AOSOP6 RESULTS FROM THE 2-YEAR OPEN-LABEL EXTENSION TREATMENT PHASE OF A PIVOTAL PHASE 3 STUDY OF DENOSUMAB IN PATIENTS WITH BREAST CANCER AND BONE METASTASES PREVIOUSLY TREATED WITH ZOLEDRONIC ACID OR DENOSUMAB

A.T. Stopeck[*,a], A. Lipton[b], M. Martín[c], J-J. Body[d], A. Paterson[e], G.G. Steger[f], K. Tonkin[g], R.H. de Boer[h], Y. Fujiwara[i], D. Yardley[j,k], J. Jassem[l], T. Takano[m], P. Solal-Céligny[n], M. Fan[o], A. Braun[o]. [a] *University of Arizona Cancer Center, Tucson, AZ, USA,* [b] *Penn State Milton S. Hershey Medical Center, Hershey, PA, USA,* [c] *Hospital General Universitario Gregorio Marañón, Madrid, Spain,* [d] *CHU Brugmann, Université Libre de Bruxelles, Brussels, Belgium,* [e] *Tom Baker Cancer Centre, Calgary, Alberta, Canada,* [f] *Medical University of Vienna, Vienna, Austria,* [g] *Cross Cancer Institute, Edmonton, Alberta, Canada,* [h] *Western and Royal Melbourne Hospitals, Melbourne, Australia,* [i] *National Cancer Center Hospital, Tokyo, Japan,* [j] *Sarah Cannon Research Institute, Nashville, TN, USA,* [k] *Tennessee Oncology, PLLC, Nashville, TN, USA,* [l] *Medical University of Gdansk, Poland,* [m] *Toranomon Hospital, Tokyo, Japan,* [n] *Clinique Victor Hugo, Centre Jean Bernard, Le Mans, France,* [o] *Amgen Inc., Thousand Oaks, CA, USA*

Background. Denosumab was superior to zoledronic acid (ZA) in reducing the risk of a first on-study skeletal-related event (SRE; HR, 0.82; 95% confidence interval (CI) 0.71, 0.95; $p = 0.01$) in patients with breast cancer and bone metastases (BMs; Stopeck et al., 2010). All patients who remained on treatment after the primary analysis were offered open-label (OL) denosumab for a pre-specified 2-year extension phase.

Methods. Women with BMs secondary to breast cancer ($N = 2046$) were randomly assigned to subcutaneous denosumab 120 mg or IV ZA 4 mg (adjusted for renal function) Q4W. Patients who completed this double-blind, double-dummy treatment phase were offered OL denosumab Q4W. Patients who did not participate in the OL phase were followed up for survival every 12 weeks for up to 2 years after their last dose of investigational drug.

Findings. Of the 752 patients who completed the double-blind phase, 667 (89%) chose to receive OL denosumab: 325 initially randomly assigned to denosumab (DD) and 342 to ZA (ZD). Total median (Q1, Q3) cumulative denosumab exposure in DD patients was 19.3 months (9.2, 32.2) (range 0.9–59.8 months). Adverse events (AEs) were comparable between groups ($n = 283/318$ [89%] for DD; $n = 303/334$ [91%] ZD) during the OL phase; 20 and 18 patients, respectively, reported osteonecrosis of the jaw; cumulative incidence was 4.7% in DD patients and 3.5% in ZD patients for the entire study duration of 5 years. Hypocalcaemia was comparable between groups ($n = 12$ DD; $n = 9$ ZD). Serious AEs were reported in 126 (39.6%) DD patients and 133 (39.8%) ZD patients. Overall survival was similar between the groups for the entire study: median 34.4 months (95% CI 31.5, 39.3) and 34.2 months (95% CI 31.0, 37.6), respectively.

Interpretation. This OL extension treatment phase confirmed the safety profile of denosumab in patients with breast cancer with BMs receiving up to 5 years of monthly denosumab therapy or switching to denosumab after up to 3 years of ZA.

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AOSOP7 ROLE OF POLYMORPHISMS OF DNA METHYLTRANSFERASES IN RISKS OF GASTRIC CANCER AND ATROPHIC GASTRITIS

J. Jiang[a], X. Cao[*,a], Z.F. Jia[a], M.S. Jin[a], F. Kong[a], S. Tokudome[b]. [a] *First Hospital of Jilin University, ChangChun, China,* [b] *National Institute of Health and Nutrition, Tokyo, Japan*

Background. DNA hypermethylation catalysed by DNA methyltransferases (DNMT) is thought to be involved in the development of gastric cancer. Single nucleotide polymorphisms (SNP) of DNMTs have been reported to be associated with susceptibility to various cancers. In this study, we investigated whether tag SNPs of DNMTs were associated with gastric cancer and, moreover, atrophic gastritis and *Helicobacter pylori* (*H. pylori*) infection, which are also risk factors for gastric cancer.

Methods. Twelve tagSNPs, rs2288349, rs2228611, rs2228612, rs16999593, and rs10420321 of *DNMT1*, rs1550117 and rs13420827 of *DNMT3a*, and rs6119954, rs4911107, rs4911259, rs8008663, and rs1569686 of *DNMT3b* were genotyped by use of the TaqMan assay in 450 patients with non-cardiac gastric cancer and 1072 healthy controls. Serum antibodies to *H. pylori* and pepsinogen I and II were also tested using ELISA kits.

Findings. Three hundred and eleven (69.1%) patients with cancer and 562 (52.4%) controls were identified as being seropositive for *H. pylori* ($p < 0.001$). In seropositive subjects, rs1550117 AA genotype of *DNMT3a* was marginally associated with increased risk of gastric cancer compared with the GG genotype (OR 3.08, 95% confidence interval (CI) 1.00–9.61, $p = 0.05$). In terms of risk of atrophic gastritis, rs6119954 AA genotype of *DNMT3b* (OR 0.58, 95% CI 0.35–0.97) in *H. pylori* seropositive controls and rs1550117 AA genotype of *DNMT3a* (OR = 7.70, 95% CI 1.84–32.1) in seronegative controls were not significant. Moreover, three SNPs of *DNMT1*, rs2288349 A allele, rs2228612 C allele, and rs10420321 G allele, and two haplotypes of *DNMT1*, GATTA and AATCA, were associated with a higher risk of *H. pylori* infection in controls.

Interpretation. SNPs of *DNMTs* might be associated with risk of gastric cancer, atrophic gastritis, and*H. pylori* infection. However, further studies are needed to confirm this conclusion.

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AOS1 PILOT CANCER SCREENING PROGRAMME ON WHEELS IN MUMBAI

Y. Kumar[*], G. Mishra, S. Gupta, S.S. Shastri. *J.N. Medical College, KLE University, Belgaum, Karnataka, India, Tata Memorial Hospital, Mumbai, Maharashtra, India*

Background. Breast, cervical, and oral cancers account for 58% of all cancers in women in India. Because India does not have an