Veterinary Oncology Clinical Trials:
Balancing Rewards and Risks for Your Clients and Patients

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Agenda

• Introduction
• Why would a clinician/hospital want to be involved?
• What do you need to run a trial?
• Types of clinical trials and associated study goals
• Discussing clinical trials and obtaining informed owner consent
• Ethics, animal welfare and patient protection
• Benefit versus risk – is this trial a good fit for my client / patient?
• Current veterinary trial consortia
• Available resource for clinical trials
• Q&A
Clinical Trials

• Conducted to collect data regarding the safety and efficacy of new drug or device
• Umbrella term for many different types of trials/levels of evidence
Why would clinicians want to conduct trials?

• Academic edge
  • Wanting more than simply seeing and treating standard patients

• Ability to offer patients something new
  • Access to new and novel therapies before others
  • For disease with no standard of care
  • Funded trials to helps owners with limited funds

• Prestige within the field
  • Clinician and hospital
  • Publications, lectures, etc.

• Financial - fully funded trials generate revenue
Why would hospitals want to be in trials?

• Academia - part of universities mission to advance knowledge
• Referral Hospital
  • Often untapped source for cases/revenue
    • Many self referrals
    • Referral from traditionally nonreferring rdvms
  • Trials may separate a practice from others
    • Considered a higher level, more academic
    • Trial data is presented at conferences and published which is free PR
    • Possible recruitment tool for potential new clinicians to the practice
• Public relations (true for academia and referral):
  • Often trial owners have limited funds thus incredibly thankful
What do you need to run a clinical trial?

• Institution needs to help create the infrastructure for running trials
  • Internal review board to provide timely review / approval of the study
  • Provide individual for signing the research agreement/NDA, etc.
  • Provide affective supportive staff to help with
    • Client inquiries regarding trials
    • Marketing and outreach
    • Study paperwork, maintenance of trials binders, data storage and protection
    • Financial aspects of study

• Trials take more time than traditional outpatient cases this needs to be factored into clinic/support staff time
What do you need to run a clinical trial?

• Clinicians and nurses need to be on board
  • Clinicians
    • Case accrual
    • Accurate and timely data capture
  • Nurses/study coordinators
    • Maintaining integrity of the study and care of cases
    • Maintaining contact with sponsor in the event of adverse events

• Make sure all personal are adequately compiling study data, intermittent communication with sponsor is helpful
  • This is extremely important and may mean discussions with those who may be falling behind with paperwork, etc.
What do you need to run a clinical trial?

• Study completion
  • Accurately updating sites that trial has accrued all cases
  • Making sure all individuals are present for study closeout
  • Keeping data (binders etc) in a secure location
The Evolution of Pet Ownership

Pets are family whose medical needs merit quality care
Why do clients enroll their pet in a trial?

• Access to novel therapy
  • Failed traditional therapies
  • Anticipated poor outcome with standard of care

• Financial assistance
  • Therapy or portion thereof paid for while on trial
  • Financial incentive upon completion

• Desire to advance veterinary medicine and animal health
  • Advancing human health is less of a motivator for pet owners
Why should primary care veterinarians be interested in clinical trials?

Where do you obtain health information for your pet?

Results from unpublished on-line survey conducted by the Flint Animal Cancer Center in 2012 (n = 465)
TYPES OF CLINICAL TRIALS / ASSOCIATED STUDY GOALS
What are clinical trials?

- **Prospective studies** to new test...
  - Drugs or drug combinations
  - Diagnostic tests
  - Surgical interventions
  - Radiation therapy protocols
  - Gene therapy/immunotherapy

- May also be sampling studies
  - Collect blood and/or tissue for molecular or genetic analysis
Clinical Trials: Examples

**Sampling Trial**
- **Enrollment**
- Pre-tx biopsy
- **Intervention**
- Post-tx biopsy
- **Study Complete**

**Treatment Trial**
- **Enrollment**
- Treatment
- Assess response to therapy
  - **Responder**
  - Continue treatment
  - **Non-responder**
  - Withdraw
Phase of drug development trials

- Phase I
- Phase II
- Phase III
- Phase IV
Phase I Trials

- **Phase I** studies assess the **safety** of a drug or device
  - Initial phase of testing with a small number of patients
  - Designed to determine the effects of the drug or device including:
    - How it is absorbed
    - Metabolized
    - Excreted
  - Investigates the side effects that occur as dosage levels are increased (maximum tolerated dose)
  - Physician based therapy: ~ 70% of experimental drugs pass this phase

**RISKS:** Side effects not fully known; may receive subtherapeutic or toxic dose; may be additional blood or tissue sampling
Phase II Trials

- **Phase II** studies test the **efficacy** of a drug or device
- Involves larger number of patients (50 - hundreds)
- Many phase II studies are randomized trials:
  - One group of patients receives the experimental drug
  - Second "control" group receives a standard treatment or placebo
- Often these studies are "blinded"
  - Owners/patients and researchers do not know who has received active drug
- Data allows pharmaceutical company and the FDA to have info regarding safety and effectiveness of the new drug
- ~ 1/3 of drugs successfully complete both Phase I and Phase II studies

**RISKS:** Drug may not be effective against disease; possibility of placebo; side effects still not fully elucidated
Phase III Trials

- **Phase III** studies involve randomized, controlled and blind testing
- Large numbers of patients (hundreds) over several years
- Provides thorough understanding of the effectiveness of the drug or device, the benefits and the range of possible adverse reactions
- Physician based therapy, ~70% to 90% of drugs that enter Phase III studies successfully complete this phase of testing
- Once Phase III is complete, a company can request FDA approval

**RISKS:** May be randomized to placebo/control arm; additional side effects possible with long term dosing
Phase IV Trials

- **Phase IV** studies are often called **Post Marketing Surveillance Trials**, are conducted *after a drug or device has been approved* for sale.
- Pharmaceutical companies have several objectives at this stage:
  - To compare a drug with other drugs already in the market
  - Monitor long-term effectiveness and impact on a patient's quality of life
  - Assess cost-effectiveness of a drug therapy relative to other therapies
- Phase IV studies can result in a drug or device being taken off the market or restrictions of use could be placed on the product

**RISKS:** Side effects generally known, but be sure report possible side effects not listed in drug brochure
Veterinary Medicine

- Path is slightly different likely due to costs
  - Discovery
  - Pilot
  - Pre-pivotal
  - Pivotal
  - Post-market
Companion animals in drug development

Preclinical models
- Small animal
- Beagle dog
- Non-human primate

Phase I human clinical trials
Phase II human clinical trials
Phase III human clinical trials

Tumour-bearing dog studies
- Activity
- Toxicity
- Pharmacokinetics
- Pharmacodynamics

Tumour-bearing dog studies
- Dose
- Regimen
- Schedule
- Biomarkers
- Responding histologies
- Combination therapies

New cancer drug

Elements of a well designed trial

• Research question/goal clearly defined

• Study design is appropriate to answer research question
  • Adequately powered sample size

• Clearly defined population of interest (inclusion/exclusion criteria)

• Assessment of response to treatment and possible risks / side effects occur at appropriate intervals
Study Training

• All individuals must have training in Good Clinical Practice
  • Important in maintaining trial integrity
• Time needs to be blocked out of clinics for this
  • Many sponsors will pay for this time to the clinic
• All individuals need to be present, taking notes and understanding their role
• Primary investigator should also follow this up with key points for all to take regarding their roles.
  • Delegation of duties for:
    • Primary investigator and secondary investigators
    • Nurses, and secondary nurses
• Understanding trial confidentiality regarding sponsor, drug, agent mech of action, etc
• Maintaining all study material in secure locations
Study Marketing

• Many sponsors will provide funding for this, but if not consider:
  • Placing a section in all referral letters that describes the trial etc
  • Social Media: Facebook, Instagram, Twitter
  • AVMA trials database
  • Hospital website
  • RDVM mailers
  • Email/fax blasts
  • Hospital Newsletters
  • Material in the waiting room:
  • Ensure all departments are aware to be on the lookout for potential cases
  • Continuing Education events
DISCUSSING TRIAL WITH CLIENTS

Obtaining informed consent
Informed consent process

Discussion with pet owner
- Good fit for pet?
- Good fit for them?

Weigh pros and cons

Ample time to review and ask questions

Obtain signatures

Enrolled!
Provide owner copy of signed consent

Update owner regarding new risks identified

Screening of owner?
Elements of Informed Consent

• Statement that study involves research
• Purpose of research
  ◦ Usual or alternative approach?
• Expected duration
• Description of procedures
  ◦ ID which are experimental
• Possible risks/discomfort
• Compensation for illness or injury that occurs on study
• Possible benefits to patient

Adapted from: https://www.hhs.gov/ohrp/regulations-and-policy/guidance/checklists/index.html
Withrow & MacEwen Small Animal Clinical Oncology, chapter 17, 2013.
Elements of Informed Consent - con’t

• Assurance of confidentiality
• Assurance that:
  • Participation is voluntary
  • Refusal to participate will not impact care
  • Patient can be withdrawn at anytime without penalty
• Approximate costs to owner
• Termination of study by PI
• Necropsy (always frightens owners)
• Study contact information
• Client and veterinarian signature
• Copy of signed document should be provided to the owner

Adapted from: https://www.hhs.gov/ohrp/regulations-and-policy/guidance/checklists/index.html
Withrow & MacEwen Small Animal Clinical Oncology, chapter 17, 2013.
Informed consent summary

• Make sure patient meets all eligibility criteria before consenting

• Should be a discussion with time for questions
  • Provide clients document beforehand for review
  • Set aside adequate time to discuss
    • Consent forms can be quite lengthy!

• Don’t sugarcoat possible risks or possible benefit to pet
ETHICS, ANIMAL WELFARE AND PATIENT PROTECTION

*How are our patients and clients protected?*

- Appropriate pre-clinical studies
- Institutional Animal Care and Use Committees (IACUC)
- Clinical Trials Review Boards (CTRB)
- Informed consent process ✓
Appropriate pre-clinical studies

• Laboratory / cell culture studies
  • Proof of principle

• Laboratory animal studies
  • Need to determine starting dose
    • Rodents: PK, efficacy, limited safety
    • Healthy, purpose bred dogs
    • Other?

• Reasonable to use in people’s pets?
Institutional Animal Care and Use Committees (IACUC)

• Ensures that procurement, housing, and care and use conform to:
  • 1) ILAR Guide for the Care and Use of Laboratory Animals
  • 2) Guide for the Care and Use of Agricultural Animals in Research and Teaching
  • 3) USDA implementation of Animal Welfare Act (AWA)
  • 4) Public Health Service’s Policy on Humane Care and Use of Laboratory Animals

• Animal facilities accredited by the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC)
Institutional Animal Care and Use Committees (IACUC)

• Primarily oversee purpose bred research animals
  • Confusion regarding role for veterinary clinical trials

• IACUC protocols focus on animal safety and welfare
  • Mitigation of painful procedures
  • Blood volumes collected do not exceed specific guidelines
  • People involved in research have appropriate training

• Not responsible for assessing scientific merit of research
Clinical Trials Review Boards (CTRB)/Internal Review Board (IRB)

• Evaluate and oversee...
  • Scientific merit of research
    • The “New York Times” test
    • Clinics worry about PR
  • Informed consent documents (i.e. client communication)

• Some institutions just have a CTRB/IRB
  • Trials exempted from IACUC review unless highly novel or invasive
  • Others have a hybrid model using both CTRB and IACUC
Protection while enrolled in clinical trial

• Training for individuals participating in clinical trials
  • Veterinary Good Clinical Practice (vGCP)
    • Ethical and scientific quality standard for veterinary clinical studies
  • IACUC 101, if applicable

• Attitude is everything
  • People’s pets, not research animals
  • Treat them the way we would any patient of ours
BENEFIT VERSUS RISK

Is this trial a good fit for my client and patient?
Is this trial a good fit for my client and patient?

*It depends...*

- **Consider your client...**
  - Goals for treatment?
  - Are they risk adverse?
  - Unable to take time away from work for extra visits?
  - How reliable are they?
  - Psychologically stable?
  - Only option for treatment?
  - Finances?
Is this trial a good fit for my client and patient?

*It depends…*

- **Consider your patient…**
  - Hospital visits
  - Performance status or comorbidities
  - Past experiences with drugs
  - Likelihood of benefit from trials
VETERINARY CLINICAL TRIALS CONSORTIA
Comparative Oncology Trials Consortium (COTC)
Animal Clinical Investigation (ACI)
Current Clinical Trials

Participation in any clinical trial being conducted at a BluePearl Veterinary Partners hospital requires a referral from your family veterinarian. If you and your veterinarian are interested in learning more about enrollment in one of our active trials, please have your family veterinarian contact the doctor conducting the study.
CLINICAL TRIALS RESOURCES
AVMA Animal Health Studies Database

Welcome to the AVMA Animal Health Studies Database (AAHSD)! Veterinary clinical studies conducted to investigate novel therapies or to collect samples or information to gain further understanding of a disease provide the best scientific evidence to guide the clinical care of animals, and oftentimes, people too. For recent examples of veterinary clinical studies in the news, see here.

Veterinarians and animal owners may search the site to find studies that might be relevant to their patient or pet, either for a particular condition or even to provide health data or a sample from a normal animal. Animal owners interested in participating in such studies are encouraged to discuss their eligibility for any relevant study with their veterinarian.

SEARCH FOR VETERINARY STUDIES

To search for a specific study, please use one or more of the search options below OR click the ‘Show all Studies’ button to view all studies in the AAHSD.

Show All Studies >

Or, to narrow your search, please use one or more of the search options below.

**DIAGNOSIS**

or keywords:

**PRIMARY FIELD**

of Veterinary Medicine:

**COUNTRY:**

- Any Country -

**SPECIES:**

- Any Species -

Search >
We found 5 result(s). Diagnosis/keyword = "arthritis"
You can narrow this search further with the filter located to the left. Animal owners interested in participating in a study are encouraged to discuss their eligibility for any relevant study with their veterinarian.

AAHSD004447 - Evaluation of MK-0674 its effect on the development and progression of osteoarthritis in dogs following cranial cruciate ligament (CCL) rupture and tibial plateau leveling osteotomy (TPLO) surgery

The VCI is conducting a clinical trial for dogs who have had a cranial cruciate ligament (CCL) rupture and meniscal tear that has been surgically repaired with a tibial plateau l...
For people...

ClinicalTrials.gov is a database of privately and publicly funded clinical studies conducted around the world.

Explore 282,668 research studies in all 50 states and in 204 countries.

ClinicalTrials.gov is a resource provided by the U.S. National Library of Medicine.

IMPORTANT: Listing a study does not mean it has been evaluated by the U.S. Federal Government. Read our disclaimer for details.

Before participating in a study, talk to your health care provider and learn about the risks and potential benefits.

Find a study (all fields optional)

Status
- Recruiting and not yet recruiting studies
- All studies

Condition or disease (For example: breast cancer)

Other terms (For example: NCT number, drug name, investigator name)

Country

Search  Advanced Search
Other resources:

• Teaching hospital websites (examples)
  • Auburn (http://www.vetmed.auburn.edu/veterinarians/clinical-trials/)
  • Colorado State (http://csu-cvmbs.colostate.edu/vth/veterinarians/clinical-trials/Pages/default.aspx)
  • North Carolina State (https://cvm.ncsu.edu/research/clinical-trials/)
• COTC (https://ccr.cancer.gov/Comparative-Oncology-Program)
• Animal Clinical Investigations (ACI; http://www.animalci.com/)
• VCA (https://vcahospitals.com/west-los-angeles/specialty/for-vets/clinical-studies)
• Blue Pearl (https://bluepearlvet.com/about-us/clinical-trials/current-clinical-trials)
What is a successful trial?

- *It is an equal balance of accrual and quality*
- *Important data was gained*
- *Owners feel their pet contributed*
QUESTIONS?

CLINICAL TRIAL

UC DAVIS VETERINARY MEDICINE

HOPE Veterinary Specialists
Thank you!

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