Glucocorticoids (GC) (or steroid hormones) are widely used to treat various inflammatory, immunologic, and allergic disorders that cause severe pain, respiratory, bowel, hepatic, hematologic, renal, and skin disorders. A decrease in bone mineral density (BMD) by 10% occurs within the first several months of starting GC therapy, although bone mineral density decreases more slowly thereafter, with the annual loss being approximately 2–4%. It is important to prevent bone loss and to decrease fracture risk as early as possible after the start of GC therapy. Based on the concept of early prevention and treatment of GO, the American College of Rheumatology (ACR) guidelines recommend this for the prevention and treatment of GO.

Based on such new evidence regarding GO, the ACR recommendations was updated to incorporate FRAX® as an assessment tool for fracture risk in the 2012 revision. The Joint GC Study Group developed a comprehensive system for the diagnosis and treatment of osteoporosis in Japan, through which it is possible to prevent bone loss and to decrease fracture risk in elderly women (≥75 years of age) at risk for osteoporosis. The Japanese Society for Bone and Mineral Research (JSBMR) has also published a framework for the development of guidelines for preventive care and treatment guidelines for physicians to initiate drug therapy in clinical practice.

In response to these international changes related to GO, the Japanese Society for Bone and Mineral Research (JSBMR) set up a Committee for the Revision of the Guidelines on the Management and Treatment of Glucocorticoid-induced Osteoporosis.

### 1. Subjects

In order to determine risk factors for fractures, the committee randomly selected data on the following Japanese GO patients: a patient in a randomized controlled trial (RCT) on the primary prevention and treatment of GC-induced osteoporosis (GO) with alendronate plus estradiol. The GO Study Group and the International Society for Clinical Densitometry (ISCD) of the C-Japan Group and the Japanese National S莫名其妙sion Hospital (Cohort B), the Comprehensive Study of the Foundation of Endocrinology and Metabolism (Cohort C), and patients in an RCT of the Ministry of Health, Labor, and Welfare (Cohort D) were the major contributing centers.

### 2. Phase 1 analysis

#### 2.1. Identification of factors predicting fractures

<table>
<thead>
<tr>
<th>Factor</th>
<th>Hazard ratio</th>
<th>95% confidence interval</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>1.077</td>
<td>1.062–1.092</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Gender (male vs. female)</td>
<td>1.373</td>
<td>1.131–1.666</td>
<td>0.0018</td>
</tr>
<tr>
<td>GC dose (mg/day)</td>
<td>1.030</td>
<td>1.016–1.044</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Lumber bone mineral density (BMD) (mg/cm²)</td>
<td>1.516</td>
<td>1.455–1.581</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>FSH/fructose ratio</td>
<td>3.412</td>
<td>2.409–4.832</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

#### 2.2. Biochemical factors

<table>
<thead>
<tr>
<th>Factor</th>
<th>Hazard ratio</th>
<th>95% confidence interval</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biochemical factors</td>
<td>2.475</td>
<td>1.774–3.441</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

### 3. Determining the optimal cut-off score for intervention and outline of the updated guideline (Phase 3)

#### 3.1. Determining the optimal cut-off score for discrimination between fracture and non-fracture patients

The cut-off score that efficiently separates fracture and non-fracture cases by ROC analysis was 0.388.

#### 3.2. Verifying the cut-off score for intervention threshold for physicians to initiate drug therapy

The cut-off score for intervention threshold for physicians to initiate drug therapy was determined to be 0.400.

### 4. Recommended pharmacotherapy of GO (Phase 4)

#### 4.1. Bone resorption inhibitors

- **Bisphosphonates**
  - Alendronate
  - Ibandronate
  - Risedronate
  - Proliferating cell nuclear antigen (PCNA) inhibitors

#### 4.2. Parathyroid hormone (PTH) analogues

- **Teriparatide**
  - Calcitriol

#### 4.3. Sclerostin monoclonal antibody

- **Dacetumab**


- **General guidance**
  - **Risk factors**
    - Bone mineral density
    - Age
    - Gender
  - **Assess clinical risk factors and calculate individual patient’s score**
    - Prior fracture (2 points)
    - Age (≥75 years, 3 points)
    - Fracture (5 points)
  - **Treatments**
    - First-line treatment: alendronate
    - Second-line treatment: denosumab
    - Tertiary: recombinant PTH

### Conclusion

The updated guidelines for GO are expected to improve the management and treatment of GO in Japan, thereby contributing to the prevention and treatment of osteoporosis.