(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

$p < 0.003$). QoL was significantly better ($p = 0.0001$) than in the control group. There was no difference in the haematological parameters or 24-month overall survival for all stages [study 74% versus control 56% ($p = 0.174$)]; however, there was a trend for longer survival in the patients treated with *W. somnifera* root extract plus chemotherapy.

Interpretation. Addition of *W. somnifera* to chemotherapy could have a positive effect on fatigue and improve QoL in patients with breast cancer. The effectiveness and toxicity of chemotherapy were not altered. Thus further study with a large sample size, uniform tumour criteria, and risk stratified patients with breast cancer could help to validate our preliminary outcome.

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AOS15 ASSESSMENT OF COGNITIVE FUNCTION IN PATIENTS WITH BREAST AND COLON CANCERS UNDERGOING CHEMOTHERAPY: RESULTS FROM AN EXPLORATORY PILOT STUDY

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Background. Memory loss after chemotherapy is one of the most commonly reported post-treatment symptoms by patients with cancer. This deterioration in cognitive function, commonly referred to as chemobrain or chemofog, was largely unacknowledged by the medical community until in recent years. An exploratory pilot study was undertaken in Tuanku Jaafar Hospital, Negeri Sembilan, Malaysia. The aim in the study was to assess the effect of chemotherapy on cognitive function of patients with breast and colon cancers.

Methods. Ten patients with cancer (6 patients with breast cancer patients and 4 with colorectal cancer) who were receiving adjuvant chemotherapy (anthracycline and/or 5-fluorouracil) were assessed using the Montreal Cognitive Assessment (MoCA) and the Mini Mental State Examination (MMSE) before the first cycle of chemotherapy and again after the third cycle.

Findings. There were mean reductions of 6.1% in MoCA and 5.3% in MMSE; no difference was noted between patients with breast and those with colorectal cancer.

Interpretation. The reductions in both the tests suggest that chemotherapy does have an impact on cognitive function, although it must be noted that the sample size was small. Based on the results of this exploratory pilot study, we aim to do a further larger scale, longer study to assess cognitive function after chemotherapy.

The authors declared no conflicts of interest.

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AOS16 CANCER CARE ISSUES DURING RECOVERY: OBSERVATIONS FROM INDIA

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Background. Because of the lack of literature about patients with cancer in the Indian setting, increasing incidence of the disease, changing trends in treatment, and residual cancer or side-effects that restrict activities of daily living (bathing, eating, using the bathroom) or functional disabilities (e.g. in walking, standing, or sitting), the care of people with cancer has been transferred to caregivers (Hewitt et al., 2003). Hence, in this study, the needs of caregivers were assessed to develop an organised programme for caregivers in the Indian setting.

Methods. Sixty caregivers were interviewed according to a schedule in a cross-sectional study. The patients receiving care had heterogeneous cancer diagnoses and were hospitalised for at least one month.

Findings. The highest need was financial followed by informational, family, personal, social, psychological, and spiritual needs by contrast with findings of the studies from the west where psychological need was the highest.

Interpretation. Changing trends in treatment have led to patients being discharged early from hospital. Consequently, there is a transition of care from hospital to family caregivers. Additionally, the residual cancer or side-effects of the disease that restrict activities of daily living (e.g. bathing and eating) or functional disabilities (e.g. difficulty in walking, standing, or sitting) or make the care recipients more dependent on the caregivers. Thus reduced hospitalisation and increased dependence of care recipients on the caregivers have resulted in increased care demands that in turn would affect the caregiver's needs.

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AOS17 *KRAS* GENOTYPES IN THAI PATIENTS WITH COLORECTAL CANCER

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Background. The reported prevalence of *KRAS* mutations, the predictive factor of efficacy of cetuximab in colorectal cancer, varies in 30–40% of patients. However, the prevalence and correlations between *KRAS* mutation and clinical outcome in Thai patients have never been investigated. We did a retrospective study to define the *KRAS* genotype in Thai patients with colorectal cancer.

Methods. Genomic DNA from patients' paraffin-embedded tumour tissues was analysed for *KRAS* mutation at codons 12 and 13 by use of direct sequencing. Their clinical characteristics and outcomes were correlated with the genotype patterns. The concordance of *KRAS* genotype between primary tumour and available metastatic tumour was analysed

Findings. One hundred and seventeen patients with colorectal cancer were enroled. Eighty-three patients (70.9%) had wild-type *KRAS* (WT-*KRAS*) whereas 34 patients (29.1%) had mutant *KRAS*. Gly12Asp (GGTGAT at codon 12) was the most common mutation (41.2%). The G13D mutation was detected in 14.7% of patients. Non-hepatic metastases were associated with mutant *KRAS* (adjusted OR = 3.699). The overall survival at 1, 2, and 5 years in patients with mutant *KRAS* was 85%, 75%, and 54%, respectively, compared with 96%, 83%, and 47%, respectively, in those with wild-type *KRAS* ($p = 0.56$). Discordance of the *KRAS* genotype (wild-type primary tumours and mutant metastatic tumours) was detected in 2 of 9 patients (22.2%). After cetuximab-chemotherapy, the PFS of one case with discordant *KRAS* was shorter than the median PFS in 10 cases with primary WT-*KRAS* (2.7 months versus 12.8 months).