (20.9)**	0.093 [X]

LBD, largest basal diameter; KW, Kruskal-Wallis F test; X, Pearson Chi-square test.
Not all clinical information was available from all patients in the registry.

Results: Survival

- **Patients with a 15-GEP Class 1A result had higher 18-month OS than patients with a Class 2 result (97% vs. 86%; P=0.02) (Figure 1).**

Figure 1. Overall survival of 15-GEP-tested uveal melanoma patients in the NCI SEER registry



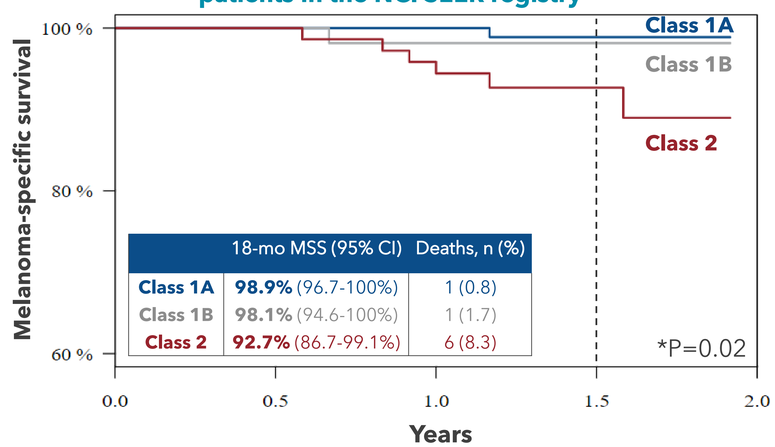
	18-mo OS (95% CI)	Deaths, n (%)
Class 1A	**97.1%** (93.9-100)	3 (2.4)
Class 1B	**94.6%** (88.8-100)	3 (5.2)
Class 2	**86.2%** (77.2-96.2)	9 (12.5)

No. at risk				
Class 1A	**125**	120	115	51
Class 1B	**58**	56	52	19
Class 2	**72**	72	68	29

*P values calculated by log-rank test

- **Patients with a 15-GEP Class 1A result also had higher 18-month MSS than patients with a Class 2 result (99% vs. 93%; P=0.02) (Figure 2).**
- **Patients with a Class 2 result had a 10 times higher event rate than those with a Class 1A result (8.3% [6/72] vs. 0.8% [1/125] melanoma mortality) (Figure 2).**

Figure 2. Uveal melanoma-specific survival of 15-GEP-tested patients in the NCI SEER registry



	18-mo MSS (95% CI)	Deaths, n (%)
Class 1A	**98.9%** (96.7-100%)	1 (0.8)
Class 1B	**98.1%** (94.6-100%)	1 (1.7)
Class 2	**92.7%** (86.7-99.1%)	6 (8.3)

No. at risk				
Class 1A	**125**	120	115	51
Class 1B	**58**	56	52	19
Class 2	**72**	72	68	29

*P values calculated by log-rank test

Results: Univariate Analysis

- **Univariate analysis of Class 1A vs. Class 2 patients showed a ten-fold greater risk of death from uveal melanoma for Class 2 patients (Table 2).**
- **In this small cohort with limited follow-up, there was no statistically significant difference in OS or MSS between patients with a Class 1A and 1B result (Table 2).**

Table 2. Univariate analysis by GEP Class result (n=255)

	Hazard ratio (95% CI) *P value*	
	Class 1A vs. 1B	**Class 1A vs. 2**
Overall survival	**2.25** (0.45-11.14) *0.321*	**5.03** (1.36-18.58) *0.015*
Melanoma-specific survival	**2.24** (0.14-35.77) *0.570*	**10.06** (1.21-83.61) *0.033*

Conclusions

- Consistent with previously published cohorts, the 15-GEP accurately stratified risk of death from uveal melanoma in this unselected, real-world contemporary cohort.
- Future analyses of NCI SEER-linked uveal melanoma patient data will include patients with 15-GEP results who were diagnosed as far back as 2009, which will provide an even larger cohort with more extensive follow-up time.

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Acknowledgments & Disclosures

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For more information: kalsina@castlebiosciences.com