The FREEDOM trial open-label extension is evaluating the long-term safety and efficacy of denosumab (DMAb) for up to 10 years. We report the intention-to-treat (ITT) results for women who participated in the first 3 years of the extension, representing up to 6 years of DMAb exposure. We also report the results for the pre-specified per protocol (PP) and modified per protocol (MPP) subsets.

During the extension, each woman is scheduled to receive 60 mg DMAb every 6 months and supplemental calcium and vitamin D daily. For the analyses here, women from the FREEDOM placebo group received 3 years of DMAb (cross-over group) and women from the FREEDOM DMAb group received 3 more years of DMAb for a total of 6 years (long-term group). The PP and MPP subsets excluded subjects who were non-compliant with the protocol and the MPP subset further excluded subjects who missed ≥ 2 doses of DMAb during the extension.

Of the 5928 women eligible for the extension, 4550 (77%) enrolled (N = 2207 cross-over; N = 2343 long-term). During the first 3 years of DMAb treatment during the extension, the cross-over group had significant gains in bone mineral density (BMD) at the lumbar spine and total hip, and further significant increases in BMD occurred over years 4 to 6 in the long-term group. Serum CTX was rapidly and similarly reduced after the 1st (cross-over) or 3rd (long-term) DMAb dose with the characteristic attenuation observed at the end of the dosing period.

In FREEDOM, DMAb reduced the risk of new vertebral (2.3% DMAb vs 7.2% placebo) and nonvertebral (6.5% DMAb vs 8.0% placebo) fractures over 3 years. In the first 3 years of the extension, for the cross-over group, incidences of new vertebral (2.8%) and nonvertebral (5.6%) fractures were similar to the FREEDOM DMAb group. In the long-term group, fracture incidences remained low (3.5% for new vertebral and 3.8% for nonvertebral fractures). The fracture efficacy results for the PP and MPP subsets were consistent with the ITT analysis. Incidences of adverse events (AEs) and serious AEs did not increase over time with DMAb. No subjects developed neutralizing antibodies to DMAb.

DMAb treatment for 3 years in the cross-over group reproduced FREEDOM efficacy observations. DMAb treatment for 6 years (long-term group) remained well tolerated, maintained reduced bone turnover, and continued to significantly increase BMD. Fracture incidence remained low in the ITT, PP, and MPP populations.

Sources of Research Support: Amgen Inc. sponsored this study.

Disclosures: HGB: Consultant, Amgen, Merck & Co., Takeda, Tarsa; Investigator, Amgen, Merck & Co., Nordic Bioscience A/S, Novartis Pharmaceuticals, Takeda, Tarsa; Speaker Bureau Member, Amgen. JPB: Investigator, Amgen, Eli Lilly & Company, Merck & Co., Novartis Pharmaceuticals, Warner Chilcott Pharmaceuticals; Advisory Group Member, Amgen, Eli Lilly & Company, Merck & Co., Novartis Pharmaceuticals, Warner Chilcott Pharmaceuticals; Speaker, Amgen, Eli Lilly & Company, Novartis Pharmaceuticals. RC: Advisory Group Member, Amgen, Eli Lilly & Company, Servier, Merck & Co., Novartis Pharmaceuticals; Speaker, Amgen, Ipsen, Servier, Roche Pharmaceuticals. NF: Employee, Amgen. EC: Investigator, Eli Lilly & Company, Novartis Pharmaceuticals, Roche Pharmaceuticals, Amgen, Pfizer, Inc., Servier, Merck Serono S.A., Astra Zeneca, Ardea Biosciences, INC Research, Shire, Biotest AG, Andromeda Biotech Ltd., Johnson & Johnson; Speaker, Amgen, Roche Pharmaceuticals, Servier, Zentiva. SCR: Advisory Group Member, Novartis Pharmaceuticals, Aventis Pharmaceuticals; Study Investigator, Bristol-Myers Squibb, Amgen, Roche Pharmaceuticals, Pfizer, Inc. JYR: Advisory Group Member, Servier, Novartis Pharmaceuticals, Nextra, Lilly USA, LLC, Wyeth Pharmaceuticals, Genzyme Corporation, Roche Diagnostics, Merck & Co., Nycomed, NPS, Theramex, UCB; Speaker, Merck Sharp and Dohme, Lilly USA, LLC, Rottapharm, JBSA, Genevrier, Novartis Pharmaceuticals, Roche Pharmaceuticals, GlaxoSmithKline, Teijin, Teva, Ebewee Pharma, Zodiak, Analis, Theramex, Nycomed, Novo Nordisk; Investigator, Bristol-Myers Squibb, Merck Sharp and Dohme, Rottapharm, Teva, Lilly, Novartis, Roche, GlaxoSmithKline, Amgen, Servier. NSD: Employee, Amgen. AW: Employee, Amgen. MLG: Employee, Amgen. RBW: Employee, Amgen. SP: Medical Advisory Board Member, Amgen, Eli Lilly & Company, Novartis Pharmaceuticals, Warner Chilcott Pharmaceuticals; Speaker Bureau Member, Amgen. NG: Employee, Amgen. EC: Investigator, Eli Lilly & Company, Merck & Co., Novartis Pharmaceuticals, Teijin, Teva, Aventis Pharma, Zodiak, Analis, Theramex, Nycomed, Novo Nordisk; Consultant, Gedeon Richter; Speaker, Amgen, Eli Lilly & Company, Merck & Co., Novartis Pharmaceuticals; Investigator, Amgen, Novo Nordisk; Speaker Bureau Member, Amgen. JPB: Investigator, Eli Lilly & Company, Merck & Co., Novartis Pharmaceuticals, Warner Chilcott Pharmaceuticals; Speaker, Amgen, Ipsen, Servier, Roche Pharmaceuticals. NF: Employee, Amgen. EC: Investigator, Eli Lilly & Company, Novartis Pharmaceuticals, Warner Chilcott Pharmaceuticals; Speaker, Amgen, Ipsen, Servier, Roche Pharmaceuticals. NF: Employee, Amgen. EC: Investigator, Eli Lilly & Company, Novartis Pharmaceuticals, Warner Chilcott Pharmaceuticals; Speaker, Amgen, Ipsen, Servier, Roche Pharmaceuticals. NF: Employee, Amgen. EC: Investigator, Eli Lilly & Company, Novartis Pharmaceuticals, Roche Pharmaceuticals, Amgen, Pfizer, Inc., Servier, Merck Serono S.A., Astra Zeneca, Ardea Biosciences, INC Research, Shire, Biotest AG, Andromeda Biotech Ltd., Johnson & Johnson; Speaker, Amgen, Roche Pharmaceuticals, Servier, Zentiva. SCR: Advisory Group Member, Novartis Pharmaceuticals, Aventis Pharmaceuticals; Study Investigator, Bristol-Myers Squibb, Amgen, Roche Pharmaceuticals, Pfizer, Inc. JYR: Advisory Group Member, Servier, Novartis Pharmaceuticals, Nextra, Lilly USA, LLC, Wyeth Pharmaceuticals, Genzyme Corporation, Roche Diagnostics, Merck & Co., Nycomed, NPS, Theramex, UCB; Speaker, Merck Sharp and Dohme, Lilly USA, LLC, Rottapharm, JBSA, Genevrier, Novartis Pharmaceuticals, Roche Pharmaceuticals, GlaxoSmithKline, Teijin, Teva, Ebewee Pharma, Zodiak, Analis, Theramex, Nycomed, Novo Nordisk; Investigator, Bristol-Myers Squibb, Merck Sharp and Dohme, Rottapharm, Teva, Lilly, Novartis, Roche, GlaxoSmithKline, Amgen, Servier. NSD: Employee, Amgen. AW: Employee, Amgen. MLG: Employee, Amgen. RBW: Employee, Amgen. SP: Medical Advisory Board Member, Amgen, Eli Lilly & Company, Novartis Pharmaceuticals, Warner Chilcott Pharmaceuticals; Speaker Bureau Member, Amgen. NG: Employee, Amgen. EC: Investigator, Eli Lilly & Company, Merck & Co., Novartis Pharmaceuticals, Teijin, Teva, Aventis Pharma, Zodiak, Analis, Theramex, Nyomed, Novo Nordisk; Consultant, Gedeon Richter; Speaker, Amgen, Eli Lilly & Company, Merck & Co., Novartis Pharmaceuticals; Investigator, Amgen, Novo Nordisk; Speaker Bureau Member, Amgen.

Sources of Research Support: Amgen Inc. sponsored this study.