

Cannabinoids, a new hope for cancer therapy?

María Muñoz Caffarel
Biodonostia, San Sebastian, Spain

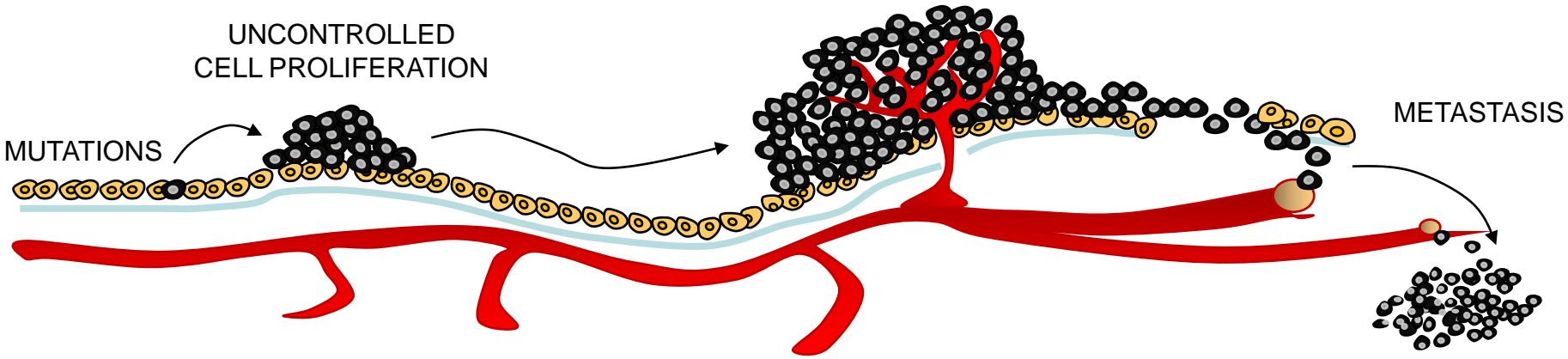
CANCER

ANGIOGENESIS

UNCONTROLLED
CELL PROLIFERATION

MUTATIONS

METASTASIS



TUMOR PROGRESSION

ONCOLOGIC PAIN

SIDE EFFECTS

← ANTI-CANCER THERAPIES

Hair loss

Anemia

Constipation/Diarrhea

Pain (bone, joint, chest, muscle)

Toxicity (heart, liver, kidneys)

Lack of appetite, nausea, vomiting

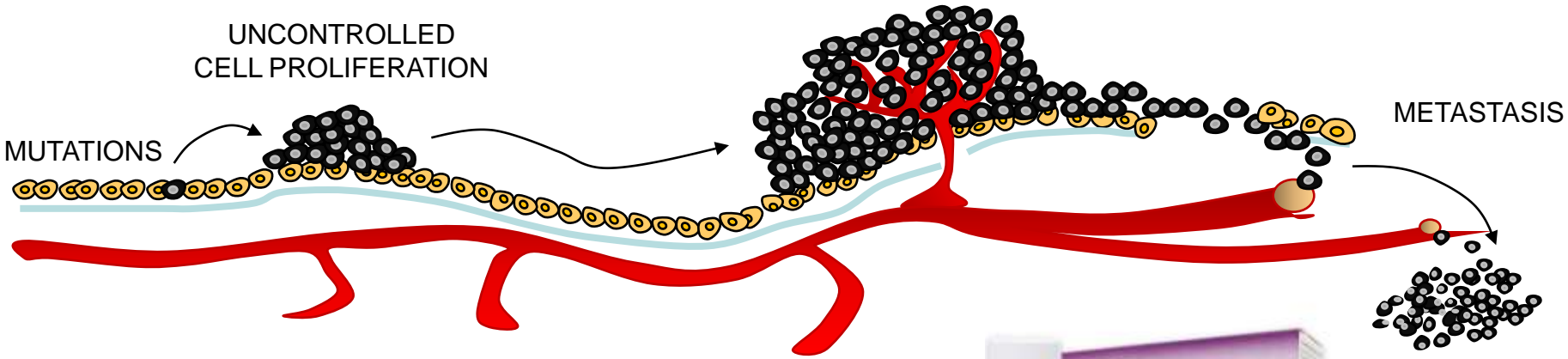
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CANNABINOIDS



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ANTI-CANCER THERAPIES



THERAPEUTIC TOOLS AGAINST CANCER

1. THEY MUST WORK

They must kill cancer cells/block cancer cell propagation

There must be targets in human patients

2. THEY MUST BE SAFE

They must not produce toxic effects on non-cancer cells

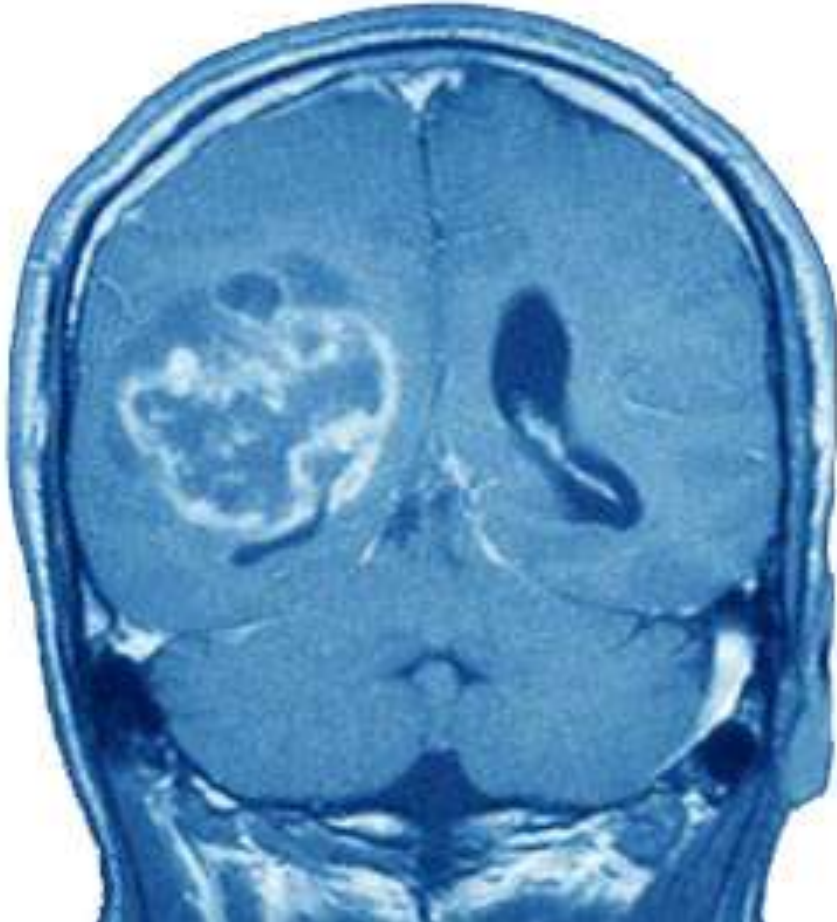
They must not produce side effects

THERAPEUTIC TOOLS AGAINST CANCER

1. DO CANNABINOIDS WORK?

2. ARE CANNABINOIDS SAFE?

1. DO CANNABINOIDS WORK as antitumor agents?



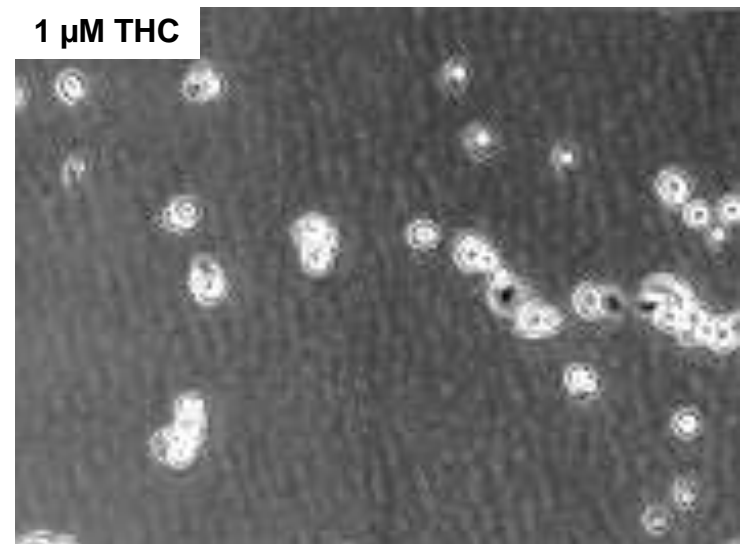
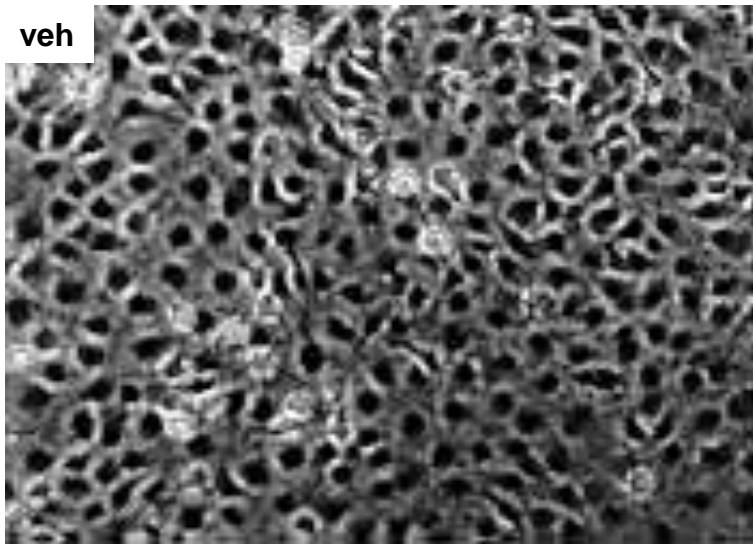
GLIOBLASTOMA MULTIFORME

Treatments: Tumor resection +
Radiotherapy +
Chemotherapy (Temozolomide)

Life expectancy of patients with GBM:
14 months after diagnosis

1. DO CANNABINOIDS WORK as antitumor agents?

LAB RESEARCH

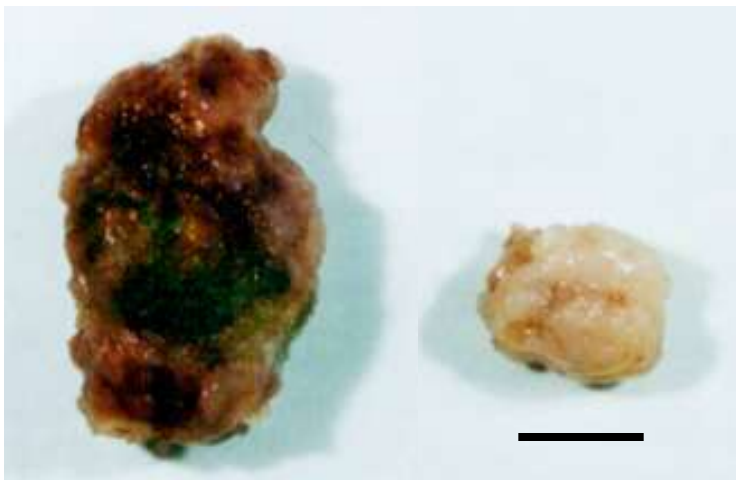
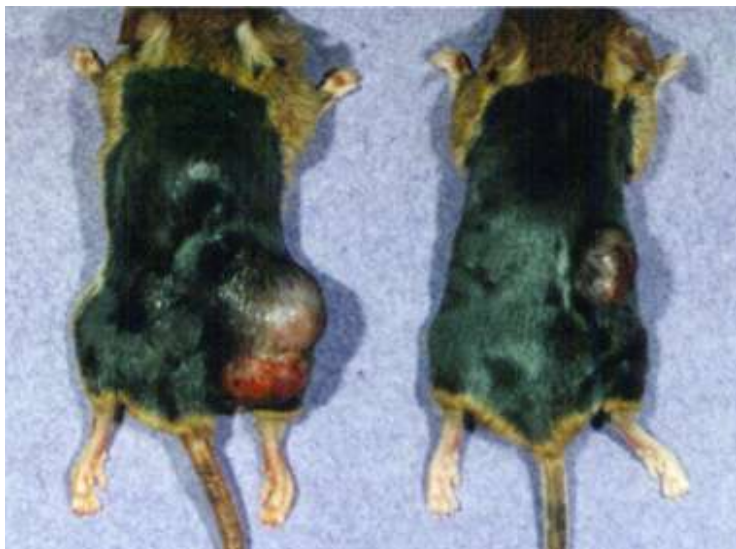


1. DO CANNABINOIDS WORK as antitumor agents?

LAB RESEARCH

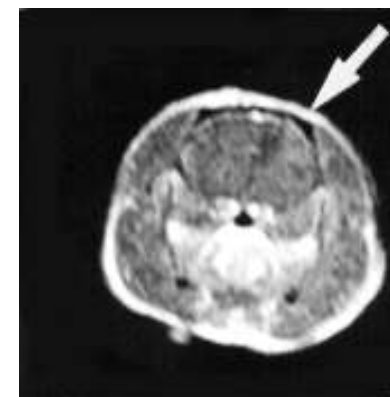
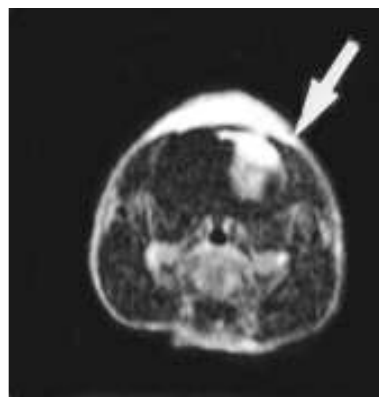
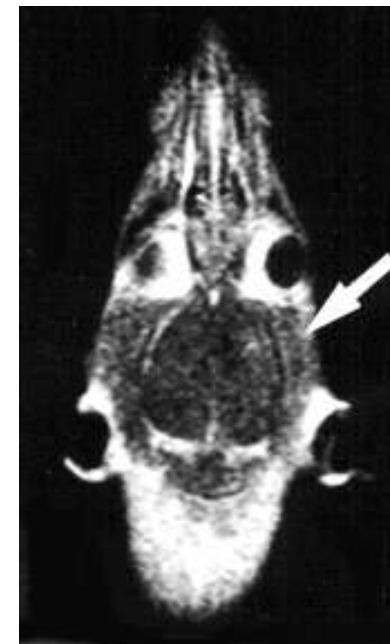
Vehicle

THC



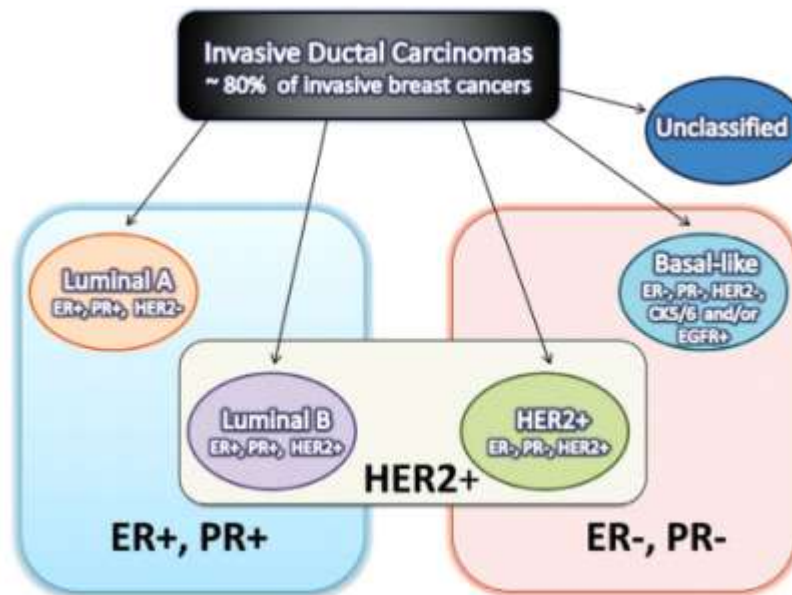
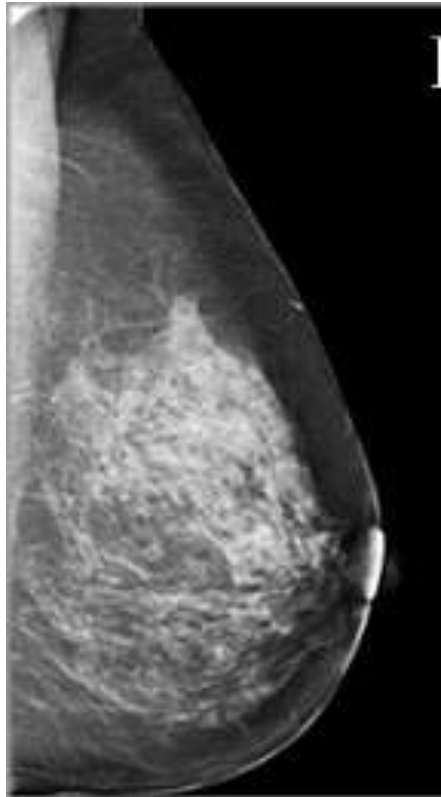
Before THC

After THC

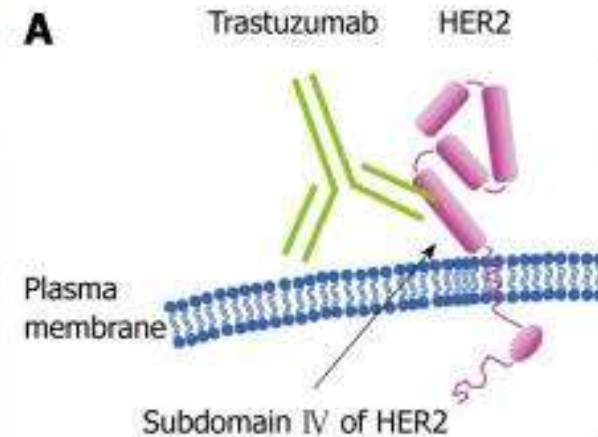


1. DO CANNABINOIDS WORK as antitumor agents?

BREAST CANCER



A



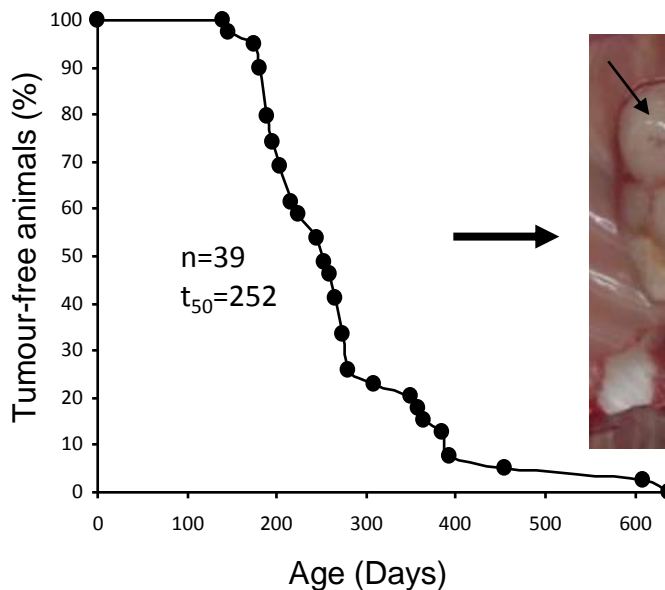
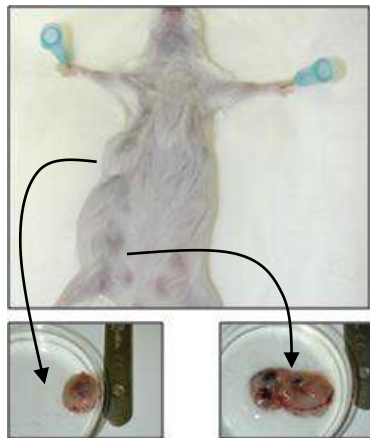
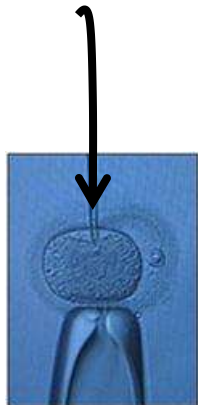
UNSOLVED ISSUES: Innate and acquired RESISTANCE to anticancer drugs
METASTASIS in the central nervous system
Anticancer drug-associated SIDE EFFECTS

1. DO CANNABINOIDS WORK as antitumor agents?

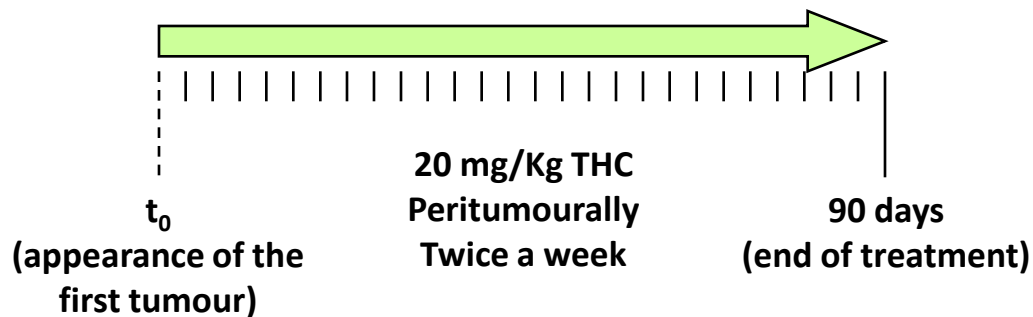
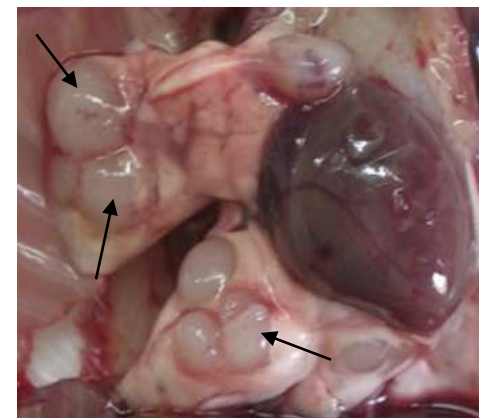
LAB RESEARCH

THE MMTV-neu MOUSE: A CLINICALLY RELEVANT MODEL OF HER2-POSITIVE METASTATIC BREAST CANCER

MMTV-neu



Lung metastases



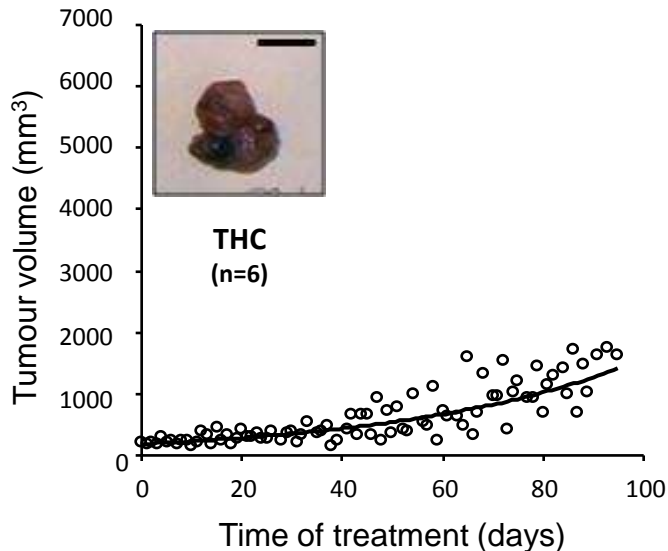
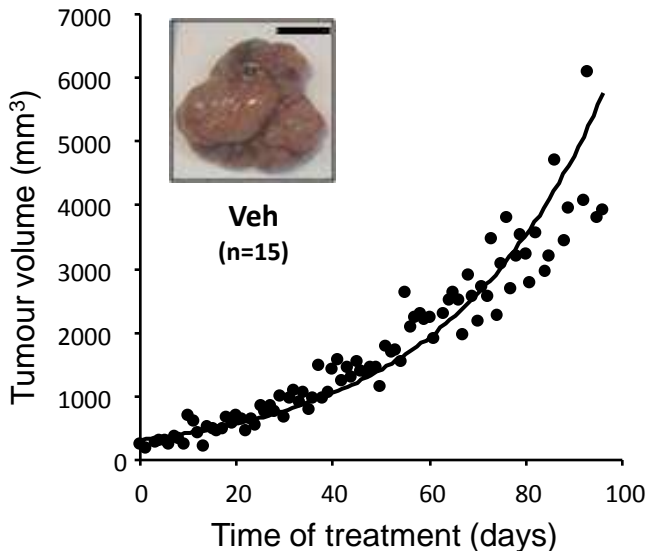
1. DO CANNABINOIDS WORK as antitumor agents?

LAB RESEARCH



MMTV-neu mouse

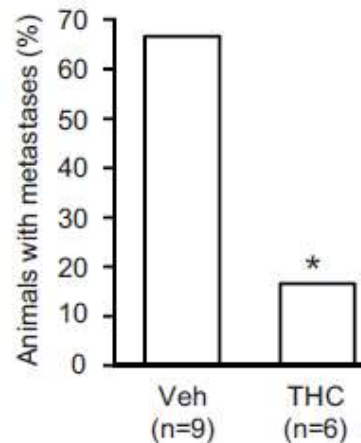
THC REDUCES TUMOUR GROWTH



THC REDUCES TUMOUR GENERATION

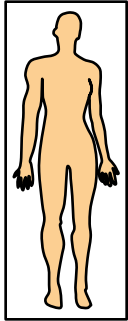
Tumors/ animal	1	2	3	4 or more
Control (n=12)	25%	8%	25%	41%
THC (n=6)	50%	17%	33%	0%

THC REDUCES LUNG METASTASES

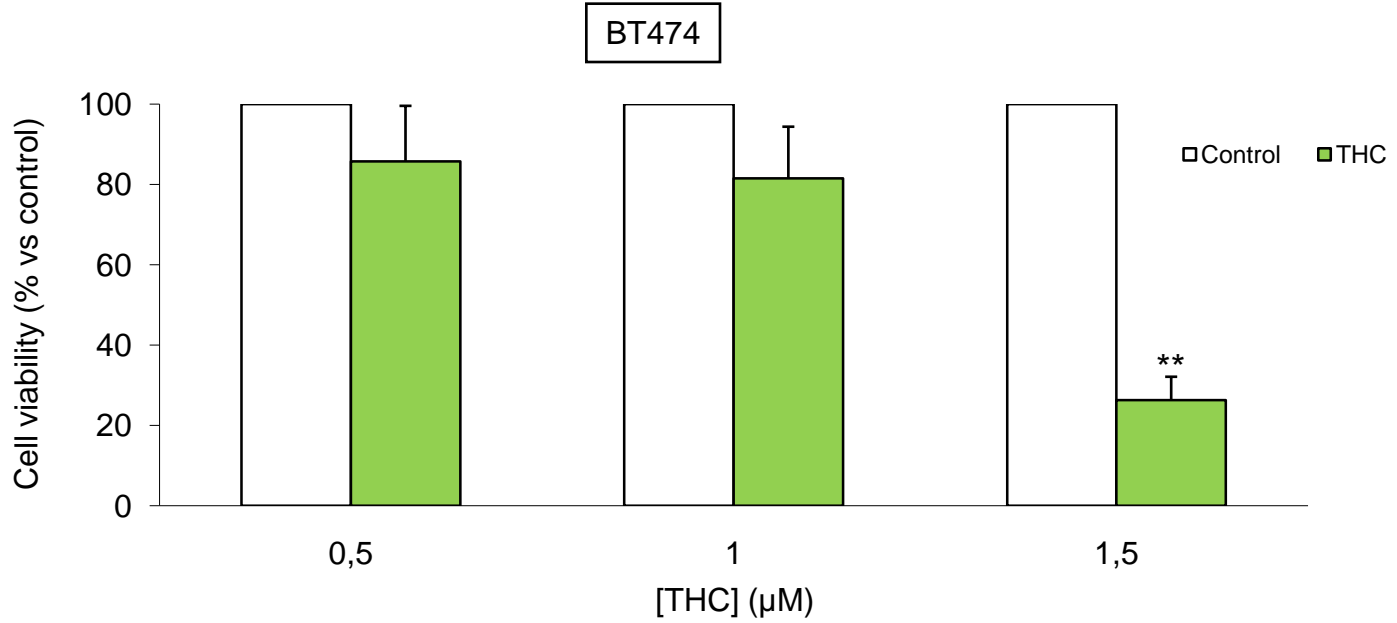


1. DO CANNABINOIDS WORK as antitumor agents?

LAB RESEARCH

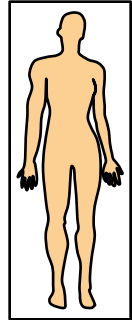


Human cells



1. DO CANNABINOIDS WORK as antitumor agents?

LAB RESEARCH



Human cells

BT474



BT474 cells
(5×10^6)



$V_0 = 200 \text{ mm}^3$

ORAL ADMINISTRATION

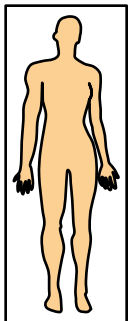


VEHICLE (sesame oil)

THC (45mg/Kg/3 days a week)

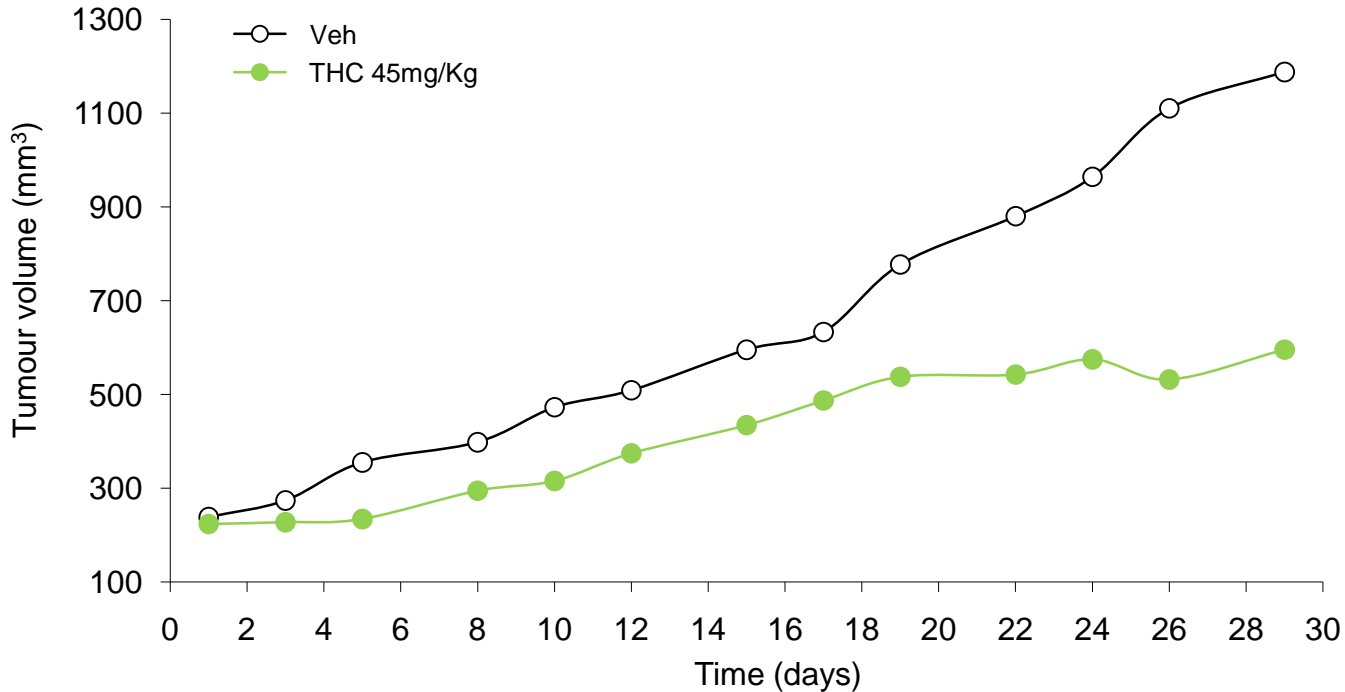
1. DO CANNABINOIDS WORK as antitumor agents?

LAB RESEARCH



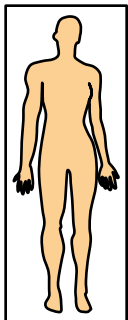
Human cells

BT474

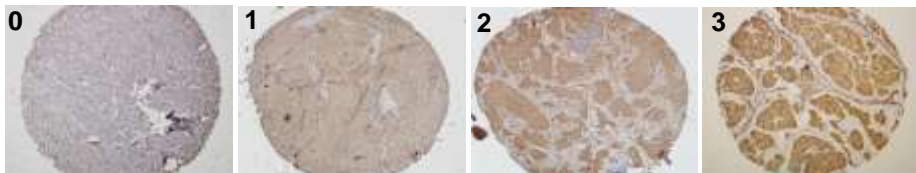


1. DO CANNABINOIDS WORK as antitumor agents?

LAB RESEARCH



Human samples



		n	CB ₂ staining				p-value
			0	1	2	3	
Hormone receptor status	Positive	504	117 (23%)	191 (38%)	135 (27%)	61 (12%)	0.655
	Negative	117	24 (21%)	41 (35%)	38 (32%)	14 (12%)	
HER2 status	Positive	92	3 (3%)	29 (32%)	39 (42%)	21 (23%)	6x10⁻⁷
	Negative	360	86 (24%)	141 (39%)	94 (26%)	39 (11%)	
Triple negative status	Positive	47	13 (28%)	20 (43%)	12 (26%)	2 (4%)	0.138
	Negative	405	76 (19%)	150 (37%)	121 (30%)	58 (14%)	

THERAPEUTIC TOOLS AGAINST CANCER

1. DO CANNABINOIDS WORK?

2. ARE CANNABINOIDS SAFE?

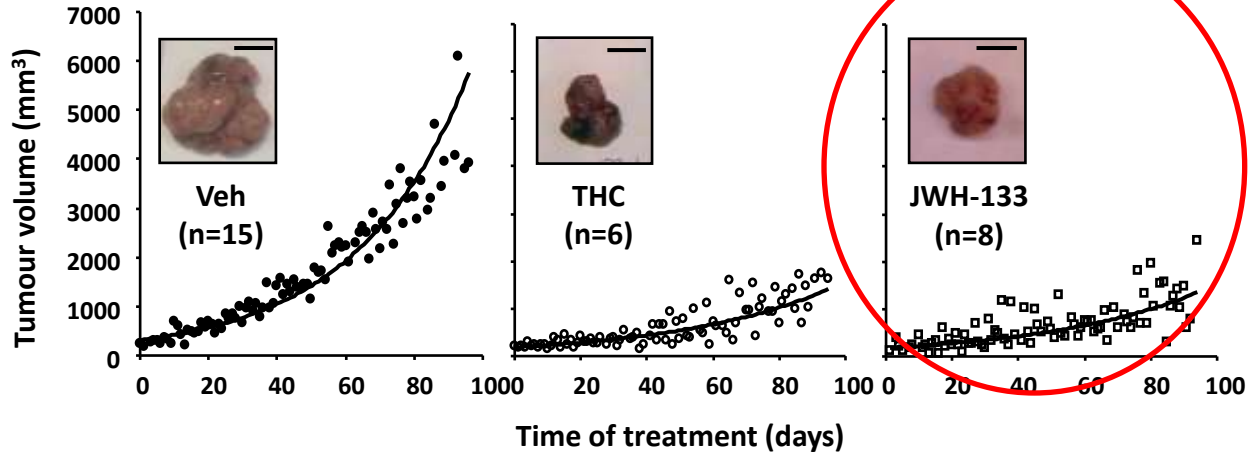
2. ARE CANNABINOIDS SAFE?

LAB RESEARCH

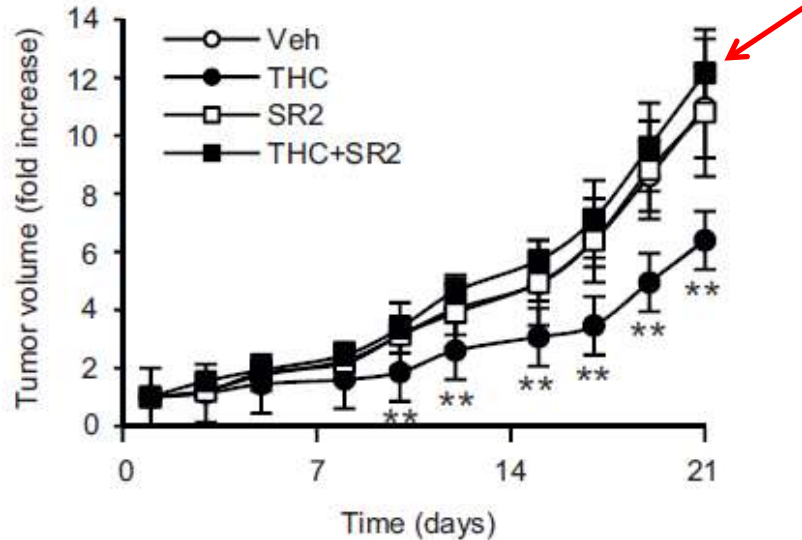


MMTV-neu mouse

EFFECT PRODUCED BY ACTIVATION OF CB2

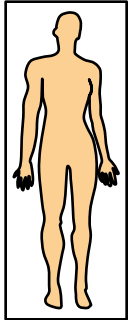


N202.1A CELLS



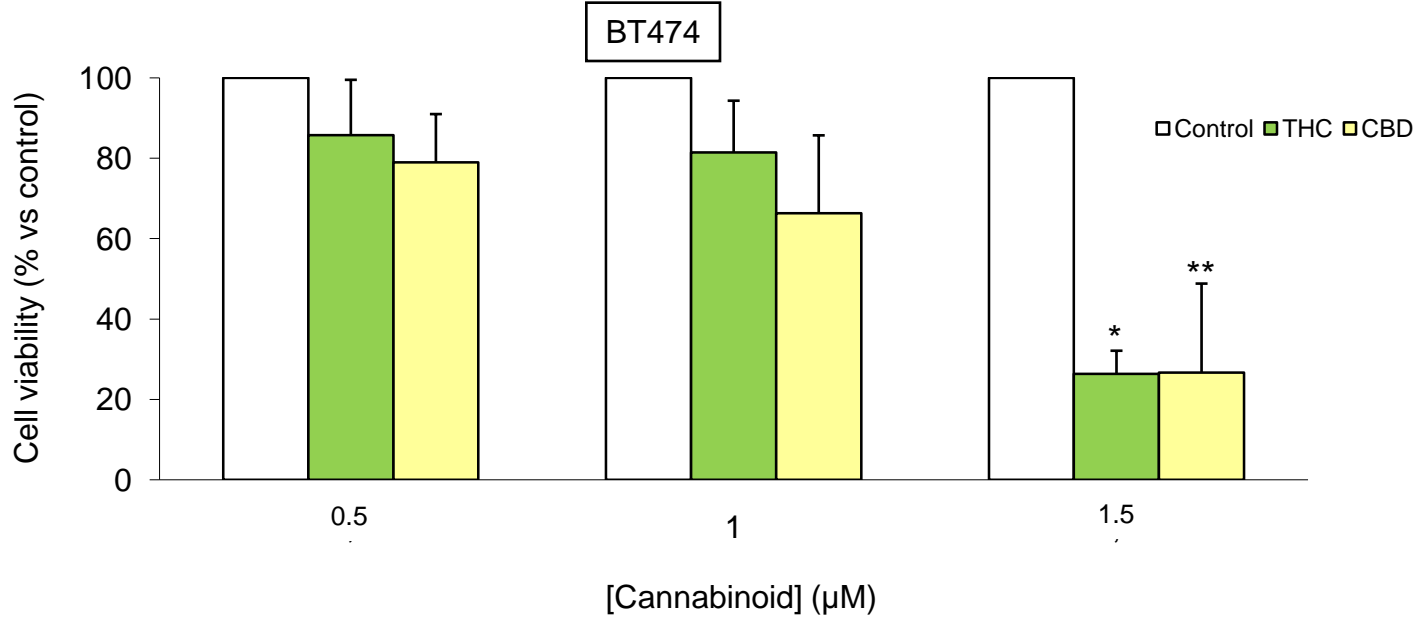
1. DO CANNABINOIDS WORK as antitumor agents?

LAB RESEARCH



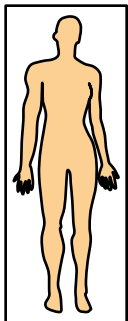
Human cells

EFFECT PRODUCED BY CBD



1. DO CANNABINOIDS WORK as antitumor agents?

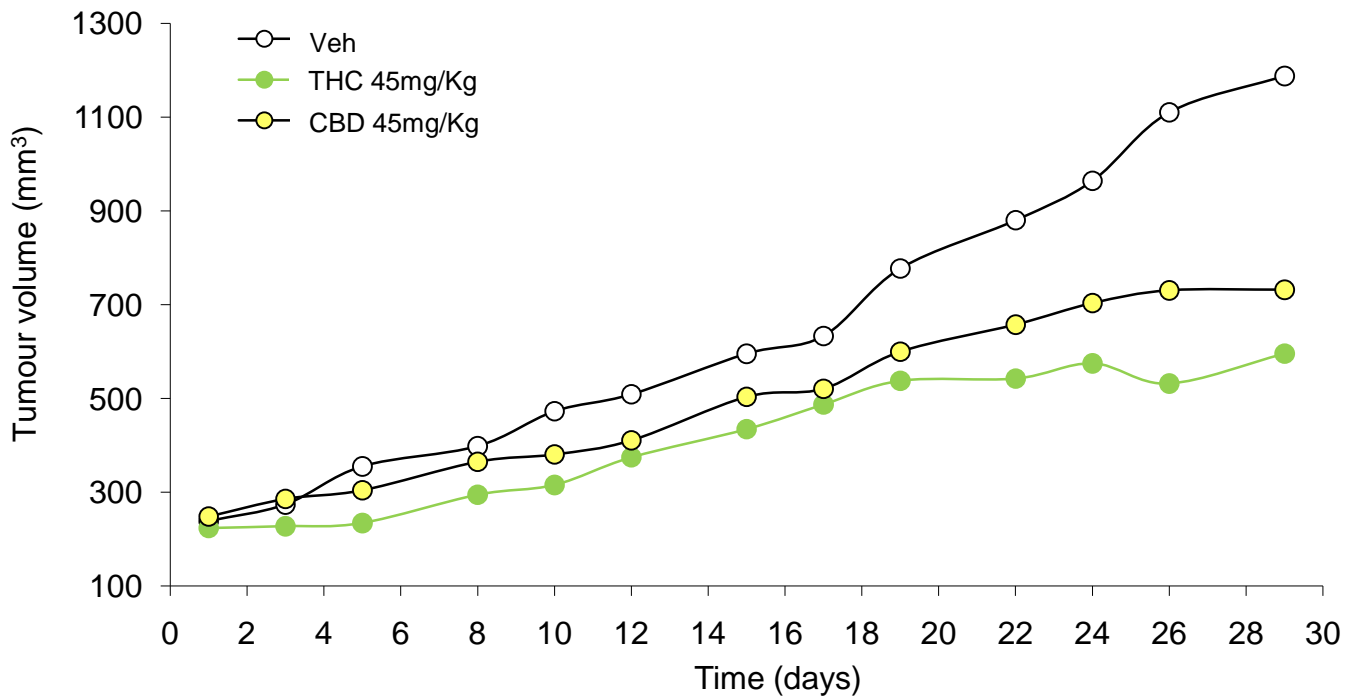
LAB RESEARCH



Human cells

EFFECT PRODUCED BY CBD

BT474



2. ARE CANNABINOIDS SAFE?

CLINICAL TRIALS

NIH U.S. National Library of Medicine

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Saved Studies (0)

ClinicalTrials.gov is a database of privately and publicly funded clinical studies conducted around the world.

Explore 256,651 research studies in all 50 states and in 201 countries.

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IMPORTANT: Listing a study does not mean it has been evaluated by the U.S. Federal Government. Read our [disclaimer](#) for details.

Before participating in a study, talk to your health care provider and learn about the [risks and potential benefits](#).

Search (all fields optional)

Condition / e.g. breast cancer

X

Disease:

Other Terms: e.g., NCT number, drug name, investigator name

X

Country:

X

Find a study to participate in

Search all studies

Advanced Search

Sativex: 371 trials completed
Marinol: 114 trials completed
CBD: 52 trials completed

THERAPEUTIC TOOLS AGAINST CANCER

1. DO CANNABINOIDS WORK?

✓ YES (in preclinical models of cancer)

2. ARE CANNABINOIDS SAFE?

✓ YES

WHAT DO WE DO NEXT?

Full Paper

A pilot clinical study of Δ^9 -tetrahydrocannabinol in patients with recurrent glioblastoma multiforme

M Guzmán^{*,1}, MJ Duarte², C Blázquez¹, J Ravina², MC Rosa², I Galve-Roperh¹, C Sánchez¹, G Velasco¹ and L González-Feria^{*,2}

¹Department of Biochemistry and Molecular Biology I, School of Biology, Complutense University, Madrid 28040, Spain; ²Department of Neurosurgery, Hospital Universitario de Canarias, La Laguna, Tenerife 38320, Spain

Primary endpoint

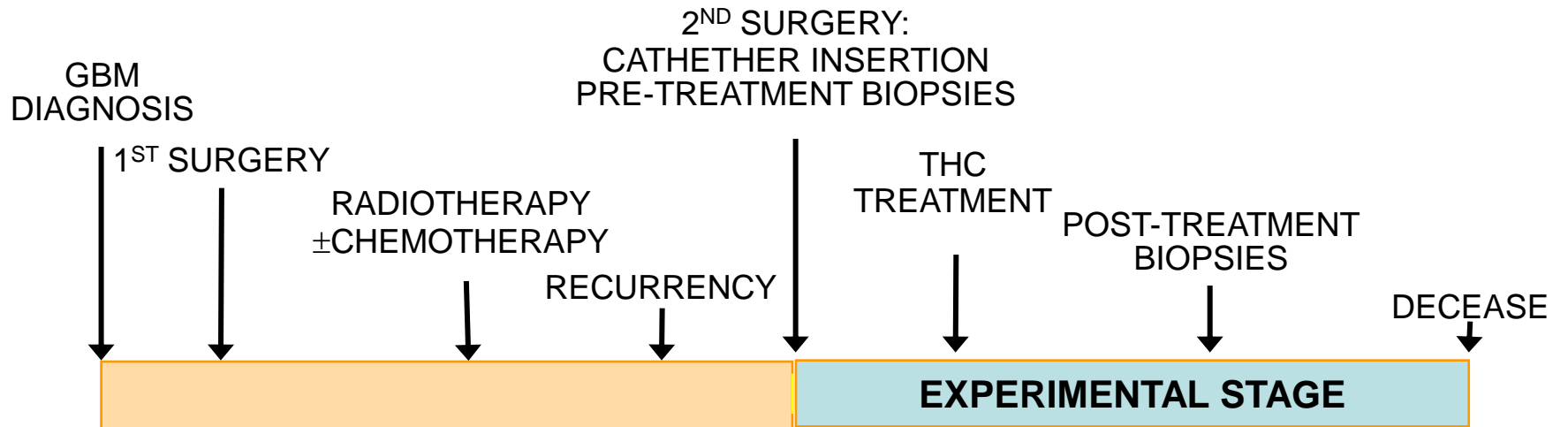
- Safety and life quality

Secondary endpoints

- Survival
- Tumor growth
- Effect on tumor markers

CLINICAL RESEARCH

THE FIRST PILOT CLINICAL STUDY



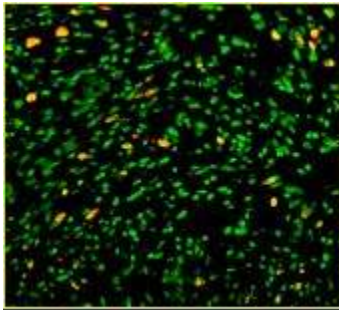
CLINICAL RESEARCH

THE FIRST PILOT CLINICAL STUDY

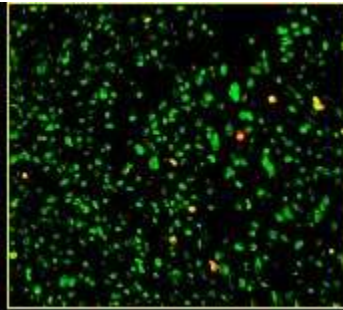
1. THC produced NO PSYCHOTROPIC EFFECTS
2. THC REDUCED TUMOR GROWTH in some patients
3. THC INCREASED LENGTH OF SURVIVAL in some patients
4. THC modulates the SAME MOLECULAR MECHANISMS as in preclinical models

CELL PROLIFERATION (Ki67)

Pre-THC

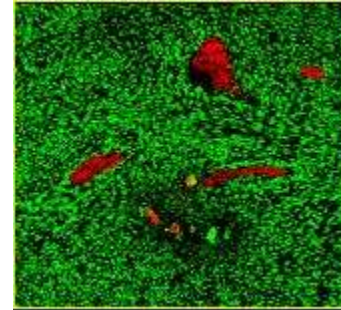


Post-THC

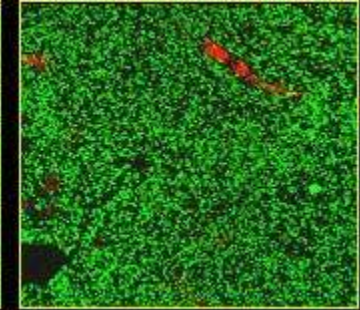


ANGIOGENESIS (CD31)

Pre-THC

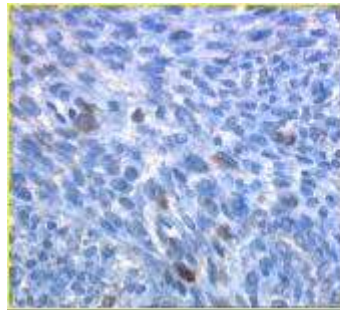


Post-THC

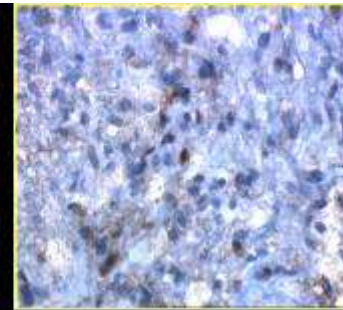


APOPTOSIS (Caspase 3)

Pre-THC



Post-THC



A Safety Study of Sativex Compared With Placebo (Both With Dose-intense Temozolomide) in Recurrent Glioblastoma Patients

Primary endpoint

- Safety in patients receiving (Sativex + TMZ) vs (Placebo +TMZ)

Secondary endpoints

- Progression-free survival at 6 months
- Overall survival



Estimated Enrollment: 20
Study Start Date: September 2014
Estimated Study Completion Date: October 2015
Estimated Primary Completion Date: October 2015 (Final data collection date for primary outcome measure)

CONCLUSIONS

PHYTOCANNABINOIDS:

- **WORK**
- **ARE SAFE:** Effects on transformed cells
 - Effects mediated by CB2
 - Effects produced by CBD
 - Clinical trials
- **HAVE ADDITIONAL ADVANTAGES:** Analgesic, orexigenic, antiemetic

NEXT STEPS

- **More preclinical data (mechanism of action, combinations with other chemotherapeutic drugs, etc)**
- **MORE CLINICAL TRIALS**

ACKNOWLEDGEMENTS

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Angela Araujo

Andrea Abaurrea

Oncology team

Cancer patients

