

FREQUENCY AND LEVEL OF EXPRESSION OF EpCAM IN NON MUSCLE-INVASIVE TRANSITIONAL CELL CARCINOMA OF THE BLADDER

M. Kowalski¹, N. Jones¹, D. Niforos¹, W. Cuthbert¹, G. MacDonald¹

¹Viventia Biotechnologies Inc., Mississauga, ON

ABSTRACT

Introduction and Objective: The epithelial cell adhesion molecule (EpCAM) appears to be over-expressed in the majority of human epithelial carcinomas and EpCAM expression levels correlate with proliferative activity and neoplastic transformation. Vicinium™ is a recombinant fusion protein comprised of a humanized scFv specific for EpCAM and a truncated fragment of *Pseudomonas* exotoxin A (ETA 252-608) that is being developed as a treatment for non muscle-invasive TCC. In order to identify patients suitable for Vicinium treatment, a semi-quantitative immunohistochemical (IHC) clinical trial assay was developed for the determination of EpCAM expression in tumor tissues. The primary objective of the study was to determine the frequency and level of EpCAM expression on bladder carcinomas with the intent of identifying and selecting those patients most likely to benefit from Vicinium therapy.

Materials and Methods: IHC was performed on formalin-fixed and paraffin-embedded tissue obtained from patients with CIS, Ta or T1 tumors being screened for entry into Vicinium clinical studies. After de-paraffinization and re-hydration, the slides were treated for antigen retrieval and then incubated with Vicinium followed with a rabbit polyclonal anti-ETA. Bound Vicinium/anti-ETA complex was detected using anti-rabbit polyclonal EnVision+HRP. Localization of the drug was visualized by the application of diaminobenzidine. Membrane staining intensity was assessed under light microscopy and graded on a 4 point scale with 0 being negative and 3+ being very strong. EpCAM positive and negative controls (human colon carcinoma and human normal heart, respectively) were included in each staining.

Results: From the 135 biopsies screened, 132 (98%) were positive and 3 (2%) were negative for EpCAM staining. Of the positive tumors screened, the staining intensity was found to be 1+ on 7 (5%), 2+ on 36 (27%) and 3+ on 89 (67%) of the patient samples. The frequency of very strong EpCAM staining was significantly higher in CIS vs. Ta tumors and in high grade vs. low grade tumors.

Conclusions: EpCAM is highly expressed in most non muscle-invasive TCC tumors as measured by IHC staining with Vicinium. EpCAM over-expression makes these tumors attractive targets for Vicinium therapy.