(gemcitabine/docetaxel). Overall median PFS was 1.5 months with no significant difference in the two groups (1.4 versus 1.9 months, respectively); 31% versus 15% of patients in the trabectedin and gemcitabine/docetaxel groups, respectively, did not have disease progression at 4 months.

Interpretation. Encouraging anti-tumour activity was noted in both treatment groups with subsets of patients achieving prolonged clinical benefit. Prospective studies are urgently needed to clarify the optimum strategy in this clinical setting.

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AOS13 DENOSUMAB VERSUS ZOLEDRONIC ACID FOR THE PREVENTION OF SKELETAL-RELATED EVENTS IN PATIENTS WITH BONE METASTASES SECONDARY TO SOLID TUMOURS: AN INTEGRATED ANALYSIS OF THREE PHASE 3 STUDIES

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Background. Skeletal-related events (SREs) cause significant morbidity in patients with solid tumours and bone metastases (BMs). An *ad hoc* analysis was undertaken to compare the effect of denosumab with zoledronic acid (ZA) in the prevention of SREs in patients with BMs secondary to solid tumours who participated in the denosumab pivotal phase 3 studies.

Methods. Patients with breast cancer ($N = 2046$), prostate cancer ($N = 1901$), or other solid tumours ($N = 1597$) and BMs were randomly assigned in a 1:1 ratio to receive subcutaneous denosumab 120 mg or IV ZA 4 mg (adjusted for renal function) every 4 weeks. Patient-level data from three identically designed, double-blind, double-dummy studies were combined. Time to first on-study SRE and time to first and subsequent SREs were analysed using the Cox proportional hazards model and Anderson–Gill method, respectively.

Findings. Patients received denosumab ($N = 2776$) or ZA ($N = 2768$). Denosumab was superior to ZA in delaying time to first on-study SRE and time to first and subsequent SREs. Denosumab reduced the risk of a first SRE by 18% compared with ZA (HR 0.82 [95% confidence interval (CI): 0.75, 0.89], $p < 0.0001$), reflecting a delay in median time to first SRE of 8.2 months. Denosumab also reduced the risk of first and subsequent SREs by 19% (HR 0.81 [95% CI: 0.74, 0.88], $p < 0.0001$) compared with ZA. Disease progression and survival were similar between groups. Incidence of adverse events (96.2% of denosumab group and 96.7% of ZA group), serious adverse events (56.2% of denosumab group and 57.3% of ZA group), and osteonecrosis of the jaw (1.7% of denosumab and 1.3% of ZA; $p = 0.18$) were similar in both groups. Hypocalcaemia was more frequent with denosumab (9.5% versus 4.8% for ZA) and acute phase reactions (first 3 days) were more common with ZA (20.4% versus 8.7% for denosumab).

Interpretation. This integrated analysis confirmed results from the individual studies; denosumab was superior to ZA in reducing the risk of both first and multiple SREs among patients with solid tumours and BMs.

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AOS14 PHASE II CLINICAL STUDY OF COMBINATION CHEMOTHERAPY WITH HERB *WITHANIA SOMNIFERA* (ASHWAGANDHA) IN BREAST CANCER

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Background. Herbal drugs are generally avoided during systemic chemotherapy because of herb–drug interaction and exaggeration of chemotherapy-related toxicity. We used a common medicinal herb *Withania somnifera* (ashwagandha) in addition to systemic chemotherapy in patients with breast cancer. This herb is haemoprotective, enhances cytotoxicity of chemotherapy, has radiosensitive properties, and improves the general wellbeing of patients.

Methods. This was a prospective non-randomised clinical trial comparing the outcomes of *W. somnifera* plus chemotherapy with chemotherapy alone (control) in women with breast cancer. Fifty patients with all stages of breast cancer that required systemic chemotherapy were alternatively assigned to study drug or no further treatment using defined selection criteria. *W. somnifera* root extract in vegetarian capsule form was given at an oral dose of 2 g tds during six courses of chemotherapy to the patients in the combination group. Piper's fatigue score (PFS), Schwartz's cancer fatigue score (SCFS), European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (QLQ) C-30 (version 3) at the beginning (1st cycle), during, and after chemotherapy (6th cycle), clinical parameters, and response to therapy in both groups were monitored. The haematological parameters were monitored during the six cycles of chemotherapy. Correlation of the quality of life (QoL) and fatigue over time as numerical covariates was evaluated using the repeated-measure analysis of covariance (ANCOVA) method, and survival analysis was done with Kaplan–Meier non-parametric estimation using SPSS (version 18, IBM) software.

Findings. Fifty patients were recruited to each group, with a median age of 51 years (range 36–70 years) in the *W. somnifera* plus chemotherapy group and 50.5 years (range 30–82 years) in the control group. Eight patients had stage I, 33 stage II, 44 stage III, and 15 stage IV breast cancer. Fifteen patients were offered palliative chemotherapy and 85 were offered adjuvant chemotherapy. Patients in the group treated with *W. somnifera* root extract and chemotherapy had less fatigue than did those in the control group (PFS $p < 0.001$ and SCFS