Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Methods: We have analyzed the multi-omic Glioma Longitudinal Analysis dataset, integrating DNA and RNA sequencing datasets from primary and post-treatment gliomas.

Results: We classified tumors as harboring temozolomide-associated hypermutation based on mutational burden increase (HM), and RT-associated signature based on small deletion burden increase (RTscars). By deconvoluting RNA profiles into cell state fractions, we observed an increase of a proliferating stem-like (PSL) cell state in 50% of patients with a RTscars+ signature which was significantly higher than RTscars−/HM− patients (P=8e-04, Fisher's exact). PSL cell state increase associated with worse overall survival outcomes (P=1.5e-03, log-rank). We observed a significant correlation between the expression change of E2F cell cycle regulator genes (R=0.91, P=6.7e-04, Pearson) and EZH2 (R=0.81, P=8.3e-03) with the increase in the PSL cell state, nominating the E2F/EZH2-pathway as regulator of the PSL cell state. Furthermore, the RTscars signature was associated with an increase in frameshift neoantigens and significantly higher neoantigen burden at recurrence (P=2.4e-02, Kruskal-Wallis). This was accompanied by a significantly higher post-treatment T-cell fraction in RTscars+ tumors (P=8.2e-04, Wilcox), suggesting an increased T-cell infiltration in these patients.

Conclusions: Our analyses revealed a longitudinal increase in the proliferating stem-like cell state associated with RT-resistance and nominates the cell cycle pathway as an actionable target. The RT-associated deletion signature (RTscars) correlated with increased frameshift-neoantigens and T-cell fractions at recurrence, suggesting a potential benefit of a combinatorial immune-targeted therapy in this specific patient population.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2022.07.433

300P The clinical results of an investigator initiated trial of allogeneic CAR-T cells targeting IL13Rα2 in the treatment of high-grade glioma

Y. Huang[1], X. Shang[2], X. Li[1]

[1]*Neurosurgery, The Dushu Lake Affiliated Hospital of Suzhou (Soochow) University, Suzhou, China;* [2]*Jiangsu T-Maximum Biotech Co., Ltd., Suzhou, China*

Background: Glioblastoma is the most common intracranial malignant tumors, which is difficult to treat and has poor prognosis. T cell immunotherapy is becoming a powerful strategy for the treatment of cancer and may provide an opportunity to improve the prognosis of patients with advanced glioma.This trial has three purposes: 1) to evaluate the safety and feasibility of allogeneic CAR-T cells in human body; 2) Lumbar injection and intratumoral injection were compared; 3) Preliminarily evaluate the effectiveness of our product in patients with advanced glioma.

Methods: We are developing allogeneic universal CAR-T cells for IL13Rα2 (IL13Rα2 UCAR-T cells) for the treatment of advanced glioma. This is a off-the-shelf anti-IL13Rα2 allogeneic CAR-T cells candidate product, which is made of a series of healthy donor materials, avoiding many shortcomings of autologous car-t products. We report here initial findings from our first-in-human clinical trial [ChiCTR2000028801].

Results: We have treated a total of 7 patients, and the longest time after the first injection has been 21 months. The most common side effects are fever and anorexia. The significant increase of inflammatory factors such as interleukin-6 and interleukin-8 can be detected in cerebrospinal fluid, but the cytokine storm seen in the application of CAR-T cells in hematologic malignancies is not seen. Among the 7 patients, one patient had complete remission (CR) and lasted for 10 months, 4 patients had partial remission (PR), which was defined as tumor regression of more than 50%, and 2 patients had disease stability (SD). Therefore, the overall effective rate was 71.42% (5 / 7) and the disease control rate was 100% (7 / 7). The patient with the longest follow-up had survived for 18 months after the first injection. We monitored the number of IL13Rα2 UCAR-T cells in cerebrospinal fluid by flow cytometry or copy number detection. We found that our IL13Rα2 UCAR-T cells could survive in cerebrospinal fluid for more than 30 days.

Conclusions: These early clinical findings suggest that lumbar puncture delivery of allogeneic IL13Rα2 UCAR-T cells is safe and well-tolerated, and that IL13Rα2 UCAR T cells are capable of eliciting potent antitumor responses against recurrent glioma.

Legal entity responsible for the study: The authors.

Funding: Jiangsu T-Maximum Biotech Co., Ltd.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2022.07.434

301P Hypofractionated radiotherapy for the treatment of newly diagnosed high-grade gliomas in younger and good performance status patients during COVID-19 pandemic

A.C. Valente[1], C. Lopes Almeida[2], M.J. Costa[3], I.C. Nogueira Costa[4], J.S. Reis[5], M.C.B. Freitas[6], C.M. Teixeira[7], M.V. Gonçalves[6], A.C. Fernandes[5], A.S.A. Costa[8], C.L.B. Caeiro[8], L. Osório[9], I.M. Augusto[10], M. Barbosa[11]

[1]*Medical Oncology Dept., CHUSJ - Centro Hospitalar Sao Joao E.P.E - SNS - Polo Porto, Porto, Portugal;* [2]*Oncology Department, CHUSJ - Centro Hospitalar Sao Joao E.P.E - SNS - Polo Porto, Porto, Portugal;* [3]*Serviço de Oncologia Médica, CHUSJ - Centro Hospitalar Sao Joao E.P.E - SNS - Polo Porto, Porto, Portugal;* [4]*Medical Oncology Service, CHUSJ - Centro Hospitalar Sao Joao E.P.E - Polo Porto, Porto, Portugal;* [5]*Medical Oncology Department, CHUSJ - Centro Hospitalar Sao Joao E.P.E - SNS - Polo Porto, Porto, Portugal;* [6]*Medical Oncology Department, Centro Hospitalar Sao Joao E.P.E - Polo Porto, Porto, Portugal;* [7]*Oncology Department, São João University Hospital Center, Porto, Portugal;* [8]*Medical Oncology Department, HSJ - Hospital de Sao Joao Centro Hospitalar Universitario, EPE - SNS, Porto, Portugal;* [9]*Radiotherapy, Centro Hospitalar e Universitário São João - Porto, Porto, Portugal;* [10]*Oncologia Médica, CHUSJ - Centro Hospitalar Sao Joao E.P.E - SNS - Polo Porto, Porto, Portugal;* [11]*Medical Oncology Department, CHUSJ - Centro Hospitalar Sao Joao E.P.E - SNS - Polo Porto, Porto, Portugal*

Background: During the initial approach to the COVID-19 pandemic, some international recommendations regarding high-grade gliomas (HGG) favored the use of hypofractionated radiotherapy (HFR) regiments, particularly in elderly and frail patients. In our institution, to reduce the risk of COVID-19 infection and the treatment interruptions, the multidisciplinary group decided to carry out a modified STUPP protocol (HFR - 40,05Gy/15 fractions over 3 weeks - with TMZ), even in younger patients with good performance status (PS). However, a few data exist about the role of HFR in this subgroup of patients.

Methods: Retrospective analysis of patients with a newly diagnosed HGG treated with chemoradiotherapy with temozolomide (TMZ) followed by adjuvant TMZ, between 2016 and 2021. Patients with $\leq$ 70 years old and ECOG PS $\leq$ 2, treated with conventional fraction RT (CFR, 60Gy/30 fractions, over 6 weeks) or HFR concurrent with TMZ (75 mg/m2/day), followed by adjuvant TMZ (150-200 mg/m2/day for 5 days, every 4 weeks) were included. Survival analysis was performed using the Kaplan-Meier method and prognostic factors assessed by univariate analysis and by the Cox regression model.

Results: A total of 157 patients were included, with a median age of 56 years old (26-69). The majority (82,2%) was submited to surgical resection. About 24% (n=37) were treated with HFR-TMZ and 76% (n=120) with CFR-TMZ. The most frequent adverse event was thrombocytopenia (n=39), with no difference between groups (p=0,828). The patients treated with HFR had a median overall survival (mOS) of 18 months vs. 21 months with CFR (p=0,221). The median progression free survival (mPFS) was 13 months for patients treated with HFR, and 10 months for CFR (p=0,418). In multivariate analysis, IDH mutation (OS: HR 0,47; 95% CI 0,26-0,86; p= 0,014. PFS: HR 0,47; 95% CI 0,27-0,84; p=0,010) and absence of corticotherapy (OS: HR 0,65; 95% CI 0,44-0,98; p=0,038. PFS: HR 0,65; 95% CI 0,44-0,97, p=0,034) had a positive impact on OS and PFS.

Conclusions: According to our data, in HGG patients with $\leq$70 years old and a good PS, the use of HFR with TMZ had no impact on median PFS and OS, when compared with CFR-TMZ. However, the role of HFR in this setting needs further research.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2022.07.435

302P A multicenter, open-label, dose-escalation (DE), first-in-human study of VEGFRs and CSF1R inhibitor SYHA1813 in patients (pts) with recurrent high-grade gliomas (HGG) or advanced solid tumors

W. Li[1], Z. Kang[1], S. Li[1], Y. Lin[1], Y. Li[2], Y. Mao[3], J. Zhang[3], T. Lei[4], H. Wang[5], Y. Su[5], Y. Yang[5], J. Qiu[5]

[1]*Neuro-Oncology, Beijing Tiantan Hospital, Capital Medical University, Beijing, China;* [2]*Medical Oncology, Chongqing Cancer Hospital, Chongqing, China;* [3]*Neurosurgery, Huashan Hospital Affiliated to Fudan University, Shanghai, China;* [4]*Neurosurgery, Tongji Hospital affiliated to Tongji Medical College of Huazhong University of Science and Technology, Wuhan City, China;* [5]*Clinical Development, CSPC Pharmaceutical Group Co., Ltd., Shijiazhuang, China*

Background: SYHA1813 is a novel small-molecule vascular endothelial growth factor receptors (VEGFRs)/ colony-stimulating factor 1 receptor (CSF1R) inhibitor, exerting synergistic antitumor effects through inhibiting angiogenesis and modulating macrophage polarity in preclinical models. We report preliminary results from a phase I, DE study of SYHA1813 in pts with recurrent or advanced solid tumors including HGG.