Silvia Martina Ferrari et al., Pharmacoeconomics 2018, Volume:3
DOI: 10.4172/2472-1042-C1-005

Lenvatinib in anaplastic thyroid cancer

Silvia Martina Ferrari, Poupak Fallahi, Ilaria Ruffilli and **Alessandro Antonelli**
University of Pisa, Italy

Statement of the Problem: *Lenvatinib* is an oral, multitargeted tyrosine kinase inhibitor (TKI) of VEGFR1-VEGFR3, FGFR1-FGFR4, PDGFRα, RET and v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog (KIT) signaling networks involved in tumor angiogenesis. The antitumor activity of lenvatinib has been investigated 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: The effect of lenvatinib (1 nM, 100 nM, 1 mcM, 10 mcM, 25 mcM and 50 mcM) was evaluated in primary ATC cells, 8305C cells, and AF cells and in AF cells injected in CD (Crohn's disease) nu/nu mice.

Findings: *Lenvatinib* significantly reduced ATC cell proliferation (P<0.01, ANOVA) and increased the apoptosis (P<0.001, ANOVA). Furthermore, lenvatinib inhibited migration (P<0.01) and invasion (P<0.001) in ATC. *Lenvatinib* inhibited EGFR, AKT and ERK1/2 phosphorylation and down-regulated cyclin D1 in ATC cells. Moreover, lenvatinib significantly inhibited 8305C and AF cell proliferation, increasing apoptosis. AF cells were injected subcutaneously into CD nu/nu mice and tumor masses were evident after 20 days. Tumor growth was significantly inhibited by lenvatinib (25 mg/kg/day), as the VEGF-A expression and microvessel density in AF tumor tissues.

Conclusion & Significance: We have shown for the first time the antitumoral effect of the multi-targeted kinase inhibitor lenvatinib, in primary human ATC cell cultures obtained from patients. These findings could open the way to the clinical use of lenvatinib in the treatment of patients with ATC.

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. Schlumberger M, Tahara M, Wirth L J, Robinson B, Brose M S et al. (2015) *Lenvatinib* versus placebo in radioiodine-refractory thyroid cancer. The New Engl. J. of Med. 372:621-630.
4. Antonelli A, Bocci G, Fallahi P, La Motta C, Ferrari SM 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

Silvia Martina Ferrari has completed her graduation in Biological Sciences cum laude in 2002 and specialized in Clinical Pathology in 2007 at the University of Pisa (Italy). Her principal areas of expertise are autoimmune thyroid disorders, chemokines and cytokines, type 1 diabetes, systemic autoimmune disorders, HCV-associated thyroid disorders and thyroid cancer. Her researches have been published in more than 154 articles in international journals (HI=38). She serves as an Editorial Board Member and is Referee and Reviewer of many scientific international journals.

sm.ferrari@int.med.unipi.it