is limited due to its high invasiveness, and immunotherapy utilizing self-immune mechanism is theoretically expected. An autologous formalin-fixed tumor vaccine (AFTV) is a vaccine that is prepared using formalin-fixed tumor tissue and recognizes tumor antigen peptides to induce cytotoxic T cells. We have previously conducted three clinical trials using AFTV for patients with newly diagnosed glioblastoma since 2004. The third trial was a double-blind multicenter phase IIb/III trial with 63 case registries, which did not make a significant difference in OS (study group 25 months, placebo group 31 months), the total removal group showed excellent clinical results (3-year survival rate; 65%, median survival; not reached). Since the study was designed to go to Phase III if the test group was not inferior to the placebo group, so it went on to go to Phase III. METHODS: Target patients will be 80 patients with newly diagnosed glioblastoma undergoing pathologic diagnosis, who have undergone total removal of contrast-enhanced lesions and receive standard chemoradiation therapy. STUDY DESIGN: Double-blind, 3-year enrollment period, 18-month observation period. Stratification factor: Photodynamic therapy (PDT), facility, age, KPS. Administration method: After standard chemoradiotherapy, in parallel with maintenance chemotherapy, a total of 9 times intradermal administration of vaccine. Primary endpoint: PFS of FAS patients, Secondary endpoints: 18 months PFS of the FAS patient, OS, PFS of the ITT analysis target case. Based on the results of the IIb trial, we limited the registered patients with total tumor removal, and in view of the fact that the prognosis of patients with combined PDT and AFTV were excellent, PDT was added to the stratification factor. We outline our efforts and problems aimed at clinical approval of AFTV for glioblastoma.

IMT-07

CLINICAL TRIAL OF A COCKTAIL WILMS' TUMOR 1 (WT1) VACCINATION USING TWO HLA CLASS I PEPTIDES AND ONE CLASS II PEPTIDE FOR RECURRENT MALIGNANT GLIOMAS

Naoki Kagawa[1], Yusuke Oji, Akihiro Tsuboi, Ryuichi Hirayama[1], Noriyuki Kijima[1], Manabu Kinoshita[1], Yoshihiro Oka, Haruo Sugiyama, Haruhiko Kishima[1]; [1]Department of Neurosurgery, Osaka University Graduate School of Medicine, Osaka, Japan

PURPOSE: Our clinical trials shows the safety and clinical efficacy of Wilms' tumor 1 (WT1) human leukocyte antigen (HLA) class I (Izumoto S et al. J Neurosurg. 2008) and class II (Tsuboi A et al. Cancer Immunol Immunother. 2019) peptide vaccination for recurrent malignant gliomas have been established. We have developed a cocktail vaccine (WT1 trio) containing two class I peptides (HLA-A*24:02 and HLA-A*02:01) and one II class peptide to improve more effective immunological response and improve patient's prognosis. Clinical trial of a cocktail vaccination using WT1 HLA class I and II peptides for recurrent malignant gliomas is planned to verify its safety, clinical efficacy and usefulness of surrogate markers. PATIENTS AND METHODS: Twenty-three patients with recurrent malignant gliomas, which showed WT1-positive in tumor samples and HLA-A*24:02 or HLA-A*02:01-positive in blood sample, were enrolled. These patients (age: 26–72 years old, average: 49.4) included 15 cases of glioblastomas and 8 of anaplastic astrocytomas. Patients received a WT1 trio vaccine intradermally, 7 times at 2-week intervals during 3 months.WT1-DTH and WT1-IgG antibody were regularly measured. Vaccine-related adverse events, best clinical response and the transfer rate of long-term administration of WT1 trio vaccination were estimated. RESULTS: WT1-DTH positive cases were 12, WT1-IgG antibody positive were in 11. In most patients, WT1 -DTH positiveness coincided with that of WT1-IgG antibody. 9 of 11 cases showed stable disease at 3 months and transferred long-term administration of WT1 trio vaccination. Transfer rate in GBM and AA of long-term administration was 33% and 25%, respectively. Grade1 skin eruption was observed at the injection sites in 15 cases, but no significant adverse events related with vaccination were shown. CONCLUSION: the safety and clinical efficacy of WT1 trio vaccination was verified for recurrent malignant gliomas. WT1-DTH and WT1-IgG antibody may be useful surrogate markers.

SURGICAL/INTRAOPERATIVE THERAPY/ MONITORING (STMO)

STMO-01

APPLICATION OF THE AMINOLEVULINIC ACID HYDROCHLORIDE FOR INTRAOPERATIVE DETECTION OF MALIGNANT BRAIN TUMORS.

Keiichi Kobayashi[1], Kuniaki Saito[1], Daisuke Shimada[1], Yoshie Matsumoto[1], Saki Shimizu[1], Shouhei Iijima[1], Akio Noguchi[1], Jyunji Shibahara, Yoshiaki Shiokawa[1], Motoo Nagane[1]; [1]Department of Neurosurgery, Kyorin University Faculty of Medicine, Tokyo, Japan

BACKGROUND: A maximal safe resection has been shown as an independent prognosis factor for high grade glioma (HGG). Intraoperative photo dynamics diagnosis (PDD) facilitates an increased rate of tumor resection, thereby taking an important role in accomplishment of " maximal safe resection " along with neuro-navigation and monitoring of motor nerve function. Since the approval of aminolevulinic acid (5-ALA) for PDD in 2013 in Japan, we have been utilizing the PDD when HGG is suspected by preoperative assessments. Here we retrospectively analyze clinical findings in PDD-mediated tumor resection. METHODS: From February 2014 to March 2019, 285 consecutive patients (132 females) with suspected HGG underwent total of 302 PDD-mediated resection. Median age was 61 yo (13–90). A single oral dose of 5-ALA 20 mg/kg was given within three hours before microsurgery. Positivity of excited fluorescence was assessed qualitatively under surgical microscope. RESULTS. Among 195 gliomas, the fluorescence positivity rates were 89.6% (120/134) for glioblastoma, 40.5% (15/37) for grade III, and 13.6% (3/22) for grade II. The positive rates for other histologies were 30.2% (13/43) for malignant lymphoma, 32.1% (9/28) for metastatic brain tumor, 0% (0/7) for meningioma (include atypical), and 4.5% (1/22) for other types. In gliomas the high positivity correlated with histological grades, while all fluorescence-positive grade II gliomas were recurrent tumors. Serious adverse events were not observed. CONCLUSIONS. The qualitative PDD showed a clinical utility to aid accurate resection in glioblastoma, whereas its positivity was inconsistent in lower grade gliomas as well as other malignant brain tumors. This unreliability might attribute, at least in part, to fluorescent intensity heterogeneity in situ, a reduced excitation by an inappropriate radiation angle of the light source, and the qualitative fluorescence detection. Impacts of introducing quantitative detection system as well as molecular and histopathological features on better discrimination will be discussed.

STMO-02

PREOPERATIVE FENCE-POST METHOD PLANNING WITH 3D-FUSION IMAGING

Hirokazu Sadahiro[1], Hisaharu Goto[1], Sadahiro Nomura[1], Michiyasu Suzuki[1]; [1]The department of Neurosurgery, Yamaguchi University Hospital

The fence-post method has been used for removal of intra-axial tumors. Preoperative detailed planning with only navigation work system is sometimes difficult to identify actual brain surface, small feeding artery and passing artery. Recently, 3-dementional imaging is well developed to integrate various anatomical findings. The purpose of this study is pursuit of perfect preoperative planning for removal intra-axial tumors with 3D-fusion imaging. From May 2017 to June 2019, 21 patients with intra-axial tumor were included. The software "AZE" was used to create 3D-fusion imaging. The brain tumor, brain surface and tractography were built from MRI, artery from digital angiography and vein from subtraction enhanced computed tomography. Then detailed preoperative planning was planned including how many fence-posts, procedure of cutting feeder, making sulcotomy or corticotomy, and finally cutting drainer. The average bleeding volume was 101±129cc, and there were no patients who had transfusion. All patients did not show additional neurological impairment after surgery. Detailed and perfect preoperative planning with 3D-sufion imaging should be effective for secure neurosurgery.

STMO-03

ROLE OF INTRAOPERATIVE COMPUTED TOMOGRAPHY IN GLIOBLASTOMA RESECTION GUIDED BY 5-ALA

Takahiro Yamauchi[1], Ryuhei Kitai, Yoshinori Shibaike[1], Mizuki Oiwa[1], Shintaro Yamada[1], Satoshi Kawajiri[1], Makoto Isozaki[1], Kenzo Tsunetoshi[1], Ken Matsuda[1], Hidetaka Arishima[1], Toshiaki Kodera[1], Ken-Ichiro Kikuta[1]; [1]Department of Neurosurgery, University of Fukui, Fukui, Japan

OBJECTIVE: To improve resection rate, multiple operative modalities have been essential for glioblastoma (GBM) surgery. Aim of this study is to clarify the impact of intraoperative computed tomography (i-CT) for GBM surgery with 5-aminolevulinic acid photodynamic diagnosis (5-ALA PDD). METHODS: Consecutive 24 patients newly diagnosed GBM were analyzed, retrospectively. To exclude 6 patients decided timing for i-CT based on neural monitoring, 18 patients performed i-CT after total resection of 5-ALA positive lesion were included, finally. RESULTS: The median age was 58 years old, and average preoperative tumor volume was 47.78 cm3. Tumor locations were frontal lobe 5 (27%), parietal lobe 3 (17%), temporal lobe 9 (50%), and corpus callosum 1 (6%). Seventeen tumors (78%) harbored in eloquent area. After i-CT performed, 7 (39%) were confirmed residual tumor, and additional resections were needed. Subtotal resection (STR) was 5 and partial resection (PR) was 2 on volumetry in i-CT before additional resection. After additional resection, those cases were judged as 2 gross total resection (GTR), 4 STR and 1 PR in postoperative magnetic resonance imaging (MRI). 11 cases without additional resection were judged as 4 GTR, 3 STR and 4 PR in postoperative MRI. In 18 patients confirmed