Update on mEHTGlio phase III trial. First results and comments.

Elisabeth Arrojo[1], Paola Navarrete[1] , Uriel Corro[1]

[1]University Hospital Marques de Valdecilla, Santander, Spain

Cite this article as:
Arrojo, E. et al. (2022): Update on mEHTGlio phase III trial. First results and comments

Oncothermia Journal 32, September 2022: 21 – 35,
http://www.oncotherm.com/sites/oncotherm/files/2022-09/Arrojo_ICHS_Update-on-mEHTGlio.pdf

ICHS 39.

39th Conference of the International Clinical Hyperthermia Society

UPDATE ON mEHTGLIO PHASE III TRIAL. FIRST RESULTS AND COMMENTS

Elisabeth Arrojo[1], Paola Navarrete[1], Uriel Corro[1].
[1]University Hospital Marques de Valdecilla, Santander, Spain

Elisabeth Arrojo Álvarez, MD, PhD

Valdecilla
Hospital Universitario Marqués de Valdecilla

Radiation Oncologist at University Hospital Marqués de Valdecilla
Medical director at INMOA (Medical Institute of advanced oncology)
ICHS President

INMOA
INSTITUTO MÉDICO DE ONCOLOGÍA AVANZADA

INTRODUCTION…

University Hospital Marqués de Valdecilla

Santander, Spain

Radiotherapy department:

- Team: 62 people.
  - 11 Radiation oncologists.
- External beam radiotherapy:
  - 3 linear accelerators:
    - Radiosurgery
    - Stereotactic RT (intra and extracraneal)
    - Image guided RT
    - Intensity modulated RT
- 2 operating rooms for Brachytherapy
  - HDR and LDR

Valdecilla
Hospital Universitario Marqués de Valdecilla

University Hospital Marqués de Valdecilla

- **The first public** hospital in **Spain** with a **mEHT** device.
- **The first public** hospital in **Spain** which will have protontherapy.

Virtual Hospital Valdecilla

- A **pioneer center in Europe** in the use of **clinical simulation for the training** of health professionals and the improvement of patient safety.
- Works in **collaboration with the Center for Medical Simulation** (Boston)

IDIVAL Research Institute

In March 2015 IDIVAL was awarded by the Spanish Institute of Health Carlos III as **one of the reference Institutes for Health Research in Spain**

Valdecilla
Hospital Universitario Marqués de Valdecilla

mEHT at Valdecilla Hospital

- Since July 2019

INMOA
INSTITUTO MÉDICO DE ONCOLOGÍA AVANZADA

Valdecilla
Hospital Universitario Marqués de Valdecilla

Medical Institute of advanced oncology INMOA - Madrid

Hyperthermia at private practice...

- 3 mEHT devices

INMOA INSTITUTO MÉDICO DE ONCOLOGÍA AVANZADA

Valdecilla Hospital Universitario Marqués de Valdecilla

ESMO OPEN | CANCER HORIZONS

ORIGINAL RESEARCH | VOLUME 6, ISSUE 3, 100157, JUNE 01, 2021

Impact of the COVID-19 pandemic on the care of cancer patients in Spain

M. Amador • X. Matias-Guiu • G. Sancho-Pardo • ... R. García-Sanz • Á. Rodríguez-Lescure • L. Paz-Ares • Show all authors

Open Access • Published: May 17, 2021 • DOI: https://doi.org/10.1016/j.esmoop.2021.100157 •

Check for updates

Highlights

- The number of new cancer patients decreased 20.8%
- Assistance protocols were adapted
- Inclusion in clinical trials decreased by 12.9%

mEHT at Valdecilla Hospital

- Stopped for 18 months

INMOA INSTITUTO MÉDICO DE ONCOLOGÍA AVANZADA

Valdecilla Hospital Universitario Marqués de Valdecilla

Hungary 28-29 September, 2018

ICHS
36th Conference of the International Clinical Hyperthermia Society

Future position of oncothermia combination with standard chemo and radiotherapy in clinical practice – Highlights of upcoming Phase III clinical studies in Hospital Universitario Marqués de Valdecilla (HUMV)

Elisabeth E. Arrojo, MD, PhD
Radiation Oncologist
University Hospital Marqués de Valdecilla, Santander, Spain

Valdecilla
Hospital Universitario Marqués de Valdecilla

INMOA
INSTITUTO MÉDICO DE ONCOLOGÍA AVANZADA

What happened with that phase III trial called mEHTGlio for GBM treated with mEHT which started 2 years ago…?

1.1 **Title: "Treatment with modulated electro-hyperthermia in high grade gliomas (grade III and IV) as an adjuvant treatment to standard radiotherapy and chemotherapy or as a unique treatment".**

INMOA
INSTITUTO MÉDICO DE ONCOLOGÍA AVANZADA

Valdecilla
Hospital Universitario Marqués de Valdecilla

What happened with that phase III trial called mEHTGlio?

- **We tend to think the results are not good if we don't have results…**

1.1 Title: "Treatment with modulated electro-hyperthermia in high grade gliomas (grade III and IV) as an adjuvant treatment to standard radiotherapy and chemotherapy or as a unique treatment".

INMOA INSTITUTO MÉDICO DE ONCOLOGÍA AVANZADA

Valdecilla Hospital Universitario Marqués de Valdecilla

What happened with that phase III trial?

- **We tend to think the results are not good if we don't have the results…**

1.1 Title: "Treatment with modulated electro-hyperthermia in high grade gliomas (grade III and IV) as an adjuvant treatment to standard radiotherapy and chemotherapy or as a unique treatment".

INMOA INSTITUTO MÉDICO DE ONCOLOGÍA AVANZADA

Valdecilla Hospital Universitario Marqués de Valdecilla

Let's remind…

5. STUDY DESIGN

This is a prospective, randomized study designed to evaluate the possible benefit in terms of better control of the disease, of adding a treatment with modulated electrohyperthermia to standard surgery, radio and chemotherapy treatments or as a single treatment in those cases that meet the inclusion criteria of the study and in which it is not possible to apply any other treatment.

It is hypothesized that treatment with modulated electrohyperthermia, will produce different beneficial effects that will impact on better oncological control such as:

- Radiosensitivity: mEHT will increase oxygenation and therefore will decrease hipoxia, improving this way radiosensitivity in those patients who will receive radiotherapy treatment concomitantly with mEHT.
- Chemosensitivity: mEHT will increase oxygenation and improve blood flow to improve the "drugs" distribution in the tumor area.
- Improve cancer cell killing: mEHT will promote cancer cell destruction through apoptosis by a mechanism of selection and modulation.

INMOA INSTITUTO MÉDICO DE ONCOLOGÍA AVANZADA

Valdecilla Hospital Universitario Marqués de Valdecilla

mEHTGlio trial: Inclusion criteria

HIGH GRADE GLIOMA
Patients able to understand and sign informed consent
Age >18 years
Karnofsky ≥ 70
• Confirmed by pathology High Grade Glioma (III and IV) • Newly diagnosed patients • Patients with relapse/progression.

INMOA INSTITUTO MÉDICO DE ONCOLOGÍA AVANZADA

Valdecilla

Update on mEHTglio phase III trial. First results and comments

- Patients diagnosed with WHO grade III/IV glioma at University Hospital Marques of Valdecilla were recruited in phase III mEHTGlio trial between August 2019 and March 2021.

- Due to COVID19's pandemic and technical reasons recruitment was **stopped for 18 months during this period**.

INMOA INSTITUTO MÉDICO DE ONCOLOGÍA AVANZADA

Valdecilla

Update on mEHTglio phase III trial. First results and comments

- Arm 1: Patients at first diagnosis randomized to:
  - Control group: Standard treatment (temozolamide + radiotherapy)
  - Experimental group: Standard treatment
    + mEHT:
    - 5 times a week (30 minutes before radiotherapy).
    - One hour treatment
    - Power between 45 and 60W.
- Arm 2: Patients with progression after standard treatment, treated with mEHT in monotherapy or concomitant with CT.
  - mEHT:
    - 3 times a week.
    - One hour treatment
    - Power between 45 and 60W.

INMOA INSTITUTO MÉDICO DE ONCOLOGÍA AVANZADA

Valdecilla

RESULTS

- Due to COVID19's pandemic and technical reasons recruitment was **stopped for 18 months during this period.**

  - 26 patients were recruited.

INMOA INSTITUTO MÉDICO DE ONCOLOGÍA AVANZADA

Valdecilla Hospital Universitario Marqués de Valdecilla

Arm 1: Randomized:

Control group: Standard treatment vs

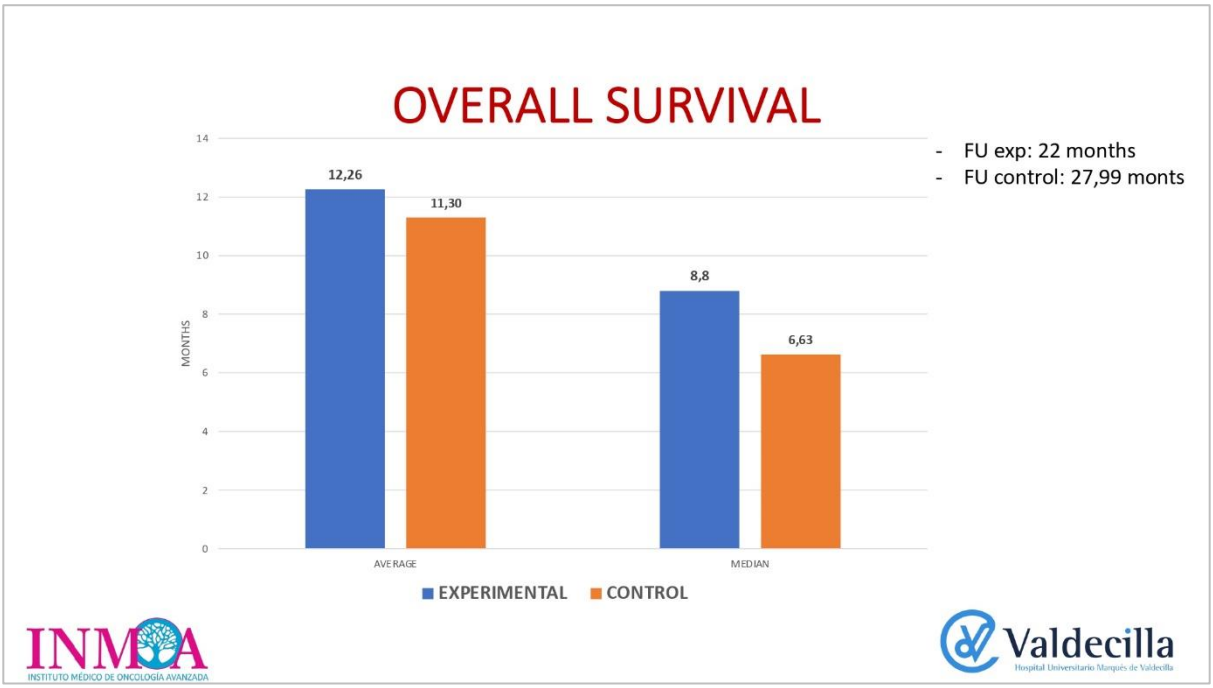
Experimental group: Standard treatment+mEHT.

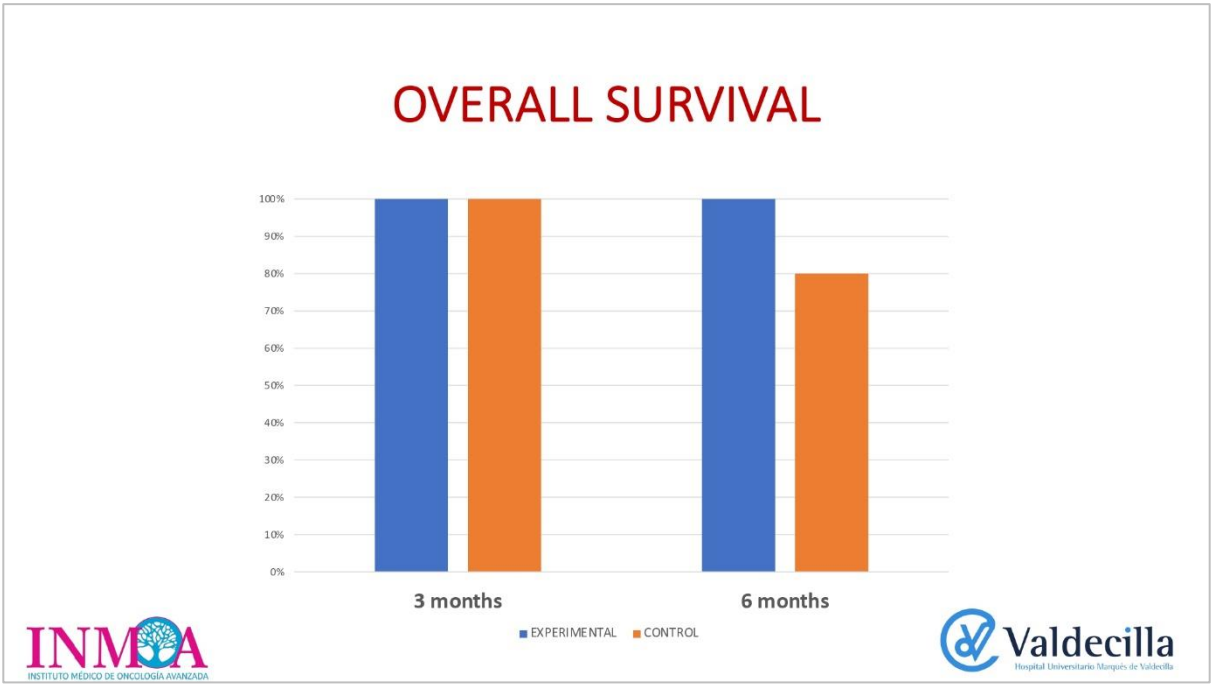
- 14 patients:
  - 8 patients randomized to Experimental group
  - 6 patients randomized to control group
- 4 patients were excluded for this report:
  - 3 did not begin/complete treatment (2E and 1C group).
  - 1 was a grade III glioma (E group). Due to the low number of patients recruited and in order to make more comparable groups the grade III patient was excluded.

ARM 1	EXPERIMENTAL	CONTROL
N (Patients evaluated)	5	5
Average Age	53	61
IDH Status	17% Positive (n=1)	17% Positive (n=1)
Average Follow-Up	22,09 months (8,8-28,4)	27,99 months (22,10-30,4)

INMOA INSTITUTO MÉDICO DE ONCOLOGÍA AVANZADA

Valdecilla Hospital Universitario Marqués de Valdecilla


OVERALL SURVIVAL
14
12
10
8
6
4
2
0
MONTHS
12,26
11,30
8,8
6,63
AVERAGE
MEDIAN
EXPERIMENTAL
CONTROL
- FU exp: 22 months
- FU control: 27,99 monts
INMA
INSTITUTO MÉDICO DE ONCOLOGÍA AVANZADA
Valdecilla
Hospital Universitario Marqués de Valdecilla


OVERALL SURVIVAL
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
3 months
6 months
EXPERIMENTAL
CONTROL
INMA
INSTITUTO MÉDICO DE ONCOLOGÍA AVANZADA
Valdecilla
Hospital Universitario Marqués de Valdecilla

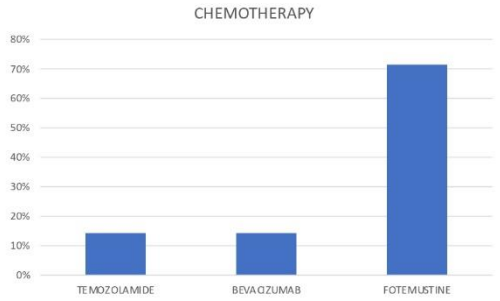
Arm 2: Patients under progression after ST, treated with mEHT in monotherapy or concomitant with CT.

- 12 patients recruited
  - 2 patients did not complete treament because of very advanced disease.
  - 2 patients treated in monotherapy showed no response (very advanced tumor. Limited Karnofsky).
  - 8 patients treated with mEHT + chemotherapy.

INMOA INSTITUTO MÉDICO DE ONCOLOGÍA AVANZADA

Valdecilla Hospital Universitario Marqués de Valdecilla

Arm 2: Patients with progression after ST, treated with mEHT concomitant with CT.



- N= 8
  - 50% progressed
  - 50% responded (4 patients)
    - 2 treated with Fotemustine:
      - 1 alive after 7 months and showing good response.
      - 1 died 7 months after beginning mEHT
    - 1 treated with Bevacizumab died 6 months after beginning mEHT
    - 1 treated with Temozolamide died 6,4 months after beginning mEHT

All but one: 4 weeks treatment → wait 8 weeks for MRI → if Ok → 4 weeks treatment → and so on..

INMOA INSTITUTO MÉDICO DE ONCOLOGÍA AVANZADA

Valdecilla Hospital Universitario Marqués de Valdecilla

CONCERN!

- One feeling…
  - Patients progress mainly when we stop treatment?
    - "Feeling" from the trial at Public hospital and experience outside the trial at private practice…

- (• 3 mEHT devices

here.
ways" there?

Arm 2: Patients with progression after ST, treated with mEHT concomitant with CT.

- 50% progressed
- 50% respo d (4 patient
  - 2 treated with Fotemustine:
    - **1 alive after 7 months and showing good response.**
    - 1 died 7 months aft ginning
  - 1 treated with Bevacizumab died 6 months after beginning mEHT
  - 1 treated with Temozolamide died 6,4 months after beginning mEHT

CONCERN!

- Patients progress mainly when we stop treatment?
- Glioblastoma is ALWAYS there.
  - Treatment should be always there?

- **We are thinking about changing trial's protocol in order to go on with treatment until progression.**

Toxicities

- Minor toxicities: <5% light headache for less than 1 hour.
- No epileptic seizures.
- **No** grade III or IV toxicities.

CONCLUSIONS:

- These are the first preliminary results from a phase III trial comparing ST vs ST+mEHT in patients diagnosed with high grade glioma.
- We don't have conclusions…
  - … Yet
- COVID19 pandemic has delave[illegible] **we don't have enough number of patients to ri[illegible]** [illegible]h groups seem to be comparable and the [illegible]er results regarding overall survival.
- Adding mEHT to RT/C[illegible] [illegible]oxicities.
- **More patients and follo[illegible] needed to rise conclusions.**

INMOA INSTITUTO MÉDICO DE ONCOLOGÍA AVANZADA

Valdecilla Hospital Universitario Marqués de Valdecilla

ICHS 39.

39th Conference of the International Clinical Hyperthermia Society

5 November, 2021

You still have to come to Spain!!!

Thank you!

earrojo@inmoa.es

INMOA INSTITUTO MÉDICO DE ONCOLOGÍA AVANZADA

Valdecilla Hospital Universitario Marqués de Valdecilla