What was hot at MASCC/ISOO Annual Meeting this year?

“Supportive Care Makes Excellent Cancer Care Possible”. This slogan of the Multinational Association of Supportive Care in Cancer (MASCC) mirrors the importance of supportive care in cancer. MASCC is dedicated to research and education in the areas of supportive and palliative care as well as psychosocial issues and survivorship. MASCC holds an annual international symposium to discuss current developments and progress in supportive and palliative care. Congress president Petra Feyer, Berlin, Germany, pointed out that improving patients quality of life was equally important as fighting the disease itself, for example by the management of side effects allowing patients to return to work. Apart from improving quality of life there is evidence that patients should receive best supportive care for other reasons as well: Improved patient reported outcomes (PROs) seem to prolong survival. A recent study presented at ASCO 2013 suggested a strong correlation of PROs with survival (Gralla R et al. J Clin Oncol 31, 2013 (suppl; abstr 8087). Median survival differences above (positive factor) or below (negative factor) medians for each global item varied by 4 months ($p < 0.003$). For monitoring, the simple LCSS HRQL-PRO Index was used.

Scientific Highlights Antiemesis

Chemotherapy-induced nausea and vomiting (CINV) are two of the greatest fears of patients with cancer. The aim of antiemetic treatment is the total prevention of nausea and vomiting for each individual, thereby conferring the best patient outcome. Total control (i.e., no nausea, no vomiting or retching, and no use of antiemetic rescue medication) during the postchemotherapy period will maximize patients' quality of life, including their ability to sustain their normal daily activities after such treatment, thereby reducing associated symptom management costs. Thus, optimum control will be associated with considerable socio- and pharmacoeconomic, as well as clinical, benefits. Some 20 years after the launch of the first-generation 5-HT₃ receptor antagonists (5-HT₃ RAs), which heralded a major advance in the treatment of acute CINV, however, some patients are still not treated adequately.

“A significant number of patients still experience nausea and vomiting despite optimal treatment. Furthermore, current antiemetics do not treat nausea effectively and more effective treatments are needed”, explained Richard Gralla, New York, USA. Unfortunately,
adherence to antiemetic guidelines is also suboptimal and many patients still suffer from CINV. But further progress is being made in controlling CINV. Two current phase-III-studies used NEPA, a fixed-dose combination of netupitant (NETU), a new NK1 RA and palonosetron (PALO), a pharmacologically and clinically distinct 5-HT3 RA. “The oral fixed-dose combination has been developed to allow patients to receive guideline-based targeted antiemetic prophylaxis in a single oral administration” commented Matti Aapro, Lausanne, Switzerland. He presented a phase-III-study comparing one single oral dose of NEPA (netupitant 300 mg + palonosetron 0.50 mg) versus one single oral 0.50 mg dose of palonosetron (PALO) for prevention of CINV following moderately emetogenic chemotherapy (MEC) (Aapro M. et al. MASCC 2013, # 433). A total of 1,455 chemotherapy-naïve patients undergoing anthracycline-based chemotherapy were randomly assigned to receive dexamethasone plus either NEPA or PALO. NEPA or PALO were taken orally one hour before chemotherapy and dexamethasone was taken 30 minutes prior to chemotherapy. NEPA exhibited superior rates of complete acute (0-24 hour post-chemotherapy) and delayed (25-120 hours post-chemotherapy) antiemetic response (no emesis and no rescue medication; \( P=0.047 \) and \( P=0.001 \), respectively). “NEPA was also superior to PALO during the delayed/overall phases for complete protection, no emesis, and no significant nausea,” he noted. “The type and frequency of adverse events were comparable between NEPA and PALO.” The most common NEPA-related adverse events were headache (3.3%) and constipation (2.1%). NEPA “has the potential to improve chemotherapy-induced nausea and vomiting control for patients,” Aapro concluded.

Karin Jordan, Halle, Germany, presented another phase-III-study with NEPA (Jordan K et al. MASCC 2013, # 434). The study was designed to examine the tolerability and efficacy of NEPA over multiple cycles of HEC and MEC. 413 patients were randomized. NEPA was well tolerated > 1900 chemotherapy cycles. Over 75% of the patients received up to 4 chemotherapy cycles. Given that only few large randomized trials have documented safety and efficacy over multiple cycles of chemotherapy, the results of this study are especially important. The fixed-dose combination was highly effective in preventing CINV and efficacy of this combination was maintained over repeated cycles. Jordan concluded: “NEPA is a convenient, active, and well-tolerated combination that offers the opportunity to improve guideline adherence and CINV prevention for patients”.

Another study evaluated the effect of the novel combination of aprepitant and granisetron for RINV prophylaxis among patients receiving moderately emetogenic radiotherapy for thoracolumbar bone metastases (Dennis K et al. MASCC 2013, # 475). Acute and delayed radiotherapy-induced nausea and vomiting (RINV) is common among patients receiving moderately emetogenic radiotherapy for bone metastases. Single fraction patients (8Gy in 1
received aprepitant 125 mg and granisetron 2 mg on the day of radiotherapy and aprepitant 80 mg on the first 2 days after the day of radiotherapy. Multiple fraction patients (20Gy in 5 fractions) received aprepitant 125 mg on the first day of radiotherapy, aprepitant 80 mg on the third and fifth days of radiotherapy, and granisetron 2 mg on every day of radiotherapy. No single fraction patients experienced nausea, vomiting, retching or required rescue antiemetics during the acute phase. **Kristopher Dennis**, Ottawa, Canada, explained: “Aprepitant and Granisetron were efficacious for the prophylaxis of RINV”. Another study showed that by adding aprepitant to standard anti-emetic therapy 7 days after high-dose chemotherapy significantly reduced chemotherapy-induced vomiting in patients undergoing high dose chemotherapy before stem cell transplantation (Svanberg A et al. MASCC 2013, # 486). Twenty-eight patients in the aprepitant group compared to 14 in the control group (standard antiemetics) experienced complete response (no vomiting) from end of HDCT to end of study regarding vomiting (p=0.0001).

Standard antiemetic prophylaxis for highly emetogenic chemotherapy recommended in the MASCC/ESMO and ASCO guidelines is a triple combination of 5-HT3 RA, dexamethasone (Dex), and aprepitant (Apr). Yamanaka and colleagues compared for the first time the efficacy of two 5-HT3 RAs (palonosetron versus granisetron) within a triple regimen for preventing CINV due to HEC. The primary endpoint of the study was complete response during the first 120 hours (day 1 through 5) after chemotherapy. Although the primary endpoint was not met study results have shown the clinical superiority of palonosetron over granisetron, especially in the delayed phase. **Takeharu Yamanaka**, Tokyo, Japan, concluded „Palonosetron is a more preferable 5-HT3 RA in the triple regimen than granisetron for preventing CINV due to HEC.”

**Scientific Highlights Mucositis**

Oral mucositis (OM) is a frequent complication of high dose melphalan (HDM) followed by autologous hematopoietic stem cell transplantation (AHSCT). A current study compared the efficacy of 3 interventions to prevent HDM-induced oral mucositis in patients with multiple myeloma (Toro J et al. MASCC 2013 # 393). One hundred and seventeen patients who received HDM were randomized to receive either oral cryotherapy (CT), saline solution rinses, or Caphosol® (calcium phosphate). Only 10 % of patients in the cryotherapy group experienced OM ≥ grade 1, compared to 64 % and 66 % in the Caphosol® and saline solution groups, respectively (P<0.0001). None of the cryotherapy patients experienced grade 3–4 oral mucositis. Duration of oral mucositis in the group with cryotherapy was significantly shorter than in the other groups. Patients in the CT group required fewer analgesics compared with the other groups (p=0.007). Patients who received cryotherapy...
experienced less oral pain when compared to the Caphosol® and saline solution groups. **Juan Toro**, San Antonio, USA, San Antonio, summarized “Cryotherapy significantly reduces oral mucositis frequency, duration and severity.” The results of this study are further evidence to support the use of oral cryotherapy for the prevention of oral mucositis in patients receiving melphalan as recommended in the MASCC/ISOO guidelines published in 2007.” Its ease of application, tolerability and lack of side effects make oral cryotherapy an important resource for reducing the incidence and severity of oral mucositis”, he added.

**Scientific Highlight Neuropathic Pain**

Neurotoxicity is a dose-limiting side effect of many different chemotherapeutic agents. In particular, platinum compounds, including oxaliplatin, are associated with neurotoxicity. Acute sensory neurotoxicity manifests as rapid onset of cold-induced distal dysesthesia and/or paresthesia, sometimes accompanied by cold-dependent muscular contractions of the extremities or the jaw. The symptoms, often occurring during or shortly after infusion, are usually transient and mild. A cumulative sensory peripheral neuropathy may also develop with prolonged treatment with oxaliplatin, eventually causing superficial and deep sensory loss, sensory ataxia, and functional impairment. In a recent study from the Netherlands on the prevalence and severity of chemotherapy induced neuropathy and its influence on quality of life among a population-based sample of colorectal cancer survivors, neuropathy-related symptoms-, especially sensory symptoms in the lower extremities among those patients treated with oxaliplatin - were reported even 2–11 years after diagnosis of CRC (Mols F., MASCC 2013, Abstract 108. Since neuropathy symptoms impair health-related QOL, more attention should be paid to screening for and treating these symptoms. “Future studies should focus on possible ways to effectively prevent and treat chemotherapy induced neuropathy”, Mols explained.

Almost 10 years ago, benefits of administering intravenous calcium and magnesium concomitant with with oxaliplatin-based chemotherapy to reduce platin-induced neuropathy were shown in a study by Gamelin et al. (Gamelin L et al, Clin Cancer Res. 2004;10:4055-4061). The authors compared the results in this series of 160 prospective patients with historical controls, and found that the rate of neurotoxicity with oxaliplatin was reduced by half. Although this was not a randomized study the report led to an enthusiastic uptake of this practice. However, the first placebo-randomized phase-III-trial of this practice has shown no benefit. The results were presented at the 2013 Annual Meeting of the American Society of Clinical Oncology (ASCO) by Charles Loprinzi, Rochester, Minnesota (abstract 3501). The trial was conducted in 353 patients with colon cancer undergoing adjuvant therapy with FOLFOX (5-fluorouracil, oxaliplatin, and leucovorin), who were randomized to receive
intravenous CaMg (1g calcium gluconate, 1 g magnesium sulfate) or placebo before and after oxaliplatin. There was also a third arm in the trial, in which patients received CaMg before and placebo after the oxaliplatin. The results showed no differences between the groups in either acute neurotoxicity or cumulative sensory neurotoxicity, as assessed both by patient and physician questionnaires. "This study did not demonstrate any activity of IV CaMg as a neuroprotectant against oxaliplatin-induced neurotoxicity. This practice should now be stopped," Loprinzi commented at the MASCC-Meeting in Berlin.