Palliative/Supportive Care

Dr. Ann Hoeben
Medisch Oncoloog MUMC+
## Disclosure

<table>
<thead>
<tr>
<th>(potentiële) belangonverstrekking</th>
<th>No</th>
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<tr>
<td>Voor bijeenkomst mogelijk relevante relaties met bedrijven</td>
<td>No</td>
</tr>
<tr>
<td>• Sponsoring of onderzoeksgeld</td>
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<td>• Honorarium of andere (financiële) vergoeding</td>
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<td>• Aandeelhouder</td>
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<tr>
<td>• Andere relatie, namelijk …</td>
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</tbody>
</table>
Overview

1. Introduction.

2. Early onset supportive/palliative care.

3. Supportive/palliative care: symptom management:
   – Neurological deficit & pain due to spinal cord compression: SCORAD III
   – Pain
   – CINV
   – Delirium

1. INTRODUCTION:
WHO definition: Palliative Care

Palliative care is an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.
1. INTRODUCTION:
Supportive/Palliative Care: what’s in a name.

Incurable Tumor (recurrent, locally advanced or metastatic)

Multidisciplinary anti-cancer treatment
Symptom relief
End of Life Palliative Care
Aftercare
Death

Concurrent Supportive/Palliative Care
Overview

1. Introduction.

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3. Supportive/palliative care: symptom management:
   - Neurological deficit & pain due to spinal cord compression: SCORAD III
   - Pain
   - CINV
   - Delirium

2. Early Onset Supportive/Palliative Care: Rationale.

- Improved Quality of Life during treatment
- Decreased depressive symptoms and anxiety

The New England Journal of Medicine

Original Article

Early Palliative Care for Patients with Metastatic Non–Small-Cell Lung Cancer

2. Early Onset Supportive/Palliative Care: Rationale.

- mOS: 11,6m (95% CI, 6,4 to 16,9)
- mOS: 8,9m (95% CI; 6,3 to 11,4)
2. Early Onset Supportive/Palliative Care: Rationale.

Early palliative care for patients with advanced cancer: a cluster-randomised controlled trial
Camilla Zimmermann, Nadia Swami, Monika Krzyzanowska, Breffni Hannon, Natasha Leighl, Amit Oza, Malcolm Moore, Anne Rydall,
VOLUME 33 · NUMBER 13 · MAY 1 2015
ORIGINAL REPORT
JOURNAL OF CLINICAL ONCOLOGY

Early Versus Delayed Initiation of Concurrent Palliative Oncology Care: Patient Outcomes in the ENABLE III Randomized Controlled Trial
Marie A. Bakitas, Tor D. Tosteson, Zhigang Li, Kathleen D. Lyons, Jay G. Hull, Zhongze Li, J. Nicholas Dionne-Odom, Jennifer Frost, Konstantin H. Dragnev, Mark T. Hegel, Andres Azuero, and Tim A. Ahles
Overall survival results of a randomized trial assessing patient-reported outcomes for symptom monitoring during routine cancer treatment (NCT00578006)

Ethan Basch, Allison Deal, Amylou Dueck, Antonia Bennett, Thomas Atkinson, Howard Scher, Mark Kris, Clifford Hudis, Paul Sabbatini, Dorothy Dulko, Lauren Rogak, Allison Barz, Deborah Schrag

From: Lineberger Comprehensive Cancer Center, University of North Carolina; Memorial Sloan Kettering Cancer Center; Mayo Clinic; Dana-Farber Cancer Institute
Standard Approach to Symptom Monitoring

Limited Time
Forget to Discuss
Reluctance to Contact
Problems Connecting

REACTIVE APPROACH
Study Hypothesis:

“Proactive symptom monitoring during chemotherapy will improve symptom management, leading to better clinical outcomes.”
Study Design

Patients receiving chemotherapy for metastatic breast, lung, GU, GYN cancer at MSKCC

**INTERVENTION ARM** \( N = 441 \)
- Self-report 12 common symptoms
- Prior to / between visits, by web
- Weekly email reminders to patients
- Alerts to nurses (by email)
- Reports to oncologists (at visits)

**CONTROL ARM** \( N = 325 \)
- "Standard" symptom monitoring

**Outcomes**
- QOL
- ER visits
- Survival

**Stratified by level of prior computer use**
Randomized 2:1 for those w/o prior use

**Treatment discontinuation, withdrawal, hospice, death**
### Patient Self-Reporting Interface

- **Example: Pain**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>None</td>
<td>I have not had pain.</td>
</tr>
<tr>
<td>Grade 1 (Mild)</td>
<td>I have had mild pain, but it does not interfere with my normal functioning.</td>
</tr>
<tr>
<td>Grade 2 (Moderate)</td>
<td>I have had moderate pain, and my pain or my use of pain medications interferes with my normal functioning. But I am still able to carry out my normal daily activities.</td>
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<tr>
<td>Grade 3 (Severe)</td>
<td>I have had severe pain, and my pain or my use of pain medications severely interferes with my normal daily activities.</td>
</tr>
<tr>
<td>Grade 4 (Disabling)</td>
<td>My pain has been disabling.</td>
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Patient Self-Reporting Interface

- **Example: Shortness of Breath (Dyspnea)**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>None</td>
<td>I have not had shortness of breath (with exercise or rest).</td>
</tr>
<tr>
<td>Grade 1 (Mild)</td>
<td>I have been short of breath with exercise, but I can walk up 1 flight of stairs without stopping.</td>
</tr>
<tr>
<td>Grade 2 (Moderate)</td>
<td>I have been short of breath with exercise but I am not able to walk up 1 flight of stairs or 1 city block without stopping.</td>
</tr>
<tr>
<td>Grade 3 (Severe)</td>
<td>I have been short of breath during my normal daily activities (dressing, showering, cleaning, cooking, etc).</td>
</tr>
<tr>
<td>Grade 4 (Disabling)</td>
<td>I have been short of breath even when I am resting in bed or in a chair.</td>
</tr>
</tbody>
</table>
Email Alert to Clinical Nurse

From: Patient Symptom Tracking <webmaster@mskcc.org>
Date: Wednesday, June 14, 2010 at 2:16 PM
To: Microsoft Office User <[REDACTED]@mskcc.org>
Subject: Patient Symptom Alert

SYMPTOM REPORTED FROM HOME

Patient Medical Record Number: [REDACTED]
Date/Time Reported: 07/14/2010 at 2:15 PM

Symptom: DYSPNEA Grade: 3

Symptoms that have worsened since 07/07/2010:
Symptom: DYSPNEA from Grade: 1 to 3

Link to FULL REPORT
Printed Report to Oncologist at Clinic Visit

**STAR SYMPTOM REPORT**

**Confidential PHI**

**Patient Name:**

**Patient MRN:**

**Primary Oncologist:**

Worsened symptoms since July 7:
- Cough: from grade 0 to grade 1

Improved symptoms since July 7:
- Dyspnea: from grade 3 to grade 1
- Fatigue: from grade 2 to grade 1
- Pain: from grade 1 to grade 0

Below is a summary of prior reported symptoms, with most recent reports on top:

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<td>07/01/10</td>
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<td>07/14/10</td>
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<td>0</td>
<td>0</td>
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<tr>
<td>07/22/10</td>
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*Clinic/Chemotherapy Visit*
Quality of Life

- Assessed at 6 months, compared to baseline

- Compared to standard care, 31% more patients in the self-reporting arm experienced QOL benefits ($P<0.001$)

Basch: J Clin Oncol 2016;34:557-565
Proportion of Patients Visiting Emergency Room

- Compared to standard care, 7% fewer patients in the self-reporting arm visited the ER, with durable effects throughout the study ($P=0.02$)
Overall Survival

- Compared to standard care, median survival was 5 months longer among patients in the self-reporting arm (31.2 vs. 26.0 months) \( (P=0.03) \)

- Remained significant in multivariable analysis: Adjusted hazard ratio 0.832 (95% CI; 0.696, 0.995)
2. Early Onset Supportive/Palliative Care: Conclusions NCT00578006.

1. Proactive symptom monitoring prompts clinicians to intervene early, before symptoms worsen and cause serious downstream complications: decrease in ER admission.

2. Symptom control enables patients to stay more functional, which is known to be associated with better survival.

3. Symptom monitoring improves control of chemotherapy side effects, enabling more intensive and longer duration of cancer treatment. (Standard care 6,3 months vs. Self-report 8,2 months; p=0,002)
2. Early Onset Supportive/Palliative Care: Abstracts.

- **Abstract 10023**: Improved coping to mediate the positive effects of integrated palliative care on quality of life and depression.
- **Abstract 10026**: Early specialist palliative care for all hospitalized, advanced cancer patients? Better outcome with ‘up-front’ versus ‘on-demand’ palliative care.
- **Abstract 10025**: Predictive value of the patient reported outcome “living with cancer” instrument on overall survival in advanced cancer patients: A tool for guiding timing of palliative care consultations.
- **Abstract LBA10002**: Web-based stress management for newly diagnosed cancer patients (STREAM): A randomized, wait-list controlled intervention study.
- **Abstract 10050**: The importance of recognizing and addressing depression in patients with advanced cancer.
- **Abstract e21678**: Strategies to embed palliative care into a culture of cancer care.
- **Abstract e21551**: The importance of evaluation and taking care of the patient and caregiver in the oncological disease experience: A multicentre study.
- **Abstract e21511**: Preference of end-of-life discussion at diagnosis in patients with advanced/recurrent cancer.
- **Abstract e21644**: Results of implementing a novel supportive oncology screening tool for comprehensive evaluation of distress and other supportive care needs.
2. Early Onset Supportive/Palliative Care: CONCLUSIONS.

Incurable Tumor (recurrent, locally advanced or metastatic)

Multidisciplinary anti-cancer treatment

- Multidimensional patient tailored PSC
- Education is key:
  ✓ Nurse practitioner
  ✓ Physician
  ✓ Paramedics

Symptom relief

End of Life Palliative Care

Aftercare

Death

Concurrent Supportive/Palliative Care
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   - Neurological deficit & pain due to spinal cord compression: SCORAD III
   - Pain
   - CINV
   - Delirium

3. Supportive/Palliative Care:
Symptom Relief: NEUROLOGICAL DEFICIT +/- PAIN
SPINAL CANAL COMPRESSION

SCORAD III

Randomised non-inferiority phase III trial of single dose radiotherapy (RT) compared to multifraction RT in patients with metastatic spinal canal compression

Peter J Hoskin, Vivek Misra, Kirsten Hopkins, Tanya Holt, Gillian Brown, Seonaid Arnott, Sharon Shibu Thomas, Krystyna Reczko, Sandy Beare, Andre Lopes, Sharon Forsyth

PRESENTED AT: ASCO ANNUAL MEETING ‘17 | #ASCO17

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**SCORAD:** Feb 2008-Apr 2016

47 sites: 43 UK, 4 Australia

Randomised: 694  
Eligible patients: 687

Stratification factors:
- Radiotherapy centre
- Ambulatory status at randomisation
- Primary tumour type
- Extent of metastases:
  - Non-skeletal metastases absent
  - Non-skeletal metastases present

1:1 randomisation

Control Arm:  
20 Gy/5 f (N=342)

Investigational Arm:  
8 Gy/1 f (N=345)

Ambulatory status, bladder/bowel function, adverse events and Quality of life assessed at:
- Baseline
- 1 week post randomisation
- 4 weeks post randomisation
- 8 weeks post randomisation
- 12 weeks post randomisation

Presented by: Peter Hoskin
## Patient characteristics

<table>
<thead>
<tr>
<th>WHO Performance Status</th>
<th>20 Gy/5 f (N=342) N(%)</th>
<th>8 Gy/1 f (N=345) N(%)</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>11 (3)</td>
<td>13 (4)</td>
</tr>
<tr>
<td>1</td>
<td>83 (24)</td>
<td>84 (24)</td>
</tr>
<tr>
<td>2</td>
<td>81 (24)</td>
<td>88 (26)</td>
</tr>
<tr>
<td>3</td>
<td>122 (36)</td>
<td>114 (33)</td>
</tr>
<tr>
<td>4</td>
<td>41 (12)</td>
<td>44 (13)</td>
</tr>
<tr>
<td>Not reported</td>
<td>4 (1)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Number of SCC sites</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>312 (91)</td>
<td>303 (88)</td>
</tr>
<tr>
<td>Multiple</td>
<td>30 (9)</td>
<td>42 (12)</td>
</tr>
</tbody>
</table>
Overall survival

HR: 1.03 (95% CI: 0.87, 1.23), p = 0.697
3. Supportive/Palliative Care: Symptom Relief: NEUROLOGICAL DEFICIT +/- PAIN SPINAL CANAL COMPRESSION

**SCORAD III**

- 8 Gy single dose was as effective as/non-inferior to 20 Gy / 5f for:
  - Ambulatory status at 8 weeks
  - Global quality of life and overall survival

- Single dose RT recommended in this setting:
  - Significant reduction in hospital visit (short survival time and cost effective)
3. Supportive/Palliative Care: Symptom Relief: PAIN

- **Opioids**: No significant differences in efficacy between strong opioids.

- **Multimodal therapy**: pharmacologic and non-pharmacologic interventions
3. Supportive/Palliative Care: Symptom Relief: PAIN

Medicinal Cannabis & Cancer Pain: An Alternative to Opioids?

Timothy Furnish, M.D.
Associate Clinical Professor
Department of Anesthesiology
University of California, San Diego
3. Supportive/Palliative Care: Symptom Relief: PAIN

• Medicinal Cannabis: Pharmacology:

  - Delta-9-tetrahydrocannabinol (THC) - main psychoactive cannabinoid

  - Cannabidiol (CBD) – non-psychoactive cannabinoid:
    ▪ Anti-convulsant, muscle relaxant, sedative, anti-inflammatory activity.
    ▪ May attenuate the psychoactive properties of THC.

  - Medicinal Cannabis NL: Transvaal apotheek – Den Haag:
    Bediol CBD 2,0% / THC 1,3%, 10 ml
    Bedica THC 2,0% , 10 ml
    Bedrocan THC 2,0%, 10 ml
    Bedrolite CBD 10%, 10 ml
3. Supportive/Palliative Care: Symptom Relief: PAIN

- Medicinal Cannabis: Pain relief?

<table>
<thead>
<tr>
<th>Cannabinoid</th>
<th>N=</th>
<th>Indication</th>
<th>Duration/Type</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoked Cannabis</td>
<td>50</td>
<td>HIV neuropathy</td>
<td>5 days/DB</td>
<td>Decreased pain and hyperalgesia (Abrams, 2007)</td>
</tr>
<tr>
<td>Smoked Cannabis</td>
<td>16</td>
<td>Diabetic Neuropathy</td>
<td>Single dose/DB/Crossover</td>
<td>Decreased pain (Wallace, 2015)</td>
</tr>
<tr>
<td>Smoked Cannabis</td>
<td>38</td>
<td>Neuropathic pain</td>
<td>Single dose/DBC</td>
<td>Decreased pain w/ highest dose, but significant psychoactive effects (Wilsey, 2008)</td>
</tr>
<tr>
<td>Dronabinol (synthetic THC)</td>
<td>24</td>
<td>Neuropathic pain in MS</td>
<td>15-21 days/DBC</td>
<td>Median numerical pain and relief improved (Svendsen, 2004)</td>
</tr>
<tr>
<td>Nabilone (synthetic THC)</td>
<td>96</td>
<td>Neuropathic pain</td>
<td>14 weeks/DBC vs dihydrocodeine</td>
<td>DHC &gt; Nabilone with fewer AE (Frank, 2008)</td>
</tr>
<tr>
<td>Nabiximols (THC:CBD SL spray)</td>
<td>125</td>
<td>Peripheral neuropathy</td>
<td>5 weeks</td>
<td>Decreased pain and alldynia, (Nurmikko, 135)</td>
</tr>
<tr>
<td>THC (Oral)</td>
<td>36</td>
<td>Cancer Pain</td>
<td>Single dose; vs codeine</td>
<td>Decreased pain similar to codeine; high dose cannabis &gt;AE than codeine, (Noyes, 1975)</td>
</tr>
<tr>
<td>Nabiximols (THC:CBD)</td>
<td>117</td>
<td>Cancer Pain</td>
<td>2 weeks</td>
<td>THC:CBD Decreased pain THC alone no better</td>
</tr>
</tbody>
</table>

- ONLY LIMITED DATA AVAILABLE – BEST EVIDENCE NEUROPATHIC PAIN
- NOT RECOMMENDED AS FIRST LINE THERAPY
  (MAY BE CONSIDERED AS AN ADJUVANT IN THE MANAGEMENT OF REFRACTORY CANCER PAIN)
- RESEARCH NEEDED CONCERNING DOSING EN DELIVERY ROUTE.
3. Supportive/Palliative Care: Symptom Relief: PAIN
3. Supportive/Palliative Care: Symptom Relief: NAUSEA & VOMITING.

Phase III study of NEPA, a fixed combination of NEtupitant and PAlonosetron, versus an aprepitant regimen for prevention of chemotherapy-induced nausea and vomiting (CINV).

<table>
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<tr>
<th>Table 1. Treatment Groups</th>
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<tr>
<td>Day 1</td>
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<td>Day 3</td>
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<td>Day 4</td>
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</table>

APR, aprepitant; GRAN, granisetron; DEX, dexamethasone; NETU, netupitant; IV, intravenous; PALO, palonosetron
3. Supportive/Palliative Care:
Symptom Relief: NAUSEA & VOMITING.

Phase III study of NEPA, a fixed combination of netupitant and palonosetron, versus an aprepitant regimen for prevention of chemotherapy-induced nausea and vomiting (CINV).

- Comparable efficacy & adverse event profile
- NEPA: simplified prophylactic anti-emetic
- **Costs**: NEPA 65,99 euro vs APR/GRAN 60,33 euro/cycle
3. Supportive/Palliative Care: Symptom Relief: DELIRIUM

Lorazepam as an Adjuvant to Haloperidol for Agitated Delirium at the End-of-Life

A Double-Blind Randomized Controlled Trial

David Hui, Susan Frisbee-Hume, Annie Wilson, Seyedeh S Dibaj, Thuc Nguyen, Maxine De La Cruz, Paul Walker, Donna S. Zhukovsky, Marvin Delgado-Guay, Marieberta Vidal, Daniel Epner, Akhila Reddy, Kimberson Tanco, Janet Williams, Stacy Hall, Diane Liu, Kenneth Hess, Sapna Amin, William Breitbart, Eduardo Bruera

MD Anderson Cancer Center, Houston, TX
3. Supportive/Palliative Care:
Symptom Relief: DELIRIUM

**Study Design**

- Double-blind, randomized controlled trial
- Single dose instead of repeated dosing
  - Short survival (i.e. hours to days)
  - Uncertain risks associated with lorazepam in a frail population
- Use of other medications was permissible as per standard of practice

Cancer patients in APCU with mixed/hyperactive delirium despite regular haloperidol use (<8 mg/d)

- Haloperidol 2 mg q6h and q1h PRN
- First occurrence of RASS ≥+1 and PRN meds needed
- Haloperidol 2 mg PLUS Lorazepam 3 mg x1 dose
- Haloperidol 2 mg PLUS Placebo x1 dose

*Presented by: David Hui, MD*
3. Supportive/Palliative Care: Symptom Relief: DELIRIUM

Secondary Outcomes

Patients on lorazepam/haloperidol arm were perceived to be more comfortable after the study medication by blinded caregivers and nurses.

- Combination of haloperidol and lorazepam was associated with a rapid sustained and clinical significant reduction of agitation compared to haloperidol alone.
- Further research is needed.
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   - Pain
   - CINV
   - Delirium

4. Conclusions

- ASCO Guideline Palliative Care 2017:

  - Concurrent supportive/palliative care alongside usual oncology care is recommended

  - Concurrent speciality care should start within 8 weeks of diagnosis and delivered by an interdisciplinary team:
    collaboration: oncologist – nurse practitioner – palliative care team
4. Conclusions

• Pro-active symptom management during treatment:
  - Increase OS, QoL, decrease in ER admissions and cost effective.
  - Needed: (IT-)infrastructure, qualified nurse practitioners, physicians.

• Structural collaboration oncology-palliative care teams:
  - Increasing expertise
  - Delivering multi-dimensional care.
Thank you for your attention.