ThT 15

PHASE II STUDIES OF 1,2,4-TRIGLYCIDYLURACOL (TGU) IN SOLID TUMORS

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TGU is a new triepoxide derivative with a wide spectrum of activity against experimental tumors. Phase II trials were initiated in breast carcinoma (23 patients), non small cell carcinoma of the lung (14), colon and rectum (14) and renal carcinoma (16). All patients had measurable disease. TGU was administered 600-800 mg/m² d 1 or 200 mg/m² d 1-5.

Out of 61 evaluable patients, 45 obtained 2 treatment cycles and could be evaluated for response. 2 showed partial remissions suggesting an overall response rate of 4.4%. Considerable leuko- and thrombocytopenia, nausea/vomiting, local reactions and 1 drug related death were observed. The data suggest minimal activity of TGU in solid tumors.

Phase-II-Studiengruppe der Arbeitsgemeinschaft für internistische Onkologie (AIO) der Deutschen Krebsgesellschaft

ThT 16

GERMAN - AUSTRIAN STUDY ON MALIGNANT SUPRATENTORIAL GLIOMAS

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This randomized study with central review of the histology started in fall 1983 and compares the efficacy of "adjuvant" BCNU as best known chemotherapy starting simultaneously with radiotherapy 2-4 weeks after surgery (biopsies included) with the combination of BCNU + VM 26. As chemotherapy per se has not a major impact on survival times in malignant gliomas we regarded a prolongation of the median survival time of 20% as therapeutically relevant. For this reason the study design requires 250 patients for each treatment group. In comparison with the similar studies of the American BTSG there are some differences: 1. age limit: (<70 years) 2. strict Karnofsky score limit: (>50%) 3. irradiation schedule: instead of 60 Gy to the whole brain 40 Gy + 20 Gy to the tumor site. 4. chemotherapy schedule: BCNU 80 mg/sqm x 3 or additionally 50 mg/sqm VM 26 x 2 are administered every 6 (instead of 8) weeks and lower doses than 75% of the original dose were not given but the time interval between the cycles was prolonged. 5. strict monitoring of the lung toxicity by pulmonary function tests. Hematological toxicity did not differ in the 2 groups. Drop out rate in both groups is about 24%. Interim analysis based on 164 pts showed no important difference in the survival curves. Median survival times are not fixed now but will reach more than 17 months in both groups. Probability to survive more than 18 months is 54% and 60%, respectively. This compares favorable to the 10-12 months median survival times and at best 23% living 18 months achieved in the previous studies of the American BTSG. This study is supported by the Bundesministerium für Forschung und Technologie. Participating centers: FU Berlin, SK Duisburg, Uni Essen, Uni Hamburg, MHH Hannover, SK Ingolstadt, Uni Innsbruck, Uni Kiel, Uni Mainz, Uni Marburg, AK Wien-Lainz, Uni Würzburg. Statistik: BZT München, Neuropathologie: Zürich^{*}
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ThT 17

EARLY STAGE NON-SEMINOMATOUS TESTIS TUMOR. CURRENT TRIALS. L. Weißbach, EA. Boedefeld, JH. Hartlapp and entire Study Group

Three prospective multicenter trials explore possibilities to diminish damages or toxic side-effects of treatment. In path. stage I modified LA is compared to radical LA regarding postop. ejaculation, and frequency of relapse, particularly retroperitoneal. Random trials in stage II after rad. LA study the feasibility of dispensing with adjuvant chemotherapy in IIA, and decreasing number of courses PVB(EINHORN) in IIB. Localisation of solitary lymph node(LN)metastases are recorded to confirm the anatomic basis of mod. LA. Stage I: Mod.LA is restricted to ipsilateral LNs, nerves essential to ejaculation are preserved. Postop. emission was intact in 94/126 mod. and 20/53 rad. pts. (75 vs. 38%). Frequency of relapse was 15% and 16%, resp., with retroperitoneal relapse below 2% in either group. Mod.LA thus permits highly accurate staging with small risk of lasting dyspermia rendering rad.LA unjustifiable in stage I. It appears superior to surveillance with >20% risk of retroper. relapse. Stage IIA(solitary mets. < 2 cm): 48 pts. were randomized to (a) observation only or (b) 2 courses PVB. 38 pts. are followed 3-24 mo (median 18 mo). 1 pt. in (a) relapsed. Stage IIB(mult. mets. < 5 cm): 173 pts. randomized to (a) 2 or (b) 4 courses PVB. 131 pts. are followed, median 17 mo. 2 pts. in (a) relapsed, 1 pt. died of pneumonia after 1 course. Toxicity is discussed by HARTLAPP, WEISSBACH, BOEDEFELD (see abstract). Localisation of solitary mets.: with left testis tumor, 32/38 paraaortic, 4/38 preaortic; with right tumor, none of 36 mets. in paraaortic or left iliac regions. Mult. mets. spread over entire retroperitoneal space yet rarely in ext. iliac region.

The Testicular Tumor Study Group includes 56 clinics in BRD, West-Berlin, Austria. Trials are supported by Federal Ministry of Research and Technology, grants ZP 041 and ZP 051.

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ThT 18

PHASE-II-STUDY: COMBINATION OF CISPLATINUM, VINDESINE AND DACARBAZINE IN ADVANCED MALIGNANT MELANOMA

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Cytostatic chemotherapy has been generally of limited benefit in disseminated malignant melanoma. Single agent treatments have yielded objective response rates (ORR) in a decreasing percentage of 10-14%, with DTIC being one of the best available agents. In polychemotherapy protocols the ORR have reached a plateau of about 25%. The EORTC-MMCG embarked on a controlled trial in melanoma patients with documented progression of measurable lesions and without prior chemotherapy with cDDP, Vds or DTIC. The treatment was repeated every 4 weeks with DTIC (450 mg/m² d1+8 i.v.), Vds (3 mg/m², d1+8 i.v.) and cDDP (50 mg/m² d1+8 i.v.) on an ambulatory basis. 104 patients from 12 institutions have entered the trial with 87 patients being available for an analysis of ORR and remission duration. In general the objective and subjective toxicity of the polychemotherapy was acceptable with 139 of 602 (23%) treatment courses to be modified because of toxicity. The preliminary response rate analysis: CR=4 (for 31, 65 and 91 weeks), PR=19 (for a median of 9.5 w), stable disease=20 and progress = 44, totalling an ORR of 26% (95% C.I., 17-36%). The preliminary response rate by site gives 29% ORR for skin- and 93% for lymphnode-metastases, 33% for lung- and 25% for liver-metastases. No additive or synergistic antitumor activity could be demonstrated with this 3-drug-regimen. Extramural review and careful interdisciplinary discussion proved to be of utmost importance for the selection of optimal treatment and the scientific evaluation of its benefit.

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