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Intravenous Ibandronate
In the Treatment of Osteoporosis

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Contents

Abstract

▲ Ibandronate (ibandronic acid) is a potent nitrogen-containing bisphosphonate that inhibits osteoclast-mediated bone resorption in women with postmenopausal osteoporosis. Recently, an intravenous (IV) formulation of ibandronate for intermittent injection, which circumvents the fasting and posture requirements associated with administration of oral bisphosphonates, was approved for use in this patient population.

▲ In initial placebo-controlled studies of 1 year's duration, IV ibandronate (≤2mg once every 3 months) increased lumbar spine bone mineral density (BMD) and reduced levels of biochemical markers of bone turnover in a dose-dependent manner. Dosages ≤1mg every 3 months were found to be suboptimal in terms of fracture prevention in a 3-year trial.

▲ Subsequently, the large randomised, double-blind, noninferiority DIVA trial showed that, in terms of increasing lumbar spine BMD (primary endpoint), IV ibandronate 3mg once every 3 months and 2mg once every 2 months for 1 year were noninferior and also superior to oral ibandronate 2.5mg once daily, a regimen with proven antifracture efficacy. Median reductions from baseline in biochemical markers of bone turnover were similar for the IV and oral regimens.

▲ IV ibandronate was generally well tolerated in clinical trials. Treatment-related adverse events included musculoskeletal events and transient influenza-like symptoms, the latter mainly associated with the first dose.

Features and properties of intravenous (IV) ibandronate (Bonviva®)	
Featured indication	
Osteoporosis in postmenopausal women	
Mechanism of action	
Nitrogen-containing bisphosphonate	Inhibits osteoclast-mediated bone resorption
Dosage and administration	
Dose	3mg
Route	IV injection (over 15–30 sec)
Frequency of administration	Once every 3 months
Pharmacokinetic profile in healthy postmenopausal women after administration of intravenous ibandronate 0.5–6mg	
Area under the serum concentration-time curve from time zero to infinity	316–908 ng • h/mL
Apparent volume of distribution	90–175L
Total clearance	≈90–130 mL/min
Renal clearance	≈60 mL/min
Terminal elimination half-life	10–23h
Treatment-related adverse events in phase III trial (IV ibandronate plus placebo tablets)	
Most frequent	Influenza-like illness, arthralgia, abdominal pain, dyspepsia

Osteoporosis is a progressive disease characterised by decreased bone mass and disordered bone architecture, leading to fragility and an increased risk of fractures, particularly of the spine, hip and wrist.[1] When described in terms of bone mineral density (BMD), osteoporosis is defined as BMD more than 2.5 standard deviations below the mean for young normal subjects of the same gender (T score < −2.5).[1] The risk of osteoporosis increases with age and, while it occurs in both men and women, it is especially common in postmenopausal women, related to a decrease in estrogen-mediated suppression of bone resorption.[1,2] At least one in three women over the age of 50 years will experience an osteoporotic fracture.[1,2]

The main aim of treatment is to reduce the risk of fractures, which can be achieved by slowing bone loss and improving bone mass and quality.[2] Lifestyle preventive measures include dietary considerations, exercise, the avoidance of smoking and limiting alcohol intake.[2] Among pharmacological approaches, bisphosphonates, which reduce bone resorption, are generally the first-line option for the treatment of postmenopausal osteoporosis.[2,3] Bisphosphonates increase BMD and reduce fracture risk.[2] Intermittent dose regimens for drugs of this class have been approved based on BMD responses being similar to those seen with daily regimens.[2]

Ibandronate (ibandronic acid; Bonviva®)[1] is a nitrogen-containing bisphosphonate. Oral ibandronate, which is available for administration in daily or intermittent regimens, has been shown to have antifracture efficacy in women with postmenopausal osteoporosis.[4] Oral bisphosphonates, including ibandronate, are poorly absorbed and can also be associated with dyspepsia or oesophageal irritation.[2] Consequently, oral preparations must be taken first thing in the morning, at least 0.5–1 hour (depending on the drug) prior to food, drink (except water) or other medications, and swallowed while in an upright position, which should then be maintained for at least an hour.[5]

An injectable intravenous (IV) formulation of ibandronate, which circumvents the fasting and posture requirements associated with oral preparations, and can be administered with an intermittent dose regimen, has recently been approved for use in women with postmenopausal osteoporosis.[6] This article reviews the pharmacological and clinical profile of IV ibandronate injection in the treatment of postmenopausal osteoporosis. Clinical data from other osteoporosis populations is also discussed briefly.

1. Pharmacodynamic Profile

- Ibandronate is a nitrogen-containing bisphosphonate that inhibits osteoclast-mediated bone resorption. Like other bisphosphonates, ibandronate binds to hydroxyapatite crystals in bone, from which it is released during bone resorption and taken up by osteoclasts (reviewed by Chapurlat[7]). Through effects on intracellular enzyme pathways (in the case of nitrogen-containing bisphosphonates, the mevalonate pathway), osteoclasts are inactivated and apoptosis is induced.[7]
- In animal models, ibandronate was shown to reduce bone turnover and increase or preserve bone mass and strength without adversely affecting bone quality or mineralisation (reviewed by Bauss and Russell[8]). Ibandronate had 2- to 500-fold greater potency than risedronate, alendronate, pamidronate or clodronate. Animal studies also showed that the benefits achieved were similar with daily or intermittent dosing regimens, and that efficacy was determined primarily by the total cumulative dose.[8]
- In postmenopausal women with[9,10] or without[11] osteoporosis, IV ibandronate dose-dependently decreased the serum and/or urinary level of C-telopeptide of type I collagen (CTX), a biochemical marker of bone resorption. Serum levels of osteocalcin, a marker of bone formation, also decreased during treatment with IV ibandronate.[10,11] See section 3 for additonal data on biochemical markers of bone turnover from clinical trials.

1 The use of trade names is for product identification purposes only and does not imply endorsement.

- On the basis of bone biopsies from postmenopausal women, after 2 years' treatment with IV ibandronate 3mg once every 3 months, bone quality and mineralisation were normal; this was also the case after 3 years' treatment with oral ibandronate 2.5mg once daily.[6]

2. Pharmacokinetic Profile

The pharmacokinetics of IV ibandronate have been evaluated in healthy men, healthy postmenopausal women, postmenopausal women with osteopenia and patients with multiple myeloma or metastatic bone disease.[12] Data specifically for the dose approved for use in postmenopausal osteoporosis (3mg) are not available.

- Serum concentration and area under the serum concentration-time curve from time zero to infinity (AUC_∞) values increase in a dose-proportional manner following administration of IV ibandronate.[12] For example, AUC_∞ values were 316, 581 and 908 ng • h/mL after single doses of IV ibandronate 2, 4 and 6mg, respectively, in healthy postmenopausal women.[12]
- Ibandronate is either distributed and rapidly binds to bone (40–50% of the circulating dose) or is excreted in the urine, and plasma concentrations decrease to 10% of maximum values within 3 hours of IV administration.[6,12] The apparent volume of distribution for IV ibandronate was 90–175L in healthy postmenopausal women (following doses of 0.5–6mg).[12] Protein binding is moderate (84–86% at therapeutic concentrations).[12]
- Ibandronate is not metabolised, and is excreted unchanged in the urine, largely within 24 hours.[12] The apparent terminal elimination half-life is generally in the range 10–72 hours[6] (10–23 hours in healthy postmenopausal women[12]). Total clearance of ibandronate is low (generally ≈84–160 mL/min across all healthy volunteers and patient groups; ≈90–130 mL/min in healthy postmenopausal women [after 0.5–6mg doses]). Renal clearance is ≈60 mL/min in healthy postmenopausal women and accounts for ≈50–60% of total clearance.[12]
- Renal clearance of ibandronate is dependent on renal function, and is directly related to creatinine clearance (CL_{CR}).[12] In patients with severe renal failure (CL_{CR} <1.8 L/h [<30 mL/min]), total, renal and non-renal clearance decreased by 67%, 77% and 50%, respectively, after administration of IV ibandronate 0.5mg, although tolerability was not affected.[6]

3. Therapeutic Efficacy

IV ibandronate injection has been assessed in the management of patients with postmenopausal osteoporosis, the approved indication and the main focus of this section. Limited data have also been reported for corticosteroid-induced osteoporosis and conditions with localised increased bone turnover.

Postmenopausal Osteoporosis

Intermittent IV ibandronate injection has been evaluated for the treatment[9,10,13,14] or prevention[11] of postmenopausal osteoporosis in several randomised, double-blind clinical trials. Although only one study used the approved dosage of 3mg once every 3 months,[13] studies using other dosages are included as they provide data pertinent to the overall development history of the IV formulation.

The DIVA trial[13] was a large (n = 1395), multicentre, noninferiority study using double-dummy methodology to compare two regimens of IV ibandronate (3mg once every 3 months [approved dosage] and 2mg once every 2 months) with oral ibandronate 2.5mg once daily (a regimen that has proven antifracture efficacy) in the treatment of postmenopausal osteoporosis. The trial was designed to evaluate noninferiority after 1 year,[13] after which treatment continued in a blinded manner, with another noninferiority analysis performed after 2 years.[15]

Prior to DIVA, several placebo-controlled trials (n = 126–2862) were performed using lower dosages of IV ibandronate.[9-11,14] Three of these assessed dose-response relationships, based on changes in BMD and biochemical markers of bone metabolism over 1 year, for IV ibandronate administered once every 3 months at dosages of 0.25, 0.5, 1 and 2mg,[9] 0.5, 1 and 2mg,[11] or 1 and 2mg (IRIS trial).[10] Two of these studies[10,11] were originally

designed to last 2 years, but were terminated early after results from another trial suggested suboptimal efficacy at dosage levels of ≤1mg.[14] The latter trial was a large phase III study evaluating antifracture efficacy over a 3-year period using IV ibandronate 0.5 and 1mg every 3 months.[14]

In most studies, women were ≥5 years past menopause and had osteoporosis (defined as mean lumbar spine [L2–L4[9,13] or L1–L4[10,14]] BMD T score ≤ −2.5[9,10] or < −2.5 but ≥ −5.0,[13] or −2.0 to −5.0[14]). In the osteoporosis prevention trial, women were postmenopausal (by 1–10 years) with a T score ≥ −2.5 and no osteoporotic fractures.[11] IV ibandronate was administered as an injection.[9,10,13,14] Patients also received oral calcium (500[10,11,13,14] or 1000[9] mg/day) and vitamin D (400 IU/day[10,13,14]) supplements.

The primary efficacy parameter was the mean change from baseline in lumbar spine BMD after 1 year (measured using dual x-ray absorptiometry) in all trials[9-11,13] except the fracture trial, in which it was the incidence of new morphometric vertebral fractures after 3 years.[14] One of the trials, DIVA, was designed to assess noninferiority.[13] The primary efficacy analysis was performed on the intent-to-treat (ITT) population in all studies[9-11,14] except DIVA, where it was performed on the per-protocol (PP) population, as this is considered more conservative for assessing noninferiority.[13]

Common secondary endpoints included change from baseline in proximal femur BMD (total hip, femoral neck, hip trochanter)[10,11,13] and in levels of biochemical markers of bone turnover (e.g. CTX[9-11,13,14] and osteocalcin[9,11,14]).

Comparisons with Placebo

- IV ibandronate administered as an injection once every 3 months dose dependently increased lumbar spine BMD and proximal femur BMD in postmenopausal women with[9,10,14] or without[11] osteoporosis. For example, in a dose-finding study (n = 126), lumbar spine BMD increased by 2.4%, 3.5%, 3.7% and 5.2% after 1 year's treatment with IV ibandronate 0.25, 0.5, 1 and 2mg, respectively; these changes were significantly ($p \leq 0.006$) greater than that seen with placebo (0.85%) for all dosages except 0.25mg.[9]

- After 1 year in the IRIS trial (n = 520), IV ibandronate 2mg once every 3 months increased lumbar spine BMD and proximal femur BMD (all regions) significantly more than IV ibandronate 1mg once every 3 months; see figure 1 for change in lumbar spine and total hip BMD.[10] Both IV regimens were significantly more effective than placebo.

- In postmenopausal women without osteoporosis, the greatest increases in BMD occurred in those who had osteopenia at baseline (T score −2.5 to −1) and were treated with the highest evaluated dosage of IV ibandronate (2mg once every 3 months).[11]

- IV ibandronate once every 3 months caused a dose-dependent reduction in bone turnover (as indicated by reductions in biochemical markers of bone resorption and formation) in postmenopausal women with[9,10,14] or without[11] osteoporosis. For ex-

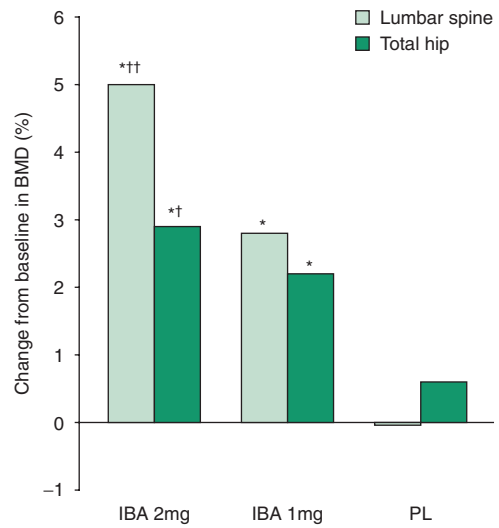

Fig. 1. Dose-response relationship with intravenous (IV) ibandronate (IBA) in postmenopausal osteoporosis. Data are from IRIS, a randomised, double-blind, placebo-controlled trial in 520 women treated for 1 year with IV IBA 1 or 2mg or placebo (PL), once every 3 months.[10] Increase from baseline in lumbar spine bone mineral density (BMD; primary endpoint) and total hip BMD are shown. Baseline lumbar spine BMD T score was −2.7 in the IBA 1mg and 2mg groups and −2.8 in the PL group; baseline values for total hip BMD were not stated. * $p < 0.001$ vs PL; † $p < 0.02$, †† $p < 0.0001$ vs IBA 1mg.

ample, in IRIS, median reductions from baseline in urinary CTX (CTX/creatinine) after 1 year were 42%, 61% and 17.4% for IV ibandronate 1 and 2mg and placebo, respectively ($p < 0.01$ for both comparisons with placebo; $p < 0.002$ for comparison of ibandronate groups).[10] Median reductions in serum osteocalcin levels were 48.3%, 53.7% and 11.2% ($p < 0.002$ for comparison of ibandronate groups; p-values vs placebo not reported).[10]

- In a large antifracture trial (n = 2862) in women with postmenopausal osteoporosis, the incidence of new morphometric vertebral fractures after 3 years was 8.7% and 9.2% with IV ibandronate 0.5 or 1mg once every 3 months compared with 10.7% for placebo; however, the difference did not reach statistical significance.[14]

- The lack of a significant reduction in fracture risk may have been due to the use of suboptimal dosages of IV ibandronate.[14] This is supported by indirect comparison (without statistical analysis) of IV ibandronate data[10,14] with results from a study of oral ibandronate (including a daily 2.5mg regimen) in which significant antifracture efficacy was demonstrated.[4] In the oral ibandronate trial, the incidence of new vertebral fractures in the overall population was reduced significantly with oral daily and intermittent ibandronate compared with placebo ($p = 0.0001$ and $p = 0.0006$), as was the risk of nonvertebral fractures in a high-risk subgroup (based on a *post hoc* analysis; $p = 0.012$), although the incidence of nonvertebral fractures in the overall population did not differ significantly between groups.[4]

- Cross-study comparisons should be interpreted with caution. Firstly, looking at the two 3-year fracture studies, the increase in mean lumbar BMD and reduction in median CTX/creatinine level after 3 years were 4% and 10.8% with IV ibandronate 1mg every 3 months,[14] compared with 5.2%[4] and 54.7%[16,17] with oral ibandronate 2.5mg once daily (placebo-subtracted values).

- Secondly, based on IRIS,[10] a higher dosage of IV ibandronate (2mg once every 3 months) achieved an improvement in lumbar spine BMD after 1 year of 5% compared with 3.8% after 1 year of daily oral ibandronate 2.5mg in the oral ibandronate fracture study[4] (placebo-subtracted values); reductions in CTX/creatinine were 43.6% versus 44% (the latter estimated from a graph).[10,16] Since the magnitude of changes in BMD and biochemical markers of bone turnover are related to fracture risk reduction,[18,19] these data suggest that higher dosages of intermittent IV ibandronate (≥2mg every 3 months) may show better antifracture efficacy than the lower dosages (≤1mg every 3 months) used in the IV ibandronate fracture study.

- Overall, data from placebo-controlled trials indicate that dosages of IV ibandronate ≤1mg every 3 months did not provide adequate antifracture efficacy;[14] however, a dosage of 2mg every 3 months provided a significantly greater reduction of bone turnover and significantly greater improvement in BMD than seen with 1mg,[10] of a magnitude that was associated with antifracture efficacy in a trial of a daily oral regimen.[4]

Comparison with Daily Oral Ibandronate

- DIVA showed that, in terms of increasing lumbar spine BMD, IV ibandronate 3mg once every 3 months or 2mg once every 2 months was both noninferior, and statistically superior, to oral ibandronate 2.5mg once daily (a regimen with proven antifracture efficacy[4]).[13]

- Increases from baseline in lumbar spine BMD after 1 year were similar in the two IV groups and were greater than that in the daily oral ibandronate group (figure 2).[13] The mean difference versus the oral group (PP population; n = 1104) was 1.31% (95% CI 0.76, 1.86) for the 2-monthly group and 1.03% (95% CI 0.49, 1.58) for the 3-monthly group. For both IV groups, the lower limit of the 95% confidence interval was above the prespecified noninferiority margin of −1%, indicating these regimens were noninferior to the daily oral regimen. Subsequently, analysis using ANOVA showed that both IV regimens were statistically superior to the daily oral 2.5mg regimen ($p < 0.001$ for both comparisons). The outcome was similar for the ITT population.[13]

- After 2 years, both IV regimens remained noninferior and also superior ($p < 0.001$) to the oral

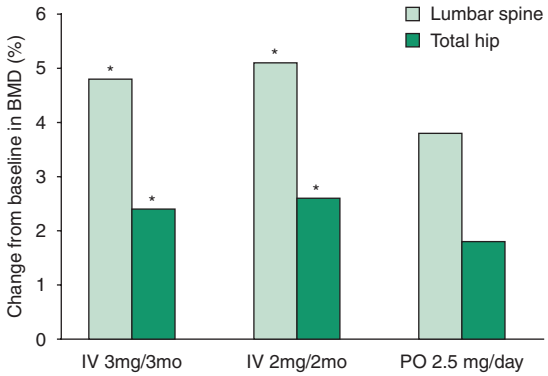

Fig. 2. Efficacy of intermittent intravenous (IV) ibandronate injection in postmenopausal osteoporosis. Data are from DIVA, a randomised, double-blind noninferiority trial in women treated for 1 year with IV ibandronate 2mg once every 2 months or 3mg once every 3 months or oral (PO) ibandronate 2.5mg once daily.[13] Increase from baseline in lumbar spine bone mineral density (BMD; primary endpoint) and total hip BMD at 1 year for the per-protocol population (n = 1104) are shown. Mean baseline lumbar spine BMD T score was −3.3 in all three groups; mean baseline total hip BMD T score was −1.9 for the IV 2mg group and −2.0 for the IV 3mg and oral 2.5mg groups. * $p < 0.05$ vs oral ibandronate 2.5mg daily.

regimen, with increases in lumbar spine BMD of 6.4% and 6.3% versus 4.8% in the 2-monthly IV, 3-monthly IV and daily oral ibandronate groups (reported in an abstract and poster).[15]

- Analyses of secondary endpoints after 1[13] and 2[15] years in DIVA generally supported the primary findings. For example, increases from baseline in proximal femur BMD (total hip, femoral neck and trochanter) at 1 year were similar for both IV ibandronate groups and significantly (both $p < 0.05$) greater than seen with oral ibandronate 2.5mg once daily, except for the femoral neck with the 2-monthly regimen (see figure 2 for total hip values).[13]

- Responder rates (proportion of patients whose lumbar spine, total hip, or lumbar spine and total hip BMD measurements were greater than or equal to baseline values) after 1 year were significantly higher in the 2- and 3-monthly groups than the daily oral group (e.g. 92.6% and 92.1% vs 84.9% for lumbar spine BMD; $p < 0.01$ for both comparisons).[13] Outcomes for these endpoints after 2 years were consistent with the 1-year results.[15]

- The median decrease from baseline in serum CTX level was similar across the IV ibandronate 2mg once every 2 months or 3mg once every 3 months and oral ibandronate 2.5mg once-daily groups after 1 year (59–65%)[13] and after 2 years (53–60%).[15] With regard to the timeframe of changes, IV ibandronate 3mg once every 3 months reduced the median serum CTX level from baseline by 43% after 3 months and 58% after 6 months, with this level of reduction maintained at 12 months (59%) and 2 years (53%).[13,15] Reductions from baseline with IV ibandronate 2mg every 2 months were 47% at 2 months, 65% at 6 and 12 months and 56% at 2 years, and with oral ibandronate 2.5mg once daily were 54% at 3 months, 63% at 6 and 12 months and 60% at 2 years.[13,15]

Other Osteoporosis Populations

Data on IV ibandronate in corticosteroid-induced osteoporosis have been reported for a nonrandomised, open-label study in 115 men and women, which compared IV ibandronate 2mg once every 3 months with daily oral alfacalcidol 1μg.[20] Pairs of patients matched for baseline characteristics were enrolled, one to each group.

Data on patients with a diagnosis of localised transient osteoporosis (based on the presence of acute leg joint pain not associated with trauma, localised bone marrow oedema and corroborative imaging evidence) come from a 6-month, noncomparative, observational study of 12 patients, each treated with a single IV injection of ibandronate 4mg and an optional second injection of 2mg after 3 months.[21]

Endpoints in these studies included change in lumbar spine and femoral neck BMD after 6 months[21] or 3 years,[20] the incidence of new fractures[20] and an assessment of pain (using a 4-point Likert scale[20] or a 10-point visual analogue scale[21]). Patients received calcium supplements (500[20] or 1000[21] mg/day).

- In patients with corticosteroid-induced osteoporosis, IV ibandronate 2mg once every 3 months was associated with significantly greater increases from baseline than daily oral alfacalcidol 1μg in mean lumbar spine BMD (13.3% vs 2.6%; $p <$ 0.001) and femoral neck BMD (5.2% vs 1.9%; $p <$

0.001) and significantly fewer new vertebral fractures (8.6% vs 22.8%; p = 0.043) after 3 years.[20] There were 13 nonvertebral fractures with ibandronate and 16 with alfacalcidol; the between-group difference was not significant. In addition, IV ibandronate recipients experienced significantly greater relief of back pain than those in the alfacalcidol group, with pain scores improving by 2 or 3 points in 86.2% versus 49.1% of patients (p < 0.001).[20]

- In patients with localised transient osteoporosis, treatment with a single dose of IV ibandronate 4mg (plus an additional dose of 2mg after 3 months in three patients) reduced pain scores by a mean of 43.3% after 1 month and 94.3% after 6 months (from 8.4 at baseline to 0.5; p < 0.0001).[21] Mean lumbar spine BMD increased by 4% from baseline. In patients with hip involvement, the mean difference in BMD between the affected and nonaffected femoral necks decreased from 10.1% to 2.6% (statistical analyses not reported).[21]

4. Tolerability

The primary focus of this section is tolerability data for the approved dosage of IV ibandronate (3mg once every 3 months) from the DIVA study in postmenopausal women with osteoporosis (section 3),[13] including relevant data from the manufacturer's prescribing information.[6] Only descriptive analyses were reported for DIVA.

- IV ibandronate was generally well tolerated in postmenopausal women with osteoporosis, with most adverse events being mild to moderate in severity.[6] In placebo-controlled trials, which used dosages of ≤2mg once every 3 months, there was no significant difference in the overall incidence of adverse events between IV ibandronate and placebo.[9,10,14]

- In DIVA, the overall incidence of adverse events with IV ibandronate 3mg once every 3 months and 2mg once every 2 months was similar to that with oral ibandronate 2.5mg once daily (a regimen that has been shown to have a tolerability profile similar to that of placebo[6]).[13] Adverse events considered possibly or probably related to treatment had occurred in 26% of patients receiving IV ibandronate 3mg once every 3 months and 20.4% of the oral ibandronate group after 1 year, and 28.6% versus 22.6% of patients after 2 years.[6]

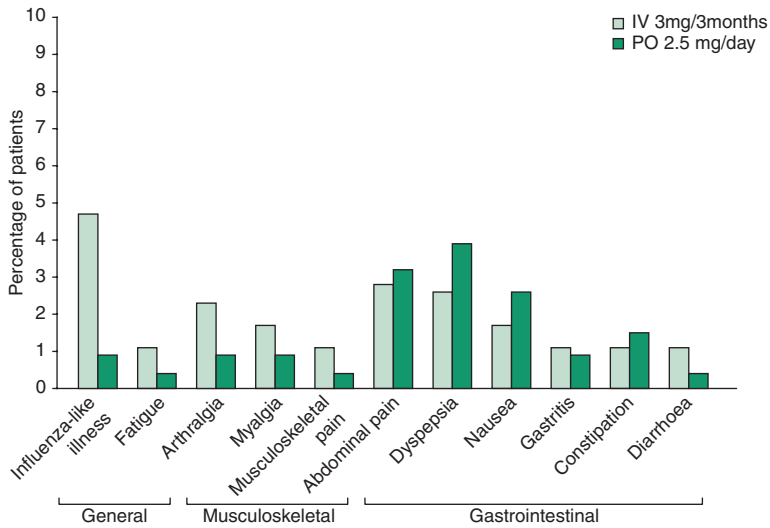

Fig. 3. Tolerability of intravenous (IV) ibandronate in women with postmenopausal osteoporosis. Incidence of general, musculoskeletal and gastrointestinal adverse events considered possibly or probably related to treatment, and occurring at a rate of >1% after 1 year in DIVA, a randomised, double-blind, phase III trial which compared IV ibandronate 3mg once every 3 months (n = 469), IV ibandronate 2mg every 2 months (data not shown) and oral (PO) ibandronate 2.5mg once daily (n = 465).[6] Double-dummy methodology was used, with patients in the IV ibandronate groups also receiving placebo tablets, and the oral group also receiving placebo IV injections.

- Treatment-related adverse events with IV ibandronate 3mg once every 3 months in DIVA included musculoskeletal events (e.g. arthralgia, myalgia) and influenza-like illness (figure 3).[6,13] Influenza-like symptoms tended to occur in association with the first IV dose of ibandronate, were mild or moderate in severity, transient (≤7 days) and did not require treatment.[13]
- Gastrointestinal adverse events were also reported for the IV ibandronate group in DIVA (figure 3).[13] Placebo tablets were administered concurrently with IV ibandronate in this double-dummy trial, and although comparisons across studies should be made with caution, the incidence of such symptoms in the IV ibandronate groups in DIVA was similar to that seen with placebo tablets in a separate oral ibandronate placebo-controlled trial.[6] In addition, in placebo-controlled trials of IV ibandronate using lower dosages than in DIVA, the incidence of gastointestinal events with IV ibandronate 0.5–2mg once every 3 months was similar to that seen with IV placebo.[9,10,14]
- No cases of acute renal failure were reported in DIVA.[13]
- No cases of avascular necrosis (osteonecrosis) of the jaw were reported in DIVA,[13] or in any other controlled clinical trial with ibandronate in postmenopausal osteoporosis.[17]

5. Dosage and Administration

IV ibandronate is indicated for the treatment of osteoporosis in postmenopausal women, at a dosage of 3mg once every 3 months.[6,22] It is available as a 3mg/3mL solution in a pre-filled syringe for injection intravenously over 15–30 seconds. Patients should also receive calcium and vitamin D supplements. Administration to patients with severe renal impairment (serum creatinine >200 μmol/L) is not recommended because of limited clinical experience in this patient group.[6] Local prescribing information should be consulted for additional information, including specific indications, differences between countries, warnings and contraindications.

6. Intravenous Ibandronate: Current Status in Osteoporosis

Intermittent IV ibandronate injection is approved for the treatment of osteoporosis in postmenopausal women, and provides an alternative method of administration to existing oral ibandronate preparations. A large, well designed trial demonstrated that IV ibandronate at dosages of 3mg once every 3 months and 2mg once every 2 months was generally well tolerated and was more effective at increasing lumbar spine and hip BMD than an oral ibandronate regimen with proven vertebral antifracture efficacy. Both IV regimens had similar efficacy and tolerability; registration was sought for the 3mg dosage regimen because the 3-monthly dose interval may be more convenient for patients.

Disclosure

During the peer review process, the manufacturer of the agent under review was offered an opportunity to comment on this article; changes based on any comments received were made on the basis of scientific and editorial merit.

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