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Title: A TRANSGENIC MOUSE MODEL FOR CARCINOGENICITY TESTING OF UROLOGIC AGENTS

Aims of Study:

Utilization of new implantation biomaterials requires extensive preclinical safety testing; carcinogenicity testing is an essential element. Heretofore, carcinogenicity bioassays have utilized two-year rodent models. However, in these models it has been difficult to differentiate foreign-body sarcomagenisis (FBS) (common in rodent species and rare in humans) from other mechanisms, more indicative of human carcinogenicity risk. A transgenic model has recently been validated for a number of chemical carcinogens, providing a promising model for the evaluation of potential bulking agents (Uryx^{TM}, Genyx Medical, Inc. Aliso Viejo, CA)).

Methods:

RasH2 transgenic mice (Tg) and non-transgenic littermates (nTg) were implanted subcutaneously with Uryx, Millipore filters (MP) of two pore sizes and filters doped with ethyl carbamate (EC). Terminal sacrifice was at 26 weeks. Gross necropsy observations included number, size and location of tumors. Histolopathology examinations of implant sites and major visceral organs are underway.

Results:

All Tg groups dosed with EC (positive control) demonstrated increased incidence of the expected lung and spleen lesions, whether applied by injection or in a gel applied to implanted filters. No treatment related lesions were observed at the site of implantation or in the major visceral organs in animals receiving implanted Uryx or negative MP control.

Conclusions:

Based on gross necropsy findings, the positive control material demonstrated a strong tumorigenic response. No such response was observed in the Uryx treated animals.

Drs. Mishra and Kammula (FDA) designed the protocol; their participation has no reflection on the regulatory status or FDA's safety assessment of Uryx.

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