Diffuse intrinsic pontine glioma treatment

- PNOC009: Convection-enhanced delivery of liposomal irinotecan in patients with newly diagnosed diffuse intrinsic pontine glioma
- Targeting the CD40 costimulatory receptor to improve virotherapy efficacy in diffuse midline gliomas
- From Seeing to Healing: The Clinical Potential of Radiotracers in Pediatric Neuro-Oncology
- Nimotuzumab Combined With Chemoradiation Therapy in Newly Diagnosed Pediatric Diffuse Intrinsic Pontine Glioma
- Exploring the tumor microenvironment in diffuse intrinsic pontine glioma: immunological insights and therapeutic challenges
- Integrative Multi-Omics Analysis Identifies Nuclear Factor I as a Key Driver of Dysregulated Purine Metabolism in DIPG
- Combination therapy of supercharged NK cells and ONC201 or ONC206 to target aggressive K27M brain tumor
- Beyond Base Camp: Promise and Pitfalls of PI3K/mTOR Inhibition in Pediatric High- Grade Gliomas

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Surgical approaches to intrinsic pontine lesions are technically difficult and prone to complications.

Early treatment of hydrocephalus presents a very low complications rate with satisfying clinical outcome, as it allows the patients to continue the neurooncological therapies being a part of the treatment armamentarium instead of a palliative solution [1)].

CAR-T

CAR-T cell therapy for diffuse intrinsic pontine glioma

Personalized treatment

Whole genome sequencing (WGS) data provided further insight into tumor evolution and fidelity of patient-derived cell models. Detection of the H3F3A or HIST1H3B K27M (H3K27M) mutation using ctDNA was successful in 92% of H3K27M mutant cases. A personalized treatment recommendation for DIPG can be rendered within a multi-center setting using comprehensive next-generation sequencing technology in a clinically relevant timeframe [2)].

Radiation therapy

Radiotherapy is the traditional therapy for newly diagnosed DIPGs. It uses high-energy rays (radiation)

from a specialized machine to damage or kill cancer cells and shrink tumors. Conventional limited-field radiation produces responses in more than 90 percent of children with DIPGs. These responses are short-lived, however, lasting about six to nine months on average. Several trials to increase the dose of radiation therapy have been performed and none have improved survival.

Chemotherapy

Diffuse intrinsic pontine glioma (DIPG) has a dismal prognosis with no chemotherapy regimen so far resulting in any significant improvement over standard radiotherapy. In this trial, a prolonged regimen (21/28d) of temozolomide was studied with the aim of overcoming O(6)-methylguanine methyltransferase (MGMT) mediated resistance. Forty-three patients with a defined clinico-radiological diagnosis of DIPG received radiotherapy and concomitant temozolomide (75 mg/m(2)) after which up to 12 courses of 21d of adjuvant temozolomide (75-100mg/m(2)) were given 4 weekly. The trial used a 2-stage design and passed interim analysis. At diagnosis median age was 8 years (2-20 years), 81% had cranial nerve abnormalities, 76% ataxia and 57% long tract signs. Median Karnofsky/Lansky score was 80 (10-100). Patients received a median of three courses of adjuvant temozolomide, five received all 12 courses and seven did not start adjuvant treatment. Three patients were withdrawn from study treatment due to haematological toxicity and 10 had a dose reduction. No other significant toxicity related to temozolomide was noted. Overall survival (OS) (95% confidence interval (CI)) was 56% (40%, 69%) at 9 months, 35% (21%, 49%) at 1 year and 17% (7%, 30%) at 2 years. Median survival was 9.5 months (range 7.5-11.4 months). There were five 2-year survivors with a median age of 13.6 years at diagnosis. This trial demonstrated no survival benefit of the addition of dose dense temozolomide, to standard radiotherapy in children with classical DIPG. However, a subgroup of adolescent DIPG patients did have a prolonged survival, which needs further exploration [3)].

Reirradiation

Diffuse intrinsic pontine glioma (DIPG) is a pediatric brain tumor with dismal prognosis despite initial radiation therapy (RT). The clinical consequences of attempting reirradiation (reRT) in these patients to alleviate both symptomatology and improve prognosis are currently unclear. Thus, the aim of this systematic review and meta-analysis was to clarify the efficacy and safety of reRT in DIPG.

Searches of seven electronic databases from inception to January 2019 were conducted following the appropriate guidelines. Articles were screened against prespecified criteria. The incidence and duration of clinical outcomes were then extracted and pooled by means of meta-analysis from the included studies.

A total of 7 studies satisfied all criteria, describing 90 cases of DIPG in which reRT was attempted 11.8-14 months after initial RT. Based on a random-effects model, the incidences of clinical improvement and radiologic response following reRT were 87% (95% CI, 78-95%) and 69% (95% CI, 52-84%), respectively. The incidence of acute serious toxicity was 0% (95% CI, 0-4%). Pooled overall survivals from initial diagnosis and time of reRT were 18.0 months (95% CI, 14.2-21.7) and 6.2 months (95% CI, 5.5-7.0), respectively.

Based on these results, the clinical consequences of reRT for DIPG when administered appropriately

and safely at first progression appear acceptable, and potentially favorable, based on the limited evidence in the current literature. Concerns regarding acute serious toxicity were not realized. It is likely that a subcohort of all DIPG diagnoses will be most amenable to improve prognosis with reRT, and greater investigation is required to identify their characteristics [4].

A proof-of-concept study provides a novel demonstration of marked DIPG cell susceptibility to low intensity electric fields delivered using intratumoral modulation therapy (IMT). The potent impact as a monotherapy and when integrated into multi-modality treatment platforms justifies further investigations into the potential of IMT as a critically needed biomedical innovation for DIPG [5].

Results support continued development of PPM1D inhibitors for Phase I/II trials in children with DIPG [6].

Bevacizumab for diffuse intrinsic pontine glioma

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