

How does disease modifying treatment fit into future cancer pain management guidelines?

Peter Lawlor
Elisabeth Bruyère & University of Ottawa



5/06/2012

EAPC Preconf P7

1

Case Example: 62yo fem with MCRC in PCU..1

- Dx Oct 2007, localized disease
 - Neoadjuvant RT, Laparoscopic Ant Resection + colostomy
- Jan 2008 Adjuvant ChemoTx with FOLFOX x 2 cycles
 - LBO in midst of 1st cycle, Rx laparotomy - adhesions divided
 - Coronary spasm in 2nd cycle ? due to 5FU
- Dx 2009 vaginal met, July 2010 Rx Irinotecan ChemoTx
 - ARF, febrile neutropenia, flank pain, Nephrostomy drain initially then Nephroureterostomy in Dec 2010
- Oct 2011: Pre-sacral mass on MRI invading S1 and S2
 - RadioTx, & Pain Team referral
- Nov 2011 – Rx Panitumumab
 - Switched to Ralitrexed (Tomudex) because of skin toxicity

5/06/2012

EAPC Preconf P7

2

Case Example: 62yo fem with MCRC in PCU..2

- May 2012: admitted to PCU for Methadone switch
 - Severe incident pain
- Unable to tolerate Methadone / Fentanyl prn
 - Intrathecal administration of opioid /local anaesthetic
- Points to note:
 - Patients personality
 - Many surgical/radiological interventions
 - Chemotherapy treatments: benefit vs burden
 - Late palliative care referral
 - Radiation Rx
 - Monoclonal Rx
 - Methadone unsuccessful, next step: intrathecal analgesia

5/06/2012

EAPC Preconf P7

3

Objectives

To evaluate

- the impact of “cancer disease modifying therapies” on cancer pain [Why?]

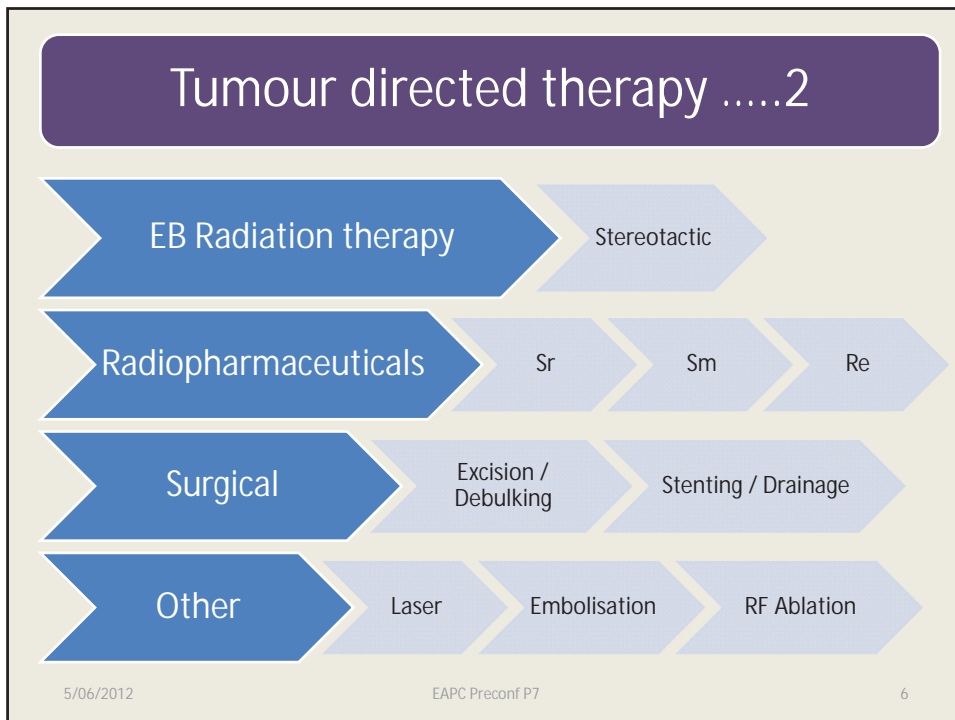
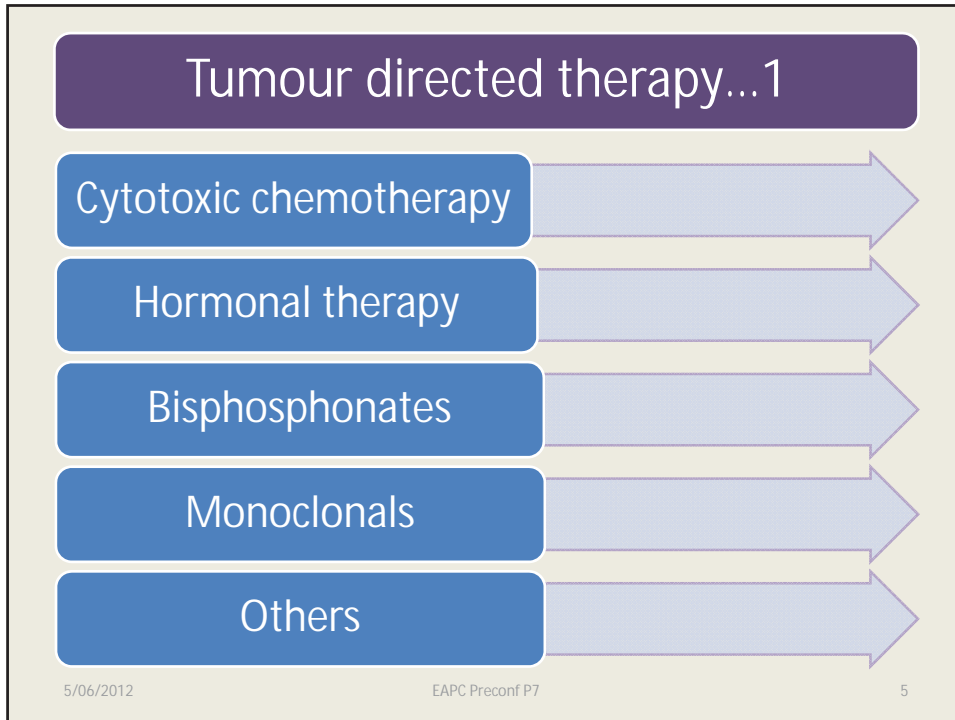
To explore

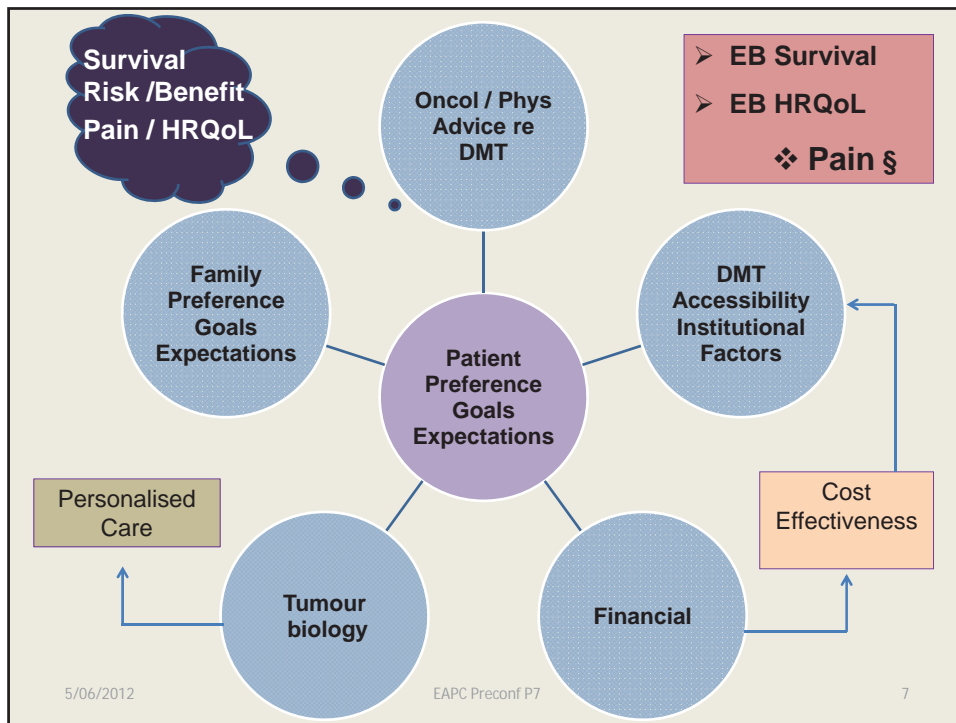
- how best to incorporate “cancer disease modifying therapies” in cancer pain guidelines [What & How?]

5/06/2012

EAPC Preconf P7

4





An evolving story...

- Developments in Cancer Care
 - Disease modification
 - RCTs: strong evidence base
 - Survival data vs HRQoL data
 - Symptom control / Supportive & Palliative Care / Hospice Care
 - Developing evidence base
 - QoL: Pall & Hospice Care



Table 3 Binary Logistic Regression Model†

	Adj Odds Ratios 2007 vs 1997	95% CIs	P Value
Central Line Use	2.62	0.94-7.31	0.065
Peripheral Line Use	4.82	3.33-6.98	<0.0001
Bisphosphonate iv	2.24	1.11-4.50	0.024
Antibiotics iv	7.94	4.34-14.5	<0.0001
Chemotherapy	7.19	2.05-25.2	0.002
Feeding oral vs other	0.40	0.18-0.88	0.022
Out of Hospice Trip	1.85	1.20-2.84	0.005
A red cell transfusion	3.26	1.67-6.37	0.0005

† Adjusted for age, admission duration, gender and referral location

Lawlor et al MASCC Rome 2009

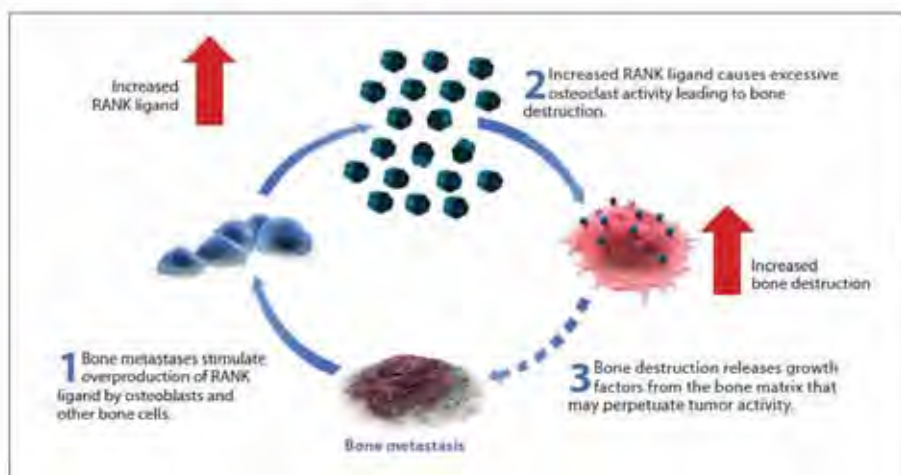


Figure 2: The Vicious Cycle of Bone Destruction From Metastases: the Role of RANK Ligand—Increased levels of receptor activator of nuclear factor- κ B (RANK) ligand are both the result of the presence of bone metastases and the cause of excessive osteoclast activity that in turn increases bone destruction. Data from: Mundy GR. *Nat Rev Cancer*. 2002[2] and Roodman GD. *N Engl J Med*. 2004[97]

cancertherapy.com

ONCOLOGY • December 2011 1369

The Economist

Log in | Register | Subscribe | Digital & mobile

World politics | Business & finance | Economics | Science & technology | Culture | Blogs | D

Multimedia

Audio, video and videographics

Previous | Next | Latest Multimedia | Latest from all our blogs

The cost of fighting cancer

Targeted therapies

May 31st 2011, 22:23 by The Economist online

Like 18 | Tweet 1

Drugs companies are charging top dollar for treatments tailored to combat specific types of cancer. Does the benefit outweigh the cost?

5/06/2012 EAPC Preconf P7 11

	Medline (R) without Revision 1996 to 2012 (May Week 3)	Hits
1	Antibodies monoclonal (MeSH) or "targeted therapy", (tw)	131,419
2	Neoplasms (MeSH) or "cancer", (tw)	626,750
3	1 + 2	22,353
4	Pain (MeSH) or "pain", (tw)	263,187
5	1 + 2 + 4	215
6	Limits: year > 2000, English, abstract available	153

5/06/2012 EAPC Preconf P7 12

Role of vertebral augmentation procedures in the management of vertebral compression fractures in cancer patients

Kamran Aghayev^a, Ioannis D. Papanastassiou^{a,b} and Frank Vrionis^a

^aDepartment of Neuro-Oncology, H Lee Moffitt Cancer Center and Department of Neurosurgery, University of South Florida, Tampa, Florida, USA and ^bDepartment of Orthopedics, General Oncological Hospital 'Agiou Anagnosti', Athens, Greece

Correspondence to Frank Vrionis, Department of Neuro-Oncology, H Lee Moffitt Cancer Center and Department of Neurosurgery, University of South Florida, 12902 Magnolia Drive, Tampa, FL 33612, USA
Tel: +1 813 745 4251; fax: +1 813 745 3713;
e-mail: fvri@usf.edu

Current Opinion in Supportive and Palliative Care 2011, 5:222-226

Purpose of review

To review the current status of vertebral augmentation procedures (VAPs) in the management of symptomatic vertebral compression fractures (VCFs) in cancer patients.

Recent findings

The natural history of VCFs in the cancer setting is presumably different from the one seen with osteoporotic fractures. Factors contributing to the poor outcome with conservative treatment in cancer patients include continued bone loss due to tumor invasion, poor nutritional status, immobilization, prolonged steroid use, gonadal ablation, chemotherapy and radiotherapy. VAPs have been shown by retrospective and prospective randomized studies to be effective in treating symptomatic VCFs. Advantages of VAPs include immediate pain relief, avoiding delays in chemoradiation, outpatient care in the majority of cases, biopsy, vertebral height restoration, and potential antitumor effect of bone cement. Results from the prospective randomized Cancer Fracture Evaluation (CAFÉ) trial show superiority of balloon kyphoplasty (BKP) over conservative management in cancer patients with VCFs with similar rate of adverse events between treatment arms. Additionally, the field is still evolving with advances such as combination with radiosurgery and spinal radiofrequency ablation (RFA), use of kyphoplasty without a balloon and highly viscous cement to prevent leakage.

Summary

VAPs are well tolerated and effective methods to provide palliative care for cancer patients with VCFs and should be offered to symptomatic patients.

Keywords

kyphoplasty, metastasis, multiple myeloma, vertebral compression fracture, vertebroplasty

5/06/2012

EAPC Preconf P7

13

Radiation for bone metastases

Daniel J. Bourgeois III^d, Stephen Kraus^{a,c}, Bassam N. Maalouf^{b,d} and Oliver Sartor^{b,c,d}

^aDepartment of Radiation Oncology, ^bMedicine, Section of Hematology-Oncology, Tulane Cancer Center and ^cTulane Medical School, New Orleans, Los Angeles and USA

Correspondence to Oliver Sartor, MD, Liborde Professor of Cancer Research, Tulane Cancer Center, New Orleans, Los Angeles and USA
Tel: +504 988 7869; fax: +504 988 5059;
e-mail: osartor@tulane.edu

Current Opinion in Supportive and Palliative Care 2011, 5:227-232

Purpose of review

To synopsize the current state-of-the-art for radiation and treatment of painful bone metastases with a focus on prostate cancer.

Recent findings

Although external beam radiation has long been known to palliate painful bone metastatic disease for patients with prostate cancer, new studies continue to evolve in this area. Data from randomized studies over the past decade emphasize that palliation can be achieved with single-fraction radiation strategies. Despite these data, and various supportive national and international guidelines, single-fraction regimens are relatively underutilized in the USA as compared with other countries. In addition to external beam radiation, beta-emitting isotopes are also effective as systemic agents for the palliation of painful bone metastases. New alpha-emitters such as Alpharadin (radium-223) are under current development but remain unproven at this time and recent data indicate that this agent can prolong survival in patients with advanced prostate cancer.

Summary

Radiation in various forms is highly effective for palliation of pain associated with bone metastases.

Keywords

bone, metastasis, palliation, radiation, radiopharmaceuticals

5/06/2012

EAPC Preconf P7

14

Original Article

Palliative Radiotherapy for Bone Metastases in the Last 3 Months of Life: Worthwhile or Futile?

K. Dennis, K. Wong, L. Zhang, S. Culleton, J. Nguyen, L. Holden, F. Jon, M. Tsao, C. Danjoux, E. Barnes, A. Sahgal, L. Zeng, K. Koo, E. Chow

Rapid Response Radiotherapy Program, Department of Radiation Oncology, Odette Cancer Centre, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada

Received 23 December 2010; received in revised form 24 March 2011; accepted 28 March 2011

Abstract**Aims:** To determine the efficacy of radiotherapy for the palliation of pain from bone metastases among patients in their last 3 months of life.**Materials and methods:** Mutually exclusive, prospectively gathered Edmonton Symptom Assessment System and Brief Pain Inventory databases compiled from patients with bone metastases receiving palliative radiotherapy were reviewed. Demographic information and response rates from patients dying within 3 months of beginning radiotherapy were analysed.**Results:** From a total of 1118 patients, 232 dying within 3 months of beginning treatment were identified. There were 148 men and 84 women. Their median age was 69 years and their median Karnofsky Performance Status was 60. The three most common primary cancers were lung (34%), prostate (18%) and gastrointestinal (14%). Fifty-eight percent of patients received single fraction treatment. A pain response was evaluable for the 309 (47%) patients with available follow-up information. The overall response rates were 70% at 1 month and 63% at 2 months, which included complete and partial responses in accordance with the International Bone Metastases Consensus definitions.**Conclusions:** Despite their limited lifespan, patients reported pain relief after palliative radiotherapy. Patients suffering from painful bone metastases with an estimated survival of 3 months should still be considered for palliative radiotherapy.

© 2011 The Royal College of Radiologists. Published by Elsevier Ltd. All rights reserved.

Key words: Bone metastases; pain; palliative care; prognosis; radiotherapy

5/06/2012

EAPC Preconf P7

15

Systemic Metabolic Radiopharmaceutical Therapy in the Treatment of Metastatic Bone Pain

Fabio M. Paes, MD, and Aldo N. Serafini, MD

Bone pain due to skeletal metastases constitutes the most common type of chronic pain among patients with cancer. It significantly decreases the patient's quality of life and is associated with comorbidities, such as hypercalcemia, pathologic fractures and spinal cord compression. Approximately 65% of patients with prostate or breast cancer and 35% of those with advanced lung, thyroid, and kidney cancers will have symptomatic skeletal metastases. The management of bone pain is extremely difficult and involves a multidisciplinary approach, which usually includes analgesics, hormone therapies, bisphosphonates, external beam radiation, and systemic radiopharmaceuticals. In patients with extensive osseous metastases, systemic radiopharmaceuticals should be the preferred adjunctive therapy for pain palliation. In this article, we review the current approved radiopharmaceutical armamentarium for bone pain palliation, focusing on indications, patient selection, efficacy, and different biochemical characteristics and toxicity of strontium-89 chloride, samarium-153 lexidronam, and rhenium-186 etidronate. A brief discussion on the available data on rhenium-188 is presented focusing on its major advantages and disadvantages. We also perform a concise appraisal of the other available treatment options, including pharmacologic and hormonal treatment modalities, external beam radiation, and bisphosphonates. Finally, the available data on combination therapy of radiopharmaceuticals with bisphosphonates or chemotherapy are discussed.

Semin Nucl Med 40:89-104 © 2010 Elsevier Inc. All rights reserved.


5/06/2012

EAPC Preconf P7

16

JOURNAL OF CLINICAL ONCOLOGY	REVIEW ARTICLE	
<p>Palliative Radiotherapy Trials for Bone Metastases: A Systematic Review</p> <p><i>Edward Chow, Kristin Harris, Ghee Fan, May Tsim, and Wei M. Xu</i></p>		
5/06/2012	EAPC Preconf P7	17

A B S T R A C T		
<p>Purpose The objective is to update previous meta-analyses with a systematic review of randomized palliative radiotherapy (RT) trials comparing single fractions (SFs) versus multiple fractions (MFs).</p> <p>Methods The analysis includes all published reports from randomized trials comparing SF or MF schedules for the treatment of painful bone metastases with localized RT. A systematic review was performed using the random-effects model with Review Manager version 4.1 (Cochrane Collaboration, Oxford, UK). The odds ratio and 95% CI were calculated for each trial and presented in a forest plot.</p> <p>Results A total of 16 randomized trials from 1988 onward were identified. For intention-to-treat patients, the overall response (OR) rates for pain were similar for SF at 1,468 (58%) of 2,513 patients and MF RT at 1,466 (59%) of 2,487 patients. The complete response (CR) rates for pain were 23% (545 of 2,375 patients) for SF and 24% (558 of 2,351 patients) for MF RT. No significant differences were found in response rates. Trends showing an increased risk for SF RT arm patients in terms of pathological fractures and spinal cord compressions were observed, but neither were statistically significant ($P = .75$ and $P = .13$, respectively). The likelihood of re-treatment was 2.5-fold higher (95% CI, 1.76 to 3.56) in SF RT arm patients ($P < .00001$). Repeated analysis of these end points, excluding dropout patients, did not alter the conclusions. Generally, no significant differences with respect to acute toxicities were observed between the arms.</p> <p>Conclusion No significant differences in the arms were observed for overall and CR rates in both intention-to-treat and assessable patients. However, a significantly higher re-treatment rate with SFs was evident.</p> <p><i>J Clin Oncol 25:1423-1436. © 2007 by American Society of Clinical Oncology.</i></p>		
5/06/2012	EAPC Preconf P7	18



Recent important developments in the management of nonspine bone metastases

Liang Zeng^a, Stephen Lutz^b, Edward Chow^a, and Peter Hoskin^c

Purpose of review
External-beam radiotherapy (EBRT) remains the most important treatment for patients with painful bone metastases. This review updates the recent information regarding therapeutic guidelines, pain flare reaction, treatment endpoints, and quality-of-life (QOL) measurements.

Recent findings
Firstly, within the framework of the Third International Consensus Conference Workshop on Palliative Radiotherapy, the American Society for Radiation Oncology has published evidence-based treatment guidelines for bone metastases which should be employed in evaluating both the care of individuals as well as the quality indices of radiotherapy centers. Secondly, the definition and proper management of pain flare following the initiation of radiotherapy for bone metastases allows for the prevention or minimization of this treatment-related phenomenon. Thirdly, the appropriate endpoints for treatment response have been updated and should be employed for all clinical trials measuring clinical efficacy. Finally, the EORTC QLQ-BM22 QOL module has been validated and should be used to measure QOL in all patients entered onto trials.

Summary
Although the treatment of bone metastases with EBRT is a well established method for providing palliative relief from painful bone metastases, recent publications have enhanced our knowledge of the best approaches to caring for this clinical scenario.

5/06/2012
EAPC Preconf P7
19

I. J. Radiation Oncology • Biology • Physics Volume 79, Number 4, 2011

Purpose: To present guidance for patients and physicians regarding the use of radiotherapy in the treatment of bone metastases according to current published evidence and complemented by expert opinion.

Methods and Materials: A systematic search of the National Library of Medicine's PubMed database between 1998 and 2009 yielded 4,287 candidate original research articles potentially applicable to radiotherapy for bone metastases. A Task Force composed of all authors synthesized the published evidence and reached a consensus regarding the recommendations contained herein.

Results: The Task Force concluded that external beam radiotherapy continues to be the mainstay for the treatment of pain and/or prevention of the morbidity caused by bone metastases. Various fractionation schedules can provide significant palliation of symptoms and/or prevent the morbidity of bone metastases. The evidence for the safety and efficacy of repeat treatment to previously irradiated areas of peripheral bone metastases for pain was derived from both prospective studies and retrospective data, and it can be safe and effective. The use of stereotactic body radiotherapy holds theoretical promise in the treatment of new or recurrent spine lesions, although the Task Force recommended that its use be limited to highly selected patients and preferably within a prospective trial. Surgical decompression and postoperative radiotherapy is recommended for spinal cord compression or spinal instability in highly selected patients with sufficient performance status and life expectancy. The use of bisphosphonates, radionuclides, vertebroplasty, and kyphoplasty for the treatment or prevention of cancer-related symptoms does not obviate the need for external beam radiotherapy in appropriate patients.

Conclusions: Radiotherapy is a successful and time efficient method by which to palliate pain and/or prevent the morbidity of bone metastases. This Guideline reviews the available data to define its proper use and provide consensus views concerning contemporary controversies or unanswered questions that warrant prospective trial evaluation.

5/06/2012
EAPC Preconf P7
20

BJUI

Impact of docetaxel-based chemotherapy on quality of life of patients with castration-resistant prostate cancer: results from a prospective phase II randomized trial

Orazio Caffo, Teodoro Sava*, Evi Comploj†, Annamaria Fariello*, Fable Zustovich‡, Romana Segati§, Cosimo Sacco¶, Antonello Vecchia and Enzo Galligioni****

*Medical Oncology Department, Santa Chiara Hospital, Trento; *Medical Oncology Department, University of Veneto, Verona; †Urology Department, San Maurizio Hospital, Bolzano; ‡Medical Oncology Department, SS. David Hospital, Sord; §Discipline Medica I, Istituto Oncologico Veneto (IOV), Padua; ¶Medical Oncology Department, Civil Hospital, Feltre; **Medical Oncology Department, Santa Maria della Misericordia Hospital, Udine; ***Medical Oncology Department, Santa Chiara Hospital, Trento, Italy*

Accepted for publication 20 January 2011

5/06/2012 EAPC Preconf P7 21

Study Type – Therapy (RCT)
Level of Evidence – 1b

OBJECTIVES

- To assess quality of life (QoL) outcomes and pain changes in patients affected by castration-resistant prostate cancer enrolled in a phase II randomized trial of 3-week docetaxel (DOC)-based chemotherapy
- To provide further data to clarify the conflicting published data concerning the impact of DOC on the patients' QoL.

PATIENTS AND METHODS

- QoL outcomes were assessed using the European Organisation for the Research and Treatment of Cancer QLQ-C30 questionnaire
- Pain changes were evaluated by means of the Brief Pain Inventory at baseline and after every two DOC courses.
- The patients completing at least four questionnaires (at baseline and before the third course) were considered evaluable.

What's known on the subject? and What does this study add?

Data on quality of life during docetaxel treatment in castration-resistant prostate cancer was mainly provided by SWOG and TAX327 trials.

In the TAX327 trial biochemical response and pain predicted survival, whereas quality of life outcomes did not.

In the present study, there were no statistically significant changes in the quality of life scores during treatment except in the case of patients receiving docetaxel and estramustine, who experienced a significant decrease in pain. Our data seem to suggest that patients with a better baseline quality of life (and consequently with fewer symptoms) are more likely to achieve a biochemical response.

RESULTS

- In all, 59 patients were evaluable.
- Asymptomatic patients and responders had a better baseline QoL than symptomatic patients and non-responders.
- There were no statistically significant changes in the QLQ-C30 scales during treatment except in the case of patients receiving DOC and estramustine, who experienced a significant decrease in pain.
- There was a progressive improvement in the mean intensity and interference scores of the Brief Pain Inventory.

CONCLUSIONS

- Our data confirm that QoL is generally maintained during chemotherapy.
- There is a substantial reduction in pain.
- Our results also suggest that baseline QoL may predict treatment response.

KEYWORDS

castration-resistant prostate cancer, chemotherapy, quality of life, docetaxel

5/06/2012 EAPC Preconf P7 22

TABLE 2. National Comprehensive Cancer Center Network Guidelines for Switching to Nonchemotherapy Palliative Care

Disease	Performance Status	Or State of Disease
Breast	≥3	No response to 3 sequential regimens*
Colorectal	≥3	If patient is not appropriate for intensive therapy, and no improvement with treatment, transition to supportive care† If appropriate for intensive therapy, after 2 or 3 progressions of disease‡
Non-small cell lung	≥3	After 2 types of chemotherapy and erlotinib§
Prostate, hormone-refractory	No statement	No statement
Pancreas	≥3	Progression after 2 regimens*

Swetz KM and Smith TJ, Ca Journal 2010;16: 467-472

5/06/2012

EAPC Preconf P7

23

Emerging Therapies to Prevent Skeletal Morbidity in Men With Prostate Cancer

Philip J. Saylor, Richard J. Lee, and Matthew R. Smith

A B S T R A C T

Skeletal morbidity is a prominent burden to men with advanced prostate cancer throughout the natural history of the disease. Bone metastases can cause pain and greatly elevate the risk for fractures and other structural complications. Distinct from the problem of metastases, treatment-related osteoporosis and associated fragility fractures are potential complications of androgen-deprivation therapy. Bone-targeted therapies for prostate cancer have therefore been the focus of considerable research and drug development efforts. The osteoclast is a validated therapeutic target in the management of prostate cancer. Osteoclast inhibition with zoledronic acid (a bisphosphonate) or with denosumab (a monoclonal antibody to RANK ligand) reduces risk for skeletal events in men with castration-resistant prostate cancer metastatic to bone. Osteoclast inhibition with any of several bisphosphonates improves bone mineral density, a surrogate for osteoporotic fracture risk. Denosumab and toremifene (a selective estrogen receptor modulator) have each been shown to reduce osteoporotic fracture risk among men receiving androgen-deprivation therapy. Beta-emitting radiopharmaceuticals reduce pain due to metastatic disease. Investigations involving alpha-emitting radium-223, endothelin-A receptor antagonists atrasentan and zibotentan, proto-oncogene tyrosine-protein kinase (SRC) inhibitor dasatinib, and tyrosine kinase inhibitor cabozantinib (XL184) are ongoing in clinical trials and are also discussed.

All authors, Massachusetts General Hospital Cancer Center, Boston, MA.

Submitted December 23, 2010; published online ahead of print at www.jco.org on August 22, 2011; accepted June 23, 2011.

Supported by Young Investigator Awards from the Prostate Cancer Foundation and American Society of Clinical Oncology (ASCO) Cancer Foundation (P.J.S.), by a Physician Research Training Award (Prostate Cancer Research Program, Department of Defense) and a Career Development Award from the ASCO Cancer Foundation (R.J.L.), and by National Institutes of Health (NIH) Midcareer Investigator Award No. 5K24CA121690-02 and awards from the Prostate Cancer Foundation (M.R.S.).

Authors' disclosures of potential conflicts of interest and author contributions.

J Clin Oncol 29:3705-3714. © 2011 by American Society of Clinical Oncology

5/06/2012

EAPC Preconf P7

24

VOLUME 29 NUMBER 5 MARCH 20 2011

JOURNAL OF CLINICAL ONCOLOGY ASCO SPECIAL ARTICLE

American Society of Clinical Oncology Executive Summary of the Clinical Practice Guideline Update on the Role of Bone-Modifying Agents in Metastatic Breast Cancer

Catherine H. Van Pozzani, Sarah Teerin, Gary C. Tee, Nara A. Janjan, William E. Barlow, J. Sybil Bierman, Linda D. Rosenman, Cindy Grayhugh, Bruce E. Hillner, Richard L. Theriault, Dan S. Zuckerman, and Jamie H. Van Boerum

ABSTRACT

Purpose
To update the recommendations on the role of bone-modifying agents in the prevention and treatment of skeletal-related events (SREs) for patients with metastatic breast cancer with bone metastases.

Methods
A literature search using MEDLINE and the Cochrane Collaboration Library identified relevant studies published between January 2003 and November 2010. The primary outcomes of interest were SREs and time to SRE. Secondary outcomes included adverse events and pain. An Update Committee reviewed the literature and re-evaluated previous recommendations.

From the University of Michigan, Ann Arbor, MI; American Society of Clinical Oncology, Alexandria, Virginia; Corning HealthCare, Plainsboro, NJ; University of Nebraska Medical Center, Omaha, NE; Cancer Research and Biostatistics, Seattle, WA; Wake Forest University Medical School, Winston-Salem, NC; Yale National Breast Cancer Organization, Cook County Cancer Center of Northwestern University, Chicago, IL; National Cancer Air Policy Analysis, Dallas; The University of Texas MD Anderson Cancer Center, Houston, TX; and Memorial Sloan-Kettering Cancer Center, New York, NY.

5/06/2012 EAPC Preconf P7 25

THE BOTTOM LINE

ASCO GUIDELINE UPDATE

The Role of Bone-Modifying Agents (BMAs) in Metastatic Breast Cancer

Intervention

- Bone-modifying agents (BMAs), including bisphosphonates

Target Audience

- Medical Oncologists, Radiation Oncologists, Surgical Oncologists, Palliative Care Providers

Key Recommendations

- BMAs are recommended for patients with metastatic breast cancer with evidence of bone destruction.
- Denosumab 120 mg subcutaneously every 4 weeks; intravenous (IV) pamidronate 90 mg over no less than 2 hours every 3 to 4 weeks; or IV zoledronic acid 4 mg over no less than 15 minutes every 3 to 4 weeks
- One BMA is not recommended over another.
- In patients with creatinine clearance > 60 mL/min, no change in dosage, infusion time, or interval is required; monitor creatinine level with each intravenous bisphosphonate dose.
- In patients with creatinine clearance < 30 mL/min or on dialysis who may be treated with denosumab, close monitoring for hypocalcemia is recommended.
- All patients should have a dental examination and preventive dentistry before using a BMA.
- At onset of cancer bone pain, provide standard of care for pain management and start BMAs.
- Use of biochemical markers to monitor BMA use is not recommended for routine care.

Methods

- Systematic review of medical literature and analysis of the medical literature by the Update Committee of an Expert Panel

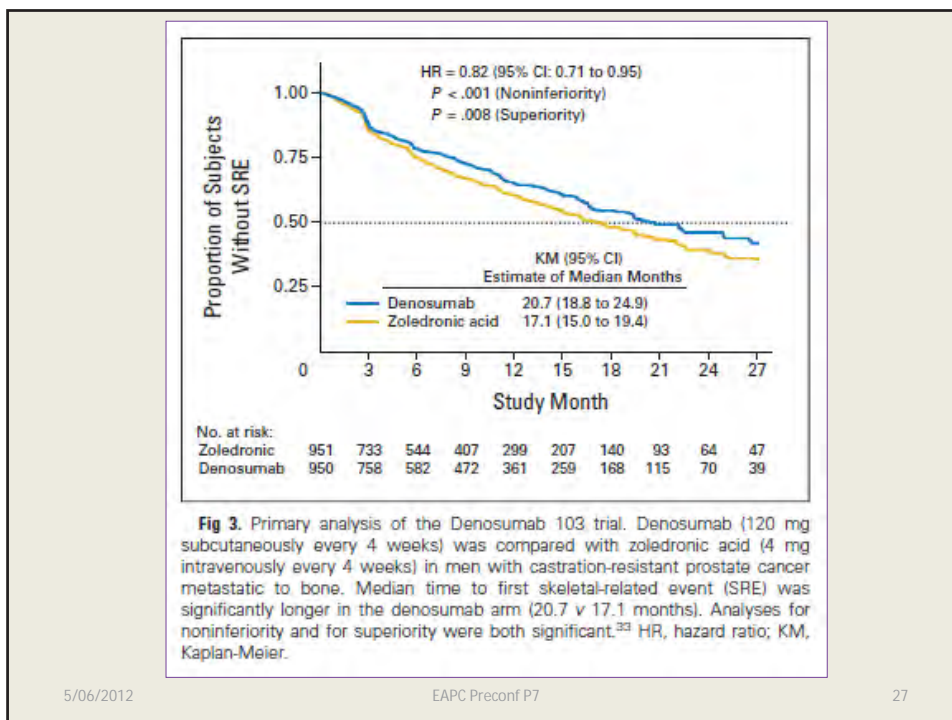
Additional Information

- The recommendations, clinical questions, and a brief summary of the literature and discussion are in this Executive Summary.

The full guideline, with comprehensive discussions of the literature, methodology, full reference list, evidence tables, and clinical tools and resources, can be found at www.asco.org/guidelines/bihsbreast.

5/06/2012 EAPC Preconf P7 26

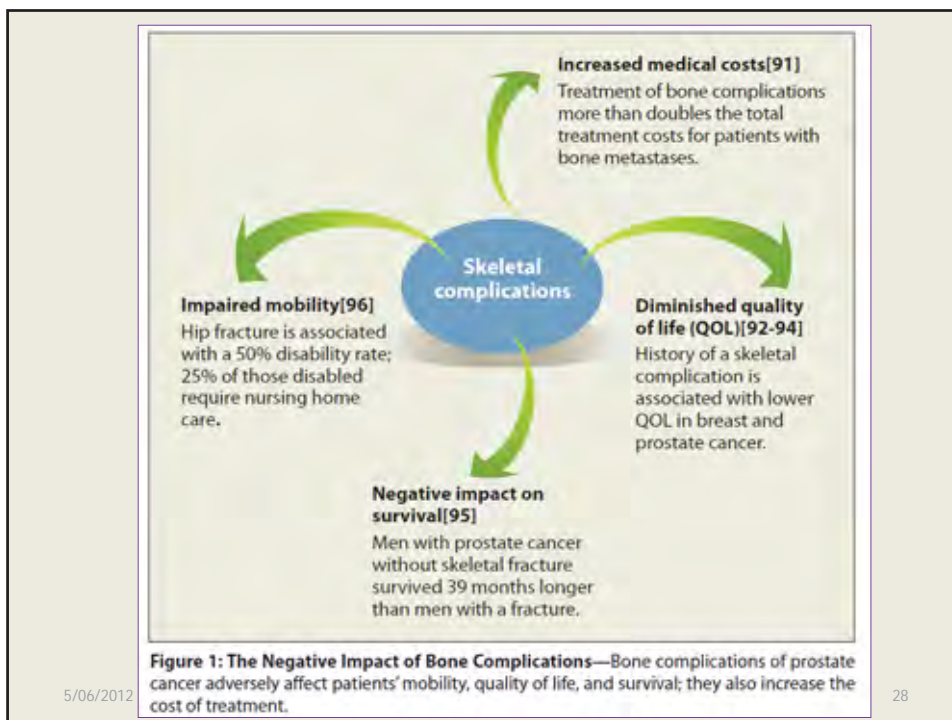
© 2011 by American Society of Clinical Oncology



5/06/2012

EAPC Preconf P7

27



5/06/2012

28

Special Article

Measuring Outcomes in Palliative Care: Limitations of QALYs and the Road to PaLYs

Charles Normand, BA, MA, DPhil, FFPH, FTCD

Centre for Health Policy and Management, School of Medicine, Trinity College Dublin, Dublin, Republic of Ireland

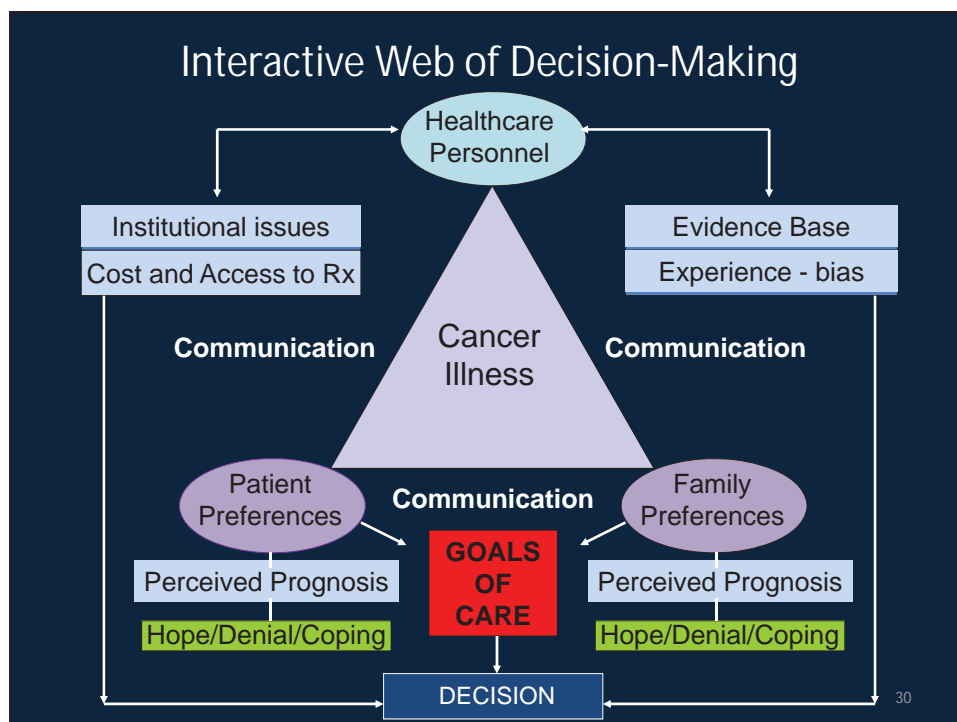
Abstract

Tools for measuring outcomes in health and social care have become key parts of the processes of evaluation and setting priorities. Measures of output that can be used in all settings and specialties have the advantage that they facilitate comparisons and choices between and within patient groups. However, the most commonly used composite measure of outcomes, the quality-adjusted life year (QALY) appears not to work well in complex interventions, such as palliative care, leading to the paradox that there is evidence that people would give priority to interventions and services that would be shown not to be cost-effective, using QALYs as an outcome measure. This article explores the possible reasons for this paradox, and looks at alternative approaches that may provide better tools for setting priorities within palliative care and for comparison of palliative and other care services. *J Pain Symptom Manage* 2009;38:27–31. © 2009 U.S. Cancer Pain Relief Committee. Published by Elsevier Inc. All rights reserved.

5/06/2012

EAPC Preconf P7

29



VOLUME 24 • NUMBER 21 • JULY 20 2006

JOURNAL OF CLINICAL ONCOLOGY REVIEW ARTICLE

Why Do Patients Choose Chemotherapy Near the End of Life? A Review of the Perspective of Those Facing Death From Cancer

Robin Masuyama, Seethkar Reddy, and Thomas J. Smith

From the Markey Cancer Center of Virginia Commonwealth University, Richmond, VA.

Submitted July 26, 2005; accepted March 7, 2006.

Authors' disclosures of potential conflicts of interest and author contributions are found at the end of this article.

Address reprint requests to Thomas J. Smith, MD, Virginia Commonwealth University, Division of Hematology/Oncology and Palliative Care, MCY Box 980200, Richmond, VA 23298-0200; e-mail: tsmith@vcu.edu.

© 2006 by American Society of Clinical Oncology
0732-183X/06/2421-3496/\$20.00
DOI: 10.1200/JCO.2005.03.6236

A B S T R A C T

Purpose
The number of patients receiving chemotherapy near the end of life is increasing, as are concerns about goals of treatment, toxicity, and costs. We sought to determine the available sources of knowledge, the choices, and concerns of actual patients, and how patients balanced competing issues.

Methods
We used a literature search from 1980 to present.

Results
Available patient sources provide little information about prognosis, choices, alternatives, consequences, or how to choose. Many patients would choose chemotherapy for a small benefit in health outcomes, and for a smaller benefit than perceived by their health care providers for their own treatment. Adverse effects are less a concern for patients than for their health care providers. There are no decision aids to assist patients with metastatic disease in making their choices, such as there are for adjuvant breast therapy.

Conclusion
The perspective of the patient is different from that of a well person. Patients are willing to undergo treatments that have small benefits with major toxicity. Receiving realistic information about the different options of care and the likelihood of successful treatment or adverse effects is difficult. These factors may explain some of the increased use of chemotherapy near the end of life. Decision aids and honest, unbiased sources to inform patients of their prognosis, choices, consequences, typical outcomes, and ways to make decisions are needed. More prospective information about how patients make their choices, and what they would consider a good choice, would assist informed decision-making.

J Clin Oncol 24:3490-3496. © 2006 by American Society of Clinical Oncology

5/06/2012 EAPC Preconf P7 31

Advanced Breast Ca Pts' Perceptions of Decision Making for Palliative ChemoTx

Grunfeld et al JCO 2006;24:1090-1098

- N=102 with advanced Br Ca
- 15 closed fixed choice Qs & 6 open-ended
- 1st Line CT: N=70 and 2nd Line CT: N=47
- 40-60 mins interview with Res Nurse mean of 20/7 and 13/7 post key consult
 - Recall of key clinical decision-making consult
 - Perceptions re info disclosure
 - Perceptions of clinical decision-making process

Table 2. Patient Recall of Clinical Decision-Making Consultation

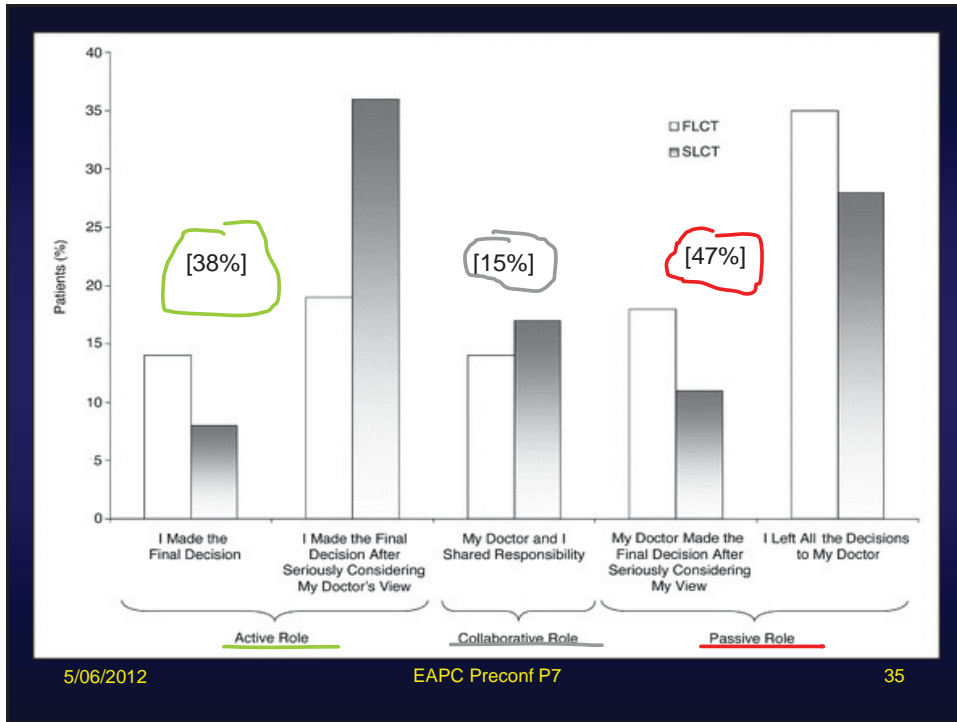
Recall of Clinical Decision-Making Consultation	All Patient Interviews (N = 117)			Interviews of <u>First-Line</u> Chemotherapy Patients (n = 70)			Interviews of <u>Second-Line</u> Chemotherapy Patients (n = 47)		
	No.	%	95% CI	No.	%	95% CI	No.	%	95% CI
Recall of discussion about management	101	86	80 to 92	69	99	92 to 100	32	68	53 to 81
Recall of topics discussed									
Type of chemotherapy proposed	69	59	50 to 68	44	63	50 to 74	25	53	38 to 68
Rationale for management plan	59	50	41 to 59	40	57	45 to 69	19	41	26 to 56
Start date and duration of chemotherapy	58	50	41 to 59	40	57	45 to 69	19	41	26 to 56
Results of investigations	48	41	32 to 50	48	68	57 to 79	0	0	0 to 6
Other tests/procedures	43	37	32 to 42	31	44	32 to 56	12	26	13 to 39
Recall of explanation about how treatment would help									
Acting directly on the cancer	88	75	67 to 83	58	83	72 to 91	30	64	49 to 77
Maintaining a sense of hope	35	30	22 to 38	15	22	13 to 33	20	43	28 to 58
Reducing symptoms	29	25	17 to 33	22	31	21 to 44	7	15	6 to 28
Recall of adverse effects									
Hair loss	66	56	47 to 65	50	71	59 to 82	16	34	21 to 49
Nausea	47	40	31 to 49	36	51	39 to 64	11	23	12 to 38
Fatigue or tiredness	24	21	14 to 27	19	27	17 to 39	5	11	4 to 23
Expressed concern about adverse effects	40	34	25 to 43	34	49	38 to 61	6	12	5 to 26
Doctor's manner									
Very caring/caring	113	98	94 to 100	66	94	86 to 98	47	100	94 to 100
Neither caring nor uncaring	2	1	0 to 3	2	3	0 to 10	0	0	0 to 6
Very uncaring/uncaring	2	1	0 to 3	2	3	0 to 10	0	0	0 to 6
Satisfaction with the consultation in general									
Very satisfied/satisfied	105	90	85 to 94	60	86	75 to 93	45	96	85 to 99
Neither satisfied nor unsatisfied	9	8	3 to 13	7	10	4 to 20	2	4	1 to 15
Very dissatisfied/dissatisfied	3	2	0 to 7	3	4	1 to 12	0	0	0 to 6

5/06/2012 EAPC Preconf P7 33

Table 4. Patient Perceptions of the Clinical Decision-Making Process

Perception of the Clinical Decision-Making Process	All Patient Interviews (N = 117)			Interviews of <u>First-Line</u> Chemotherapy Patients (n = 70)			Interviews of <u>Second-Line</u> Chemotherapy Patients (n = 47)		
	No.	%	95% CI	No.	%	95% CI	No.	%	95% CI
Doctor directly recommended this approach to your treatment/care	108	92	87 to 97	65	93	84 to 98	43	91	80 to 98
How much did you agree with your doctor about your treatment and care?									
Agreed completely about most issues	110	94	90 to 98	66	94	86 to 98	44	94	82 to 99
Neither agreed nor disagreed	5	4	0 to 8	2	3	0 to 10	3	6	1 to 18
Disagreed completely	2	2	0 to 5	2	3	0 to 10	0	0	0 to 6
How do you feel about the time taken to reach the decision?									
Too long	18	15	13 to 17	13	19	10 to 30	5	11	4 to 23
About the right amount of time	91	84	77 to 91	51	72	61 to 83	40	85	72 to 94
Too quickly	9	1	0 to 3	6	9	3 to 18	2	4	1 to 15
How satisfied are you with how your treatment and care plan has been decided?									
Very satisfied/satisfied	106	91	86 to 96	65	93	84 to 98	41	87	74 to 95
Neither satisfied nor dissatisfied	5	4	0 to 8	4	6	2 to 14	1	2	0 to 11
Very dissatisfied/dissatisfied	6	5	1 to 9	1	1	0 to 8	5	11	4 to 23

5/06/2012 EAPC Preconf P7 34



original article

Annals of Oncology 21: 360-366, 2010
doi:10.1093/annonc/mdp378
Published online 4 August 2009

European Society for Medical Oncology (ESMO) Program for the Integration of Oncology and Palliative Care: a 5-year review of the Designated Centers' incentive program

N. Cherny^{1*}, R. Catano², D. Schrijvers³, M. Klocke⁴ & F. Strasser⁵

¹Department of Oncology, Cancer Pain and Palliative Medicine, Sheba Medical Center, Ramat Gan, Israel; ²Department of Hemato-Oncology, Ziekenhuis Zuyderland, Arnhem, Belgium; ³Center for Palliative Medicine, Kibibon, Essen Mills, Essen, Germany; and ⁴Oncological Palliative Care, Oncology Department Internal Medicine and Palliative Care Center, Cantonal Hospital, St Gallen, Switzerland

Received 23 March 2009; revised 4 May 2009; accepted 3 May 2009

Background: In 1999, the National Representatives of European Society for Medical Oncology (ESMO) created a Palliative Care Working Group to improve the delivery of supportive and palliative care (S + PC) by oncologists, oncology departments and cancer centers. They have addressed this task through initiatives in policy, education, research and incentives. As an incentive program for oncology departments and centers, ESMO developed a program of Designated Centers (DCs) for programs meeting predetermined targets of service development and delivery of a high level of S + PC.

Method: The history, accreditation criteria and implementation of the DC incentive program is described.

Results: Since 2004, 75 centers have applied for designation and 48 have been accredited including 34 comprehensive cancer centers (CCCs) in general hospitals and seven freestanding CCCs. Perceived benefits accrued from the accreditation included the following: improved status and role identification of the center, positive impact on daily work, positive impact on business activity and positive impact on funding for projects.

Conclusions: The accreditation of DCs has been a central to the ESMO initiative to improve the palliative care provided by oncologists and oncology centers. It is likely that many other oncology departments and cancer centers already meet the criteria and ESMO strongly encourages them to apply for accreditation.

Key words: European Society for Medical Oncology, education, Oncology, palliative care, supportive care

5/06/2012

EAPC Preconf P7

37

Supporting Treatment Decision Making in Advanced Cancer: A Randomized Trial of a Decision Aid for Patients With Advanced Colorectal Cancer Considering Chemotherapy

Natasha B. Leigh, Heather L. Shepherd, Phyllis N. Butow, Stephen J. Clarke, Margaret McLennan, Philip J. Beale, Nicholas R.C. Wilcken, Malcolm J. Moore, Eric X. Chen, David Goldstein, Lisa Horvath, Jennifer J. Knox, Monika Krzyzanowska, Amit M. Oza, Ronald Feld, David Hedley, Wei Xu, and Martin H.N. Tattersall

A B S T R A C T

Purpose

Decision making in advanced cancer is increasingly complex. We developed a decision aid (DA) for patients with advanced colorectal cancer who are considering first-line chemotherapy and reviewing treatment options, prognostic information, and toxicities. We examined its impact on patient understanding, treatment decisions, decisional conflict, decision making, consultation satisfaction, anxiety, and quality of life by using a randomized trial design.

Patients and Methods

In all, 207 patients with colorectal cancer who were considering first-line chemotherapy for metastatic disease were randomly assigned to receive a standard medical oncology consultation or a consultation in which the DA (take-home booklet with audio recording, reviewed by an oncologist) was used. Participants completed questionnaires postconsultation, postdecision, and 1 month later.

Results

In this study, 100 patients were randomly assigned to the control arm, and 107 received the DA. Median age of the sample was 62 years, 58% were male, 89% had a performance status of 0 or 1, and 98% had received prior adjuvant chemotherapy. Patients receiving the DA demonstrated a greater increase in understanding of prognosis, options, and benefits, with higher overall understanding ($P < .001$). Decisional conflict, treatment decisions, and achievement of involvement preferences were similar between the groups. Anxiety was similar across groups and decreased over time. Most patients were confident in a decision during the first consultation; 74% chose chemotherapy, 7% supportive care alone, and 10% observation.

Conclusion

This randomized trial of a decision aid in advanced cancer showed that its use in advanced colorectal cancer improved patient understanding of prognosis, treatment options, risks, and benefits without increasing anxiety. DAs can improve informed consent and can be tested through randomized trials even in the advanced cancer setting.

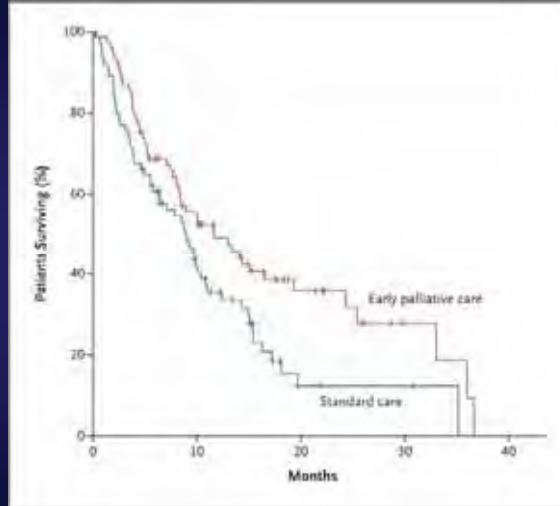
J Clin Oncol 29:2077-2084. © 2011 by American Society of Clinical Oncology

5/06/2012

EAPC Preconf P7

38

K-M Estimates of Survival According to Study Group.



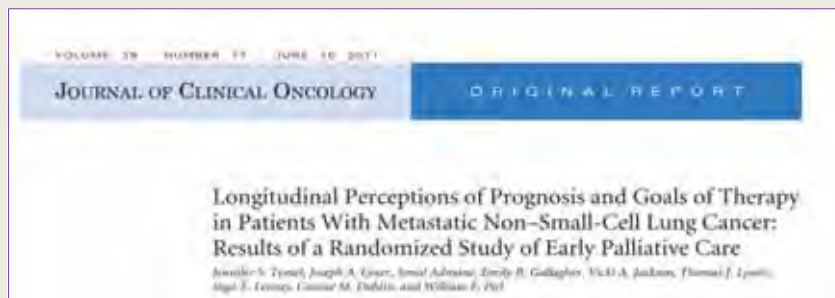
Temel JS et al. N Engl J Med 2010;363:733-742.

5/06/2012

EAPC Preconf P7



39



5/06/2012

EAPC Preconf P7

40

A B S T R A C T

Purpose
Understanding of prognosis among terminally ill patients impacts medical decision making. The aims of this study were to explore perceptions of prognosis and goals of therapy in patients with metastatic non-small-cell lung cancer (NSCLC) and to examine the effect of early palliative care on these views over time.

Patients and Methods
Patients with newly diagnosed metastatic NSCLC were randomly assigned to receive either early palliative care integrated with standard oncology care or standard oncology care alone. Participants completed baseline and longitudinal assessments of their perceptions of prognosis and the goals of cancer therapy over a 6-month period.

Results
We enrolled 151 participants on the study. Despite having terminal cancer, one third of patients (46 of 145 patients) reported that their cancer was curable at baseline, and a majority (86 of 124 patients) endorsed getting rid of all of the cancer as a goal of therapy. Baseline perceptions of prognosis (ie, curability) and goals of therapy did not differ significantly between study arms. A greater percentage of patients assigned to early palliative care retained or developed an accurate assessment of their prognosis over time (82.5% v 59.6%, $P = .02$) compared with those receiving standard care. Patients receiving early palliative care who reported an accurate perception of their prognosis were less likely to receive intravenous chemotherapy near the end of life (9.4% v 50%, $P = .02$).

Conclusion
Many patients with newly diagnosed metastatic NSCLC hold inaccurate perceptions of their prognoses. Early palliative care significantly improves patient understanding of prognosis over time, which may impact decision making about care near the end of life.

J Clin Oncol 29:2319-2326. © 2011 by American Society of Clinical Oncology

5/06/2012 EAPC Preconf P7 41

JOURNAL OF CLINICAL ONCOLOGY **ASCO SPECIAL ARTICLE**

American Society of Clinical Oncology Statement: Toward Individualized Care for Patients With Advanced Cancer

Jeffrey M. Peppercorn, Thomas J. Smith, Paul R. Helff, David J. DeBono, Scott R. Berry, Dana S. Wolins, Daniel M. Hayes, Jamie H. Von Roenn, and Lowell E. Schnipper

See accompanying article doi: 10.1200/JCO.2010.29.2599

A B S T R A C T

Patients with advanced incurable cancer face complex physical, psychological, social, and spiritual consequences of disease and its treatment. Care for these patients should include an individualized assessment of the patient's needs, goals, and preferences throughout the course of illness. Consideration of disease-directed therapy, symptom management, and attention to quality of life are important aspects of quality cancer care. However, emerging evidence suggests that, too often, realistic conversations about prognosis, the potential benefits and limitations of disease-directed therapy, and the potential role of palliative care, either in conjunction with or as an alternative to disease-directed therapy, occur late in the course of illness or not at all. This article addresses the American Society of Clinical Oncology's (ASCO's) vision for improved communication with and decision making for patients with advanced cancer. This statement advocates an individualized approach to discussing and providing disease-directed and supportive care options for patients with advanced cancer throughout the continuum of care. Building on ASCO's prior statements on end-of-life care (1998) and palliative care (2008), this article reviews the evidence for improved patient care in advanced cancer when patients' individual goals and preferences for care are discussed. It outlines the goals for individualized care, barriers that currently limit realization of this vision, and possible strategies to overcome these barriers that can improve care consistent with the goals of our patients and evidence-based medical practice.

J Clin Oncol 28. © 2011 by American Society of Clinical Oncology

5/06/2012 EAPC Preconf P7 42



PAIN® 147 (2009) 20–28

PAIN®
www.elsevier.com/locate/pain

Research papers:

Multidisciplinary pain management based on a computerized clinical decision support system in cancer pain patients

Thilo Bertsche^{a,b}, Vasileios Askoxyllakis^c, Gregor Hahl^c, Friederike Laidig^b, Jens Kaltschmidt^d, Simon P.W. Schmitt^e, Hamid Ghaden^d, Angelika Zabel-du Bois^e, Stefanie Milker-Zabel^e, Jürgen Debus^e, Hubert J. Bardenheuer^d, Walter E. Haefeli^{a,c}

^aDepartment of Internal Medicine VI, Clinical Pharmacology and Pharmacokinetics, University of Heidelberg, Im Neuenheimer Feld 410, 69120 Heidelberg, Germany
^bDepartment of Pharmacy, University of Heidelberg, Germany
^cDepartment of Radiation Oncology, University of Heidelberg, Germany
^dDepartment of Neurosurgery, University of Heidelberg, Germany

5/06/2012 EAPC Preconf P7 43

Conclusions

- Decision-making re DMT is complex: individualized approach and further studies needed
- Trend towards more aggressive use of DMTs ? reflecting advances: need to evaluate PROs
- Increasing evidence that Pall Care referral / integrated care is associated with better coping, QoL, decision-making and even survival
- Tactful communication – time and training
- Guidelines / MDT conferences / Decision Aids help
- Cost is an arbiter in relation to decisions regarding newer therapies (? PALYs vs QUALYs)