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Research Article

Denosumab for the Treatment of Osteoporosis in Hong Kong Chinese Women

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Abstract

A study was conducted on Hong Kong women with osteoporosis or osteopenia with risk factors for fracture. Among 655 subjects, 49.2% received a fifth injection, while 15.3% received an eleventh injection. Among 283 subjects in the DEXA follow up study, the mean bone mineral density (BMD) increase at the 5th year (6 months after the tenth injection) was 7.0% (SD=3.7%) at the hip and 10% (SD=7.1%) at the spine. No osteonecrosis of the jaw nor atypical fracture were reported. It is concluded that Denosumab is an effective treatment for preventing bone loss in Hong Kong Chinese women with osteoporosis.

Key words: Denosumab, osteoporosis, Hong Kong Chinese women, efficacy, compliance

Introduction

Osteoporosis is a major health problem in Asia. In 2018, the Asian Federation of Osteoporosis Societies (AFOS) study projected that there would be 2.56 million hip fracture in Asia by 2050 [1]. In 2023, Chandran et al reported a prevalence of osteoporosis between 10-30% in adult Asian women [2]. In Hong Kong, Lo et al reported a prevalence of 24% for osteoporosis among women aged 65 years or above [3].

The incidence of hip fracture in Hong Kong rose 2.5 folds from 1966 to 1985 [4]. In 1995, the incidence of hip fracture was 11/1000 in women and 5/1000 in men who were 70 years and older [4]. Early detection and treatment of osteoporosis are essential in preventing osteoporotic fractures.

The fully human monoclonal antibody Denosumab was approved for treatment of osteoporosis in 2010. The FREEDOM trial program [5, 6] provided evidence of the drug's efficacy in increasing bone mineral density (BMD) and reducing fracture risk.

In 2022, a study on the effectiveness of Denosumab for fracture prevention in Hong Kong and Taiwan was published [7]. The effectiveness of Denosumab, or were found to be consistent with global clinical trials [5, 6].

The objectives of the current study are to investigate the compliance and efficacy and adverse events of Denosumab in Hong Kong women with osteoporosis on osteopenia with risk factors for fracture.

Materials and methods

The study was conducted from 2011 to 2022. Denosumab was used as one of the first-line drug for women who had a T-score of ≥-2.5 at either the total hip or the total spine; or who had a T-score of ≥-1.0 and have additional major risk factors of fracture, or already had an osteoporotic fracture. Denosumab was administered subcutaneously every 6 months. Dual X-Ray densitometry (DEXA) was performed annually. All patients were prescribed elemental calcium of 1200 mg and vitamin D supplement of 1000 IU per day.

Only subjects who consented to participate in the study were included. For compliance, all subjects were included. For the BMD Study, only subjects who had at least 3 Denosumab injection and 2 BMD measurements were included. All BMD was measured by a Lunar DEXA machine (GE, Prodigy P11 Compact). Adverse events and fractures were based only on subjects in the DEXA study, by self-report. Follow up data for up to 5 years is presented here. SPSS was used for data- analysis.

Results

A total of 655 subjects were followed up in the compliance study. The compliance is shown in (Table 1). The compliance dropped quite rapidly and was only 49.2% for the fifth injection. A total of 15.3% of subjects were still receiving the 11th injection.

Injection	Total Number	% Compliance
Baseline (first)	655	--
Second	549	83.8
Third	469	71.6
Fourth	407	62.1
Fifth	322	49.2
Sixth	271	41.4
Seventh	211	32.2
Eighth	185	28.2
Ninth	146	22.3
Tenth	121	18.5
Eleventh	100	15.3

Table 1: Compliance of study subjects to denosumab injection

A total of 283 subjects were included in the DEXA study. The mean age of the women were 68.1 years (SD=10.2), the Body Mass Index was 21.3 Kg/M2 (SD=3.07), the mean number of injections received was 7.8 (SD=2.9), and the mean duration of follow up was 3.43 (SD=1.6). At baseline, the mean total hip T-score (N=284) was -1.95 (SD = 0.75) and the mean total spine T-score (N=260) was -2.6 (SD = 0.81).

The distribution of T-score according to the WHO criteria for osteoporosis and osteopenia is shown in (Table 2). The percent of subjects classified as osteoporosis at the total hip was 19.8% and at the total spine was 59.6%.

T-score	Total Hip	Total Spine
≥ -2.5	19.8%	59.6%
-1.0 to -2.49	71.4%	36.5%
< -1.0	8.8%	3.9%

Table 2: Distribution (by percentage) of T-scores of DEXA study subjects at Total Hip (n=283) and Total Spine (n=260) at baseline

The percentage increase in BMD at the hip and spine are shown in (Table 3). There were steady increase in BMD with Denosumab injection. No osteoporosis of the jaw nor atypical femoral fractures were observed. Only one patient developed skin reactions which led to discontinuation of Denosumab injection. It was diagnosed as pseudolymphoma by a board-certified dermatologist. This occurred after 5 injections of Denosumab.

	Baseline	1st year	2nd year	3rd year	4th year	5th year
		6 monthsafter 2nd injection	6 monthsafter 4th injection	6 monthsafter 6th injection	6 monthsafter 8th injection	6 monthsafter 10thinjection
Total hip						
Total number	283	283	207	144	99	63
BMD (gm/cm^2)	0.711±0.094	0.730±0.094	0.739±0.095	0.738±0.098	0.743±0.103	0.736±0.096
Percentage change frombaseline		2.69±2.55	4.11±3.22	4.90±3.20	6.44±3.66	6.99±3.68
Total spine						
Total number	260	256	184	127	84	53
BMD (gm/cm^2)	0.800±0.097	0.832±0.100	0.840±0.094	0.838±0.091	0.845±0.088	0.860±0.091
Percentage change frombaseline		4.33±4.18	6.24±4.52	7.20±5.31	8.89±6.67	10.08±7.09
1st year DEXA was conducted 6 months after the second injection and so on.						

Table 3: Percentage change in BMD at the total hip and total spine

The percentage increase in BMD was lower than observed in the Freedom Study [5,6]. For instance, the BMD increase in the total hip in Hong Kong subjects at 3 years was 4.9%, as opposed to 6% in the Freedom Study; and at 5 years was 7%, as opposed to 7.8% observed in the Freedom Study.

The percentage increase at in BMD at the spine in the Hong Kong subjects at spine was 7% at 3 years, as opposed to 9.2% in the Freedom Study; while at 5 years, the BMD increase was 10% in the Hong Kong subjects, as opposed to 13.0% in the Freedom Study.

There was a total of 7 clinical vertebral fracture, 7 forearm fractures and 3 hip fractures reported in 5 years. This was based only on self-report by subjects. The number was much lower that observed in Denosumab treated patients in the freedom study. This could be partly due to under reporting of fractures in the current study.

Discussion

A study was conducted in Hong Kong and Taiwan on the effectiveness of Denosumab for fracture prevention in real world postmenopausal women [7]. The effectiveness of Denosumab for fracture reduction in East Asian women was found to be consistent with the efficacy demonstrated in a global clinical trial [5,6]. The current study is the first of its kind conducted in Hong Kong to investigate the compliance and efficacy of Denosumab in osteopenic and osteoporotic patients. The short comings are a relatively small sample size, a substantial number of drop outs and reliance on self-reporting for adverse events and fractures. Despite shortcomings, the study provided some insight into the usefulness of Denosumab in treating osteoporosis in Hong Kong women.

The compliance to Denosumab injection decreased quite rapidly with time. A formal survey was not conducted into the reasons for dropping out of treatment, but reasons described in clinical consultations included cost, not convinced about the "need" for long term treatment, or just a loss of interest. We observed that BMD increased consistently from baseline at both the total hip and spine. The mean cumulative percentage increase in BMD was slightly lower than the percentage change in BMD in the Freedom Trial [5,6]. Most of the adverse events observed were mild. Only one patient had to be taken off Denosumab due to side effects.

Fracture reporting in the current study was based on self-reporting, and some fractures would have been missed. It is hard to conclude on the efficacy of Denosumab on fracture prevention in this study. Nevertheless, efficacy was demonstrated by increase in BMD.

Remedies to increase compliance can include more health education on the important health consequences of osteoporotic fractures, and more frequent reminder calls to subjects. The cost of treatment remains a challenge.

Conflict of interest: None

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