

Canine Survival Analysis upon Excision of Mammary Tumors and Complementary Dendritic Cell-Based Treatment

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Background & Objective

Mammary gland tumors account for over 40% of all tumors in intact female dogs^{1,2}. Surgical resection is the standard medical treatment. This applies to dogs with benign tumors and to approximately 50% of dogs with malignant tumors^{3,4}. An additional option is complementary follow-up care with various treatment protocols such as chemotherapy, radiation therapy, or immunotherapy. The latter, based on autologous dendritic cells, was used in 40 privately owned dogs between 05/2017 and 07/2023. We report here on the median survival rate and time based on the preliminary endpoint of July 31, 2025.

¹Sleedix N., de Ooster H., Velthuis Kroeze, E.J., Van Ginneken, C., van Brantegem, L., 2011. Canine mammary tumours, an overview. *Reprod. Domest. Anim.* 46, 1112-1131. ²Doorn, C.T., Taylor, D.O., Schneider, R., Hibbard, H.H., Klausner, M.R., 1968. Survey and animal neoplasms in Alameda and Contra Costa Counties, California. II. Cancer morbidity in dogs and cats from Alameda County. *J. Natl. Cancer Inst.* 1968, 40, 307-318. ³Misdorp, W., Hart, A.A., 1979. Canine mammary cancer. II Therapy and causes of death. *J. Small Anim. Pract.* 20, 395-404. ⁴Straw, R., 2005. Treatment of Mammary Gland Tumours and Perianal Neoplasia, pp. 672-675, North American Veterinary Conference, Orlando, 2005.

Materials and Methods

Selection of Cases

- Review of medical records of the period from 05/16/2017 to 07/18/2023.
- Confirmed diagnosis of histologically classified malignant mammary tumor^{5,6}, tumor excision and no additional treatments.
- 40 privately owned female dogs, 11/40 neutered.
- American Stafford Terrier (2), Australian Shepherd (3), Bavarian Mountain Hound (1), Bernese Mountain Dog (1), Bolonka Zwetna (1), Cairn Terrier (1), Cavalier King Charles Spaniel (1), Chihuahua (1), English Cocker Spaniel (1), French Bulldog (2), Flat Coated Retriever (1), Goldendoodle (1), Golden Retriever (1), Hovawart (1), Magyar Vizsla (1), mixed breed (5), Poodle (3), Rhodesian Ridgeback (3), Siberian Husky (1), Small Münsterländer (1), Tibet Terrier (1), unknown breed (3), Whippet (1), Wire-haired Dachshound (1), Wolfspitz (1), Yorkshire Terrier (1).
- Body weight (kg): Mean 19,96, Median 19,45, Min-Max 2,00-40,6.
- Age (year) at the time of surgical removal: Mean 9,12, Median 9,24, Min-Max: 1,92 -12,74.
- Age (year) at the time of first treatment: Mean 9,16, Median, 9,29, Min-Max 2,00-12,75.
- Days between surgery and 1st treatment: Mean 35,08, Median: 26,50, Min-Max: 13,00-146,00.

⁵Goldschmidt, M., Pena, L., Rasotto, R., Zappulli, V., 2011. Classification and grading of canine mammary tumors. *Vet. Pathol.*, 48 (1), 117-131. ⁶Schmidt JM, Meichner K (2022). In: Kessler M (Hrsg.): *Kleintieronkologie*. 4. Aufl. Georg Thieme Verlag, Stuttgart, 809-815.

Immunotherapy Based on Autologous Dendritic Cells (DCs)⁷

- DCs derived from peripheral blood monocytes of the animal patient.
- Dosis: DCs $\geq 5 \times 10^6$ cells required for in-vitro culture in RPMI 1640, rGM-CSF and rIL-4, GMP, seven days.
- Acceptance criteria for release: $\geq 10\%$ of CD-1b positive cells, cell viability $\geq 90\%$.
- Dispers: DCs $\geq 5 \times 10^4$ / 2ml of isotonic sodium chloride solution (0.9 %); quantity varied with cell number initially separated from blood.
- Intradermal injection within 24 hours.
- Number of treatments: Mean 4,58, Median 4, Min-Max 3-10.
- Schedule: three injections in four-week interval followed by injections upon demand.

⁷Spiller V., Vetter M., Dettmer-Richard C., Grammel T. (2024). *Vet J* 306:106-96. doi: 10.1016/j.tvjl.2024.106196.0

Analysis

- Kaplan-Meier curve analysis to determine median survival time, defined by the endpoint of July 31, 2025.
- For each degree of malignancy, hazard ratio calculated including comparison of survival curves (log-rank test).
- To compare survival rates with canine non-DC treated cohort, Rasotto et al., 2017⁸.

⁸Rasotto, R., Berisato, D., Goldschmidt, M. H., Zappulli, V., 2017. *Vet. Pathol.* 54, (4), 571-578. <https://doi.org/10.1177/0300985817698208>

Results

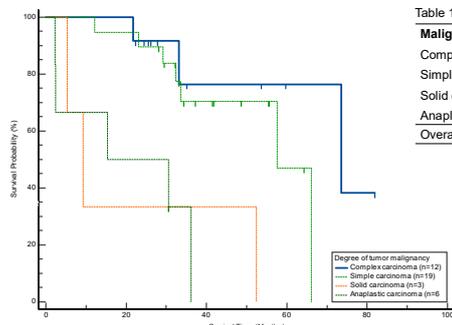


Table 1. Case summary.

Malignancy	Number of events	Number censored
Complex carcinoma	3 (25%)	9 (75%)
Simple carcinoma	7 (36,84%)	12 (63,16%)
Solid carcinoma	3 (100%)	0 (0%)
Anaplastic carcinoma	5 (83)	1 (16,67)
Overall	18 (45%)	22 (55%)

Table 2. Hazard ratios (HR) with 95 % confidence interval in comparison to cohort study, Rasotto et al., 2017⁸.

Canine study group (n=40) with tumor excision and DC-based immunotherapy					Canine cohort (n=229) with tumor excision alone ⁸	
Malignancy	Complex carcinoma	Simple carcinoma	Solid carcinoma	Anaplastic carcinoma	Malignancy	HR, P value
Complex carcinoma	Reference	1.74	8.44	8.30	Complex carcinoma	Reference
Simple carcinoma	0.64-4.71	Reference	0.83-85.42	1.31-52.37	Simple tubular carcinoma	5.6, non-significant
Solid carcinoma	0.58	0.21-1.56	Reference	4.85	Simple tubulopapillary carcinoma	10.4, 0.037
Anaplastic carcinoma	0.12	0.01-1.20	0.02-2.02	0.98	Solid carcinoma	33.7, 0.001
	0.02-0.76	0.04-1.27	1.02	Reference	Anaplastic carcinoma	153.4, < 0.001
			0.06-16.07	Reference		

Abbreviations: SE, standard error; SR, survival rate; CI, confidence interval

Results

- A number of 18 dogs (45 %) died within observation period, 22 dogs (55%) were still alive (Table 1).
- Solid carcinoma had the lowest median survival time followed by anaplastic carcinoma, simple carcinoma, and complex carcinoma (Figure 1).
- The risk ratio for solid carcinoma was slightly higher than that for anaplastic carcinoma (Table 2).
- Survival time differed significantly between malignancy grades, chi-square 18.35, degrees of freedom 3, P = 0.004 (log-rank test).
- In cases of anaplastic carcinoma, survival rates in dogs were 66% (year 1) and 50% (year 2) compared to surgical removal alone (0%) (Table 3). The survival rates of dogs with simple carcinoma treated surgically and with DC were higher (100%, year 1; 89%, year 2) than in dogs that underwent tumor removal alone (84%, year 1; 70%, year 2). For solid and complex carcinomas, both treatment methods showed similar survival rates (Table 3).

Table 3. Median and mean survival time (months) and survival rates (years) in comparison to cohort study without DC treatment, Rasotto et al. (2017)⁸.

Malignancy	Canine study group (n=40) with tumor excision and DC-based immunotherapy								Canine cohort (n=229) with tumor excision alone ⁸			
	Median	95%CI	Median	Mean	SE	95%CI	Mean	SE	Median	Mean	SR Year 1	SR Year 2
Complex carcinoma	73.51	33.11-73.51	66.24	7.67	51.21-81.28	100% (12/12)	83% (10/12)	33% (4/12)	33% (4/12)	8% (1/12)	8% (1/12)	
Simple carcinoma	57.60	33.53-66.08	52.46	4.81	43.02-61.89	100% (19/19)	89% (17/19)	47% (9/19)	31% (6/19)	10% (2/19)		
Solid carcinoma	9.27	5.39-52.44	22.37	15.08	-7.18-51.92	33% (1/3)	33% (1/3)	33% (1/3)	33% (1/3)			
Anaplastic carcinoma	15.39	2.27-36.16	20.50	6.66	7.45-33.56	66% (4/6)	50% (3/6)	16% (1/6)				

*Death by car accident.

Discussion & Conclusion

- During the period from 05/2027 to 07/2023, 40 privately owned dogs with mammary tumors were treated by surgical removal and dendritic cell-based immunotherapy with up to six-year follow-up.
- In anaplastic carcinoma, DC treatment appeared to prolong the survival rate of dogs compared to surgical removal alone. DC treatment also supported the survival rate of dogs with simple carcinoma. Regardless of the treatment method, no obvious differences in survival rates were observed for solid and complex carcinomas.
- In contrast to studies published elsewhere^{9,10} solid carcinoma rather than anaplastic carcinoma had the poorer prognosis. This could be due to intrinsic differences in the study population or to interobserver variability⁹.
- To conclude: The results of this prospective study must be interpreted with caution, as there is no true comparison group, only a reference group⁸ that underwent surgery alone. Interestingly, there is evidence that DC treatment would improve survival rates in highly malignant anaplastic carcinomas and less malignant simple carcinomas. Evidence-based approaches are currently being developed to further evaluate the efficacy of immunotherapy based on autologous dendritic cells.

⁹Chang, S.C., Chang, C.C., Chang, T.J., Wong, M.L., 2005. Prognostic factors associated with survival two years after surgery in dogs with malignant mammary tumors: 79 Cases (1998-2002). *J. Am. Vet. Med. Assoc.*, 227, (10), 1625-1629. ¹⁰Pena, L., De Andres, P.J., Clemente, M., et al., 2013. Prognostic value of histological grading in non-inflammatory canine mammary carcinomas in a prospective study with two-year follow-up: relationship with clinical and histological characteristics. *Vet. Pathol.*, 50 (1), 94-105.