INTERNATIONAL SOCIETY FOR ORAL ONCOLOGY

Newsletter 2009-2010

Editor: Andrei Barasch  Associate Editor: Rajesh V. Lalla
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(meeting announcement)
As the Vancouver scientific meeting rapidly approaches, it is fitting to bring you greetings from the ISOO Board, and to provide a brief update on ISOO activities. Our organization has participated enthusiastically in contributing to the Vancouver scientific program. First, the annual continuing education workshop will be held on Saturday morning and is entitled “Management of Oral Complications of Cancer Therapy”. This exciting session has an interdisciplinary mix of presenters who will discuss selected oral complications in a two-part program. The first part addresses taste changes, nutrition, and jaw dysfunction, while the second part addresses viral, fungal, and bacterial infections. Interdisciplinary panel discussions will enable audience participation, and local outside speakers will enhance the clinical applicability of the presentations. Second, the Oral Care Study Group is presenting a parallel session on Saturday afternoon entitled “Xerostomia: All You Need to Know and More”. This important session will discuss guidelines from the systematic reviews conducted by the Oral Care Study Group. It will also include a panel discussion and proffered papers.

In addition, the ISOO Board will meet at the Vancouver conference, and will host an ISOO General Membership Meeting on Thursday June 24 from 9-10am. All ISOO members are encouraged to attend this annual meeting and learn what’s going on with the organization. Finally, the ISOO Board is currently reviewing the organization’s non-profit and U.S. tax filing status. This examination is important in helping to determine ISOO’s future organizational structure and its relationship with MASCC. The Board has recently sent an email to all ISOO members asking them to vote on granting a one-year extension of the current ISOO Board in order to complete this work.

On behalf of the entire ISOO Board, I thank you for your commitment to our organization and look forward to seeing you in Vancouver.

Deborah B. McGuire, PhD, RN, FAAN
President, ISOO
The View from the Corner Office

Andrei Barasch

This is a swan song. Not a sad one, as my years as Editor of this Newsletter have been fulfilling. I simply think it is time to cede the position to someone with fresh views and ideas who will hopefully be able to continue to improve this publication from where I leave off. Someone with the desire to keep ISOO as an entity and able to reflect that identity and its strengths in the pages of this Newsletter. I think the it has been an important means of filling in the gaps between MASCC meetings to enhance our communications. I look forward to facilitating the transition for our new newsletter editor, whoever that may be!

As typical for a departing salvo, thanks are due, and they go to those who made significant contributions to the Newsletter. Their selfless work is highly appreciated. I may forget a few names and I hope those left out will forgive me for that. The folks who made the short list in my similarly limited mind include (in no particular order) Sharon Elad, Mike Brennan, Judith Raber-Durlacher, and Ourania Nicolatou-Galitis. And last but not least, my sincere thanks go to those who have taken the time to read the Newsletter and made our contributions worth the effort.

So I will say good-bye as editor and look forward to returning to these pages as a contributor to future issues!

Note

Please send all your communications electronically to Andrei Barasch at abarasch@uab.edu
The year is 2015 and last year’s phase III trials of Ulcernotmumab® have convinced the authorities (FDA in the US) to approve marketing of the drug for prevention of mucositis. Results of the phase III study indicated that Ulcernotmumab® is extremely effective at preventing alimentary mucositis induced by both chemotherapy and ionizing radiation. Side effects of the drug are minimal and the Oncology community is very excited at the prospect of a patient population that is virtually mucositis-free.

The 2016 meeting of MASCC/ISO in Tirana, Albania, will have a plenary session that will carry the congratulatory message to the membership, for this success was in no small part due to efforts of the organization’s members. Well done!

So, where do we go from here?

Since ISOO’s inception, the members’ efforts have been intensely focused on oral mucositis, with some space for salivary gland hypofunction and short spurts of interest in other issues, such as osteonecrosis of the jaws. As a result, we deserve a claim of substantial contribution to bringing the issue of mucositis to the fore of the research community and our members have done much of the work that led to the current maturity of this topic. Whether it will be 2015 or later (earlier?), we are approaching the time when these efforts will be crowned by success (see the insulin-like growth factor news item in the Science News of Interest below).

With that day in the periscope, I feel that our organization can make even greater contributions to the Oncology world. The direction I propose is treatment of oral cancer. The vast majority of malignant diseases are typically the territory of both oncology and the medical subspecialty that focuses on the affected system. Skin cancer is treated by dermatologists, lung cancer by pulmonologists, bone cancer by orthopods and blood cancers by hematologists. Can oral cancer be treated by stomatologists? The likely answer at this point in time is “no” but I believe we can and should change that. And that change should naturally start within the Oral Oncology community.

In the current climate, graduates of dental schools or stomatology universities are trained (and perceived) as mostly tooth doctors. Some curricula do include more advanced training in oral medicine, and all those I am aware of include some lectures about oral cancer. However, I do not know of any program where clinical students get to see, touch, and participate in the treatment of oral cancer patients. The paradigm that so far has gone unchallenged is that patients suspected of malignant disease must be referred to a medical doctor. This pattern of training continues in advanced education programs, though some Oral and Maxillofacial Surgery residencies have broken the mold. Nevertheless, no program I am aware of, including Oral Medicine residencies in the USA, encourages its residents to think in terms of cancer treatment. Or research the topic. Why not?
While I may agree that the overcrowded dental school curriculum may not be able to accommodate advanced training in oncology, advanced programs should open the door to such a possibility. With adequate training, a dental specialist should be able to treat cancer that is limited to the oral cavity and does not require surgical excision. Those of us who are hospitalists are already familiar with blood tests and necessary scans. Most of us also prescribe cytotoxic medication to treat other diseases such as pemphigoid or lichen planus. Some of us have already treated Kaposi’s sarcoma in HIV infected patients. New research may provide additional local therapeutic solutions. So why not?

The current financial crisis in the medical field should make now a propitious moment to expand the reach of Oral Oncology into the treatment of limited malignant disease. And from there, perhaps further. I think this is an exciting direction for a talented group like ours to tackle, and I propose that is where we should go from here. Why not?

ISOO News

Athens, Greece (Ourania Nicolatou-Galitis)

1. Dental Oncology Unit

   Educational activities

Dental Oncology Unit continues to be active on the education/motivation of general dentists in the treatment of cancer patients. Two courses are being organized each year, always overbooked, with 50 dentists attending each course. After the course, most of the attending dentists apply for HASCOCC membership, so HASCOCC is steadily growing.

   Treatment of cancer patients

   A large number of cancer patients are being followed in the Unit, with the help of graduate students.
   Bisphosphonate-related osteonecrosis of the jaws lesions were had a low prevalence (1.6%), after the prevention protocol that we implemented (Nicolatou-Galitis et al, under review).

   Head and neck cancer patients, who received cetuximab, in addition to radiotherapy and cisplatin were appropriately supported and the prevalence of severe mucositis was not higher than that of patients who received radiotherapy and cisplatin alone (Nicolatou-Galitis et al, under review).

   Research plans under way

   We are happy to participate in two Quality of Life (QoL) questionnaire modules development with colleagues in the EORTC.

   A graduate student has undertaken a project on QoL and xerostomia in head and neck cancer patients who have received radiotherapy, with the kind collaboration of Radiation Oncologists.
Two other graduate students will undertake a research project on bone metabolism, apoptosis and other inflammation factors in patients with metastatic bone disease.

Within our fruitful collaboration with radiation oncologists, we are preparing a project to evaluate the benefit of devices for oral mucositis.

2. Hellenic Association of Supportive Care of the Oral Cavity in Cancer – HASCOCC

Grant and financial supportive activities
HASCOCC kindly supports the secretarial assistance of the Dental Oncology Unit, Clinic of Hospital Dentistry, School of Dentistry, University of Athens. HASCOCC also offers small scholarships to graduate students.

Symposium activities

(a) Mediterranean Multidisciplinary Oncology Forum – MMOF

The 1st Meeting was held in September 2009, in Athens. It was quite successful, with more than 500 participants from different Mediterranean countries. Professor Douglas Peterson and Dr Sharon Elad were invited lecturers and highlighted the “Oral Oncology” subject. MMOF is expanding and the President, Professor Dimitris Bafaloukos, has embraced the development of the “Oral Supportive Oncology Section” of MMOF. New members are welcome to offer their ideas and serve in every multidisciplinary way.

(b) HASCOCC is organizing the 2nd Meeting in Athens, scheduled for 24 and 25 April. Please see the preliminary program and call for abstracts in MASCC event calendar and in www.oraloncology.gr, English version. HASCOCC is grateful to MASCC/ISOO for their kind support. We also thank all the international speakers for their kind participation.

(c) A scientific event has also been arranged and Professor Mark Schubert will honour us as an invited speaker to highlight the subject of Oral Oncology in Haematopoietic Stem Cell Transplantation.

3. MASCC / ISOO 2011 Symposium in Athens

Professors Dimitris Bafaloukos, Kostas Syrigos and Ourania Nicolatou-Galitis cordially welcome all the MASCC and ISOO members, colleagues and friends to attend the Symposium and enjoy the Greek spirit and hospitality.
Adelaide, Australia
Reported by Richard Logan

Animal models
The Mucositis Research Group has developed animal models of both chemotherapy- and radiotherapy-induced mucositis to investigate the changes both along the alimentary canal and through its depth after chemotherapy and radiotherapy treatments. The group has an international reputation in this area, with Professor Keefe acting as a consultant to many of the pharmaceutical companies that have drugs in development for mucositis, as well as collaborating to investigate the potential of new anti-mucotoxic agents in a pre-clinical setting. Current pharmaceutical collaborations include Nestle and Glaxo-Smith Kline, and studies include the development of a new animal model using targeted therapy.

Human clinical trials
A number of clinical studies are currently underway, investigating possible mechanisms for the development of mucositis in cancer patients. The Triad Burden of Illness studies are prospectively investigating the clinical and quality of life implications and health-care costs associated with mucositis from multi-cycle chemotherapy and chemo-radiotherapy.

Preliminary results from a pilot clinical study led to funding from Cancer Australia and Cure Cancer to investigate the mechanisms of chemotherapy-induced mucositis in more detail, specifically looking at the gut bacteria and inflammatory cytokines. Research in animal models this year has led to the findings that chemotherapy has an effect on the gut bacteria, and this effect varies with the drug administered; mucus production is altered following chemotherapy, and may leave the gut lining vulnerable to damage; and inflammatory cytokines are increased following chemotherapy (both in the gut and in the circulation), which may add to the damage through downstream signaling. Knowledge of the components involved in the development of mucositis will allow more detailed studies investigating the signaling pathways involved, which will hopefully identify new targets for intervention.

Oral Care Study Group Updates
Reported by Michael Brennan, Co-chair OCSG, and Douglas Peterson

Members of the Oral Care Study group of MASCC/ISOO have been working hard to complete the systematic reviews of oral complications from cancer therapies. In the last part of 2009, approximately 60 individuals worked together to complete 12 manuscripts- all of which are currently in review with the Journal of Supportive Care in Cancer (JSCC). A total of 531 articles were evaluated by 2 reviewers and an extensive amount of data was extracted from each article.

Depending on funding, these manuscripts will be presented in serial issues or as a supplement of JSCC. The Oral Care Study group will continue to go over the enormous amount of data from these reviews and will work on future publications- more to follow!
In addition to the publication of the systematic reviews, the evidence is also being incorporated into a comprehensive update of the National Cancer Institute's PDQ website on oral complications of cancer therapies. The previous version of the PDQ text had been updated by Douglas Peterson, Mark Schubert and Cesar Migliorati. The systematic reviews now being completed represent important new information that will provide a foundation for this major update of the PDQ website. This modeling extends the impact of the reviews, and enhances the visibility and contribution of ISOO with the NCI.

Board members 2009-2010:

President: Deborah B. McGuire, PhD, RN, FAAN, United States
Vice President: Inger von Bültzingslöwen, DDS, PhD, Sweden
Vice President for Communication: Ourania Nicolatou-Galitis, DDS, Greece
Immediate Past President: Judith E. Raber-Durlacher, DDS, PhD, the Netherlands
Secretary: Sharon Elad, DDS, Israel
Treasurer: Michael T. Brennan, DDS, MHS, United States
MASCC Liaison: Joel B. Epstein, DMD, MSD, FRCD(c), FRCDEd, United States
Educational Initiatives in the Field Of Oral Cancer – A Growing Demand

Sharon Elad, DMD, MSc, Head of Hospital Oral Medicine Service, Hadassah University Medical Center and Hebrew University-Hadassah School of Dental Medicine, Jerusalem and Chairperson of the Israeli Society of Oral Medicine.

The interest in oral cancer and oral complications in cancer patients has resulted in an increased demand for educational activities by various audiences. During the last year, an unprecedented number of scientific events related to oral cancer and related oral complications were organized in Israel. The conference halls were crowded with general and specialist dental practitioners, often joined by nurses and physicians. As expected, the role of the Oral Oncology specialist was pivotal. These educational programs were organized by the Israeli Society of Oral Medicine (ISOM), the universities of Jerusalem and Tel-Aviv, regional medical centers and dental centers.

The main catalyst for the increased number of conferences this year is the growing interest in bisphosphonate-related osteonecrosis of the jaws (BRONJ). This subject is currently under extensive research, with numerous publications reporting on suggested guidelines by well-recognized medical societies, such as the American Academy of Oral and Maxillofacial Surgery. Dentists here in Israel were especially interested in attending forums that discussed updated guidelines on dental treatment for patients being treated with bisphosphonates.

At the ISOM annual scientific meeting, another type of educational activity relating to oral cancer was discussed. The theme was oral mucosal lesions and open discussions were
dedicated to the management of lichen planus and lichenoid lesions. At this meeting, a series of clinical cases were presented, each with a clinical dilemma. Most of the dilemmas were related to the potential malignant transformation of lichen planus and lichenoid conditions. The panel of experts and the audience were requested to recommend a treatment approach. Although the risk of cancer in lichen planus is not a new topic, recent developments in our understanding of the molecular nature of lichen planus may change our approach in patient treatment planning. One example of this research can be found in a recent publication by Yarom et al in the Journal of Dental Research.[1]

After a long registration procedure with the health authorities in Israel, the marketing of Visilight plus kit was started this year. Based on personal experience of several oral medicine specialists, ISOM decided to offer its assistance to the company that distributes Visilight in Israel. We have included in the Visilight kit a letter that offers assistance to patients using Visilight, along with a list of oral medicine specialists who are available for consultations regarding oral lesions. We hope that this innovative approach will greatly improve the early detection of abnormal oral conditions.

As we enter the year 2010, we hope that this popular enthusiasm for issues relating to oral cancer and its complications will continue, as they greatly benefit the dental community and general population.

Acknowledgment: Thanks to Dr. Sharon Akrish for assisting in composing this article.

Reference:
Case of the Year

School of Dentistry and Attikon University Hospital, School of Medicine, University of Athens, Athens, Greece

Emerging oral complications for targeted therapies?
Unusual gingival bleeding in a patient with renal cell carcinoma receiving sunitinib,

A 19 year old female, diagnosed with renal clear cell carcinoma, stage pT3N0, associated with Xp11.2 translocation/TFE3 gene fusion, underwent nephrectomy in 2007. Two years later, in 2009, she developed a recurrence, and, on July 15 2009, the patient was started on cisplatin 100mg/m2 every 3 weeks and Sunitinib at a daily dose of 50mg. On August 3rd, 2009, the patient presented with mouth pain, malodor, and profound oral bleeding. Her complete blood count was normal. Oral clinical examination revealed extensive necrotic, painful, haemorrhagic areas at the gingival crests and the interdental papillae, on maxilla and mandible (Photos below).

Figure 1. Maxilla. Arrow and arrow head show the necrotic gingivae and the blood clots.
These findings were consistent with necrotizing ulcerative gingivitis (NUG), whereas primary herpetic gingivostomatitis and oral chemotherapy-induced mucositis were excluded, based on the clinical picture. Metronidazole (500mgX3) was administered for six days. Two days later, the patient reported to be well and one week later her oral examination was normal.

Necrotizing ulcerative gingivitis is a rapidly destructive gingival bacterial infection, characterized by necrosis of the interdental papillae, bleeding, pain, and halitosis. Metronidazole is the treatment of choice.

NUG is usually seen in immunocompromized patients, in the present case on the grounds of the underlying malignancy. The antiangiogenetic/antiendothelial effect of sunitinib most probably acted synergistically, intensifying the NUG-related bleeding. To our knowledge, this is the first report of NUG with unusual bleeding, following treatment with sunitinib.

**Science News of Interest**

**Increased thyroid cancer risk among women**

This year more than 27,000 women and 10,000 men will be diagnosed with thyroid cancer. In women, the incidence is increasing by an astounding 6.3% a year. It remains unclear why “women are more susceptible to thyroid problems than men. It has been long known that radiation can cause thyroid cancer, but for women, there’s no solid evidence about the cause of this increasing problem.”
Vitamin E extract shrinks tumors within days

"A vitamin jab that shrinks tumors in a day is being hailed as a powerful new treatment for cancer." Researchers at the University of Glasgow and the University of Strathclyde found that "injecting an extract of vitamin E," called tocotrienol, "into the bloodstream" shrank tumors "within 24 hours...and after ten days they had almost completely disappeared." The study targeted skin cancers by disguising tocotrienol "inside thousands of microscopic bubbles made from fat," which travelled "through the body without damaging healthy cells." (Daily Mail)

Melanoma incidence increasing 2.4% annually in the United States

According to a study published in the Dec. issue of the Archives of Dermatology, "melanoma incidence nationwide has been increasing at a rate of 2.4% per year, with certain groups having distinctly higher rates of annual increase." After analyzing data on "41,072 cases of melanoma," researchers found that "the highest rates of advanced melanoma...were seen in blacks," while "Hispanics had a higher proportion of advanced melanomas than whites."

Denosumab to treat osteoporosis, cancer.

Finally, a biologic compound will compete with bisphosphonates. Amgen Inc.’s search for a way to strengthen bones led scientists to a medicine that may stop tumors from spreading beyond soft tissue. The FDA is "weighing whether to clear the drug, denosumab, to treat the bone-thinning disorder osteoporosis in aging women." In addition, the first indication on whether denosumab can also "help keep bone tissue strong enough to fight off the invasion of cancer cells" will come "sometime this year when Amgen will release initial results of a 1,400-patient study begun in 2006 in cancer patients, said Christine Regan, an Amgen spokeswoman." Notably, results of the phase III trial have shown that 2.4% of the patients developed osteonecrosis of the jaws (ONJ).

Mouthwash may help prevent cancer therapy-induced mucositis

Caphosol, a mouthwash intended to treat mucositis, is now being used in some hospitals in Great Britain. In a clinical trial, the treatment, "made from a special combination of...calcium and phosphate," was found to benefit patients "having bone marrow transplants." In fact, over "twice as many patients using the mouthwash avoided mucositis altogether," while for those who "did develop it their symptoms lasted half as long and they needed 72% less morphine." Still, "Cancer UK doesn't recommend Caphosol yet," because the group is "'waiting for more results from bigger trials,' says a spokesperson." (Daily Telegraph)

Sentinel node biopsy may predict absence of lymphatic metastasis in oral cancer.

"In early oral squamous cell carcinoma, a sentinel node biopsy correctly predicted an absence of lymphatic metastasis in all but 4% of patients," according to a study published in the Journal of Clinical Oncology. Researchers found that "for T1 and T2 lesions that were clinically node-negative, the procedure -- combined with additional sectioning and immunohistochemistry -- yielded a negative predictive value of 96%." They noted that the results "may position the procedure as an intermediate option between watchful waiting and selective neck dissection." (MedPage Today)

Gene suppression may reduce chemotherapy side effects.

Researchers from the University of Southern California introduced new research this week that may provide hope for chemotherapy patients -- in the form of a pill. Researchers said that "mice with melanoma that were genetically modified to have reduced expression of...the insulin-like growth factor I (IGF-I)...were less
vulnerable to side effects of chemo, and had better survival rates than mice without this gene suppression.” The “IGF-I suppression protected healthy cells from chemo, but not cancerous cells.” (LA Times)

The Mucositis Study Group of MASCC/ISOO invites you to the Fourth Annual

**Mucositis Research Workshop**

**Tuesday - June 22, 2010 - 8.30 AM - 5:00 PM**

The British Columbia Cancer Research Centre, 601 West 10th Avenue, Vancouver, Canada

Following the outstanding success of last year’s workshop, the Mucositis Study Group of MASCC/ISOO is once again hosting a one-day research workshop in conjunction with the 2010 MASCC/ISOO symposium in Vancouver. This is the place to be if you have interest in research related to mucositis. Attendees typically include a broad cross-section of academia and industry with interests ranging from basic to pre-clinical and clinical mucositis research. The program will include proffered papers, invited lecture(s), and an Expert Panel Question and Answer session.

Registration for the workshop is separate from registration for the main meeting. Workshop registration costs $85 and includes coffee breaks, lunch, and printed materials for workshop attendees. Please submit registration requests in the attached form to crittenberg@mascc.org. Space is limited to 70 participants so please register early to avoid disappointment.

**CALL FOR ABSTRACTS**

Abstract guidelines are the same as those for the main MASCC meeting and include a word limit of 300 words (not including the title and authors’ names).

Abstracts may cover any aspect of mucositis research. The presenting author must be specified.

Please submit your abstract(s) for the workshop to Lalla@uchc.edu by February 15, 2010. Selected presenters will be notified by April 1, 2010.

Please remember to submit your abstract(s) separately for the main MASCC/ISOO meeting!
Fourth Annual Mucositis Research Workshop

Tuesday, June 22, 2010  8:30AM – 5:00PM
The British Columbia Cancer Research Centre, 601 West 10th Avenue, Vancouver, Canada • ph: (604) 877-6000

Please submit Registration Form to: crittenberg@mascc.org
Please submit abstracts (same format as main meeting) to: lalla@uchc.edu
Workshop attendees should register separately for the main MASCC meeting.
Attendees must be registered for some portion of the MASCC/ISOO Symposium.

Registration Form

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Authorized Signature:
If e-mailing this form and you do not have an electronic signature, your printed name will act as your signature.
If paying by **Check or Money Order** return this form with payment to the Symposium Organizer:

**MASCC; Attn: Cynthia Rittenberg; 500 Rue St. Ann Suite 223; Metairie, LA 70005 USA**

*Please Note: This Form will act as your Receipt.*
ORAL HEALTHCARE FOR PEOPLE LIVING WITH CANCER

7 credits of Verifiable Continuing Professional Development (CPD)

Date: June 11th (Friday) 2010

Venue: London, de Vere Conference Centre, Canary Wharf

A single day CPD meeting, in London, in parallel sessions, organized by Professor Crispian SCULLY CBE, and supported by International Academy of Oral Oncology (IAOO), Multinational Association of Supportive Care in Cancer (MASCC) and Royal College of Surgeons of Edinburgh.

Given by a European faculty, the day is aimed at:

- Dentists, and specialists mainly in maxillofacial surgery, oral medicine, oral surgery, special care dentistry, and otorhinolaryngology.
- Dental care professionals [DCPs], and the cancer support team.

Faculty:

Professor Jose BAGAN (Spain)

Professor Marco CARROZZO (UK)

Professor Luca Di ALBERTI (Italy)

Professor Pedro Diz DIOS (Spain)

Professor Jose-Pedro FIGUEIREDO (Portugal)

Professor Michele GIULIANI (Italy)

Professor Miguel GONZALEZ-MOLES (Spain)

Dr Vinod JOSHI (UK)

Mr Nick KALAVREZOS (UK)

Mr Cyrus KERAWALA (UK)

Dr Carlos MADRID (Switzerland)

Professor Jukka MEURMAN (Finland)
Professor Tim NEWTON (UK)

Dr Chris NUTTING (UK)

Professor Stephen PORTER (UK)

Dr Judith RABER-DURLACHER (Netherlands)

Professor Crispian SCULLY (UK)

Professor Simon ROGERS (UK)

Dr Rosie SHOTTS (UK)

Professor Isaac van der WAAL (Netherlands)

Professor Saman WARNAKULASURIYA (UK)

Course costs including all day coffee and restaurant lunch:

Dentists, surgeons and medics = £125

All others = £95

Register at: http://www.eventassociates.co.uk/

Additional information can be obtained at the MASCC website or by contacting Dr. Judith Raber-Durlacher (jraber@worldonline.nl).