INCONTRI SARDO EUROPEI DI TERAPIA DEL DOLORE E CURE PALLIATIVE

Palliative Care and Pain Therapy: Sardinia Meets Europe.

3-5 OTTOBRE 2008, BUDONI - Sardegna (OT)

EAPC

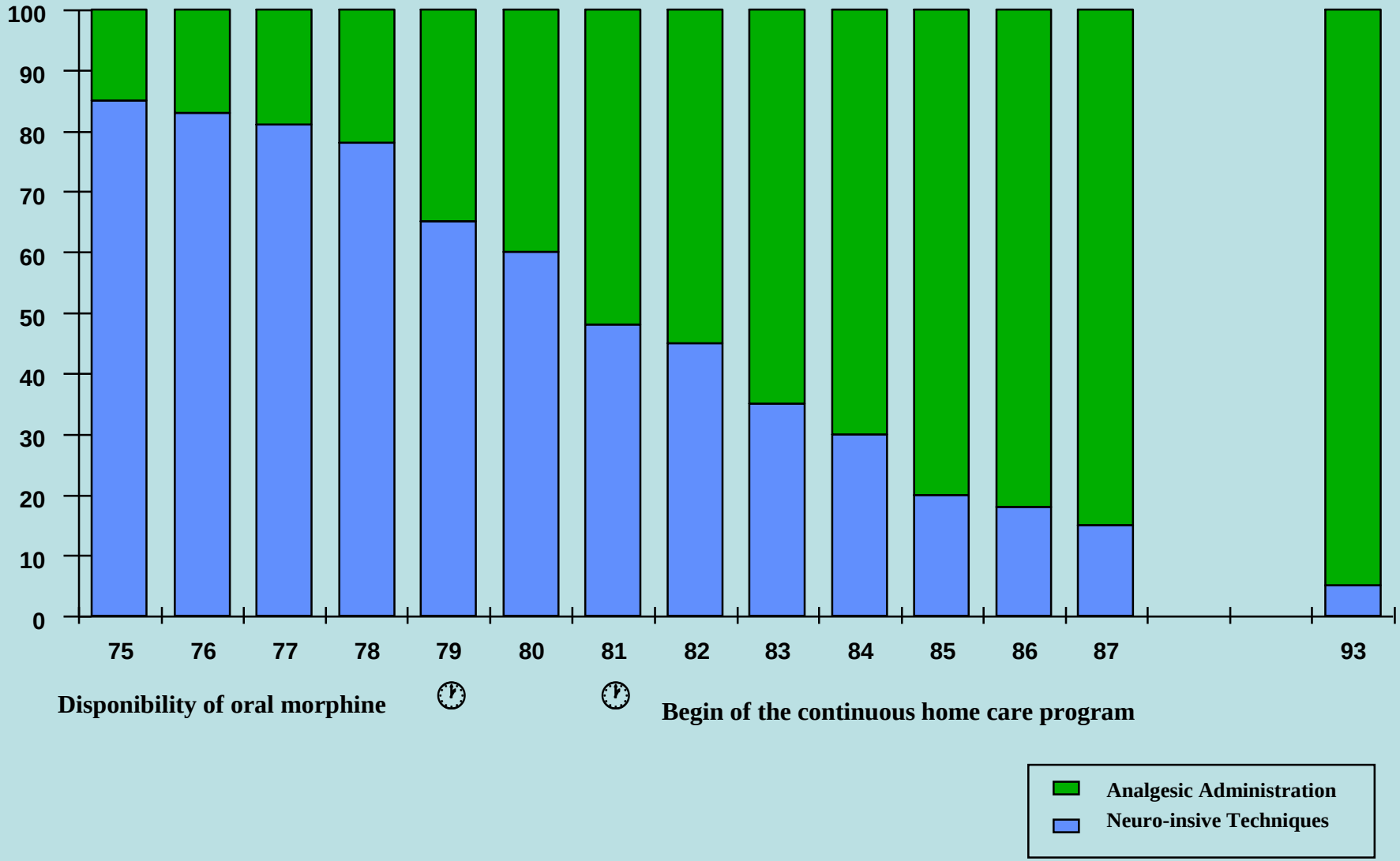
SICP

AIOM

WHO: secondo scalino? Titolazione?

Franco De Conno
Fondazione IRCSS Istituto Nazionale dei Tumori di Milano

Percentage of the use of neuro-invasive techniques versus the administration of analgesic drugs for the treatment of cancer pain in the National Cancer Institute of Milano from 1975 to 1993.



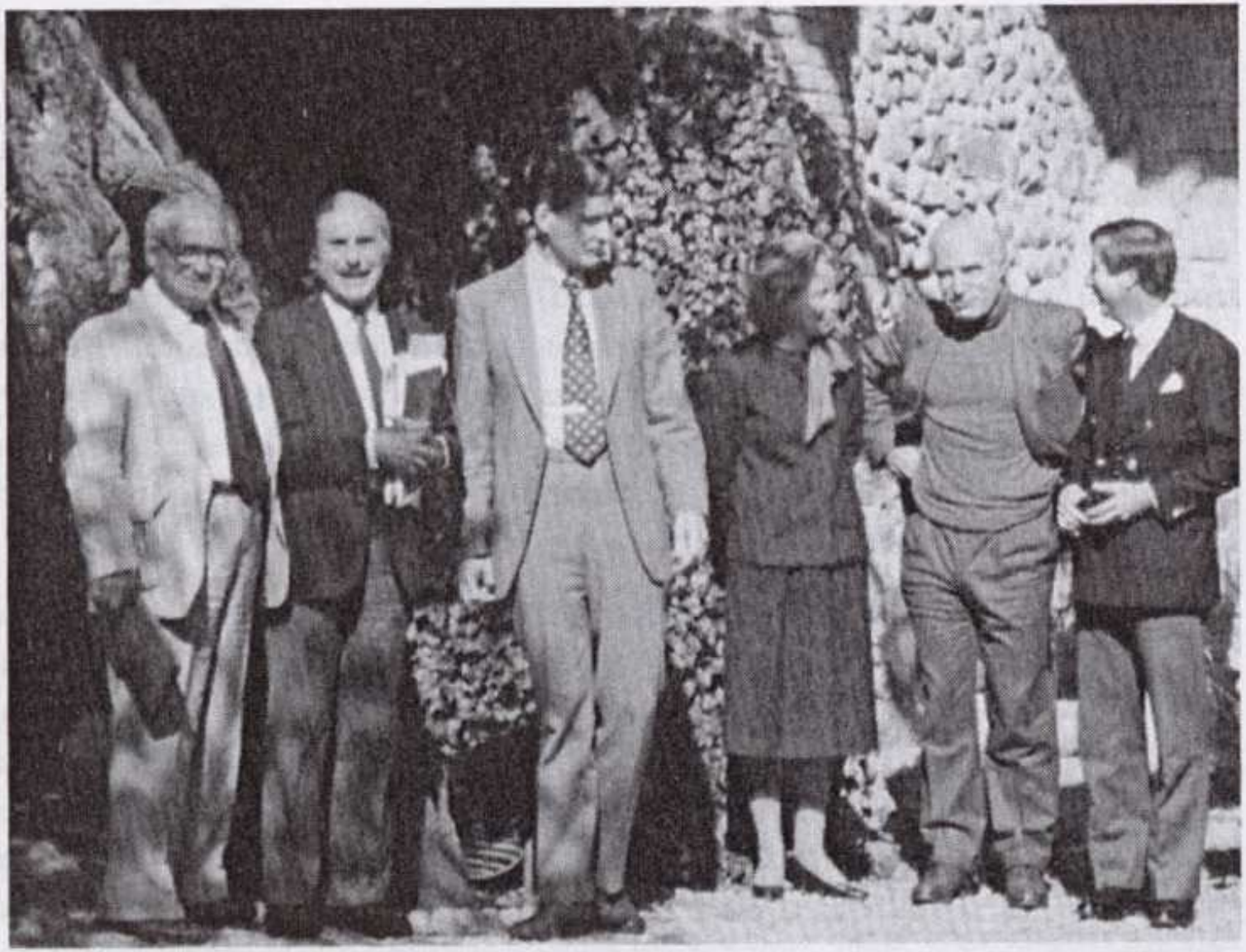
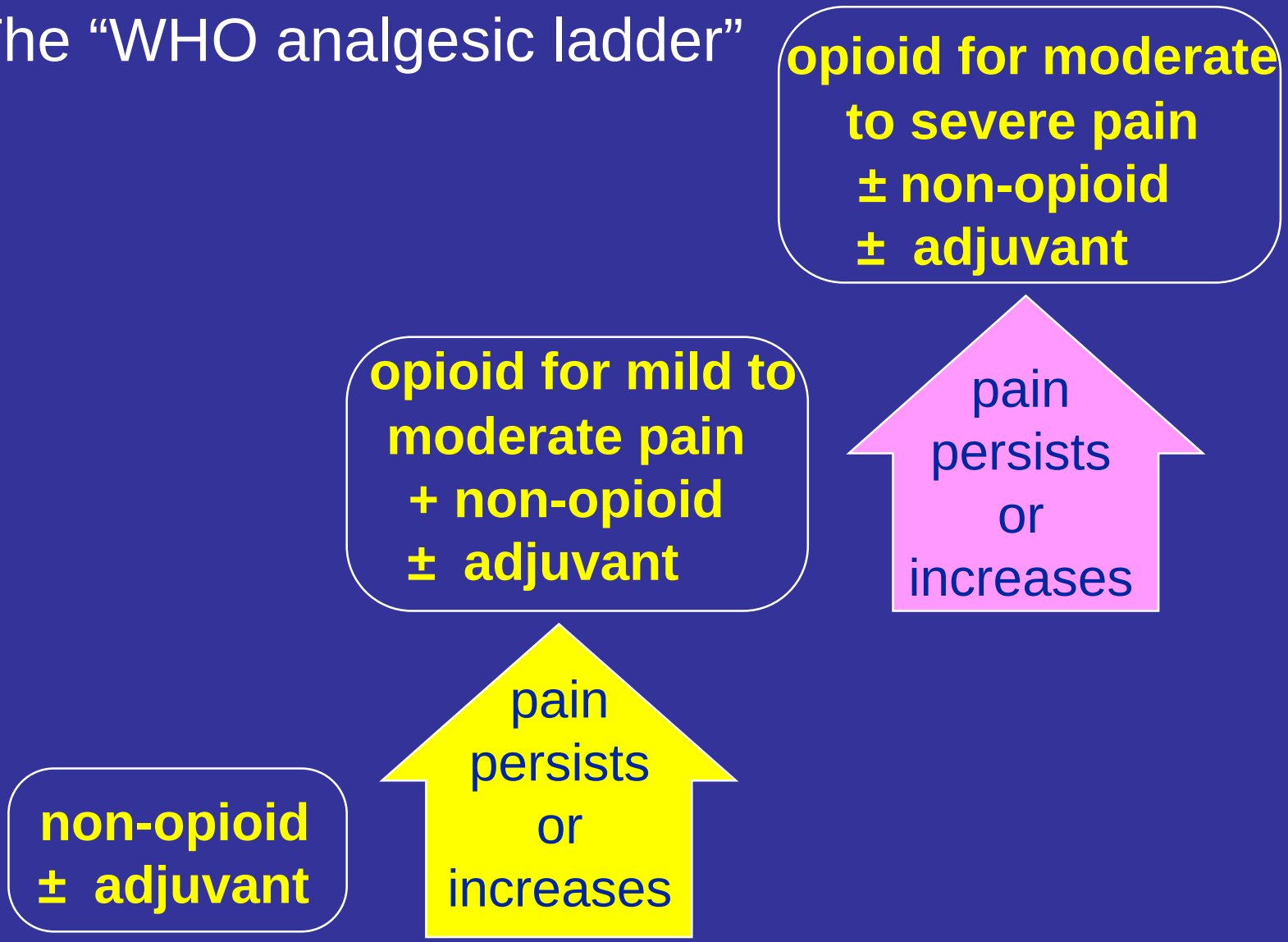
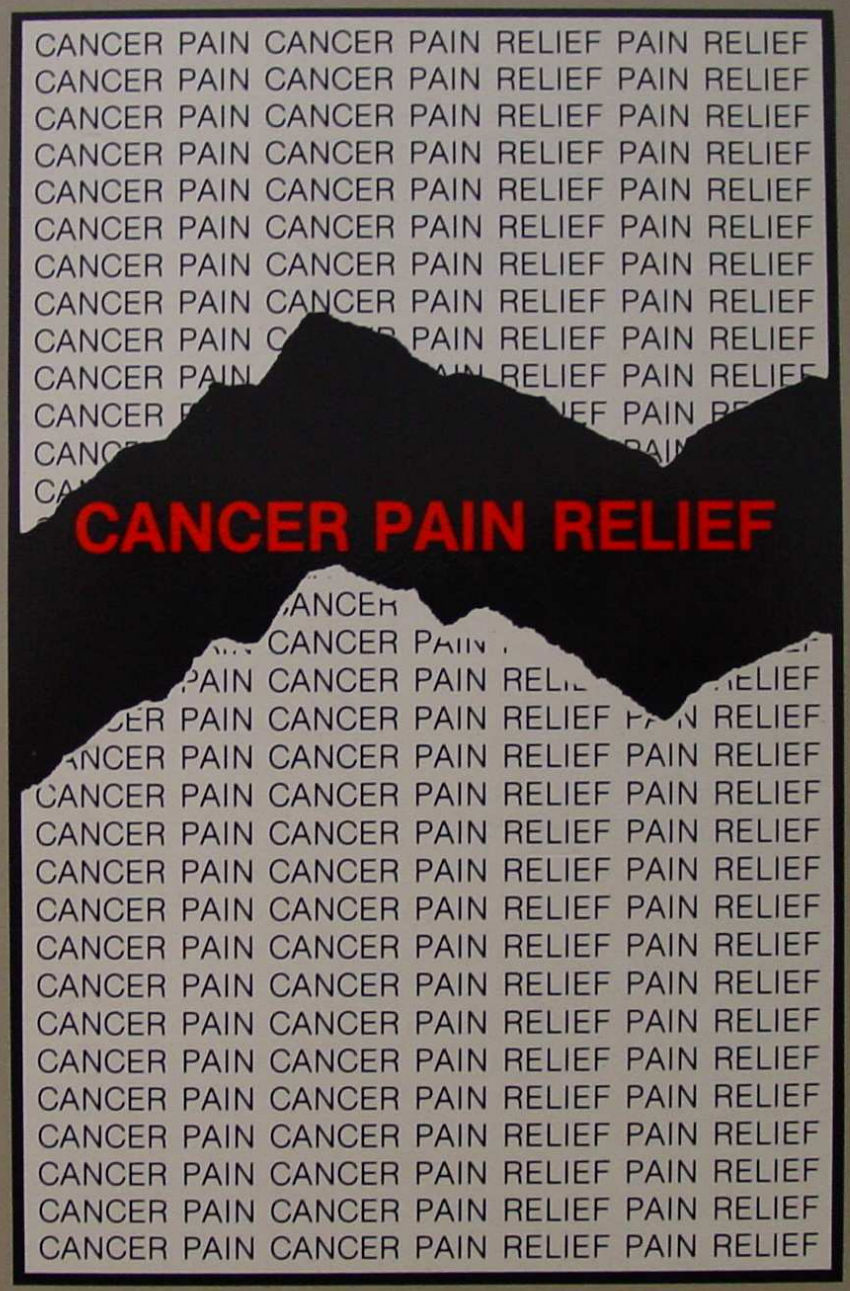


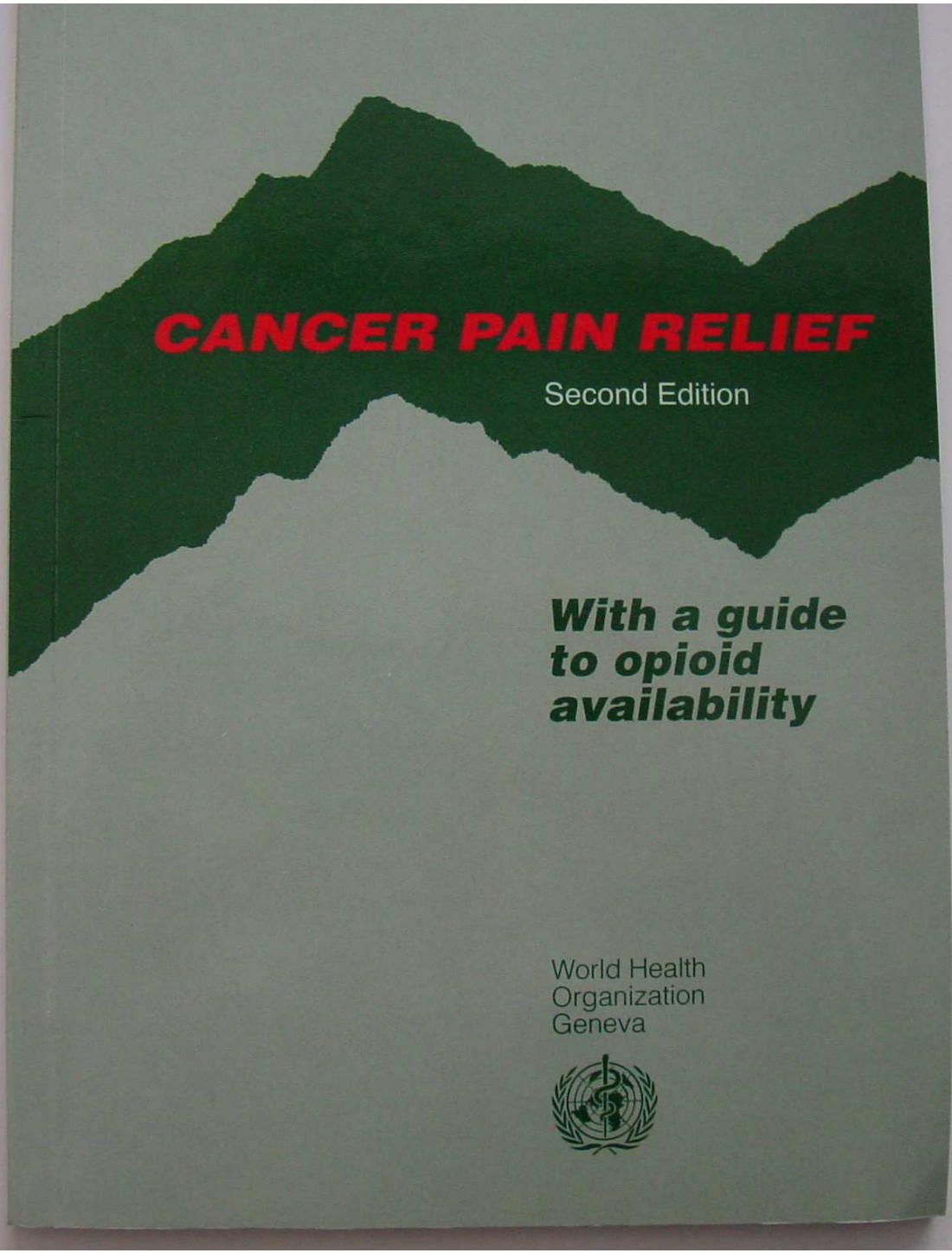
Figure 4: Some of the 1982 WHO group at the Villa D' Este on Lake Como, Italy.
L to R: John Bonica, Mark Swerdlow, Robert Twycross, Kathleen Foley, Vittorio Ventafridda, and Jan Stjernswärd.

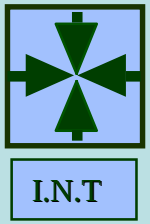
The “WHO analgesic ladder”





World Health Organization, Geneva


CANCER PAIN RELIEF
Second Edition
With a guide to opioid availability
World Health Organization
Geneva



Jadad et al.

J.A.M.A. 1995

Morphine in cancer pain: modes of administration

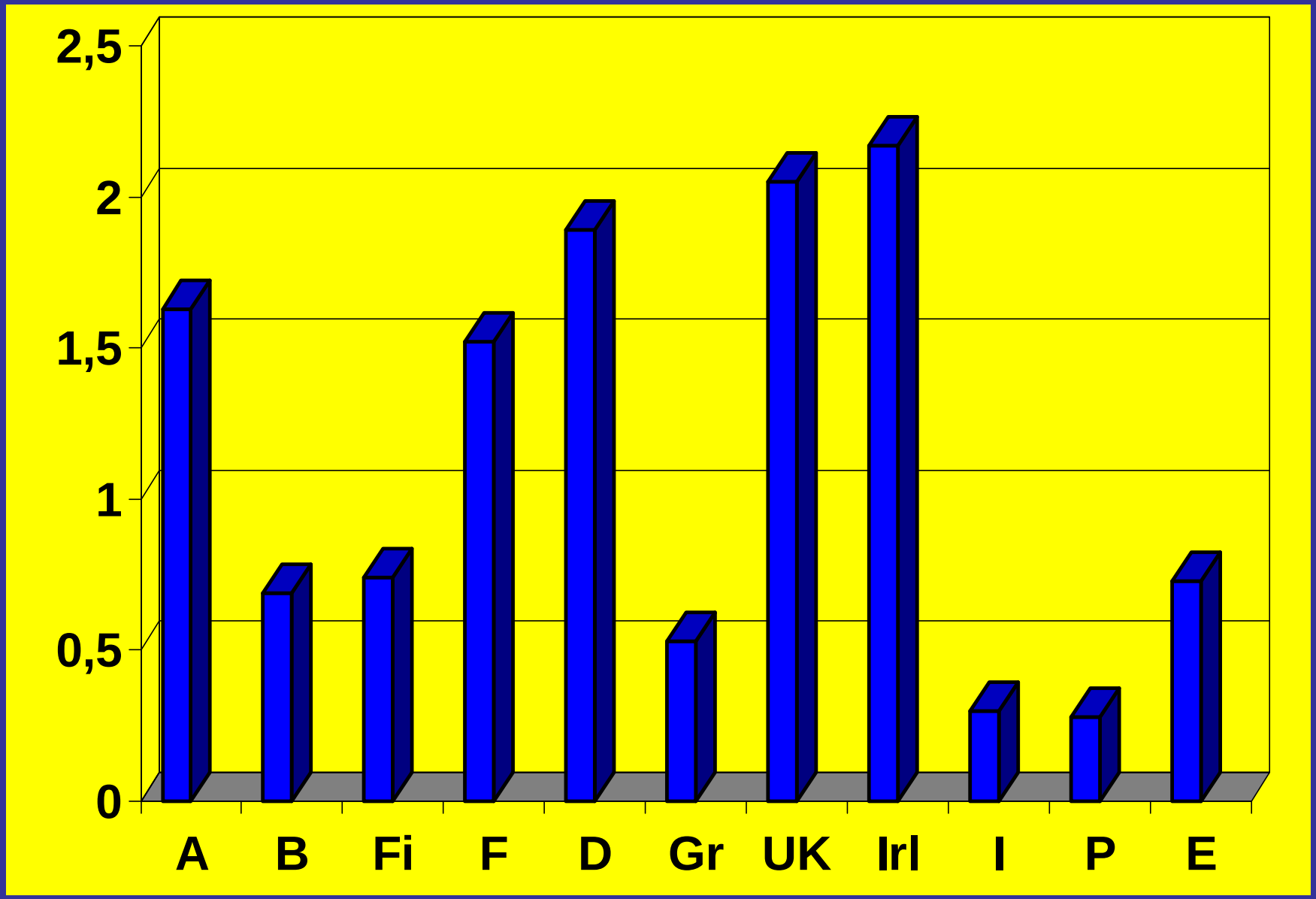
Expert Working Group of the
Research Network of the
European Association for Palliative Care

British Medical Journal 1996; 312: 823-826

Morphine and alternative opioids in cancer pain: the EAPC recommendations

Expert Working Group of the
Research Network of the
European Association for Palliative Care

British Journal of Cancer 2001; 84: 587-593



Consumo dei farmaci oppiacei in Europa (% sul totale della spesa farmaceutica)

SECONDO SCALINO??

TITOLAZIONE??

J Pain Symptom Manage. 2004 May;27(5):409-16

Use of strong opioids in advanced cancer pain: a randomized trial

Marinangeli F, Ciccozzi A, Leonardis M, Aloisio L, Mazzei A, Paladini A, Porzio G, Marchetti P, Varrassi G

Department of Anesthesiology and Pain Medicine, University of L'Aquila, L' Aquila, Italy

The purpose of this randomized study was to prospectively compare the efficacy and tolerability of strong opioids as first-line agents with the recommendations of the WHO in terminal cancer patients.

One hundred patients with mild-moderate pain were randomized to treatment according to WHO guidelines or to treatment with strong opioids

No between-treatment differences were observed for changes in quality of life or performance status, but patients started on strong opioids had significantly better pain relief than patients treated according to WHO guidelines (P=0.041)

Support Care Cancer. 2005 Nov;13(11):888-94.
Epub 2005 Apr 8. Links

A validation study of the WHO analgesic ladder: a two-step vs three-step strategy.

Maltoni M, Scarpi E, Modonesi C, Passardi A, Calpona S, Turriziani A, Speranza R, Tassinari D, Magnani P, Saccani D, Montanari L, Roudnas B, Amadori D, Fabbri L, Nanni O, Raulli P, Poggi B, Fochessati F, Giannunzio D, Barbagallo ML, Minnotti V, Betti M, Giordani S, Piazza E, Scapaticci R, Ferrario S.

Palliative Care Unit, Forlimpopoli Hospital, Via Duca d'Aosta 33, 47034 Forlimpopoli (FC), Italy.
ma.maltoni@ausl.fo.it

GOALS OF WORK: The aims of the present study were to verify whether an innovative therapeutic strategy for the treatment of mild-moderate chronic cancer pain, passing directly from step I to step III of the WHO analgesic ladder, is more effective than the traditional three-step strategy and to evaluate the tolerability and therapeutic index in both strategies.

Preliminary data would seem to suggest that a direct move to the third step of the WHO analgesic ladder is feasible and could reduce some pain scores but also requires careful management of side effects.

J Pain Symptom Manage. 2006 Mar;31(3):242-7.
Links

Low morphine doses in opioid-naive cancer patients with pain.

Mercadante S, Porzio G, Ferrera P, Fulfaro F, Aielli F, Ficorella C, Verna L, Tirelli W, Villari P, Arcuri E.

Anesthesia & Intensive Care Unit, La Maddalena Clinic for Cancer, and Department of Anesthesiology and Intensive Care, University of Palermo, Palermo, Italy. terapiadeldolore@la.maddalena.it

The aim of this multicenter study was to evaluate the efficacy and tolerability of very low doses of morphine in advanced cancer patients no longer responsive to non opioid analgesics

A sample of 110 consecutive opioid-naive patients with moderate-to-severe pain were given oral morphine at a starting dose of 15 mg/day (10 mg in those older than 70 years). Doses were then titrated according to the clinical situation. Pain intensity, morphine doses, symptom intensity, quality of life, and the requirement for dose escalation were monitored for a period of 4 weeks

The treatment was effective and well tolerated by most patients, who were able to maintain relatively low doses for the subsequent weeks (mean dose 45 mg at Week 4).

Eur J Pain. 2007 Nov;11(8):823-30. Epub 2007 Feb 28. Links

Opioid titration in cancer pain: a critical review

Mercadante S

Anesthesia and Intensive Care Unit & Pain Relief and Palliative Care Unit, La Maddalena Cancer Center, Palermo, Italy.
terapiadeldolore@la-maddalena.it

This review assesses the principal titration methods and outcomes regarding the different opioid drugs and their modalities of administration, in different clinical contexts.

M.E.R.I.T.O. Study

The MERITO Study: A multicenter trial of the analgesic efficacy and tolerability of immediate-release oral morphine during 'titration phase' in patients with cancer pain

Franco De Conno M.D., Carla Ripamonti M.D., Elena Fagnoni M.D., Cinzia Brunelli ScD, Massimo Luzzani M.D.°, Marco Mal toni M.D.§, Edoardo Arcuri M.D.^; Oscar Bertetto M.D.* on behalf of MERITO Study Group

MERITO

Morphine with Rapid onset Efficacy as Start Therapy in Oncology (Morfina ad Efficacia Rapida nell'Inizio della Terapia in Oncologia)

M.E.R.I.T.O. Study

Primary objective

The primary objective of this study was to measure the duration (percentage of time) of pain control during the 5 days of Start Therapy in cancer patients with pain given oral immediate release morphine (Oramorph)

Definition of Pain Control :

pain reduction by at least 50% vs baseline

M.E.R.I.T.O. Study

DEMOGRAPHICS

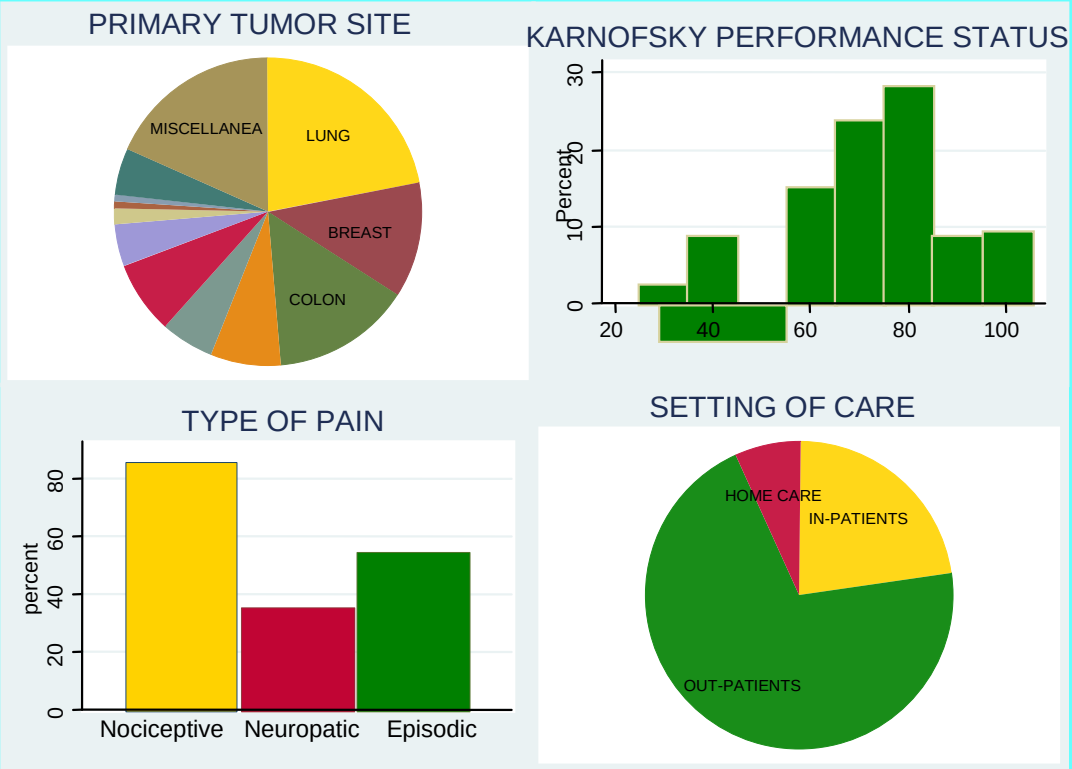
Number of Centers: 16

Total Patients ITT population: N=156

SEX: Male 102 (65%) Female 54 (35%)

AGE (years): Mean 64.9

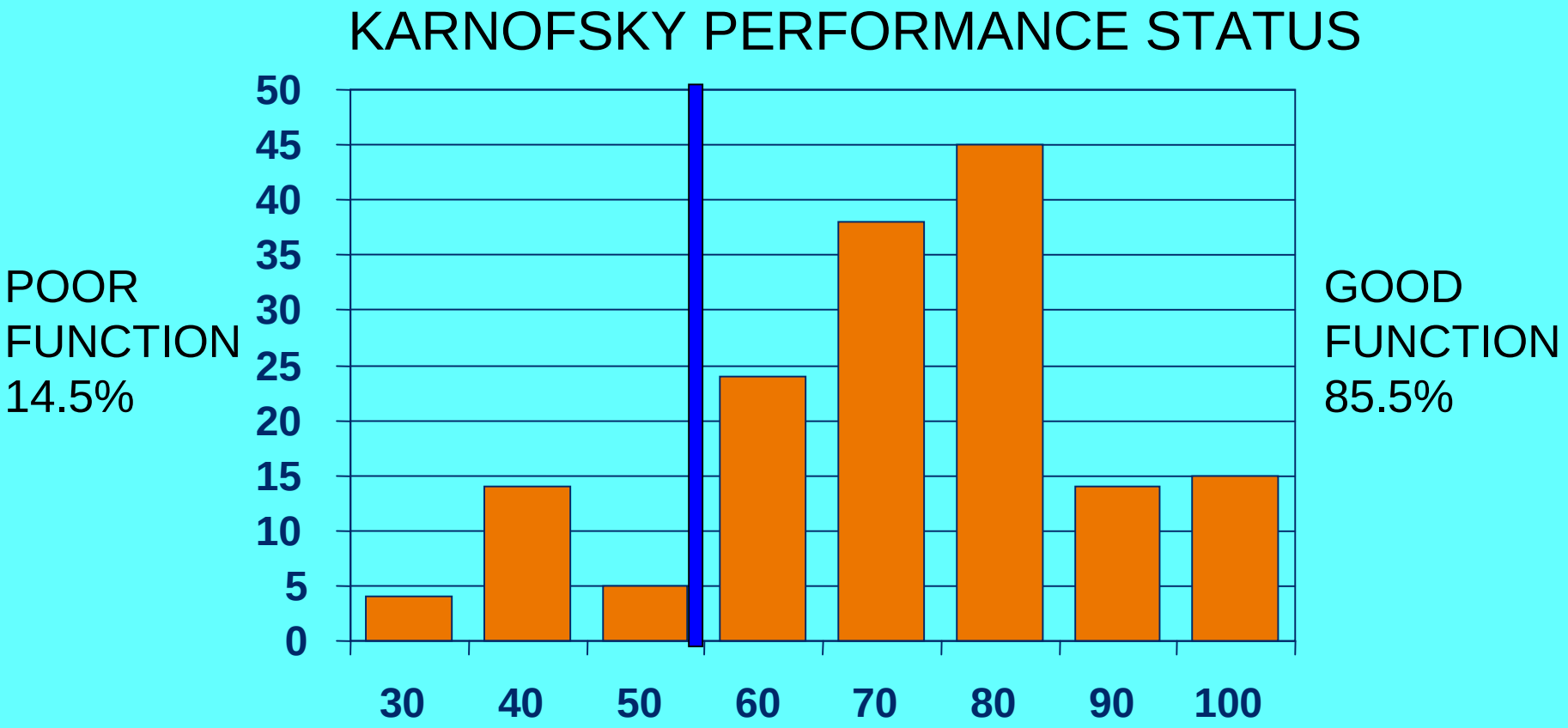
M.E.R.I.T.O. Study



Baseline characteristics

M.E.R.I.T.O. Study

Pts by KP Status:Most of Pts have still good function



M.E.R.I.T.O. Study

Immediate Release Oral Morphine Start Therapy
Posology

2 Groups of Patients (N=156)

Step I
WHO (29%)

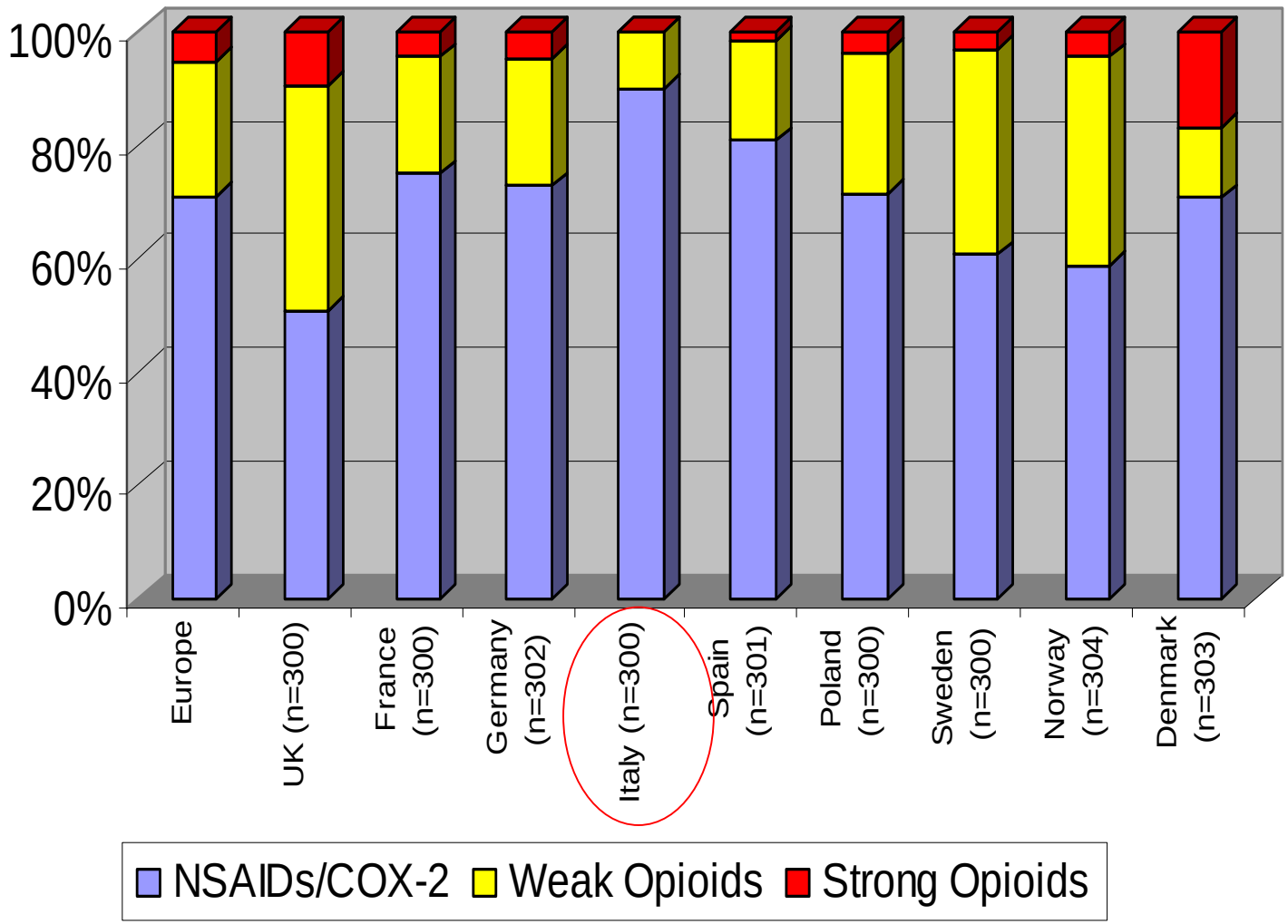
Step II
WHO (71%)

ORAMORPH DROPS

5 mg/4h **5 DAYS** **10mg/4h**

+ Rescue doses administered according to EAPC

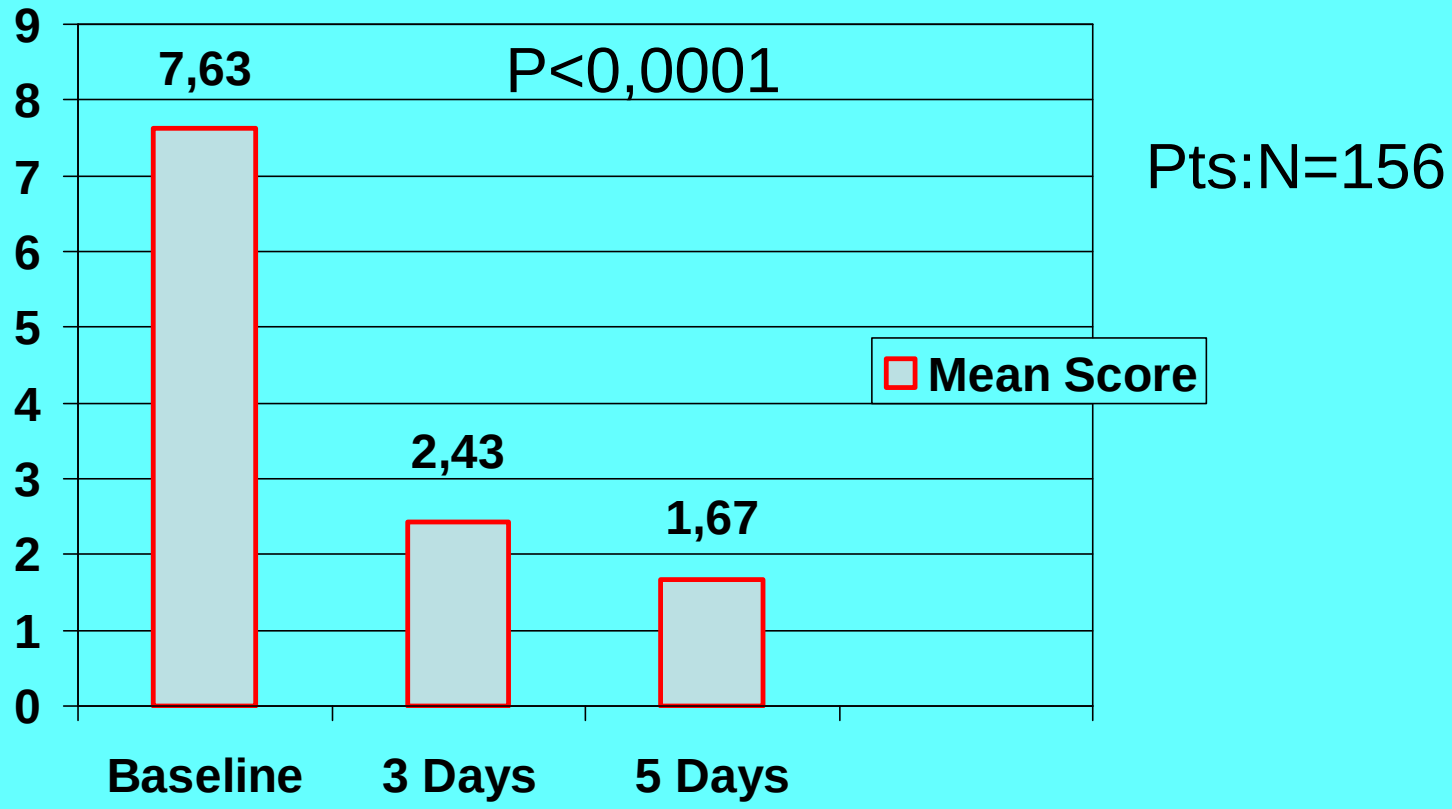
Trattamento farmacologico



M.E.R.I.T.O. Study

Persistent Pain Control

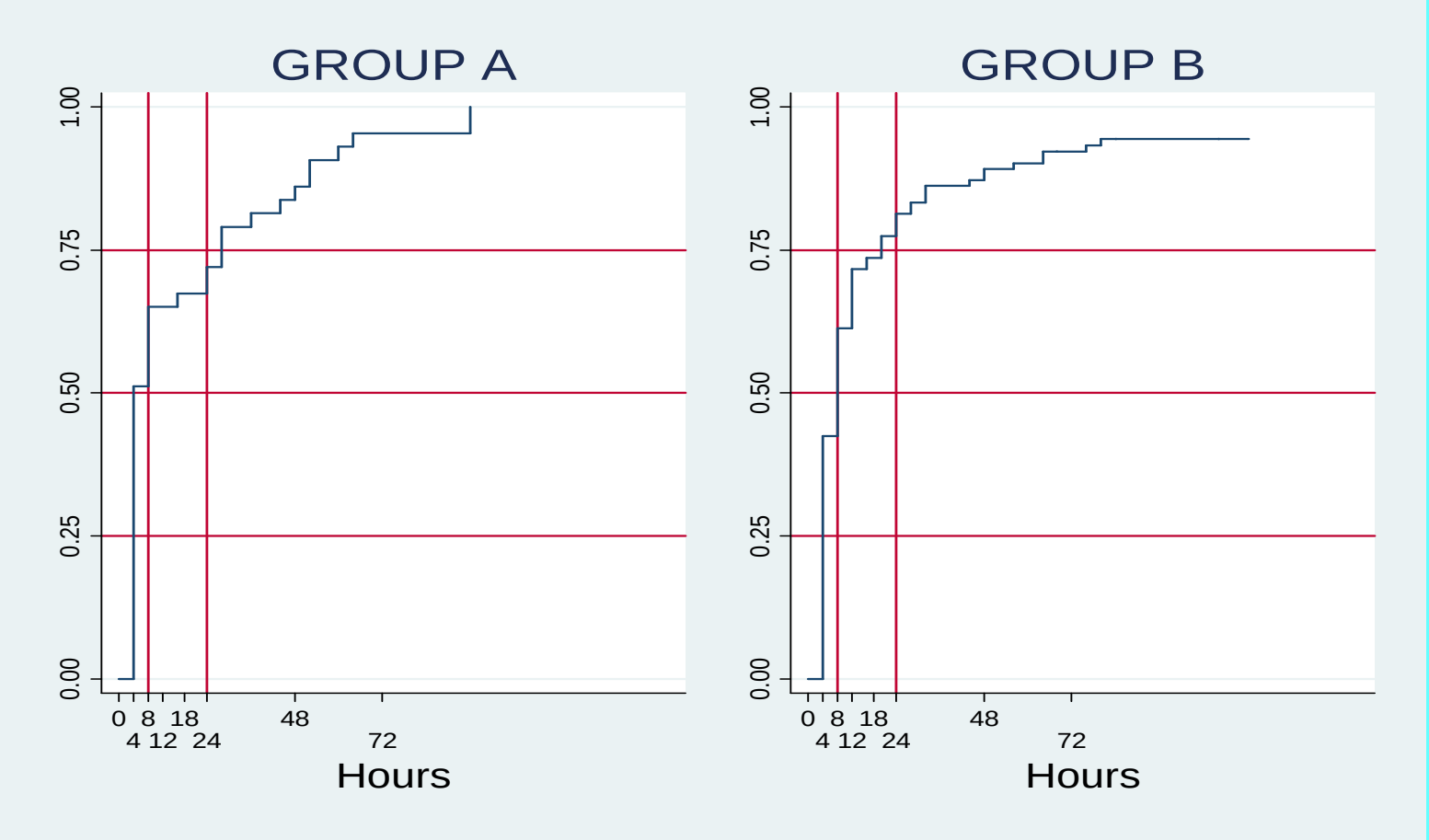
The Mean Score of Pain Numeric Rating Scale decreased with a high Statistical significance after 3 and 5 days of Immediate Release Oral Morphine Therapy



Pts:N=156

M.E.R.I.T.O. Study

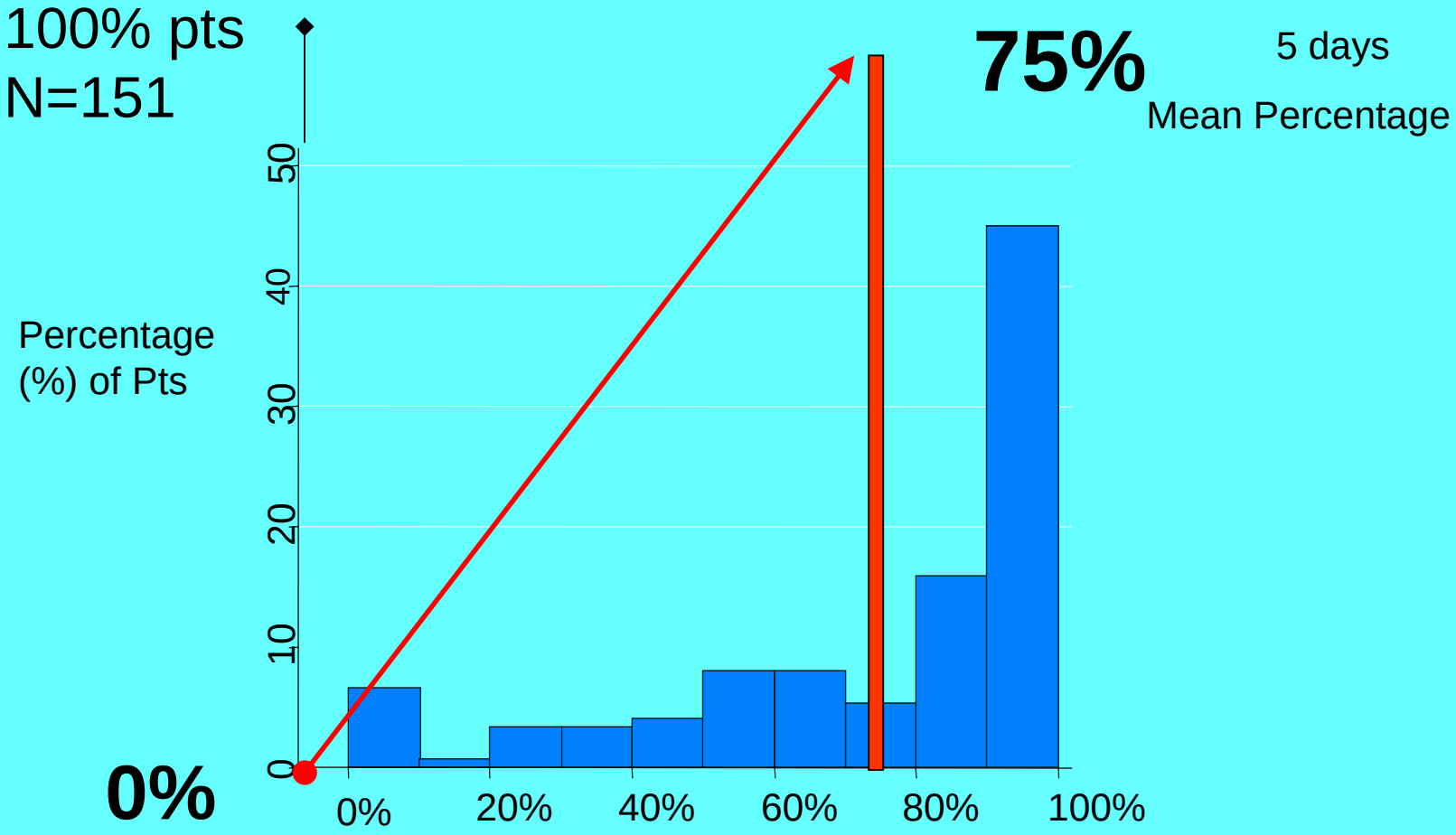
Time needed to reach the first pain control



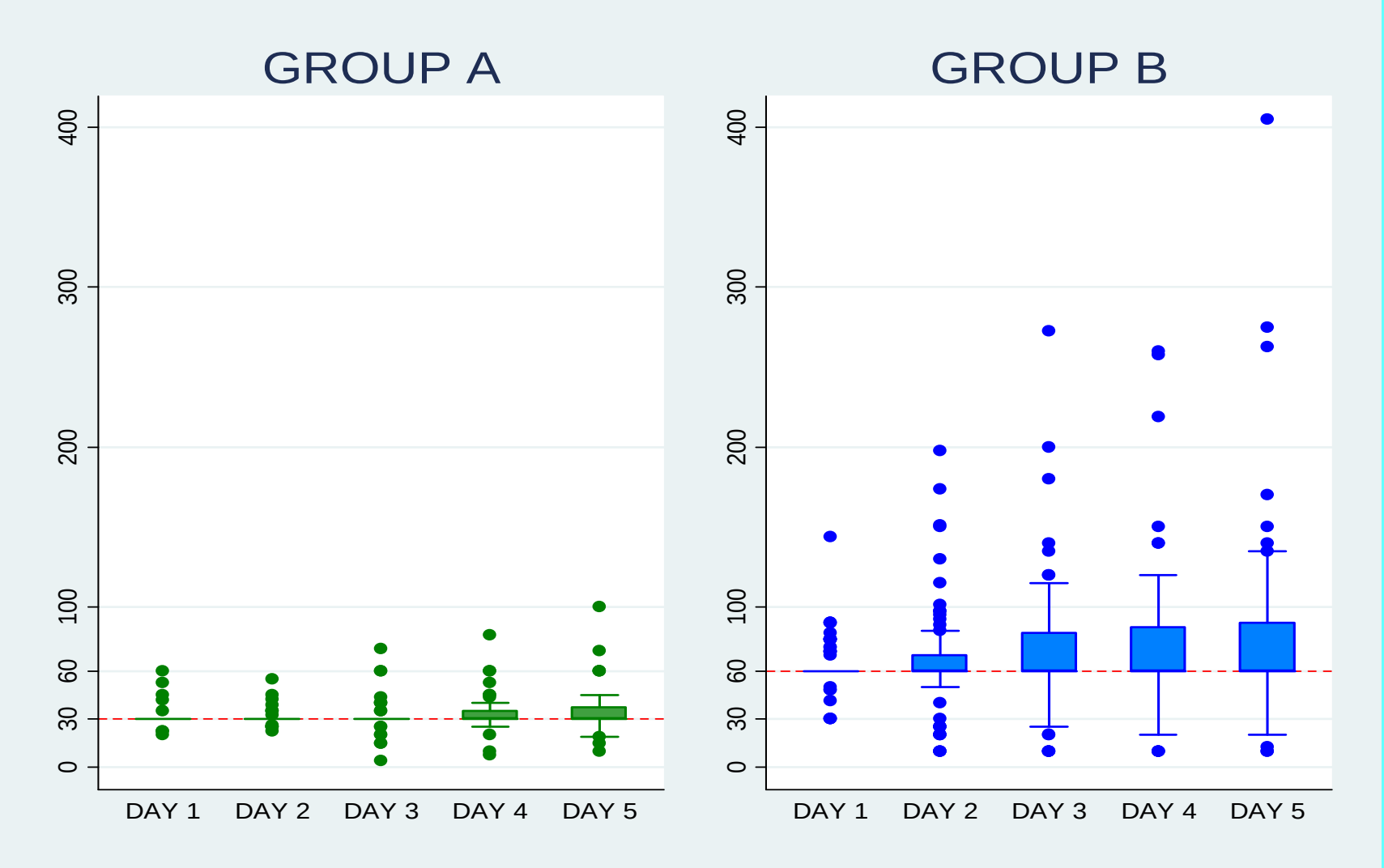
M.E.R.I.T.O. Study

Time Covering pain control

Percentage of time in 5 days “free of pain”



M.E.R.I.T.O. Study



MERITO STUDY

Safety

5 Deaths: Not related to Oramorph

No SUSAR (Suspected Unexpected Serious Adverse Reaction) related to Oramorph

ithdrawals for Serious AEs possibly related to Study Drug: 1 (Sedation)

ithdrawals for Not-Serious AEs possibly related to study drug: 15 (Confusion:

M.E.R.I.T.O. Study

Among all the factors examined those which proved to be associated with the response were KPS and episodic pain; the percentage of response to IRM
is higher in pts with a KPS ≥ 60 (52% vs 19%) and in patients without episodes of pain in the 24 hours before starting IRM treatment (30% vs 49%).

M.E.R.I.T.O. Study

CONCLUSIONS

MERITO Study data indicate that stable doses of Immediate Release Oral Morphine as Start Therapy (titration) are able to get a satisfactory,quick and stable control of pain in cancer patients, especially the opioid naïve ones.

Fixed dose posology IRM could be proposed as Start Therapy in cancer patients with pain.

M.E.R.I.T.O. Study

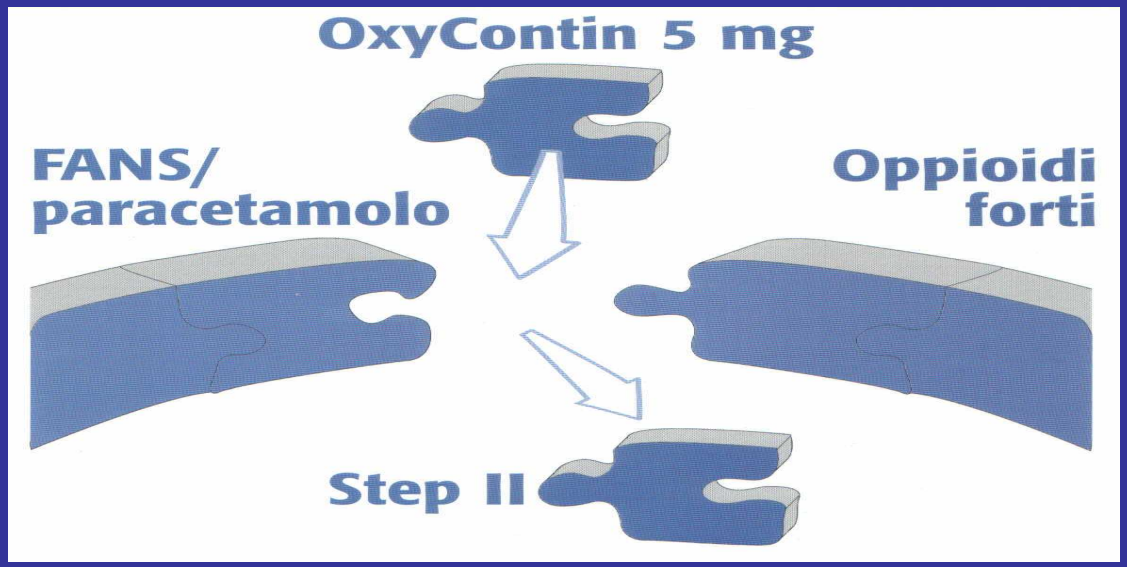
CONCLUSIONS

MERITO Study data indicate that patients with cancer pain and a KPS $\geq$ 60 before starting Immediate Release Oral Morphine (IRM) are more likely to have better pain control than patients with cancer pain and KPS < 60.

The analgesic response to IRM as starting therapy is better if IRM is administered to pain cancer patients as fast as possible instead to wait patients decline.

LINEE GUIDA ESMO 2007

L’utilizzo di formulazioni a rilascio controllato di oppioidi a basso dosaggio consentono un buon controllo anche del dolore moderato



Il passaggio diretto dal I al III gradino della scala OMS consente un buon controllo del dolore

“Management of Cancer Pain: ESMO Clinical Recomendation” Annals of Oncology 18 (Supplement 2): 1192-1194. 2007

Le linee guida pubblicate dall'OMS indicano la terapia orale come il trattamento di prima scelta per la gestione del dolore oncologico cronico.

la MORFINA, somministrata per via orale (IR-CR)è l'oppioide più utilizzato per il controllo del dolore da moderato a grave.

Il 30% dei pazienti con dolore da cancro non può essere trattato con successo con morfina orale per una scarsa risposta analgesica ad una dose che provoca effetti indesiderati insopportabili.

altri farmaci oppioidi maggiormente utilizzati :

FENTANYL TRASDERMICO(14%)

OSSICODONE (4%)

METADONE(2%)

DIAMORFINA(2%)

IDROMORFONE (1%).

For more information

visit

www.eapcnet.org