ACT-26

ABT-414 (DEPATUX-M) IN NEWLY DIAGNOSED AND RECURRENT GLIOBLASTOMA: WHERE DO WE STAND?

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Epithelial growth factor receptor (EGFR) amplifications are found in approximately half of glioblastoma cases and targeting of the EGFR axis is an attractive treatment paradigm in this tumor type. However, several anti-EGFR drugs have failed to achieve significant and meaningful improvements in clincial trials. ABT-414 (Depatux-M) is an antibody-drug conjugate (ADC) that combines a cytotoxic agent with an antibody targeting EGFR, thus aiming at specific tummor cell killing through intracellular toxin delivery. The activity of ABT-414 has been evaluated in two large clinical trials enrolling glioblastoma patients. Intellance-2 enrolled 260 patients with first recurrence of EGFR-amplified glioblasoma into a chemotherapy control arm (temozolomide or lomustine) or one of two experimental arms (ABT-414 monotherapy or ABT-414 combined with temozolomide). Depatux-M in combination with temozolomide showed a trend towards improved survival times compared to temozolomide/lomustine alone, with patients relapsing more than 4 months after the last adjuvant temozolomide cycle deriving the greatest benefit. Intellance-1 was a randomized, placebo-controlled Phase 3 study and was designed to evaluate the efficacy and safety of Depatux-M versus placebo when administered with concurrent radiation and temozolomide and with adjuvant temozolomide in subjects with newly diagnosed EGFR-amplified glioblastoma. The primary endpoint was overall survival. Recently, it was announced that a preplaned interim analysis based on data from 639 patients showed the lack of a survival benefit for patients exposed to Depatux-M. In summary, the currently available data do not support routine use of Depatux-M in glioblastoma patients and further studies are needed to understand resistance mechanisms limiting therapeutic efficacy of EGFR-targeting in glioblastoma.

Key words: epithelial growth factor receptor, glioblastoma, antibody-drug-conjugate

PEDIATRIC CLINICAL TRIALS/THERAPEUTIC STUDIES (PEDT)

PEDT-02

DIAGNOSIS, TREATMENT AND CLINICAL OUTCOME OF ATYPICAL BRAINSTEM TUMOUR IN CHILDHOOD

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BACKGROUND: Brainstem tumours account for 10–15% of brain tumors in childhood. Diffuse intrinsic pontine glioma (DIPG) accounts for 60–80% of them and are diagnosed based on clinical findings and radiologic features. All the rest of tumours excluding DIPG are very rare, heterogeneous group of tumours including low-grade glioma and malignant embryonal tumors. It is often difficult to diagnose and decide treatment strategy for their rarity. METHODS: To present our experience with atypical brainstem tumours, a retrospective chart review was conducted to identify eligible cases treated over a ten-year period. All tumors involving brainstem, felt not to be DIPGs for absence of clinical/neuroimaging features were included. Demographic information, pathological findings, neuroimaging characteristics, surgical and nonsurgical management plans, and survival data were collected for analysis. RESULTS: Between April 2007 and March 2017, 16 patients (14 initial and 2 recurrent) aged from 3 to 20 years were identified. 14 of them were symptomatic and 4 of them were asymptomatic at reference. Of 10 symptomatic cases, 10 were biopsied and pathological diagnosis was low-grade glioma in 8, glioblastoma in 2 cases. They had treatment depending on the pathological diagnosis. Of 4 asymptomatic cases, one with small focal tumour, with no findings suggesting malignant tumour with 11C-methioninePET or MRS, progressed to show typical clinical and image findings of DIPG in a year. For other three, they remain asymptomatic without progression with no treatment for 25months, 60months, and 65 months respectively. Malignant transformation was observed in one with biopsy-conformed oligoastrocytoma with no K27M-H3 mutations treated with chemotherapy and another with pilocytic astrocytoma treated with chemotherapy and radiotherapy. CONCLUSIONS: Though molecular findings such as K27M-H3 mutations can predict clinical outcome in some cases, it still remains difficult to diagnose and find treatment strategy of atypical brainstem tumours. The need and usefulness of nationwide registry study is warranted.

PEDT-04

SIX CASES OF RETINOBLASTOMA WITH CNS INVOLVEMENT

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Although the survival rate of intraocular retinoblastoma (RB) is nearly 100%, the outcome of central nervous system (CNS) involvement or Trilateral retinoblastoma (TRb: very rare RB which associated with brain tumor) is dismal. We retrospectively reviewed our six cases of these rare tumors. Their ages at diagnosis are 0y3m-1y10m (median 1y3m) (Male 4, Female 2). Only one had RB family history. Their affected eyes were bilateral 2, unilateral 3 and no 1. Their CNS diseases were suprasellar tumor 3, pineal tumor 1 and cerebrospinal fluid (CSF) cytology positive 2. Two of the suprasellar tumor patients had spinal metastasis. Three of the six patients were TRb. One TRb patient was treated with chemotherapy and high-dose chemotherapy without radiotherapy. Although he suffered with secondary osteosarcoma seven years later, he got complete remission and alive 5 years more without any tumor recurrence. The second TRb patient was treated with chemotherapy and local radiotherapy but relapsed 20 months later. The third TRb patient was chemotherapy resistant. Two CSF positive patients had optic nerve invasion. One patient with chiasm invasion died 11 months later because of treatment resistance. The other patient with optic nerve invasion before optic canal had no CNS tumor nor CSF involvement at diagnosis. Chemotherapy before enucleation was given to avoid dissemination. However, CSF cytology became positive after enucleation and remained even with intensified chemotherapy. Finally, he got remission with radiotherapy and high-dose chemotherapy, and alive without disease for 3.8 years. The last patient had suprasellar genetically classified retinoblastoma tumor and cerebrospinal metastasis. This patient showed good chemotherapy response and is still under treatment. Even with &quotso called° fatal RB cases, some case could survive with intensified therapy. Data accumulation is necessary for better survival of these tumors.

PEDT-05

USEFULNESS OF BEVACIZUMAB IN MAINTAINING QOL AT DIPG RELAPSE

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INTRODUCTION: Even in the age of molecular diagnosis, diffuse intrinsic pontine glioma (DIPG) is still a dismal disease, and there is no effective treatment. The usefulness of bevacizumab for DIPG relapse is reported. SUBJECTS AND METHODS: The treatment and outcomes of 10 patients with DIPG who were treated at our institute since 2001 were retrospectively reviewed. All patients were diagnosed with DIPG by MRI imaging and underwent radiation therapy first. Chemotherapy was performed in combination with radiation therapy in 4 cases, and 3 of them did not receive chemotherapy at the time of relapse (Untreated Group). In 7 cases, chemotherapy was performed at the time of relapse with ACNU/vincristine or interferon beta (Other Treatment Group), and 2 cases with bevacizumab (Bv Group). The change in the Karnofsky Performance Status Scale (KPS) from the time of relapse was compared.

RESULTS: The average overall survival (OS) for all 10 cases was 10.0 months, 8.1 months in the Untreated Group, 9.5 months in the Bv Group, and 11.4 months in the Other Treatment Group. No prolongation of OS by bevacizumab was observed. However, it was only in the Bv Group that the KPS increased from the time of relapse. Comparison of the KPS at the time of relapse and the KPS after 4 months showed that the Bv Group remained unchanged or increased from 80 to 90, while the Untreated Group decreased by 60–100, and the Other Treatment Group also decreased by 20–50. In the Other Treatment Group, hospitalization was required for treatment, and side effects of bone marrow suppression were observed. However, in the Bv Group, outpatient treatment was possible, there were no side effects, and all could be observed at home. CONCLUSION: From the above results, bevacizumab appears useful for palliative treatment for maintaining quality of life after DIPG relapse.

PEDT-06

THERAPEUTIC STRATEGY FOR DISSEMINATED PILOCYTIC ASTROCYTOMAS

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