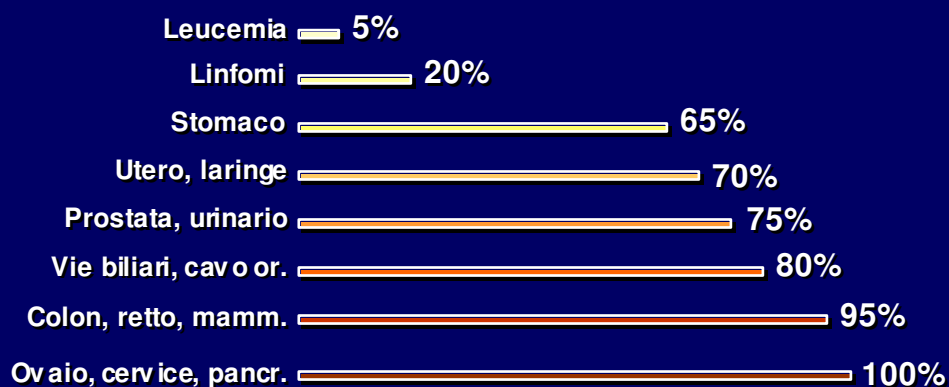


Prevalenza del dolore neoplastico

- **Prevalenza media in qualunque stadio (23 studi)**
48% (range 38-100%)
- **Prevalenza media in fase avanzata (27 studi)**
74% (range 53-100%)

• Hearne Higginson, Cancer pain epidemiology: a systematic review, 2003

Prevalenza del dolore correlato al cancro



Dolore da cancro: incidenza in base ai meccanismi fisiopatologici

- Dolore nocicettivo “puro”: **49%**
- Dolore neuropatico “puro”: **10%**
- Dolore misto: **41%**

Cherny, Neurology, 1994

SINDROMI DOLOROSE

2266 pazienti

4542 sindromi dolorose anatomicamente distinte

30%	1
39%	2
31%	≥ 3

Grond, Pain, 1996

SINDROMI DOLOROSE IN ONCOLOGIA

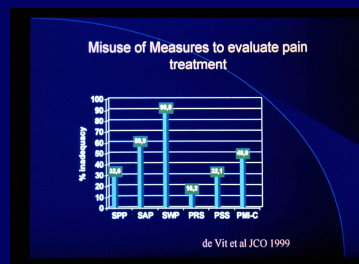
	ricoverati	esterni
Da neoplasia	78%	62%
Da terapie	19%	25%
Ne' da neoplasia, né da terapie	3%	10%

Foley, OTPM, 2004

MISURAZIONE DEL DOLORE

- **Scale di intensità**
 - scale analgesiche visive (VAS)
 - scale numeriche (NRS)
 - scale verbali (VRS)
- **Scale di sollievo**
- **Questionari multidimensionali**
 - Mc Gill Pain Questionnaire (MPQ)
 - Brief Pain Inventory (BPI)
 - Memorial Pain Assessment Card (MPAC)

A seconda della modalità di rilevazione, la percentuale di pazienti trattati "in modo inadeguato" variava **da 16% a 91%**



Centro Studi e Ricerche Osservatorio Italiano Cure Palliative

- **Due studi trasversali:**
il primo su “malati oncologici in carico alle Cure Palliative” (2002),
il secondo su”malati oncologici seguiti in setting di cure non specificamente palliative” (2003)
- **Dolore medio Studio I: 3.43 +- 2.47**
- **Dolore medio Studio II: 5.46 +- 2.45**
(6.55+- 2.14 per i pazienti con metastasi)

(Corli O, Pizzuto M)

Symptoms during cancer pain treatment following WHO-guidelines: a longitudinal follow-up study of symptom prevalence, severity and etiology

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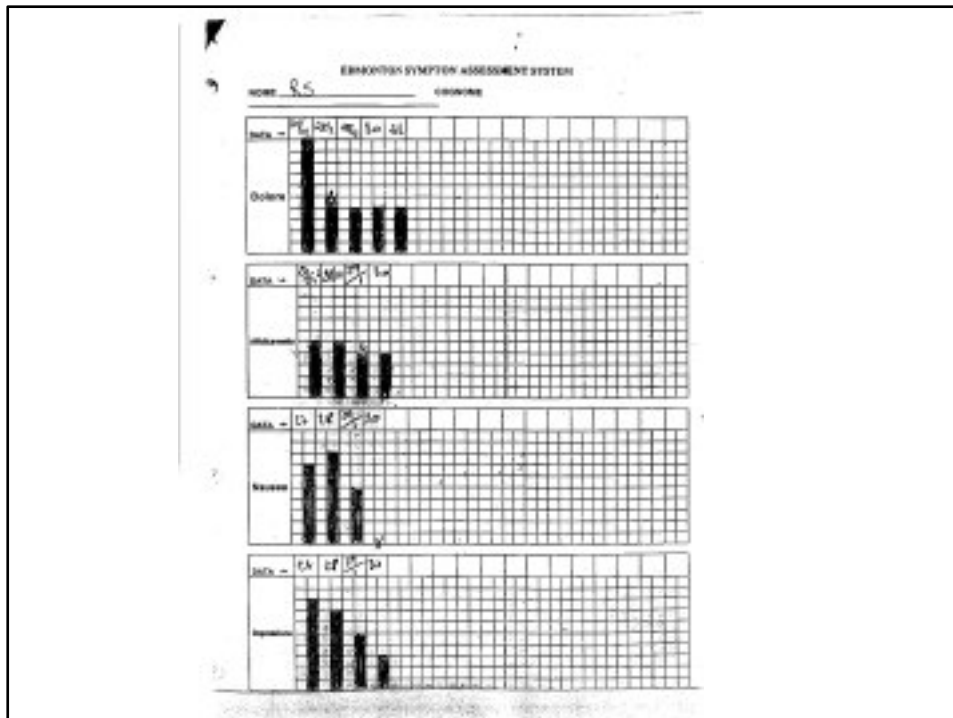
Abstract

Most patients with advanced cancer develop diverse symptoms that can limit the efficacy of pain treatment and undermine their quality of life. The present study surveys symptom prevalence, etiology and severity in 503 cancer patients treated by a pain service. Non-opioid analgesics, opioids and adjuvants were administered following the WHO-guidelines for cancer pain relief. Other symptoms were systematically treated by appropriate adjuvant drugs. Pain and symptom severity was measured daily by patient self-assessment; the physicians of the pain service assessed symptom etiology and the severity of confusion, coma and gastrointestinal obstruction at each visit. The patients were treated for an average period of 53 days. Efficacy of pain treatment was good in 30%, satisfactory in 16% and inadequate in 14% of patients. The initial treatment caused a significant reduction in the average number of symptoms from four to three. Prevalence and severity of anorexia, impaired activity, confusion, mood changes, insomnia, constipation, dyspepsia, dyspnoea, coughing, dysphagia and urinary symptoms were significantly reduced; those of sedation, other neuropsychiatric symptoms and dry mouth were significantly increased and those of coma, vertigo, diarrhea, nausea, vomiting, intestinal obstruction, erythema, pruritus and sweating remained unchanged. The most frequent symptoms were impaired activity (74% of days), mood changes (22%), constipation (23%), nausea (23%) and dry mouth (20%). The highest severity scores were associated with impaired activity, sedation, coma, intestinal obstruction, dysphagia and urinary symptoms. Of all 23 symptoms, only constipation, erythema and dry mouth were assessed as being most frequently caused by the analgesic regimen. In conclusion, the high prevalence and severity of many symptoms in far advanced cancer can be reduced, if pain treatment is combined with systematic symptom control. Nevertheless, general, neuropsychiatric and gastrointestinal symptoms are experienced during a major part of treatment time and pain relief was inadequate in 14% of patients. Cancer pain management has to be embedded in a frame of palliative care, taking all the possibilities of symptom management into consideration. © 2001 International Association for the Study of Pain. Published by Elsevier Science B.V. All rights reserved.

Hospice Forlimpopoli: un anno di attività

Pazienti con sintomo >4 all'ingresso

Sintomo	Pazienti	Giorno 1	Giorno3	Giorno7
Nausea	24	7.12	3.75	1.96
Dispnea	37	7.08	5.73	3.86
Anoressia	90	7.33	5.80	4.33
Malessera	66	6.83	4.88	3.85
Dolore	74	7.12	4.95	4.23
Ansia	83	7.13	5.67	5.14
Depressione	78	7.26	5.83	5.28
Astenia	104	7.46	6.28	5.68
Sonnolenza	80	7.42	6.69	6.40



Percentuale di pazienti oncologici nei programmi nazionali di cure palliative

- UK, 1994-1995, **96%** (NCHPCS,1997)
- USA, 1990, **80.2%** (Christakis,NEJM,1996)

Oncology/PC relationships: Concurrent Model



Palliative Care Home care

Diagnosis
Advanced
Cancer

Refractoriness
to ChemoRx

Death

- Continuity of Care
- Flexible primary care coordination: patient or condition determined
- Always goal appropriate

Trends in aggressiveness of cancer care near the end of life (28,777 pts 65 ys+ dead in 1 y)

	1993	1996	p
Chemo last 2 weeks	13.8	18.5	<.001
Emergency dept visit last month	7.2	9.2	<.001
Hospitalization last month	7.8	9.1	=.008
Admission ICU last month	7.1	9.4	=.009
Last 3 days hospice	14.3	17.0	=.004
Acute care hospital death	32.9	29.5	<.001
Hospice service use	28.3	38.8	<.001

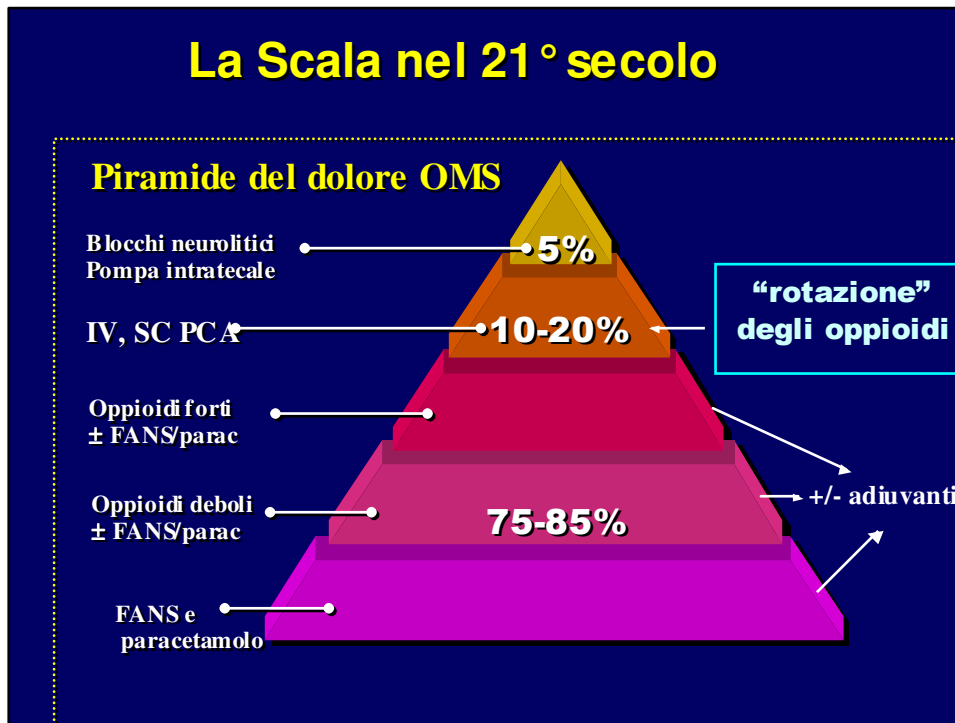
Earle, JCO, 2004

Implementing guidelines for cancer pain management: results of a randomized controlled clinical trial

(Du Pen SL, JCO, 1999)

- 81 pz, studio prospettico, longitudinale, randomizzato
- Pratica standard nella gestione del dolore verso l'utilizzo di un algoritmo di trattamento basato sulle Agency for Health Care Policy and Research (AHCPR) Guidelines for Cancer Pain Management
- Impatto su dolore, altri sintomi, qualità di vita
- Risultato significativo sul dolore: $p < .02$

La Scala nel 21° secolo



Randomized clinical trial of the effectiveness of a self-care intervention to improve cancer pain management

(Miaskowski C, JCO, 2004)

- **Programma psicoeducazionale individualizzato vs trattamento “standard”**
- **Impatto del trattamento individualizzato:**
riduzione significativa degli score del dolore rispetto al basale
(peggiore -27%, medio -32.5%, minore -28.4%; $p < .0001$)
(dati per standard: peggiore -1.2%, medio + 1.9%, minore +14.6%)
- **Terapia appropriata**
braccio sperimentale: 28.3% → 37.0% ($p = .008$);
braccio standard: 29.6% → 32.5%.

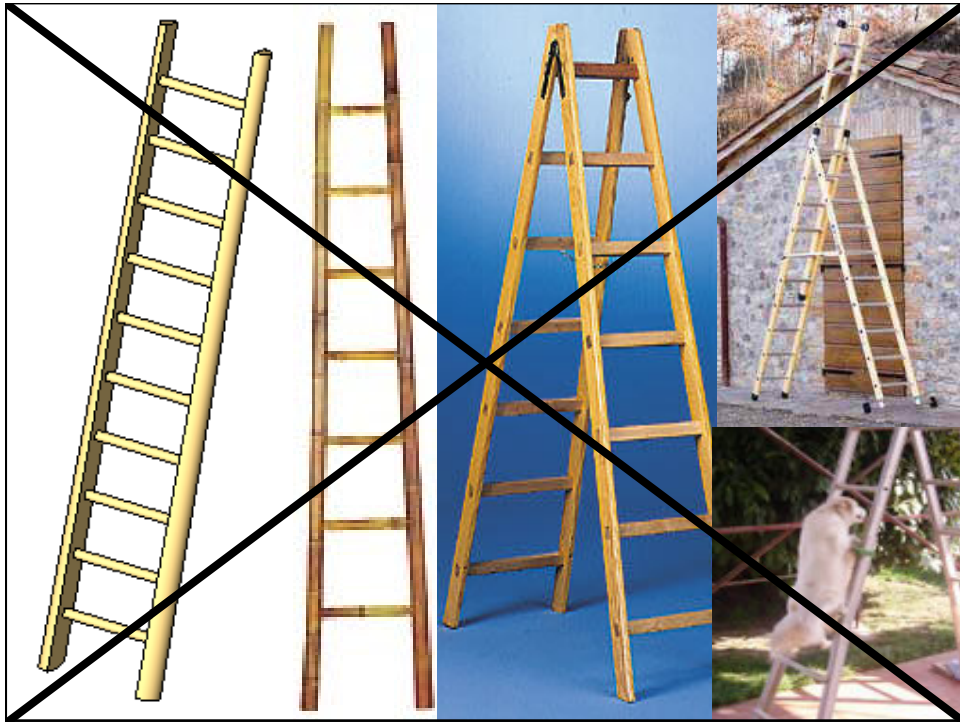
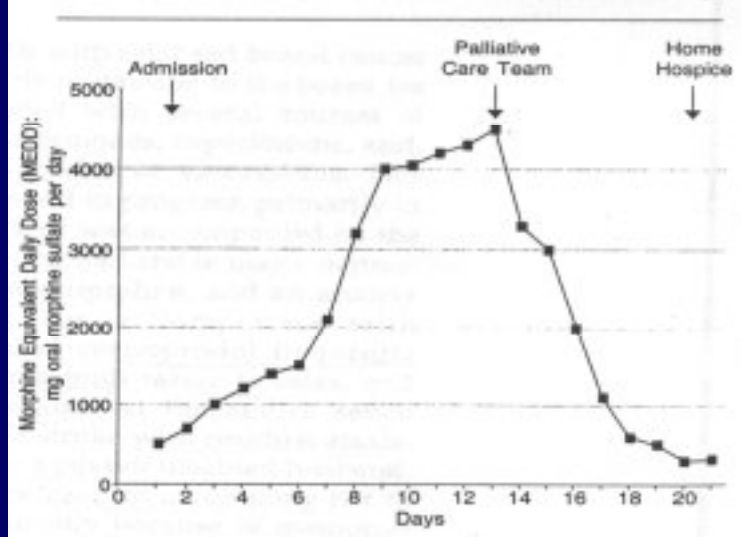
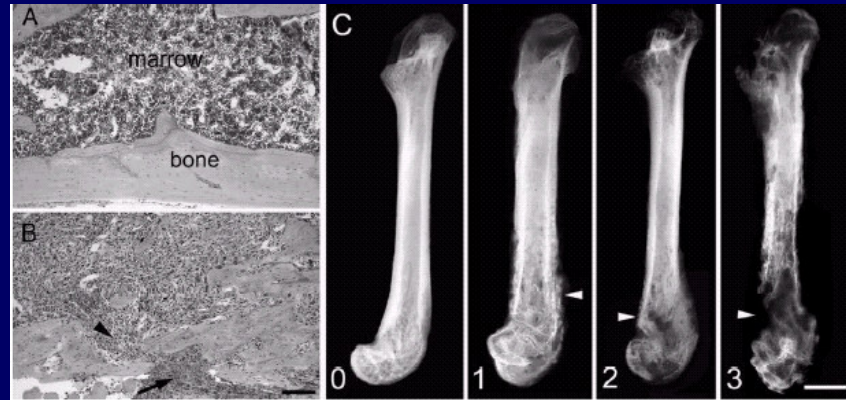


Figure 1 / MORPHINE EQUIVALENT DAILY DOSE (MEDD) CURVE OF CASE 1 (ADMISSION UNTIL DISCHARGE TO HOME HOSPICE)



Modello di dolore da cancro nel topo

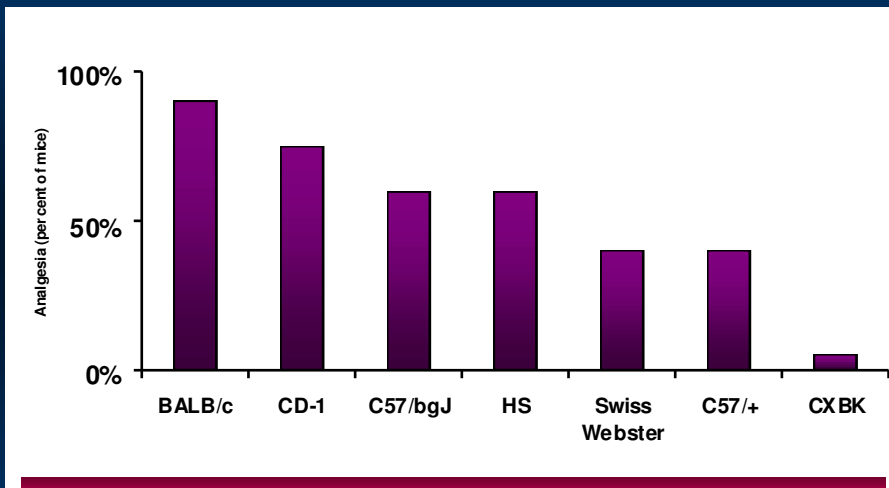


Schwei M, J Neurosci, 1999

Approccio etiopatogenetico al dolore osseo

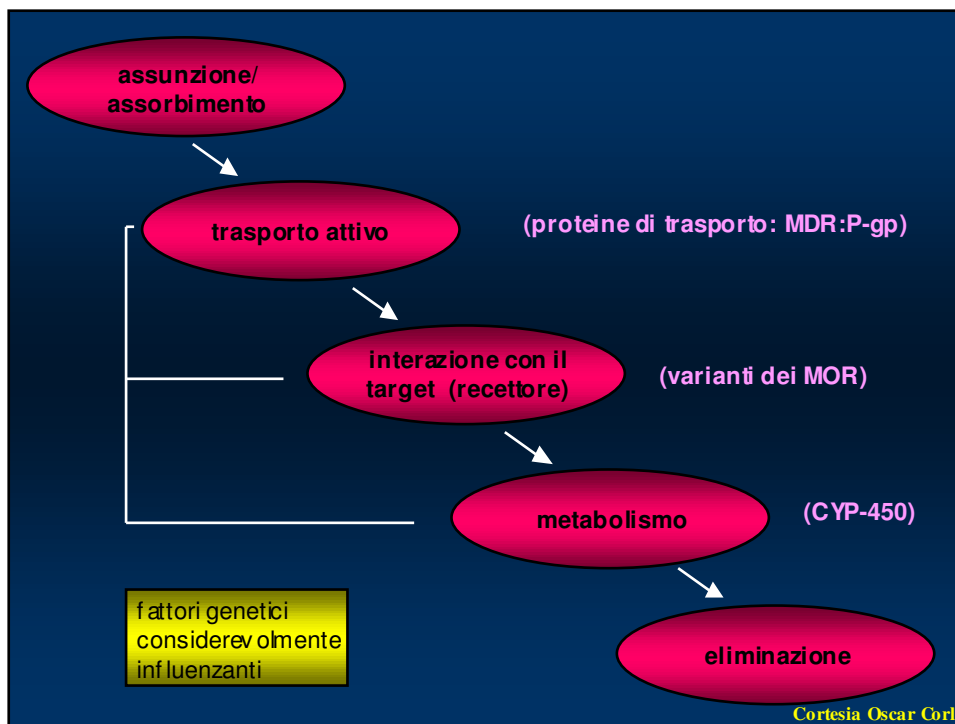
- Dolore pre-distruzione ossea da **fattori proiperalgesci**, quali prostaglandine ed endoteline: COX-inibitori ed antagonisti delle endoteline
- Proliferazione e ipertrofia **osteoclasti**: OPG e difosfonati
- **Danno terminazioni nervose**: gabapentin, pregabalin, artemina
- Cellule neoplastiche che riempiono del tutto lo spazio midollare con elevata apoptosi che produce **acidosi**: ASICs o TRPV-1
- Coinvolgimento del periostio e dolore associato al **movimento**: antagonisti dei canali regolati meccanicamente e/o dei recettori ATP

“OPIOID SENSITIVITY”



Differenti risposte alla stessa dose di morfina dopo stimolo doloroso (*tail-flick*) in diversi ceppi di topi.

(Heck, 1991), Cortesia Oscar Corli



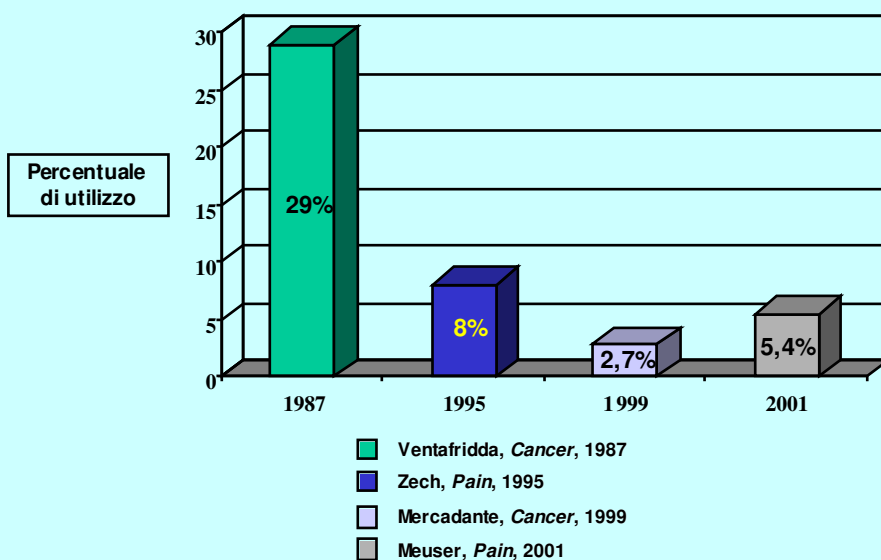
European Pharmacogenetics Opioid Study (EPOS)

- **Obiettivi farmacogenetici:** prevalenza mutazioni enzimi metabolismo ed effetti sulle concentrazioni sieriche, prevalenza mutazioni recettori oppioidi ed effetti sull'efficacia clinica, effetti del polimorfismo del gene MDR1 sull'efficacia clinica
- **Obiettivi farmacologici:** concentrazioni sieriche degli oppioidi rispetto a sesso, età, peso, Indice Massa Corporea, funzionalità renale, dose e via di somministrazione del farmaco e rispetto a risultati (efficacia/effetti collaterali)
- **Obiettivi clinici:** effetti collaterali dei diversi oppioidi, correlazione fra dolore e qualità di vita

Frequenza della rotazione degli oppioidi

Autore	Rivista	Anno	Pz	Pz con RO	%	RO
De Stoutz	JPSM	1995	191	80	42	111
Cherny	Cancer	1995	100	64 80 (farmaco e via)	64 80 (farmaco e via)	88 182 (farmaco e via)

Utilizzo di metodiche invasive nel sollievo del dolore in pazienti in cure palliative



Controversies in pharmacotherapy of pain management

(Davis M, Lancet Oncol, 2005)

- La morfina rimane ancora l'oppioide di prima scelta?
- Oppioidi diversi possono essere usati in combinazione?
- Quando va utilizzata la via spinale?
- Qual è la dose rescue appropriata?
- I Cox2 inibitori sono utili?
- Quali sono gli adiuvanti per il dolore neuropatico?
- C'è evidenza dell'efficacia dei bifosfonati?

Motivi per un ridotto controllo del dolore

- Barriere istituzionali
- Barriere di pazienti e familiari
- Barriere professionali
- Peculiarità patogenetica e genetica



