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Renal Function And Safety Results After One Year Treatment With Zoledronic Acid In Chinese Women With Postmenopausal Osteoporosis

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INTRODUCTION

- Osteoporosis is a systemic skeletal disease, characterized by low bone mass and microarchitecture deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture.
- Zoledronic Acid (Zol) has been demonstrated to be an effective therapy to treat postmenopausal osteoporosis (PMO) in Chinese women in a 12-months post-marketing observational study (ZOOM study). As an intravenous bisphosphonate, Zol is exclusively excreted via the kidneys.

OBJECTIVE

- The present report aimed to assess the renal function, safety data and tolerability for all the patients enrolled in the ZOOM study with once-yearly Zol 5mg treatment.

METHODS

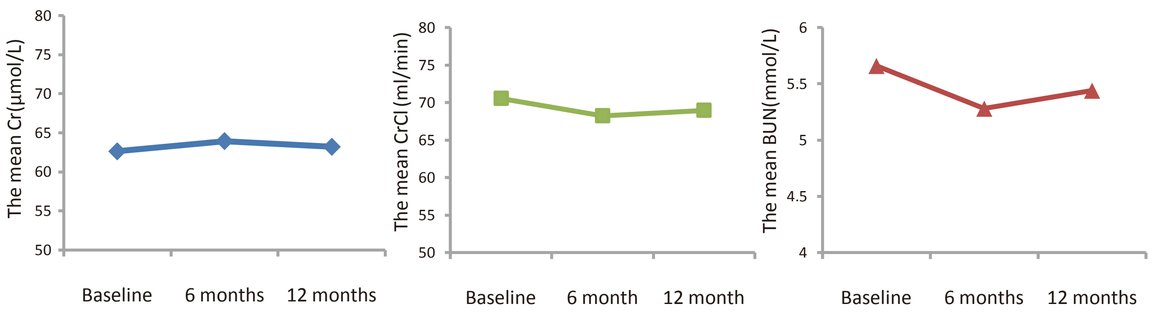
- This was a 12-month, multicenter, non-interventional, post-marketing observational study.
- A total of 373 PMO patients from 30 different centers in China with baseline creatinine clearance (CrCl) >35ml/min, bone mineral density (BMD) T score ≤–2.5 or T score >-2.5 with previous fragility fractures were recruited in the study. All the eligible patients received a single 15-minute infusion of Zol 5mg and followed up for 12 months. The BMD change at 12 month was the primary objective.
- Renal function [serum creatinine, CrCl, and blood urea nitrogen(BUN)] was tested at baseline, 6 months and 12 months after the Zol infusion.
- Safety was assessed from adverse events and serious adverse events recorded by the investigators.
- Tolerability satisfactions were evaluated by investigators and patients using the categories “very good”,“good”,“ordinary” and “bad” .

RESULTS

Renal Safety

- Renal function assessment for all the patients showed that mean serum creatinine, CrCl and BUN maintained 12 months after treatment (creatinine 62.64±14.59 μmol/L vs. 63.21±15.04 μmol/L ,CrCl 70.57±23.67 ml/min vs. 68.94±21.85 ml/min , and BUN 5.66±3.46 vs. 5.44±3.18 mmol/L, respectively).(Figure 1)

Figure 1.The mean Cr, CrCl and BUN at baseline,6 months and 12 months during follow-up period.



- Creatinine increase of more than 0.5mg/dl compared to baseline was found in only one patient (0.38%) at 12 month.
- The patients’ baseline average CrCl was 70.57±23.67 ml/min. During one year follow-up, CrCl decline under 35 ml/min was found in 9 patients (9/257, 3.50%) with moderate renal impairment at baseline. (Table 1)

Table 1. Patients with CrCl ＜35ml/min at follow-up

Patient	CrCl baseline (ml/min)	CrCl at 6 months (ml/min)	CrCl at 12 months (ml/min)
1	39.08	-	33.83
2	35.52	33.03	28.85
3	37.48	31.58	35.23
4	47.63	48.33	33.44
5	38.80	33.21	32.51
6	46.34	31.33	42.61
7	38.39	34.20	35.12
8	40.01	38.41	34.29
9	36.61	39.20	34.76

RESULTS(Cont’d)

Adverse Events

- A total of 42 patients (11.26%) experienced adverse events (AEs). (Table 2)
- The most common AEs were fever (6.17%) and musculoskeletal pain (1.61%), while other AEs occurred below 1 percent.
- Serious adverse events were reported in 4 patients, including 3 deaths due to pneumonia, lung cancer and gastric perforation, which were not considered by the investigators to be drug related.

Table 2.Adverse Events

AEs	No. of pts	Frequency of events	Rate (%)
Systemic events	27	30	7.24
Pyrexia	23	23	6.17
Pain	3	3	0.80
Fatigue	3	3	0.80
Influenzalike symptoms	1	1	0.27
Musculoskeletal system events	8	8	2.14
Myalgia	6	6	1.61
Bone Pain	2	2	0.54
Gastrointestinal system events	6	9	1.61
Nausea	3	3	0.80
Vomiting	3	3	0.80
Diarrhea	2	2	0.54
Gastrointestinal reactions	1	1	0.27
The central and peripheral nervous system events	5	6	1.34
Dizziness	3	3	0.80
Drowsiness	2	2	0.54
Headache	1	1	0.27
Skin and its accessories events	2	3	0.54
Pruritus	2	3	0.54
Urinary system events	1	1	0.27
Abnormal renal function	1	1	0.27

Adverse events were categorized according to codes used in the WHO Drug Adverse Reactions Database.

Tolerability

- After treatment for 12 month, the tolerability satisfactions evaluated by investigators were significant consistent with those by patients (P<0.001). The proportion of “very good” tolerability evaluations in patients was 96.28%, which was similar to that in investigators (96.43%).
- 81.01% (290) of all enrolled patients were willing to continue the Zol treatment. And 91.79% of patients who completed the study continued Zol infusion in the next year.

CONCLUSIONS

- Once yearly zoledronic acid administration was associated with a good safety profile and generally well tolerated in Chinese PMO patients.

REFERENCES

- The main result of ZOOM study was accepted as posters on ASBMR Annual Meeting (Minneapolis, Minnesota, October 12-15,2012.Poster # LB-SA 19) and IOF Regionals-3rd Asia-Pacific Osteoporosis Meeting (Kuala Lumpur, Malaysia,December 13-16,2012.Poster # P321).

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