Hipster Oncology

What's New and Matters to You

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Leading Specialty Healthcare for Pets

Summary

- New and old kids on the block
  - Mast cell: **STEL**FONTA®
  - Lymphoma: Laverdia ®
  - Hemangiosarcoma: Propanolol
  - Carcinomas: NSAID use
- How do they work
  - MOA
- Patient selection
  - When to reach for these therapies/refer
- Concepts on the horizon

STELFONTA® for Mast Cell Tumors

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STELFONTA® : What is it

- **STEL**FONTA® (tigilanol tiglate injection) is an Intralesional therapy for local canine mast cell tumors
- Discovered by Australian company Qbiotics
- seed of the blushwood plant *(Fontainea picrosperma)*

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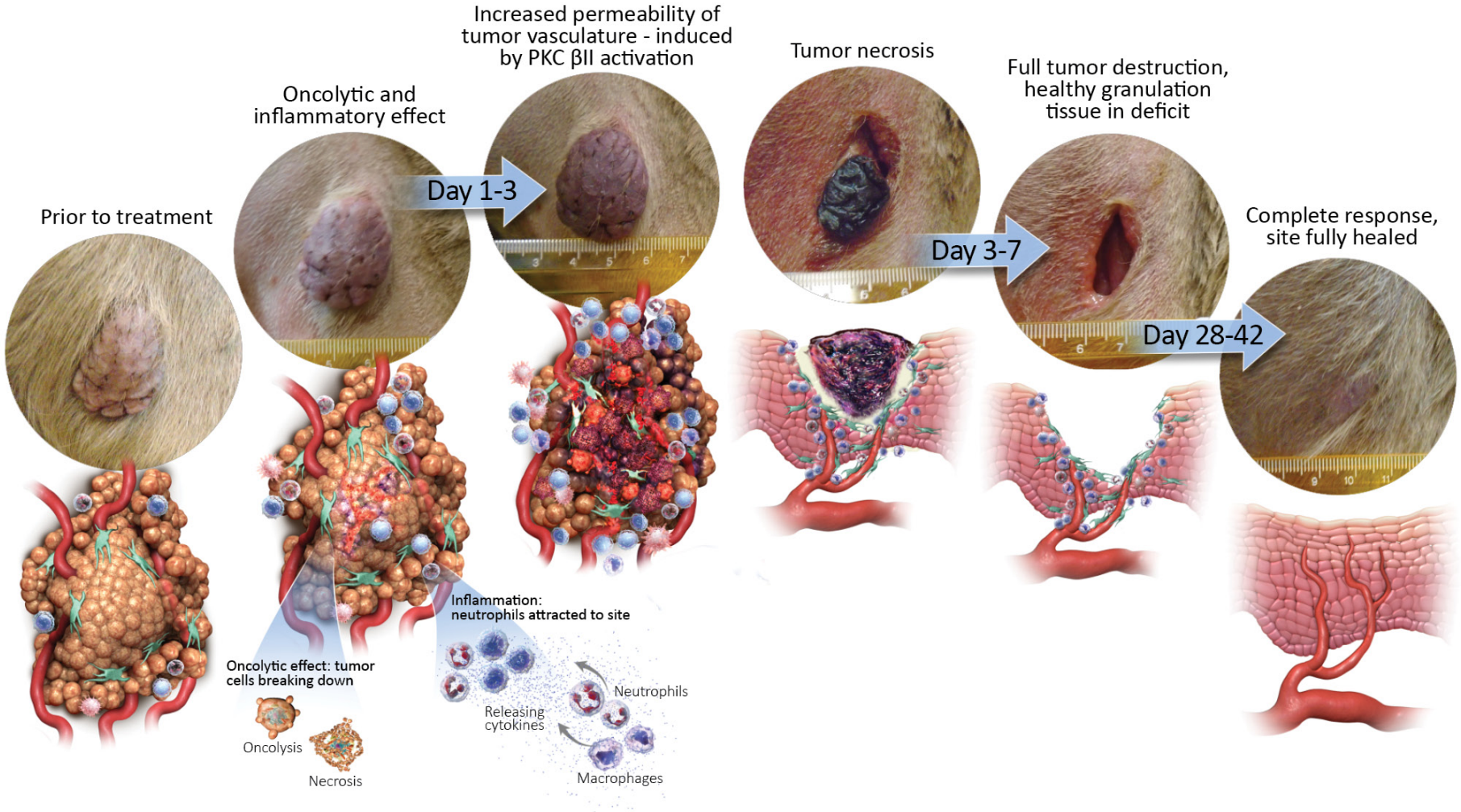
STELFONTA® : How it works

- Stimulates the activation of the enzyme protein kinase C
- Direct tumor cell death
- Increased permeability of tumor blood vessels

STELFONTA® : How it works



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STELFONTA® : Guidelines for Case Selection

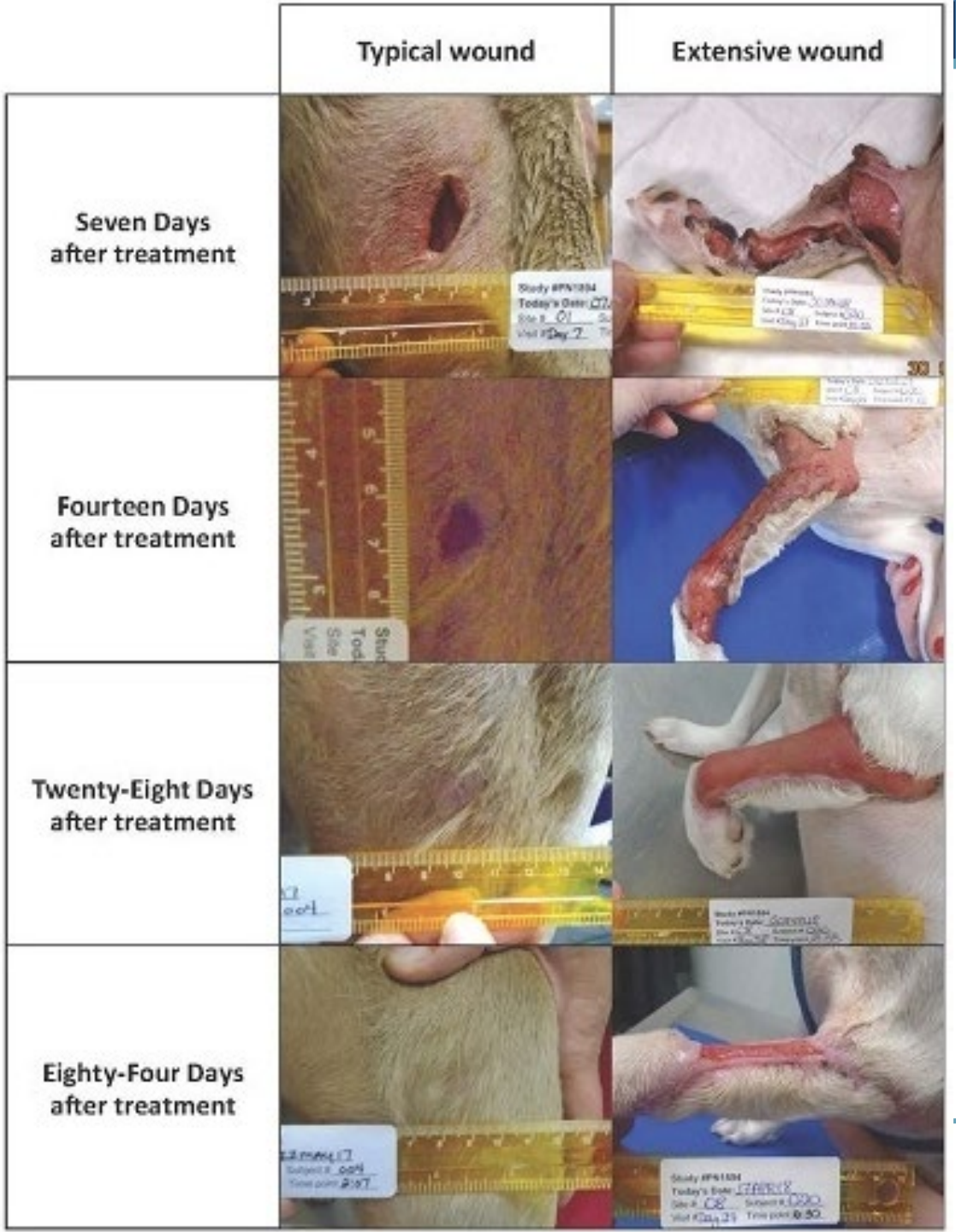
- Size: 3 cm x 3 cm x 1 cm max dimension
- Non-surgical mast cell tumors
- Subcutaneous mast cell tumors located at or distal to the elbow or the hock in dogs

STELFONTA®

- Disadvantages
  - Risk of self-injection
  - Local therapy
    - Grade
      - Predictive value on prognosis
        - May interfere with a systemic approach
  - Degranulation event
  - Healing

Owner Preparation

- Cost
  - $1000+
- Degranulation risk
- Hospitalization for pain control
  - 24 hours
- Wound healing > 4 weeks to 4 months



Laverdia-CA1 ® : What is it?

- Anivive life sciences
- Oral medication for canine lymphoma
- Targeted therapy

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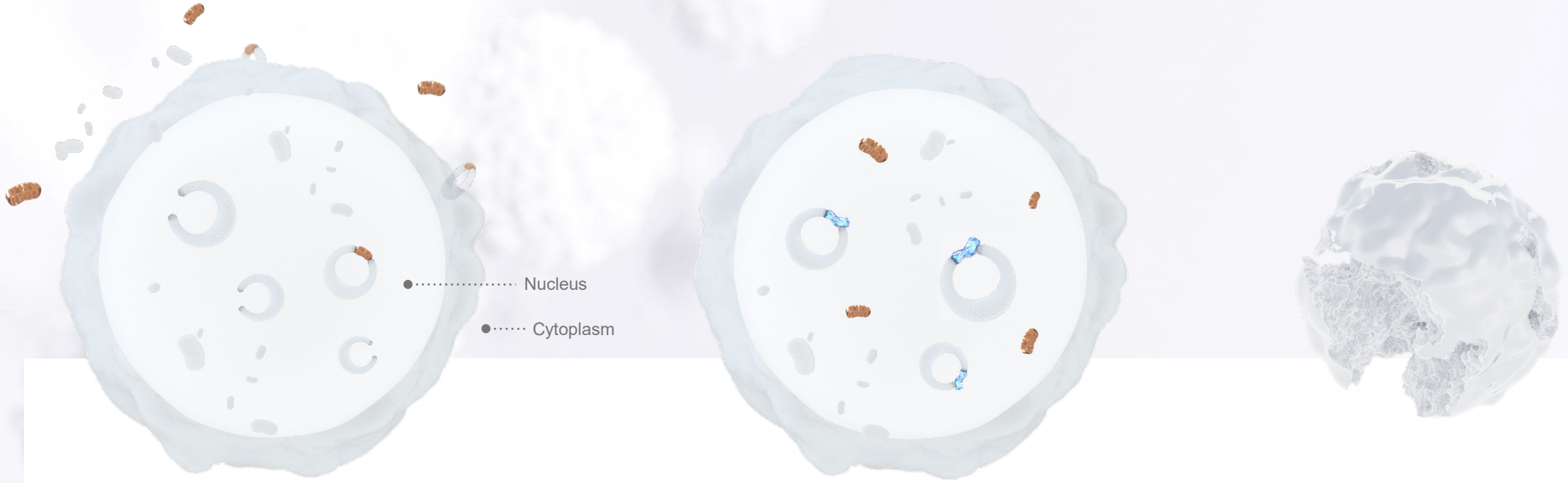
Lymphoma: Laverdia-CA1®

- Mechanism
- Selective inhibitor of nuclear export (SINE) KPT-355
  - Increases nuclear XPO1 tumor suppressor proteins
    - Nuclear export is stopped
    - Accumulation of XPO1 and cell death
      - Keeps tumor suppressor proteins in the nucleus reversibly



Lymphoma Cells Overproduce XPO1

LAVERDIA-CA1 Blocks XPO1

XPO1 inhibition results in nuclear retention and reactivation of TSPs leading to selective indtion of apoptosis of lymphoma cells

Lymphoma Cells Quickly Die

Healthy cells are spared in this process while TSPs accumulate in lymphoma cells and cause apoptosis

XP01

XPO1 is the sole nuclear exporter of several major tumor suppressor and growth regulatory proteins including p53, Rb1, and p27 among others

LAVERDIA-CA1

Binds to XPO1 and selectively inhibits nuclear export of TSPs. This binding functionally inactivates XPO1 and targets the protein for proteasome degradation, resulting in restoration of TSPs cellular localization and function. The binding is slowly reversible, contributing to relatively low toxicity for healthy cells

TSPs

TSPs (Tumor Suppressor Proteins) act inside the cell nucleus to suppress tumor growth

Lymphoma: Laverdia-CA1®

- Advantages
  - Oral at home therapy
  - Not cytotoxic
  - Not bone marrow suppressive

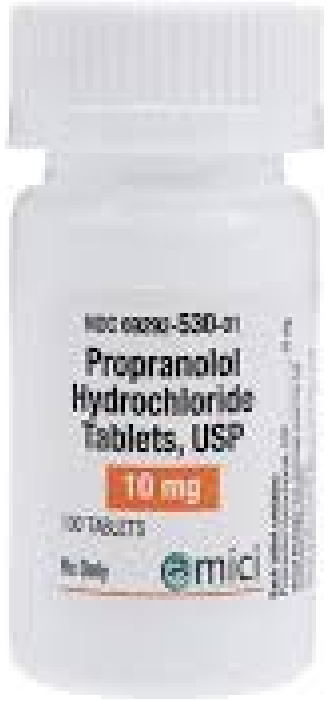
Lymphoma: Laverdia-CA1®

- Disadvantages
  - Cost +/-
    - Tablet size
  - GI toxicity
  - Novel: Effectiveness

Lymphoma: Laverdia-CA1®

- Future directions
  - Maintenance therapy
  - Palliative care
  - Appointment wait times or distance concerns
  - Aggressive or difficult to handle patients
  - In conjunction with standard of care
  - Additional cancers

Hemangiosarcoma: Propranolol



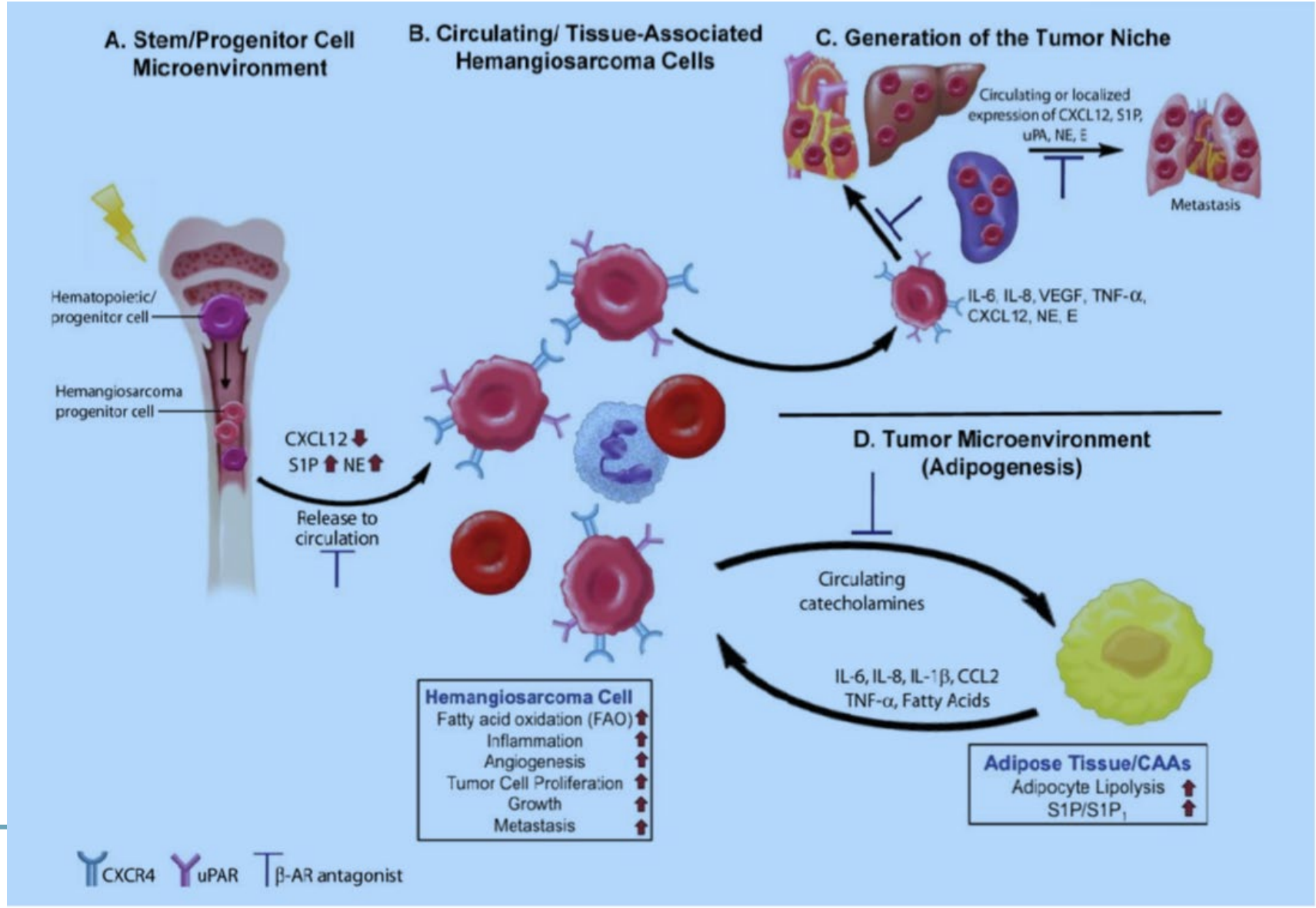
Propranolol: Hemangiosarcoma

- Hemangiosarcoma pathophysiology
  - Hematocytoblast
    - →Circulation
    - →Niche development
      - →Fatty acid oxidation, inflammation/cytokines, catacholamines
    - →Scouting
    - →Vascular compromise
    - →Rupture

Propranolol : MOA

- Beta blockade
- Competitive blocks both B1 and B2 adrenergic receptors (non-selective)

Propranolol : MOA in Hemangiosarcoma



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Propranolol : MOA in Hemangiosarcoma

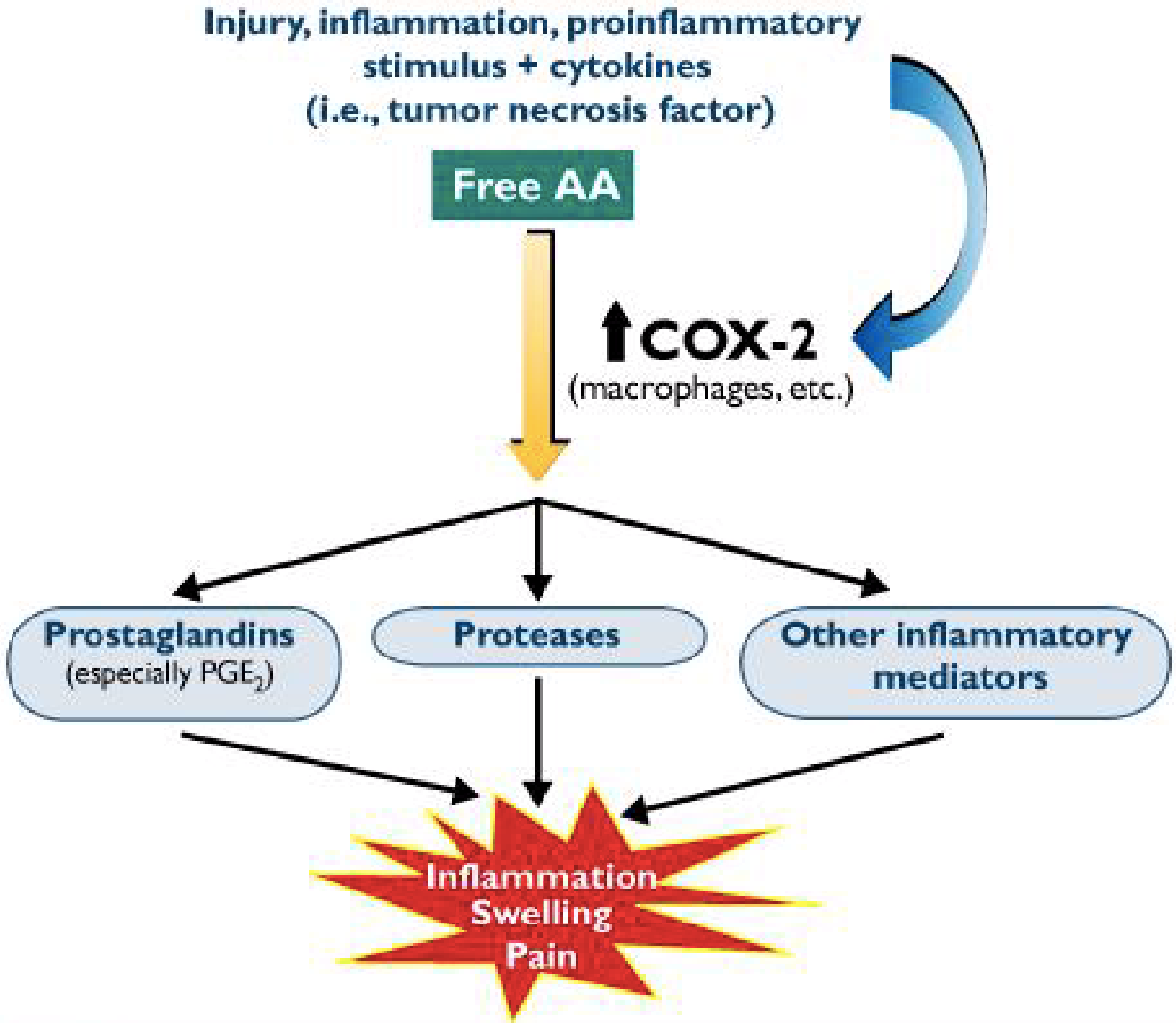
- Pros
  - Treat from home
  - Cost effective
  - Low risk with gradual increase
- Cons
  - Monitoring
    - Disease progression
    - Hypotension
  - Efficacy

Propranolol : Hemangiosarcoma

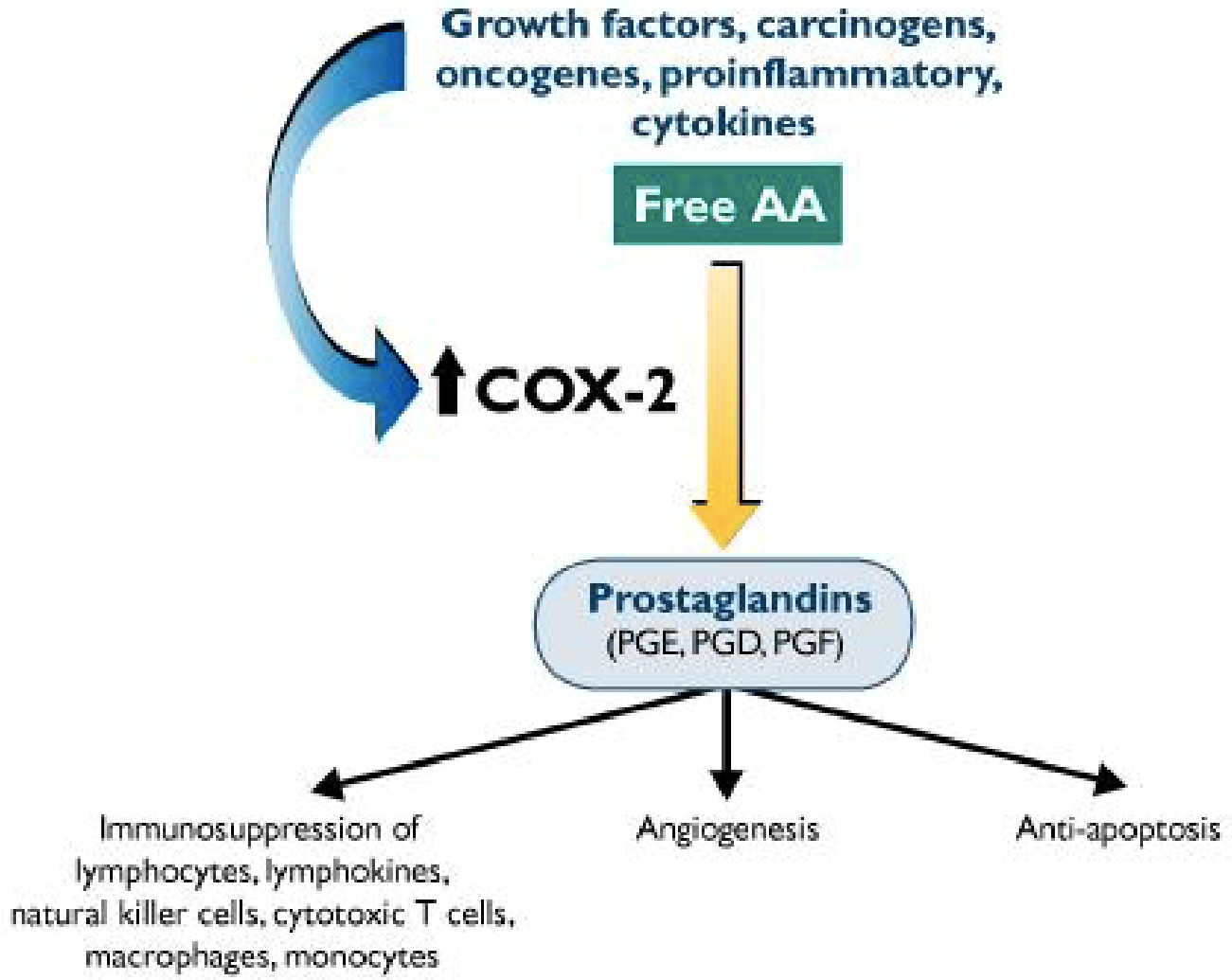
- Canine dose:
  - 0.1-0.2 mg/Kg orally every 8 hours
  - Recheck BP 1 and 2 weeks post
  - Increase to 0.5 mg/kg if tolerated every 8 hours
    - maximum 1.5 mg/Kg per day

NSAIDS:MOA

- Cox inhibition



NSAIDS:MOA cancer



NSAIDs

- All created equal?
  - Heavily debated with some studies conferring benefit with certain drugs
  - Piroxicam, Meloxicam, Deramaxx> Rimadyl

- Carcinomas

NSAIDs

- Pros
  - Affordable
  - Treatment from home
  - Pain relief
- Cons
  - Monitoring
    - GI
    - Renal and hepatic
      - Renal limitations common in urogenital tumors

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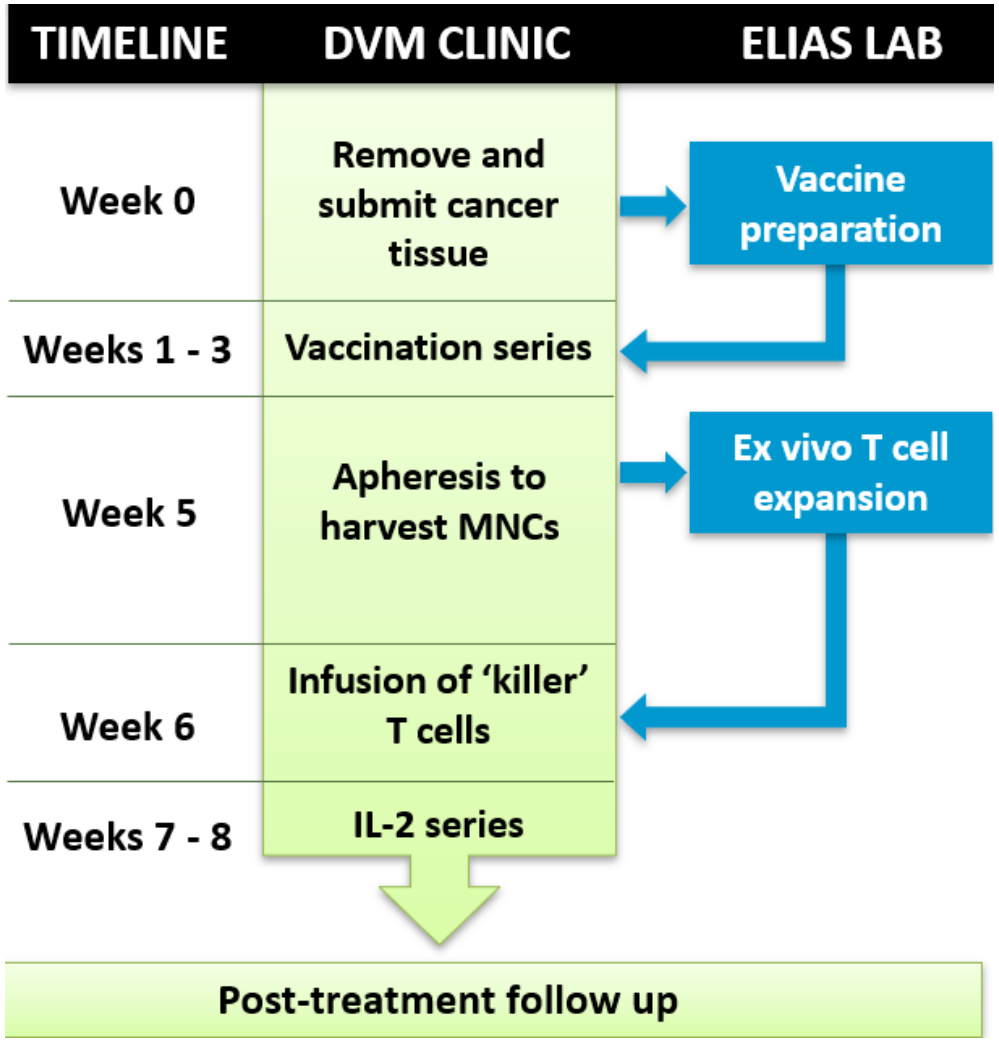
New Directions

- Osteosarcoma immune therapy
- Genomics and mutational assessment
- Drug repurposing

Osteosarcoma: Elias Cancer Treatment Platform



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Osteosarcoma: Elias personalized treatment

Initial OSA study[1] (n = 14)

- Osteosarcoma-bearing dogs demonstrated a 415-day median survival time
  - Five dogs (36%) survived > 730 days

USDA licensure OSA study (n = 100)

- Conducted at 10 sites across the U.S.
- Fully enrolled April 2021 (data expected in mid-2022)
  - Randomized, two-arm study
  - Comparator = amputation + carboplatin
  - Study endpoints include overall survival time and QOL

Genomics and mutational assessment

- Cancer genomics
  - Searchlight DNA Biomarkers
- Standard of care therapy
  - ImpriMed drug response
- Targeted therapy
  - FidoCure mutational targeting

Genomics and Mutational Assessment

Genomics and Mutational Assessment

- Benefits
  - Personalized medicine
- Disadvantages
  - Effectiveness
  - Time frame for culture varies
  - Adverse effect profiles of newer therapies
  - Cost
    - Price point varies
    - Plan on 1500-2500/culture
    - Does not include therapy

Drug Repurposing in Cancer

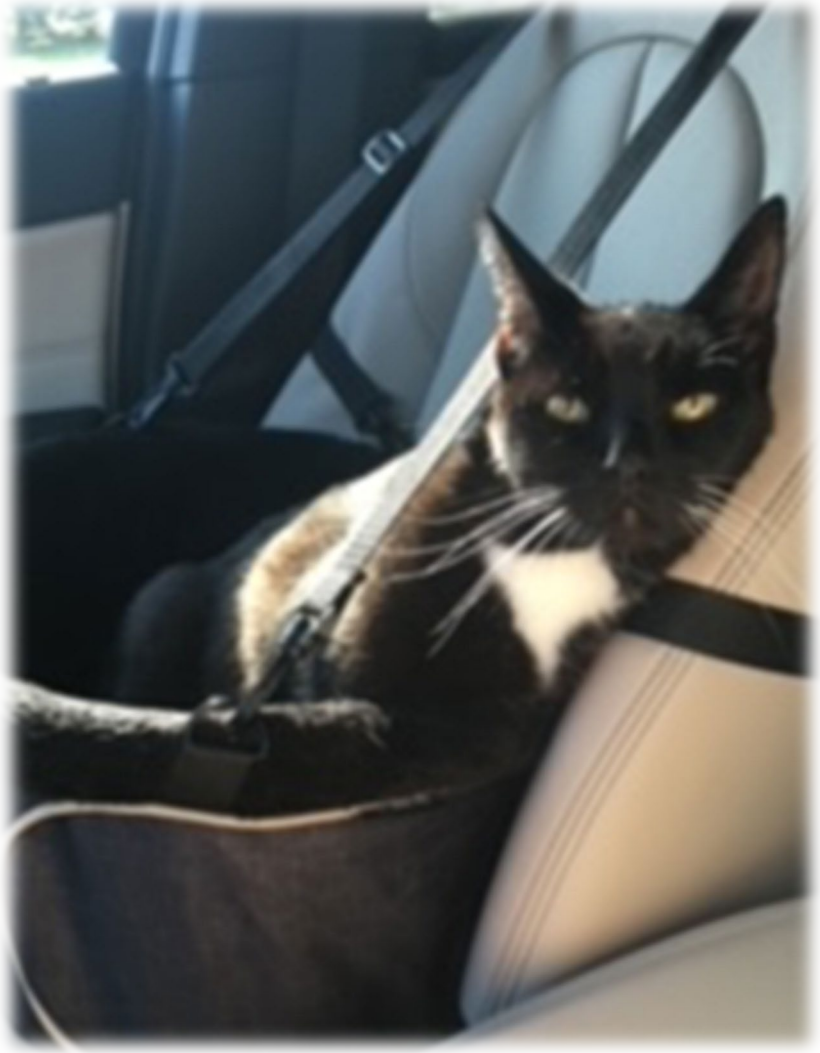
- Drug repurposing (the ReDO project)
  - Anti-fungals→Itraconazole
    - MOA
      - Anti-angiogenic factors and tumor hypoxia
      - Pro-death signals
      - Anti-metastatic signals
    - Human trials: carcinomas - skin, lung, prostate, colon
    - Veterinary literature: 2019 pulmonary SCC case study + NSAID

Are We There Yet?

Current--> Stelfonta, Laverdia, Fidocure…

Case considerations?

Monday → Thursday 216-362-6001



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