

DEVELOPMENT OF NEW CLASS PHOTOACTIVATED ANTICANCER-ANTIFUNGAL COMPOUNDS: CONJUGATES OF GOLD NANOPARTICLE-SUPPORTED QUINONE METHIDES-ANTICANCER DRUGS, FOR MULTIMODAL TREATMENT OF URINARY BLADDER TUMORS

The aim of the project is to develop the multifunctional system on the base of gold nanoparticles conjugated with quinone methide and anticancer substance i.e. imatinib, sunitinib, lapatinib or pemetrexed. The system will be potentially applicable as a second stage local treatment of urinary bladder cancer with additional protection against candidemia. The application of gold nanoparticles allows site-specific activation of the system using laser irradiation for photothermal purposes.

The most common malignancy of the urinary tract is the Bladder Cancer (BC) it is the 7th most common cancer in men population and the 17th in women. The age standardized incidence of BC worldwide is 9 per 100 000 for men and 2 per 100 000 for women . For European Union the mean age standardized incidence of BC is almost three times higher and 27 per 100 000 for men and 6 per 100 000 for women. According to data collected by GLOBOCAN only in 2012 about 430 000 new BC cases were registered worldwide and 165 000 of the deaths occurred.

The therapeutic strategy of BC treatment depends on the molecular subtype of the cancer. It covers radiotherapy, cystectomy, chemotherapy, instillation therapies. The local treatment of BC is especially interesting because it allows, to maximize the concentration of a therapeutic agent in the neighborhood of the cancer changes without exposure of the patient for side effects of the active substance. The intravesical therapies do not belong to the first line treatments. The option of improving of intravesical chemotherapy is a combination of standard local administration of active anticancer agents with physical factors e.g. temperature. The examples of such approaches cover microwave-induced hyperthermia (Synergo) or electromotive drug administration (EMDA) in patients with high-risk tumours.

The application of local BC therapies is connected with the risk of infections, which is connected with application of medical devices, urinary tract instruments, catheters, etc. Among the infections the risk of candidoses should not be underestimated. Although in number of studies report the development of candidemia in patients with identified candiduria (presence of *Candida* strains in urine) is rather rare (1-8%) it must be pointed out that the presence of BC together with chemotherapy treatment significantly increase the risk of development of invasive ascensional infections. In the case of current proposal the gold nanoparticles will be applied as a carrier for anticancer and antifungal substances together with application as photothermal agent, which should increase the effectiveness of the system .

The planned research will cover the range of activities from designing and development of small molecules with fungistatic and fungicidal activity, verification of their in vitro activity, preliminary toxicity tests of the compounds in in vitro and in vivo, synthesis of the series of gold nanoparticle gels stabilized with biocompatible organogelators with discovered pharmacologically active compounds, effectiveness tests of the gold nanoparticle gels in in vivo under condition of photo activation.