Denosumab Therapy in Postmenopausal Women with Osteoporosis: Results from the First Two Years of the Freedom Trial Extension

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Denosumab (DMAb) is an approved therapy for postmenopausal women with osteoporosis at increased risk for fracture. The favorable risk/benefit of DMAb was shown in the pivotal, placebo-controlled, 3-year FREEDOM trial. All women who completed FREEDOM were invited to participate in an extension study to monitor DMAb safety and efficacy for up to 10 years. In the extension, all women receive 60 mg DMAb every 6 months. For the FREEDOM placebo group, the data here reflect up to 4 DMAb doses (2 years; cross-over group). For the FREEDOM DMAb group, the data reflect up to 10 DMAb doses (5 years; long-term group). The efficacy and general safety long-term data were previously presented. Here, we report the cross-over data and additional safety data.

Of those who completed FREEDOM, 4550 (70%) enrolled in the extension (2207 cross-over; 2343 long-term). During the first 2 years of DMAb, the cross-over group had significant ($P<0.0001$) gains in lumbar spine (7.9%) and total hip (4.1%) BMD, similar to those in the DMAb group in the first 2 years of FREEDOM. CTX was rapidly and similarly reduced after the 1st (cross-over) or 7th (long-term) DMAb dose with the characteristic attenuation of this effect at the end of the dosing period. In the cross-over group, yearly incidences of new vertebral and nonvertebral fractures were lower than in the FREEDOM placebo group. Fracture incidence remained low in the long-term group.

Incidences of adverse events (AEs) and serious AEs (SAEs) in the cross-over group were similar to or lower than in the placebo and DMAb FREEDOM groups, and AEs or SAEs did not increase over time with long-term DMAb. In particular, subject incidence rates of SAEs of...
infection in years 4 and 5 of DMAb were similar to or lower than yearly rates in the FREEDOM placebo group. This was also the case for individual SAEs of infection including pneumonia, urinary tract infection, diverticulitis, gastroenteritis, cellulitis/erysipelas, and bronchopneumonia. Two oral AEs were adjudicated to ONJ in the cross-over group and none in the long-term group; both healed completely and 1 woman continued DMAb. No atypical fractures occurred. The FREEDOM extension study safety and efficacy results are consistent with the original FREEDOM study observations and provide long-term exposure data for up to 5 years in 2343 women.

Disclosures: HGB: Investigator, Amgen, Merck & Co., Nordic Bioscience; Advisory Group Member, Amgen, Merck & Co., Novartis Pharmaceuticals; Honoraria, Amgen, Merck & Co.; Speaker Bureau Member, Amgen. RC: Investigator, Servier, Merck & Co., Sanofi-Aventis, Novartis Pharmaceuticals, Warner Chilcott; Consultant, Servier, Novartis Pharmaceuticals, Amgen, Merck & Co. MLB: Speaker, Amgen, Merck & Co., Servier, Warner Chilcott, GlaxoSmithKline, Eli Lilly & Company. JPB: Coinvestigator, Abbott Laboratories, Roche Pharmaceuticals; Principal Investigator, Amgen, Eli Lilly & Company, Merck & Co., Novartis Pharmaceuticals, Pfizer, Inc., Sanofi-Aventis, Serono, Servier, Warner Chilcott; Advisory Group Member, Amgen, Eli Lilly & Company, Novartis Pharmaceuticals, Warner Chilcott; Speaker, Amgen, Eli Lilly & Company, Merck & Co., Novartis Pharmaceuticals, Roche Pharmaceuticals; Consultant, Sanofi-Aventis. EC: Investigator, Eli Lilly & Company, Novartis Pharmaceuticals, Roche Pharmaceuticals, Amgen, Pfizer, Inc., Servier, Merck & Co., Serono, Astra Zeneca, Merck Sharp & Dohme, SantoSolve AS, Danone Research; Speaker, Servier, Roche Pharmaceuticals. NSD: Employee, Amgen. AG: Employee, Amgen. ZM: Principal Investigator, Amgen, Astra Zeneca, Bayer, Inc., Eli Lilly & Company, Merck & Co., Novartis Pharmaceuticals, NPS Allelix, Proctor & Gamble, Aventis Pharmaceuticals, Sanofi-Aventis, Roche Pharmaceuticals, Wyeth Pharmaceuticals; Medical Advisory Board Member, GlaxoSmithKline, Sanofi-Aventis; Speaker, Novartis Pharmaceuticals, Sanofi-Aventis, Roche Pharmaceuticals; Committee Member, Novartis Pharmaceuticals. SR: Principal Investigator, Amgen; Speaker, Eli Lilly & Company; Principal Investigator, Novartis Pharmaceuticals, Pfizer, Inc., Roche Pharmaceuticals; Speaker Bureau Member, Sanofi-Aventis. J-YR: Consultant, Servier, Novartis Pharmaceuticals, Negma, Eli Lilly & Company, Wyeth Pharmaceuticals, Amgen, GlaxoSmithKline, Roche Pharmaceuticals, Merck & Co., Nycomed, NPS, Theramex, UCB; Speaker, Merck Sharp & Dohme, Eli Lilly & Company, Rottapharm, IBSA, Genevrier, Novartis Pharmaceuticals, Servier, Roche Pharmaceuticals, GlaxoSmithKline, Teijin, Teva, Ebewe Pharma, Zodiac, Analis, Thermamex, Nycomed, Novo Nordisk; Investigator, Bristol-Myers Squibb, Merck Sharp & Dohme, Rottapharm, Teva, Eli Lilly & Company, Novartis Pharmaceuticals, Roche Pharmaceuticals, GlaxoSmithKline, Amgen, Servier. CR: Investigator, Amgen; Consultant, Amgen; Speaker, Amgen. SRC: Speaker, Amgen; Consultant, Amgen. CL: Employee, Amgen; Employee, Amgen. SP: Consultant, Amgen, Merck & Co., Novartis Pharmaceuticals, Eli Lilly & Company, Proctor & Gamble; Consultant, GlaxoSmithKline. Nothing to Disclose: M-AK, DM, HR, JAR

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