Updates in Supportive Care From ASCO 2014

Summaries of selected presentations on key aspects of supportive care in oncology, from the 2014 American Society of Clinical Oncology (ASCO) Annual Meeting, held May 30-June 3, 2014, in Chicago, IL

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Overview

This CME activity features data from 5 abstracts presented at the 2014 American Society of Clinical Oncology Annual Meeting in the area of supportive care in cancer. The abstracts represent a broad range of topics that highlight the importance of supportive care measures to optimize quality of life, symptom management, and outcomes in patients with cancer. The topics are as follows:

- The relationship between memory problems and sleep duration/ insomnia in adults with cancer
- Prevention of chemotherapy-induced nausea and vomiting in patients receiving paclitaxel plus carboplatin
- Distress and psychiatric morbidity in patients with cancer
- Intensity of end-of-life care in adolescents and young adults with cancer
- Risk of diarrhea in ipilimumab-treated patients with cancer

Target Audience

This activity is directed toward medical oncologists and hematologists who treat patients with solid tumors and hematologic malignancies. Fellows, nurses, physician assistants, nurse practitioners, and other healthcare providers may also participate.

Learning Objectives

After participating in this CME activity, learners should be better prepared to:

- Review recent data presented at national society meetings for symptom and adverse-event mitigation and management

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Effect of Insomnia and Sleep Duration on Self-Reported Memory Problems in Adults With Cancer

Summary based on abstract 9588 presented by Pascal Jean-Pierre, MPH, PhD

Cognitive dysfunction can be a serious consequence of cancer and the various strategies used in its treatment. Data suggest that cognitive impairment occurs in up to 75% of patients with cancer, and that up to 3.9 million individuals in the United States may be living with long-term cognitive deficits due to cancer and cancer-related therapy.[1] Although it has been shown that cancer and cancer-related therapy may adversely affect attention, verbal and visual memory, and verbal, psychomotor, spatial, and executive functioning,[2] much remains to be elucidated about the size, duration, and pattern of the cognitive effect.[3,4] Sleep disorders, such as insomnia, are common in patients with cancer[5] and could potentially have a detrimental effect on memory.

The purpose of the study conducted by Jean-Pierre and colleagues[6] was to investigate the relationship between self-reported memory problems (SRMPs) and sleep disorders in adult-onset cancer survivors.

Study Design and Methods

Epidemiologic data from the 2007-2008 National Health and Nutrition Examination Survey (NHANES) were used to investigate the relationship between SRMPs and insomnia/sleep duration in cancer survivors aged 41 to 64 years. Individuals with a history of brain cancer or stroke were excluded from the study given the potential for associated memory problems. NHANES data from adults aged 41 to 64 years who had no history of cancer were also examined for SRMPs.

The presence of SRMPs, the primary outcome measure, was investigated using population-weighted binary logistic regression analysis; covariates included age, sex, education, race/ethnicity, income, and overall health status. Insomnia was stratified by type (initial, middle, late, and combined) and occurrence (none, mild, and severe); sleep duration was categorized as very short, short, normal, and long (**Table**).

Results

Complete data on insomnia and sleep duration were presented for 161 cancer survivors (mean age, 54.1 years; female, 55.71%; and non-Hispanic white, 84.26%). About one-third of the study population had a college degree, nearly one-half earned more than $75,000 per year, and more than two-thirds self-reported their health as "good" or "very good."

Initial insomnia was reported by 108 patients (mild, n=93; severe, n=15), and 53 patients reported no initial insomnia (P = .0498). Middle insomnia was reported by 112 patients (mild, n=93; severe, n=19), and 49 patients reported no middle insomnia (P = .6464). Late insomnia was reported by 104 patients (mild, n=92; severe, n=12), and 57 patients reported no late insomnia (P = .3749).

Normal sleep duration was reported by 73 patients. Short, very short, and long sleep duration were reported by 64, 13, and 11 patients, respectively (P = .682). Of interest, the analysis showed a negative correlation between SRMPs and long sleep duration, potentially suggesting that long sleep may confer a neuroprotective effect on memory.

The presence of insomnia was found to be significantly correlated with SRMPs in adults with a history of cancer (P < .0001), but did not predict memory problems in those without a history of cancer. Severe initial insomnia was associated with SRMPs (P = .006), as well as mild and severe middle insomnia (P = .007 and P < .0001, respectively). Severe late insomnia also seemed to be associated with SRMPs (P = .037).

TABLE. Study Definitions of Insomnia and Sleep Duration

Insomnia Type	**Definition**
Initial	Difficulty falling asleep
Middle	Difficulty maintaining sleep
Late	Waking too early
Combined	Presence of severe insomnia of any type (initial, middle, or late)
Insomnia Occurrence	**Definition**
None	No occurrence of insomnia
Mild	Occurrence of insomnia on <15 days/months
Severe	Occurrence of insomnia on ≥15 days/month
Sleep Duration	**Definition**
Very Short	≤4 hours
Short	5-6 hours
Normal	7-8 hours
Long	≥9 hours

Conclusions

Insomnia may be a "mechanistic pathway" through which cancer and cancer-related therapy affect memory. Further investigation is needed to more fully clarify the relationship between sleep and memory problems in patients with a history of cancer.

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Efficacy and Toxicity of Palonosetron in Combination With 1-day vs 3-day Dexamethasone in Women With Gynecologic Cancer Receiving Paclitaxel and Carboplatin

Summary based on abstract 9608 presented by Naoto Furukawa, MD

Paclitaxel plus carboplatin (TC) is a common treatment approach in gynecologic cancers. Patients receiving TC are usually given palonosetron (on day 1) in combination with dexamethasone (on days 1-3) to prevent chemotherapy-induced nausea and vomiting (CINV). Although palonosetron has been effective in preventing delayed CINV, dexamethasone administered for 3 days has been associated with toxicity in the week following chemotherapy.[1] Data suggest that administering dexamethasone on day 1 only is not associated with inferior antiemetic control.[2,3]

The purpose of the study conducted by Furukawa and colleagues[4] was to compare the efficacy and toxicity of palonosetron in combination with 1-day vs 3-day dexamethasone in women with gynecologic cancers who received TC.

Study Design and Methods

The study was a prospective, randomized, 2-arm, phase II study in chemotherapy-naïve women aged ≥20 years with a confirmed diagnosis of a gynecologic cancer (ovarian, cervical, or endometrial). Patients were stratified by age (<50 or ≥50 years) and alcohol intake (habitual [≥5 times per week] or nonhabitual).

Patients in arm 1 of the study received palonosetron (0.75 mg) and dexamethasone (20 mg) on day 1 and dexamethasone (8 mg) on days 2 and 3. Patients in arm 2 of the study received palonosetron (0.75 mg) and dexamethasone (20 mg) on day 1 only.

The primary endpoint was complete response (CR) in *delayed CINV*, which was defined as no emetic events and no rescue medication. Secondary endpoints included CR in acute and overall CINV; complete control (no emetic events, rescue medication, or significant nausea) in acute, delayed, and overall CINV; and toxicity (incidence of treatment-related adverse events [AEs]). The Multinational Association for Supportive Care in Cancer antiemesis tool was used to assess nausea and vomiting.

A sample size of 42 patients per treatment arm was deemed adequate to test the null hypothesis with 80% power and an alpha error of 0.05, taking into consideration a dropout rate of 10%. Logistic regression was performed to determine factors predictive of delayed CR.

Results

In total, 88 patients were randomized to arm 1 (n=44) or arm 2 (n=44) of the study between April 2012 and December 2013. Five patients in arm 1 and 1 patient in arm 2 discontinued the study because of paclitaxel-induced anaphylactic reactions; the remaining 82 patients were assessed for efficacy and toxicity.

The median age of patients in arm 1 was 62 years (range, 43 to 83 years) and 59 years (range, 36 to 76 years) in arm 2. Three patients in arm 1 and 4 patients in arm 2 were habitual alcohol users, and 7 patients in arm 1 and 5 patients in arm 2 had ascites.

Delayed CR was reported by 76.9% and 69.8% of patients in arms 1 and 2, respectively (P = .465). Acute CR was similar in arms 1 and 2 (94.9% vs 95.4%, respectively; P = .920), as was overall CR (76.9% vs 67.4%, respectively; P = .340).

The most common treatment-related AEs were grade 1 constipation and grade 1 insomnia. Grade 1 constipation occurred

in 20.5% of patients in arm 1 and 18.6% of patients in arm 2 (P = .828); grade 1 insomnia occurred in 12.8% and 16.3% of patients, respectively (P = .658).

Logistic regression analysis showed that age <50 years vs ≥50 years was predictive of a lower probability of delayed CR (univariate odds ratio [OR], 3.92; 95% confidence interval [CI], 1.30 to 12.12).

Conclusions

Antiemetic treatment with palonosetron plus dexamethasone on day 1 only seemed to be as effective in preventing CINV as palonosetron on day 1 plus dexamethasone on days 1-3 in patients receiving TC chemotherapy. Antiemesis beyond treatment with dexamethasone plus palonosetron may be required in patients aged <50 years.

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Prevalence of Distress and Psychiatric Morbidity in the Cancer Setting and Its Effect on Mortality

Summary based on abstract 9529 presented by Caryn Mei-Hsien Chan

Psychiatric morbidity, commonly observed in patients with cancer,[1] has been shown to be correlated with worse outcome.[2] Depression and anxiety, for example, have been linked to poorer performance status and quality of life.[2] Furthermore, data also suggest that depression in the cancer setting may be associated with mortality.[3-6]

The purpose of the study conducted by Chan and colleagues[7] was to prospectively investigate the prevalence of distress and psychiatric morbidity in the cancer setting and its effect on mortality.

Study Design and Methods

Adult patients (aged ≥18 years) with cancer undergoing oncology follow-up at a single academic medical center were recruited between November 1, 2011 and October 31, 2013, to participate in this 24-month longitudinal study. Patients with a previous psychiatric history, a life expectancy of <3 months, or lack of awareness of their cancer diagnosis were ineligible for participation.

Two assessments were performed: (1) the Hospital Anxiety and Depression Scale (HADS) was used at baseline and at 4 to 6 weeks to determine probable cases; and (2) the Structured Clinical Interview for DSM-IV-TR was used at 6 months and at 12 to 18 months to confirm caseness.

Overall survival was calculated using the Kaplan-Meier method; all patients were followed for up to 24 months. Comparisons were made between comorbid psychiatric cases and noncases.

Results

A total of 480 patients were asked to participate in a baseline interview; of these, 13 patients (2.4%) declined study enrollment, and 467 patients (97.6%) enrolled in the study.

The mean age of the study participants was 56.21 years (range, 18 to 93 years), 74.7% of the patients were female, and 45.6% of the patients had stage IV cancer. A total of 191 patients (40.7%) had breast cancer, 102 patients (21.7%) had gastrointestinal cancer, and 174 patients (37.6%) had other cancer types. Using HADS, 247 of the 467 patients were categorized as nonpsychiatric cases, and 220 patients were categorized as psychiatric cases.

Two hundred seventeen patients with total HADS scores ≥16 at baseline and at 4 to 6 weeks met criteria for a DSM-IV-TR axis I disorder (ie, major mental disorders) at 6 months. At 12- to 18-month follow-up, 102 of 115 re-interviewed patients were assigned a diagnosis of a psychiatric disorder. Overall, psychiatric comorbidity was found to be present in about 46% of the patients with cancer.

Seventy-four patients (noncase group, n=27; case group, n=47) died during the 24-month study period, mainly due to disease progression. Mean survival in cancer patients with and without

psychiatric morbidity was 20.87 months (95% confidence interval [CI], 20.06 to 21.69) vs 23.11 months (95% CI, 22.78 to 23.43), respectively ($P < .001$); the survival benefit in cancer patients without psychiatric morbidity was 2.24 months (67 days). The HR of psychiatric morbidity on survival before and after adjustment was 2.18 (95% CI, 1.34 to 3.53; $P = .002$) and 4.12 (95% CI, 1.54 to 11.07; $P = .005$), respectively.

Conclusions

The findings suggest that psychiatric morbidity is associated with reduced survival in patients with cancer. Appropriate interventions to monitor and actively treat psychiatric conditions could potentially lead to improved quality of life and longer survival in affected patients.

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Intensity of Medical Care at End of Life in Adolescents and Young Adults With Cancer

Summary based on abstract 9541 presented by Jennifer W. Mack, MD

Nearly 70,000 individuals aged 15 to 39 years are diagnosed with cancer each year in the United States, and cancer remains the main disease-related cause of death in adolescents and young adults.[1] Some studies suggest that nonelderly adults are less likely than elderly adults to receive hospice and/or palliative care and are more likely to receive intensive treatment in the last month of life.[2] At present, data on end-of-life medical care are lacking in younger patients, who nonetheless face numerous short- and long-term physical and psychosocial challenges.[1,2]

The purpose of the study conducted by Mack and colleagues[3] was to evaluate the intensity of medical care that adolescents and young adults with cancer received prior to dying.

Study Design and Methods

End-of-life care was evaluated in adolescent and young adult patients with stage IV/disseminated cancer who received treatment at Kaiser Permanente Southern California (KPSC) and died between 2001 and 2010. KPSC, an integrated healthcare delivery system, is a Cancer Research Network site.

Patients who were between the ages of 15 and 39 years at the time of death were included in the study. Patient characteristics and medical care strategies used at end of life were based on data from KPSC's Surveillance, Epidemiology and End Results–affiliated cancer registry and electronic medical records.

Intensive end-of-life medical care strategies included: (1) chemotherapy use in the last 14 days of life; (2) care in an intensive care unit in the last 30 days of life; (3) more than 1 emergency room visit in the last 30 days of life; (4) hospitalization in the last 30 days of life; and (5) any medically intensive end-of-life care.

Results

The records of 381 patients (males, 50%; white, 48%) aged 15 to 39 years were evaluated in the study. Primary cancers included leukemia (25%), lymphoma (12%), colorectal (9%); lung (8%), breast (7%), bone/soft tissue (6%); and other (34%).

At death, 23%, 34%, and 43% of the patients were aged 15 to 24 years, 25 to 34 years, and 35 to 39 years, respectively.

Overall, 76% of patients received at least one type of medically intensive care at the end of life. Eleven percent of patients received chemotherapy in the last 14 days of life; 17% of patients received care in an intensive care unit in the last 30 days of life; 48% of patients had more than 1 emergency room visit in the last 30 days of life; and 66% of patients were hospitalized in the last 30 days of life.

Conclusions

Adolescents and young adults with cancer often receive medically intensive end-of-life care, but the extent to which aggressive

care can be attributed to patient preference remains unknown. Additional research is needed to further evaluate end-of-life care and the availability of palliative strategies in this patient population.

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Risk of Severe Diarrhea in Ipilimumab-Treated Patients With Cancer

Summary based on abstract 9634 presented by Robert Charles Hendler, MD

Ipilimumab, a human cytotoxic T-lymphocyte antigen 4–blocking antibody, is approved by the US Food and Drug Administration in the treatment of unresectable or metastatic melanoma.[1] Although ipilimumab has shown promise in the treatment of other tumor types, its use has been associated with an increase in the incidence of diarrhea.[2-5] The overall risk of diarrhea in patients treated with ipilimumab, however, has not yet been well documented.

The purpose of the study conducted by Hendler and colleagues[6] was to systematically review relevant clinical trial data and perform a meta-analysis to determine the incidence and relative risk (RR) of ipilimumab-related diarrhea in patients with cancer.

Study Design and Methods

Relevant clinical trials were identified by searching PubMed articles published between January 1998 to November 2013, and abstracts presented at American Society of Clinical Oncology meetings up to 2013. The incidence and RR of diarrhea were calculated using random-effects or fixed-effects models.

Results

In total, 1571 patients with cancer from 10 clinical trials were included in the meta-analysis. The overall incidence of all-grade diarrhea and high-grade diarrhea was 41.6% (95% CI, 33.6% to 50.0%) and 8.4% (95% CI, 5.5% to 12.7%), respectively.

Ipilimumab versus controls was shown to significantly increase the risk of all-grade diarrhea (RR, 1.63; 99% CI, 1.37 to 1.95; $P < .001$) and high-grade diarrhea (RR, 2.19; 95% CI, 1.11 to 4.34; $P = .025$).

Conclusions

The risk of severe diarrhea is significant in ipilimumab-treated patients with cancer.

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