Azolium Salts for Treatment of Non-Muscle Invasive Bladder Cancer

(Ref. No. 498-PA)

Background

The long-time standard-of-care of high-grade superficial bladder cancer is the administration of Bacillus Calmette Guerin (BCG). Although effective, BCG actually only reduces the risk of cancer progression and reduces the need for radical cystectomy (removal of the bladder). Second-line therapies, such as gemcitabine, valrubicin, and docetaxel, predictably have little chance of success because they only act at specific points in the cell cycle and cannot practically be retained in the bladder long enough to have an effect. One of the advantages of the currently available treatments is the use of intravesical administration. Systemic absorption and symptoms associated with intravesical administration are significantly reduced compared to parenteral or oral administration. However, BCG can still cause systemic symptoms such as fever, malaise, and, in rare cases, sepsis, as well as local symptoms such as urinary urgency/ frequency/dysuria by virtue of its nature as a live bacterial immunogenic vaccine. Thus, it is clear that there is an urgent and genuine need for better intravesical chemotherapeutic agents to help circumvent existing therapies and their relative ineffectiveness. Therefore, avoiding radical cystectomy is probably the first priority for patients, and this is reflected in the medical literature and new clinical studies.

Summary of the Invention

Researchers at Fox Chase Cancer Center have developed a group of therapeutic imidazolium compounds for the effective diagnosis and treatment of human bladder cancers. For any compound to be a practical and effective intravesical agent for bladder cancer, it must elicit a cell-killing effect in 1 hour or less. Patients cannot retain a drug for long periods, and this likely contributes to the ineffectiveness of intravesical chemotherapy. Therefore, due to the brisk and effective induction of cell death in bladder cancer cell lines by imidazolium compounds, and with the absence of histological damage in the normal bladder of murine models after intravesical instillation, imidazolium compounds appear to behave as cancer-selective agents and possess potent antineoplastic activity toward bladder cancer.

Intravesical imidazolium salts have several favorable characteristics compared to existing therapies including ease of manufacture, apparent mechanism of action, short duration of exposure with maximum cytotoxicity, and potentially the ability to induce a significant effect on bladder cancer with less treatments (one to two) than current standards (six).

Patent Status: A patent application has been filed.

For Licensing/Partnering information, please contact:

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