Outcomes in severe osteoporotic women in Korea using sequentail treatment

Background

- Osteoporosis is a progressive disease characterized by decreases in the density and quality of bone. The most common osteoporosis in women occurs after menopause and is called postmenopausal osteoporosis (PMO).
- Bone mineral density (BMD) is used as an indicator of osteoporosis. BMD is measured and quantified by T-score, whose units are standard deviations relative to the young, healthy adults (Young Adult Mean (YAM)). The International Osteoporosis Foundation (IOF) defines osteoporosis as a T-score of -2.5 or less. The FRAX® tool also considers the presence of at least one fragility fracture.
- As bone turnover increases, progression of osteoporosis in women occurs. In postmenopausal women, BMD is greatly increased. Other important fracture risk factors are age and fracture history, such as previous fractures and family history. Estrogen and non-estrogen fractures are associated with increased risks of further fractures. Hip and vertebral fractures are also associated with increased fracture risks.
- Drug treatment interventions such as Fosfatid (teripatide GON origin) lead to a decreased risk of the risk of fractures. Teriparatide is approved for up to 24 months of use.
- Clinical management of osteoporosis often involves different pharmacologic therapies in a sequential manner. After completion of the teriparatide regimen, antiresorptive (AR) bisphosphonate therapies such are commonly considered.
- Real-world outcomes based on sequential teriparatide-bisphosphate treatment of severe PMO in Korea are lacking.

Objectives

- A cost-effectiveness analysis (CEA) model was developed to support a study of the treatment in the treatment of osteoporosis in Korea. The purpose of this study was to estimate fracture (Fx) and health-related quality of life (HRQoL) outcomes for severe PMO patients using teriparatide followed by AR bisphosphonate alendronate versus only alendronate.

Methods

- Analytical Model Structure
  - Monte Carlo simulation model based on a published computer-based simulation model (Figure 1)
  - 6-month fixed time advance
  - Natural mortality and fracture-related excess mortality modeled
  - Lifetime horizon (maximum age 105 years)
  - Fractures included in the analytic hip, clinical vertebral, wrist, and other fractures (proximal humerus, finger, toe, etc.)
  - Patients with previous (TPTD2+ALN3) or a given 6-month period
- QALYs and LTVs discounted at 5% per year

- Base Case Demographics
  - BMD T-score -2.5
  - Ages 65-69 years as distributed in Korea population;
  - T-score (previous osteoporotic fractures (clinical vertebral fractures) T-score -2.5.
  - One of the two previous clinical vertebral fractures is designated to be a historical fracture, which occurred more than 6 months before the beginning of simulation
  - The other clinical vertebral fracture is designated to be an incident fracture, which occurred in the six-month period immediately before the beginning of simulation
  - The two fractures, in combination with the T-score of -2.5, are used to represent severe PMO.
  - The occurrence of the second fracture, i.e., the incident fracture, can be a prompt for the potential use of teriparatide.

- Treatments (Tx)
  - 2 years of teriparatide followed by 3 years of alendronate (TPTD2+ALN3) vs. 5 years of alendronate (ALN5)
  - Efficacy for fracture relative risk reduction (RRR) sourced from literature
  - 100% therapy persistence assumed
  - Teriparatide modeled as having fracture RRR while on treatment (Table 1) and off treatment (RR) values, where RR = 1.0 – RRR.
  - Fractures are assigned during treatment and subsequent fracture RRR phaseout period to the duration of the treatment.
- For sequential teriparatide-bisphosphate treatment, during the post-teriparatide sustained fracture RRR and subsequent fracture RRR phaseout period the patients experience the sustained fracture-specific RRRs, where RRR is the reduction in the number of vertebral fractures.

Results

- In the TPTD2+ALN3 vs. ALN5 T-score -2.5, 2 Fxs analysis, the fracture count reduction of 177 fractures (compared to 173) is the primary and in the case of clinical vertebral fractures and non-hip fractures over 6-month period, and in the case of clinical vertebral fractures and non-hip fractures over 6-month period, and in the case of clinical vertebral fractures and non-hip fractures over 6-month period. The impact on long- and short-term fracture-specific RRRs is minimal.
  - This is because in the 24 months of teriparatide use, its clinical vertebral fracture 50% RRR is much higher than alendronate’s 10%.
  - Additionally in the 18-month post-treatment (sustained) clinical vertebral fracture RRR, teriparatide’s clinical vertebral fracture 57% RRR is higher than alendronate’s clinical vertebral fracture 10% RRR. Thus, using extension of the effective teriparatide clinical vertebral fracture RRR to 42 months (24+18) for TPTD2+ALN3.
  - The teriparatide post-treatment (sustained) non-vertebral fracture RRR (27%) is lower than alendronate’s hip fracture RRR (35%), so the effective hip fracture RRR is the reason used for the 24 months of teriparatide treatment. Thus the impact on long- and short-term hip fracture counts is minimal for TPTD2+ALN3 vs. ALN5.

- The teriparatide post-treatment (sustained) non-vertebral fracture RRR (27%) is higher than alendronate’s non-vertebral fracture RRR (16%), but this extension of the effective teriparatide non-vertebral fracture RRR to 54 months (24+30) for TPTD2+ALN3.

- All fractures have an associated acute and continuing disutilities, so the reductions in clinical vertebral, wrist, and other fractures result in an increase on QALYs for TPTD2+ALN3 vs. ALN5.

- Clinical vertebral fractures are modeled as having increased mortality risks, so there are resultant increases in both LTVs, and thus QALYs, for TPTD2+ALN3 vs. ALN5 due to osteoporosis mortality.

- The lifetime horizon model of the analysis reduces to the positive impact of 24-month teriparatide use. Teriparatide’s superior fracture RRR compared to alendronate manifests itself in fewer fractures in this 24-month period, and in the case of clinical vertebral fractures and non-hip fractures over additional 18- and 30-month periods, respectively.

- For TPTD2+ALN3 vs. ALN5 hip, wrist, and other non-hip fractures are discounted at 5% per year, and LTVs and QALYs are discounted at 5% per year.

Discussion & Conclusions

- Teriparatide followed by alendronate may lead to improved fracture and HRQoL outcomes when compared to alendronate only in severe PMO women in Korea.
- Benefits of teriparatide in sequential therapy increase with the severity of PMO as measured by BMD.
- Benefits of sequential therapy after a full regimen of teriparatide depend on subsequent administration of alendronate.

Limitations

- Real-world fracture RRRs for sequential teriparatide-bisphosphate treatment were not available.
- Efficacy assumptions were made based on the utilization of optimal longitudinal fracture-specific RRRs.

- Sensitivity Analyses
  - Tables 6 and 7 show results for TPTD2+ALN7 vs. ALN7 for patients with T-score -2.5 and no previous osteoporotic fractures.
  - Tables 8 and 9 show results for TPTD2+ALN5 vs. ALN7 for patients with T-score -3.0 and two previous fractures.

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References


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