ELCC 2016

Integrating supportive care in the treatment of lung cancer patients

Matti Aapro MD

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Member ESMO supportive care Faculty

Board member and Past-President of

MASCC

(Multinational Association for Supportive Care in Cancer)

And Honorary President of AFSOS

(French-speaking Association for Supportive Care)

COI for this talk

- Consultant and/or investigator or speaker for:

Amgen, Hospira, JnJ, Kyowa Hakko Kirin, Mundipharma, Novartis,

Roche, Sandoz, Taiho, Teva

- Executive Committee member of

MASCC and AFSOS

and ESMO supportive care Faculty

TOPICS

- The key role of supportive care
- BONE
- ANTIEMETICS
- FN PREVENTION
- PAIN
- DYSPNEA

SUPPORTIVE AND PALLIATIVE CARE

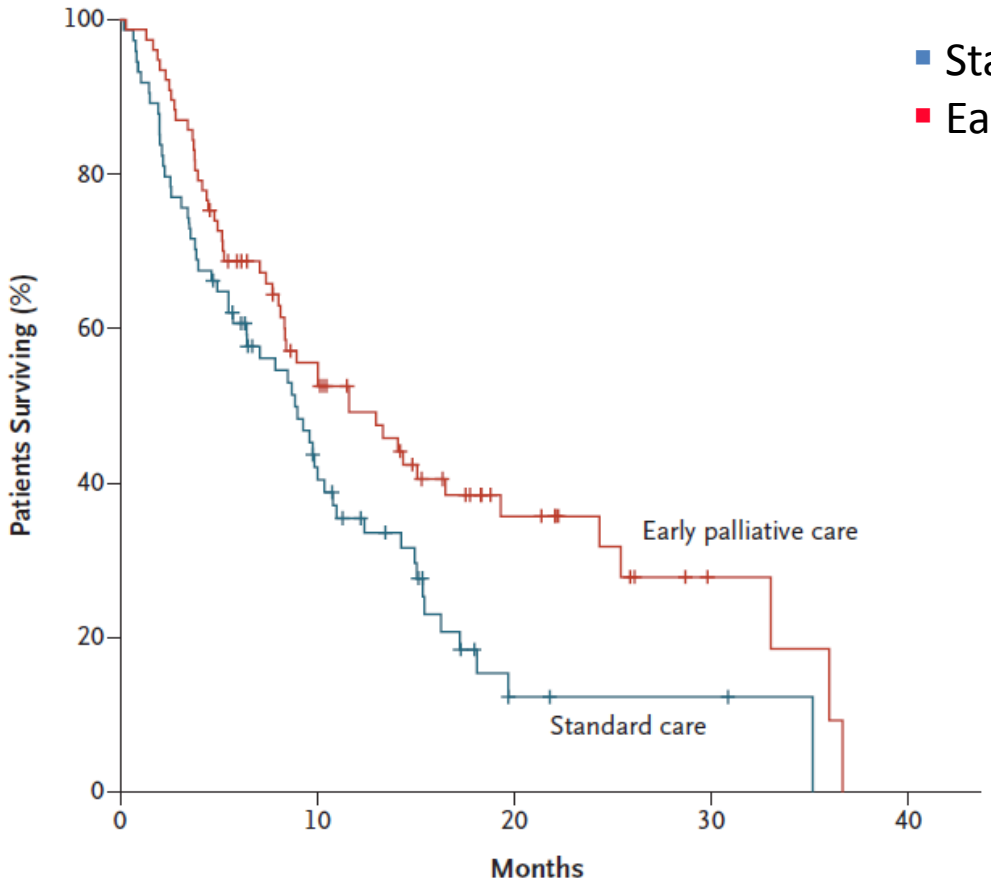
Annals of Oncology 23: 1932–1934, 2012
doi:10.1093/annonc/mds239

Supportive care and palliative care: a time for unity in diversity

emotional burden of patients and caregivers, helps cancer survivors with psychological and social problems [1].

Matti S. Aapro*
IMO Clinique de Genolier, Department of Medical Oncology

« Early Palliative Care »



- Standard Care
- Early Palliative Care

Temel J et al. NEJM 2010

TOPICS

- The key role of supportive care

- **BONE**

- ANTIEMETICS
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- PAIN
- DYSPNEA

TAKE HOME MESSAGE

clinical practice guidelines

Annals of Oncology 25 (Supplement 3): iii124–iii137, 2014
doi:10.1093/annonc/mdu103
Published online 29 April 2014

Bone health in cancer patients: ESMO Clinical Practice Guidelines†

R. Coleman[1], J. J. Body[2], M. Aapro[3], P. Hadji[4] & J. Herrstedt[5] on behalf of the ESMO Guidelines Working Group*

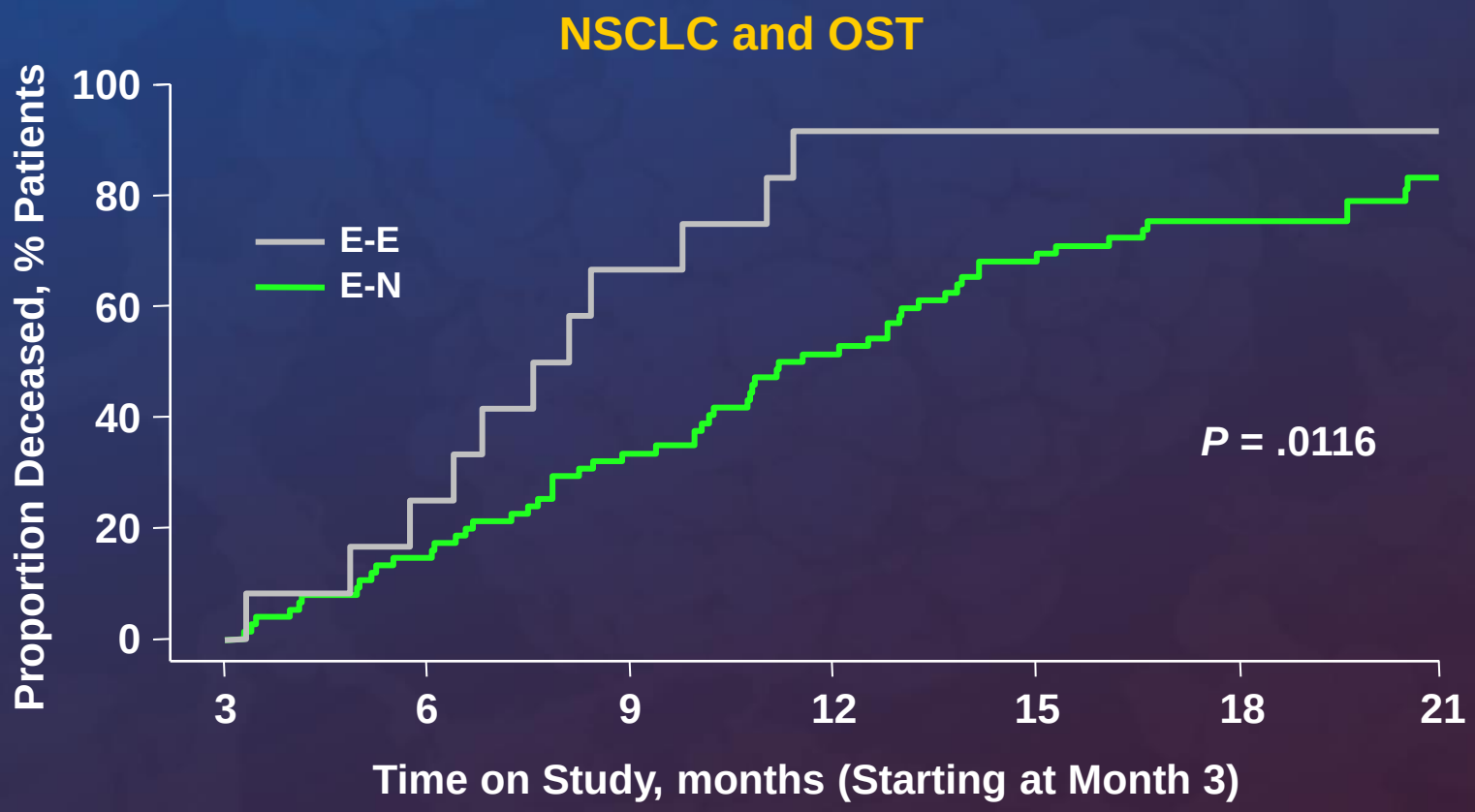
[1]Weston Park Hospital, Cancer Research-UK/Yorkshire Cancer Research Sheffield Cancer Research Centre, Sheffield, UK; [2]CHU Brugmann, Université Libre de Bruxelles, Brussels, Belgium; [3]Multidisciplinary Oncology Institute, Genolier, Switzerland; [4]Department of Gynecology, Endocrinology and Oncology, Philipps-University of Marburg, Marburg, Germany; [5]Department of Oncology, Odense University Hospital, Odense, Denmark

Incidence of bone metastasis in cancer

METASTATIC BONE DISEASE PREVALENT IN PATIENTS WITH LUNG CANCER			
Cancer type	**Incidence of BM in cancers (%)**	**Median survival (months)**	**5-year survival (%)**
Myeloma	95-100	20	10
Prostate	65 - 75	40	25
Breast	65 - 75	24	20
Thyroid	60	48	40
Lung	**30 - 40**	**<6**	**<5**
Kidney	20 - 25	6	10
Melanoma	14 - 45	<6	<5

Coleman, Cancer 1997

NTX Normalization Within 3 Months Is Associated With Improved Survival



Abbreviations: E-E, Patients whose NTX levels remained elevated at 3 months; E-N, Patients whose NTX levels normalized at 3 months from elevated baseline levels; NSCLC, Non-small cell lung cancer; NTX, N-telopeptide of type I collagen; OST, Other solid tumors.

Reprinted from Lipton A, et al. *Cancer.* 2008;113(1):193-201.

Lung cancer post-hoc subgroup of randomised, double-blind, active-controlled, Phase 3 trial

- **Key inclusion**
- Adults with lung cancer and bone metastases
- **Key exclusion**
- Current or prior intravenous bisphosphonate administration

1.1

Denosumab 120 mg SC
+
Placebo IV* Q4W **(n = 411)**

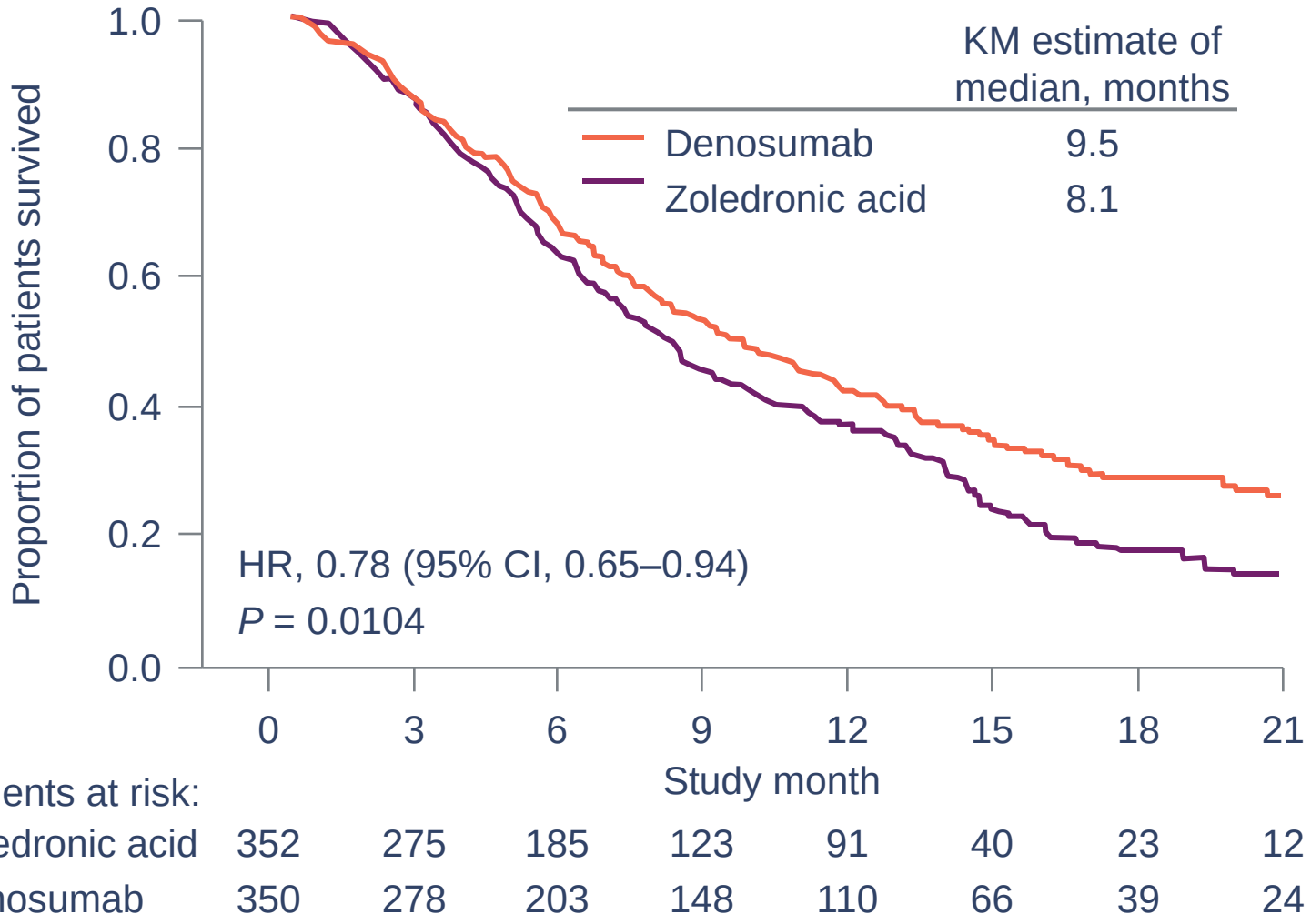
Calcium (500 mg) and Vitamin D (400 IU) strongly recommended

Zoledronic acid 4 mg IV*
+
Placebo SC Q4W **(n = 400)**

Lung cancer type, n (%)	Zoledronic acid	Denosumab	Total
NSCLC	352 (88)	350 (85)	702 (100)
Adenocarcinoma	211 (60)	189 (54)	400 (57)
Squamous Cell	75 (21)	88 (25)	163 (23)
Other	66 (19)	73 (21)	139 (20)
SCLC	48 (12)	61 (15)	109 (100)

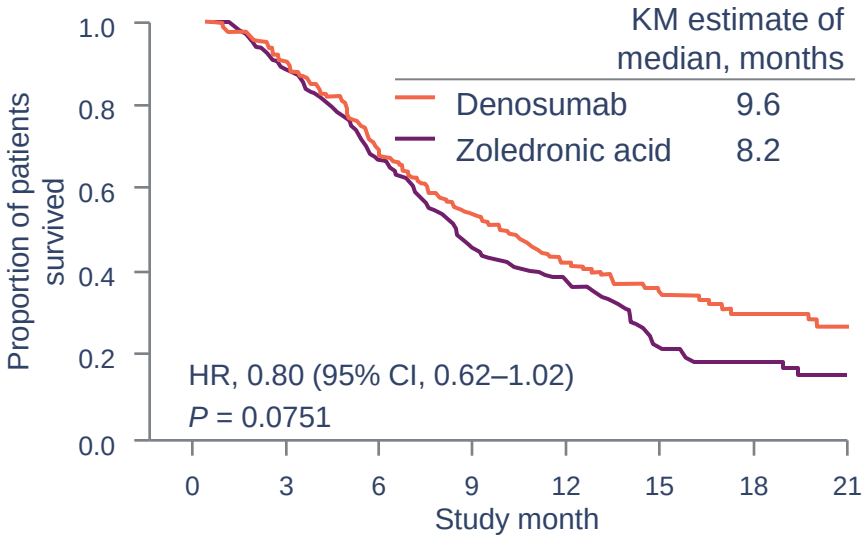
Scagliotti, WCLC 2011

Overall survival: patients with NSCLC Retrospective analysis (Scagliotti et al)



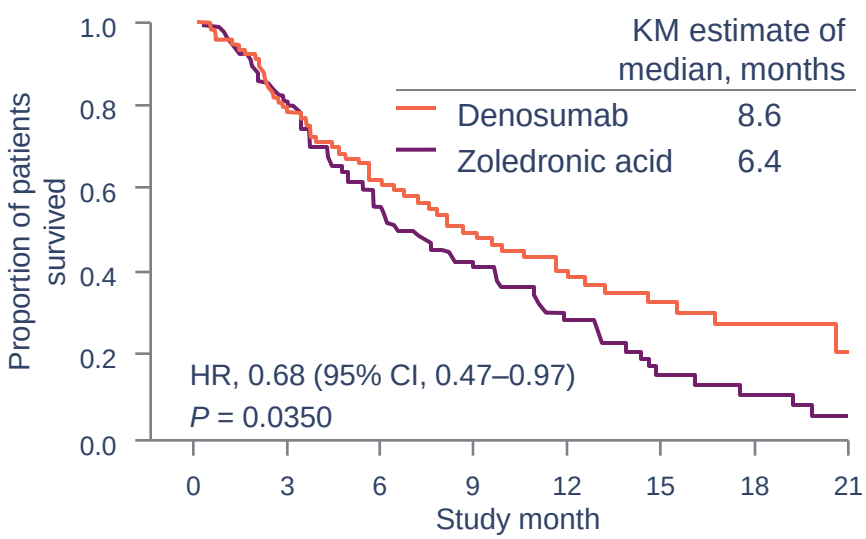
Overall survival: NSCLC by histological types

Adenocarcinoma



Patients at risk:								
Zoledronic acid	211	169	113	71	55	21	14	8
Denosumab	189	154	114	83	59	40	22	16

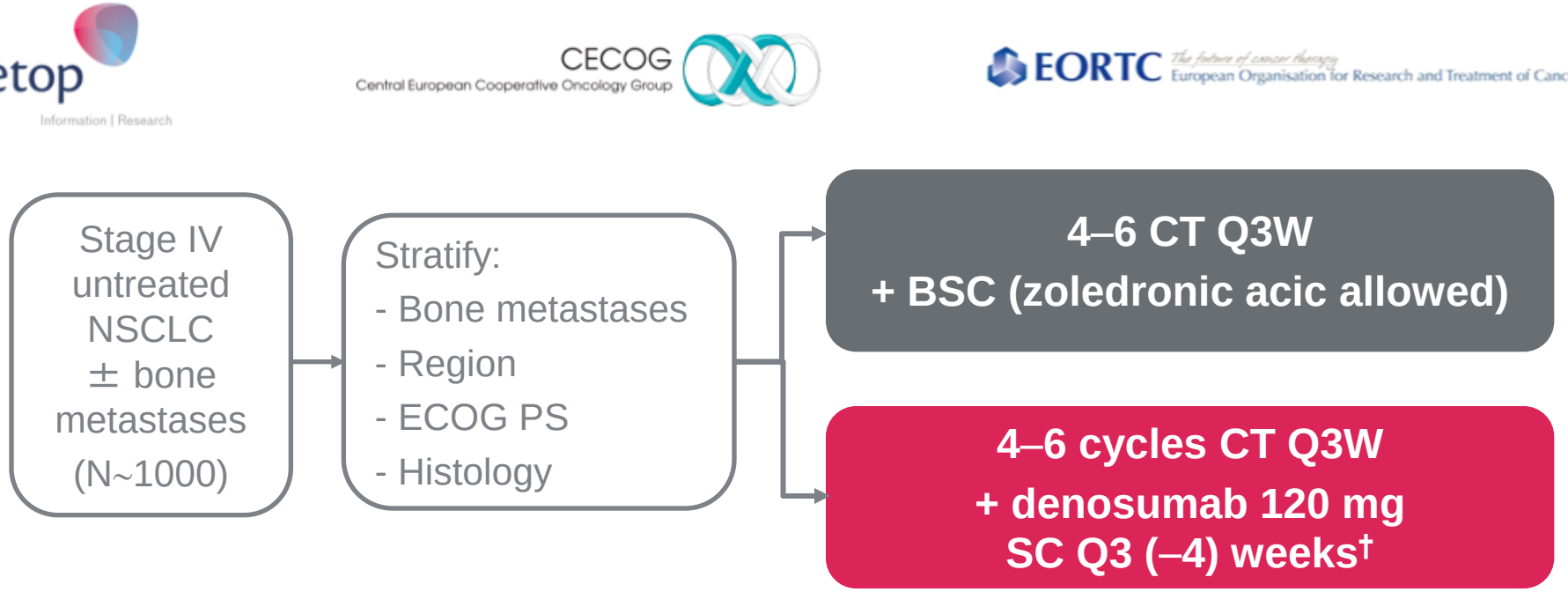
Squamous cell carcinoma



Patients at risk:								
Zoledronic acid	75	56	38	28	17	7	4	2
Denosumab	88	66	47	34	25	13	10	3

Scagliotti et al, WCLC 2011

SPLENDOUR: Phase III trial of denosumab in patients with Stage IV NSCLC



- Primary objective: overall survival
- Secondary objectives: PFS (RECIST 1.1); safety (CTCAE v 4); determination of biomarkers for translational research

†To be continued on tumour progression and concomitantly to subsequent lines of systemic treatment.
CT, chemotherapy, ECOG, Eastern Cooperative Oncology Group; IV, intravenously; Q3W, every 3 weeks; SC, subcutaneously.

TOPICS

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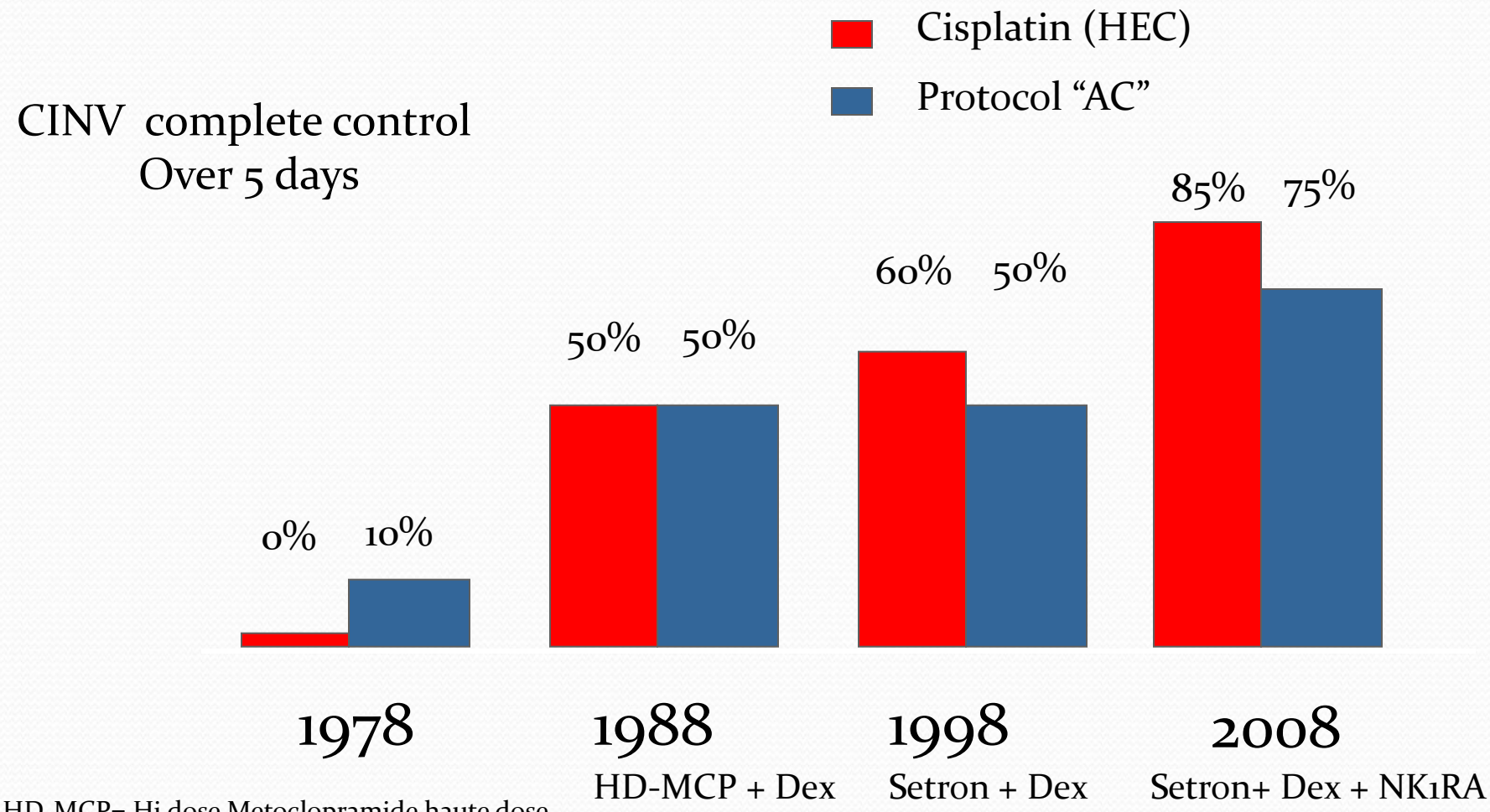
CINV Control
PROGRESS SINCE the 80's



HD-MCP= Hi dose Metoclopramide haute dose
Dex = Dexamethasone

CINV Chemo induced Nausea and Vomiting

Jordan K and Feyer P, 2012

MASCC/ESMO ANTIEMETIC GUIDELINE 2016

Multinational Association of Supportive Care in Cancer

Organizing and Overall Meeting Chairs:
Matti Aapro, MD
Richard J. Gralla, MD
Jørn Herrstedt, MD, DMSci
Alex Molassiotis, RN, PhD
Fausto Roila, MD

ACUTE Nausea and Vomiting: SUMMARY

EMETIC RISK GROUP	ANTIEMETICS
High Non-AC	**5-HT$_3$** + **DEX** + **NK$_1$**
High AC	**5-HT$_3$** + **DEX** + **NK$_1$**
Carboplatin	**5-HT$_3$** + **DEX** + **NK$_1$**
Moderate (other than carboplatin)	**5-HT$_3$** + **DEX**
Low	**5-HT$_3$** or **DEX** or **DOP**
Minimal	No routine prophylaxis

5-HT$_3$ = serotonin$_3$ receptor antagonist

DEX = DEXAMETHASONE

NK$_1$ = neurokinin$_1$ receptor antagonist such as APREPITANT or FOSAPREPITANT or ROLAPITANT or NEPA (combination of netupitant and palonosetron)

DOP = dopamine receptor antagonist

NOTE: If the NK$_1$ receptor antagonist is not available for AC chemotherapy, palonosetron is the preferred 5-HT$_3$ receptor antagonist.

DELAYED Nausea and Vomiting: SUMMARY

EMETIC RISK GROUP	ANTIEMETICS
High Non-AC	**DEX** or (if APR 125mg for acute: (**MCP** + **DEX**) or **APR**)
High AC	None or (if APR 125mg for acute: **DEX** or **APR**)
Carboplatin	None or (if APR 125mg for acute: **APR**)
Oxaliplatin, or anthracycline, or cyclophosphamide	**DEX** can be considered
Moderate (other)	No routine prophylaxis
Low and Minimal	No routine prophylaxis

DEX = DEXAMETHASONE | **MCP** = METOCLOPRAMIDE | **APR** = APREPITANT

COMMITTEE IX (1a/3): Advanced Cancer

Treatment of Nausea and Vomiting in Advanced Cancer: Drugs of Choice

The antiemetic drug of choice in advanced cancer is metoclopramide (titrated to effect).

MASCC Level of Consensus: High
MASCC Level of Confidence: Moderate
ESMO Level of Evidence: III
ESMO Grade of Recommendation: C

COMMITTEE IX (1b/3): Advanced Cancer

Treatment of Nausea and Vomiting in Advanced Cancer: Drugs of Choice

Alternative options include haloperidol, levomepromazine, or olanzapine.

MASCC Level of Consensus: High
MASCC Level of Confidence: Low
ESMO Level of Evidence: V
ESMO Grade of Recommendation: D

The use of cyclizine or 5-HT_3 receptor antagonists is poorly defined to date and may be used when dopamine antagonists are contraindicated or ineffective.

MASCC Level of Consensus: Low
MASCC Level of Confidence: Low
ESMO Level of Evidence: V
ESMO Grade of Recommendation: D

NOTE: The evidence to support combinations of drugs with antiemetic effect and different mechanisms of action is minimal (except in bowel obstruction)

COMMITTEE IX (3/3): Advanced Cancer

Treatment of Nausea and Vomiting in Advanced Cancer: Opioid-induced Emesis

No recommendation can be made about specific antiemetics, although various antiemetics may help. Opioid rotation and route switching may be effective approaches. There is no data to support prophylactic antiemetics in this situation.

MASCC Level of Consensus: High
MASCC Level of Confidence: Low
ESMO Level of Evidence: V
ESMO Grade of Recommendation: D

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ESMO Clinical Practice Guidelines (2010)
Application of Hematopoietic Growth Factors (hGFs)

Indications for Primary Prophylaxis of FN by hGFs*

- Reasonable only if
  - Probability of FN of ~20% based on chemotherapy and/or special situations, or
  - Dose reduction deemed detrimental to outcome [A]
- Efficacy parameters
  - Affected
    - ANC recovery [I]
    - Fever [I]
    - Infection rate [I]
    - Use of intravenous (IV) antibiotics [II]
    - Hospital discharge [I]
  - Controversial
    - Infectious mortality [I]
    - Early mortality
  - Not affected
    - Survival [I]

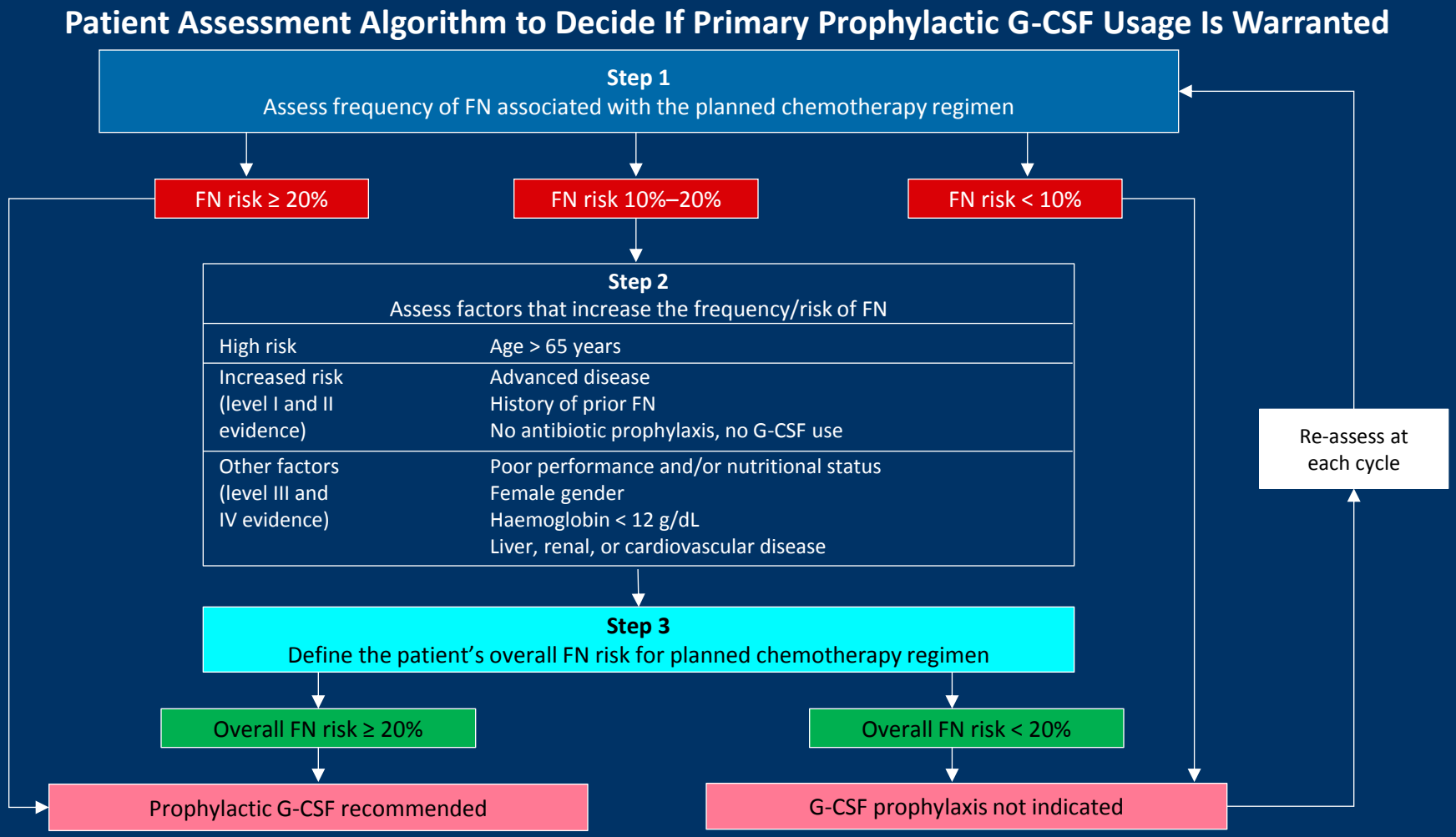
Special Situations for the Use of hGFs for Standard Therapy

Indication	Special Situation	Use of hGF
Primary prophylaxis	▪ Reduced marrow reserve (eg, ANC < 1.5 × 10^9/L) due to radiotherapy of > 20% marrow	Yes
	▪ Human immunodeficiency virus	Yes
	▪ Patients aged ≥ 65 years treated with curative intention (CHOP or more-intensive regimens for patients with aggressive NHL)	Yes
Secondary prophylaxis	▪ Further infections in the next treatment cycle considered life threatening	Yes
	▪ Dose reduction below threshold	Yes
	▪ Delay in chemotherapy	Yes
	▪ Lack of protocol adherence if compromising cure rate, OS, or disease-free survival	Yes
Therapy of afebrile neutropenia	–	No
Therapy of FN	General	No
Therapy of high-risk FN	Protracted FN (> 7 days), hypotension, sepsis, pneumonia, or fungal infection	Yes

*Roman numerals are the levels of evidence and the letters are their grades for recommendations. Everything not labelled as such is based on reasonable consensus/clinical practice

Crawford J, et al. *Ann Oncol*. 2010;21(suppl 5):v248-v251.

EORTC Guidelines (2010)



Aapro MS, et al. *Eur J Cancer.* 2011;47;8-32.

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PAIN

clinical practice guidelines

Annals of Oncology 23 (Supplement 7): vii139–vii154, 2012
doi:10.1093/annonc/mds233

Management of cancer pain: ESMO Clinical Practice Guidelines†

C. I. Ripamonti[1], D. Santini[2], E. Maranzano[3], M. Berti[4] & F. Roila[5], on behalf of the ESMO Guidelines Working Group*

[1]*Supportive Care in Cancer Unit, Fondazione IRCCS, Istituto Nazionale Tumori, Milan, Italy;* [2]*Oncologia Medica, Università Campus Bio-Medico, Rome, Italy;* [3]*Department of Oncology, Radiation Oncology Centre, S. Maria Hospital, Terni, Italy;* [4]*Anaesthesiology Intensive Care and Pain Therapy, University Hospital Parma, Parma, Italy;* [5]*Department of Medical Oncology, S. Maria Hospital, Terni, Italy*

An overview of cancer pain prevalence

According to a systematic review	
PHASE	**Prevalence**
After curative treatment	33%
On anticancer treatment	59%
Metastatic, advanced or terminal phase	64%

Ripamonti CI, et al; ESMO Guidelines Working Group. Ann Oncol 2012;23 Suppl 7:vii139
Van den Beuken-van Everdingen MHJ, et al. Ann Oncol 2007; 18: 1437

Prevalence of cancer pain: Meta-analysis of 52 studies

Type of cancer	% Pain
Head/neck	70 %
Gastrointestinal	59 %
Lung/bronchus	55 %
Breast	54 %
Urogenital	52 %
Gynaecological	60 %

Despite clear recommendations from the World Health Organization, cancer pain control is still a major issue.

van den Beuken-van Everdingen MH, et al. Ann Oncol. 2007;18:1437

Treatment of cancer pain

STRONG RECOMMENDATION

Mild pain → **STEP 1 NRS 1-3** → **NSAIDs-PARACETAMOL** → Periodical reassessment of cancer pain. Use rescue medications. If pain not controlled go on the next step

WEAK RECOMMENDATION

MILD-MODERATE PAIN → **STEP 2 NRS 4-6** → **WEAK OPIOIDS +/- NSAIDs-PARACETAMOL** → Periodical reassessment of cancer pain. Use rescue medications. If pain not controlled do not change opioid but go on the next step

STRONG RECOMMENDATION

MODERATE-SEVERE PAIN → **STEP 3 NRS 7-10** → **STRONG OPIOIDS +/- NSAIDs-PARACETAMOL**

Increase the dose of opioid every day, considering the number of opioid rescue doses used, till pain control or side effects

Side effects

Go on or, if necessary,opioid or route of opioid administration switching, using an equianalgesic dose of the same or different opioid:
- ✓ Oral or transdermal Long acting opioid
- ✓Symptomatic treatment

Use always rescue doses to treat Breakthrough Pain

Persisting Pain

- ✓Reasses the pain intensity and its causes
- ✓Consider the type and/or doses of adjuvants
- ✓Consider opioid or route of opioid administration switching
- ✓Consider invasive interventions
- ✓Team decision

VIENNA 2012 ESMO congress

www.esmo2012.org

Adjuvant drugs such as corticosteroids,anticonvulsants,antidepressants, should be considered at any step when necessary

TOPICS

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- **DYSPNEA**

Dyspnea:

the hardest symptom to control?

Causes: CAAPPAAC

Cardiac…
Asthma (+ chronic obstructive pulmonary disease)
Airway obstruction
Pleural effusion
Pulmonary embolism
Anemia
Anxiety
CANCER AND TREATMENT

Evaluating dyspnoea

Medical Research Council (MRC)

American Thoracic Society-Division of Lung Disease (ATS-DLD) questionnaire

Numeric scales (0 to 10)

VAS 0 to 100 mm

Verbal scale: Likert 4 (6) levels: no =1, some=2, a lot=3, extrme=4

Support Team Assessment Schedule (STAS)

EORTC QLQC30

The Borg Category Scale

Chronic Respiratory Questionnaire (CRQ)

The Oxygen Cost Diagram (OCD)

The Baseline Dyspnea Index (BDI)

Symptom relief

Anticholinergic drugs and mucolytics

Physical therapy and methods of respiratory management (Level 1 evidence)

Radiation therapy

Laser desobstruction

Thoracocentesis / pleurodesis (permanent pleural catheters)

Guidelines for treatment/prevention of subsequent pulmonary emboli

VTE / PE

clinical practice guidelines

Annals of Oncology 22 (Supplement 6): vi85–vi92, 2011
doi:10.1093/annonc/mdr392

Management of venous thromboembolism (VTE) in cancer patients: ESMO Clinical Practice Guidelines

M. Mandalà[1], A. Falanga[2] & F. Roila[3]

On behalf of the ESMO Guidelines Working Group*

[1]*Unit of Medical Oncology;* [2]*Division Immunohaematology and Transfusion Medicine, Haemostasis and Thrombosis Center, Department of Oncology and Haematology, Ospedali Riuniti, Bergamo;* [3]*Department of Medical Oncology, S. Maria Hospital, Terni, Italy*

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ASCO SPECIAL ARTICLE

Venous Thromboembolism Prophylaxis and Treatment in Patients With Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update

Gary H. Lyman, Alok A. Khorana, Nicole M. Kuderer, Agnes Y. Lee, Juan Ignacio Arcelus, Edward P. Balaban, Jeffrey M. Clarke, Christopher R. Flowers, Charles W. Francis, Leigh E. Gates, Ajay K. Kakkar, Nigel S. Key, Mark N. Levine, Howard A. Liebman, Margaret A. Tempero, Sandra L. Wong, Ann Alexis Prestrud, and Anna Falanga

Gary H. Lyman, Nicole M. Kuderer, and Jeffrey M. Clarke, Duke University and Duke Cancer Institute, Durham; Nigel S. Key, Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, NC; Alok A. Khorana, Taussig Cancer

SYMPTOM RELIEF

Oxygen therapy for patients who are not hypoxaemic is no more effective than medical air. If a therapeutic trial is indicated, any symptomatic benefit is likely within the first 72 hours.

SYMPTOM RELIEF

Regular, low dose, sustained release oral morphine (Level 1 evidence) titrated to effect (with regular aperients) is effective and safe.

Cancer Care Ontario
Action Cancer Ontario

Cancer Care Ontario's Symptom Management Guide-to-Practice: Dyspnea

Take Home Message

“Supportive care makes excellent cancer care possible”

Dorothy M.K. Keefe, MASCC president


MASCC/ISOO 2016
International Symposium on Supportive Care in Cancer
Save The Date...Adelaide, Australia - June 23-25 2016
ADELAIDE
SOUTH AUSTRALIA

Punctuality