COTC Questionnaire
Completed 2008

This questionnaire was designed to assess the use and associated adverse events of human oncology drugs within the practice of veterinary oncology. The questionnaire is divided into three sections (off label use of approved human drugs, agents in early human clinical trials, general questions) and all answers are tallied in red. The questionnaire was distributed to seventeen COTC institutions and was completed and returned by nine. The results from the questionnaire have been used in several presentations and recent publications. For additional information please contact Christina Mazcko at mazckoc@mail.nih.gov.

I. Off-label use of approved human drugs:

1. How many dogs have you treated with cancer therapies currently available for the treatment of cancer in humans in the last year?
    a. <100 **0/9 (0%)**
    b. 101-200 **3/9 (33%)**
    c. 201-500 **6/9 (66%)**
    d. >501 **0/9 (0%)**

2. How many distinct classes of agents in this group of drugs have you used in the treatment of cancer in the last 3 years?
    a. <3 **0/9 (0%)**
    b. 4-6 **3/9 (33%)**
    c. 7-9 **5/9 (55%)**
    d. >10 **1/9 (11%)**

3. How many "unexpected" adverse events or severe adverse events have you seen in association with the use of these drugs?
"Unexpected" adverse or severe adverse events that have not been reported in human patients or in experimentally treated research dogs.

    Of the patients treated:
    a. 0-10% **9/9 (100%)**
    b. 11-25% **0/9 (0%)**
    c. 26-50% **0/9 (0%)**
    d. 51-100% **0/9 (0%)**

II. Agents either in early human clinical trials or not yet in human clinical trials:

4. How many dogs have you entered into clinical trials using novel cancer agents either in early human trials or not yet in human clinical trials in the last year?

a. <10 **4/9 (44%)**
b. 11-26 **3/9 (33%)**
c. 27-99 **2/9 (22%)**
d. >100 **0/9 (0%)**

5. How many distinct agents in this group of drugs have you used in the treatment of cancer in the last 3 years?

a. <3 **7/9 (77%)**
b. 4-6 **2/9 (22%)**
c. 7-9 **0/9 (0%)**
d. >10 **0/9 (0%)**

6. How many "unexpected" adverse events or severe adverse events have you seen in association with the use of these drugs?
"Unexpected " adverse or severe adverse events that have not been reported in experimentally treated research dogs.

Of the patients treated:
a. 0-10% **9/9 (100%)**
b. 11-25% **0/9 (0%)**
c. 26-50% **0/9 (0%)**
d. 51-100% **0/9 (0%)**

III. General questions:

8. Do you expect differences in the types of toxicity, the MTD, or the PK of drugs when assessed in tumor bearing dogs compared to research dogs? If so provide examples.

Yes **6/9 (66%)**
No **3/9 (33%)**

If yes, please explain

- **Yes, Due to differences in drug metabolism and underlying organ dysfunction, I would expect that pharmacokinetics may be altered and animals with borderline organ function and occult organ dysfunction could develop clinically apparent organ dysfunction.**

- **In one of our trials, we are concerned about an investigational immunotherapy that links a monoclonal antibody to a cytokine. We are suspicious that tumor-bearing dogs may have greater toxicity since the cytokine will be retained in the tumor rather than being cleared with the unbound antibody.**

- **Waddle JR et al. Cancer Chemother Pharmacol (1999) 44:74-80 showed that there was greater variability of orally administered tamoxifen in tumor-bearing as compared to normal dogs. Tumor-bearing dogs are typically older than normal dogs and often have concurrent disease such as renal insufficiency that may influence tumor PK, and are client owned so may be on different diets and supplements. Diet may influence PK as well (Maguire PJ et al. J Am Vet Med Assoc (2000) 217:847-852)**

- **Unless there is underlying concurrent of metabolic disease.**

- **MTD is often lower with higher PK at similar dose in research dogs**

- **We have been doing some studies with intravesical therapy for urinary bladder cancer. We expect greater drug absorption in tumor bearing dogs than in normal lab dogs because of the increased vasculature in the tumors.**

9. What is your estimate of the relative MTD for specific anticancer drug in tumor bearing dogs compared to humans?

a. 0-24% **0/8 (0%)**
b. 25-49% **3/8 (37%)**
c. 50-74% **3/8 (37%)**
d. 75-100% **2/8 (25%)**

10. What is your estimate of the relative MTD for specific anticancer drug in tumor bearing dogs compared to normal research dogs?

a. 0-24% **0/8 (0%)**
b. 25-49% **0/8 (0%)**
c. 50-74% **3/8 (37%)**
d. 75-100% **5/8 (62%)**