

TERAPIE SISTEMICHE DELL'EPATOCARCINOMA IN FASE AVANZATA

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***ISTITUTI CLINICI DI PERFEZIONAMENTO,
MILANO***

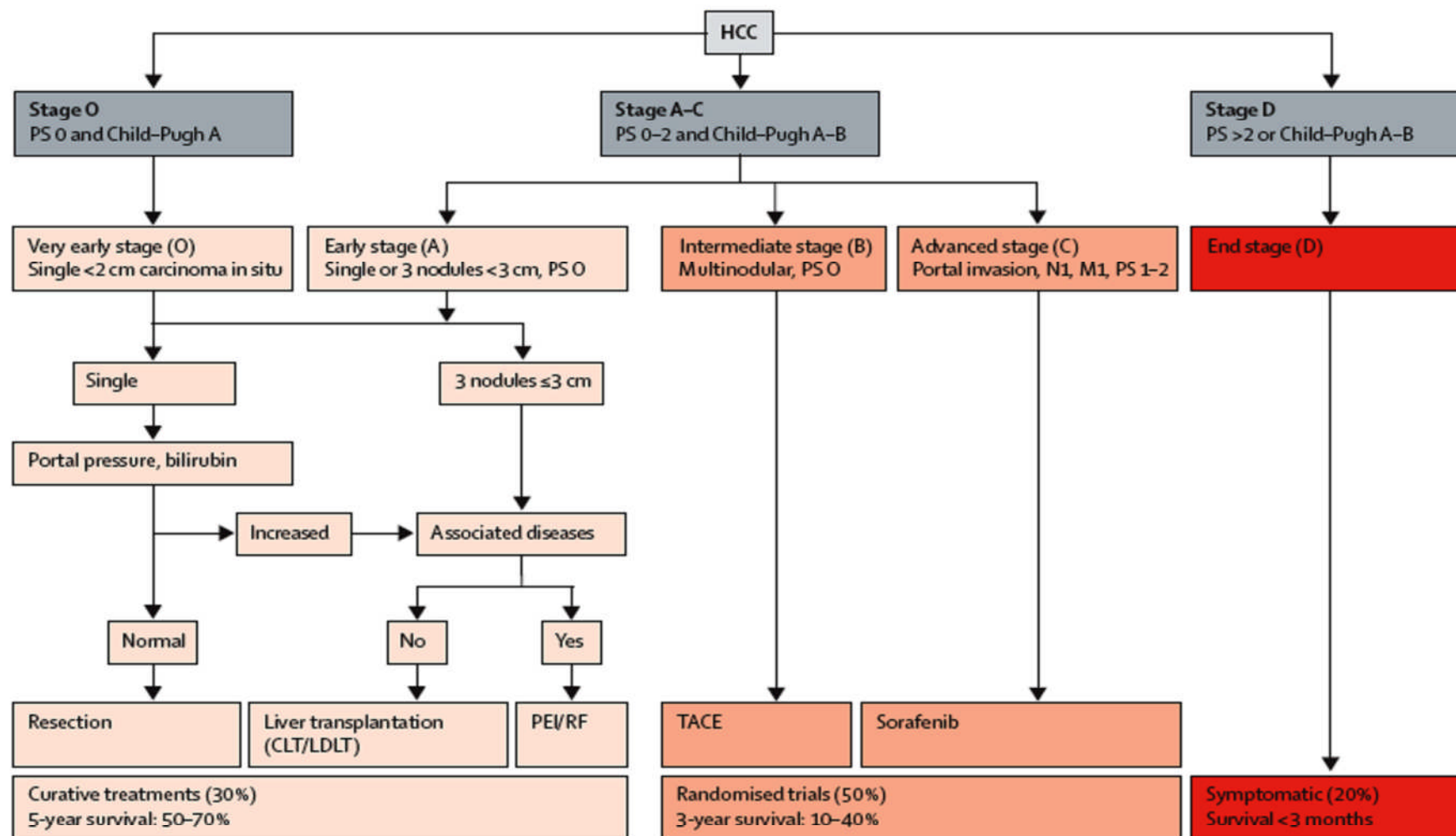
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Società Italiana di Ultrasonologia in Medicina e Biologia

BARCELONA CLINIC LIVER CANCER STAGING AND TREATMENT APPROACH

Bruix J and Llovet JM - Lancet 2009 and J Natl Cancer Inst 2008



HCC : SOPRAVVIVENZA MEDIANA A SECONDA DEL DIVERSO TRATTAMENTO SISTEMICO

TRATTAMENTO (RANGE)	SOPRAVVIVENZA MEDIANA IN MESI
Interferon in monoterapia	3-4
Interferon + chemioterapia	5-10
Monochemioterapia	4-10
Polichemioterapia	8-10
Tamossifene	3-6
Megestrol	4-18
Octreotide	4-13

Treiber G – Dig Dis 2001

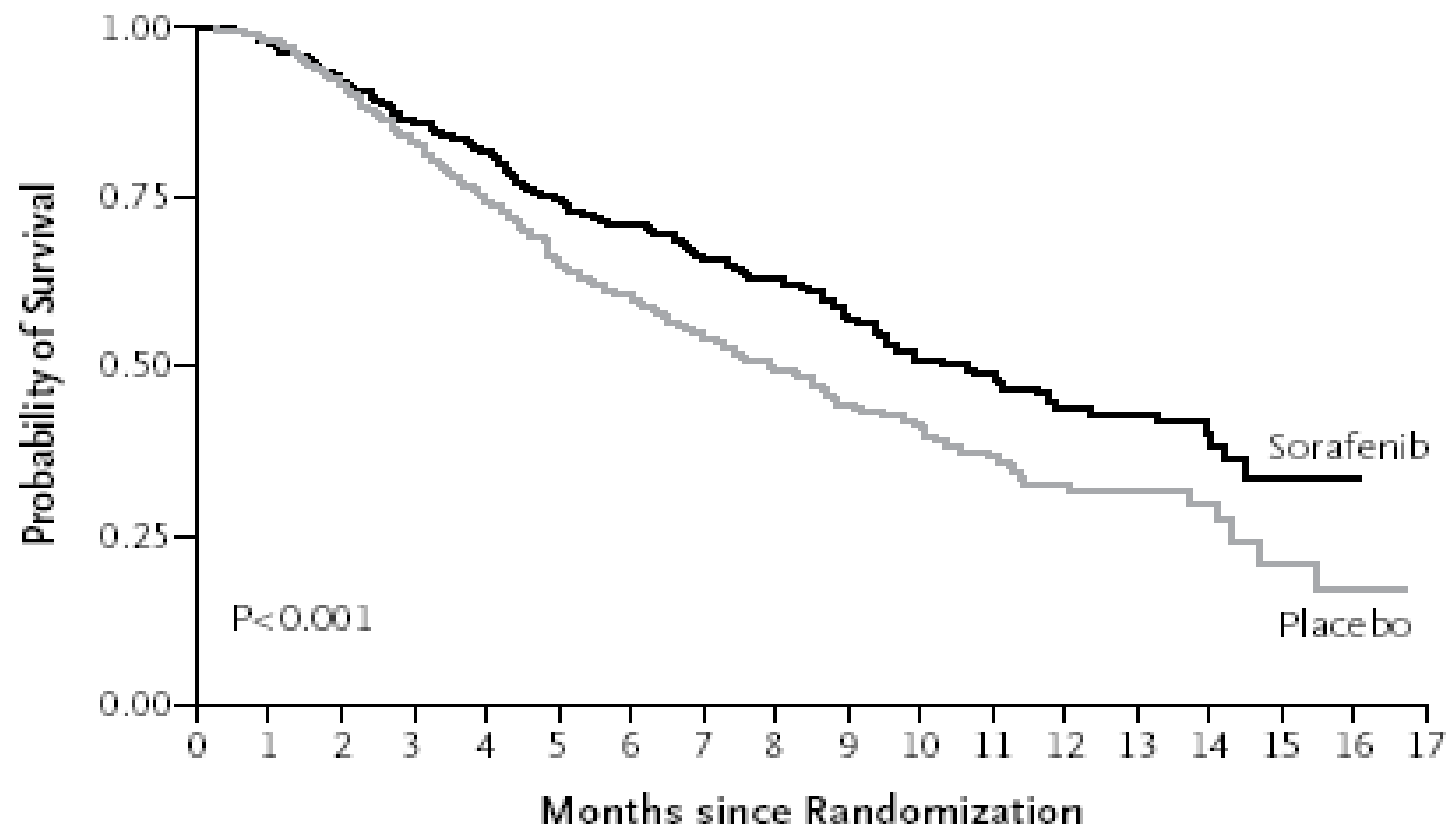
Tali dati ed altri non dissimili hanno portato per decenni a un senso di nichilismo nei confronti dell'HCC da parte degli oncologi ed epatologi

Sorafenib: mediana di sopravvivenza = 10,7 mesi.

Placebo = 7,9 mesi

Llovet JM et al. - NEJM 2008

A Overall Survival



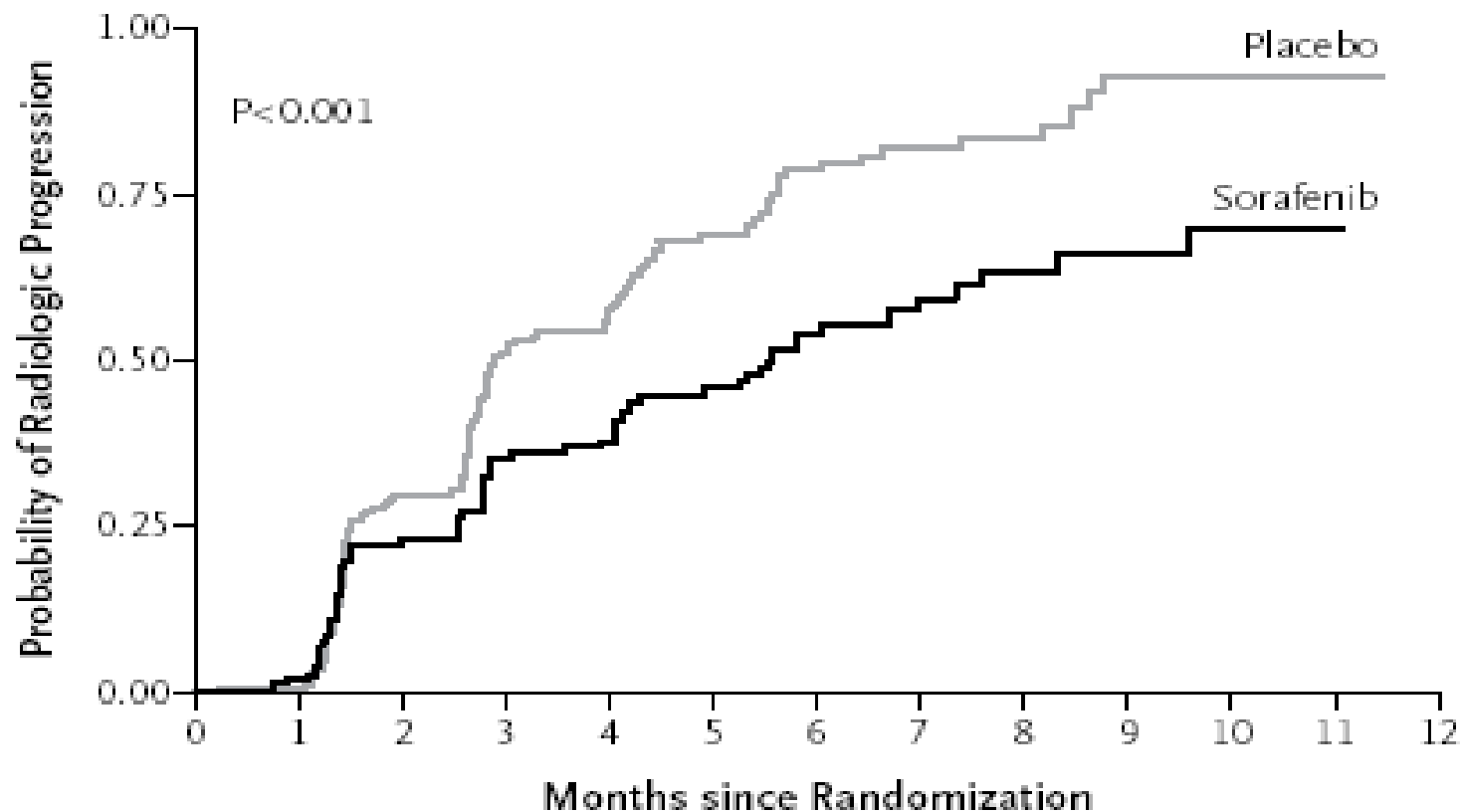
No. at Risk

Sorafenib	299	290	270	249	234	213	200	172	140	111	89	68	48	37	24	7	1	0
Placebo	303	295	272	243	217	189	174	143	108	83	69	47	31	23	14	6	3	0

Sorafenib: mediana di progressione radiologica = 5,5 mesi.

Placebo = 2,8 mesi

C Time to Radiologic Progression



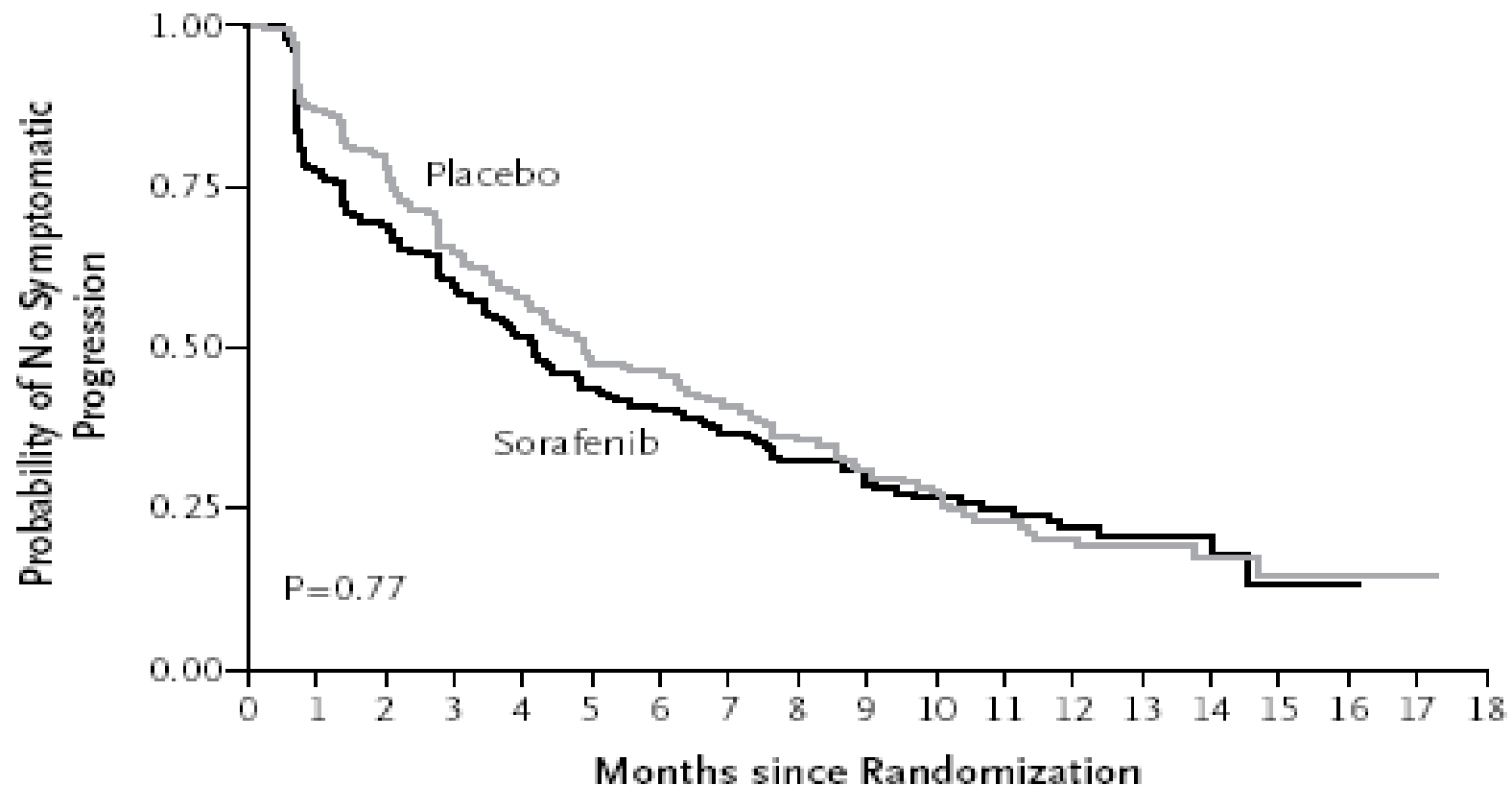
No. at Risk

Sorafenib	299	267	155	101	91	65	37	23	18	10	4	2	0
Placebo	303	275	142	78	62	41	21	11	10	3	1	1	0

Sorafenib: mediana di progressione sintomatica = 4,1 mesi.

Placebo = 4,9

B Time to Symptomatic Progression



No. at Risk

Sorafenib	299	226	196	161	137	111	99	78	59	47	36	27	18	14	7	1	1	0	0
Placebo	303	259	229	184	157	126	117	87	63	47	39	28	18	13	8	5	3	1	0

Radioembolizzazione con microsfere di Yttrio-90

- Diversamente dalla chemioembolizzazione si può praticare anche in pazienti con trombosi portale
- Studi non controllati
- Tassi di risposta alti, vicini al 50% o anche superiori
- Sopravvivenza molto variabile a seconda della presenza o meno di trombosi portale, di una branca, lobare o massiva e di cirrosi



- **Trombosi portale di una branca con cirrosi = 261 giorni (8,7 mesi)**

Kulik LM et al. Hepatology 2008

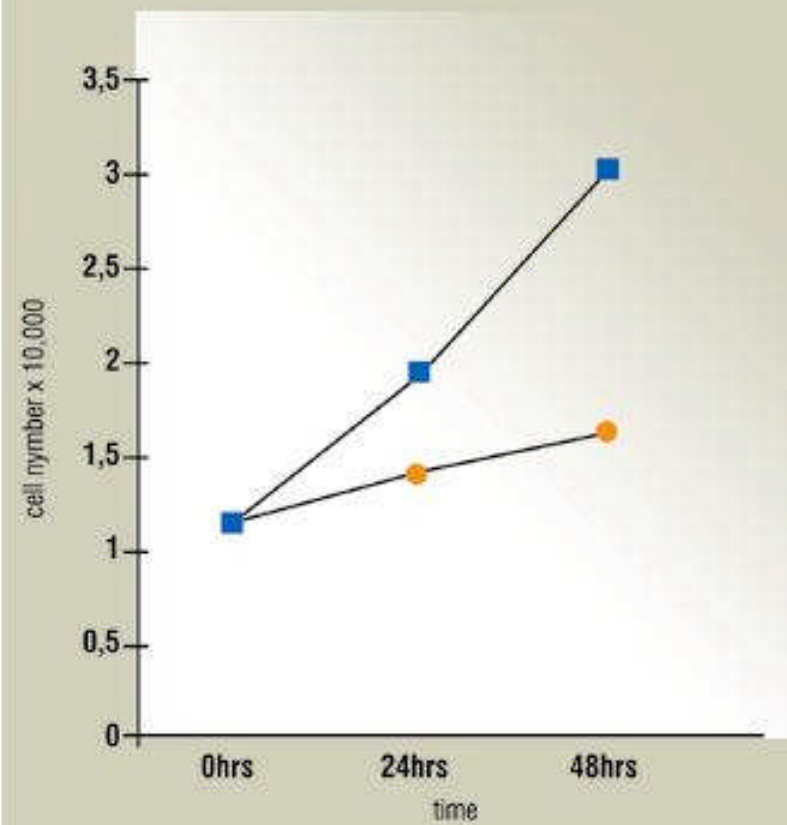


Fig.5

Cell proliferation curve of A172 (glioblastoma cells) after the treatment with zebrafish stem cells differentiation stage factors.

- control cells.
- stage I (50% of epiboly) treated cells.

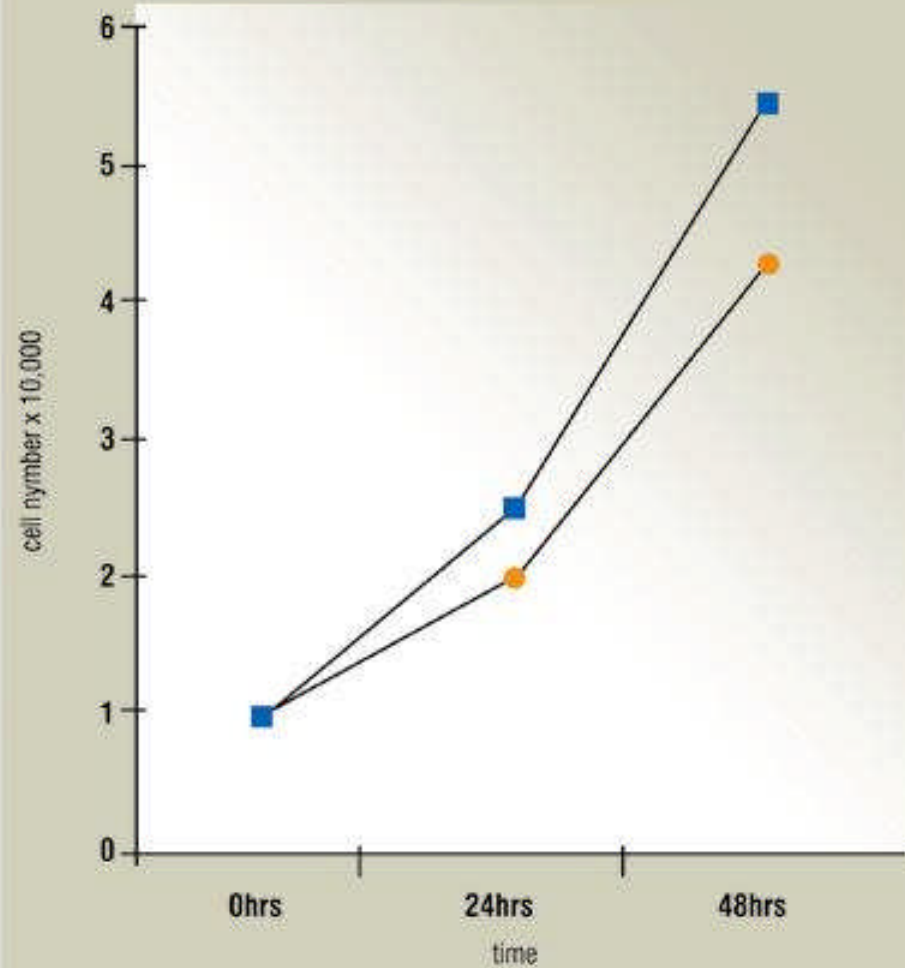


Fig.6

Cell proliferation curve of A375 (melanoma cells) after the treatment with zebrafish stem cells differentiation stage factors.

- control cells.
- stage I (50% of epiboly) treated cells.

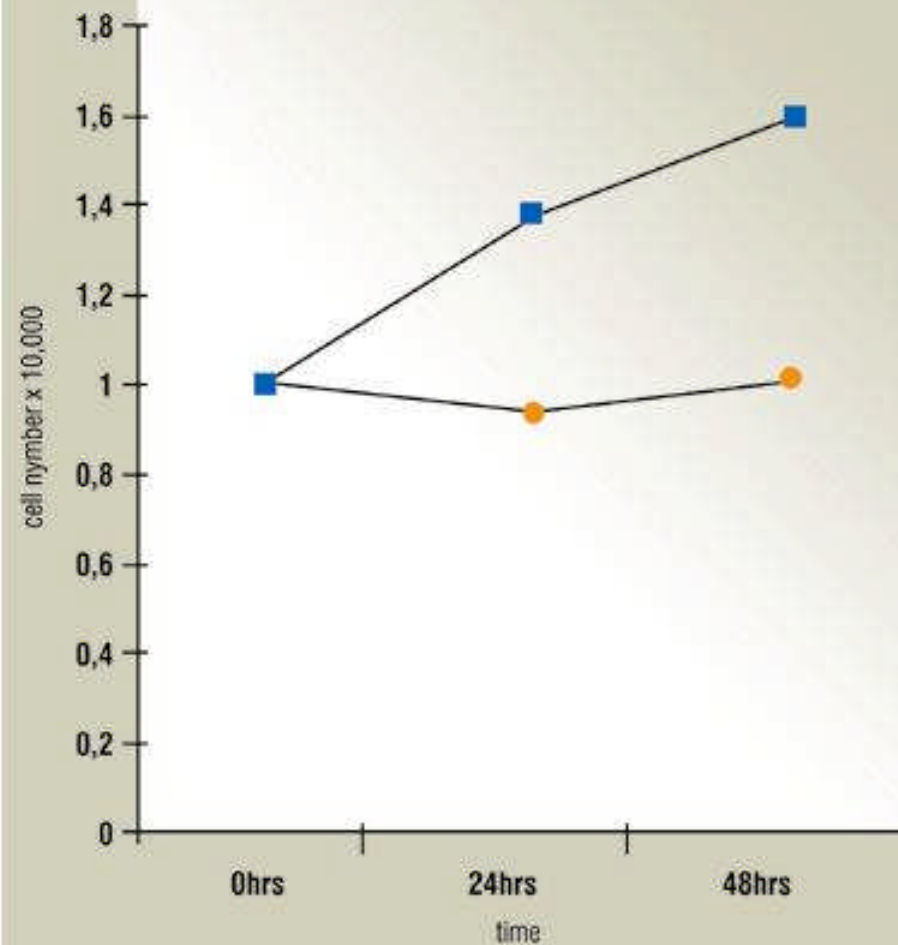


Fig.8

Cell proliferation curve of lymphoblastic leukemia after the treatment with zebrafish stem cells differentiation stage factors.

- control cells.
- stage I (50% of epiboly) treated cells.

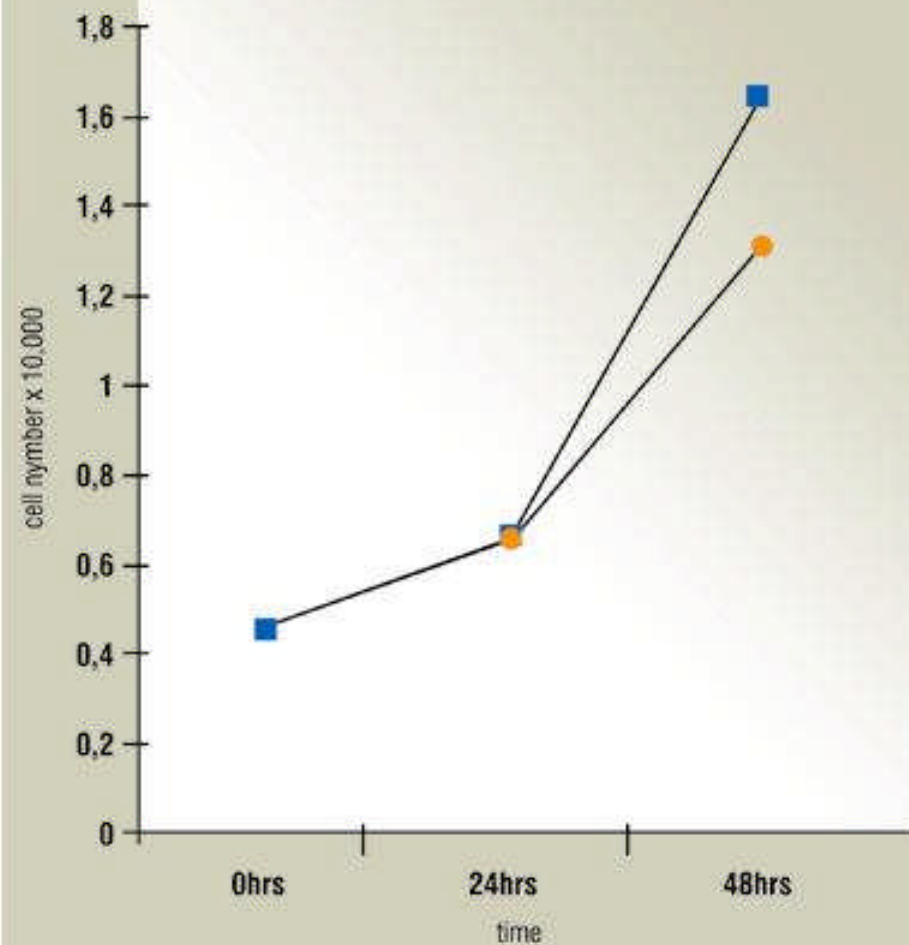


Fig.9

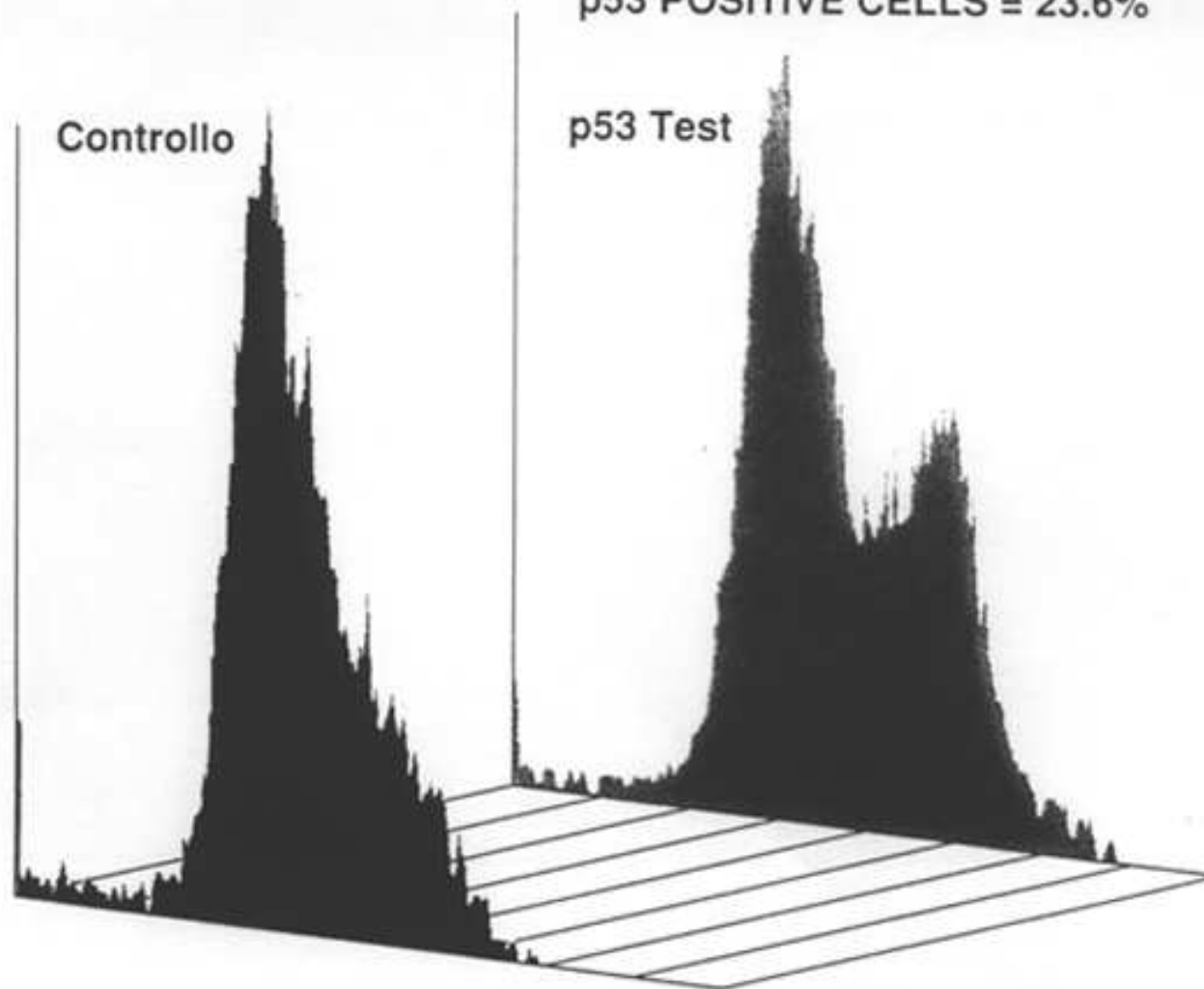
Cell proliferation curve of ACHN (kidney adenocarcinoma cells) after the treatment with zebrafish stem cells differentiation stage factors.

- control cells.
- stage I (50% of epiboly) treated cells.

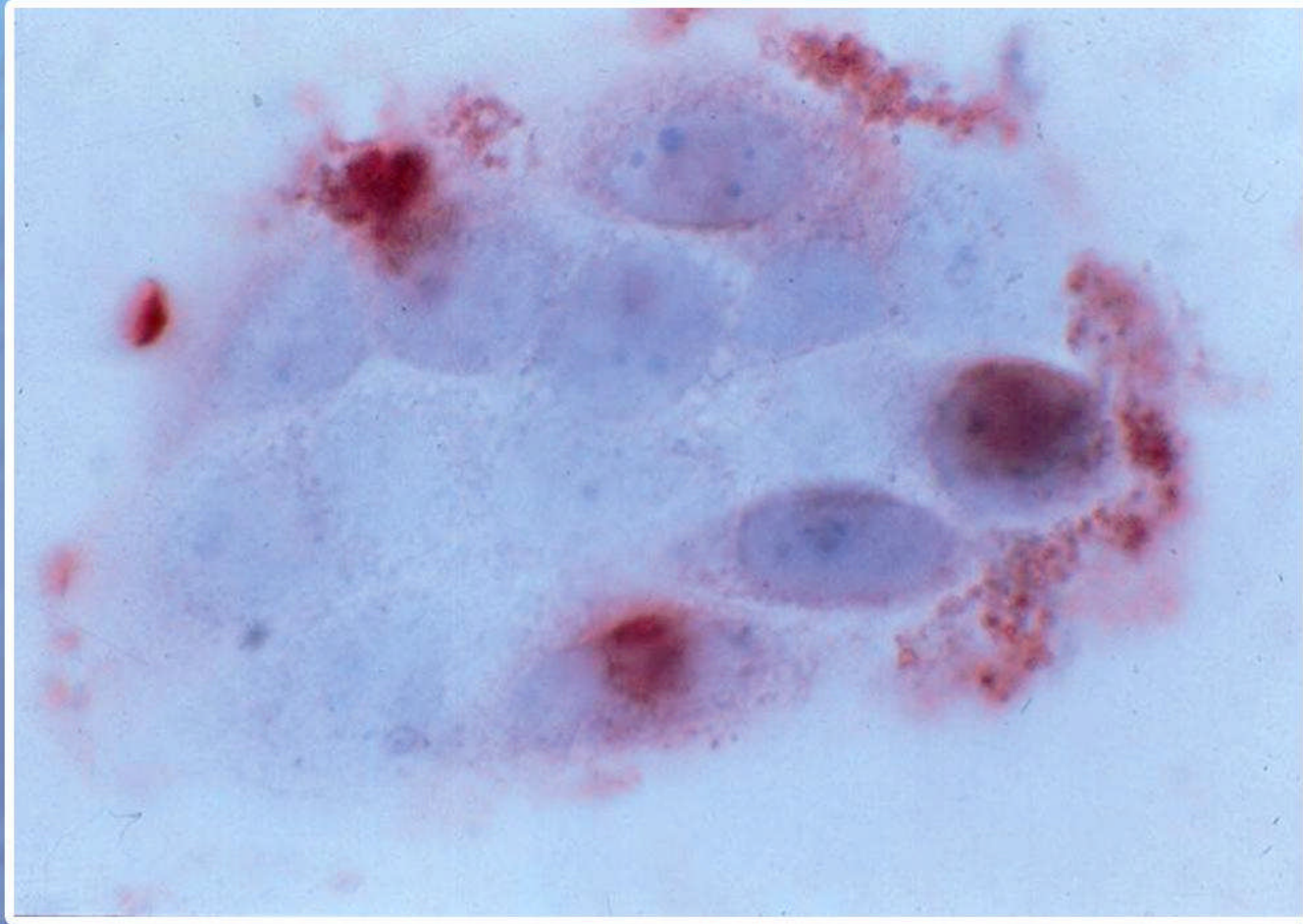
GLIOBLASTOMA

LINEA CELLULARE + 10% FCS +100UL XI

p53 POSITIVE CELLS = 23.6%

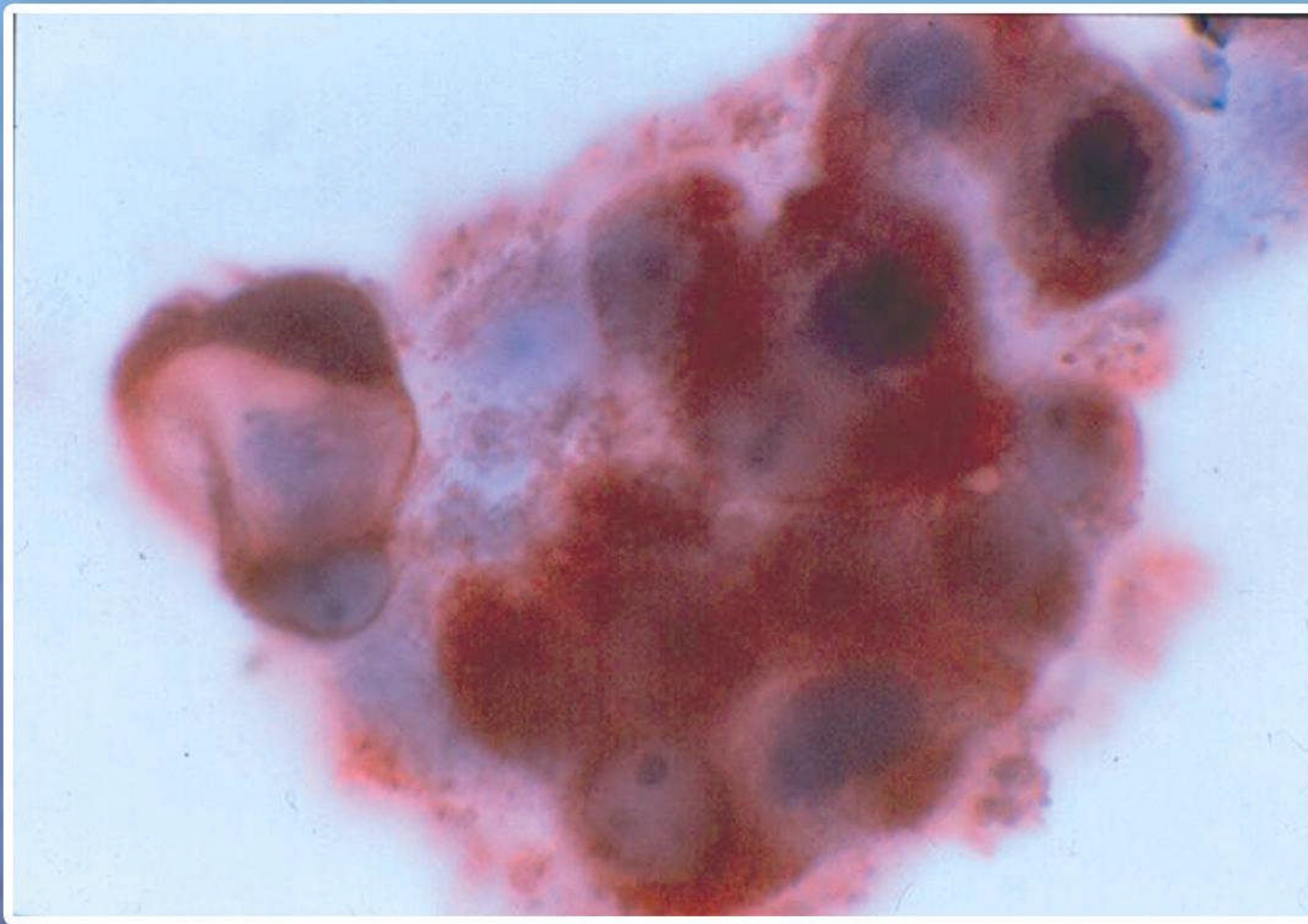


**Espressione di p53 in cellule di melanoma non trattate con
stem cell differentiation stage factors (SCDSF)**



(immunoistochimica, 1000x)

**Espressione di p53 in cellule di melanoma trattate con
stem cell differentiation stage factors (SCDSF)**



(immunoistochimica, 1000x)

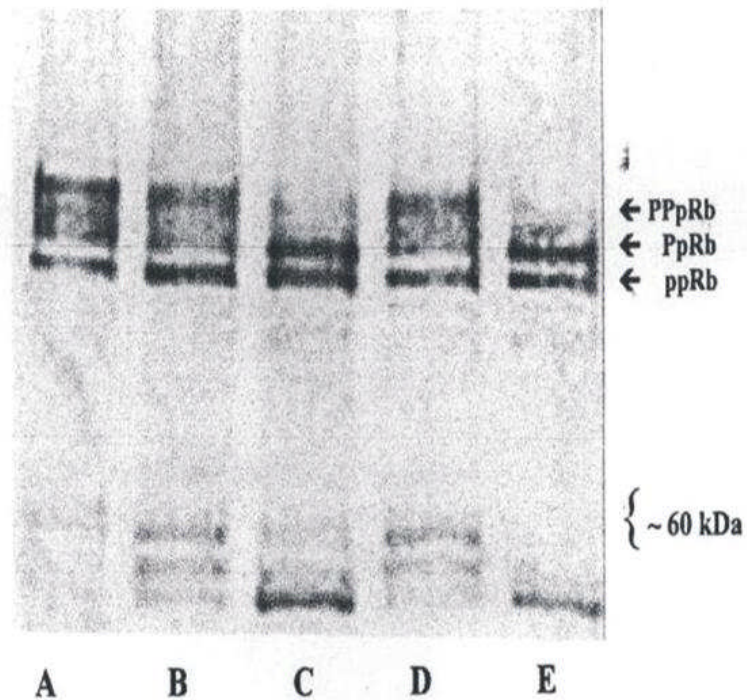


FIG. 4

Immunostaining of whole ACHN cell lysates with α -pRb antibody after fractionation of proteins on a 5% SDS-PAGE and Western Blotting. A: untreated cells. B: 24-hours treated cells with 3 μ g of extract. C: 48-hours treated cells with 3 μ g of extract. D: 24-hours treated cells with 15 μ g of extract. E: 48-hours treated cells with 15 μ g of extract.

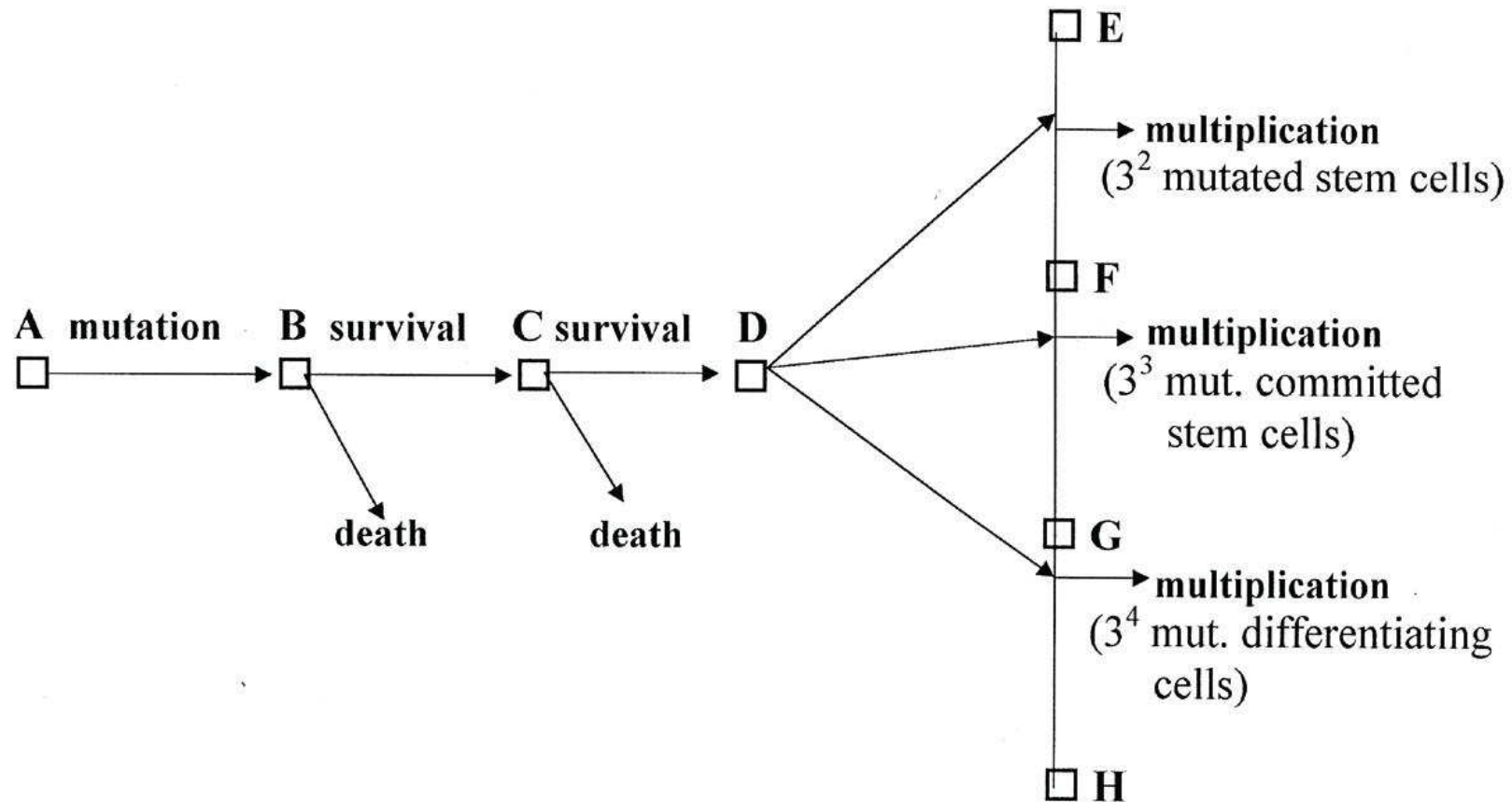
PPpRb: hyperphosphorylated pRb. PpRb: phosphorylated pRb. ppRb: hypophosphorylated pRb

Fig. 18 CANCER AS A PROCESS OF DETERMINISTIC CHAOS - Legend

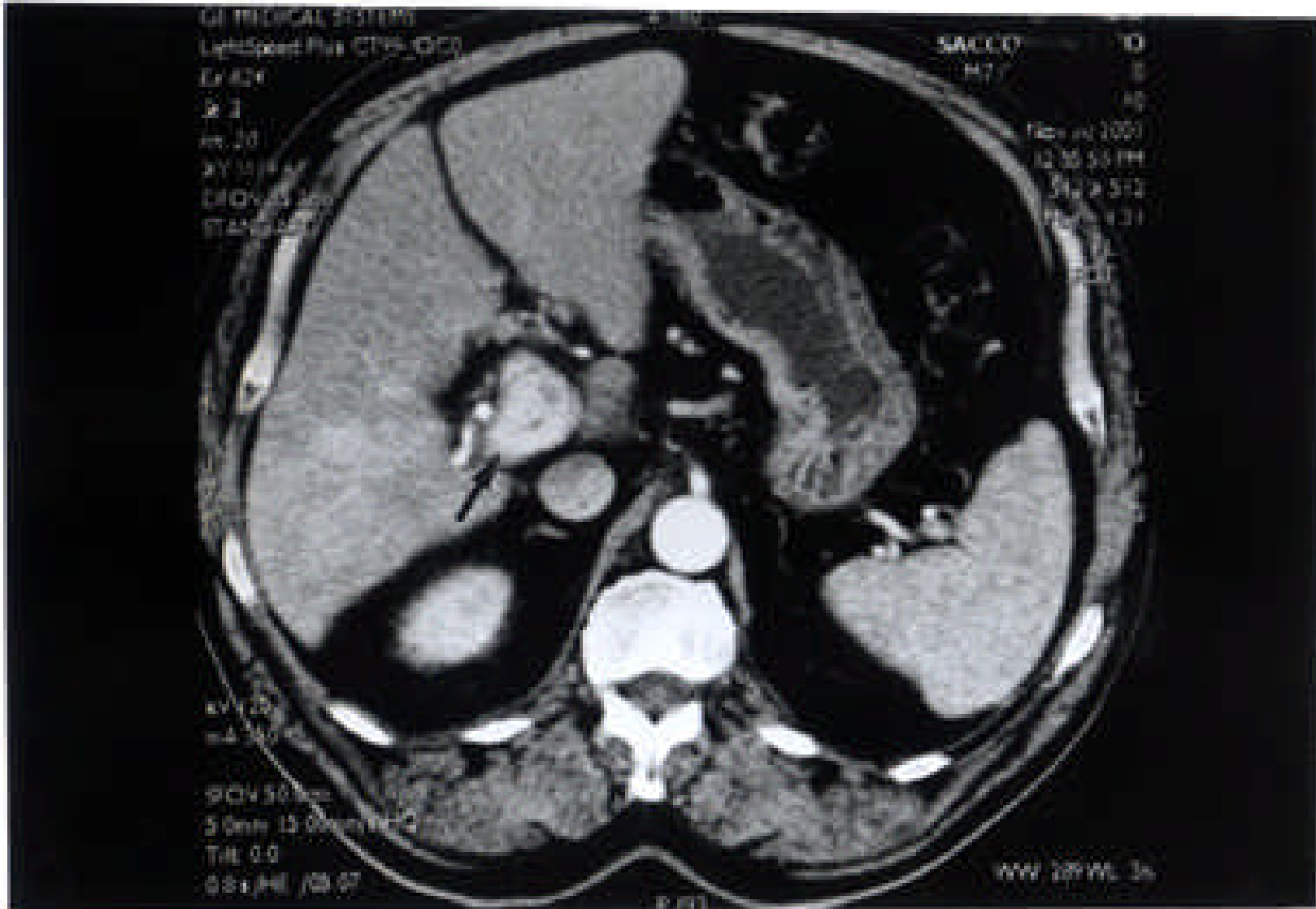
A: normal cell **B:** cell with damaged DNA **C:** cell with rampant genetic instability

D: cancer cell: stable gene configuration with uncoupled steps of cell multiplication and differentiation.

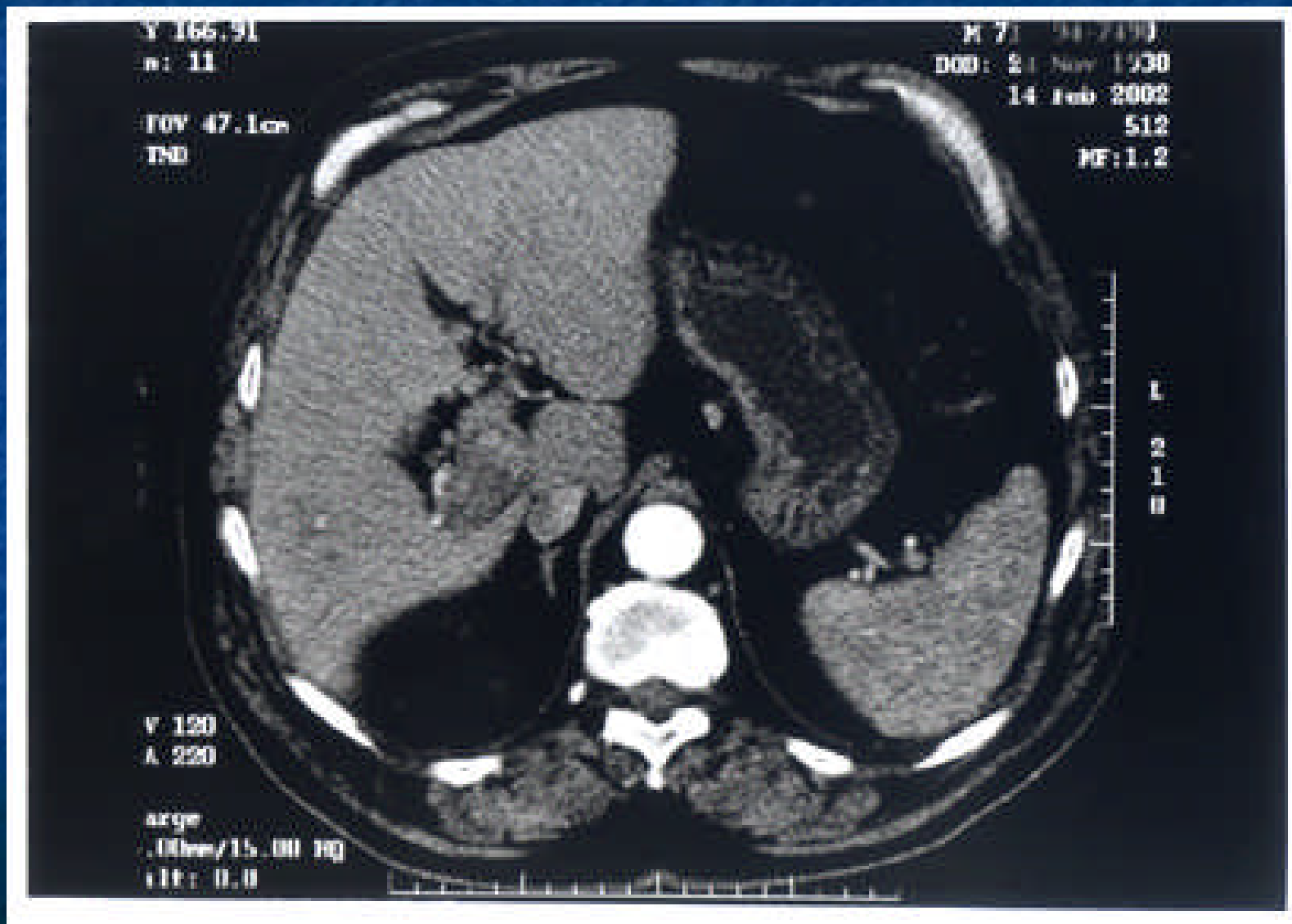
E: stem cell **F:** committed stem cell **G:** differentiating cell **H:** differentiated cell.



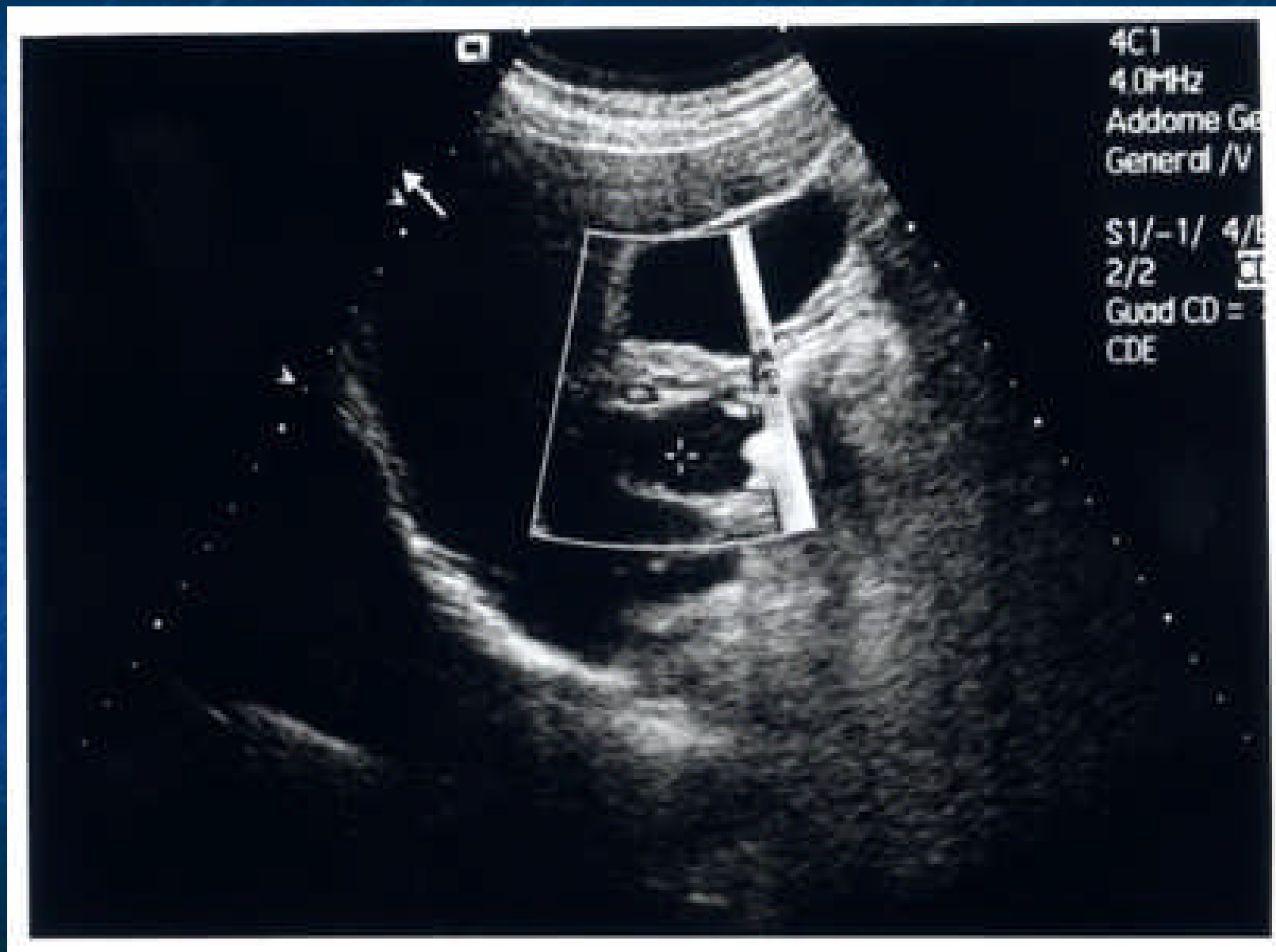
La TC in fase arteriosa prima del trattamento con **stem cell differentiation stage factors** (SCDSF) dimostra un HCC avanzato del lobo dx, con un trombo occupante la branca dx della porta (freccia), fino al ramo principale



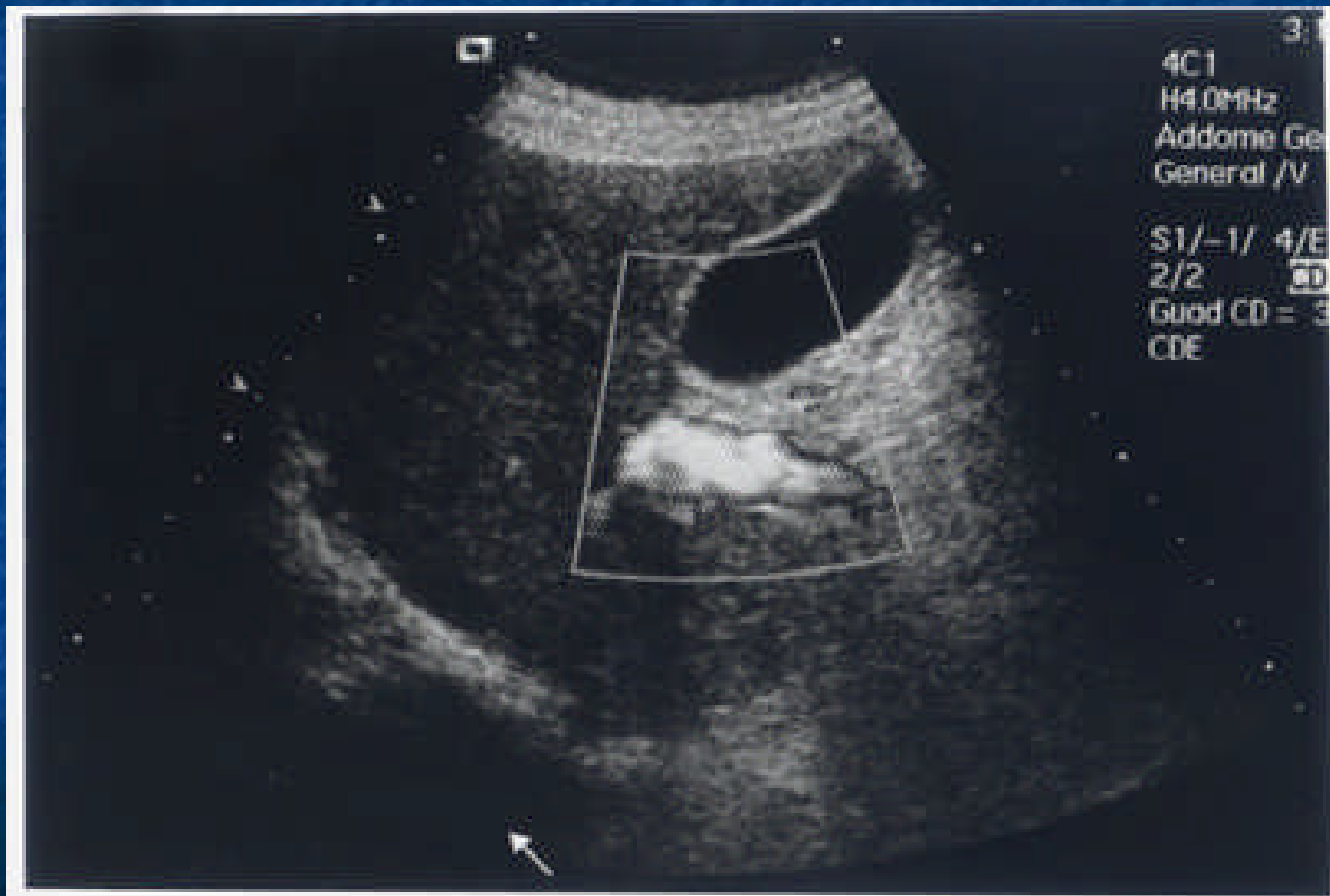
TC in fase arteriosa 3 mesi dopo il trattamento con SCDSF: scomparsa dell'area neoplastica ed evidente riduzione della trombosi portale



Nello stesso paziente, la power doppler conferma la trombosi portale (asterisco)



L'esame power doppler dopo la terapia con **SCDSF** conferma la regressione della trombosi portale e la pervietà della porta



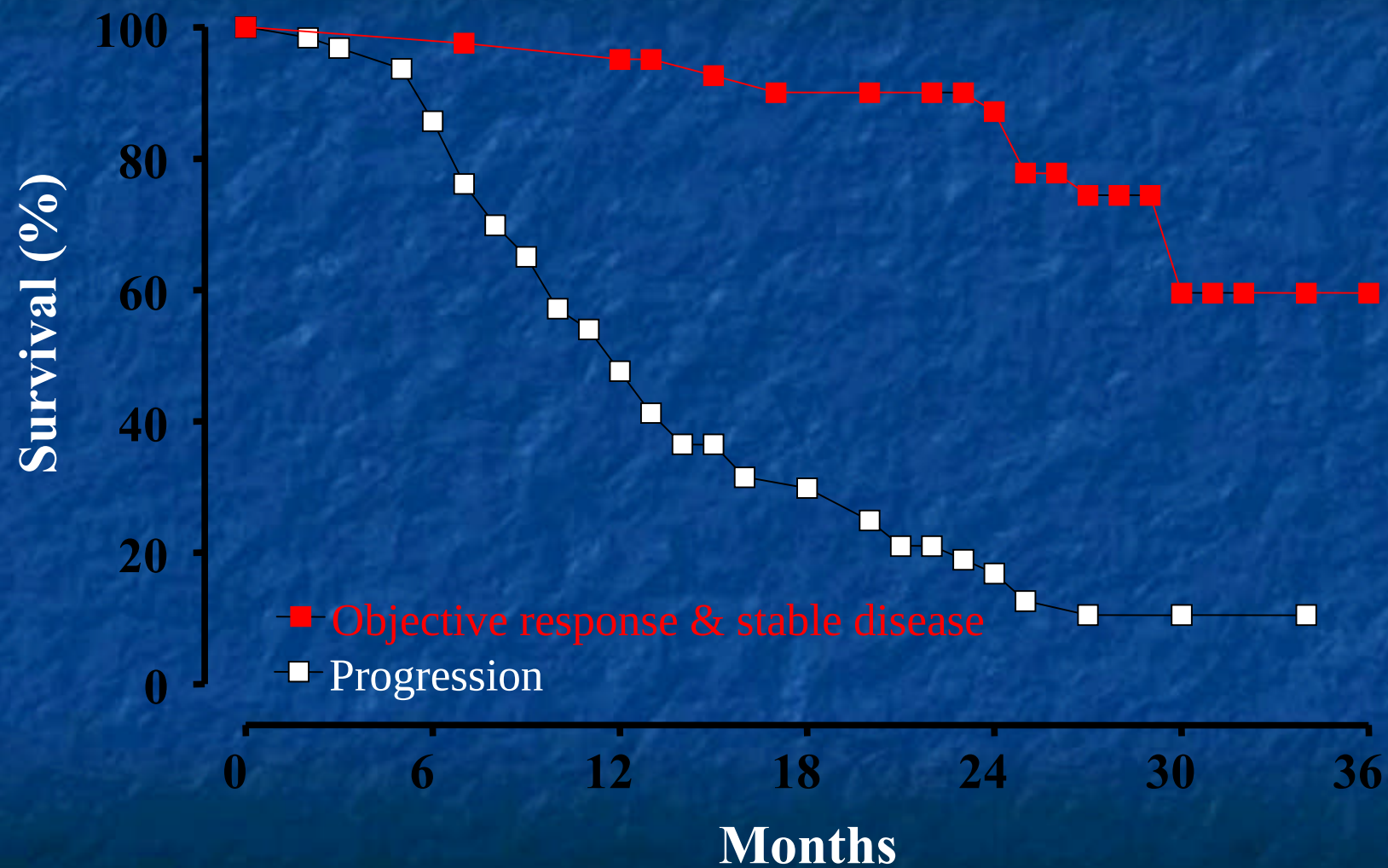
In un altro caso, la TC in fase arteriosa prima del trattamento con SCDSF, evidenzia molti noduli ipervascolarizzati di HCC nel lobo dx



La TC 6 mesi dopo il trattamento con SCDSF dimostra la scomparsa dell'ipervascolarizzazione neoplastica all'interno dei noduli di HCC



**Treatment with stem cell differentiation stage factors of intermediate-advanced HCC:
an open randomized clinical trial.**



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MODIFICATA

