SHORT REPORT

# Somatostatin receptor positron emission tomography/computed tomography imaging in Merkel cell carcinoma

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## Abstract

**Background** Merkel cell carcinoma (MCC) is an uncommon aggressive primary cutaneous carcinoma with neuroendocrine differentiation. However, literature data about the use of somatostatin receptor positron emission tomography/computed tomography (PET/CT) imaging in MCC are limited and its role is not clearly stated.

**Objective** To investigate the role of PET/CT using somatostatin analogues radiolabelled with gallium-68 in patients with MCC.

**Methods** All patients affected by MCC who performed a somatostatin receptor PET/CT imaging from October 2007 to May 2014 were retrospectively analysed. The diagnostic performances of PET/CT were evaluated on a patient-based analysis and compared to final diagnosis (histology = 3 or clinical/radiological follow-up = 20).

**Results** We evaluated 23 consecutive MCC patients [18 men; median age 71 years (range 47–87)]. Primary tumour was located in ear (1/23), cheek (3/23), arm (2/23), hand (1/23), back (1/23), anal canal (1/23), gluteus (4/23), thigh (3/23) and popliteal fossa (1/23). In 6/23 patients, the site of primary tumour was unknown. PET/CT was performed to detect primary tumour site (4/23) or to stage (8/23) or re-stage (11/23) patients. PET/CT resulted positive in 14/23 patients and according to the final diagnosis was defined true positive, true negative, false positive (FP) and false negative in 11/23, 8/23, 3/23 and 1/23 cases respectively. FP PET/CT results were due to unspecific liver uptake, post-surgical inflammation and pancreatic neuroendocrine tumour. PET/CT was unable to detect primary tumour site in all patients with unknown primary MCC. Sensitivity, specificity and diagnostic accuracy of PET/CT were 92%, 73% and 83% respectively.

**Conclusions** In our experience, somatostatin receptor PET/CT imaging resulted useful in patients with MCC and presented high diagnostic performances with a significant impact in disease management although in patients with unknown primary MCC, it was unable to identify the primary tumour site.

Received: 20 May 2015; Accepted: 5 August 2015

## Conflicts of interest

All authors declare no competing financial interests.

## Funding sources

None.

## Introduction

Merkel cell carcinoma (MCC) is an uncommon aggressive primary cutaneous carcinoma with high mortality.[1–3] Establishing the exact extent of the disease may ensure an optimal choice of treatment; therefore due to the metastatic potential of MCC, the role of imaging is crucial. Despite most of these tumours have ultrastructurally and immunocytochemically neuroendocrine characteristics, few cases (manly case reports or small series) have been evaluated by somatostatin receptor (SSTR) positron emission tomography (PET) or positron emission tomography/computed tomography (PET-CT).[4–10]

In this study, we aimed to evaluate $^{68}$Ga-labelled somatostatin (SST) analogues PET/CT in patients with MCC.

†Martina Sollini and Silvia Taralli have contributed equally to the manuscript and share the first authorship.

## Materials and methods

### Patients

Between October 2007 and May 2014, a total of 23 consecutive patients [18 men and five women; median age 71 years (range 47–87 years)] with pathologically confirmed MCC, referred for $^{68}$Ga-DOTA-peptides PET/CT, were retrospectively evaluated. PET/CT studies were performed in Nuclear Medicine Units of 'Arcispedale Santa Maria Nuova – IRCCS Reggio Emilia' (Centre A) and 'Università Cattolica del Sacro Cuore' in Rome (Centre B). The use of $^{68}$Ga-somatostatin analogues was approved by Local Ethics Committee of each centre (EudraCT numbers 2008-000983-17 and 2010-023827-34 for centres A and B respectively). All patients provided informed consent for PET/CT and for personal data use.

Inclusion criteria for the above-mentioned studies were: age >18 years, cytohistological diagnosis of neuroendocrine tumor (NET), signed informed consent. In Merkel cell carcinoma of unknown primary origin (MCCUP), diagnosis of MCC was made by analysing lymph node(s). Radiological imaging results were also collected.

### Positron emission tomography/computed tomography imaging

Positron emission tomography/computed tomography was performed on a hybrid scanner (Discovery STE; GE Healthcare, Chalfont St. Giles, UK in Centre A and Gemini GXL; Philips Medical Systems, Cleveland, OH or Biograph; Siemens Healthcare, Malvern, PA in Centre B). Images were acquired 60 ± 10 min after tracer injection (2 MBq/kg) as whole body (vertex-feet) in both Centres according to protocols previously described.[11,12]

All PET/CT scans were re-evaluated (qualitative analysis), independently, by two experienced nuclear physicians aware of patients' clinical history and of results of prior conventional imaging. PET/CT was considered positive in case of radiopharmaceutical uptake higher than background activity (mediastinum), and negative in case of no evidence of abnormal radiotracer uptake. PET/CT results were compared to reference standard (i.e. final diagnosis).

### Statistical analysis

A descriptive analysis was performed. Sensitivity, specificity and accuracy of PET/CT imaging were calculated with 95% confidence interval (CI). A *P*-value <0.05 was considered significant by chi-square test.

## Results

Table 1 summarizes patients' characteristics and main results of the study.

The AJCC stages of disease[13] at enrolment for patients who performed PET/CT for staging (8/23) were I (1/8), II (3/8) and III (4/8).

Grade of differentiation was G3 in all available (6/23) cases (Ki-67 = 70%, range 30–90%).

Final diagnosis was obtained by histology/cytology (3/23) or clinical and radiological follow-up (20/23). Median time of follow-up was 303 days (range 74–2233). According to final diagnosis, 12/23 patients had at least one MCC-related lesion, whereas 11/23 patients had no evidence of disease.

$^{68}$Ga-DOTA-peptides PET/CT resulted positive in 14/23 (Fig. 1) and negative in 9/23 cases.

$^{68}$Ga-DOTA-peptides PET/CT presented 92% (CI: 65–98) sensitivity, 73% (CI: 43–90) specificity and 83% accuracy. Diagnostic accuracy was higher for $^{68}$Ga-DOTANOC compared to $^{68}$Ga-DOTATOC or $^{68}$Ga-DOTATATE (100% vs. 71% and 75% respectively; *P*-value = 0.56) and for staging compared to re-staging (88% vs. 73%; *P*-value = 0.7).

In MCCUP (6/23), PET/CT not identified primary site of disease resulting positive for metastases in four cases and negative in the remaining two cases.

Based on a per-lesion analysis, 76 lesions were identified (considering only the 14 positive scans). In the majority of cases lymph nodes were involved (61/76). Other sites of radiotracer uptake were soft tissues (7/76), skin (3/76), adrenals (2/76), pancreas (1/76), colon (1/76) and liver (1/76). Seventy-two lesions resulted as true positive (TP) (lymph nodes $n$ = 61, soft tissues $n$ = 7, skin $n$ = 2, adrenals $n$ = 2), while in 4/76 cases radiotracer uptake was not MCC-related. Particularly, in patient #9 the area of $^{68}$Ga-DOTATATE uptake observed in the site of MCC surgery was subsequently diagnosed as post-surgical inflammation; in patient #11 liver uptake was unspecific; while in patients #23 and #20 a pNET and a synchronous MCC metastases plus primary colon cancer (Fig. 2) were diagnosed respectively.

Clinical stage of disease was not modified by PET/CT in patients who performed examination to stage disease (8/23). PET/CT changed patients' management in 7/23 cases (Table 2).

## Discussion

In our experience, SSTR PET/CT resulted very useful in MCC and provided information impacting in patients' management even if it was unable to identify primary tumour in MCCUP.

The role of PET/CT in the identification of primary tumours in MCCUP has not been definitely studied. A potential role of PET/CT has been suggested in detecting primary occult lesions (>5–8 mm) in MCCUP,[14] however positive results using [$^{18}$F] FDG have been reported only to confirm lymph nodes disease involvement or to identify unknown metastases.[15] Similarly, our approach based on SSTR imaging, confirmed the role of PET/CT to identify metastases in MCCUP. Unfortunately PET/CT failed in the identification of primary tumour site also in our experience, possibly due to the intrinsic characteristics of such tumours. Nevertheless, from a clinical perspective, SSTR PET/CT may significantly impact in patients' management especially to rule out tumour spread.

**Table 1** Baseline patients' characteristics and main results of the study

| Pt | Sex, age (year) | Site of primary MCC | Previous surgery for MCC | Previous malignancy and co-morbidities | SSTR PET/CT | | | Final diagnosis | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | Clinical purpose | Radiolabelled peptide | Results | Method | Result |
| 1 | M, 74 | Ear | Partial excision of primary tumour | Prostate cancer + chronic lymphocytic leukaemia | Staging | DOTANOC | TP | Follow-up (CT + SSTR PET/CT) | PD |
| 2 | M, 72 | Thigh | Excision of primary tumour + SLn biopsy | Any | Re-staging (suspected recurrence at CT) | DOTANOC | TP | Follow-up (clinical) | Death |
| 3 | M, 74 | Arm | Excision of primary tumour + local lymphadenectomy | Any | Re-staging (increase chromogranin A) | DOTANOC | TN | Follow-up (CT) | NEoD |
| 4 | M, 80 | Unknown | Ln excisional biopsy | Colorectal cancer + melanoma | Detect primary site | DOTANOC | TP (Ln) | Histology | Mts |
| 5 | F, 80 | Cheek | Excision of primary tumour + local lymphadenectomy | Chronic myelogenous leukaemia | Staging | DOTANOC | TN | Follow-up (CT) | NEoD |
| 6 | M, 73 | Hand | Excision of primary tumour + local lymphadenectomy | Gilbert's syndrome | Re-staging (suspected recurrence at CT) | DOTANOC | TN | Follow-up (US) | NEoD |
| 7 | M, 47 | Cheek | Partial excision of primary tumour | Any | Staging | DOTANOC | TP | Follow-up (CT + MRI) | SD |
| 8 | M, 71 | Unknown | Ln excisional biopsy | Any | Re-staging (evaluation at the end of chemotherapy) | DOTANOC | TP | Follow-up (CT) | PD |
| 9 | M, 58 | Thigh | Excision of primary tumour + local lymphadenectomy | Any | Staging | DOTATATE | FP | Follow-up (US) | NEoD |
| 10 | M, 67 | Cheek | Excision of primary tumour + SLn biopsy | Seronegative arthritis + hypertrophic cardiomyopathy | Staging | DOTATATE | TN | Follow-up (CT) | NEoD |
| 11 | M, 79 | Back | Excision of primary tumour + local lymphadenectomy | pNET | Re-staging (evaluation at the end of chemotherapy) | DOTATOC | FP | Follow-up (US) | NEoD |
| 12 | M, 81 | Thigh | Excision of primary tumour + SLn biopsy | Melanoma + acute myocardial infarction + chronic renal failure | Re-staging (suspected clinical Lns recurrence) | DOTATOC | TP | Follow-up (clinical) | Death |
| 13 | F, 41 | Gluteus | Excision of primary tumour + SLn biopsy | Chronic anaemia | Staging | DOTATOC | TN | Follow-up (CT) | NEoD |
| 14 | F, 70 | Unknown | Ln excisional biopsy | Any | Detect primary site | DOTATOC | TN | Follow-up (CT) | NEoD |
| 15 | M, 80 | Unknown | Ln excisional biopsy | Any | Re-staging (Lns mts) | DOTATOC | TP | Follow-up (CT) | PD |
| 16 | M, 74 | Gluteus | Excision of primary tumour + local lymphadenectomy | Acute myocardial infarction | Re-staging (evaluation at the end of chemotherapy) | DOTATATE | TP | Follow-up (CT) | PD |
| 17 | M, 59 | Unknown | Ln excisional biopsy | Any | Detect primary site | DOTATATE | TP (Ln) | Histology | Mts |
| 18 | F, 74 | Gluteus | Excision of primary tumour + SLn biopsy | Any | Staging | DOTATATE | TN | Follow-up (CT) | NEoD |
| 19 | M, 68 | Anal canal | Partial excision of primary tumour | Any | Re-staging (evaluation at the end of EBRT) | DOTATOC | FN | Follow-up (CT) | PD |
| 20 | M, 87 | Popliteal fossa | Excision of primary tumour + local lymphadenectomy | Benign prostatic hypertrophy | Re-staging (follow-up) | DOTATOC | TP | Histology | Mts* |
| 21 | M, 69 | Gluteus | Excision of primary tumour + SLn biopsy | Any | Staging | DOTATATE | TP | Histology | Mts |
| 22 | F, 54 | Unknown | Ln excisional biopsy | Diabetes | Detect primary site | DOTATATE | TN | Follow-up (US) | NEoD |
| 23 | M, 68 | Arm | Excision of primary tumour | Renal cancer | Re-staging (suspected recurrence at CT) | DOTATATE | FP† | Follow-up (CT) | NEoD |

*Patient with concomitant MCC abdominal metastases and primary colon cancer identified by PET/CT.

†Patient subsequently diagnosed as pNET (cytology); follow-up examinations (CT and US) did not show evidence of MCC recurrence (stable pNET).

CT, computed tomography; F, female; FN, false negative; FP, false positive; Ln, lymph node; M, male; MRI, magnetic resonance imaging; Mts, metastases; n.e., not evaluable; NEoD, no evidence of disease; PD, progressive disease; PET/CT, positron emission tomography/computed tomography; SLn, sentinel lymph node; SD, stable disease; SSTR, somatostatin receptor; TP, true positive; TN, true negative; US, ultrasound.

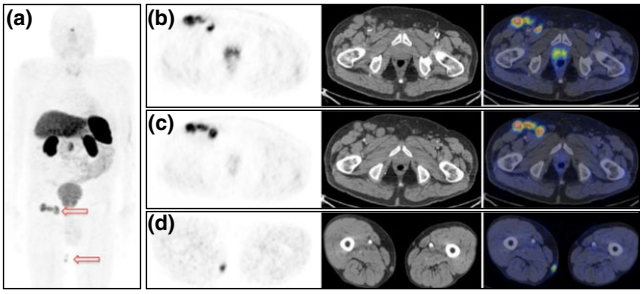


**Figure 1** $^{68}$Ga-DOTATOC positron emission tomography/computed tomography in a patient (#15) with Merkel cell carcinoma (MCC). MIP (a) shows two sites of $^{68}$Ga-DOTATOC uptake (red arrow). Axial images identify MCC disease in right inguinal lymph nodes (b,c) and in subcutaneous nodule of the right thigh (d).

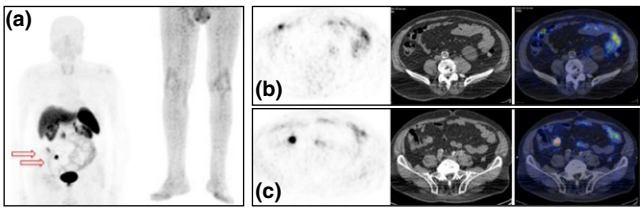


**Figure 2** $^{68}$Ga-DOTATOC positron emission tomography/computed tomography in a patient (#23) with Merkel cell carcinoma (MCC). MIP (a) shows two sites of $^{68}$Ga-DOTATOC uptake (red arrow). Axial images localizes radiotracer uptake in intestinal loop diagnosed as colon cancer (b) and in a MCC metastatic abdominal lymph node (c).

**Table 2** Change in management (expected vs. undertaken) according to $^{68}$Ga-DOTA-peptide PET/CT results

| Patient | Site of primary MCC | Clinical purpose | Tracer uptake (site) | Management | |
|---|---|---|---|---|---|
| | | | | Expected | Undertaken |
| 3 | Arm | Re-staging | Any | Individualized treatment | Follow-up |
| 6 | Hand | Re-staging | Any | Individualized treatment | Follow-up |
| 8 | Unknown | Re-staging | Multiple Lns | Any | 'Cold' somatostatin analogue therapy |
| 17 | Unknown | Detect primary site | Ln | Radiation therapy | Surgery (second look) |
| 20 | Popliteal fossa | Re-staging | Ln + bowel* | Chemotherapy | Surgery (second look) |
| 21 | Gluteus | Staging | Ln | Adjuvant chemotherapy or radiation therapy | Surgery (second look) |
| 23 | Arm | Re-staging | Pancreas† | Individualized treatment | Follow-up |

*Patient with concomitant MCC abdominal metastases and primary colon cancer.
†Patient diagnosed as pNET (cytology).
CT, computed tomography; Ln, lymph node; MCC, Merkel cell carcinoma; PET/CT, positron emission tomography/computed tomography; T, primary tumour.

Overall, $^{68}$Ga-DOTA-peptides PET/CT presented good diagnostic performances in our series of MCC. Moreover, if we considered TP also the patient subsequently diagnosed as pNET (radiolabelled peptides imaging identifies SSTR expression independently from the site of NET origin), the diagnostic performances of SSTR PET/CT further improved (92% sensitivity, 80% specificity and 87% accuracy).

Comparing the diagnostic performances of $^{68}$Ga-DOTATOC, $^{68}$Ga-DOTATATE and $^{68}$Ga-DOTANOC PET/CT, we observed a higher accuracy using $^{68}$Ga-DOTANOC compared to $^{68}$Ga-DOTATOC and $^{68}$Ga-DOTATATE (100%, 71% and 75% respectively). However, despite the sample size of patients for each tracer we used is similar, the heterogeneity of our population and the different clinical purposes for PET/CT examinations, make unreliable any speculation. Nonetheless, direct comparison of PET/CT using $^{68}$Ga-DOTATOC and $^{68}$Ga-DOTATATE[16] in NET, showed comparable diagnostic accuracy despite their different SSTR2 affinity. Notably, we reported the first series of MCC patients imaged by $^{68}$Ga-DOTANOC. In fact, the only case of MCC previously studied with $^{68}$Ga-DOTANOC was included in a series of patients published by Ambrosini *et al.*[5] in which PET/CT was performed to assess bone metastases.

$^{68}$Ga-DOTA-peptides PET/CT lead to a change in therapeutic patients' management in a high percentage of subjects, avoiding unnecessary treatment in three cases. Very recently, Buder *et al.*[10] used PET ($n = 19$) or PET/CT ($n = 5$) with $^{68}$Ga-DOTATOC/$^{68}$Ga-DOTATATE to stage MCC. Although the

 

number of patients evaluated in this series was comparable to our, they performed PET alone in the majority of cases, thus we reported the largest series of MCC studied by SSTR PET/CT. Buder *et al.*[10] found high sensitivity of SSTR PET to detect metastases which translate in an upstaging of disease in three cases, and lead to a change in therapeutic management in a lower proportion of patients compared to our series (13% vs. 30%). The higher proportion of patients in whom SSTR imaging impacted in our series may be partially explained by the use of PET/CT (instead of PET alone) and the inclusion of other than staging examinations.

The demonstration of SSTR expression using $^{68}$Ga-DOTA-peptides PET/CT may be also used to offer a therapeutic option (i.e. PRRT) to MCC patients[4,7,8] since the current treatment regimens for metastatic disease have a limited impact on the overall survival.[17]

[$^{18}$F]FDG-PET/CT, currently considered an accurate imaging modality in MCC, upstaged disease in 16% of cases in a review of 97 patients[15] and changed the stage of disease as well as treatment in 22% of cases in a review of 102 patients.[18] In our series $^{68}$Ga-DOTA-peptides PET/CT findings did not change the pre-PET disease stage but impacted on patients' management also in the staging setting. According to a meta-analysis of six studies, the sensitivity and specificity of [$^{18}$F]FDG-PET/CT in the staging are 90% and 98% respectively.[19] We found high sensitivity and specificity of $^{68}$Ga-DOTA-peptides PET/CT in the staging (100% and 80% respectively), while both sensitivity and specificity decreased during re-staging (86% and 50% respectively). However, a head-to-head comparison of both imaging approaches (SSTR expression vs. [$^{18}$F]FDG metabolism) is lacking in literature and it warrants an interesting tool for further research.

Despite these promising results, our study is affected by some limitations, mainly represented by patient population. First, the number of enrolled subjects is limited (but it should be into account the orphan disease status of MCC) and PET/CT was performed with different clinical purposes. Second, phenotype tumour properties (i.e. proliferative index) and immunohistochemical characteristics were available only in a very small subset of patients avoiding the possibility to correlate tumour features and PET/CT results. Finally, although data reported in literature confirmed that $^{68}$Ga-DOTA-peptides have similar diagnostic accuracy, we performed PET/CT using three different $^{68}$Ga-DOTA-peptides even if the number of patients in each subgroup and the images acquisition protocol employed were comparable, making reproducible the results deriving from both Centres.

## Conclusions

$^{68}$Ga-DOTA-peptides PET/CT resulted useful in MCC to identify site(s) of disease, presenting high diagnostic performances and a significant impact in disease management. However, in patients with MCCUP, SSTR PET/CT was unable to identify primary tumour site.

## References


1 Allen PJ, Bowne WB, Jaques DP, Brennan MF, Busam K, Coit DG. Merkel cell carcinoma: prognosis and treatment of patients from a single institution. *J Clin Oncol* 2005; **23**: 2300–2309.
2 Bichakjian CK, Lowe L, Lao CD *et al.* Merkel cell carcinoma: critical review with guidelines for multidisciplinary management. *Cancer* 2007; **110**: 1–12.
3 Lemos BD, Storer BE, Iyer JG *et al.* Pathologic nodal evaluation improves prognostic accuracy in Merkel cell carcinoma: analysis of 5823 cases as the basis of the first consensus staging system. *J Am Acad Dermatol* 2010; **63**: 751–761.
4 Koukouraki S, Strauss LG, Georgoulias V *et al.* Evaluation of the pharmacokinetics of 68Ga-DOTATOC in patients with metastatic neuroendocrine tumours scheduled for 90Y-DOTATOC therapy. *Eur J Nucl Med Mol Imaging* 2006; **33**: 460–466.
5 Ambrosini V, Nanni C, Zompatori M *et al.* (68)Ga-DOTA-NOC PET/CT in comparison with CT for the detection of bone metastasis in patients with neuroendocrine tumours. *Eur J Nucl Med Mol Imaging* 2010; **37**: 722–727.
6 Schneider C, Schlaak M, Bludau M, Markiefka B, Schmidt MC. $^{68}$Ga-DOTATATE-PET/CT positive metastatic lymph node in a 69-year-old woman with Merkel cell carcinoma. *Clin Nucl Med* 2012; **37**: 1108–1111.
7 Schmidt MC, Uhrhan K, Markiefka B *et al.* (68)Ga-DotaTATE PET-CT followed by peptide receptor radiotherapy in combination with capecitabine in two patients with Merkel cell carcinoma. *Int J Clin Exp Med* 2012; **5**: 363–366.
8 Salavati A, Prasad V, Schneider CP, Herbst R, Baum RP. Peptide receptor radionuclide therapy of Merkel cell carcinoma using (177)lutetium-labeled somatostatin analogs in combination with radiosensitizing chemotherapy: a potential novel treatment based on molecular pathology. *Ann Nucl Med* 2012; **26**: 365–369.
9 Epstude M, Tornquist K, Riklin C *et al.* Comparison of (18)F-FDG PET/CT and (68)Ga-DOTATATE PET/CT imaging in metastasized merkel cell carcinoma. *Clin Nucl Med* 2013; **38**: 283–284.
10 Buder K, Lapa C, Kreissl MC *et al.* Somatostatin receptor expression in Merkel cell carcinoma as target for molecular imaging. *BMC Cancer* 2014; **14**: 268.
11 Filice A, Fraternali A, Frasoldati A *et al.* Radiolabelled somatostatin analogues therapy in advanced neuroendocrine tumors: a single centre experience. *J Oncol* 2012; **2012**: 320198.
12 Treglia G, Castaldi P, Villani MF *et al.* Comparison of 18F-DOPA, 18F-FDG and 68Ga-somatostatin analogue PET/CT in patients with recurrent medullary thyroid carcinoma. *Eur J Nucl Med Mol Imaging* 2012; **39**: 569–580.
13 Edge S, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A. AJCC Cancer Staging Manual, 7th edn. Springer, New York, NY, 2010.
14 Enzenhofer E, Ubl P, Czerny C, Erovic BM. Imaging in patients with merkel cell carcinoma. *J Skin Cancer* 2013; **2013**: 973123.
15 Hawryluk EB, O'Regan KN, Sheehy N *et al.* Positron emission tomography/computed tomography imaging in Merkel cell carcinoma: a study of 270 scans in 97 patients at the Dana-Farber/Brigham and Women's Cancer Center. *J Am Acad Dermatol* 2013; **68**: 592–599.
16 Poeppel TD, Binse I, Petersenn S *et al.* Differential uptake of (68)Ga-DOTATOC and (68)Ga-DOTATATE in PET/CT of gastroenteropancreatic neuroendocrine tumors. *Recent Results Cancer Res* 2013; **194**: 353–371.
17 Voog E, Biron P, Martin JP, Blay JY. Chemotherapy for patients with locally advanced or metastatic Merkel cell carcinoma. *Cancer* 1999; **85**: 2589–2595.
18 Siva S, Byrne K, Seel M *et al.* 18F-FDG PET provides high-impact and powerful prognostic stratification in the staging of Merkel cell carcinoma: a 15-year institutional experience. *J Nucl Med* 2013; **54**: 1223–1229.
19 Treglia G, Dabbagh Kakhki VR, Giovanella L, Sadeghi R. Diagnostic performance of fluorine-18-fluorodeoxyglucose positron emission tomography in patients with Merkel cell carcinoma: a systematic review and meta-analysis. *Am J Clin Dermatol* 2013; **14**: 437–447.