Abstracts

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INTRODUCTION: There exist controversies on recurrence and aggressiveness after use of first-line bevacizumab (BEV) which has been approved in Japan and is being beneficial. Therefore, we analyzed the clinical impact of BEV approval by investigating the overall clinical course and glioblastoma (GBM) relapse pattern.

METHODS: We included 100 patients with IDH-wildtype GBM between September 2006 and February 2018 from our institution. They were subdivided into pre-BEV (n=51) and post-BEV (n=49) groups. Overall, progression-free, deterioration-free, and post-progression survivals (OS, DFS, and PPS, respectively) were compared. We analyzed the relapse pattern of 72 patients, whose radiographic progressions were confirmed.

RESULTS: Significant improvements in DFS (median DFS in the pre-BEV and post-BEV era were 8.5 and 13.8 months, P=0.0046), and PFS (7.5 and 9.9 months, P=0.0153) after BEV approval were observed. These survival prolongations were strongly correlated (r: 0.91, P<0.0001). Non-enhancing tumor emerged as a novel recurrence pattern in the post-BEV era (five of 33; 15.2%). Changes in relapse pattern did not significantly impact OS, DFS, and PFS. No significant difference in PFS between pre-BEV and post-BEV era was observed (6.7 and 5.5 months, P=0.2319). The rate of early (within 6 months) focal recurrence was significantly lower (P=0.0155) in the post-BEV era (four of 33; 12.1%) than in the pre-BEV era (18 of 39; 46.2%). A significant decrease in early focal recurrence after BEV approval was observed exclusively in patients with unresectable tumors (P=0.0110). Treatment era was the only parameter significantly correlated with decreased early focal recurrence rate (P=0.0021, univariate analysis; P=0.0144, multivariate analysis).

CONCLUSIONS: We found that, first-line BEV in Japan for unresectable tumors has a positive impact on the prevention of early recurrence and clinical deterioration of GBM without accelerating the clinical course after recurrence.

ACT-03

OBJECTIVE: To report the clinical outcome in newly diagnosed glioblastoma multiforme after treatment with bevacizumab.

METHODS: A retrospective analysis of 116 consecutive patients with newly diagnosed glioblastoma treated with bevacizumab was performed. All patients received 1672 cycles of BEV. The median period of treatment was 172 days (range 0-1413 days). The safety and efficacy of BEV was assessed using T1-weighted (T1w), T2-weighted (T2w), diffusion-weighted (DW), and contrast-enhanced T1w images.

RESULTS: The median survival was 266 days, and overall survival 693 days. Patients without progressive disease had a median survival of 333 days, while patients with progressive disease had a median survival of 713 days than those with progressive disease (n=8; P=0.0003). The radiological findings varied by patients, tumor lesions, and follow-up imaging; thus, it was difficult to correlate with survival. Our data implied that the 2-circumscribed lesion was accompanied by no enhancement at T1 but hypoperfused at arterial spin labeling imaging, indicating that blood-brain barriers were intact and vascularization is activated. CONCLUSION: Although our cohort included patients with relatively high age, some had prolonged post-BEV survival. T2-circumscribed or double-positive was not useful to predict the survival; however, MRI at 6 months post-BEV can be an indicator for two years of post-BEV survival.

ACT-07

CLINICAL TRIALS OF 11C-METHIONINE PET FOR BRAIN TUMORS

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BACKGROUND: Although 11C-Methionine (MET) PET has widely used, 11C-MET tracer has not been approved in Japan. We conducted multi-center prospective clinical trials using MET for drug approval in diagnosis of brain tumors. Methods: Two trials using 11C-MET PET were performed in Hokkaido University, Osaka University and Fukushima Medical University. 1) Diagnostic accuracy in differentiating tumor recurrence from radiation injury after radiotherapy in brain tumors. 2) Diagnostic efficiency in newly-diagnosed gliomas. 3) The patients with suspected brain tumor recurrent underwent MET PET and then the target lesion showed MET and FDG uptake, the patients underwent target resection for pathological confirmation. Positive prediction values of each tracer uptake were assessed as primary outcome measure, and the sensitivities and specificities of each PET exams were also assessed. 2) The patients with suspected gliomas underwent MET PET. Tissue samplings were performed from MET uptake lesions without contrast-enhancement on MRI in each patient, and evaluated the existence of tumor cells. Diagnostic additional value of MET PET on contrast-enhanced MRI was also investigated. Safety of MET PET was also assessed in each trial. 1) 75 cases were investigated. 38 cases underwent surgery and 32 cases (84%) were confirmed tumor recurrence histopathologically. MET and FDG uptake in 32 recurrence cases were 100% and 50%, respectively. Sensitivities and specificities of tumor recurrence were 84% and 89% in MET, and 100% and 56% in FDG. 2) 53 glioma cases were enrolled. Viable tumor cells were proven in 98% in MET uptake lesion without contrast-enhancement. In 42 out of 53 cases (78%), MET PET depicted tumor area beyond the contrast-enhancement area on MRI. No severe adverse events were observed in both trials. 3) MET PET were effective in diagnosis of brain tumors, and safety of MET PET was demonstrated.

ACT-17

PROTOCOL DESIGN OF A MATRIX-TYPE OF NOVEL CLINICAL TRIAL FOR LOWER-GRADE GLIOMAS

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INTRODUCTION: Differentiation between glioma grade 2 and 3 was performed based on histological findings. The current grade is an important prognostic factor due to its widespread use, economic efficiency, and data accumulation. However, analog elements remain and the genetic marker is unknown. The concept of Lower-grade glioma including G2/3 is spreading. On the other hand, WHO grade is the criteria of clinical trials, and evidence is established for G2 with low risk and high risk, G3 alone or with G4. In Japan, JCOG 1303 and 1016 have been implemented for high-risk G2 and G3, respectively and will be finished next year. Therefore, we examined the feasibility and design of novel clinical trial for patients with grade 2/3 glioma.