Background. This study was designed to identify the factors affecting survival in patients with leptomeningeal metastases from solid tumours and define the role of various treatments.

Methods. Medical records of 82 patients who were diagnosed with leptomeningeal metastases from solid tumours from January 1, 2004, to May 31, 2011, were retrospectively reviewed. The most frequent site of origin was the lung (57.1%) followed by breast (25%) and stomach (15.5%). Median age of patients was 54 years (range 27–78). Two-thirds of patients had an Eastern Cooperative Oncology Group (ECOG) performance status class of 1 or 2. Patients were treated with various combinations of intrathecal chemotherapy (85.7%), whole brain radiotherapy (65.5%), systemic chemotherapy (31%), and spinal radiotherapy (22.7%). 29.3%, 42.7%, and 23.2% of patients were treated with single, dual, and triple modalities, respectively.

Findings. Median survival was 2.6 months and the 1-year survival rate was 9.7%. Univariate analysis showed significantly different survival rates according to age, site of origin, cerebrospinal fluid (CSF) leukocytosis, CSF cytology, intrathecal chemotherapy, systemic chemotherapy, and combined modality. Furthermore, there was a trend towards improved survival with an increase in the number of cycles of chemotherapy and whole brain radiotherapy. Multivariate analysis showed that positive cytology in CSF (positive [6.3 months] versus negative [2.2 months], $p = 0.003$), intrathecal chemotherapy (done [2.7 months] versus not done [2.1 months], $p = 0.009$), systemic chemotherapy (done [7.6 months] versus not done [1.9 months], $p = 0.029$), and combined modality treatment (single [1.2 months] versus dual [3.5 months] versus triple [8.3 months], $p = 0.002$) had statistically significant effects on survival.

Interpretation. Unlike previous reports, no factors among the characteristics of patients and symptoms at the time of diagnosis of leptomeningeal metastases affected survival, including performance status, and survival in patients with primary non-small cell lung cancer (NSCLC) tumours was comparable with that in patients with primary breast tumours. Furthermore, survival improvement was significant with combined modality treatment over single modality treatment. Thus, multimodality treatment should be sought for patients with feasible performance in tolerating treatment and those with not only breast primary but also NSCLC primary tumours.

The authors declared no conflicts of interest.

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AOS11 TRABECTEDIN IN SARCOMA: INITIAL EXPERIENCE IN THE ASIAN SETTING

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Background. Trabectedin has recently been approved for treatment of soft tissue sarcoma (STS) and has shown interesting anti-tumour activity in a wide spectrum of bony sarcomas. Published literature about its use in Asian patients is limited.

Methods. Twenty consecutive patients with histology-confirmed sarcoma treated with trabectedin at our institution were included in this single-centre retrospective study. Per institutional guidelines, imaging studies were done after 2–3 cycles of treatment; response rates and drug-emergent toxicities were evaluated using Response Evaluation Criteria in Solid Tumors (RECIST) (version 1.1) and CTACE (version 4), respectively.

Findings. Median age was 57 years (range, 22–72), 60% of patients were female and 95% had STS. Common histotypes included undifferentiated pleomorphic sarcoma (UPS, 30%), leiomyosarcoma (LMS, 20%), and liposarcoma (LPS, 15%). Eighty-five per cent of patients had bulky primary tumours (>5 cm); the lung was the most common metastatic site (44%). Patients had previously been given a median of 1 line of chemotherapy (range 0–4). A total of 59 cycles of trabectedin was administered with a median dose of 1.2 mg/m^2 (range 0.6–1.5 mg/m^2) and a median of two cycles (range 1–10). At a median follow-up of 4 months, 2 patients were still on drug treatment; the most common reason for discontinuing trabectedin was disease progression. Objective response rate was 5% (patient with LMS) and 25% of patients achieved stable disease as the best response. Three patients (15%) received more than six cycles of trabectedin; 20% of patients did not have evidence of disease progression at 6 months (2 patients with LPS, 1 each with LMS and UPS). Median PFS was 1.5 months. Trabectedin was generally well tolerated; the most common grade 3/4 toxicity was self-limiting ALT/AST elevations.

Interpretation. Trabectedin is safe and well tolerated in Asian patients with sarcoma. A significant subset of patients achieved prolonged clinical benefit. Biomarker development is urgently needed to better identify this group of patients.

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AOS12 EFFICACY AND SAFETY OF TRABECTEDIN VERSUS GEMCITABINE/DOCETAXEL IN PATIENTS WITH SARCOMA AFTER FAILURE OF ANTHRACYCLINE AND/OR IFOSFAMIDE

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Background. Trabectedin and gemcitabine/docetaxel are routinely used in the treatment of advanced sarcoma after failure of anthracycline and/or ifosfamide. The optimum regimen remains unclear. We aimed to assess the efficacy and safety of trabectedin versus gemcitabine/docetaxel in patients with sarcoma after failure of standard therapy.

Methods. Twenty-nine patients with advanced sarcoma who had received trabectedin or gemcitabine/docetaxel after failure of anthracycline and/or ifosfamide were included in this single-centre study. Three patients received both regimens and were included in the initial treatment group for the purpose of this analysis. Per institutional guidelines, imaging studies were repeated after 2–3 cycles of treatment; response rates and drug-emergent toxicity were evaluated using Response Evaluation Criteria in Solid Tumors (RECIST) (version 1.1) and CTACE (version 4), respectively.

Findings. Sixteen and 13 patients received trabectedin and gemcitabine/docetaxel, respectively. Median age (53 versus 56 years) and sex (44% versus 46% males) were not significantly different between the two groups. Patients in both cohorts had previously received a median of 1 line of chemotherapy (range 1–3). A median of two cycles were administered in both cohorts (range 1–10 and 1–6, respectively). Median administered dose of trabectedin was 1.2 mg/m^2 (range 0.9–1.5 mg/m^2) and, per institutional practice, gemcitabine was administered routinely at 900 mg/m^2 on days 1 and 8 and docetaxel at 75 mg/m^2 day 8, supported by growth factors. With the exception of self-limiting grade 3/4 ALT elevations in 50% of patients in the trabectedin group versus none in the gemcitabine/docetaxel ($p = 0.003$), both treatments were generally well tolerated with no significant differences in toxicity profiles. Objective response rates were 6% (trabectedin) versus none

(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