CASE REPORT

Everolimus Induced Mucocutaneous Toxicity

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A 45 Years old female case of ductal cell carcinoma of breast with ER/PR positivity diagnosed in year 2009 and presently was on tamoxifen 20 mg once daily. Presented with bone pains and bone scan was showing increased tracer uptake in D9/D10 vertebral bodies suggestive of metastasis. In view of progression of disease on hormonal agents she was started on treatment with Everolimus 10 mg once daily and Exemestane 25mg once daily. During second month of treatment she started with painful oral lesions and acniform skin rash on face, neck and upper trunk. Treatment was withheld and she improved. Once treatment was reintroduced with everolimus she again started with similar skin and oral lesions which were more severe than earlier lesions. (Fig.1, 2). Treatment was stopped.

Everolimus is a potent inhibitor of the mammalian target of rapamycin (mTOR). mTOR is a serine/threonine kinase that senses mitogen, energy levels, and nutrients in cells and has been shown to regulate cell growth in response to various environmental stimuli, acting as a gatekeeper for cell cycle progression^{1,2}. In cancer development and metastasis, mTOR activity may be increased by multiple signaling pathways³, resulting in increased transcription and translation of proteins involved in regulation of cell growth, cell cycle progression, and cellular metabolism. Through the synthesis of hypoxia-inducible factor 1 (HIF-1), mTOR regulates the production of proteins involved in

angiogenesis and other responses to further increase supplies of nutrients and energy required by the growing cell⁴. Everolimus is a highly specific and potent mTOR inhibitor that forms a complex with FKBP12, inhibiting the kinase activity of mTOR20 and leading to decreased synthesis of tumor promoting proteins and inhibition of downstream signaling involved in tumor growth and progression. The common side effects of oral Everolimus are asthenia, fatigue, mucositis, oral ulceration, skin rash, infections, interstitial pneumonias, myelosuppression, mild hepatotoxicity, hyperlipidemia and hyperglycemia. Most of the side effects are grade ½ in severity and are managed conservatively. However in grade ¾ toxicity the drug is stopped.

Fig 1. Acniform skin lesions.

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Fig 2. Glossitis with mucositis.

REFERENCES

1. Shaw RJ, Cantley LC. Ras, PI(3)K, and mTOR signaling controls tumor cell growth. *Nature*. 2006; 442:424-430. 2009; 115:3618-3630.
2. Bjornsti M-A, Houghton PJ. The TOR pathway: A target for cancer therapy. *Nat Rev Cancer*. 2004; 4:335-348.
3. Kapoor A, Figlin RA. Targeted inhibition of mammalian target of rapamycin for the treatment of advanced renal cell carcinoma. *Cancer*.
4. Samlowski WE, Vogelzang NJ. Emerging drugs for the treatment of metastatic renal cancer. *Expert Opin Emerg Drugs*. 2007; 12:605-618.