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

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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

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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

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

organised cancer screening programme, specialists are trying to reach the masses through different approaches.

Methods. This pilot study was done in Mumbai in coordination with different non-governmental organisations (NGOs). After women had participated in a health education programme (HEP), they were screened for breast cancer (clinical examination), cervical cancer (visual tests namely visual inspection with acetic acid and visual inspection with Lugol's Iodine), and oral cancers (visual examination). Women screened positive were referred to Tata the Memorial Hospital (TMH) for further diagnosis and management.

Findings. Three hundred and seventy-two women participated in HEP. Twenty-three (12.43%) of 185, 32 (17.88%) of 179, and 18 (35.29%) of 51 women screened positive for breast, cervical, and oral cancers, respectively. The compliance among these women to undergo further diagnostic investigations at TMH was poor. One case of cervical pre-cancer and one of cervical cancer were diagnosed.

Interpretation. Affordable, effective, and acceptable outreach cancer screening services as part of an awareness programme are needed in India. The NGOs should take responsibility for motivating women who screen positive for cancer to comply with further confirmatory diagnostic investigations at the referral hospital.

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AOS2 PREVALENCE OF SYMPTOMATIC DEEP VEIN THROMBOSIS IN PATIENTS WITH CANCER ADMITTED TO THE NATIONAL KIDNEY AND TRANSPLANT INSTITUTE IN THE PHILIPPINES

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Background. Prevention of cancer-associated thrombosis is important for reducing the burden of disease, yet it has received little attention from clinicians. In this study we aimed to assess the prevalence of deep venous thrombosis (DVT) in patients with solid and haematological malignancies who were admitted to the National Kidney and Transplant Institute (NKTI) and to define the profile of patients with cancer who developed DVT.

Methods. In this retrospective study, charts of inpatients with cancer who developed DVT from January 2005 to December 2010, were reviewed. ICD-10 codes for DVT and pulmonary embolism were used to search for patients. The total number of patients with cancer was obtained from the medical records section of the electronic database.

Findings. Ten thousand two hundred and ninety-nine patients with cancer were admitted to NKTI from 2005 to 2010. Forty-six developed DVT (prevalence 0.45%). Prevalence in solid and haematological malignancies was 0.44% and 0.43%, respectively. DVT commonly occurred within 6 months of cancer diagnosis, and in patients with stage IV malignancies and those who were obese. Lung cancer was the most common malignancy that presented with DVT. Leg oedema was the most common initial manifestation. Doppler venous ultrasonography frequently showed proximal DVT with or without distal involvement. Twnety-one deaths were known to have occurred after diagnosis of DVT. Most patients died within 1–3 months of the onset of DVT. Septic shock was the most common cause of death.

Interpretation. The results suggest that DVT in patients admitted to NKTI occur in those with late-stage cancer and that the thrombosis is usually extensive, symptomatic, and arises early after the initial diagnosis of cancer. Also, after the onset of DVT, most patients died within 1–3 months, which is lower than the median survival cited in previous studies.

The authors declared no conflicts of interest.

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AOS3 CONTROL OF URINARY, RECTAL, AND SEXUAL SYMPTOMS AFTER 3-D CONFORMAL RADIOTHERAPY FOR BLADDER CANCER

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Background. Radical cystectomy remains the standard of care for muscle-invasive transitional cell carcinoma of the bladder. A combination of maximum transurethral resection of the bladder tumour, radiation, and concurrent chemotherapy is the hallmark of modern bladder function preserving strategies. Our aim is to describe bladder, rectal, and sexual dysfunctions in survivors after radical radiotherapy for urinary bladder cancer.

Methods. Twenty patients were treated with 3-D conformal radiotherapy (60–66 Gy in 2 Gy fractions, five fractions per week) on a linear accelerator machine. Median follow-up time was 30 months. For comparison, 20 controls were selected from our annual cancer register. Information was collected anonymously to avoid investigator-related bias using a questionnaire about changes in daily life after radiotherapy.

Findings. Of the irradiated patients, 80% reported little or no distress from urinary symptoms. Twenty per cent of patients reported that radiotherapy had a moderate to severe impact on their present bladder function, causing dysuria, incontinence, or stenosis that required the use of a bladder catheter. Thirty per cent of irradiated patients reported moderate to severe impact on their present sexual function. Impotence and lack of sexual desire were significantly higher among the male patients who received radiotherapy. Forty per cent of the male patients had regular sexual intercourse (half of whom used aids like sildenafil to sustain erection) and 70% of the male patients reported they had ejaculation. Moderate distress from symptoms of the gastrointestinal tract was reported by 30% of irradiated patients. Diarrhoea was most common, followed by faecal urgency and faecal incontinence.

Interpretation. After radical radiotherapy, most patients had a well functioning bladder. Radiotherapy is associated with considerable long-term intestinal side-effects because the treatment field includes the bowel. Moreover, radiotherapy can result in sexual dysfunction. Although we do not suggest that selective bladder-sparing treatment should replace radical cystectomy, sufficient data now exists to indicate that it is a valid alternative.

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AOS4 DETECTION OF HUMAN PAPILLOMAVIRUS DNA IN PATIENTS WITH DIFFERENT CERVICAL LESIONS IN KURDISTAN REGION, IRAQ

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