Novel Genomic Prognostic Biomarkers for Canine Cancer Patients

Esther Chon[1], Jonathan Adkins[1], Natalie Duran[1], Sara Aman[1], Darwin Tsinajinnie[1], Manisha Warrier[1], Sharadha Sakthikumar[1], Salvatore Facista[1], Derick Whitley[1], David Haworth[1], Min Tang[2], William Hendricks[1], Guannan Wang[1]

[1]Vidium Animal Health, Scottsdale, AZ
[2]STATBEYOND Consulting LLC, Irvine, CA

ACVIM American College of Veterinary Internal Medicine FORUM

vidium ANIMAL HEALTH®

Oncology

INTRODUCTION

- **Background**
  - Growing evidence from dogs and humans supports the existence of abundant mutation-based biomarkers in canine cancers.
  - Increasing use of clinical genomic diagnostics now provides another powerful data source for biomarker discovery.
- **Hypothesis/Objectives**
  - We analyzed clinical outcomes from cancer cases profiled with SearchLight DNA®, a canine cancer gene panel, to identify mutations with prognostic value.

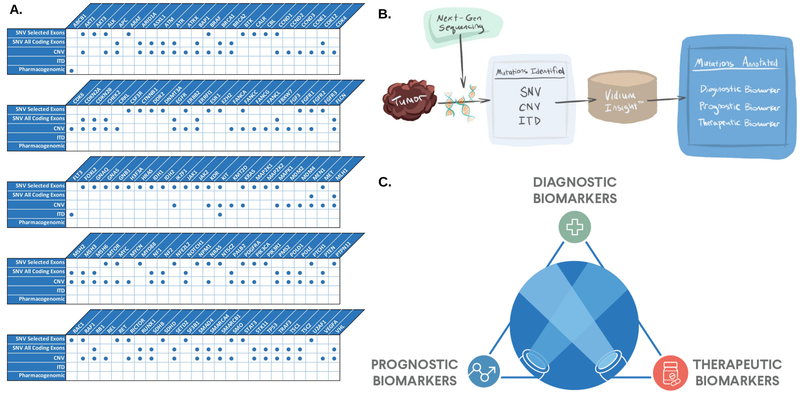

Figure 1. SearchLight DNA® is a tumor-only, next-generation sequencing, hybrid-capture, canine gene panel. A. SearchLight DNA® covers 120 genes associated with canine or human cancer. Mutation types identified include single nucleotide variants (SNV), copy number variants (CNV), and internal tandem duplications (ITD). **B.** Next generation sequencing is performed on a submitted tumor to identify mutations that then go through Vidium's bioinformatics pipeline to get annotated as a biomarker of diagnosis, prognosis, and/or therapy based on published literature curated and stored within Vidium's knowledgebase, Vidium Insight™. **C.** Annotation of each mutation diagnostic support, prognostic information, and targeted therapeutic options.

MATERIALS AND METHODSS

- **SearchLight DNA reports between September 2020 and May 2022 were searched for the following inclusion criteria:**
  - At least 3 months elapsed since SearchLight DNA analysis was performed
  - At least 1 genomic biomarker (diagnostic, prognostic, therapeutic) on the SearchLight DNA report
  - Reports not meeting these inclusion criteria were excluded

MATERIALS AND METHODS *cont.*

- **Veterinarians overseeing dogs for whom they had ordered SearchLight DNA reports which met the inclusion criteria were contacted in 1 of 2 methods:**
  - Direct completion of an online questionnaire
  - Sending dog's medical records to Vidium for completion of online questionnaire by medical oncologist (EC)
- **Demographic** (age, gender, breed) **and clinical** (initial cancer diagnosis, initial treatments, first and subsequent progressions, death) **data points were collected.**
- **Genomic data** (mutated genes, mutation types) **were collected.**
- **Statistical analyses were performed.**
  - Progression-free survival (PFS) was the time from initial diagnosis to first progression or death.
  - Mutated genes, mutation types, cancer diagnosis, signalment, whether targeted therapy was administered, and whether the dog received standard of care[#] were fitted with univariate analysis and multivariate Cox proportional hazard models for association with PFS
  - The log-rank test compared Kaplan-Meier curves of PFS between dogs that received and did not receive targeted therapy prior to first progression, and between dogs that received genomically informed targeted therapy vs. any therapy that was not genomically informed.

[#]general standard practice to treat the specific cancer type, as defined by EC

RESULTS

- **n = 127 dogs were included for PFS analysis.**
- **Diagnoses spanned 26 cancer histologies.**
- **Six genes (CCND1, SMARCB1, FANCG, CDKN2B, MSH6, CCND3) were significantly associated with PFS (Figure 2)**

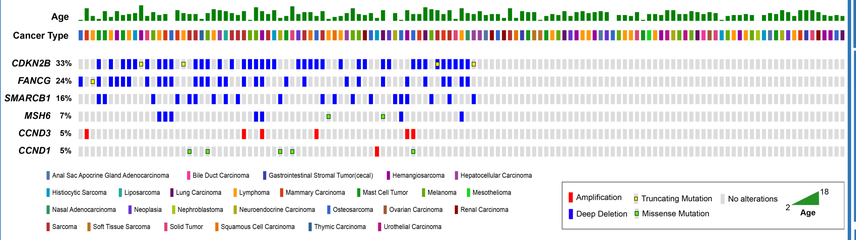

Figure 2. Oncoprint depicting the distribution of genes, mutation types, cancer diagnoses, and age in 127 dogs included for clinical outcome analysis. Each column of bars represents 1 patient.

RESULTS *cont.*

- **Dogs that received targeted therapy prior to first progression or death (n = 45) experienced significantly longer PFS compared to those that did not (n = 82; *P* = 0.012, Figure 3A).**
- **Dogs that received genomically informed targeted therapy (n = 29) experienced significantly improved PFS compared to dogs that received therapy that was not genomically informed (n = 98, *P* = 0.050, Figure 3B).**

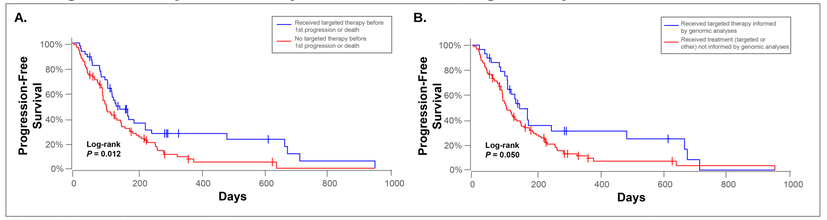

Figure 3. Kaplan-Meier plots of PFS between dogs that received targeted therapy vs. those that didn't (A), and between dogs that received genomically informed targeted therapy vs. those that received therapy that was not genomically informed (B).

- **The most common targeted therapies given in the genomically informed setting were olaparib, sirolimus, and trametinib (Table 1).**

Drug	Dose	Schedule	n
Olaparib	2 - 3.2 mg/kg	once daily	9
	1.4 mg/kg	twice daily	1
	2 mg/kg	twice daily	1
	2.8 mg/kg	once daily x 7 days starting day of carboplatin chemotherapy*	1
Sirolimus	0.08 - 0.1 mg/kg	once daily	7
	0.1 mg/kg	every other day	1
Trametinib	0.4 - 0.5 mg/m2	once daily	3
	0.02 mg/kg	once daily	1
	not reported	not reported	1
Palbociclib	0.2 mg/kg	once daily	1
Toceranib	2.8 mg/kg	every other day	1
Lapatinib	2 mg/kg	once daily while receiving concurrent carboplatin**	1
Trametinib + Sirolimus	not reported	once daily for both	1

Table 1. Doses and schedules of targeted therapies given to the 29 dogs that received these in the genomically informed setting.
*After completion of carboplatin course, this dog received continuous olaparib at the same dose once daily.
**After completion of carboplatin course, this dog received continuous lapatinib at 11 mg/kg once daily.

SUMMARY and CONCLUSIONS

- **Using a comprehensive cancer gene panel, we identified novel mutations with prognostic value, across multiple cancer types.**
- **We demonstrate the benefit of genomically informed targeted therapies.**
- **This work provides a compelling view of the significant potential in genomics and precision medicine for dogs with cancer.**

CONFLICT OF INTEREST DISCLOSURE

- All authors, excluding Min Tang, are full-time employees of Vidium Animal Health. SearchLight DNA is a product developed and provided by Vidium Animal Health.