IMIQUIMOD, AN IMMUNE-RESPONSE MODIFIER, IN THE TREATMENT OF TRANSITIONAL CELL CARCINOMA OF THE BLADDER

Douglas Scherr, M.D.

Department of Urology
New York Presbyterian Hospital-Weill Cornell Medical Center
Introduction

• **Imiquimod is a potent synthetic immunomodulator**

• **Currently used as a first-line treatment for genital condyloma (Aldara, 3M)**

• **Effective against several skin cancers including melanoma and basal cell carcinoma**
Introduction

- Induces both innate and acquired immune responses
- Toll-like receptor 7 (TLR-7) agonist
- Stimulates dendritic cells to mature and secrete pro-inflammatory cytokines
- Mechanism strikingly similar to bacillus Calmette-Guerin (BCG)
Introduction

• **Hypothesis:**
  - Imiquimod may have therapeutic potential against transitional cell carcinoma of the bladder

• **Objectives:**
  - To determine if Imiquimod has direct effects on bladder cancer cells *in vitro*
  - To determine if Imiquimod has anti-tumor effects *in vivo* in an intact immune system
In vitro Methods

Imiquimod

Cell Viability (MTT Assay)

Bladder Cancer Cell Lines (J82, T24, TCC-SUP)

24 hrs

Apoptosis (TUNEL Assay)

Cytokine Production (ELISA)
Cell Viability

MTT Proliferation Assay after 24hrs

Fractional %

Imiquimod Concentration (mcg/ml)

- J82
- T24
- TCCSUP
Apoptosis

Control (PBS) Group

Imiquimod Group
Apoptosis

Control (PBS) Group

Imiquimod Group
Apoptosis in vitro

- PBS treated: 0.8%
- Imiquimod treated: 17.1%
Cytokine Production

IL-6 Secretion

- PBS treated: 480 pg/ml
- Imiquimod treated: 1340 pg/ml

TNF-alpha Secretion

- PBS treated: 425 pg/ml
- Imiquimod treated: 930 pg/ml
In vivo Methods

• Orthotopic, syngeneic, immune competent mouse model *(Bochner et al J. Urology, 2003)*

• Murine bladder tumor (MBT-2) cells instilled intravesically into C3H mice

• Treatment regimen:
  – Day 0: Tumor cells instilled
  – Day 1: Treatment with Imiquimod or PBS
  – Day 8: Retreated
  – Day 15: Mice sacrificed
Conclusions

• Imiquimod is a potent immune-response modifier

• Has direct biological effects on bladder cancer cell lines

• Preliminary data suggests anti-tumor effects \textit{in vivo}

• Imiquimod may be a potential immunotherapy for bladder cancer
Acknowledgements

Pl: Douglas Scherr, MD

Contributors:

Hideki Kawamoto, MD
Xuecke You, MD
Mathew Albert, PhD