Safety and Compliance of Intravenous and Oral Dosing Regimens

GRAHAM JACKSON

Department of Hematology, University of Newcastle-Upon-Tyne, Newcastle, United Kingdom

The recent article by Conte and Guarneri highlights numerous safety and compliance issues of intravenous and oral bisphosphonates in patients with metastatic bone disease [1]. I believe it is essential that readers of The Oncologist are made aware of a few of the inaccuracies within the article, particularly those renal safety statements that contradict the approved product labeling for ibandronate.

First, the authors imply that the nephrotoxic potentials of intravenous bisphosphonates are similar. This is misleading. The product labeling for zoledronic acid contains a number of renal safety cautions not contained in the label of other bisphosphonates like ibandronate. In 2004, the US labeling for zoledronic acid was updated three times to provide additional safety guidance, and renal safety letters were sent to European physicians [2-4]. Various studies have reported renal safety issues with zoledronic acid [5-11], yet these are not discussed by Conte and Guarneri. For example, the Food and Drug Administration has received reports of renal deterioration progressing to renal failure and dialysis with the use of zoledronic acid [6]. Moreover, in a retrospective review, 23% of patients receiving zoledronic acid had substantial deterioration in renal function [8].

In contrast to zoledronic acid, available data suggest that ibandronate has a renal safety profile comparable to placebo [12-15]. Unlike zoledronic acid, monitoring of renal function is not required prior to each infusion of ibandronate. The approved product labeling for ibandronate in the European Union states that “according to clinical assessment of the individual patient, it is recommended that renal function, serum calcium, phosphate and magnesium should be monitored in patients treated with ibandronate” (i.e., monitoring with ibandronate is at the discretion of the physician) [12]. The statements by Conte and Guarneri about the use of ibandronate in patients with severe renal impairment (page 32) are somewhat unsubstantiated and imply a lack of clinical efficacy.

According to the approved product labeling, both the oral and intravenous formulations of ibandronate can be used with a dose adjustment to compensate for lost renal excretion in patients with severe renal failure (creatinine clearance <30 ml/min), unlike zoledronic acid where it is contraindicated [12, 16]. Clearly, the conclusion of the abstract that “newer, more potent bisphosphonates … can be administered via relatively short i.v. infusions without adversely affecting renal function” is unjustified for zoledronic acid. Due to time constraints, many physicians rely entirely on reading the abstract, hence patient safety could be compromised.

It is important that physicians appreciate the differences between bisphosphonates to make informed treatment decisions.

DISCLOSURE OF POTENTIAL CONFLICTS OF INTEREST

Dr. Jackson is a consultant for Roche.

REFERENCES


Correspondence: Graham Jackson, M.D., Department of Hematology, University of Newcastle-Upon-Tyne, Queen Victoria Road, Newcastle. United Kingdom. Telephone: 0191 282 4763; Fax: 0191 282 5042; e-mail: graham.jackson@ncl.ac.uk


