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LETTER TO THE EDITOR

Treatment of aggressive recurrent meningiomas: spinning towards peptide receptor radionuclide therapy

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Sir,

With a worldwide incidence of 45,000 cases, meningioma is the most common nonglial primary intracranial tumour. Although the tumour is often associated with indolent behaviour, in many patients it shows aggressive features and is associated with poor outcomes. After complete resection, the 5-year recurrence rates for grade I (benign), grade II (atypical) and grade III (anaplastic) tumours have been estimated to be 5%, 40% and 80%, respectively [1, 2]. Very few treatment options are available at this stage. The progression-free survival (PFS) in patients with aggressive recurrent meningiomas is less than 30% at 6 months, while the median overall survival is 3 years in patients with grade III tumour [3]. It is therefore of major importance to develop new treatment options.

In recent years, peptide receptor radionuclide therapy (PRRT) with somatostatin analogues (SSAs) has become increasingly important in the treatment of patients with tumours expressing somatostatin receptor (SST), identified and selected with a theranostic approach with the use of a companion diagnostic agent corresponding to the same SSA labelled with ^{111}In or preferably ^{68}Ga for molecular imaging. In this regard, the PRRT results obtained in the NETTER-1 trial in patients with advanced midgut neuroendocrine tumours (NET) have given a new impetus to the use of therapeutic nuclear medicine in oncology [4]. Although NET are the prime example of SST-positive tumours, meningiomas express comparable amounts of SST and, unlike NET, also express this profile in aggressive forms [5]. This could potentially open the therapeutic window for PRRT in meningiomas. From a biological standpoint, a recent study has confirmed that meningiomas overexpress SST2, with a high expression pattern in 67% of tumours, comparable to the pattern in gastroenteropancreatic NET [5]. These findings agree with those of imaging studies with ^{68}Ga-DOTA-SSAs showing highly elevated tumour uptake [6, 7]. ^{68}Ga-DOTA-SSA PET/CT is currently recommended in meningioma patients by the international RANO group for differential diagnosis, grading, delineation, radiation planning, follow-up, evaluation of response and progression [1].

To date, PRRT has been used to treat meningioma mainly on a compassionate basis. Approximately 120 patients with meningioma treated with PRRT have been reported [8–15]. These studies were limited by the inclusion of various types of meningiomas, and by the use of different PRRT schedules and follow-up imaging studies. In addition, the growth rate before treatment was not always documented, limiting interpretation of the PFS, particularly in patients with grade I and "low" grade II meningioma. Although half of these patients were treated with external radiotherapy prior to PRRT, safety and clinical tolerance were excellent. Moreover, one study showed that concomitant treatment with PRRT and external radiotherapy is also well tolerated [14]. Regarding oncological endpoints, these promising studies showed disease stabilization in most patients with grade I and less aggressive grades II meningioma, with 6-month PFS ranging from 57% to 100%. By contrast, no clear benefit has so far been found in more aggressive grade II and III meningioma.

Beyond the expression of the molecular target, overview of these studies underlines the need for the PRRT schedule to be

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tailored to each situation with integration of several factors in the decision-making process, such as the extent of disease, growth rate, grade, molecular genetics and SST expression. Regarding dosimetry, the relationship between absorbed dose and response rate is not well established. To increase the absorbed dose while preserving at-risk organs, two main options have been proposed [16]: the standard 7.4 GBq per cycle with the number of cycles increasing until the biological effective dose limits for the kidney and bone marrow are reached [17, 18], or a fixed number of four cycles with variable activity per cycle to reach the dose limits [19].

A prospective evaluation of PRRT in patients with meningioma with an integrated dosimetry-based approach, especially for at-risk organs, would be an important step towards a new spin on treating patients with meningioma. Improvement roadmaps include the use of various therapeutic isotopes depending on the situation, radiosensitizers, computational intelligence, and potential meningioma-directed applications. Further development may also include the evaluation of early postoperative PPRT in patients with grade II meningiomas as an alternative or in combination with classical radiotherapy.

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Compliance with ethical standards

Conflicts of interest None.

Ethical approval This article does not describe any studies with human participants performed by any of the authors.

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