

# **PHASE I TRIAL OF GL-ONC1 WITH CONCURRENT CISPLATIN AND RADIOTHERAPY IN LOCOREGIONALLY ADVANCED HEAD AND NECK CARCINOMA**

---

Loren K. Mell, M.D.

Director, Division of Clinical and Translational Research

Chief, Head / Neck Radiation Oncology

Department of Radiation Oncology, University of California San Diego

June 8, 2011

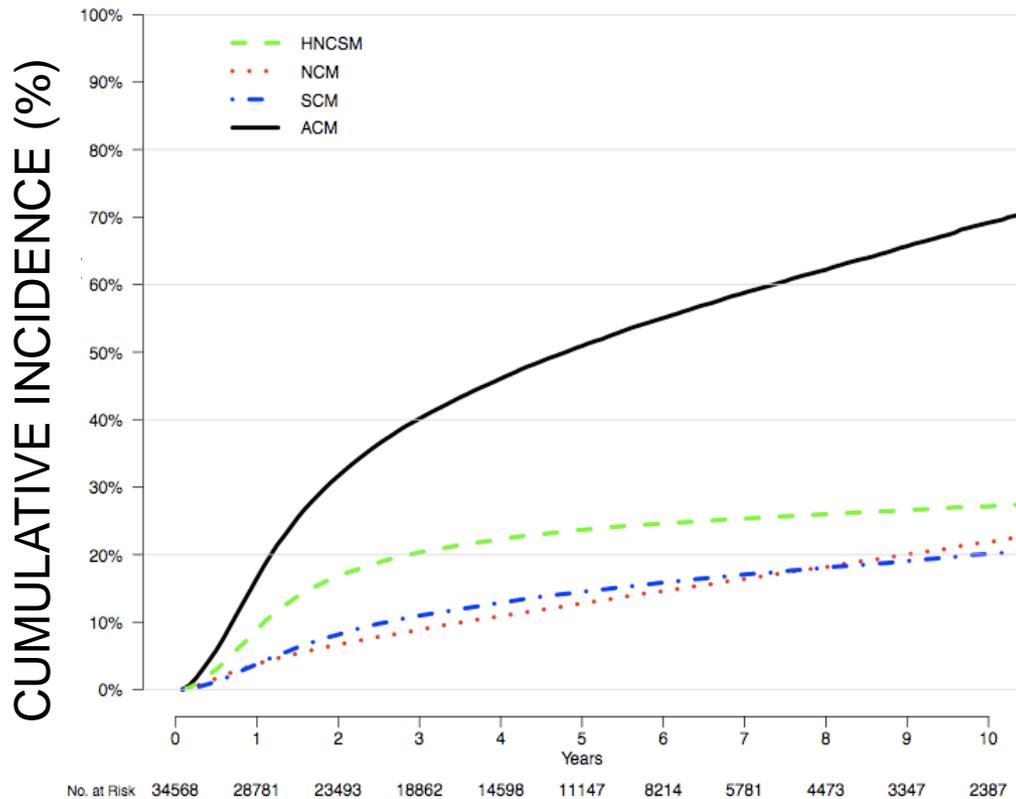


# Head and Neck Cancer: A Significant Problem

---

- 50,000 new cases in U.S. each year
- >350,000 deaths annually worldwide
- Patients commonly present with locoregionally advanced disease

# Outcomes Poor with Standard Treatment



- High Incidence of Mortality (70%/10 yrs)
- Innovative Treatment Strategies Needed

Mell et al. JCO 2011 (in press)



# Phase I Trial of GL-ONC1

---

- 12-24 HNC patients undergoing primary chemoradiotherapy
- Escalating doses of Intravenous GL-ONC1
- Open-label
- Standard 3+3 design
- DLT
  - Grade  $\geq 4$  hematologic / mucositis
  - Grade  $\geq 3$  non-hematologic/mucosal

# Phase I Treatment Scheme

---

Cohort -1:  $1 \times 10^8$  pfu

Cohort 1:  $3 \times 10^8$  pfu

Cohort 2:  $1 \times 10^9$  pfu

Cohort 3:  $3 \times 10^9$  pfu

Cohort 4:  $3 \times 10^9$  pfu x 2 cycles

- IMRT (70 Gy) + Cisplatin (100 mg/m<sup>2</sup> weeks 1,4,7)
- Virus on day #3 of chemoRT (plus day #6 in cohort 4)
- Follow-up:
  - Weekly during chemoRT
  - Weeks 1, 4, 8, 16 post chemoRT



# Key Eligibility Criteria

---

- Stage III-IV Newly Diagnosed Unresected HNC
- Adequate performance status and immune, hepatic, renal, and pulmonary function
- Exclusions:
  - HPV+ oropharynx
  - Distant metastasis
  - Pregnancy



---

# **REVIEWER CRITIQUES**

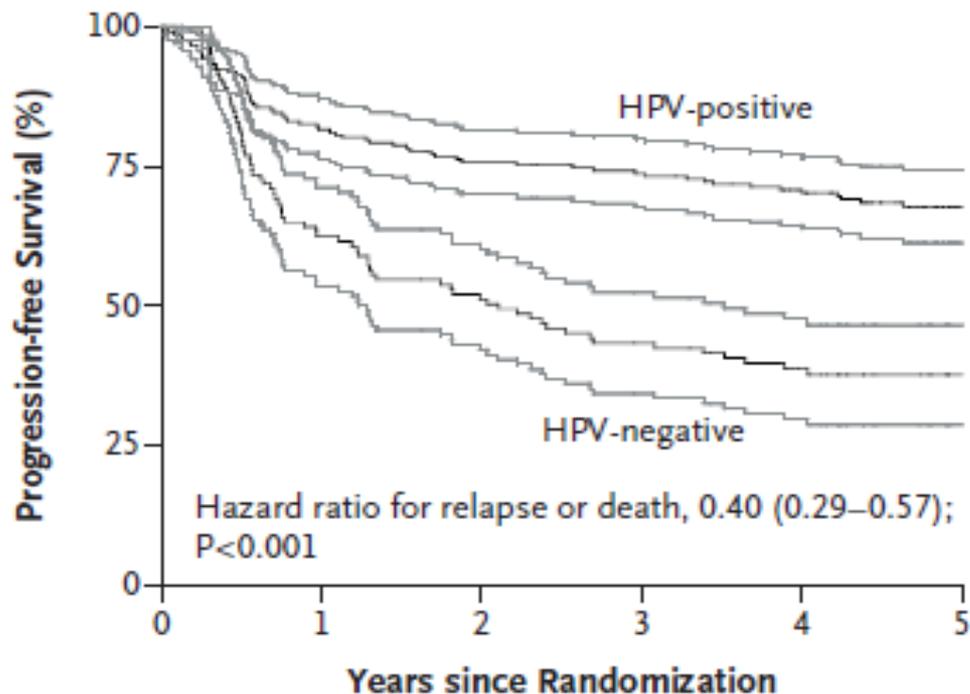
## Why are HPV+ patients excluded from the protocol? (Ornelles, Strome)

---

- HPV+ oropharyngeal cancer patients are excluded because of their superior prognosis (Ang et al. NEJM 2010)
- Strategies looking at de-intensifying treatment in HPV+ population (RTOG 1016 RT/cisplatin vs. RT/cetuximab)

# Outcomes by HPV Status

**B** Progression-free Survival According to Tumor HPV Status



No. at Risk	
HPV-positive	206    168    155    148    136    65
HPV-negative	117    73    59    49    37    15



## How do you propose to tell if toxicities are viral in origin? (Strome, Yankaskas)

---

- Phase I trial design is standard
- DLTs are severe and outside of the norm of what would be observed in standard clinical practice
- DLT definition based on previous published phase I trials in similar population

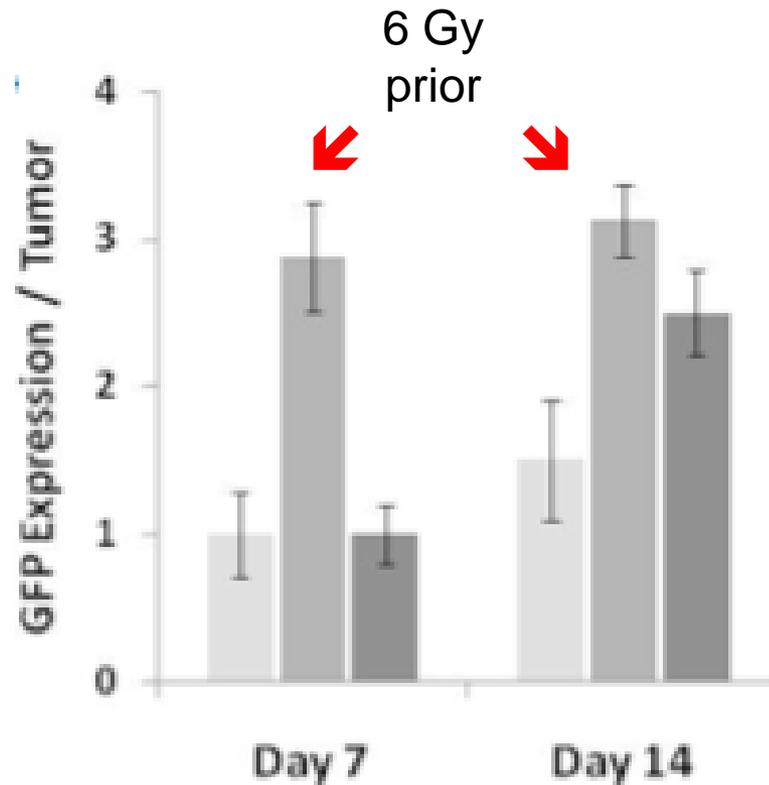


## **What are anticipated outcomes and use of tissue harvested for analysis? (Ornelles)**

---

- Secondary aim of trial: correlative science
- We will use data to assess variation in head / neck cancer susceptibility to viral infection
- Proof of principle

# Why was the time point for virus delivery after RT chosen? (Strome)



Early Onset of Effects Seen with  
RT given 1 Day Before Virus



## **Adding virus could increase liver damage, immune compromise (Strome, Yankaskas)**

---

- Patients with poor hepatic, immune function excluded
- Patients will be closely monitored for hepatotoxicity and hematologic toxicity
- Baseline incidence of high-grade events is low (~2%)
- Was not observed to be a problem in Royal Marsden trial

# Should study be in patients with locoregional recurrence? (Strome) - NO

---

- Outcomes with untreated disease poor → justifies treatment intensification
- We include similar population to RTOG 0522
- We exclude subgroups with good prognosis (resectable, HPV+)
- Untreated population larger → wider applicability
- Re-treatment standard of care not widely established, patients more heterogeneous
- Therefore, favor trial in untreated disease

# Should subgroup with advanced salivary malignancies be removed? (Strome) - NO

---

- Outcomes in unresectable salivary gland malignancies dismal (Mendenhall Cancer 2005)
- Other Phase I trials have included salivary gland tumors (Langer Cancer Inv 2006)
- Cisplatin / RT under active investigation in salivary gland (e.g. RTOG 1008) and commonly used clinically despite limited data
- Inclusion would not taint toxicity data
- Therefore, favor including salivary gland



# Conclusion

---

- New treatment strategies needed for advanced head/neck cancer patients who have poor prognosis with chemo-RT
- Hypothesize that the regimen of RT/Cisplatin + GL-ONC1 is safe based on clinical and pre-clinical data
- Plan to test this hypothesis in phase I trial