Nivolumab

Nivolumab is a programmed cell death 1 (PD-1) receptor inhibitor antibody that enhances immune system antitumor activity.

Bi et al. performed a phase II study of nivolumab among patients with grade ≥ World Health Organization grade 2 meningioma. that recurred after meningioma surgery and radiation therapy.

Twenty-five patients received nivolumab (240 mg biweekly) until progression, voluntary withdrawal, unacceptable toxicity, or death. Tumor mutational burden (TMB) and quantification of tumor infiltrating lymphocytes (TIL) were evaluated as potential immunocorrelative biomarkers. Change in neurologic function was prospectively assessed using The Neurologic Assessment in Neuro-Oncology scale (NANO).

Enrolled patients had multiple recurrences including ≥3 prior surgeries and ≥2 prior courses of radiation in 60% and 72%, respectively. Nivolumab was well tolerated with no unexpected AEs. PFS-6 was 42.4% (95% CI: 22.8, 60.7) and the median OS was 30.9 months (95% CI: 17.6, NA). One patient achieved radiographic response (ongoing at 4.5 years). TMB was > 10/Mb in 2 of 15 profiled tumors (13.3%). Baseline TIL density was low but increased post-treatment in 3 patients including both patients with elevated TMB. Most patients who achieved PFS-6 maintained neurologic function prior to progression as assessed by NANO.

Nivolumab was well tolerated but failed to improve PFS-6, although a subset of patients appeared to derive benefit. Low levels of TMB and TIL density were typically observed. NANO assessment of neurologic function contributed to outcome assessment. Future studies may consider rationally designed combinatorial regimens [1].

Although it is used for treating advanced non-small-cell lung cancer (NSCLC), its actual efficacy has not been determined.

Zhao et al. searched PubMed, the Cochrane Library, Embase, MEDLINE, and Web of Science for related noncomparative clinical studies and randomized controlled trials (RCTs) to assess nivolumab benefit and risk in NSCLC. The main outcomes were objective response rate (ORR), 1-year overall survival rate (1-yOS rate), and progression-free survival rate at 24 weeks (PFS at 24 weeks rate), any-grade adverse effects rate (any-grade AEs%), and grade 3-4 AE rate (grade 3-4 AEs%). Relative risk (RR) was used to compare ORR in patients with positive and negative programmed cell death ligand 1 (PD-L1) expression. Random-effects models were used to determine pooled effect size and two-sided 95% confidence intervals (95% CI). We included 20 studies (17 noncomparative open-label cohort studies, three RCTs) involving 3404 patients in our meta-analysis. The modified nivolumab ORR was 18% (95% CI: 15-20%), the 1-yOS rate was 45% (95% CI: 40-50%), PFS at 24 weeks rate was 42% (95% CI: 37-48%), any-grade AEs% was 61% (95% CI: 50-73%), and grade 3-4 AEs% was 12% (95% CI: 9-16%). PD-L1 expression was related with the nivolumab ORR. Nivolumab potentially causes ongoing response, long-term PFS, and reduced treatment-related AEs. PD-L1 expression predicts the outcome of nivolumab immunotherapy. More high-quality and well-designed RCTs with large sample sizes are warranted to prove our findings [2].

Case reports

A 57-year-old man presented with visual deterioration and bitemporal hemianopsia. MRI of the brain demonstrated a sellar mass suspected to be pituitary macroadenoma with a displacement of the stalk and optic nerve impingement. The patient underwent stereotactic endoscopic transsphenoidal resection of the mass. Postoperative MRI demonstrated gross total resection. Pathology revealed a sparsely granulated corticotroph adenoma with malignant transformation. Immunohistochemistry showed a loss of expression of MLH1 and PMS2 in the tumor cells. Proton therapy was recommended given an elevated Ki67 index and p53 positivity. Before radiotherapy, there was no radiographic evidence of residual tumor. Temozolomide therapy was initiated after surveillance MRI showed recurrence at 16 months postoperatively. However, MRI demonstrated marked progression after 3 cycles. Next-generation sequencing using the MSK-IMPACT platform identified somatic mutations in MLH1 Y548lfs*9 and TP53 R337C. Immunotherapy with ipilimumab/nivolumab was initiated, and MRI demonstrated no residual tumor burden 34 months postoperatively.

APA is a tumor with frequent recurrence and a short median expected length of survival. Shah et al. demonstrated the utility of immunotherapy in a single case report of APA, with complete resolution of recurrent APA and improved survival compared with a life expectancy [3].

A 67-year-old man presented with recurrent AM post gross total resection with adjuvant radiotherapy in 2012, 2014, and 2016. The patient was deemed a poor candidate for additional therapies. Tumor vasculature mapping was performed to determine TARE candidacy. Super-selective angiography and contrast-enhanced cone-beam computed tomography angiosomes demonstrated predominant pial collaterals and minor supply from a middle meningeal artery branch. Particle simulation was performed by infusing 0.3 mCi of 99mTc-macroaggregated albumin (99mTc-MAA). SPECT/CT-MRI fusion demonstrated conformal activity solely within the tumor volume perfused by the middle meningeal artery branch with a lung shunt fraction of 54.7%. The patient subsequently received off-label Nivolumab (PD-1 inhibitor). Mapping angiography for AM using 99mTc-MAA is feasible. It may identify candidates for TARE and potential AM patients with favorable blood supply. The potential for conformal intracranial vascular brachytherapy is intriguing, however, altered arterial supply in recurrent tumors is challenging.

The treatment of refractory meningiomas remains a challenge for both neurosurgeons and neuro-oncologists. There have been no clinical reports of the use or effects of anti-PD-1 therapy in patients with meningioma. We describe a patient whose intracranial meningioma decreased significantly in size after treatment with nivolumab, a monoclonal antibody targeting PD-1, for a concomitant advanced lung cancer. This is the first clinical report suggesting that antibodies targeting PD-1 are effective in treating meningioma. It should encourage further research into the use of checkpoint inhibitors in meningioma [4].

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Bi WL, Nayak L, Meredith DM, Driver J, Du Z, Hoffman S, Li Y, Lee EQ, Beroukhim R, Rinne M, McFaline-Figueroa R, Chukwueke U, McCluskey C, Gaffey S, Cherniack AD, Stefanik J, Doherty L, Taubert C, Cifrino M, LaFrankie D, Graillon T, Wen PY, Ligon KL, Al-Mefty O, Huang RY, Muzikansky A, Chiocca EA, Santagata S, Dunn IF, Reardon DA. Activity of PD-1 blockade with Nivolumab among patients with recurrent atypical/anaplastic meningioma: Phase II trial results. Neuro Oncol. 2021 May 20:noab118.

doi: 10.1093/neuonc/noab118. Epub ahead of print. PMID: 34015129.

2) Zhao B, Zhang W, Yu D, Xu J, Wei Y. The benefit and risk of nivolumab in non-small-cell lung cancer: a single-arm meta-analysis of noncomparative clinical studies and randomized controlled trials. Cancer Med. 2018 Mar 23. doi: 10.1002/cam4.1387. [Epub ahead of print] PubMed PMID: 29573217.

3) Shah S, Manzoor S, Rothman Y, Hagen M, Pater L, Golnik K, Mahammedi A, Lin AL, Bhabhra R, Forbes JA, Sengupta S. Complete Response of a Patient With a Mismatch Repair Deficient Aggressive pituitary neuroendocrine tumor to Immune Checkpoint Inhibitor Therapy: A Case Report. Neurosurgery. 2022 May 13. doi: 10.1227/neu.0000000000002024. Epub ahead of print. PMID: 35544035.

4) Gelerstein E, Berger A, Jonas-Kimchi T, Strauss I, Kanner AA, Blumenthal DT, Gottfried M, Margalit N, Ram Z, Shahar T. Regression of intracranial meningioma following treatment with nivolumab: Case report and review of the literature. J Clin Neurosci. 2017 Mar;37:51-53. doi: 10.1016/j.jocn.2016.11.011. Epub 2017 Jan 12. Review. PubMed PMID: 28089420.