We’ll Be *Raising The Stakes Against Cancer* at the 2012 Annual Conference!

Las Vegas has a tremendous amount to offer, with great shows, world-class dining and nightlife, and endless options for entertainment, gambling, and socializing. The location of the conference, The M Resort, Spa and Casino, is a truly special facility, with an exceptional assortment of appealing options for meeting, dining and gathering within the resort.

The organizing committee is also excited to announce that the 2012 VCS conference will be held jointly with the annual meeting of the American College of Veterinary Radiologists (ACVR). Given this joint structure, we have arranged a great set of keynote speakers that encompasses a broader variety of cancer-related topics. We are making a concerted effort to broaden the horizon of our conferences outside their traditional medical oncology focus, with inclusion of more topics pertaining to diagnostic imaging, surgical oncology, cancer pathology, and other ancillary areas of cancer management. Keynote speakers who have committed to presenting at the Las Vegas conference include Dr. Bruce Chabner, Dr. Landis Griffeth, and Dr. Julius Liptak. This year we will live stream the keynote speakers for those who are unable to attend.

A lot of your questions about this conference can be answered by visiting the conference website and we encourage you to do so. If you still have questions, please contact VCS at your convenience. Looking forward to seeing you all in Las Vegas in October!

Dr. Andrew Vaughan
2012 Conference Co-Chairman
Can’t make it to the conference this year?

For the first time, VCS will live stream the Keynote Speakers each morning at 8 am. For a nominal fee of $15, you can watch one or all three. Watch your email in early October for more information and registration details.

Members may also purchase a copy of the conference proceedings after the conference for $30. Non-members pay $40. You simply need to log in to your account and order through the online store after October 22nd.

For more information on these keynote speakers, the conference schedule, registration, hotel accommodations and more visit

www.vetcancersociety.org/conference
Welcome to the Fall 2012 edition of our Newsletter!

As the weather starts to cool off a bit, our thoughts turn to our Annual Conference. Scheduled for October 18-21 in Las Vegas, the conference will be held in conjunction with the annual American College of Veterinary Radiology meeting at the M Casino and Resort. Both the conference chair, Andrew Vaughan, and co-chair Pam Jones have worked incredibly hard to identify a great venue, create a stimulating scientific program and secure top notch keynote speakers. Andrew, especially, has put forth an amazing effort and please thank him for his attention to detail when you see him.

We are taking a slightly new direction this year with our keynote speakers. For better or worse, our Society has had an emphasis on medical oncology in the past and the vision embraced by the Executive Committee is to diversify our conference content to all things oncology, including surgery, radiation, imaging, and pathology. With our goal being to intentionally broaden the content of our meeting, we invited Dr. Julius Liptak to speak about veterinary surgical oncology. More ‘traditional’ keynotes include Drs. Landis Griffeth and Bruce Chabner. Landis Griffeth is boarded by the American Board of Nuclear Medicine and his special interests include PET, PET/CT and oncologic nuclear imaging. He is currently the Director of Nuclear Medicine and PET at Baylor University Medical Center in Dallas. Bruce Chabner spent the early part of his distinguished career at the NCI, where he influenced cancer drug development. He is currently a Professor of Medicine at Harvard Medical School, and Clinical Director of the Cancer Center at Massachusetts General Hospital.

The other on-going effort with our conference is our continuing attempts to only have the best abstracts presented, whether that be in oral or poster format. At the risk of getting crazy, we can also consider stretching our oral presentation time from 12 to 15 minutes. That will allow a more in-depth presentation but it will also cut down on the number of abstracts that can be presented in an oral format. To continue to hold the interest of all, the science of what is presented must be ratcheted up. For discussion on this topic, and more, plan to attend the Member Meeting on Saturday afternoon following the oral presentations. The EC wants to hear your thoughts and opinions and the Member Meeting is your opportunity to express them.

I look forward to seeing you in Vegas, both in and out of the conference halls.
Discussion and News Forum Update

The VTCS has its very own News and Discussion Forum that was launched this summer shortly after ACVIM. An invite was sent out to all current members of VTCS. We are encouraged by those members who responded and are hopeful that you will join them in participating fully in some great discussion. Invites do expire digitally, so if you wish to receive a new invite drop us a line at vettechcancersociety@gmail.com so we can get you signed up today. This is a no additional cost benefit of your membership and a great way to stay on top of current events in your field and network with other oncology technicians. Don’t miss out!

Wet Lab Registration is open for Technicians at Las Vegas Meeting

The cytology wet lab will take place at the beautiful and innovative Oquendo Center. Registration for the wet lab will be limited, so we urge you to register early. Transportation to and from the site will be provided as well as refreshments during this innovative and interactive session. The wet lab will take place on Sunday morning so as not to take away from an exciting two-day workshop for all registered members.

Case Report Presenters Announced

This year, VTCS is proud to be holding a session of peer-reviewed case reports. Presentations were judged by a panel, and the top chosen presentation will receive a $150.00 award. Presenters have been chosen and we would like to thank all of the technicians who submitted some fantastic case reports. The following members will be presenting their reports: Elizabeth Atencio, Lindsay Carroll, CVT, BS; Gina Gaylon, LVMT; and Dierdre Meehan, LVT, VTS (ECC). The reports will be published in the proceedings for Las Vegas, and the top presenter will have their report published in the newsletter following the meeting.

Call for Journal Review Submissions

Beginning with the last published newsletter, the VCS quarterly newsletter format underwent a change to primarily journal reviews. Unfortunately due to publishing and copyright issues, it is difficult for us as technicians to obtain access to the necessary journal articles. We are searching for solutions to this, but in the meantime, we encourage any technician with access to scientific journals to consider keeping their eyes peeled for articles that may be reviewed with particular interest for oncology technicians. If you feel you cannot write a review yourself, we would appreciate it if you could alert us to the article at vettechcancersociety@gmail.com.

Conference Scholarships for 2012 Conference

Three Technicians will receive scholarships in the form of registration to this year’s annual meeting in Las Vegas, NV. The VTCS EC has been accepting applications since July 15 and will be announcing the recipients in September. This is something that the general membership felt strongly about at our last annual meeting and the EC has been proud to see it through. We look forward to meeting our recipients in Vegas!

VTCS on Facebook

Do you spend time on Facebook? Perhaps more than you do say on your email, even? Don’t miss out on Timely news, information, and deadlines concerning VTCS. Like us on Facebook today to ensure you stay up to date on what is happening in your organization!
### Friday, October 19th

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<tr>
<th>Time</th>
<th>Speaker(s)</th>
<th>Topic</th>
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<tbody>
<tr>
<td>8:00 am—9:00 am</td>
<td>Dr. Landis Griffeth, Keynote Speaker</td>
<td>PET/CT: Fundamentals &amp; Clinical Applications in Humans</td>
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<tr>
<td>9:15 am—10:00 am</td>
<td>Dorothy Sharp</td>
<td>Nuclear Medicine Use in Veterinary Medicine Bone &amp; Thyroid Scintigraphy</td>
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<tr>
<td>10:30 am—12:00 pm</td>
<td>Dr. Silke Hecht VTCS Keynote Speaker</td>
<td>Comparative Imaging in Veterinary Oncology</td>
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<tr>
<td>1:45 pm—2:30 pm</td>
<td>Dr. Lenore Mohammadian</td>
<td>Ultrasound Imaging in the Veterinary Cancer Patient</td>
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<tr>
<td>2:30 pm—3:00 pm</td>
<td>Elizabeth Atencio, Lindsay Carroll, LVT, BS Gina Gaylon, LVMT Dierdre Meeham, LVT, VTS (ECC)</td>
<td>Case Report Presentations</td>
</tr>
<tr>
<td>3:30 pm—5:00 pm</td>
<td>Jo Tootell, RVT, CVT</td>
<td>Radiation Planning 101 for Veterinary Technicians</td>
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### Saturday, October 20th

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<tr>
<th>Time</th>
<th>Speaker(s)</th>
<th>Topic</th>
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<tr>
<td>8:00 am—9:00 am</td>
<td>Dr. Bruce Chamber, Keynote Speaker</td>
<td>Cancer: The Pit Bull of Human and Canine Medicine</td>
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<tr>
<td>9:15 am—10:00 am</td>
<td>Dr. Kim Selting</td>
<td>Clinical Trials: Cutting Edge Opportunities for the Motivated Pet Owner</td>
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<tr>
<td>10:30 am—11:15 am</td>
<td>Mr. Mark Tillinger</td>
<td>Charitable Funding: A Journey of Hope and Inspiration</td>
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<tr>
<td>11:15 am—12:00 pm</td>
<td>Dr. Holly Burr</td>
<td>Chemotherapy Extravasation</td>
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<tr>
<td>2:00 pm—3:00 pm</td>
<td>Dr. Deb Kamstock</td>
<td>Critical Aspects of Tumor Biopsy Submission</td>
</tr>
<tr>
<td>3:00 pm—4:00 pm</td>
<td>Dr. Chelsea Tripp</td>
<td>Electro-Chemotherapy: The Wave of the Future</td>
</tr>
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### Sunday, October 21st

**Cytology Wet Lab** 9 am-12 pm  
Separate Ticket Required

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The VTCS Workshop is sponsored by [ivo](https://www.ivoncology.com) and [amatheon pharmaceuticals](https://www.amatheonpharmaceuticals.com).
Thank You To Our Conference Sponsors

The Executive Committee of the Veterinary Cancer Society wishes to thank the following companies and organizations for sponsoring portions of the Scientific and Social Programs. Their generosity is passed onto registrants in the form of a lower registration fee.

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*Product indications: vaccine aids in extending survival times of dogs with stage II or stage III oral melanoma and for which local disease control has been achieved.

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VCS Welcomes New EC Members in 2013

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**Dr. Dave Ruslander**  
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Veterinary Specialty Hospitals of the Carolinas

**Dr. Carlos Rodriguez**  
*Secretary*  
Univ. of California, Davis

**Dr. Elaine Caplan**  
*Member at Large*  
Capital Area Veterinary Specialists

**Dr. Jenna Burton**  
*Member at Large*  
Colorado State University

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Next issue: December 2012  
Guest Editor: Dr. Iain Grant  
Deadlines: November 15 - Advertising & Articles

The articles published in this newsletter should be treated as personal communication and cited only as such with the consent of the author.

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**VCS Executive Committee**

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Andrew Vaughan, DVM, DACVIM  
Katherine Skorupski, DVM, DACVIM

Past-President: Barbara Kitchell, DVM, DACVIM  
Executive Director: Sandi Strother

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**Mark Your Calendar**

**2013 VCS Annual Conference**  
October 17-20  
Minneapolis Marriott City Center  
Minneapolis, Minnesota

**2014 VCS Mid-Year Conference**  
March 16-19  
Grove Park Inn  
Asheville, North Carolina

**2014 VCS Annual Conference**  
October 9-12  
Hyatt Regency St. Louis at the Arch  
St. Louis, Missouri

**2015 VCS Annual Conference**  
October 15-18  
Sheraton Premiere at Tysons Corner  
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- Lysodren
- Mitoxantrone
- Mustargen
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- Vinblastine
- Vincristine

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Online Discussion Forum

If you are a member of the OPWG and have not yet accessed the online forum site, please click this link to set up your account. Once your account is established, please click on the “OPWG (Onc-Path)” link in the top navigation panel to gain access to the OPWG Forum. VCS has sponsored this site to facilitate ongoing communication discussions amongst OPWG members throughout the year. For clarification, your initial account is with VCS as a whole after which you will need to click on the ‘OPWG (Onc-Path)’ link, as indicated above, for access to the OPWG discussion forum.

Upcoming Meeting

The next Oncology-Pathology Working Group Meeting will be held on Saturday, October 20th from 12:00-1:00 in Las Vegas, NV during the Annual Conference. An optional boxed lunch is available for purchase but must be pre-ordered so be sure to mark this option on your registration form if desired.

Some topics which will be covered during this one-hour meeting include the OPWG constitution and bylaws to include member definitions and voting eligibility, an update by the Mast Cell Tumor subgroup regarding grading of canine cutaneous MCTs, request for feedback/input regarding the online discussion forum, and future directions of the OPWG including new tumor subgroups.

If you’re interested in working with the OPWG or have colleagues which may be interested, please email information including name, specialty, affiliation, email and phone number to OPWG.VCS@gmail.com or to Erin Malone at Erin_Malone1@yahoo.com. For additional information about the OPWG please visit http://www.vetcancersociety.org/opwg/.

Looking forward to seeing everyone in Vegas as well as online on the discussion boards.

VCS Oncology-Pathology Working Group
~Because we can do better~

INTERESTED IN SUBMITTING INFORMATION FOR THE FALL NEWSLETTER?
WANT TO SHARE INFORMATION ABOUT ONGOING TRIALS OR THERAPIES?

If you would like to share information with the VCS membership in the Fall 2012 newsletter please submit that information in WORD format no later than November 15th to vetcancersociety@yahoo.com. All submissions will be reviewed by the Guest Editor and Editor for appropriateness prior to publication. No advertisement of products or therapies through editorial means will be allowed.
Retrospective study of cytologic features of well differentiated hepatocellular carcinoma in dogs

Masserdotti C, Drigo M.
Vet Clin Pathol. 2012 May 22, pp1-9

The authors report the cytological features that may help to distinguish well differentiated hepatocellular carcinomas from non-neoplastic hepatic parenchyma. Cytological diagnosis of hepatocellular carcinoma is possible when the hepatocytes have prominent criteria of malignancy but poses a clinical problem when hepatocytes have relatively normal morphologic appearance in well differentiated tumors.

From 33 cytological criteria, the most useful and significant distinguishing cytological features were identified: dissociation of hepatocytes (loss of cohesiveness of peripheral cells), acinar or pallisading arrangement of cells, the presence of naked nuclei, capillaries and necrosis, together with mild anisocytosis, anisokaryosis, multinuclearity and increased N:C ratios. Archived samples were collected from 15 histologically confirmed cases of WD-HCC and 15 cases of either normal liver or liver affected by non-neoplastic disease using a 25-gauge spinal needle under ultrasound guidance. The manuscript is generally well written and contains comprehensive tables of cytological criteria and some nice cytology images.

It would have been ideal to have included the appearance of the neoplastic and non-neoplastic lesions on ultrasound, as the reader ends up assuming that a large mass lesion in a single lobe or multiple lesions in contiguous lobes was not mistaken for non-neoplastic hepatic parenchyma. Perhaps of greater relevance to the clinical oncologist would be to compare a similar broad range of cytological features in WD-HCC and adenomas (hepatomas) versus hyperplastic nodules, as this could influence decision making on the need for surgical intervention in this frequently encountered and challenging clinical scenario.

Reviewed by Iain Grant, BVSc, DACVIM (Oncology)

Intensity-modulated and image-guided radiation therapy for treatment of genitourinary carcinomas in dogs

Nolan MW, Kogan L, Griffin LR, Custis JT, Harmon JF, Biller BJ, Larue SM.
J Vet Intern Med (2012); 26; 87-995

Genitourinary carcinomas in dogs (CGUC) include transitional cell carcinomas, adenocarcinomas and solid carcinomas of the urinary bladder, urethra and prostate. These tumors are locally invasive and have moderate to high risk of loco-regional and distant metastases. Death is most frequently attributable to local obstruction in spite of the potential for distant metastases. Radiation therapy may play an important role in loco-regional control of CGUC but has traditionally been associated with a high incidence of late radiation side effects. The advent of intensity modulated, image guided RT (IM/IGRT) allows for the use of smaller, better targeted treatment fields which limits the dose exposure of normal tissues.

In this retrospective study, the authors describe the extent of tumor control and acute and late treatment associated toxicoses in 21 dogs treated with IM/IGRT for CGUC (prostatic tumors n=10, bladder tumors n=9, urethral tumors n=2). An anonymous questionnaire provided to the dog owners aimed to assess the impact of RT on the patient and owner, logistical challenges associated with treatment administration, quality of life during RT, overall outcome and client satisfaction. Although somewhat subjective and also prone to bias in that the clients were typically highly committed owners, this was an interesting aspect of the data analysis.

Various novel techniques relating to patient positioning, standardization of daily urination and defecation times and interventions to standardize bladder volume in the treatment field were employed to create a PTV with minimal intra- and inter-fraction variations thus limiting dose to normal tissues amongst the organs at risk. 14 dogs had nodal irradiation in a second target field. The target prescription to the tumor was 54-58Gy in 20 daily fractions on a Monday to Friday basis (2.7-2.85Gy per fraction). Sixteen dogs were staged T2-3N0M0, 4 were staged T2-3N1M0 and 1 dog was staged T3N0M1. Neoadjuvant therapy (NSAIDs n=14, chemotherapy n=6 and surgery n=3) and adjuvant therapy (NSAIDs n=12, chemotherapy n=12) were frequently employed.

- Continued on page 13
Acute RT associated GI complications were the most common and were mild-moderate (grade 1 colitis n=7; grade 2 colitis n=1; grade 1 haematuria n=1, grade 2 stanguria n=1; grade 1 integumentary toxicoses n=4). Late RT complications were infrequent but severe (rectal stricture n=1; ureteral stricture n=1, urethral stricture n=2), occurring 6-18 months after completion of RT. Stenting procedures were employed to manage complications, again showing the commitment of these owners. The authors do not discuss the occurrence of late side effects at length. Studies by Anderson et al (2002) and Arthur et al (2008) have demonstrated that a higher dose per fraction was associated with a greater incidence of late side effects. By maintaining a lower dose per fraction (<3Gy) and/or by more accurately targeting the radiation, the authors here have limited the occurrence of late toxic effects to 4/21 dogs.

Median time to first event was 317 days in all dogs and the median overall survival time was 654 days. Interestingly 2 dogs suffered a geographic miss and 5 experienced in-field progression of their tumours; 1 underwent a second course of RT without adverse event. Three dogs developed distant metastatic disease. Due to the novel nature of treatment planning and RT delivery it is hard to compare this study to previous studies but this represents a favorable outcome compared to no treatment, surgery alone, NSAIDs alone, chemotherapy and multimodal protocols including palliative intraoperative RT and fractionated RT in the management of CGUC.

64.3 % of clients found the distance to be travelled and the duration of treatment challenging and this is valuable information as few other studies have considered the opinion of the clients with respect to the time commitment, expense and potential inconvenience of definitive RT as a treatment protocol. 15.4% of owners reported a decline in quality of life during or immediately following RT and 10% of respondents indicated that their pet's quality of life was worse after RT. Unfortunately 7.1% of owners reported that they were very inadequately informed of potential radiation side effects and 14.3% were very inadequately informed about tumour control and expected prognosis indicating the importance of effective and adequate communication between oncologist and client when prescribing oncologic treatment.


 Reviewed by Iain Grant, BVSc, DACVIM (Oncology)

Prevalence of 5-Lipoxygenase expression in canine osteosarcoma and the effects of the dual 5-lipoxygenase / cyclooxygenase inhibitor on osteosarcoma cells in vitro and in vivo

R.C. Goupil, J.J.Bushey, J. Peters-Kennedy and J.J. Wakshlag
Vet Path Online First doi: 10.1177/0300985811432350

NSAIDs inhibit the COX-1 and COX-2 isoforms of cyclooxygenase enzymes. The expression and inhibition of COX-2 has been the subject of much interest in both canine and human oncology. Through arachidonic acid metabolism, the downstream product of COX-2 activity, PGE2, is a prostaglandin with promitogenic and prometastastic properties. Deracoxib and meloxicam (COX-2 inhibitors) have demonstrated in vitro activity against canine OSA cell lines however at concentrations unachievable in vivo.

Dual inhibition of COX and 5-LOX (5-lipoxygenase) may be significant due to aberrant expression of 5-LOX in certain human cancers and demonstration that 5-LOX inhibition produces anti-proliferative effects. 5-LOX expression in canine neoplasms has not been extensively studied although Goodman et al. (2011) demonstrated there was no differential expression of 5-LOX in prostatic neoplasia versus benign prostatic disorders.

In this study, the authors examined 5-LOX expression patterns in archived tissue blocks from 60 cases of canine OSA (axial skeleton n=30, appendicular skeleton n=30) by immunohistochemistry. Although two thirds of the samples indicated positive labeling, the staining was scored mild-moderate in virtually all cases, making its relevance questionable.

Cell culture studies were then performed using 3 canine OSA cell lines: OS2.4, HMPOS and D17. 5-LOX expression was pronounced in 2 of the 3 cell lines. Following treatment with the 5-LOX inhibitor tepoxalin, significant reduction in cell viability was achieved, although

- Continued on page 14
cell lines showed varying sensitivity to its inhibitory effects. Achieving physiologically active concentrations of tepoxalin may therefore not be achievable in all clinical cases using standard oral dosing regimens.

Finally, using an OSA xenograft model in irradiated mice (n=12), treated with oral 0.9% NaCl or tepoxalin at doses of 10mg/kg or 50mg/kg PO once daily (n=4 mice in each group), the rate of increase in tumor volume was significantly reduced in mice treated with tepoxalin at both concentrations. Mice treated with the higher dose of tepoxalin lived significantly longer than those treated with saline, due to inhibition of the rate of tumor growth. All the mice did develop histologic evidence of pulmonary metastatic disease. There were no signs of normal tissue toxicity associated with the use of tepoxalin at the dosing regime employed and this fell within the safe dosing regimen used in dogs in a 6-month toxicity study.

The retrospective, in vitro and in vivo aspects of this publication make it a comprehensive research study and the first investigating 5-LOX in canine OSA. The exact mechanism of action for anti 5-LOX activity of tepoxalin is not clear however and merits further investigation. While the inhibition of tumor progression in the mouse xenograft model shows promise for the use of tepoxalin as an anti-proliferative drug in canine tumor patients, the authors point out that there are species specific variations in drug pharmacokinetics meriting further investigation in this area. The variable sensitivity in different osteosarcoma cell lines would suggest variable response in clinically affected patients.

Reviewed by Iain Grant, BVSc, DACVIM (Oncology)

Antitumor effects of deracoxib treatment in 26 dogs with transitional cell carcinoma of the urinary bladder

McMillan SK, Boria P, Moore GE, Widmer WR, Bonney PL, Knapp DW. JAVMA 2011; 239(8); 1084-1089.

The use of the NSAID piroxicam is a well-established treatment for TCC and other forms of cancer. The major mechanism of efficacy is thought to be in part through COX-2 inhibition. However because this drug has non-selective inhibition of both COX 1 and 2 enzymes, it has limited use in a percentage of animals developing associated renal or GI toxicity. The purpose of this study was to evaluate the tolerability and efficacy of a more COX-2 selective drug, deracoxib, as an antineoplastic agent in dogs with confirmed TCC. A total of 26 dogs with measurable disease (via abdominal ultrasonography) were evaluated. Eight dogs had received and had evidence of tumor progression after prior treatments including piroxicam alone, cisplatin and piroxicam and Mitoxantrone and piroxicam prior to entry into the study. All dogs received a standard dose of deracoxib given once daily. 17% of dogs achieved a partial response, 71% maintained stable disease and 13% experienced disease progression. The overall MST was 323 days, which compares favorably to other studies. Those dogs that went on to receive other chemotherapy treatments after evidence of progressive disease had a significant survival advantage over dogs that did not. Toxicity was minimal and included grade I or II GI tox which did not limit its use in these dogs. Azotemia was noted and thought to be a consequence of tumor location, inflammation or tumor progression. Eleven dogs experienced mild increases in serum liver enzyme activities with no dogs developing any clinical manifestations of liver disease. The results of this study support the use of this well tolerated COX-2 selective NSAID in treating TCC in dogs.

Reviewed by Kristine Burgess, DVM, DACVIM (Oncology)

Use of histologic margin evaluation to predict recurrence of cutaneous malignant tumors in dogs and cats after surgical excision

The purpose of this study was to evaluate the usefulness of histologic margins to predict local recurrence of cutaneous malignant tumors in dogs and cats after surgical excision. A total of 40 dogs and 20 cats with 60 surgically excised tumors consisting of an equal distribution (20 each) of soft tissue sarcomas, mast cell tumors and carcinomas. Animals were followed for a period of 24 months after surgical excision. Tumor type, size, grade and location varied with the majority arising from the trunk followed by extremities then head/neck. Nine of the 60 tumors were reported as local recurrences. None of the animals received additional therapy (chemotherapy or radiation therapy). The authors classified excised tumors as clean (>2mm of normal tissue from inked edges); close (tumors cells to within 2 mm of inked edges); or infiltrated (tumor cells extending to inked edges). Overall tumor recurrence occurred in 16/20 tumors with infiltrated margins, 8/11 tumors with close margins and 3/29 tumors with clean margins. The mean recurrence free interval (RFI) was 229 days for all animals. Those animals with primary tumors had a longer RFI (256 days) vs. animals with recurrent tumors (151 days). Comparing tumor types: the RFI for soft tissue sarcomas was 294 days; for mast cell tumors it was 167 days and for carcinomas it was 184. Prognosis depended on tumor size (>2 cm), grades (>grade II) and if greater than one surgery was performed. Prognosis was not influenced by tumor type or location. The results of this study confirm an association with histologic evidence of tumor infiltration and residual disease at the margins of resected tissue and local tumor recurrence (80% recurrence rate). Also the extent of tumor infiltration was prognostic for recurrence with diffuse tumor cell infiltration recurring in 14/15 animals vs. only 2/5 recurring with focally positive margins.

Expression of PDGFR-β and Kit in canine anal sac apocrine gland adenocarcinoma using tissue immunohistochemistry


Receptor tyrosine kinase (RTK) inhibitors are an active area of investigation in veterinary oncology. Toceranib phosphate is a well-established RTK with FDA approval for use in dogs with mast cell tumors. An early phase I clinical trial evaluating toceranib phosphate in a population of dogs with various tumor types demonstrated biologic activity in a number of histologies, including anal sac apocrine gland adenocarcinomas (ASAGAC). In this study toceranib phosphate was given to dogs with advanced stage anal sac apocrine gland adenocarcinoma and demonstrated 87.5% biologic activity. Thus this study was completed in order to demonstrate expression of toceranib phosphate targets Kit and PDGFR-β. This was completed using immunohistochemical staining of paraffin embedded canine ASAGAC. A total of 77 tissues samples with an established diagnosis of ASAGAC were identified and evaluated via IHC. The authors used 5 normal anal sac tissues obtained from non-cancer bearing dogs at the time of necropsy as controls for the study. Results demonstrated that two of 77 neoplastic samples had positive Kit staining. Positive PDGFR-β labeling was noted within the neoplastic cells of 15 samples with variable intensity and location of maximum staining uptake. None of the samples were positive for both Kit and PDGFR-β. All histologically normal canine anal sac epithelium were negative for both Kit and PDGFR-β labeling. The results of this study demonstrate that Kit was present in very small numbers (2.6%) as well PDGFR-β labeling was detected in low levels in the tissues evaluated (19.5%) suggesting that there may be other targets mediating the efficacy seen with toceranib phosphate in treating canine anal sac adenocarcinoma.

A dose-finding study with a novel water-soluble formulation of paclitaxel for the treatment of malignant high-grade solid tumors in dogs


Paclitaxel has broad efficacy against human tumors, but its use in veterinary medicine has been limited by hypersensitivity reactions to the carrier required to attain water solubility. This phase I study was aimed at assessing toxicity and identifying the maximum tolerated dose of a micelle nanoparticle paclitaxel formulation (Paccal Vet). Dogs with measurable disease and any tumor type were included and a standard 3x3 dose escalation scheme was planned. Pharmacokinetic analysis was performed during the first 24 hours after dosing. Thirty-two dogs were enrolled and mast cell tumors,
mammary tumors, and lymphoma were the most common diagnoses. Due to severe toxicity at the starting dose of 175 mg/m², dose de-escalation occurred, though the new dose-finding scheme was not specified. All other dogs received doses between 100 and 150 mg/m² every 3 weeks. Adverse events were reported in all dogs, with neutropenia being the most common serious adverse event. Hypersensitivity occurred in one dog. Nineteen dogs achieved CR or PR (including 7 dogs with mast cell tumor, 4 with squamous cell carcinoma, and 3 with lymphoma). The results of this study suggest that the Paccal Vet formulation may have significant efficacy against certain tumor types including mast cell tumors, though toxicity rates may also be high at doses used in this study.

Prognostic value of histologic grading in noninflammatory canine mammary carcinomas in a prospective study with two-year follow-up: Relationship with clinical and histological characteristics.


Several different histologic grading schemes have been published in an attempt to predict biologic behavior of canine mammary carcinomas (CA), but there is no consensus as to which scheme is most clinically useful. This study prospectively applied the Pena grading system to dogs with mammary CA in an attempt to determine the usefulness of this method in providing prognostic information and treatment guidance. Dogs were treated only with surgery and spay and those with sarcomas, carcinomas, inflammatory mammary CA, or distant metastasis were excluded. Histologic factors included in the grading scheme were tubule formation, nuclear pleomorphism, and mitotic index. Sixty-five dogs were included. Grade was found to predict recurrence and/or metastasis (evaluated together) and also survival. Fifty-nine percent of dogs with grade III tumors died of mammary CA compared to 16% of dogs with grade II tumors and 0% of dogs with grade I tumors. Other factors that were found to predict at least one outcome variable in this study included spay status, age, stage, breed size, tumor size, lymph node status, histologic subtype, and myoepithelial proliferation. Grade and stage were significantly correlated with outcome in multivariate analysis. The results of this study suggest that histologic grade, in addition to previously published prognostic factors, can be used to help predict risk of metastasis and cancer-related death in dogs with mammary CA. Adjuvant chemotherapy may be indicated in dogs with high grade tumors.

Reviewed by Katherine Skorupski, DVM, DACVIM (Oncology)

The MTAP-CDKN2A locus confers susceptibility to a naturally occurring canine cancer


Genome wide association studies have been useful in identifying potential cancer risk-associated alleles in humans. Because dogs have high rates of breed-related cancer, but less genetic diversity than humans, these types of studies may more quickly and easily identify causal alleles. The purpose of this study was to identify loci with a potential causal relationship in Bernese Mountain Dogs with histiocytic sarcoma (HS). Genomic DNA was collected from a total of 236 Bernese Mountain Dogs with HS and 228 Bernese controls from both North America and Europe. Genome wide association studies were used to identify cancer-associated loci and fine mapping and sequencing were used to narrow results. Ninety-six percent of affected Bernese Mountain Dogs were found to have a disease-associated haplotype that lies across MTAP and continues through CDKN2A. Real-time PCR showed no significant changes in MTAP expression, but significantly higher amounts of CDKN2A and B in individuals with 2 copies of the haplotype. These results identify the major histiocytic sarcoma locus and suggest that the disease, and possibly other cancers common in this breed, are caused by dysregulation of the CDKN2A and B genes as well as altered expression of INK4A/ARF/INK4B. The Bernese Mountain Dog may be an excellent model for the study of cancer susceptibility due to dysregulation in a location where alterations are frequently found in human cancers.

Reviewed by Katherine Skorupski, DVM, DACVIM (Oncology)
Exploring mechanisms of sex differences in longevity: lifetime ovary exposure and exceptional longevity in dogs

Waters DJ, Kengeri SS, Clever B, Booth, JA, Maras AH, Schlittler DL and Hayek MG.
Aging Cell (2009) 8: 752-755

Female survival advantage has been documented in certain mammalian species, most notably in humans: women that live to 100 years of age outnumber men by 4:1. The mechanisms of this sex-related difference in longevity are not clearly understood although the recent Nurses’ Health study (Parker et al. Obst Gynecol. 2009) did indicate that ovariohysterectomy was generally associated with earlier mortality compared to hysterectomy with ovary sparing. Pet dogs provide an interesting research model for comparison as a substantial proportion of dogs are spayed at a young age, presenting a novel opportunity for evaluating the relationship between endogenous estrogens and overall longevity.

This retrospective cohort study assessed two groups of pet female Rottweilers to examine the impact of lifetime ovarian hormone exposure on longevity. 83 dogs with “exceptional” longevity (survival beyond 13 years) were compared to 100 dogs with “usual” longevity (survival between 8 and 10.8 years). Pets with the longest period of ovary exposure (6.1-8.0 years) were 3.2 times more likely to reach exceptional longevity than those dogs spayed between 0.4 and 2 years of age. This trend persisted in a multivariate analysis that also considered other factors that might influence longevity (height, weight, family history). The major cause of death in the “usual” longevity group was cancer, giving rise to 73% of all deaths. More than half of these dogs (38% overall) died of bone cancer. In the exceptional longevity group, documented cancer accounted for only 25% of deaths with only 8% attributable to bone cancer. The largest single reported cause of death in the exceptional longevity group was generalized “frailty” accounting for 21% of patients.

Clearly this study does have some deficiencies given that it is a retrospective study of a single breed of pet dogs and is thus likely hampered by variable medical record keeping, uncertainty regarding the diagnosis of “frailty”, and potential selection bias. In spite of such deficiencies, however, this study indicates that female Rottweilers may be living shorter lives because of juvenile ovariohysterectomy. Although such recommendations may continue to have a positive impact on pet over-population and on reducing the incidence of mammary and gynecologic tumors in dogs, there may be a substantial negative impact on overall longevity that should be further evaluated.

Reviewed by Andrew Vaughan, DVM, DACVIM (Oncology)

Phase I Evaluation of STA-1474, a prodrug of the novel HSP90 inhibitor Ganetespib, in dogs with spontaneous cancer

PLoS ONE 2011 November; Volume 6 (11): e27018

Heat shock protein 90 (HSP90) is a molecular chaperone that promotes the conformational maturation and stabilization of a wide variety of client proteins. Many oncoproteins, including EGFR family members and other tyrosine kinase proteins, are known HSP90 clients. HSP90 inhibition gives rise to apoptosis selectively in many malignant cell types and there are no known resistance mutations to reverse such effects. STA-1474 (Synta Pharmaceuticals Corp, Lexington, MA, USA) is a highly water soluble prodrug of ganetespib which induces degradation of multiple HSP90 client proteins. Previous in vitro studies have indicated that ganetespib has activity against canine osteosarcoma (OSA) and mast cell cancer (MCT).

This study is a phase I dose-escalating clinical trial in which STA-1474 was administered intravenously to 25 client-owned dogs with selected spontaneous cancers. Patients’ diagnoses included OSA (n =10), MCT (n= 4), thyroid carcinoma (n= 3), lymphoma (n= 3), other carcinoma (n= 2), nasal chondrosarcoma (n= 1), oral malignant melanoma (n= 1), and oral fibrosarcoma (n= 1). A maximally tolerated dose of 9.5mg/kg/week was identified using once weekly dosing over a 1 hour period. Other investigated dosing regimens included once weekly dosing (9.5mg/kg) over an 8 hour period and twice weekly dosing (5mg/kg/dose) over a one hour period. Extensive pharmacokinetics were performed on each patient with each dosing regime. Side-effects entirely consisted of gastrointestinal upset and/or lethargy without documented hematologic or biochemical toxicities.

Reviewed by Andrew Vaughan, DVM, DACVIM (Oncology)
Responses were not seen in the 12 patients receiving the drug over a one hour infusion time aside from one patient in this group with melanoma who accidentally had drug extravasation with resultant prolonged drug exposure. Of 6 dogs initially treated with the 8 hour infusion protocol, there were two partial responses (metastatic thyroid carcinoma for 36 weeks and metastatic OSA for 20 weeks), one mixed response (metastatic MCT for 16 weeks), and two dogs with stable disease (both with metastatic OSA for 12 weeks). In 7 patients in the twice per week dosing group, 2 experienced partial responses to therapy (both MCTs that were subsequently excised). The authors also documented rapid up-regulation of HSP70 expression in tumor samples and PBMCs as is expected secondary to HSP90 inhibition.

Overall this report is a concise and intriguing evaluation of the use of a well-tolerated, water-soluble HSP90 inhibitor that may prove valuable in the management of several challenging malignancies in dogs.

Reviewed by Andrew Vaughan, DVM, DACVIM (Oncology)
Oncology

Medications

Adriamycin (Doxorubicin)
Alkeran (Melphalan)
Anzemet (Dolasetron Mesylate)
Carboplatin (compares to Paraplatin®)
CeeNu (Lomustine)
Cisplatin
Cyclophosphamide (compares to Cytoxan®)
Cytarabine (compares to Cytosar®)
Dacarbazine (compares to DTIC®)
Elspar (Asparaginase)
Epirubicin (Ellence®)
Fluorouracil (Adrucl, 5FU)

Gemzar (Gemcitabine HCL)
Ifex (Ifosfamide)
Leukeran (Chlorambucil)
Lysodren (Mitotane)
Mitoxantrone (compares to Novantrone®)
Pamidronate
Vinblastine (compares to Velban®)
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In honor of all the amazing animals who have sadly passed away from cancer, and to the Doctors and Technicians that cared for them. VCS honors them, and their families, below.

**Donor: Dr. Sarah Gillings**  
*Summit Veterinary Referral Center*

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