FAST FACTS

 A211801 - **BRCA-P: A Randomized, Double-Blind, Placebo-Controlled, Multi-Center, International Phase 3 Study to determine the Preventive Effect of Denosumab on Breast Cancer in Women carrying a *BRCA1* Germline Mutation**

**Inclusion criteria**

1. **Women with a confirmed deleterious or likely deleterious BRCA 1 germline mutation (Variant class 4 or 5).**
2. Age ≥ 25 years and ≤ 55 years at randomization
3. **No evidence of breast cancer by MRI or MG and clinical breast examination within the last 6 months prior to randomization**
4. **No clinical evidence of ovarian cancer at randomization**
5. **Negative pregnancy test at randomization for women of childbearing potential**
6. **No preventive breast surgery planned at time of randomization**
7. **Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1**
8. **Written informed consent before any study-specific procedure is performed**

**Exclusion criteria**

1. **Prior bilateral mastectomy**
2. **History of ovarian cancer (including fallopian and peritoneal cancer)**
3. **History of breast cancer**
4. **History of invasive cancer except for basal cell or squamous cell skin cancer or carcinoma in situ of the cervix, stage 1 papillary or follicular thyroid cancer, atypical hyperplasia or LCIS (Lobular Carcinoma In Situ)**
5. **Pregnant or lactating women (within the last 2 months prior to randomization)**
6. **Unwillingness to use highly effective contraception method during and within at least 5 months after cessation of denosumab/placebo therapy in women of childbearing potential. (Note: Women of childbearing potential should be monitored for pregnancy prior to each denosumab/placebo injection)**
7. **Clinically relevant hypocalcaemia (history and current condition), or serum calcium <2.0 mmol/L (<8.0 mg/dL)**

**Hypocalcemia defined by calcium below the normal range (a single value below the normal range does not necessarily constitute hypocalcemia, but should be ‘corrected’ before dosing the subject). Monitoring of calcium level in regular intervals (usually prior to IP administration) is highly recommended**

1. **Tamoxifen, raloxifene or aromatase inhibitor use during the last 3 months prior to randomization or for a duration of more than 3 years in total (current and prior HRT is permitted)**
2. **Prior use of denosumab**
3. **Subject has a known prior history or current evidence of osteonecrosis or osteomyelitis of the jaw, or an active dental/jaw condition which requires oral surgery including tooth extraction within 3 months of enrollment**
4. **Concurrent treatment with a bisphosphonate or an anti-angiogenic agent**
5. **Any major medical or psychiatric condition that may prevent the subject from completing the study**
6. **Known active infection with Hepatitis B virus or Hepatitis C virus**
7. **Known infection with human immunodeficiency virus (HIV)**
8. **Use of any other investigational product (current or prior Aspirin or NSAIDs are permitted)**

 