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SIOP CNS GCT II aimed to establish if 24Gy Whole Ventricular Radiotherapy (WVRT) in localised germinoma is sufficient for tumour control. After central review of radiological response after 'CarboPEI' chemotherapy, patients in complete remission (CR) were consolidated with 24Gy WVRT. Between 2/2012 and 7/2018, 182 patients from 8 European countries with histologically-confirmed fully-staged localised germinoma were registered. 70 patients were in CR after chemotherapy, 98 in partial remission (PR), seven had stable disease, two progressive disease, and in five no response data were documented. Of the 70 patients in CR, 58 received 24Gy WVRT alone; two of these relapsed, one local and one disseminated, two and six years after diagnosis. Of the 98 patients in PR after chemotherapy, 86 received 24Gy WVRT and 16Gy boost, of which five relapsed (three local, two distant) 12–24 months from diagnosis. Twelve patients in each of the CR/PR groups received non-protocol or undocumented radiotherapy fields/doses. Median follow-up was 3.7 years. Event-free survival (EFS) for patients in CR and with WVRT only (n=58) was 98% at 4 years. 4-years EFS of patients with PR and WVRT 24Gy and 16Gy tumor boost (n=86) was 95%. Localised germinoma in CR after chemotherapy had an excellent outcome with 24Gy WVRT alone; 24GY WVRT can therefore be considered standard consolidation treatment in this group. International consensus on radiological response criteria is of utmost importance to avoid over- and undertreatment of such patients and to pave the way for further treatment reduction in this group of patients.

HIGH GRADE GLIOMA

HGG-01. ENTRECTINIB IN RECURRENT OR REFRACTORY SOLID TUMORS INCLUDING PRIMARY CNS TUMORS: UPDATED DATA IN CHILDREN AND ADOLESCENTS

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STARTRK-NG (phase 1/2) is evaluating entrectinib, a CNS-penetrant oral, TRK/ROS1/ALK tyrosine kinase inhibitor, in patients <21 years with recurrent/refractory solid tumors, including primary CNS tumors. After determining the recommended dose, 550mg/m^2/day, in all-comers, expansion cohorts with gene-fusion-positive CNS/solid tumors (*NTRK1/2/3*, *ROS1*) are being enrolled. As of 5Nov2019 (data cut-off), 39 patients (4.9m–20y; median 7y) have been evaluated for response, classified as complete (CR) or partial response (PR), stable (SD) or progressive disease (PD) using RANO (CNS), RECIST (solid tumors), or Curie score (neuroblastoma). Responses in patients with fusion-positive tumors were Investigator-assessed (BICR assessments are ongoing) and occurred at doses ≥400mg/m^2. Best responses in fusion-positive CNS tumors (n=14) were: 4 CR (*GKAP1-NTRK2, ETV6-NTRK3* [n=2], *EML1-NTRK2*); 5 PR (*KANK1-NTRK2, GOPC-ROS1, ETV6-NTRK3, TPR-NTRK1, EEF1G-ROS1*); 3 SD (*BCR-NTRK2, ARHGEF2-NTRK1, KIF21B-NTRK1*); 2 PD (*PARP6-NTRK3, EML4-ALK*); and in fusion-positive solid tumors (n=8) were: 3 CR (*ETV6-NTRK3* [n=2], *DCTN1-ALK*); 5 PR (*EML4-NTRK3, TFG-ROS1* [n=3], *KIF5B-ALK*). Responses (Investigator-assessed) in non-fusion tumors (n=17) were: 1 CR (*ALK F1174L* mutation), 3 SD, 10 PD, 3 no data/unevaluable. The objective response rate (CR+PR/total) in patients with fusion-positive tumors was 77% (17/22) versus 6% (1/17) in those with non-fusion tumors. All 39 patients experienced ≥1 adverse event (AE); the most frequent AEs included weight gain and anemia (both 48.7%); increased ALT, increased AST, cough and pyrexia (all 46.2%); increased creatinine and vomiting (both 43.6%); and bone fractures (n=10, in 9 patients). Entrectinib has produced striking, rapid, and durable responses in solid tumors with target gene fusions, especially high-grade CNS neoplasms.

HGG-02. ADOLESCENT AND YOUNG ADULT (AYA) GLIOMA WITH BRAF V600E-MUTANTATION

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BACKGROUND: Biological features of pediatric glioma differ significantly from those of adult glioma, and limited data are available on those of AYA patients. Here, we focused on AYA patients with glioma, especially those harboring BRAF V600E mutation, and investigated their clinical and genetic features. METHOD: We retrospectively analyzed AYA patients with brain tumors harboring BRAF V600E, who were treated in two hospitals in Japan. RESULTS: Clinical information was available for 14 patients. The median age at diagnosis was 25 years (range: 15–38). Five patients were diagnosed with glioblastoma (GBM), including one epithelioid type. These patients were over 25. Although one patient with GBM died of the disease 6.9 years after initial diagnosis, the remaining patients were alive. Two patients were alive without recurrence at 38 and 51 months after the treatment. The patient with epithelioid glioblastoma experienced early recurrence. The remaining nine patients (64%) were diagnosed with low-grade glioma, including ganglioglioma, pilocytic astrocytoma, diffuse astrocytoma, oligodendroglioma, pleomorphic xanthoastrocytoma, and polymorphous low-grade neuroepithelial tumor of the young. No patients died of the disease, and four patients are alive without recurrence after initial operation without adjuvant treatment. Two patients are (epithelioid glioblastoma and ganglioglioma) currently undergoing treatment with a BRAF inhibitor for recurrent tumors. DISCUSSION: Although the number of this study is limited, our study suggested that the prognosis of AYA patients with BRAF-V600E positive GBM may not be as dismal as that of children or adults.

HGG-04. ZINC ENHANCES TEMOZOLOMIDE CYTOTOXICITY IN PEDIATRIC GLIOBLASTOMA MULTIFORME MODEL SYSTEM

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BACKGROUND: Temozolomide (TMZ) is an alkylating agent that has become the mainstay treatment of the most malignant brain cancer, glioblastoma multiforme (GBM). Unfortunately only a limited number of patients respond to it positively. We have shown that zinc metal reestablishes chemosensitivity in adult GBM in vitro and also in vivo but this effect has not been tested with pediatric GBM. METHODS: Using Human pediatric glioblastoma cell lines- KNS42 (mutant p53/ MGMT [+]) and SF188 (mutant p53/ MGMT [-]), we investigated whether addition of zinc to TMZ enhances its cytotoxicity against GBM. RESULTS: *In vitro* cell viability analysis showed that the cytotoxic activity of TMZ was substantially increased with addition of zinc and this response was accompanied by an elevation of p21, PUMA, BAX and a decrease in growth fraction as manifested by low ki67. Beta gal analysis showed that most of the remaining cells after the combination therapy are in senescence state. In order to eliminate the senescent population created as a result of the combined treatment of TMZ and Zinc, we decided to use a senolytic agent Navitoclax (ABT-263) that was demonstrated to be effective in reducing senescent cells by specific in-