



INSTITUTE OF MEDICINE WORKSHOP

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“The Role of Clinical Studies for Pets with Naturally Occurring Tumors in Translational Cancer Research”

Workshop Overview

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Duke Cancer Institute

A National Cancer Institute-designated
Comprehensive Cancer Center

The Cancer Challenge



Cancer is common in humans – a public health problem

- 1 of every 3 women will develop cancer
- 1 of every 2 men will develop cancer
- >1.4 million Americans will be diagnosed with cancer this year
- >600,000 Americans will die from cancer this year
- ~14 million cancer survivors in the U.S.

The Cancer Challenge



- While cancer outcomes are improving (for many, but not all cancers), short-term and long-term toxicities from current cancer therapies are quite significant.
- Cancer survivors frequently have significant health problems caused by surgery, radiation therapy, chemotherapy toxicities; includes cardiovascular disease, metabolic disorders, organ dysfunction (kidney, liver, heart, etc).

The Cancer Challenge



There is a great need for new cancer therapies – better efficacy, less toxicity

The process of developing new cancer therapies is both slow and costly:

- Average of 13-16 years to bring a new therapeutic from target validation to marketplace
- <<10% of new drugs developed make it to the marketplace
- ~\$1.8 billion to bring a new drug to market

The Cancer Challenge



- Many novel drug cancer drug candidates fail in human clinical trials despite evidence of efficacy in traditional pre-clinical murine models
- These models frequently lack key characteristics of human cancers
 - Long latency
 - Natural causation
 - Genomic instability
 - Tumor heterogeneity
 - Tumor microenvironment characteristics

The Cancer Challenge and Opportunity



Cancer is common in Pets

- >170 million pets in U.S. (80 million dogs; >90 million cats)
- 47% of U.S. households own at least one dog
- ~1 million dogs treated for cancer in U.S. yearly
- Cancer kills 50% of dogs >10yo (33% of younger dogs)
- 33% of cats die from cancer
- Pet owners are highly motivated to enroll in clinical studies

The Cancer Opportunity



Many canine tumors share many characteristics with human cancers (e.g. sarcomas, melanoma, lymphoma, glioma, etc.)

- Histologic appearance
- Tumor genetics (some genomics information available; need more)
- Biologic behavior
- Molecular targets
- Therapeutic response
- Acquired resistance
- Recurrence
- Metastasis

The Cancer Opportunity



- Many canine tumors share many characteristics with human cancers



The Cancer Opportunity



Humans and dogs have lived together for thousands of years



The Cancer Opportunity



?Convergent Evolution?



The Cancer Opportunity



Cancer Development

Environmental Exposures (contribute to the majority of
human cancers)

+

Genetic Susceptibility

- Human familial cancer susceptibility syndromes
- Dog breed cancer susceptibilities
(can provide insights into how environmental
exposures lead to cancer development)

The Cancer Opportunity



NCI Comparative Oncology Trials Consortium

- Infrastructure and resources to integrate clinical trials for pet dogs with naturally occurring cancers into the development of new drugs, devices, and imaging techniques for human cancers
- 18 veterinary academic centers

How best to integrate these clinical trial data for human cancer research advancement and integrate clinical studies in pets with cancer within the cancer research continuum?

The Cancer Opportunity



“The FDA Animal Rule” - 21 CFR314.600 and 21 CFR601.90 – Approval of drugs and biological products when human efficacy studies are neither ethical or feasible

- *Testing under Animal rule is a surrogate for human efficacy/clinical studies*
- *Safety must still be demonstrated in human subjects*
- *FDA may approve a product for which:*
 - *Human safety has been established*
 - *“Animal rule” requirements are met – based on adequate and well-controlled animal studies, the results of which establish that the product is reasonably likely to provide clinical benefit when administered in humans*

The Cancer Opportunity



“The FDA Animal Rule” - continued

- *Reasonably well-understood pathophysiologic mechanism*
- *Animal study outcome is clearly related to the desired benefit in human (reduced morbidity/mortality)*
- *Data on pharmacology parameters of the product in animals and humans allows selection of an effective dose in humans*
- *Does not apply if product approval can be based on standards described elsewhere in FDA regulations*
- *Not a shortcut to approval*



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The Cancer Opportunity



This Workshop

- Challenges and opportunities in cancer drug development
- State of canine tumor biology and genetics
- Opportunities in imaging and other biologic endpoints
- Opportunities and challenges in current human and canine clinical trials infrastructures
- Ensuring that the needs of pet animals are addressed
- Interface with regulatory bodies and pharma/biotech

The Cancer Opportunity



Who will benefit?

- Human patients
 - Canine patients
 - Canine owners
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- Faster, less costly drug approvals?
 - Better informed clinical trials design

The Cancer Opportunity



This would be an iterative process

