Poupak Fallahi, Pharmacoeconomics 2018, Volume:3
DOI: 10.4172/2472-1042-C1-004

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Vandetanib in anaplastic thyroid cancer

Statement of the Problem: The antitumor activity of vandetanib (a multiple signal transduction inhibitor including the RET tyrosine kinase, epidermal growth factor receptor (EGFR), vascular endothelial growth factor (VEGF) receptor (VEGFR), ERK and with antiangiogenic activity), has been evaluated in primary anaplastic thyroid cancer (ATC) cells, in the human cell line 8305C (undifferentiated thyroid cancer) and in an ATC-cell line (AF).

Methodology & Theoretical Orientation: Vandetanib (1 nM, 100 nM, 1 mcM, 10 mcM, 25 mcM, 50 mcM) was tested: in primary ATC cells, in the 8305C continuous Kcell line, and in AF cells; and in 8305C cells injected in CD nu/nu mice.

Findings: Vandetanib was able to reduce significantly ATC cell proliferation ($P<0.01$, ANOVA), induced apoptosis in a dose-dependent manner ($P<0.001$, ANOVA), and inhibited migration ($P<0.01$) and invasion ($P<0.001$). Moreover, vandetanib inhibited EGFR, AKT and ERK1/2 phosphorylation and down-regulated cyclin D1 in ATC cells. In 8305C and AF cells, vandetanib inhibited significantly the proliferation, inducing also apoptosis. 8305C cells were injected sc in CD nu/nu mice and tumor masses became detectable after 30 days. Vandetanib (25 mg/kg/die) inhibited significantly tumor growth and VEGF-A expression and microvessel density in 8305C tumor tissues.

Conclusion & Significance: The antineoplastic activity of vandetanib in ATC is the result of: a) an anti-proliferative activity; b) an increased apoptosis; c) inhibition of both migration, and invasion; d) and inhibition of the cancer neovascularization, too. The antitumor and antiangiogenic effect of vandetanib is promising in ATC, opening the way to a future clinical evaluation.

Recent Publications

1. Antonelli A, Fallahi P, Ulisse S, Ferrari S M, Minuto M, et al. (2012) New targeted therapies for anaplastic thyroid cancer. Anti-Cancer Agents in Medicinal Chemistry. 12(1):87-93.
2. Antonelli A, Bocci G, La Motta C, Ferrari S M, Fallahi P, et al. (2012) CLM94, a novel cyclic amide with anti-VEGFR-2 and antiangiogenic properties, is active against primary anaplastic thyroid cancer *in vitro* and *in vivo*. The Journal of Clinical Endocrinology and Metabolism 97(4):E528-E536.
3. Di Desidero T, Fioravanti A, Orlandi P, Canu B, Giannini R, et al. (2013) Antiproliferative and proapoptotic activity of sunitinib on endothelial and anaplastic thyroid cancer cells via inhibition of Akt and ERK1/2 phosphorylation and by down-regulation of cyclin-D1. The Journal of Clinical Endocrinology and Metabolism. 98(9):E1465-E1473.
4. Antonelli A, Bocci G, Fallahi P, La Motta C, Ferrari S M, et al. (2014) CLM3, a multitarget tyrosine kinase inhibitor with antiangiogenic properties, is active against primary anaplastic thyroid cancer *in vitro* and *in vivo*. The Journal of Clinical Endocrinology and Metabolism 99(4):E572-E581.
5. Smallridge R C, Ain K B, Asa S L, Bible K C, Brierley J D, et al. (2012) American Thyroid Association guidelines for management of patients with anaplastic thyroid cancer. Thyroid. 22(11):1104-1139.

Biography

Poupak Fallahi graduated in Medicine and Surgery in 1993 and specialized in Occupational Health Medicine in 1999 at the University of Pisa (Italy). Her principal areas of expertise are autoimmune thyroid disorders, type 1 diabetes, chemokines and cytokines, systemic autoimmune disorders, HCV-associated thyroid disorders, thyroid cancer and occupational medicine. Her researches have been published in more than 218 articles on International journals (HI=47). She serves as an Editorial Board Member and is Referee and Reviewer of many scientific international journals.

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