LETTERS TO THE EDITOR

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PHARMACOLOGY

New therapies and challenges

Sir, among new drugs impacting on oral healthcare are a range of molecules designed to inhibit the growth or effects of tumours. Thus agents with the acronyms BP, RANK and VEGF are becoming increasingly commonplace in clinical practice and all may be associated with a risk of developing osteonecrosis of the jaws (ONJ) – a conundrum for all in oral health care. ONJ is a particular issue following invasive dental or oral surgery, since many such procedures impact on bone.

Bisphosphonates (BPs) are potent inhibitors of osteoclast-mediated bone resorption, which is increased when cancers invade bone. BPs are an established treatment for cancer spread to bone, and effectively reduce pain and other skeletal-related events. Denosumab is a fully human monoclonal antibody with high affinity and specificity for Receptor Activator of Nuclear factor-Kappa B Ligand (RANKL), a cytokine that is the main final mediator of osteoclastic bone resorption.

Angiogenesis inhibitors block various steps in the binding of signalling molecules, such as vascular endothelial growth factor (VEGF), to receptors on endothelial cells to prevent the formation of new blood vessels; molecules such as bevacizumab, sorafenib and sunitinib are used clinically to stop or slow tumour growth or spread.

ONJ may develop in patients exposed to anti-resorptive (BPs, denosumab) and anti-angiogenic (bevacizumab, sunitinib) drug therapy and, although to date there are no documented cases with other anti-angiogenics (eg sorafenib, sunitinib), there may be a potential risk.¹

The risk of ONJ is about 1% for cancer patients receiving intravenous BPs (zoledronate), and there is a comparable figure for cancer patients exposed to denosumab while the risk for patients on VEGF inhibitors is lower (eg 0.2% with bevacizumab).^{2,3} There appears to be an increased risk in those patients on combination anti-resorptive and anti-angiogenic therapy – ONJ may be as

WHAT ABOUT AUSTERITY?

Sir, I am a dentist working in the salaried service (PDS) and am extremely concerned about the level of proposed increase in the annual retention fee.

In the salaried service, we have had pay increases of around 1% per annum, ie from 2010 till the present, a total of approximately 5%. The Government has stated that this is to reflect current austerity measures, and has also stated that there is unlikely to be any increase in this over the next few years.

Nevertheless, the GDC wishes to increase the ARF by 64% – compare that to 5%! Has the GDC not heard of austerity?

It is somewhat disingenuous to try to mollify the effects of this increase by stating that it is tax allowable.

While I understand that the costs of running the GDC have increased dramatically, this has not happened suddenly and must have been recognised over the last few years. Why have increases not been applied over the period since 2010?

Presumably much of the increase relates to the cost of travel and accommodation. Why has more use not been made of facilities available due to information technology, teleconferencing etc?

Surely it is time for the GDC to become more accountable to the registrants?

I hope that this will be brought to the attention of the Chairman, Mr Moyes, and my comments considered.

J. S. Pairman, by email

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frequent as 10% in those on combined BP and sunitinib therapy.⁴

For patients with exposure to the above agents and in whom surgical intervention is required, cessation or interruption of anti-resorptive and anti-angiogenic medication (a drug-holiday) has been advocated to minimise the risk of developing ONJ.

However, robust data on the effectiveness of drug holidays are lacking and this has been a controversial topic. A recent AAOMS position paper now suggests that for those who have been exposed to more than four years of oral BPs therapy and for whom a surgical intervention is planned, a drug-holiday of about two months prior to surgery and three months following surgery be undertaken to reduce the risk of ONJ.⁵

This paper makes no recommendation for patients on other agents but we suggest, based on the pharmacology of denosumab, that a drug interruption of six months would possibly reduce the risk of ONJ. For VEGF inhibitors, recommendations in the medical literature and adopted by surgical oncologists and plastic surgeons, to minimise wound healing impairment, might be used as a guide: bevacizumab has a median half-life of about 20 days (range 11–50 days) and on this basis they

have advocated a 6–8 week interruption of bevacizumab treatment before surgery and four weeks after surgery, to lower the risk of wound complications. Sunitinib has an elimination half-life of 40–60 hours: expert opinion has suggested cessation of sunitinib therapy one week before surgery, restarting after wound healing has commenced at a minimum of one week following surgery.^{6–8}

A. Robinson, Singapore

C. Scully, London

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