P-05 – Prof. Dr. Andras Szasz - Brain glioma results by oncothermia

oncotherm high tech medicine

Brain glioma results by oncothermia

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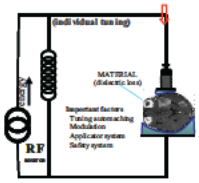
Objective

None of the established state of the art treatments in malignant primary brain tumors, especially in glioblastoma multiform (GBM), could show effective or commonly accepted curative potential until today The editorial question of JAMA [1] in 2005 is actual even now "Where to go from here?" Our objective to show a feasible way to go, summarizing the results obtained till now made by modulated electro hyperthermia (oncothermia) in various clinics in EU

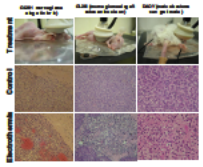
Method

Data are collected from GBM and anaplastic astrocytoma (AA) published observational studies The method is transcranially applied modulated RF current capacitive coupled at 13 56 MHz carrier frequency, (Oncotherm, EHY2000+) described in details elsewhere [2] The applied protocol was unified step up heating, 40 150 W RF power with water bolus cooling Treatment is applied in combination with chemo and/or radio therapy or used as monotherapy if the conventional therapies fail

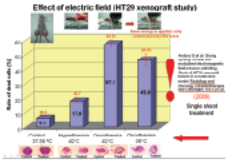


Specialties of the method

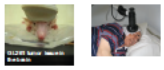
Detailed laboratory experiments had proven the efficacy of oncothermia on brain glioma cell lines



It is effective on low temperatures also Consequence applicable for brain



Due to the low temperature It is applicable near the eye



Easy to manage the treatment

Results

Study 1 Prospective single-arm Phase I/II study, [21], [22];

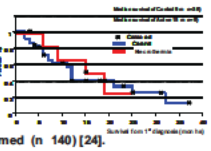
(Neurology Clinic, Regensburg University, Germany) Investigators Prof U Bogdahn & Prof P Hau Electrothermia is NON TOXIC (even by high dose escalation) It could stabilize the state of patients in highly advanced cases (n 15) **Examples:**

Patient: RE 013 4 48y mae Anapastic Oligoastrocytoma WHOIII 2 resections (partial) 3 relapses **1st therapy:** Radio Tx **2nd therapy:** PCV (Procarbazine CCNU and Vincristne); **3rd therapy:** Temizo omide (Temodal); **4th therapy:** Nimustin(ACNU) + **Electrothermia,** Cycles of ACNU: 3 Cycles of electrothermia 3 Sessions of electrothermia: 60 (5/w); **Karnofsky** score at start: 70 **Karnofsky** score at end: 60 Best performance: **STABLE DISEASE (SD)**

Patient: RE 014 4 49y mae Glioblastoma multiforme WHOIV 2 resections (partial) 3 relapses **1st therapy:** Radio Tx + Tem zolomide (Temodal)/PEG Dox **2nd therapy:** Epothilone **3rd therapy:** Temizo omide (Temodal) Int ; **4th therapy:** Nimust n(ACNU) + **Electrothermia,** Cycles of ACNU: 2 Cycles of electrothermia 3 Sess ons of electrothermia: 55 (5/w); **Karnofsky** score at start: 80 **Karnofsky** score at end: 80 Best performance: **STABLE DISEASE (SD)**

Study 2 Prospective double-arm Phase II study, [23].

Prospect ve double arm braingl oma study (control arm n=36 act ve arm n=9) study or advanced primary brain tumors (gl omas WHO IV) was done in Nurnberg (Klinkum Nürnberg Nord Nürnberg Germany Investigabr: Prof Dr H Ranner) Trimodal therapy was app ied: radiotherapy (50 60 Gy) chemotherapy (Temodal) and electrothermia (6 12x 60 min) The med an survival was measured on control arm as 9m while in the active e actrothermia arm it was 15m

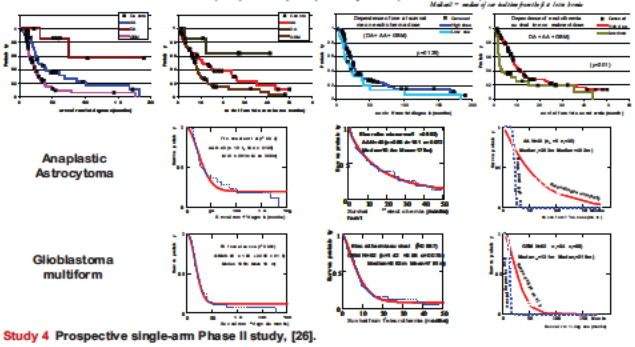


Study 3 Retrospective single-arm Phase II/III study was performed (n 140) [24].

Retrospective single arm brain glioma study for advanced primary brain tumors was done (in all cases the gold standards were failed)

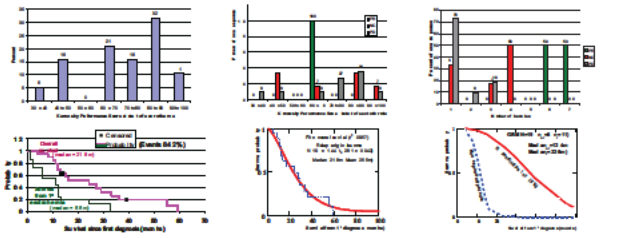
WHO grade	# Pts	Median (m)	(min - max)	n	Median (m)	(min - max)	n	Average (m)	(Std er)	n	Average (m)	(Std er)
DA	8	58.2	22 190	11 6	1 1 41	25 6	18 6	1 56	5 3			
AA	48	25 6	3 6 18	9 1	1 4 50	49 3	7 0	1 34	3 0			
GBM	82	18 0	1 4 13	5 1	0 3 48	20 0	2 5	0 0	0 0			

DA = diffuse astrocytoma AA = anaplastic astrocytoma GBM = glioblastoma multiforme Median = median of overall survival time Median = median of survival time from first relapse

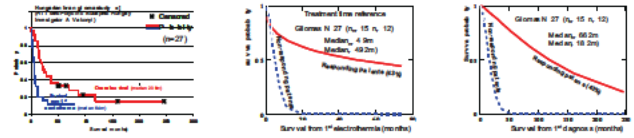


Study 4 Prospective single-arm Phase II study, [26].

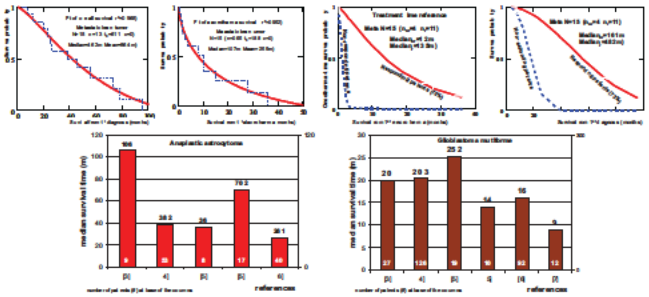
ACNU combinat on (60 mg/m2) which was used for sa ety (Phase I; dose escala ion) tr al had bee used in Phase II as well for recurrent glob astoma (n=19) (Klink St Georg Bad Aibling Germany Investigator: Dr F Douwes [19]) The quality of life of patients was measured by standard Karnofsky Performance Score (KPS) The obtained median of overal survival was 21 8m (average survival 25 5m); while the median survival from first electrothermia was 8 8m (average survival 13 5m) Fig 24 The ocal cl nical response had no complete remission and 58% of the patients were in progressive disease (not responding on electrotherm a) The ratio of responding patents is 59% (failing 41%) calculated by the parametric selection This difference could be caused by the relatively short follow up in the trial

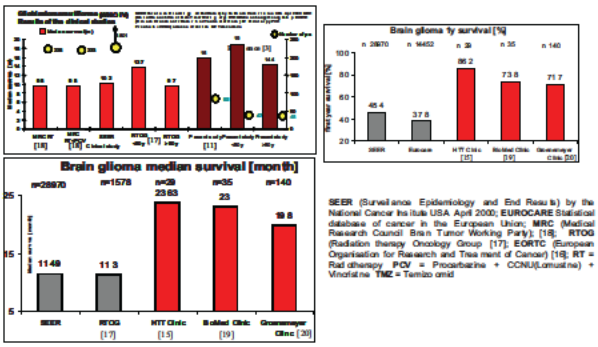


Study 5 Retrospective single-arm Phase II study [25].



Study 6 Retrospective single-arm study for metastatic brain tumors (n 15) [27]





SEER (Surveil ance Epidemiology and End Resu ts) by the National Cancer Ins tute USA April 2000; **EUROCARE** Statistical database of cancer in the European Union; **MRC** (Medical Research Council Brain Tumor Working Party); [18]; **RTOG** (Radiation therapy Oncology Group [17]; **EORTC** (European Organisation for Research and Trea ment of Cancer) [18]; **RT** = Rad ctherapy **PCV** = Procarbazine + CCNU(Lomustine) + Vincristne **TMZ** = Temizo omid

Toxicity

A well designed Phase I study shows the safety of the method [8] The dose escalation has no extra hazard even in very frequent applications

Conclusion

The results are strongly indicating the feasibility and the benefit of the oncothermia showing a valid treatment potential and safe application Oncothermia is a potential way to escape from the present impasse situation and treat brain gliomas successfully Performing prospective, randomized clinical trials in the future is mandatory

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