

Fotoafèresis extracorpòria a la MECR agut



JORDI LÓPEZ PARDO
MERITXELL ESTRADA
DRA. ALBA BOSCH



HOSPITAL DE LA
SANTA CREU I
SANT PAU

UNIVERSITAT AUTÒNOMA DE BARCELONA



Parc Taulí Sabadell
Hospital Universitari

CORPORACIÓ SANITÀRIA
PARC TAULÍ



BANC DE SANG
I TEIXITS

Cas Clínic

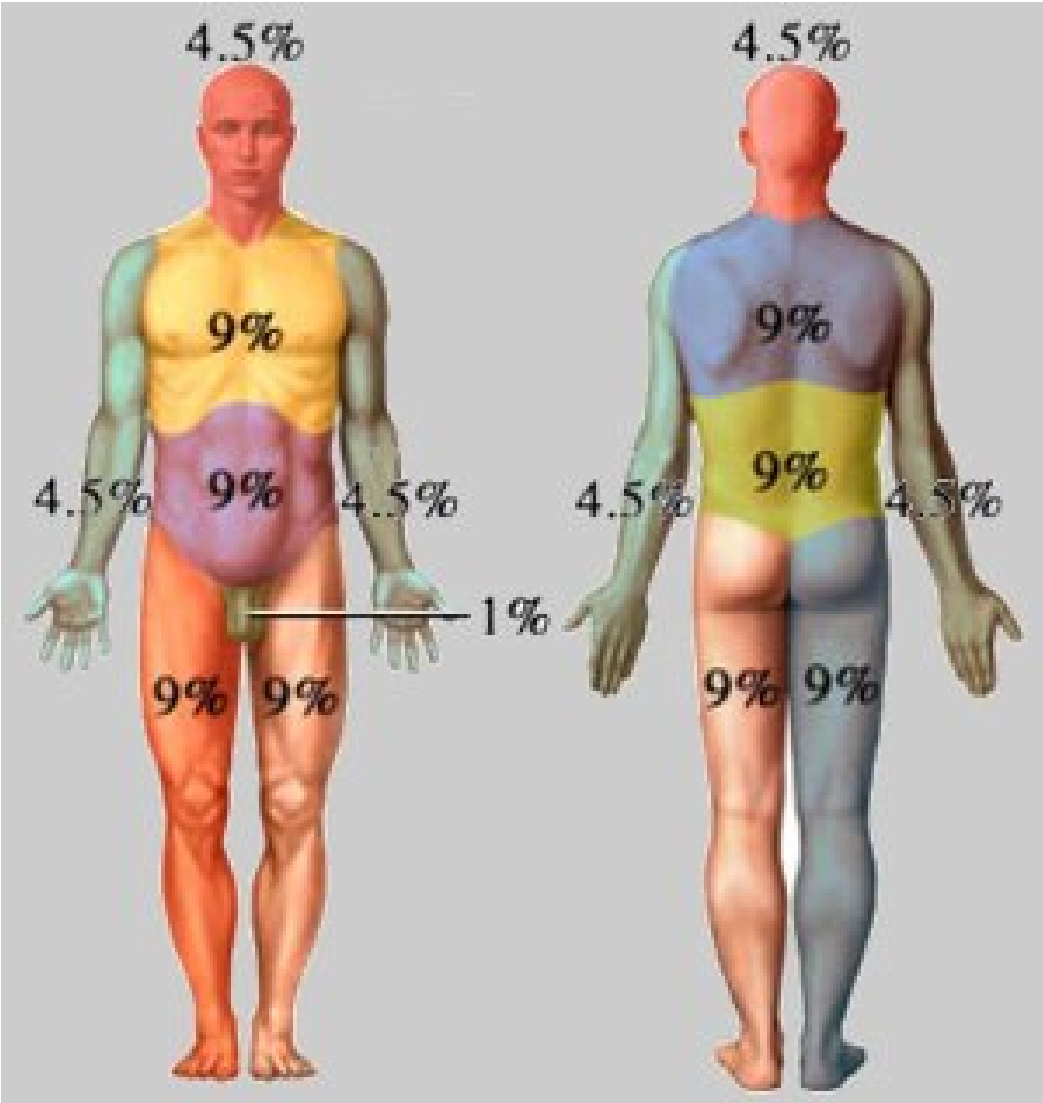
- Home de 62 anys
- No al·lèrgies medicamentoses conegudes
- No HTA, DM ni DLP
- Ex fumador des de juny 2015
- Historia hematològica
 - Gener 2014: Bicitopenia
 - AREB-1 (8% blasts) Ctg 46XY IPSS intermig-1
 - TTO:
 - EPO sense resposta.
 - Aza 75mg/m² x5d x5 cicles sense resposta.

AloTIR

- Alotransplantament d'intensitat reduïda de donant no emparentat HLA 10/10
- Acondicionat amb Fludarabina i Busulfan
- Profilaxis MECR Sirolimus-Tacrolimus
- Dia 0 25/11/2015: $5,361 \times 10^8/\text{Kg}$ CN, $6,019 \times 10^6/\text{Kg}$ CD34+ i $1,736 \times 10^8/\text{Kg}$ CD3+
- Recuperació granulocitària: 12/12/2015
- Recuperació plaquetar: 07/12/2015

- Ingrés dia +54
 - MECR gastrointestinal grau II
 - Metriprednisolona 2mg/Kg/24h
 - Reactivació CMV
 - Ganciclovir à Foscarnet
 - Quimerisme mixt
 - 29.12.15 Donant: 100% granulòcits 83% limfòcits.
 - 24.02.16 Donant: 100% granulòcits 35% limfòcits.
 - Microangiopatia trombòtica
 - Retirada d'immunosupressió

- Dia +121: Rash cutani pruriginós
 - Cara y tronc
 - TTO: AT 0,1% + Prednisona 1 mg/Kg/24h
- Dia +123: Lesions maculo-papulars amb formació de vesícules
 - Extensió a extremitats
 - MERC cutani grau III à IV
 - Metilprednisolona 2 mg/Kg/24h
 - AT 0,1%
 - Linitur + silvederma / 12 hores
 - Sirolimus
 - Sense resposta a 72 hores de tractament corticoide.





Fotoafèresis extracorpòria

– 30/03/16

– 31/03/16

– 06/04/16

– 07/04/16

– 14/04/16

– 15/04/16

– 21/04/16

– 22/04/16

– 28/04/16

– 29/04/16

– 11/05/16

– 12/05/16

– 26/05/16

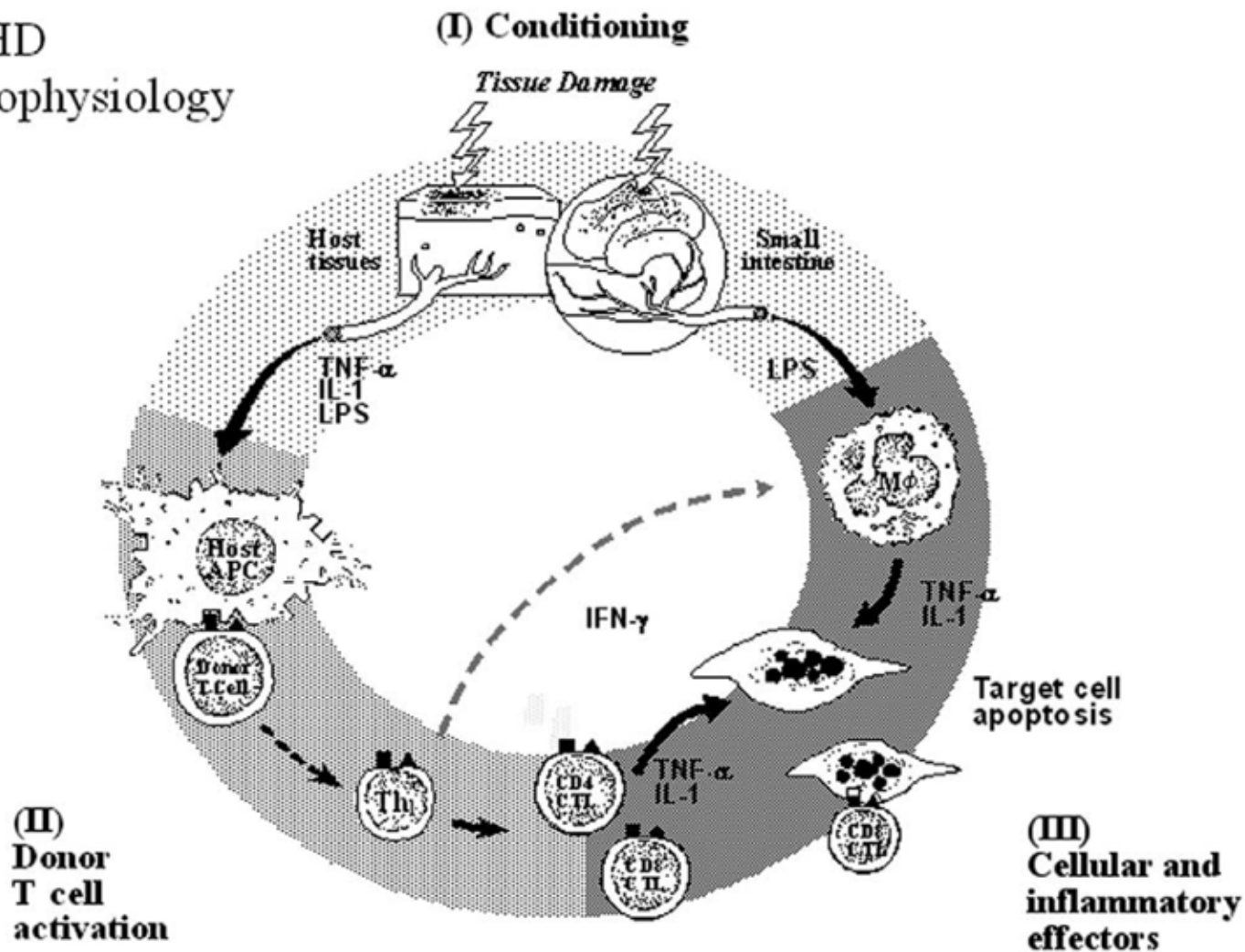
– 27/05/16

– 09/06/16

– 10/06/16

MERC agut

GVHD
Pathophysiology



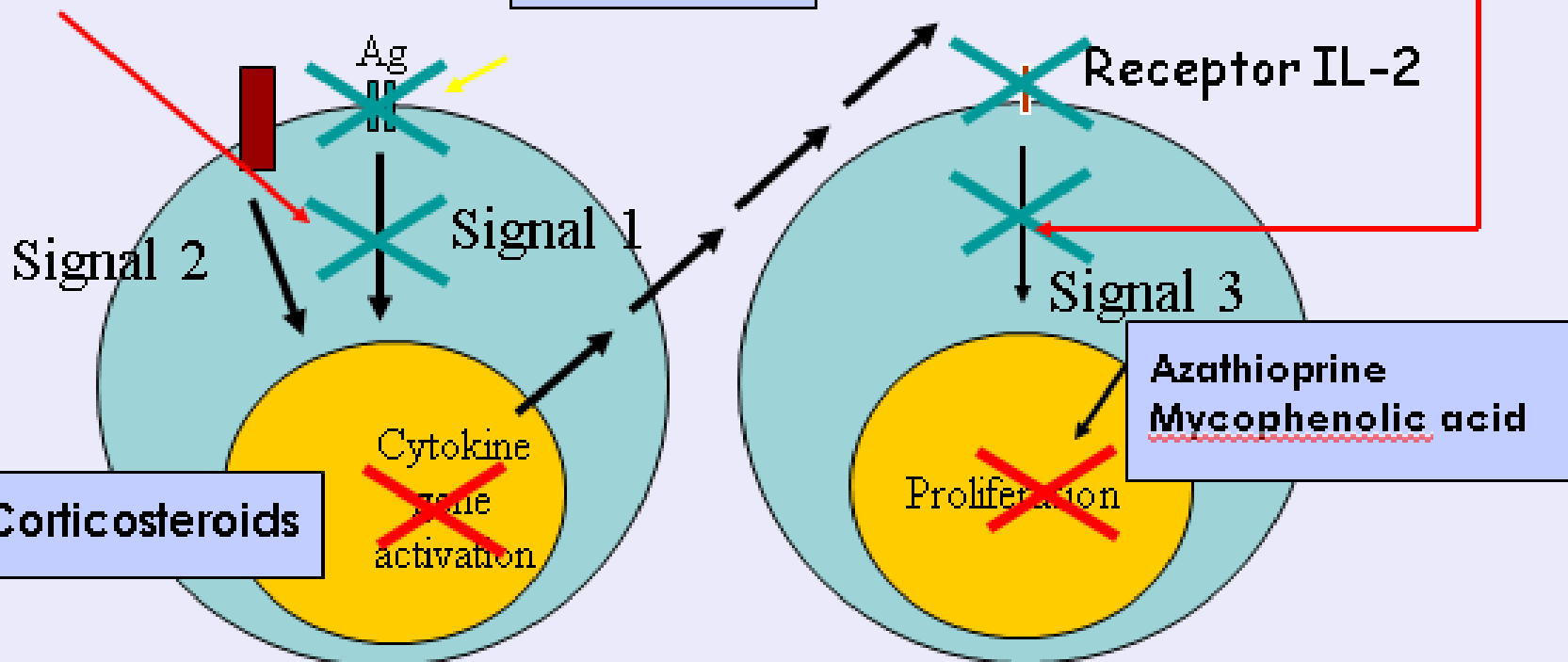
IMMUNOSUPPRESSIÓ

Calcineurin inhibitors
cyclosporin
tacrolimus

ATG

Anti-TNF receptor Abs
infliximab
etanercept

Sirolimus
Everolimus



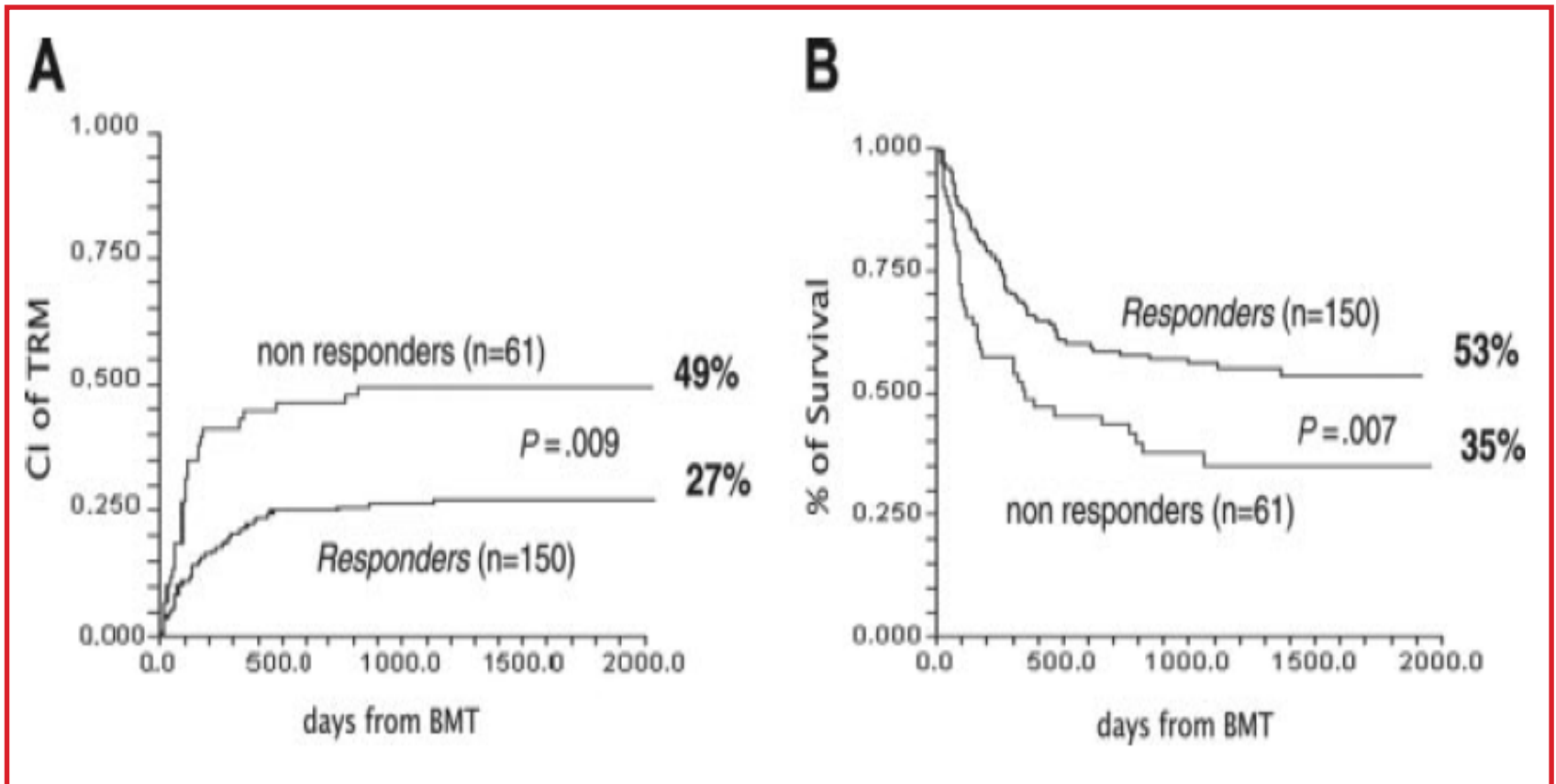
Corticosteroids

Cytokine
gene
activation

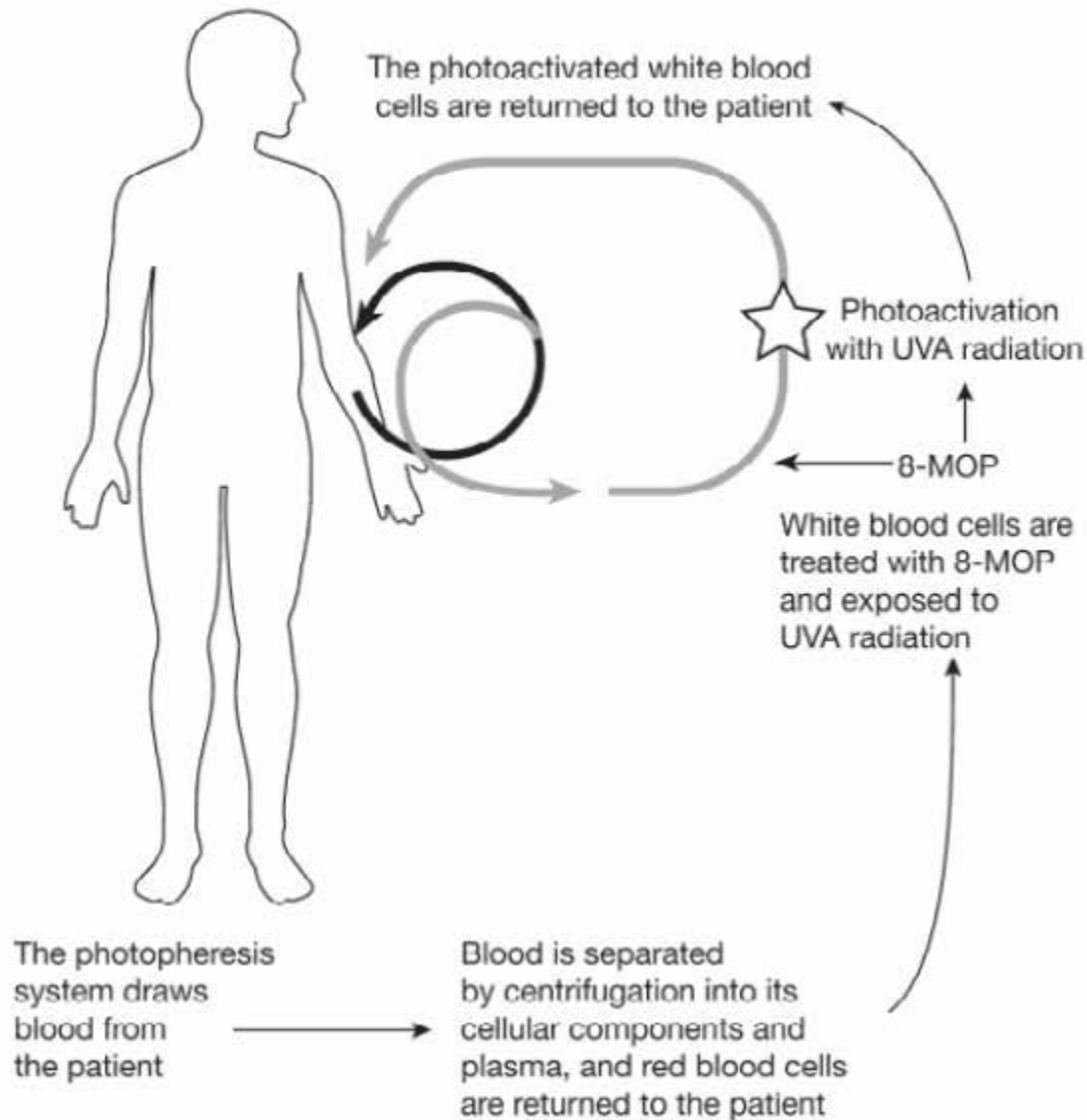
Proliferation

Azathioprine
Mycophenolic acid

Corticoides: la linea Maginot



Fotoafèresi Extracorpòrea



Fotoafèresi Extracorpòrea

- } Leucoafèresi
- } Fotosensibilització i Fotoactivació
 - 8-Methoxypsoralen (8-MOP)
- } Reinfusió

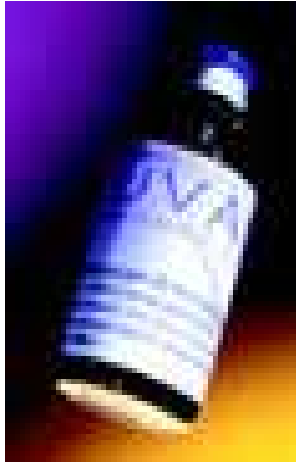
Sistema Online

Sistema off -line

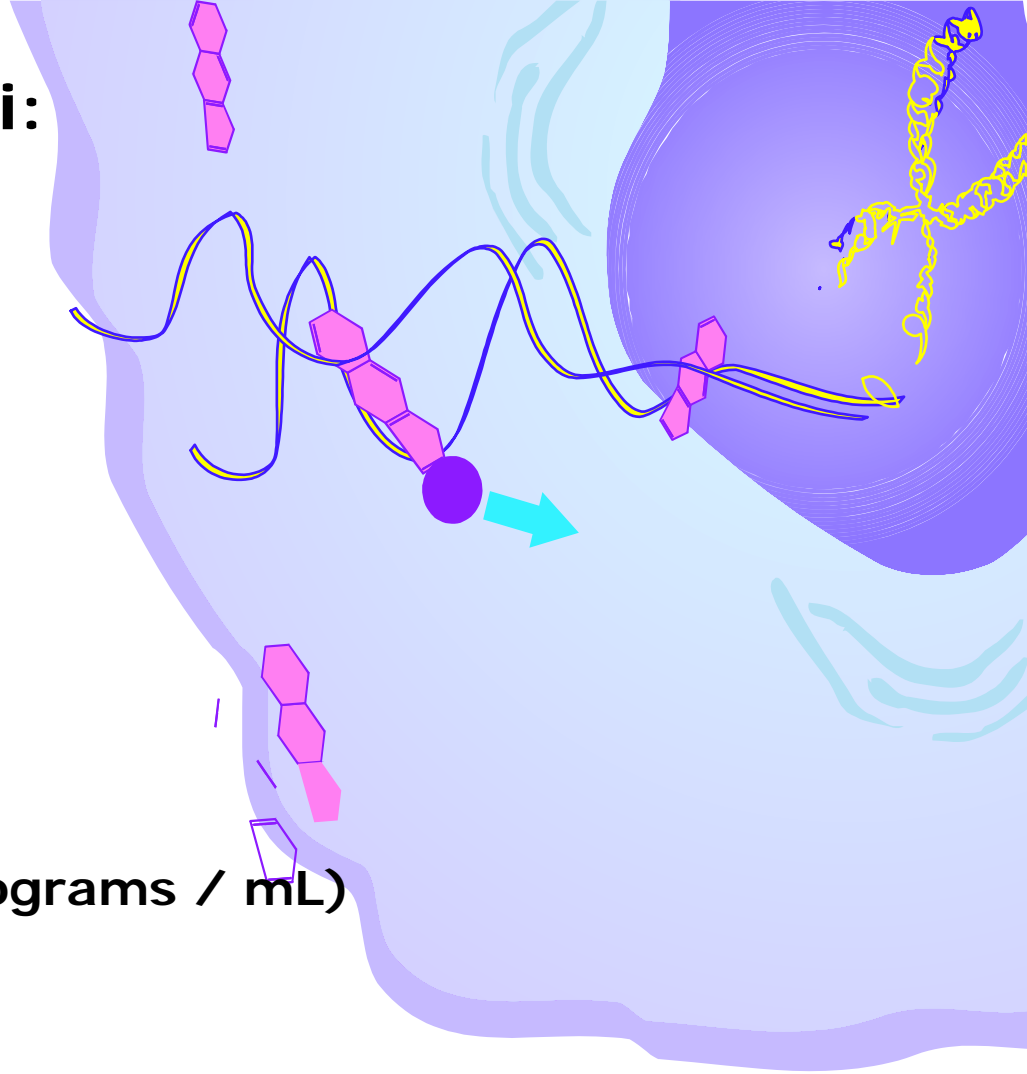
Sistema off -line



Psoralè en Fotofèresi: Mecanisme d'acció



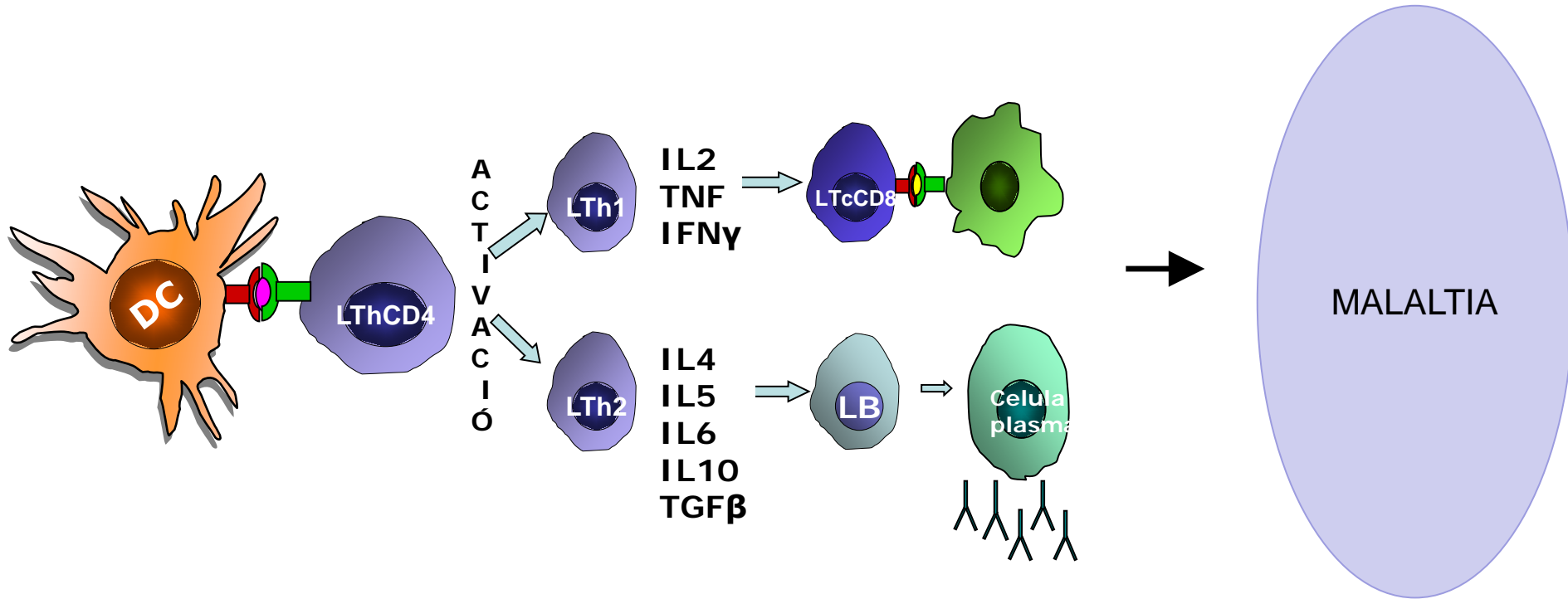
Methoxsalen (20 micrograms / mL)
(injectable psoralen)



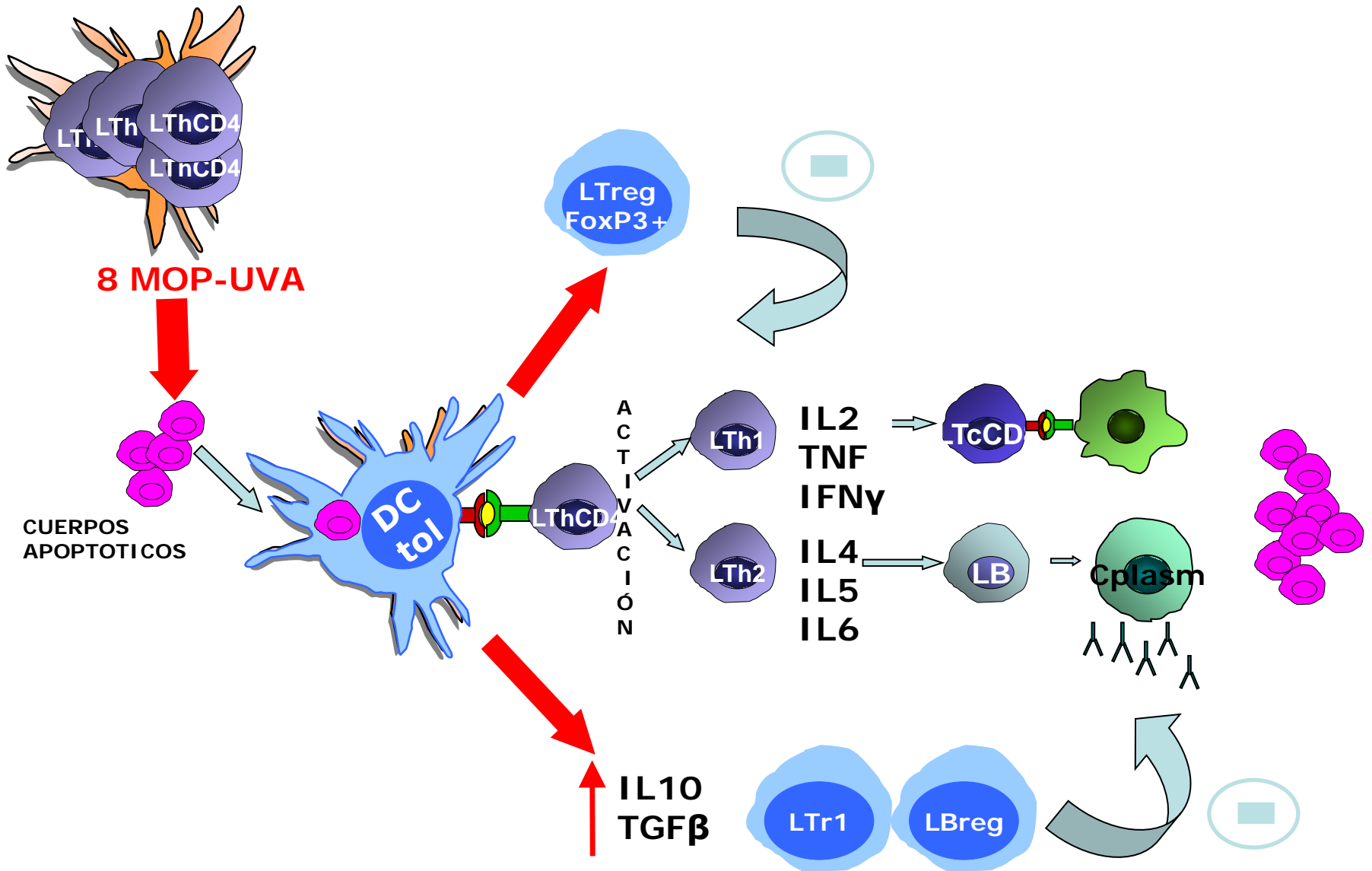
El psoralè fotoactivat lesiona el DNA, encaminant a la cèl·lula
a l' **APOPTOSIS**.

Què pretèn?

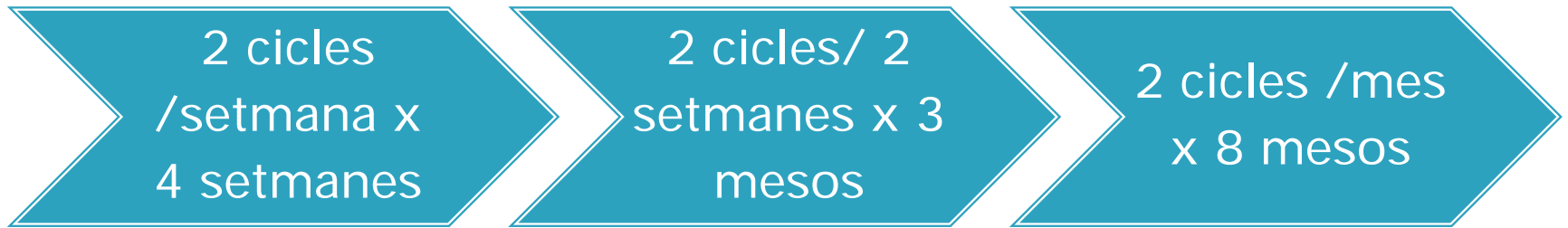
ANTIGEN PROPI



Mecanisme d'acció



Esquema de Tractament



Indicaciones

Patología	Categoría	Grade	Tiaféresis
1. Linfoma T Cutáneo, Micosis Fungoide, Sdre Sèzary			
eritrodérmico	I	1B	Fotoféresis
no eritrodérmico	III	2C	Fotoféresis
2. EICH cutáneo crónico	II	1B	Fotoféresis
EICH cutáneo agudo	II	1C	Fotoféresis
EICH no cutáneo (agudo /crónico)	III	2C	Fotoféresis
3. Rechazo trasplante cardíaco			
profilaxis	II	2A	Fotoféresis
Tto rechazo celular	II	1B	Fotoféresis
Tto rechazo humoral	III	2C	Recambio RPT
4. Rechazo trasplante pulmón			
bronquiolitis obliterante (bos)	II	1C	Fotoféresis
Rechazo humoral	III	2C	Recambio RPT
5. Pénfigo vulgar	III	2C	Fotoféresis
6. Fibrosis sistémica nefrogénica	III	2C	Fotoféresis
7. Esclerodermia sistémica	III	2A	Fotoféresis
8. Enf Inflamatoria crónica intestinal (Crohn, C.Ulcerosa)	III	2C	Fotoféresis
	III	2B	Adsorción citaf

Resposta MECRa

TABLE 2. Details of aGVHD patients and ECP characteristics*

GVHD diagnosis (days)	18 (9-92)			
Age at GVHD diagnosis (years)	12 (2-49)			
Patient weight (kg)	39 (10-98)			
Karnofsky/Landsky score at GVHD (%)	80 (60-100)			
Maximum GVHD staging				
Grade II	16 (47)			
Grade III	12 (35)			
Grade IV	6 (18)			
	GVHD 0-I	GVHD II	GVHD III	GVHD III-IV
Skin GVHD	2	2	27	5
Liver GVHD	27	2	2	5
Gut GVHD	23	1	6	6

TABLE 4. ORR for patients with aGVHD

Variables	aGVHD response (n = 34)	
	Number (%)	p value*
Age at ECP		
≥Median	8/16 (50)	0.15
<Median	14/18 (78)	
Sex		
Male	10/16 (62)	1
Female	12/18 (67)	
Stem cell source		
BM	15/22 (68)	0.22
PB	4/9 (44)	
CB	3/3 (100)	
Sex mismatch		
Female > male	5/7 (71)	1
Other	17/27 (63)	
GVHD grade		
II	14/16 (87)	0.0005
III	8/12 (67)	
IV	0/6 (0)	
Donor type		
MFD	6/8 (75)	0.68
MUD	16/26 (61)	
First-line therapy		
Steroids	22/30 (73)	0.01
Steroids plus other	0/4 (0)	
Visceral aGVHD		
Yes	11/13 (85)	0.07
No	11/21 (52)	

Resposta MECRa

Author (reference)	Year	Patients	CR/PR skin, %	CR/PR liver, %	CR/PR gut, %	Overall survival, %
Greinix et al. [23]	1998	6	100	100		100
Greinix et al. [24]	2000	21	81	67	0	57
Salvaneschi et al. [68]	2001	9	89	20	60	67
Dall'Amico et al. [69]	2002	14	79	57	70	57
Messina et al. [34]	2003	33	82	60	75	69
Garban et al. [70]	2005	12	67	0	40	42
Greinix et al. [25]	2006	59	93	65	74	59
Kanold et al. [71]	2007	12	100	67	83	75
Perfetti et al. [72]	2008	23	66	27	40	48
Calore et al. [73]	2008	15	92	100	71	85
Perotti et al. [74]	2010	50	83	67	73	64

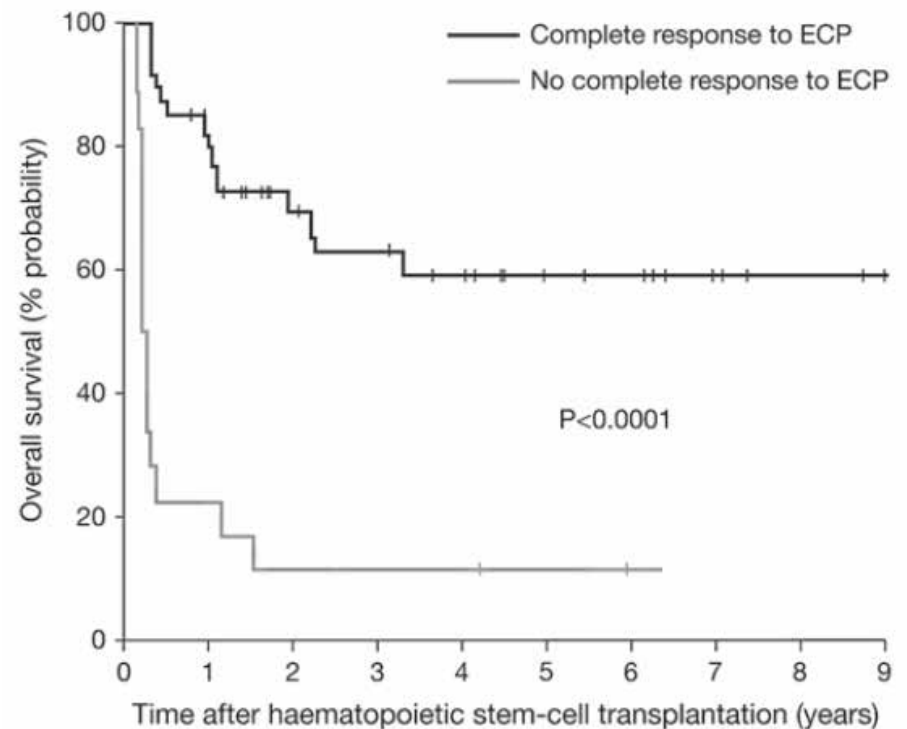
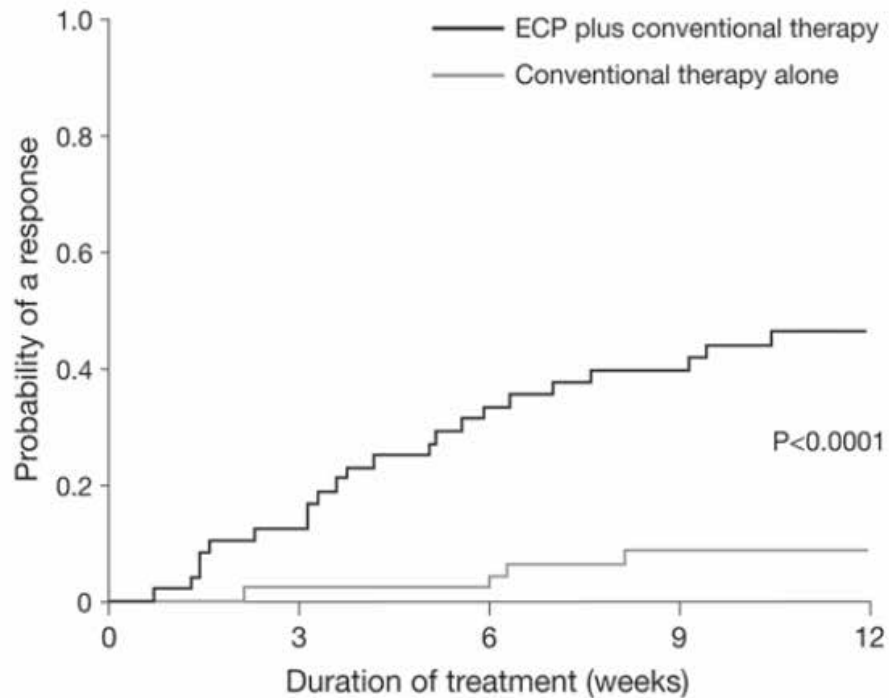
CR = Complete response; PR = partial response (>50% improvement in organ involvement).

Resposta MECRc

Author (reference)	Year	Patients	ORR (%)	Survival
Greinix et al. [23]	1998	15	8 CR, 6 PR (93)	14/15 (93%) at 15 mo
Smith et al. [75]	1998	18	3 CR, 3 PR (33)	7/18 (39%) at 2 y
Salvaneschi et al. [68]	2001	14	4 CR, 5 PR (64)	11/14 (79%) at 3 y
Messina et al. [34]	2003	44	15 CR, 10 PR (68)	34/44 (77%)
Seaton et al. [76]	2003	28	10 PR (36)	24/28 (86%)
Apisarnthanarax et al. [77]	2003	32	7 CR, 11 PR (56)	19/32 (59%)
Foss et al. [78]	2005	25	16 PR (64)	15/25 (60%)
Rubegni et al. [79]	2005	32	9 CR, 13 PR (69)	
Couriel et al. [35]	2006	71	14 CR, 29 PR (61)	13/71 (18%) at 5 y
Greinix et al. [25]	2006	47	23 CR, 16 PR (83)	42/47 (89%)
Perseghin et al. [80]	2007	25	11 CR, 9 PR (80)	19/25 (76%) at 2 y

ORR = Overall response rate; CR = complete response; PR = partial response; mo = months; y = years.

Resposta MECRc



Moltes mercès

