TARGET THERAPY OF BLADDER CANCER BY INHIBITING THE SIGNALING OF FGFR3

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One of the most studied currently in oncology are receptors for fibroblasts growth factor, as well as ligands to it. In this study, we will focus on the molecular processes that arise when the receptors are activated to the growth factor of fibroblasts, and also consider the frequency with which the expression of the components of the signal pathway of a given receptor is disturbed in bladder cancer.

Keywords: bladder cancer, target therapy, signaling.

The FGF family includes 22 protein molecules. By the principle of action they can be divided into the following groups: ligands to FGFR: FGF1-10, 16-23; the ligands possessing autoaction: FGF1-10, 16-18, 20, 22; the ligands functioning as hormones: FGF19, 21, 23; the factors not capable to contact receptors, also known as FGF homologous factors: FGF11-14. They act in cages and also participate in regulation of operation of membrane sodium channels [1].

Feature of a receptor of FGFR3 – duality of its properties. The expression of superficial FGFR3 in epitelialny fabrics and his activation by the corresponding ligands, generally FGF2 and FGF9, is associated with activation of an alarm way of STAT1, suppression of division and, in certain cases, initiation of apoptosis.

In spite of the fact that anti-FGFR therapy is at an early stage of clinical studying in oncology, certain difficulties in realization of this medical approach – high toxicity, need of selection of patients depending on activity of FGF-FGFR of a way and also depending on existence of mutations in molecules of underlying alarm ways are visible already now [2].

We will review the examples of means of targetny therapy directed to FGFR3 signaling inhibition:

1. Ponatinib/Iclusig – the medicine intended for treatment of patients with rare diseases of blood and marrow. The main target for active agent of medicine is BCR-ABL. The mechanism of effect of the medicine consists in oppression of activity of a protein – a squirrel, taking part in growth and development of tumor cells.

2. Lenvatinib – the targetny means which is the multiple inhibitor of receptors of tyrosinekinases which is selectively suppressing activity of receptors of a factor of growth of vessels (VEGF) – VEGFR1 (FLT1), VEGFR2 (KDR) and VEGFR3 (FLT4). Also Lenvatinib makes the inhibiting impact on other receptors of tyrosinekinases including receptors of a factor of growth of fibroblast of 1–4 types (FGFR 1-4).

3. Pazopanib – the antineoplastic means contacting receptors of an endotelial factor of growth of vessels allocated from growth factor platelets and a receptor of a factor of growth of stem cells.

4. Nintedanib – the threefold inhibitor of an angiokinaza blocking growth factor receptors of vessels 1–3 (VEGFR 1-3), receptors of a Tr factor of growth an alpha and a beta and receptors of a factor of growth of fibroblast 1-3 (FGFR 1-3). Competitively interacts with the ATP-connecting site of these receptors and blocks intracellular signaling which is extremely important for proliferation and survival.

5. Palifermin – it is appointed the patient having leukemia and a lymphoma. Palifermin is 16,3 kD the protein received from genetically modified E.coli strain. The strain of E.coli contains the truncated version of the nucleotide sequence of factors of growth of Kt of KGF [3].

Thus, one may say, that factors of FGF and their receptors potentially are clinically significant and effective markers and targets which can, presumably, be used for therapy or inhibition of a progression of cancer of bladder.

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