ABSTRACT 371P : LOW-DOSE BEVACIZUMAB FOR THE TREATMENT OF FOCAL POST-RADIATION NECROSIS OF THE BRAIN

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BACKGROUND

- Focal post-radiation necrosis of the brain (fRNB)
  - Relatively rare but often symptomatic complication following treatment of of benign or malignant brain lesions with stereotactic radiation therapy (SRT) or stereotactic radiosurgery (SRS) resulting in permanent focal necrosis of brain tissue [1]
  - Usually occurs within 1 year but late fRNB has been reported up to 5 years after treatment
  - Clinical features: headache, seizures and/or focal neurologic deficits
  - Radiologic characteristics: gadolinium-enhancing lesion on T1 magnetic resonance imaging with important perilesional edema; hypometabolic lesion on brain 18F-FDG-PET/CT
  - Has an increased incidence in patients treated with immune-checkpoint inhibitors[2]
- Bevacizumab (BEV) is a vascular endothelial growth factor (VEGF)-neutralizing monoclonal antibody
  - BEV at a dose of 5-7.5 mg/kg Q2W x4 has shown to be an effective treatment for fRNB [3]
  - Based on pharmacokinetic/-dynamic data[4], a "low-dose regimen" was used to treat fRNB in symptomatic patients in a "real world" setting

METHODS

- Single-center, retrospective case series
- Inclusion criteria: patients with benign or malignant cerebral lesions who were treated with SRT or SRS between 2016-2021, developed symptomatic fRNB and were treated with a low-dose BEV regimen
- Database lock: 10th May 2021

TREATMENT DISPOSITION

- All patients except one (n: 9) received a loading dose of 400 mg bevacizumab iv
- Every 3-4 weeks patients received a maintenance dose of 100 mg bevacizumab iv
- Treatment is currently ongoing in 3 patients. 7 patients were able to stop treatment and are in remission at the latest follow-up. 3 patients had to restart therapy after elective discontinuation.

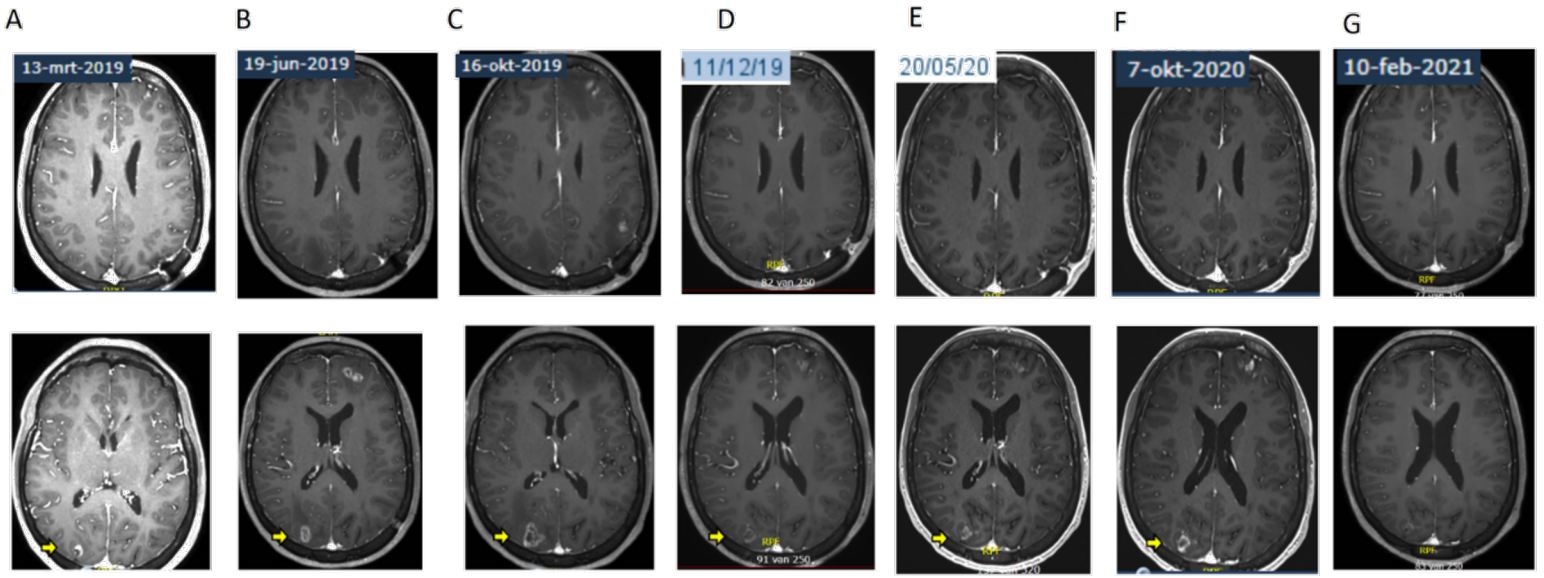
RESULTS

TABLE 1. BASELINE CHARACTERISTICS	*n* = 10
Sex (*n* [%])	
Male / Female	6 (60) / 4 (40)
Age (median [range])	50.74 (31-68)
Primary pathology (*n* [%])	
Melanoma	5 (50.0)
Non-small cell lung cancer	2 (20.0)
Medulloblastoma	1 (10.0)
Renal cell carcinoma	1 (10.0)
Arteriovenous malformation	1 (10.0)
Rechallenge after initial full dose BEV (y/n)	3 (30.0) / 7 (70.0)
Symptomatic at initial presentation (*n* [%])	10 (100.0)

TABLE 2. CLINICAL OUTCOMES	*n* = 10
Symptomatic improvement in presenting symptoms (*n* [%])	
Epileptic seizures	6 (60.0)
Headache	1 (10.0)
Neurologic deficit	2 (20.0)
Alive (*n* [%])	10 (100.0)

TABLE 3. ADVERSE EVENTS	All-grade	Grade 3-4
Any AE (*n* [%])	8 (80.0)	0 (0)
Arterial hypertension	6 (60.0)	2 (20.0)
Wound dehiscention	1 (10.0)	0 (0)
Proteinuria	1 (10.0)	0 (0)
Epistaxis	1 (10.0)	0 (0)
Headache	1 (10.0)	0 (0)
Diarrhea	1 (10.0)	0 (0)
Mouth ulcers	1 (10.0)	0 (0)
AE leading to treatment interruption (*n* [%])	1 (10.0)	

CASE ILLUSTRATION (45Y, F)



Case illustration of a 45-year-old female patient with stage IV-M1d $BRAF^{V600}$ wild-type melanoma who initially presented with a grand-mal epileptic seizure due to melanoma brain metastasis. Systemic therapy with ipilimumab/nivolumab (immune checkpoint-inhibitors) was initiated and two brain metastases were treated with SRS (20Gy). Initial response was positive, but after 4 months four new brain metastases appeared. These were subsequently stereotactically irradiated (20Gy), concurrent temozolomide chemotherapy was initiated (6 cycles) and the patient successfully went into remission. 1.5 year later, a gradual increase in gadolinium-enhancement, dimensions of the lesion and perilesional edema was observed at the site of a previously irradiated lesion (A,B,C). BEV was initiated at a dose of 400mg Q4W. The patient remained asymptomatic, and the gadolinium-enhanced T1-weighted MRI image improved (D), after which treatment was electively interrupted. However, four months after the last dose a slight increase in contrast enhancement was noted (E). Five months later, she presented with a new epileptic seizure accompanied with a further increase in gadolinium-enhancement of the lesion (F). BEV therapy was restarted with a loading dose of 400 mg followed by a maintenance dose of 100mg Q4W. Upon confirmed improvement of the MRI images (G) and as the patient remained asymptomatic, treatment was electively discontinued in February 2021 (after 4 months of therapy). The patient remained asymptomatic up to the latest follow-up visit.

CONCLUSION

In this single-center retrospective case series, treatment of fRNB with a low-dose regimen of BEV is an effective and cost-lowering alternative for standard-dose BEV.

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REFERENCES: 1. Vellayappan, B. *et al.* Front Oncol 2018; 2. Du Four, S. *et al.* Cancer Med 2018; 3. Wong, E.T. *et al.* J Clin Oncol 2008; 4. Gordon, M.S. *et al.* J Clin Oncol 2001

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