INTRODUCTION: There exist controversies on recurrence and aggressiveness after use of first-line bevacizumab (BEV) which has been approved in Japan. 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 2009 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, PFS, 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 months, P=0.0046), and PFS (7.3 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, PFS, and DFS. No significant difference in PPS 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=0.0153) 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 progression and clinical deterioration of GBM without accelerating the clinical course after recurrence.

ACT-03

CLINICAL OUTCOME AND RADIological FINDINGS OF PATIENTS WITH RECURRENT GLIOBLASTOMAS TREATED BY BEvacizumab

Hajime Handa1, Ichiyo Shibahara1, Takuchiro Hude1, Toshichiro Kumabe1, 2

1Department of Neurosurgery, Kitasato University School of Medicine, Japan

OBJECT: Seven years have passed since the approval of bevacizumab (BEV) in Japan. We retrospectively reviewed the clinical outcome and radiological findings of patients with recurrent glioblastomas (GBM) treated by BEV.

METHOD: We reviewed 116 patients, including 27 cases of newly diagnosed GB and 89 cases of recurrent GB, treated by BEV during the study period (between 2013 June and 2019 September). Cumulatively, 116 patients received 1672 cycles of BEV. Among those, we focused on 74 patients with newly diagnosed GB treated by BEV at recurrence to examine clinical characteristics, outcome, and radiological findings of T2-circumscribed or double-enhancement area on MRI. No severe adverse events were observed in both subgroups. 1672 cycles of BEV were administered to 74 patients: 251 cycles to 51 patients with recurrent GB and 1,421 cycles to 23 patients with recurrent GB who did not receive adjuvant chemotherapy. Overall, 1,906 cycles of BEV were administered to 74 patients: 251 cycles to 51 patients with recurrent GB and 1,655 cycles to 23 patients with recurrent GB who did not receive adjuvant chemotherapy.

RESULTS: Significant improvements in DFS (median DFS in the pre-BEV and post-BEV era were 8.5 and 13 months, P=0.0046), and PFS (7.3 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, PFS, and DFS. No significant difference in PPS 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=0.0153) 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 progression and clinical deterioration of GBM without accelerating the clinical course after recurrence.

ACT-07

CLINICAL TRIALS OF 11C-METHIONINE PET FOR BRAIN TUMORS

Shigeru Yamaguchi1, Tohru Shiga2, Kenji Hirata3, Shunsuke Terasaka4, Hiroki Kobayashi5, Eku Shimosegawa5, Naoya Kagawa6, Ryuichi Hirayama6, Manabu Kinoshita6, Haruhiko Kijima6, Masazumi Fuji1, Masahiro Ichikawa1, Noboru Oriuchi8, Yoji Kuge7, Nagara Tamaki7, 8

1Department of Neurosurgery, Graduate School of Medical Science, Kyoto University, Japan

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 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) The diagnostic efficacy in newly-diagnosed gliomas. 1) The patients with suspected brain tumor recurrence underwent MET and FDG PET imaging. MET PET depicted tumor area. MET PET is considered as a sensitive imaging tool for the target lesion showed MET and/or FDG uptake, the patients underwent target resection for pathological confirmation. 2) Probability positive 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.[Result] 1) 57 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 (98%) in MET uptake lesion without contrast-enhancement. In 42 (78%), MET PET depicted tumor area beyond the contrast-enhancement area on MRI. None severe adverse events were observed in both trials. [Conclusions] MET PET were effective in diagnosis of brain tumors, and safety of MET was demonstrated.