

## MGMT methylation: Prevalence in Head and Neck Squamous Cell Carcinoma and response to treatment



### Epidemiology

#### Head & Neck Squamous Cell Carcinoma

- 6th in incidence in the US
- 50 000 new cases / yr
- 12 000 deaths / yr

### Problem

#### Chemotherapy and radiation therapy

- Low survival rates
- Important functional defects



### Challenge

#### Target therapy

- Stratification
- Predict response to treatment
- ↓ Side effects

### DNA repair

- Our DNA is subject to multiple alterations
- Our organism repairs them

### MGMT

O6-methylguanine-DNA-methyltransferase)



## MGMT methylation: Prevalence in Head and Neck Squamous Cell Carcinoma and response to treatment



### Methylation

- Gene expression regulation
- Hypermethylation => Inactivation of gene transcription and function
- Hypermethylation MGMT => cancer ?

### MGMT and cancer

- Predictor of bad prognosis
  - Hepatocellular, gastric, breast and lung CA
- Predictor of good prognosis
  - Astrocytoma, glioma, lymphoma

### MGMT and chemotherapy

- MGMT allows cancerous cells to resist to the toxicity of alkylating agents
- **Hypermethylation (inactivation) = enhanced response to chemotherapy**

### MGMT and HNSCC

- Published studies
  - Heterogeneous groups
    - Treatment modality
    - Stage
  - N (21 to 99 patients)
  - Prevalence 32% (20 to 41%)
  - Bad prognostic factor, *Zuo et al.*

### Need

Study on locally advanced HNSCC treated by chemoradiation therapy only



# MGMT methylation: Prevalence in Head and Neck Squamous Cell Carcinoma and response to treatment



## Objectives

- Determine the prevalence of MGMT methylation in HNSCC
- Assess the impact of MGMT methylation on response to treatment and survival

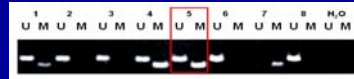
## Laboratory study (199 patients)

- DNA extraction
- Bisulfite modification
- Methylation Specific PCR (MSP)
- Migration on gel – Electrophoresis

## Inclusion Criteria

- HNSCC patients (larynx, oropharynx, hypopharynx, nasopharynx)
- Stage III or IV
- Treated primarily with chemoradiation
- Minimum follow-up period: 3 years

## Results



133♂, 40♀

### Sites

- Oropharynx 111
- Larynx 26
- Other 36

### Stage

- III 31
- IV 135



# MGMT methylation: Prevalence in Head and Neck Squamous Cell Carcinoma and response to treatment



## Methylation prevalence 41% (71pts)

Tumour grade	1	2	3
Methylated	13	47	37
Unmethylated	13	40	14

### Toxicities

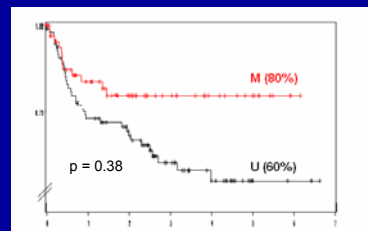
- Neutropenia
- Dermatitis
- Mucositis
- Tube feeding
- N & V
- Hospital admission
- Death

∅ association

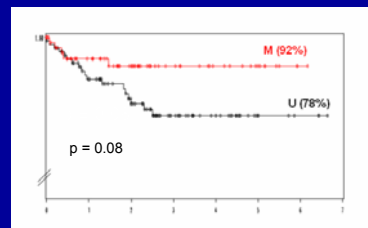
### Response rates

- Methylated 71%
  - Unmethylated 73%
- p = NS

## Disease Free Survival



## Distant metastasis free survival



## Conclusions

- 1<sup>st</sup> study
  - Big  $n$
  - Homogeneous population
- MGMT methylation is a frequent event in HNSCC
- Possible positive effect on survival in HNSCC patients treated with chemoradiation
- Avenue for future studies

