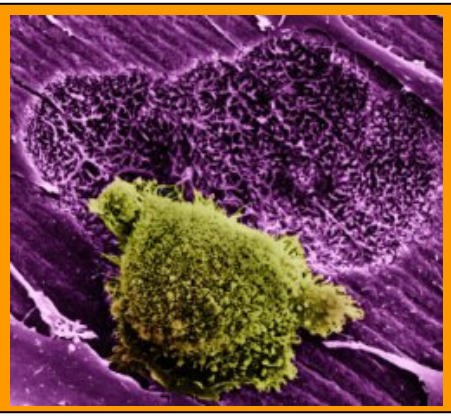
CELLULE DEL TESSUTO OSSEO:

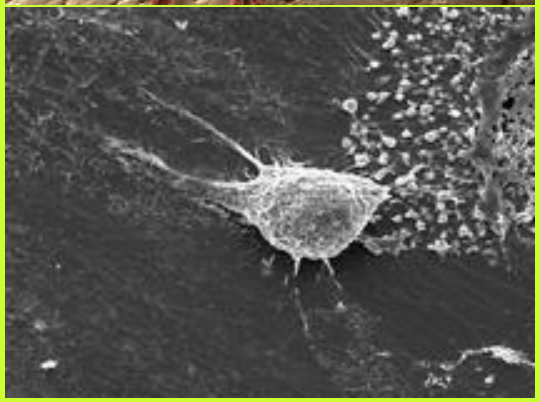


Osteoclasti

Originano da cellule ematopoietiche

Osteoblasti

Osteociti

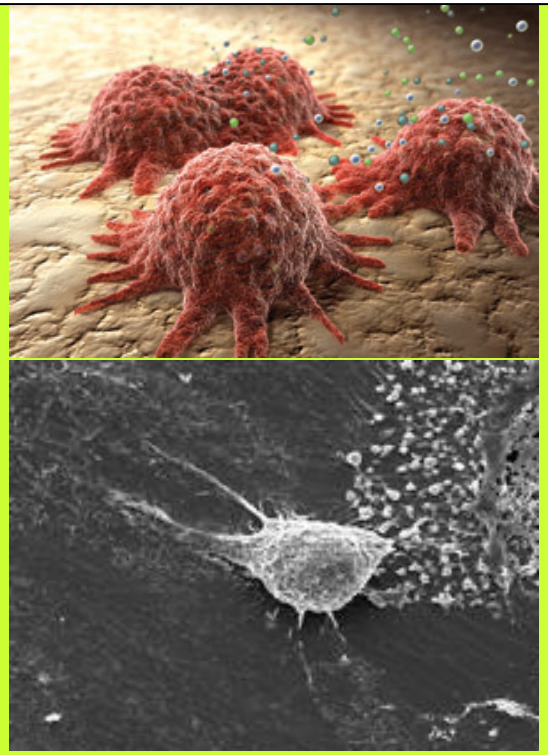


Originano da cellule mesenchimali

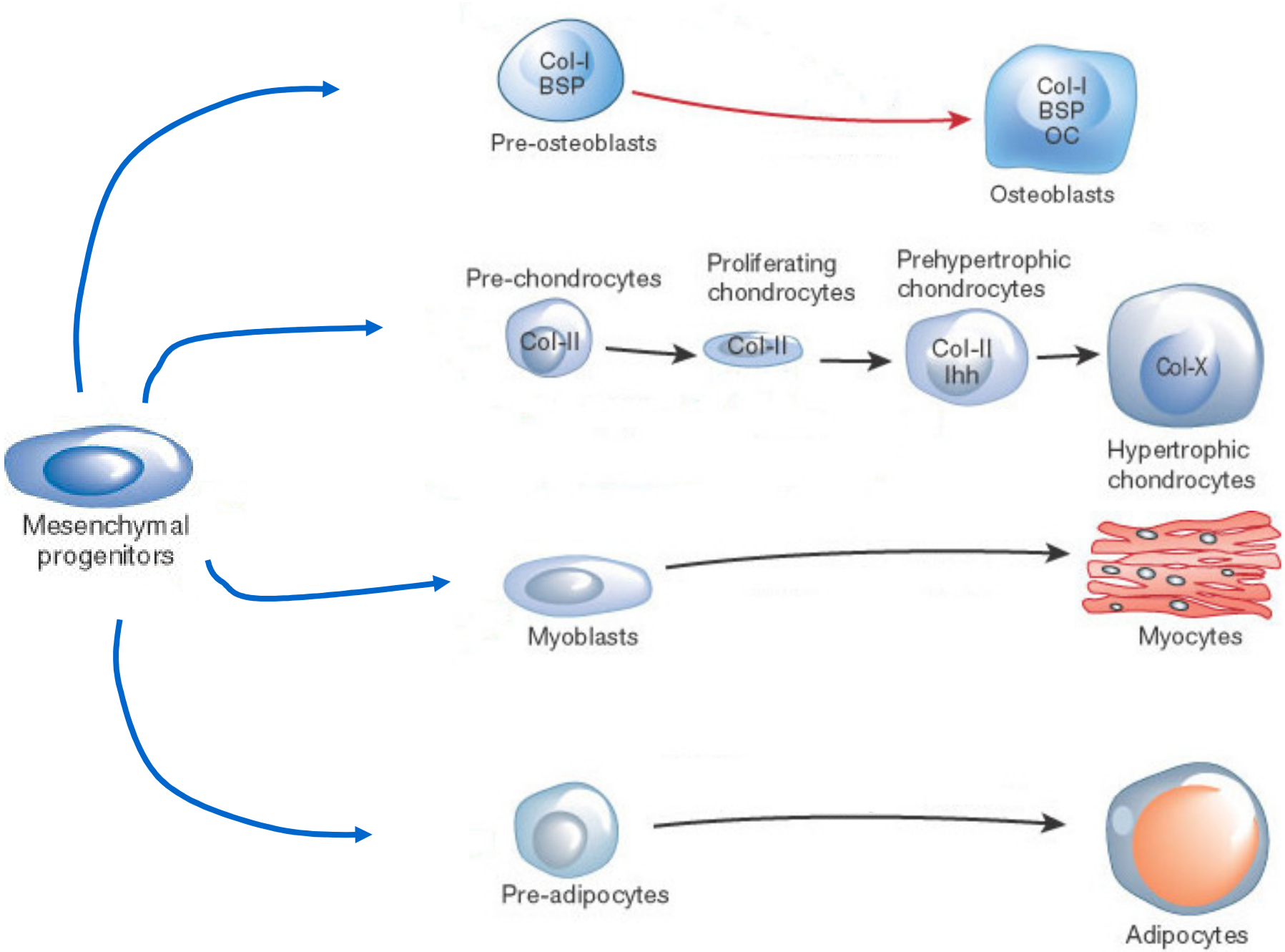
CELLULE DEL TESSUTO OSSEO:

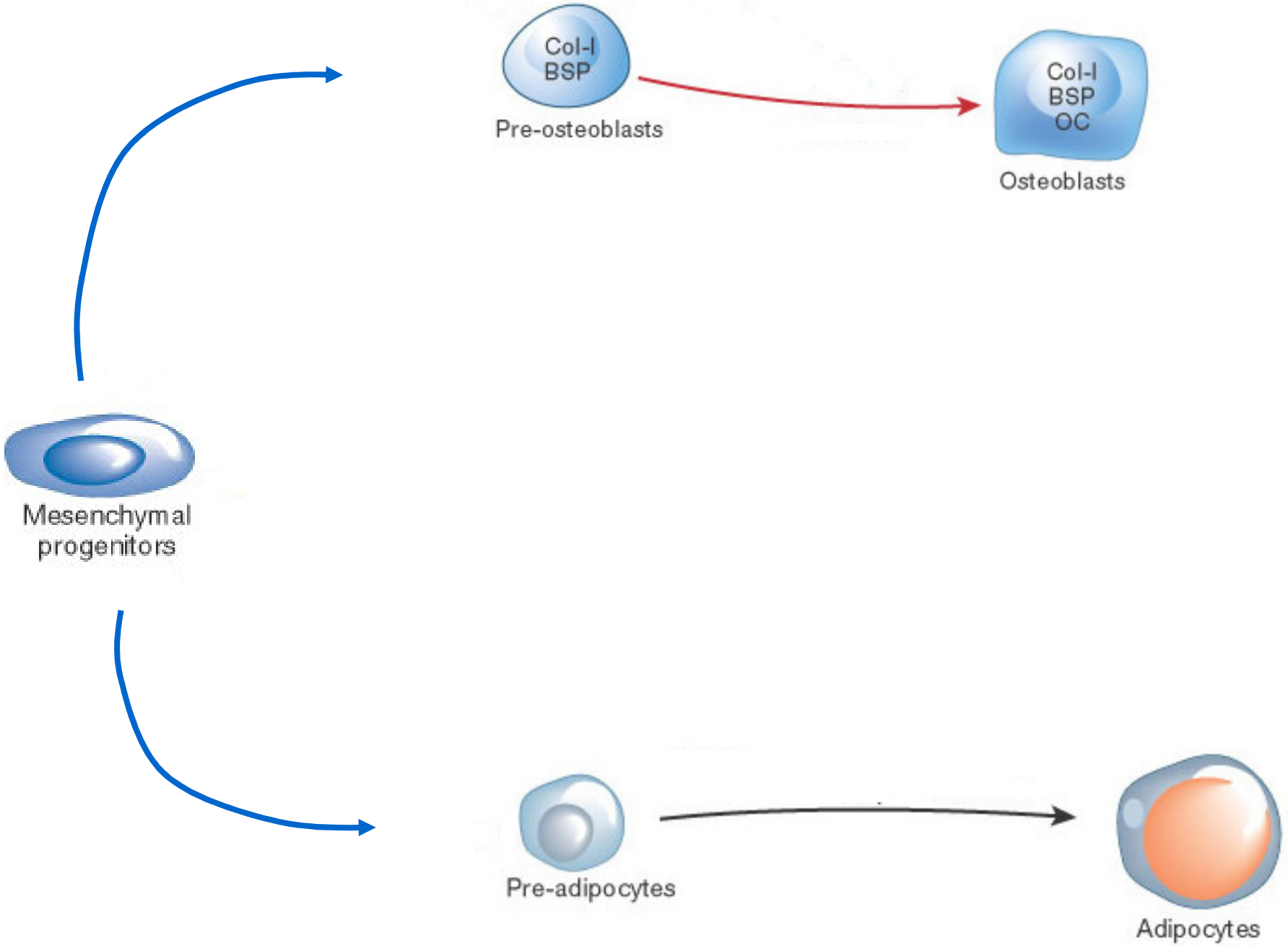
Osteoblasti

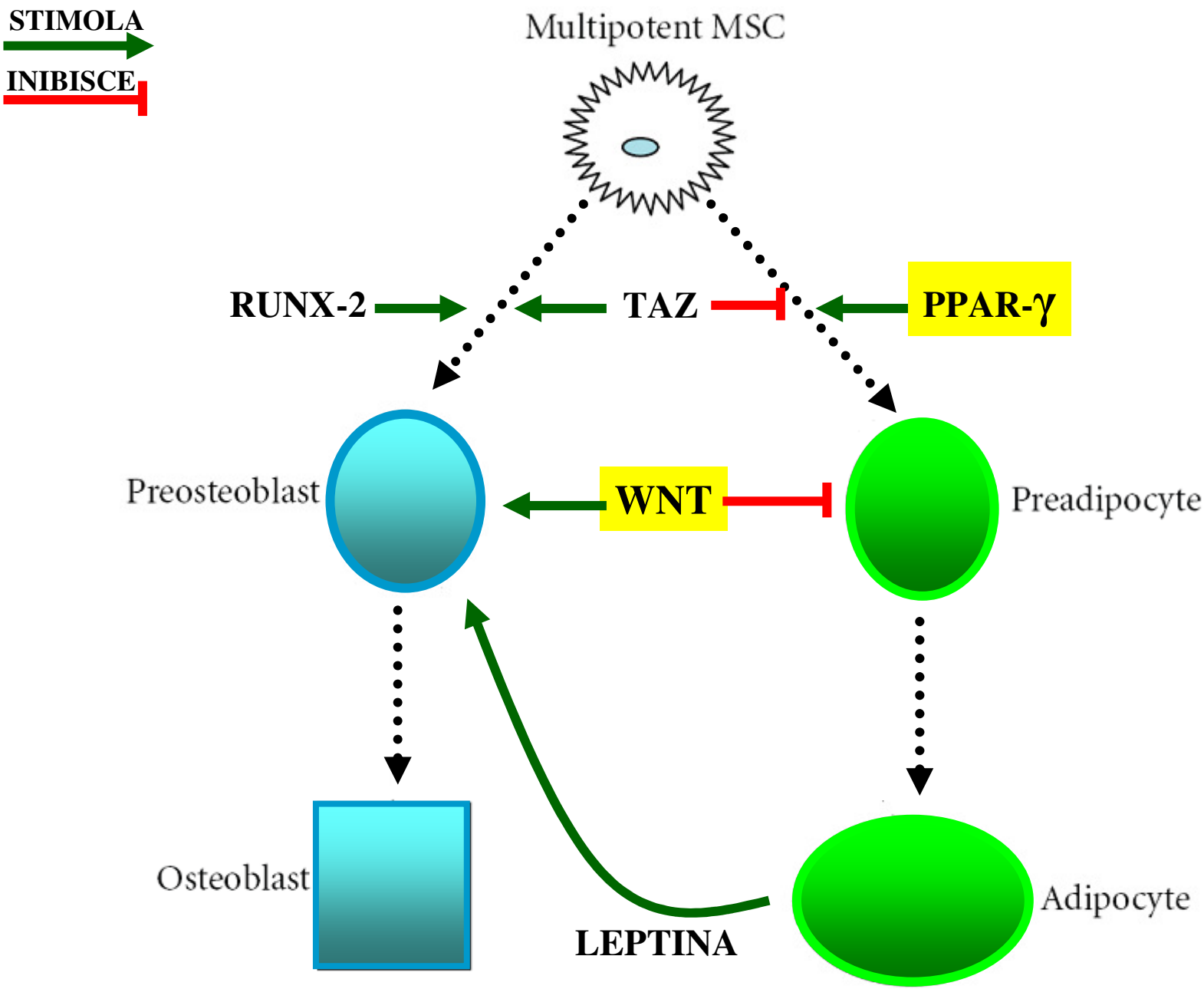
Osteociti

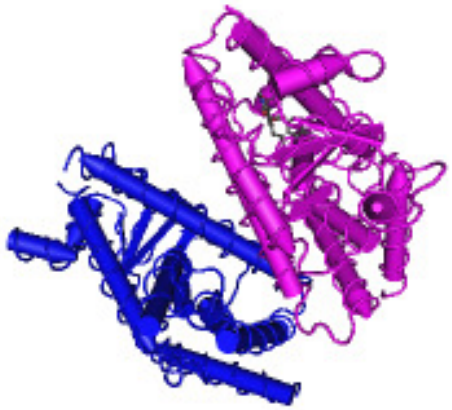


Originano da cellule mesenchimali


Col-I
BSP
Pre-osteoblasts
Col-I
BSP
OC
Osteoblasts
Pre-chondrocytes
Proliferating
chondrocytes
Prehypertrophic
chondrocytes
Col-II
Col-II
Col-II
Ihh
Col-X
Hypertrophic
chondrocytes
Mesenchymal
progenitors
Myoblasts
Myocytes
Pre-adipocytes
Adipocytes


Col-I
BSP
Pre-osteoblasts
Col-I
BSP
OC
Osteoblasts
Mesenchymal
progenitors
Pre-adipocytes
Adipocytes


STIMOLA
INIBISCE
Multipotent MSC
RUNX-2
TAZ
PPAR-γ
Preosteoblast
WNT
Preadipocyte
Osteoblast
LEPTINA
Adipocyte

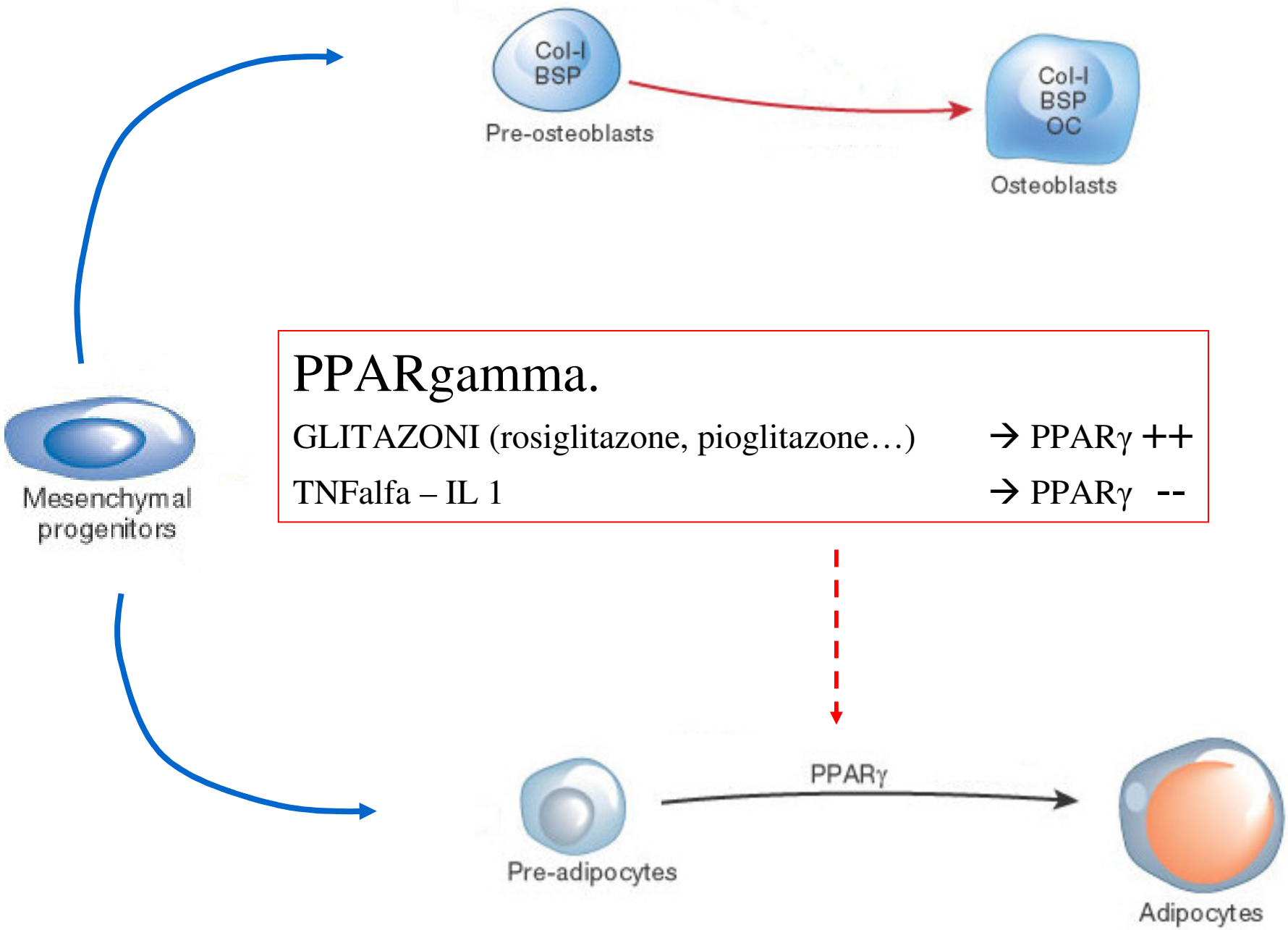


The Peroxisome Proliferator-Activated Receptor (PPAR)

PPAR — α, β/δ, γ **(con varianti 1, 2 e 3)**

PPARs

- famiglia di fattori nucleari di trascrizione (attivatori dei perossisomi) che fanno parte della superfamiglia dei recettori nucleari steroidei
-modulano l'espressione di svariati geni coinvolti nel metabolismo lipidico e del tessuto adiposo
- ubiquitari ma con distribuzione tessuto-specifica
- tutti identificati nelle cellule delle linee osteoblastica e osteoclastica.


Col-I
BSP
Pre-osteoblasts
Col-I
BSP
OC
Osteoblasts
Mesenchymal
progenitors
PPARgamma.
GLITAZONI (rosiglitazone, pioglitazone…) → PPARγ ++
TNFalfa – IL 1 → PPARγ --
PPARγ
Pre-adipocytes
Adipocytes

CMAJ • JANUARY 6, 2009 • 180(1)

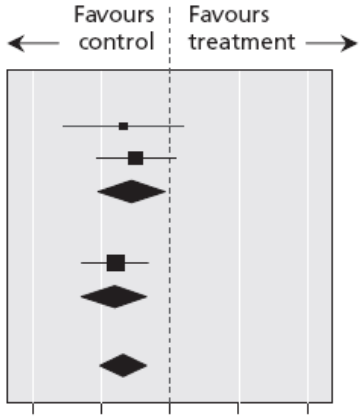
(IMPACT FACTOR 2007 = 7,1)

Long-term use of thiazolidinediones and fractures in type 2 diabetes: a meta-analysis

Yoon K. Loke MBBS MD, Sonal Singh MD MPH, Curt D. Furberg MD PhD

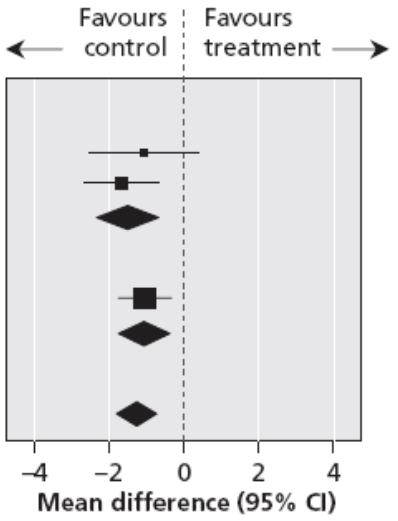
A. Lumbar spine

Study or subgroup	Treatment Mean % change (SD)	*n*	Control Mean % change (SD)	*n*	Mean difference (95% CI)
Randomized controlled trial					
Glintborg et al.[36]	−1.02 (2.66)	30	0.34 (2.78)	14	−1.36 (−3.10 to 0.38)
Grey et al.[35]	−1.2 (2.1)	25	−0.2 (2.1)	25	−1.00 (−2.16 to 0.16)
Subtotal		55		39	−1.11 (−2.08 to −0.14)
Observational study					
Yaturu et al.[37]	0.69 (2.4)	32	2.3 (2.9)	128	−1.61 (−2.58 to −0.64)
Subtotal		32		128	−1.61 (−2.58 to −0.64)
Overall		**87**		**167**	**−1.36 (−2.05 to −0.67)**



B. Hip

Study or subgroup	Treatment Mean % change (SD)	*n*	Control Mean % change (SD)	*n*	Mean difference (95% CI)
Randomized controlled trial					
Glintborg et al.[36]	−0.41 (2.03)	30	0.67 (2.46)	14	−1.08 (−2.56 to 0.40)
Grey et al.[35]	−1.9 (2)	25	−0.2 (1.6)	25	−1.70 (−2.70 to −0.70)
Subtotal		55		39	−1.50 (−2.34 to −0.67)
Observational study					
Yaturu et al.[37]	−1.19 (1.8)	32	−0.14 (1.9)	128	−1.05 (−1.76 to −0.35)
Subtotal		32		128	−1.05 (−1.76 to −0.35)
Overall		87		167	−1.24 (−1.78 to −0.70)



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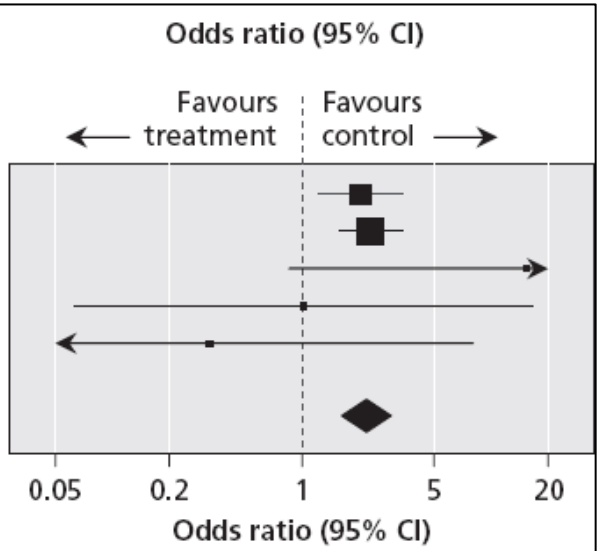
Yoon K. Loke MBBS MD, Sonal Singh MD MPH, Curt D. Furberg MD PhD

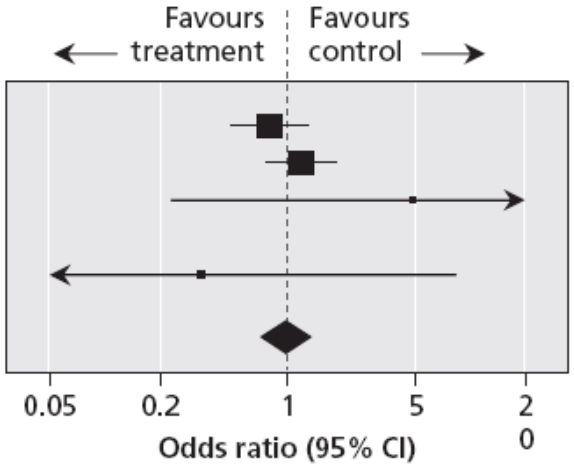
B. Fractures in women

Study	No. of fractures: Thiazolidinedione	No. of fractures: Control	Odds ratio (95% CI)
Dormandy et al.[24]	44/870	23/905	2.04 (1.22–3.41)
Kahn et al.[23]	60/645	51/1195	2.30 (1.56–3.39)
Nissen et al.[30]	6/84	0/93	15.48 (0.86–279.18)
Seufert et al. (a)[32]	1/156	1/159	1.02 (0.06–16.44)
Seufert et al. (b)[32]	0/148	1/145	0.32 (0.01–8.03)
Overall	**111/1903**	**76/2497**	**2.23 (1.65–3.01)**



C. Fractures in men

Study	No. of fractures: Thiazolidinedione	No. of fractures: Control	Odds ratio (95% CI)
Dormandy et al.[24]	30/1735	37/1728	0.80 (0.49–1.31)
Kahn et al.[23]	32/811	57/1700	1.18 (0.76–1.84)
Nissen et al.[30]	2/186	0/180	4.89 (0.23–102.60)
Seufert et al. (a)[32]	0/161	0/154	Not estimable
Seufert et al. (b)[32]	0/171	1/175	0.34 (0.01–8.38)
Overall	**64/3064**	**95/3937**	**1.00 (0.73–1.39)**



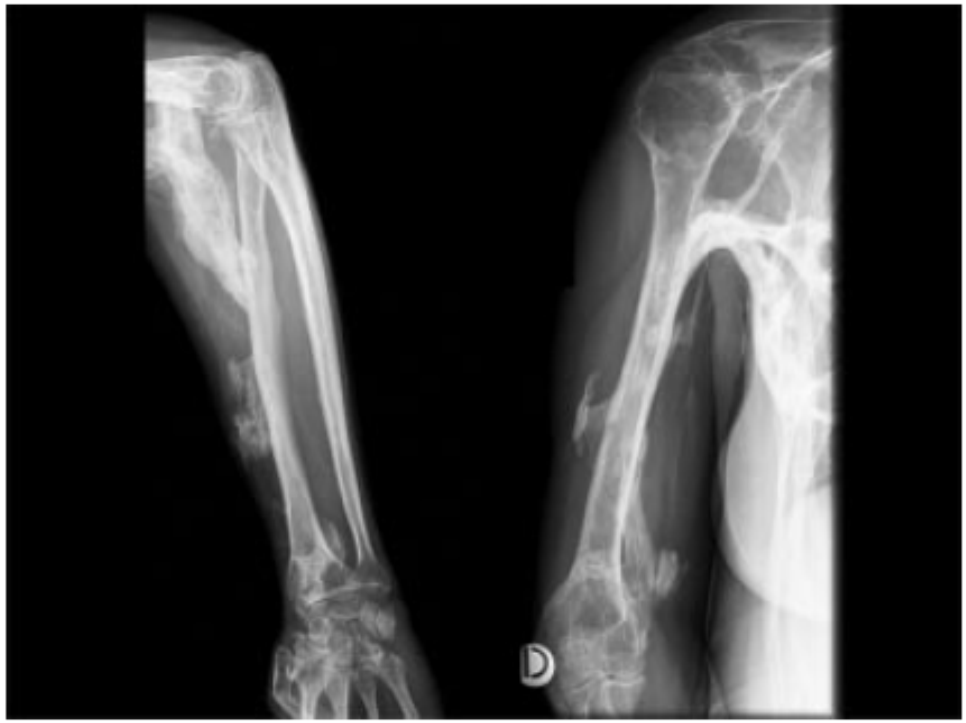
CASE REPORT

JBMR

Rosiglitazone Therapy Is Associated with Major Clinical Improvements in a Patient with Fibrodysplasia Ossificans Progressiva

Davide Gatti, Ombretta Viapiana, Maurizio Rossini, and Adami Silvano

University of Verona, Rheumatology Unit, Valeggio, Verona, Italy



LA STAMPA.it ESTERI

24/9/2010 (12:52) - ALLARME PER I PAZIENTI

Farmaco per diabetici ritirato dall'Ue Sotto accusa l'Avandia: rischio ictus

Aumenta la probabilità di malattie cardiovascolari L'Ema: "Problemi anche per Avandamet e Avaglim. Si chieda al proprio medico prima di sospendere le cure"

ROMA

L'antidiabetico Avandia (rosiglitazone), prodotto dalla britannica GlaxoSmithKline, sarà ritirato dal mercato europeo nei prossimi mesi a causa di un aumento del rischio cardiovascolare. L'ente regolatorio europeo Ema ha deciso che i medicinali a base di rosiglitazone dovranno «smettere di essere disponibile in

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 14, 2007 VOL. 356 NO. 24

Effect of Rosiglitazone on the Risk of Myocardial Infarction and Death from Cardiovascular Causes

Steven E. Nissen, M.D., and Kathy Wolski, M.P.H.

> 6 mesi di terapia

Table 4. Rates of Myocardial Infarction and Death from Cardiovascular Causes.

Study	Rosiglitazone Group	Control Group	Odds Ratio (95% CI)	P Value
	no. of events/total no. (%)			
Myocardial infarction				
Small trials combined	44/10,285 (0.43)	22/6106 (0.36)	1.45 (0.88–2.39)	0.15
DREAM	15/2,635 (0.57)	9/2634 (0.34)	1.65 (0.74–3.68)	0.22
ADOPT	27/1,456 (1.85)	41/2895 (1.42)	1.33 (0.80–2.21)	0.27
Overall			1.43 (1.03–1.98)	0.03
Death from cardiovascular causes				
Small trials combined	25/6,845 (0.36)	7/3980 (0.18)	2.40 (1.17–4.91)	0.02
DREAM	12/2,635 (0.46)	10/2634 (0.38)	1.20 (0.52–2.78)	0.67
ADOPT	2/1,456 (0.14)	5/2895 (0.17)	0.80 (0.17–3.86)	0.78
Overall			1.64 (0.98–2.74)	0.06

Io gioco 1 schedina

Io ne gioco 2

Rischio di vincere
2,0= +100%

1 su 622.614.630

2 su 622.614.630

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DREAM	15/2,635 (0.57)	9/2634 (0.34)	1.65 (0.74–3.68)	0.22
ADOPT	27/1,456 (1.85)	41/2895 (1.42)	1.33 (0.80–2.21)	0.27
Overall	**86/14.376 (0,62%)**	**72/11.635 (0,60%)**	1.43 (1.03–1.98)	0.03
Death from cardiovascular causes	**2 su 10.000**			
Small trials combined	25/6,845 (0.36)	7/3980 (0.18)	2.40 (1.17–4.91)	0.02
DREAM	12/2,635 (0.46)	10/2634 (0.38)	1.20 (0.52–2.78)	0.67
ADOPT	2/1,456 (0.14)	5/2895 (0.17)	0.80 (0.17–3.86)	0.78
Overall	**39/10.936 (0,36%)**	**23/9.509 (0,24 %)**	1.64 (0.98–2.74)	0.06

1 su 1.000

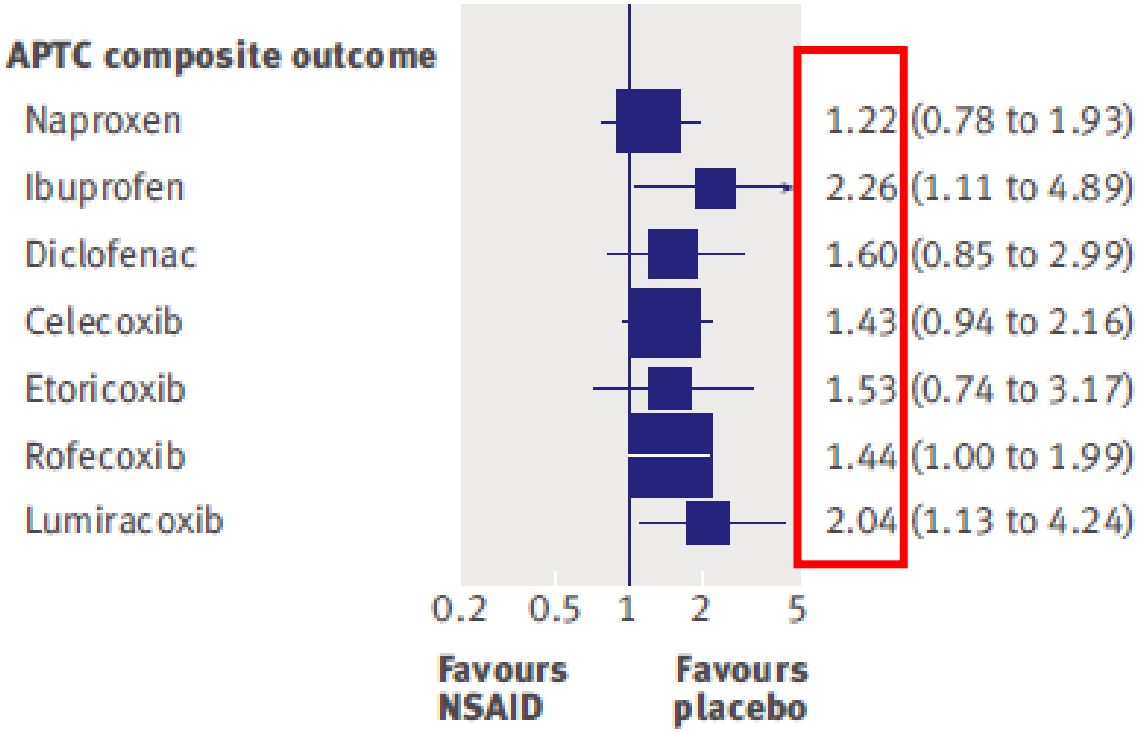
BMJ

Cite this as: *BMJ* 2011;342:c7086

RESEARCH

Cardiovascular safety of non-steroidal anti-inflammatory drugs: network meta-analysis

Sven Trelle, senior research fellow,[1,2] Stephan Reichenbach, senior research fellow,[1,4] Simon Wandel, research fellow,[1] Pius Hildebrand, clinical reviewer,[3] Beatrice Tschannen, research fellow,[1] Peter M Villiger, head of department and professor of rheumatology,[4] Matthias Egger, head of department and professor of epidemiology and public health,[1] Peter Jüni, head of division and professor of clinical epidemiology[1,2]



Agenzia Italiana del Farmaco

AIFA

N. RSC/120148/P

Risposta al Foglio del

N.

Roma, 15 ottobre 2010

Prof. Silvano Adami e Dott. Davide Gatti
S.S.O. Reumatologia
Azienda Ospedaliera Universitaria integrata
P.le Stefani, 1
37126 Verona

pc Comitato etico
Azienda Ospedaliera Universitaria integrata
P.le Stefani, 1
37126 Verona

pc Direzione Generale
AIFA
via del Tritone, 181
00187 Roma

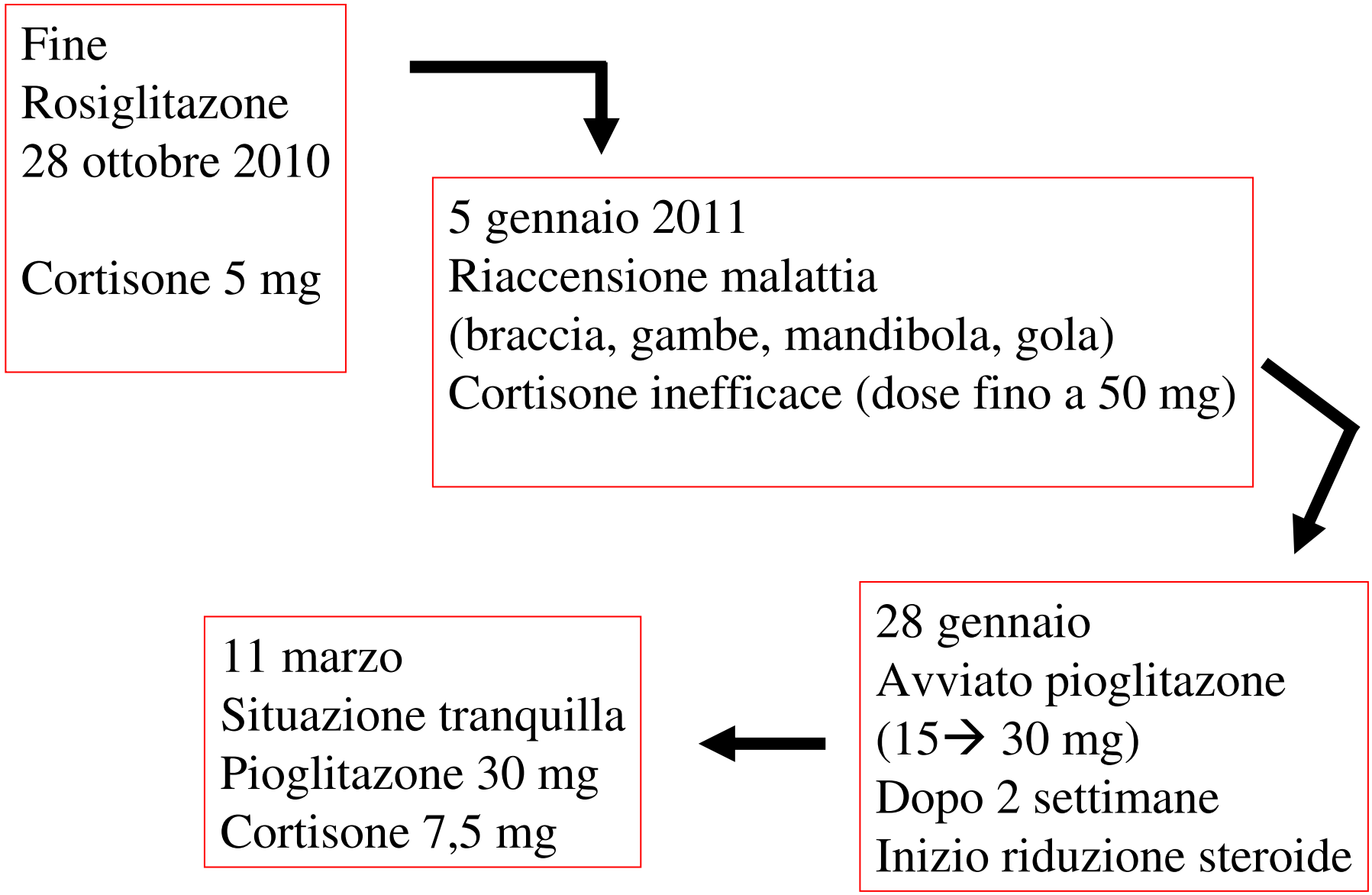
Dott. F. Ferrazin – Farmacovigilanza
Dott. A.R. Marra – Valut. ed Autorizz.

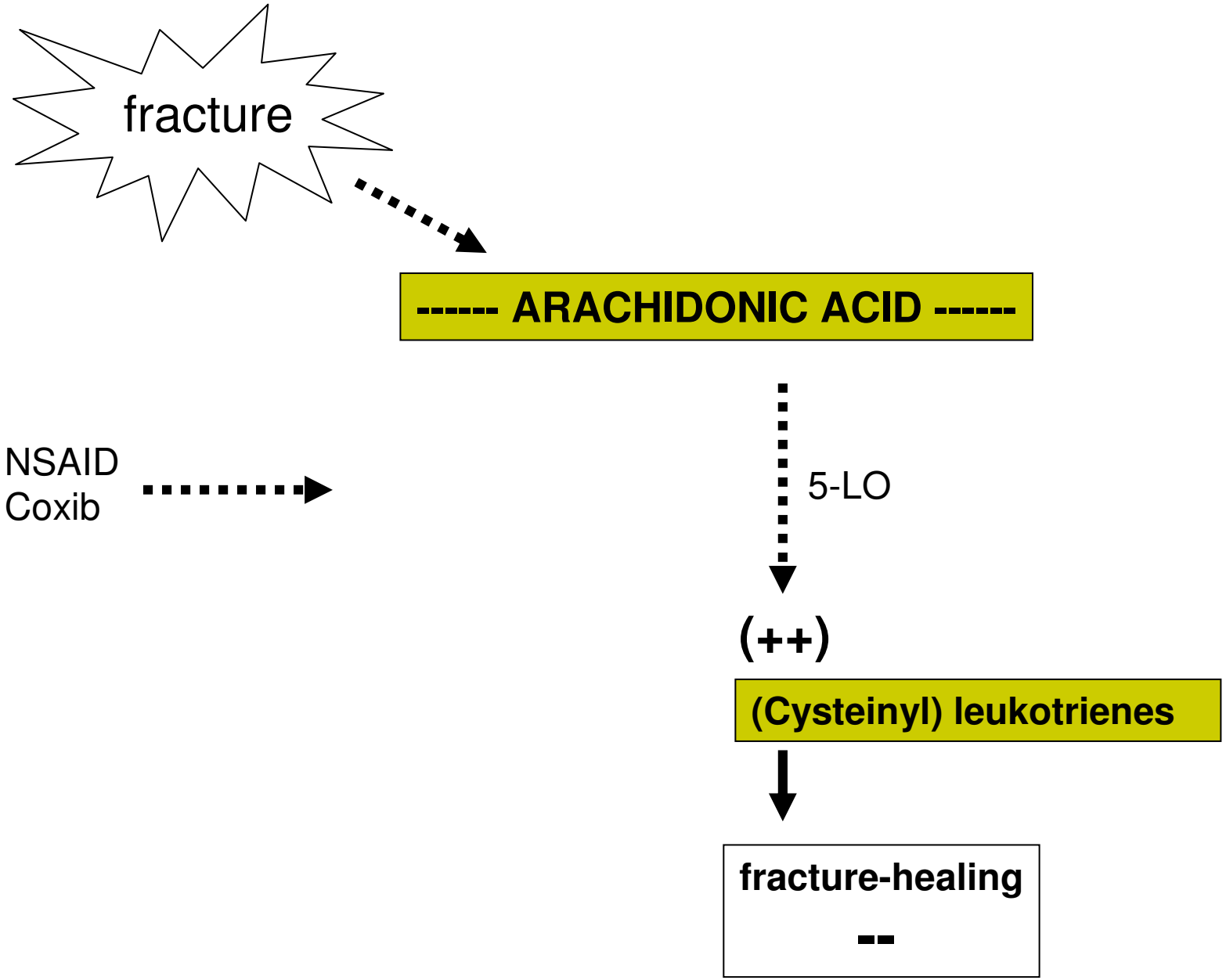
OGGETTO: ritiro dal mercato del farmaco ROSIGLITAZONE

In riferimento alla Vs nota del 29.09.10 di pari oggetto, data la gravità e la rarità della patologia (fibrodisplasia ossea progressiva) e non avendo sollevato obiezioni gli altri Uffici competenti dell'AIFA, *nulla osta* alla presentazione della *Clinical Trial Application* al Comitato etico / Autorità competente e alla successiva fornitura del rosiglitazone da parte della casa produttrice.
Si suggerisce di valutare l'eventuale utilizzo del pioglitazone.

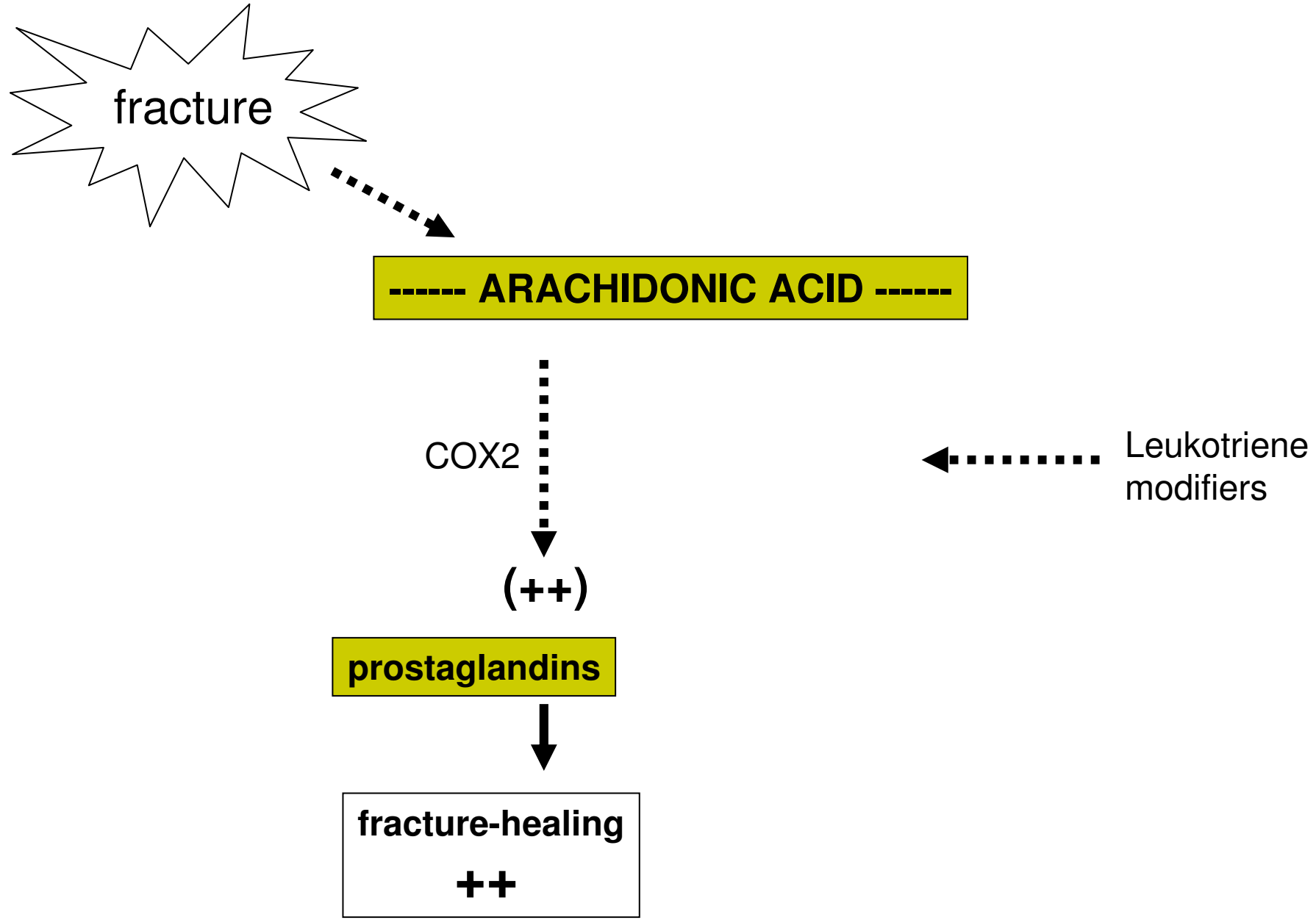
Direttore Ricerca e Sperimentazione Clinica
Dott. Carlo Tomino

Agenzia Italiana del Farmaco - Sperimentazione e Ricerca
Via della Sierra Nevada, 60 – 00144 Roma – tel. 0659784303 – fax. 0659784110 – e-mail: sperimentazione.clinica@sanita.it - www.agenziafarmaco.it


Fine
Rosiglitazone
28 ottobre 2010
Cortisone 5 mg
5 gennaio 2011
Riaccensione malattia
(braccia, gambe, mandibola, gola)
Cortisone inefficace (dose fino a 50 mg)
28 gennaio
Avviato pioglitazone
(15→ 30 mg)
Dopo 2 settimane
Inizio riduzione steroide
11 marzo
Situazione tranquilla
Pioglitazone 30 mg
Cortisone 7,5 mg



Gatti et al 2011 in press



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