KRAS Mutation in Dog Gastrointestinal Tumors

Maria Monjarás Edo
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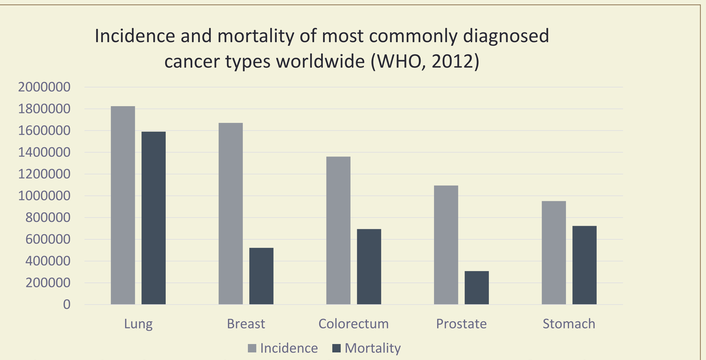
Universitat Autònoma de Barcelona

FACULTAT DE VETERINÀRIA

OBJECTIVES

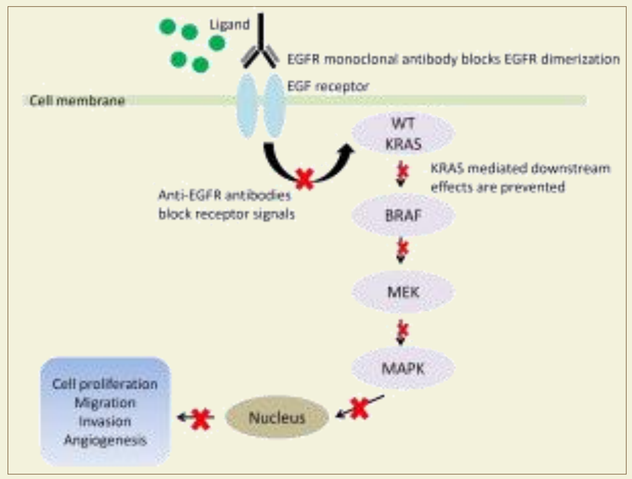
The objective of this retrospective study is to **evaluate the prevalence of KRAS mutation** in canine gastrointestinal tumors, through the study of KRAS expression in conserved tissue samples. A further aim, is to study the **influence** of other factors, such as **stage** and **treatment,** on survival time.

INTRODUCTION

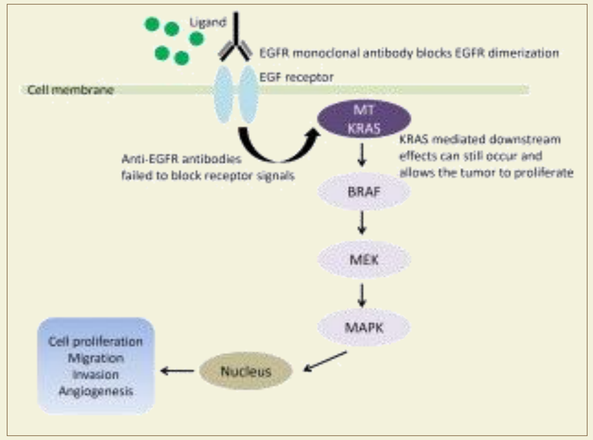


Colorectal and stomach cancer, affect **2.312.196 people** and cause **1.417.006 deaths** annually. 95% of these tumors are adenocarcinomas.

EFGR play a crucial role in tumorigenesis due to its function in cell signaling pathway. Therefore, current medical therapies in humans are based on the use of EFGR inhibitors.



A lack of response in some tumors to targeted therapy has led to the study of predictive biomarkers such as KRAS. This oncogene also plays a role in cell signaling and so, mutations may cause an upregulation of the cell cycle enhancing proliferation, migration, angiogenesis and evasion of apoptotic signals. About **40% of gastrointestinal human tumors carry the mutated form of KRAS** and it's considered a **poor prognostic factor.**

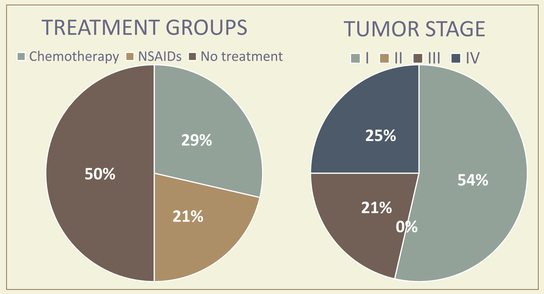


METHODS

- **Criteria for Case Inclusion:** tissue simple, minimal clinic record and staging of the tumor (human TNM criteria)
- **DNA extraction and KRAS gene analysis:** cell lysis (EZ1 DNA Tissue kit, QUIAGEN), DNA fragment measurement, KRAS determination (Therascreen KRAS RGQ PCR) with real-time PCR cycler (QUIAGEN)
- **Statistical analysis:** Kaplan-Meier survival curves, Log Rank test, Chi squared test

RESULTS

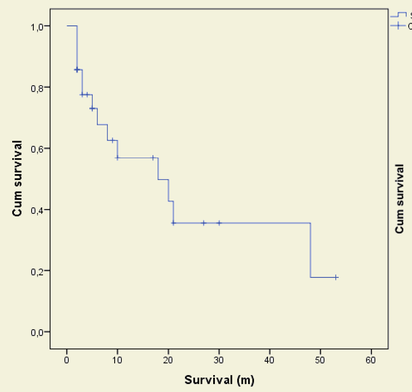
28 dogs were included in the database, all of them diagnosed with any solid gastrointestinal tumor. The mean age at diagnostic was 9'3 years old, with ages ranging from 4 to 14 years old.



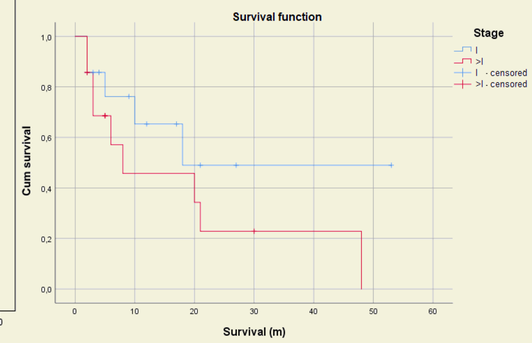
The survival mean time was 12,1 months after diagnostic, being the most common death cause clinical euthanasia.

Group		Mean	Median	Censored
Total		12,1	5,5	14 (50%)
Treatment	No treatment	11,7	4,5	8 (57,1%)
	Chemotherapy	11,25	7	2 (25%)
	NSAIDs	14,7	16,5	4 (66,7%)
Stage	I	13,2	9,5	9 (60%)
	>I	11,2	5	5 (38,5%)

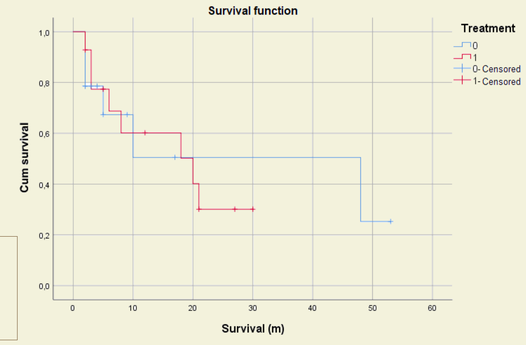
Global survival mean time



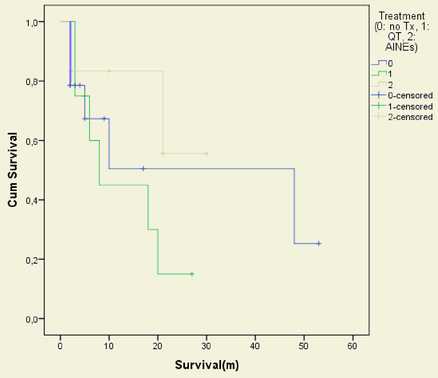
Survival mean time per stage



Survival mean time per treatment (None (0)/Ch-NSAIDs (1))



Survival mean time per treatment (None (0)/ Ch (1)/NSAIDs (2))



There are differences among stage and treatment groups, but according to Chi square test, they are **not statistically significant**.

On the other side, all 28 tissue samples, resulted negative to the KRAS mutation.

CONCLUSIONS

1. The incidence of the KRAS mutation in dog gastrointestinal tumors couldn't be defined in this study.
2. There are differences in the survival mean time depending on treatment and stage of the tumor but they are not statistically significant according to Log Rank and Chi sqaured test results.
3. The lack of follow up in a high percentage of the cases, and the small size of the simple (N) may have influenced the survival results