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Review article

Asia-Pacific consensus on long-term and sequential therapy for osteoporosis

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ABSTRACT

Objectives: This study aimed to present the Asia-Pacific consensus on long-term and sequential therapy for osteoporosis, offering evidence-based recommendations for the effective management of this chronic condition. The primary focus is on achieving optimal fracture prevention through a comprehensive, individualized approach.

Methods: A panel of experts convened to develop consensus statements by synthesizing the current literature and leveraging clinical expertise. The review encompassed long-term anti-osteoporosis medication goals, first-line treatments for individuals at very high fracture risk, and the strategic integration of anabolic and anti-resorptive agents in sequential therapy approaches.

Results: The panelists reached a consensus on 12 statements. Key recommendations included advocating for anabolic agents as the first-line treatment for individuals at very high fracture risk and transitioning to anti-resorptive agents following the completion of anabolic therapy. Anabolic therapy remains an option for individuals experiencing new fractures or persistent high fracture risk despite antiresorptive treatment. In cases of inadequate response, the consensus recommended considering a switch to more potent medications. The consensus also addressed the management of medication-related complications, proposing alternatives instead of discontinuation of treatment.

Conclusions: This consensus provides a comprehensive, cost-effective strategy for fracture prevention with an emphasis on shared decision-making and the incorporation of country-specific case management systems, such as fracture liaison services. It serves as a valuable guide for healthcare professionals in the Asia-Pacific region, contributing to the ongoing evolution of osteoporosis management.

1. Introduction

Osteoporosis is characterized by bone microarchitecture deterioration and reduced bone mass and heightens the risk of fragility fractures. The burden of such fractures is especially high in the Asia-Pacific (AP) region, with projections indicating a significant increase in hip fractures from 1,124,060 cases in 2018 to 2,563,488 cases in 2050. This increase will be accompanied by an increase in the financial burden from 9.5 billion USD to 15 billion USD [1]. Lifestyle modifications and pharmacological treatments play pivotal roles in osteoporosis management, underscoring the importance of a holistic approach [2]. Effective support systems such as fracture liaison services (FLSs) have proven successful in mitigating fracture risks [3].

As a chronic condition, osteoporosis necessitates long-term management, but patient adherence to long-term drug regimens remains unsatisfactory [4,5]. Additionally, certain therapies have notable adverse effects, ranging from musculoskeletal discomfort to rare but severe complications, such as medication-related osteonecrosis of the jaw (MRONJ) and atypical femoral fractures (AFFs), when used for prolonged use [6,7]. Evaluating the strengths, limitations, and long-term benefit-to-risk ratios of each medication is crucial, as is a specific focus on advancements in long-term and sequential treatment strategies.

Recognizing the significance of long-term and sequential therapy

[8–10], the Taiwanese Osteoporosis Association (TOA) organized the "Asia-Pacific Consensus Meeting on Long-term and Sequential Therapy for Osteoporosis" in Taiwan on October 12 and 13, 2023. Endorsed by the Asian Federation of Osteoporosis Societies (AFOS), the conference convened AP experts to assess and refine strategies for preventing fragility fractures. The detailed outcomes and recommendations from this conference are presented in this manuscript.

2. Methods

To establish consensus recommendations, experts in osteoporosis from the Asia-Pacific region were solicited to reach a consensus through a comprehensive review process. All the panelists participated in a preliminary phase to formulate a provisional draft of the statements. The subsequent consensus meetings in Taiwan along with the Congress of the Asian Federation of Osteoporosis Societies in 2023 facilitated in-person discussions among the on-site panelists. The panelists included representatives from Hong Kong (Ching-Lung Cheung), Japan (Satoshi Mori and Akira Taguchi), Korea (Yoon-Sok Chung and Kwang-Kyoun Kim), Malaysia (Joon-Kiong Lee and Swan Sim Yeap), the Philippines (Julie Li-Yu), Singapore (Seng Bin Ang), Taiwan (Ding-Cheng Chan, Chung-Hwan Chen, Hsuan-Yu Chen, Jung-Fu Chen, Hai-Hua Chuang, Chun-Feng Huang, Jawl-Shan Hwang, Sung-Yen Lin, Chien-An Shih, Ta-Wei Tai, Shih-Te Tu, Chih-Hsing Wu, and Rong-Sen Yang), and Thailand (Natthinee Charatcharoenwitthaya, Unnop Jaisamrarn, and Vilai Kuptniratsaikul). The panelists critically examined the most recent data and engaged in thorough discussions on each assertion during the consensus meetings until a unanimous agreement was reached.

Furthermore, the final statements were scrutinized by additional offsite reviewers from various regions, including Australia (Peter Ebeling), China (Huipeng Shi), India (Sanjay Bhadada), Korea (Kyu Ri Hwang), Macau (Wai Sin Chan and Hou Ng), Malaysia (Fen Lee Hew), Nepal (Dipendra Pandey), New Zealand (Ian Reid), Singapore (Manju Chandran), Spain (Fernando Marin and Francisco Javier Nistal Rodríguez), Sri Lanka (Sarath Lekamwasam), Switzerland (Serge Ferrari), Taiwan (Yin-Fan Chang, Fang-Ping Chen, and Keh-Sung Tsai), the UK (Eugene McCloskey), the USA (Michael Lewiecki) and Vietnam (Lan T Ho-Pham, Tuan Van Nguyen, Van Hy Nguyen). This comprehensive review process ensured the robustness and validity of the consensus statements.

3. Results

Experts in the panel agreed that long-term and sequential therapy is necessary for the modern-day management of osteoporosis. As a chronic disease, osteoporosis should be treated or monitored throughout life. Patients may receive more than one anti-osteoporosis medication during their lifetime. A general recommendation for principles of sequential therapy may help physicians and patients make decisions regarding their treatment plans. The following 12 statements of recommendations were made (Table 1).

Table 1
Summary of the 12 statements in the Asia-Pacific consensus on long-term and sequential therapy for osteoporosis.

Goals	**Drug holidays**
1. Osteoporosis is a chronic disease. Long-term and sequential therapy are essential strategies for primary and secondary fracture prevention.	8. Drug holidays following bisphosphonate therapy should be considered only for people who have achieved adequate increases in BMD and/or remained fracture free. Regular fracture risk reassessments are needed.
2. The goal of long-term anti-osteoporosis medications is to reduce fragility fracture risk.	**Transitions due to adverse effects**
Choices of transition	9. Teriparatide or selective estrogen receptor modulators can be considered treatment options for people with osteoporosis who have developed medication-related osteonecrosis of the jaw instead of stopping anti-osteoporosis medications.
3. For people at very high fracture risk, anabolic agents are recommended as the first-line treatment. Injectable antiresorptive agents can be prescribed as alternatives to anabolic agents.	10. Teriparatide can be considered a choice of sequential therapy for people with osteoporosis who have developed atypical femoral fractures.
4. Antiresorptive agents should be prescribed after the completion of anabolic therapy as a sequential therapeutic strategy.	**Considerations for policy making**
5. Anabolic therapy should be considered for people who develop new fractures or who have ongoing high fracture risk despite antiresorptive treatment.	11. Long-term and sequential therapy should be individualized based on shared decision-making. Country-specific case management systems, such as fracture liaison services, should be implemented to enhance treatment compliance, adherence, and fracture prevention.
6. Switching to a more potent bisphosphonate, denosumab, or anabolic agent is an option for people with inadequate response to initial anti-osteoporosis medications.	12. Long-term and sequential therapy for osteoporosis is cost-effective for the healthcare system.
7. Bisphosphonates should be prescribed after stopping denosumab to prevent rebound phenomenon with accelerated bone loss and/or multiple vertebral fractures. A selective estrogen receptor modulator is an alternative option for patients who are unable to take bisphosphonates.	

3.1. Statement 1: osteoporosis is a chronic disease. Long-term and sequential therapy are essential strategies for primary and secondary fracture prevention

Osteoporosis is considered a chronic disease. The incidence of osteoporosis in postmenopausal women increases with advancing age. The life expectancy of women in AP countries is currently more than 80 years, and the population is continuing to age. Many women have long postmenopausal periods and are at high risk of fragility fractures. However, osteoporosis is underdiagnosed even among people who have fragility fractures. Like other chronic diseases, osteoporosis management is compromised by suboptimal medication adherence, resulting in an increased risk of fractures and all-cause mortality [11]. The dropout rate from anti-osteoporosis treatment is still high. Approximately 50%–70% of patients discontinue their anti-osteoporosis medications within one year of initiating therapy [5]. These people may have a higher risk of fractures than people who continue their therapy [12,13].

The specialists attending the consensus meeting highlighted the concept that long-term and sequential therapy are essential strategies for primary and secondary fracture prevention [14,15]. Therefore, developing a strategy for prolonged periods of time and sequential therapy for osteoporotic medication treatment that is both effective and safe is mandatory [8–10].

3.2. Statement 2: the goal of long-term anti-osteoporosis medications is to reduce fragility fracture risk

The goal of current long-term anti-osteoporosis medications is to reduce fracture risk by achieving meaningful increases in bone mineral density (BMD). While improving BMD is a measurable outcome, the ultimate objective is to reduce the risk of fragility fractures. By minimizing the risk of fractures, individuals can maintain their quality of life, independence, and overall well-being. Therefore, the panelists of the consensus meeting all agreed that fracture prevention is the most crucial goal of osteoporosis treatment, ensuring the long-term health and mobility of patients.

3.3. Statement 3: for people at very high fracture risk, anabolic agents are recommended as the first-line treatment. Injectable antiresorptive agents can be prescribed as alternatives to anabolic agents

For individuals at very high risk of fracture, anabolic agents are recommended as first-line treatments because anabolic agents tend to increase BMD more rapidly and reduce fracture risk in a shorter time than antiresorptive agents [16–20]. In a study comparing teriparatide with risedronate in postmenopausal women with osteoporotic vertebral fractures, teriparatide was found to be more effective at reducing back

pain and improving fracture outcomes [21]. Additionally, the VERO trial demonstrated that among postmenopausal women with severe osteoporosis, patients receiving teriparatide had a significantly lower risk of new vertebral and clinical fractures than did those receiving risedronate [22]. In another study of glucocorticoid-induced osteoporosis (GIOP), teriparatide was also more effective at increasing BMD and reducing new vertebral fractures than was alendronate [23].

In the ARCH study, which compared romosozumab and alendronate for fracture prevention in 4093 women with postmenopausal osteoporosis and a fragility fracture, the results also showed that patients who received romosozumab treatment for 12 months followed by alendronate had significantly lower risks of fracture than did those who received alendronate alone [24]. Abaloparatide is the other anabolic agent for people at very high risk of fracture. However, it was not marketed in the AP region at the time of this consensus.

While anabolic agents are recommended as first-line treatments in very high-risk patients, parenteral antiresorptive agents can be considered alternative treatments. The AACE guidelines and guidelines from AP regions also suggest the use of the injectable antiresorptive agents such as denosumab and zoledronate [16–19].

3.4. Statement 4: antiresorptive agents should be prescribed after the completion of anabolic therapy as a sequential therapeutic strategy

Most of the clinical guidelines from the AP region and other areas recommend treatment with antiresorptive osteoporosis therapies after completing a course of anabolic agents to maintain bone density gains [16–19,25]. The FRAME study revealed that patients receiving denosumab after 12 months of romosozumab treatment had a sustained reduction in fracture risk and further increase in BMD through the 2-year treatment sequence [26] and after an additional year of denosumab treatment [27]. The sequential use of alendronate or ibandronate following romosozumab treatment maintained the BMD at the lumbar spine and total hip [24,28].

The DATA-Switch study showed that subjects who received teriparatide for 2 years and then switched to sequential therapy with denosumab for 24 months had substantially increased BMD [29]. Alendronate after parathyroid hormone therapy was also proven to maintain or increase the BMD [30]. The ACTIVExtend study further demonstrated that 24 months of alendronate after a complete course of abaloparatide for postmenopausal osteoporosis is an effective strategy for sequential therapy [31]. A Japanese randomized trial confirmed the effectiveness of sequential bisphosphonate or denosumab treatment after a course of teriparatide and revealed that denosumab treatment was more effective at increasing BMD and potentially beneficial for greater fracture prevention [32]. Another European retrospective, observational study also showed that sequential denosumab treatment appeared to yield more additional BMD gain after stopping teriparatide therapy than did bisphosphonate treatment [33]. Furthermore, raloxifene may maintain spine BMD and increase hip BMD after the discontinuation of teriparatide [34].

3.5. Statement 5: anabolic therapy should be considered for people who develop new fractures or who have ongoing high fracture risk despite antiresorptive treatment

Despite treatment with antiresorptive agents, some people still suffer new or recurrent fractures. More aggressive treatment is needed for those people because they are at very high risk of fractures. However, as indicated in statement 3, anabolic agents are the preferred first-line treatment for people who have very high risks of fractures, and there is evidence supporting the transition from antiresorptive agents to anabolic therapy. The STRUCTURE study revealed that both romosozumab and teriparatide can further increase BMD at the lumbar spine after the transition from alendronate. Romosozumab also led to gains in hip BMD, which was not observed in patients who used teriparatide [35]. Another study showed that switching to romosozumab after 1 year of denosumab treatment improved lumbar spine BMD, maintained total hip BMD and possibly prevented the rapid increase in the levels of bone turnover markers expected upon denosumab discontinuation [36]. According to the same study and AACE guidelines, retreatment with romosozumab is possible even if the patients have been treated with a course of romosozumab previously [16,36].

Adding teriparatide to antiresorptive agents might also be a therapeutic strategy for people at very high risk of fracture. The DATA Switch study showed that the combination of teriparatide and denosumab had a greater effect on the increase in BMD than the individual drugs [29]. In a study of women with osteoporosis treated with antiresorptives, greater bone turnover increases were observed after switching to teriparatide, while greater BMD gains were achieved after adding teriparatide [37]. Whether switching to teriparatide from an antiresorptive agent for patients at very high fracture risk can further decrease fracture risk is still under debate. Transient bone loss after the transition to teriparatide is a major concern, especially in the hip area [29,37].

3.6. Statement 6: switching to a more potent bisphosphonate, denosumab, or anabolic agent is an option for people with inadequate response to initial anti-osteoporosis medications

Poor adherence to oral antiresorptive agents might contribute to suboptimal outcomes after anti-osteoporosis treatment [38]. In such circumstances, switching to a more potent bisphosphonate might be a solution. The transition from oral alendronate to yearly zoledronate infusion may maintain therapeutic efficacy while improving drug adherence [39]. Another study also showed that the transition from alendronate to zoledronate yields an increase in BMD at the lumbar spine and total hip [40]. Intravenous ibandronate can also be considered according to availability.

The STAND study showed that the transition to denosumab led to greater increases in BMD at all measured skeletal sites and a greater reduction in bone turnover than continued alendronate treatment [41]. The transition from oral alendronate to denosumab also seems more effective than the transition to zoledronate. Denosumab was associated with greater increases in BMD than zoledronate at all measured skeletal sites and greater inhibition of bone remodeling [40]. For long-term bisphosphonate users, switching to denosumab or teriparatide may still increase BMD at the spine, but switching to denosumab was associated with greater increases in BMD at the total hip and femoral neck. The transition to teriparatide causes transient bone loss at the hip for the first year, but whether this change affects fracture risk is unknown [42]. At present, the role of strontium is very limited, and additional solid evidence is needed. People at very high fracture risk should consider directly transiting to anabolic therapy, as previously discussed in statement 5.

3.7. Statement 7: bisphosphonates should be prescribed after stopping denosumab to prevent rebound phenomenon with accelerated bone loss and/or multiple vertebral fractures. A selective estrogen receptor modulator is an alternative option for patients who are unable to take bisphosphonates

Rapid bone loss after denosumab discontinuation causes an increase in the risk of multiple vertebral fractures. The duration of previous denosumab use also affects the risk of multiple vertebral fractures. Compared with people who received denosumab for less than 3 years, those who received denosumab for more than 3 years might have an increased risk of vertebral fractures after discontinuation [43]. Sequential therapy with other antiresorptive agents is critical for this population.

Bisphosphonates, especially zoledronate, may prevent rapid bone loss after the discontinuation of denosumab [44–47]. A retrospective study revealed that bone loss after denosumab discontinuation is

prevented by alendronate and zoledronate [44]. However, although zoledronate was proven to be the most powerful antiresorptive agent for stopping bone loss after denosumab discontinuation, it did not fully prevent increased bone turnover and bone loss during the first year [45]. At least 2 years of sequential treatment with zoledronate has been suggested based on the current evidence [46,47].

The evidence that SERMs prevent bone loss after denosumab discontinuation is limited. SERMs only partially preserve BMD after this transition. Decreases in spine and total hip BMD in patients who switched from denosumab to raloxifene were still significant [48]. We recommend the transition to SERMs after denosumab treatment only if other antiresorptive agents are unavailable or appropriate.

3.8. Statement 8: drug holidays following bisphosphonate therapy should be considered only for people who have achieved adequate increases in BMD and/or remained fracture free. Regular fracture risk reassessments are needed

Like denosumab, discontinuation of bisphosphonates may also increase fracture risk [49,50]. Anti-osteoporosis treatment should be continued until the patients have achieved adequate increases in BMD and/or remained fracture free [17–19]. Initial anti-osteoporosis treatment should be maintained for at least 5 years with oral agents or 3–6 years with intravenous bisphosphonates. If the fracture risk remains high, it is recommended to continue treatment with the bisphosphonate or switch to other agents for another 3–5 years, and the fracture risk should be reassessed [17,19,49].

For people who cannot tolerate bisphosphonate treatment but are still at high risk of fracture, prescribing another anti-osteoporosis medication as sequential therapy is strongly recommended instead of just stopping treatment. For patients at very high fracture risk, anabolic therapy may be considered subsequently [16].

3.9. Statement 9: teriparatide or selective estrogen receptor modulators can be considered treatment options for people with osteoporosis who have developed medication-related osteonecrosis of the jaw instead of stopping anti-osteoporosis medications

For people who receive antiresorptive treatment and need invasive oral surgery, whether to stop antiresorptive medications is a matter of debate. Although some specialists have suggested stopping bisphosphonate before dental surgery [51], there is little evidence that short-term discontinuation of bisphosphonates helps to prevent the occurrence of MRONJ resulting from surgical dental procedures [52]. Bone turnover markers are also not useful tools for assessing MRONJ risk [53]. A recent Japanese position paper on MRONJ announced that discontinuation of antiresorptive agents is no longer necessary because fracture risk increases after discontinuation of anti-osteoporosis treatment [54]. Cooperation between physicians and dentists is the key to managing this situation [55].

Drug transition should be considered instead of discontinuation of anti-osteoporosis treatment because the increase in fracture risk makes discontinuation more harmful than beneficial [56,57]. For people who have developed MRONJ with bisphosphonates, teriparatide is the first choice because there is some evidence that it can treat osteoporosis and promote healing of MRONJ [58,59]. SERMs may also be considered because they are associated with only a low risk of MRONJ [60]. Another option is romosozumab, which has also shown a low risk of MRONJ in clinical trials [24,35,61]. However, additional data are needed to confirm the safety of its use in this situation.

Anabolic therapy should be followed by antiresorptive therapy, which is still relatively contraindicated in patients who have MRONJ. The benefits and risks should be considered case by case. This issue remains clinically challenging.

3.10. Statement 10: teriparatide can be considered a choice of sequential therapy for people with osteoporosis who have developed atypical femoral fractures

AFFs are uncommon complications that develop after long-term use of antiresorptive agents. Anabolic agents can be considered sequential therapies for osteoporosis in patients who have or are at high risk of AFFs. Teriparatide is the first choice because some evidence suggests the benefits of teriparatide over other anabolic agents, including improving fracture healing, shortening the fracture healing time, and decreasing the risk of fracture nonunion [62,63]. After teriparatide treatment, raloxifene or denosumab might be considered sequential therapies [64]. If teriparatide is unavailable or contraindicated, raloxifene might be considered an alternative treatment after the occurrence of AFFs.

3.11. Statement 11: long-term and sequential therapy should be individualized based on shared decision-making. Country-specific case management systems, such as fracture liaison services, should be implemented to enhance treatment compliance, adherence, and fracture prevention

Shared decision-making plays a crucial role in osteoporosis treatment, especially in sequential therapy, because there is no single sequence or strategy that can fit all situations. This approach recognizes that patients have unique preferences, values, and goals that should be considered when determining the most appropriate treatment plan. By engaging in shared decision-making, patients and physicians or other healthcare providers can collaboratively discuss the benefits, risks, and potential outcomes and adverse effects of different treatment options. This helps ensure that the chosen treatment aligns with the patient's preferences and goals, leading to improved treatment adherence and patient satisfaction.

Recognizing the diverse healthcare landscapes across the AP region, the consensus emphasizes the need for a country-specific approach, such as FLS. Given that osteoporosis is a chronic disease, long-term management or follow-up is mandatory to optimize outcomes [65,66]. FLSs are crucial for the appropriate management of patients with osteoporosis. Early identification, comprehensive assessment, and rapid treatment initiation are possible. FLSs also facilitate communication and coordination between various healthcare providers involved in the management of osteoporotic patients.

It is known that better adherence to anti-osteoporosis treatment may yield better outcomes and survival [67]. The education and support provided by FLS case managers regarding osteoporosis, fracture prevention strategies, and medication adherence could also contribute to a reduction in subsequent fractures and improved patient outcomes.

3.12. Statement 12: long-term and sequential therapy for osteoporosis is cost-effective for the healthcare system

Long-term and/or sequential therapy for osteoporosis has been shown to be cost-effective for the healthcare system [14,15]. Osteoporosis is a chronic condition that requires ongoing management to sustainably maintain a low risk of fracture. Universal screening for the elderly and treatment were estimated to be cost-effective [68,69]. Studies from Taiwan have also demonstrated that continuous treatment with appropriate medications can significantly reduce the risk of fractures and related healthcare costs, especially in the population aged > 70 years [70,71]. By reducing fracture risk, the costly hospitalizations, surgeries, and rehabilitative care that often accompany osteoporotic fractures can be minimized.

Additionally, sequential therapy, which involves switching to different medications over time, might also theoretically improve outcomes and cost-effectiveness [72]. However, limited studies investigating the cost-effectiveness of sequential therapy with various strategies have been conducted. However, further research is needed to

prove this concept [73].

4. Discussion

The successful development of this consensus represented a significant milestone in osteoporosis management in the AP region. The 12 statements addressed the complexities of long-term treatment strategies and underscored the critical importance of adopting a long-term and sequential approach to osteoporosis treatment. Acknowledging the chronic nature of the disease, our recommendations emphasized sustained efforts in osteoporosis treatment and lowering the fracture risk over the patient's lifetime.

A pivotal recommendation emerging from this consensus was the prioritization of anabolic therapy for individuals at very high fracture risk, followed by the strategic introduction of antiresorptive agents. This tailored strategy was particularly crucial for those who have very high fracture risk [16–20]. We also emphasized drug transitions instead of discontinuation of treatment while facing difficult situations such as adverse effects or poor response. Tailoring interventions to the unique challenges and resources of each country ensured the feasibility and effectiveness of long-term strategies. A clinical path diagram is postulated as a reference for practical consideration in the transition of anti-osteoporosis medication (AOM) (Fig. 1).

This consensus also advocated for the integration of long-term and sequential osteoporosis therapy considerations into healthcare policies and insurance systems. As osteoporosis poses a substantial burden on individuals and healthcare systems in the AP region, policy makers and insurance providers should recognize the cost-effectiveness of comprehensive, sustained treatment strategies [14,15,68,70,71].

5. Conclusions

In conclusion, this consensus provides a robust foundation for enhancing the management of osteoporosis and serves as a valuable guide for healthcare professionals, policymakers, and stakeholders investing in optimizing osteoporosis care across the AP region.

Conflicts of interest

The authors disclosed the following conflicts of interest.

1. **Ta-Wei Tai** received honoraria for lectures, meetings, and/or travel from Amgen and Alvogen/Lotus.
2. **Swan Sim Yeap** has received honoraria for lectures from Amgen.
3. **Natthinee Charatcharoenwitthaya** received honoraria for lectures, meetings, and/or travel from Amgen, Alvogen, and Zuellig Pharma.
4. **Akira Taguchi** has received lecture fees from Asahi Kasei Pharma Corp., Daiichi Sankyo Co. Ltd, Chugai Pharmaceutical Co. Ltd, and Teijin Pharma Ltd.
5. **Peter R Ebeling** has received research funding from Amgen, Alexion and Sanofi, and honoraria from Amgen, Alexion and Kyowa Kirin.
6. **Fernando Marin** has received honoraria for lectures from DKSH and Zuellig Pharma. He is a former employee of Eli Lilly and Company.
7. **Yoon-Sok Chung** has received research funding from Samsung Bioepis and honoraria from Amgen, Alvogen, Celltrion, Daewoong, Hanlim, and Yuyu.
8. **Ian R Reid** has received speaking fees from Amgen and Medison Pharma.

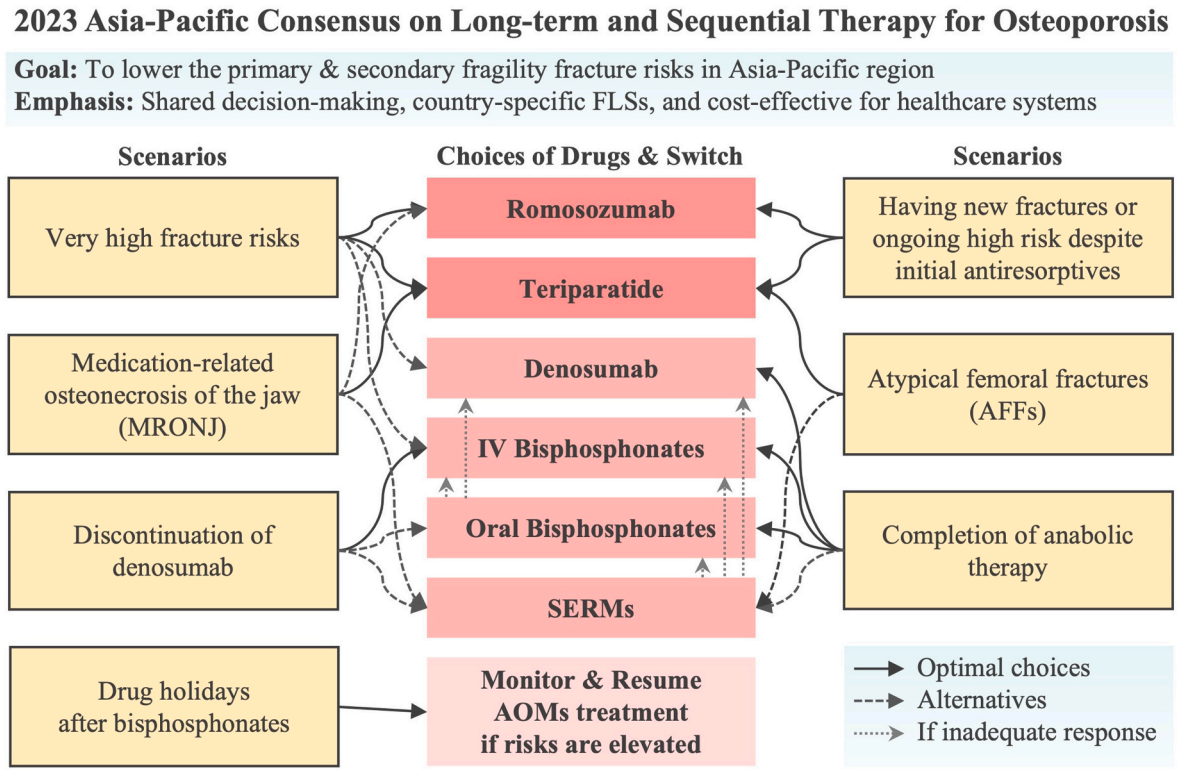

Fig. 1. Diagram of major concepts of the Asia-Pacific consensus on long-term and sequential therapy for osteoporosis.
FLS, fracture liaison service; IV, intravenous; SERMs, selective estrogen receptor modulators; AOM, anti-osteoporosis medication.

9. **Manju Chandran** has received honoraria and travel sponsorships from Amgen, DKSH, and Kyowa Kirin.
10. **E. Michael Lewiecki** - Amgen: investigator, consultant, speaker; Radius: investigator, consultant; Kyowa Kirin: consultant, speaker; Ultragenyx: investigator; Angitia: consultant; Ascendis: consultant.
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15. **The other authors** reported that they have nothing to declare for potential conflicts of interest.

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