OPEN

A Patient With Metastatic Sarcoma was Successfully Treated With Radiolabeled Somatostatin Analogs

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Abstract: We present a sarcoma patient with a tumor reduction of more than 50% in lung metastasis after 2 single courses of the investigational medical product Lutathera (^{177}Lu-DOTA0-Tyr3-octreotate). She was resistant to more than 6 lines of therapy including all the available active drugs in soft tissue sarcomas. The high expression of somatostatin receptors was shown by microarrays and Octreoscan. The overall duration of response exceeded 1 year.

Key Words: microarray expression, Octreoscan, peptide receptor radionuclide therapy, radiolabeled somatostatin analogs, sarcoma, somatostatin receptors, synovial sarcoma

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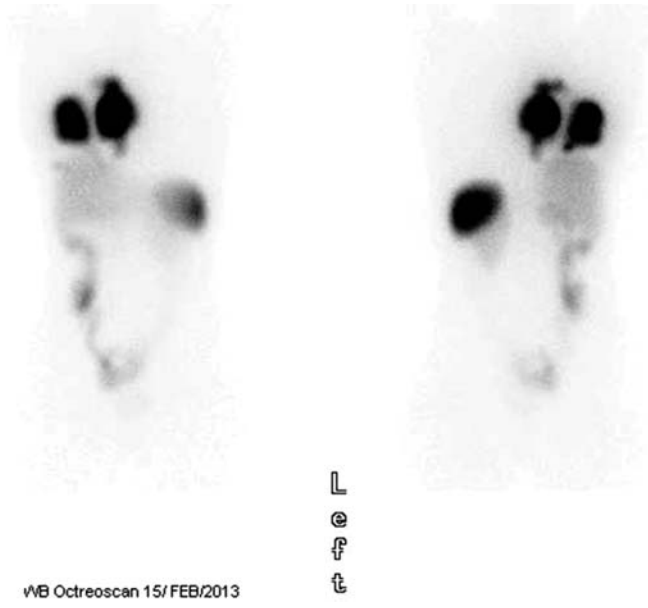

FIGURE 1. A 36-year-old woman with a diagnosis of a left popliteal synovial sarcoma treated with surgery and chemotherapy (adryamicin/ifosfamide). A local recurrence required additional surgery followed by chemoradiotherapy (70 Gy plus ifosfamide). She had a disease-free interval of 4 years until lung metastasis was detected. Between October 2007 and May 2012, she was treated with several drug combinations (in total, she had been resistant to >6 lines of therapy including all the available active drugs in soft tissue sarcomas) and operated by thoracotomy in 3 stages. Pazopanib treatment was initiated in November 2012 and then interrupted because of hemoptysis. She was referred to our institution in February 2013 presenting extreme weight loss and a performance status of 2. The most recent scan showed lung metastasis in more than 50% of the right side of the thorax, with large pleural disease and mediastinum involvement. Traqueal compression at carina level was present. A computed tomography–guided needle biopsy from a lung metastatic lesion was performed for an expression microarray. A highly significant expression of the somatostatin receptor 2 (SSTR2) gene (in excess of 10-fold) and to a lesser extent SSTR5 (>5-fold) as compared with the normal control tissue was apparent in the normalized microarray data. There are references in literature identifying SSTR in more than 80% of the soft tissue tumors analyzed by reverse transcriptase–polymerase chain reaction,[1,2] as well as positive uptake in molecular imaging.[3,4] Figure 1 shows the high uptake in the right hemithorax in the Octreoscan confirming the potential indication for somatostatin analog–based treatments. She began lanreotide 30 mg intramuscularly every 2 to 3 weeks until May 31, 2013, reaching disease stabilization.

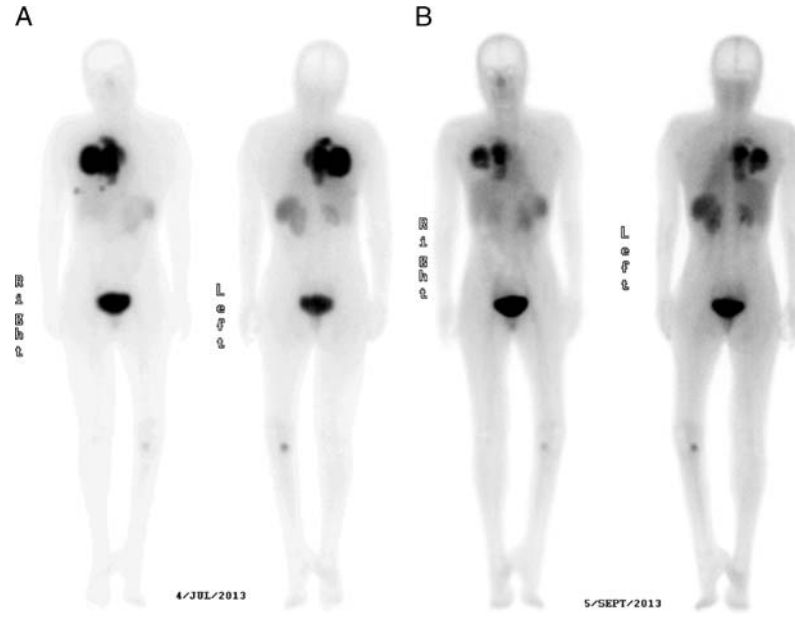

FIGURE 2. She underwent 2 cycles with Lutathera, a radiolabeled somatostatin analog that has been shown to be an effective and safe treatment for somatostatin receptor–positive gastroenteropancreatic neuroendocrine tumors[5–7]: 5.55 GBq in July 2013 and 7.4 GBq in September 2013. Figure 2 shows posttherapy ^{177}Lu-octreotate whole-body scans (**A**, first course, July 2013; **B**, second course, September 2013). A superior uptake than the baseline Octreoscan can be shown in the first ^{177}Lu-octreotate scan and additionally 2 implants upon the chest wall and a new local recurrence of the primary lesion in the left knee. Tolerance was excellent as it has been previously reported.[8,9] After the first cycle, 1 episode of hemoptysis was observed, without any hematologic disturbance, and resolved with symptomatic medication. The patient had a very important clinical improvement from the beginning of the treatment, better quality of life, performance status, and daily life activities. In addition, a significant reduction of lung masses can be shown by comparison of both ^{177}Lu-octreotate scan after the first single course.

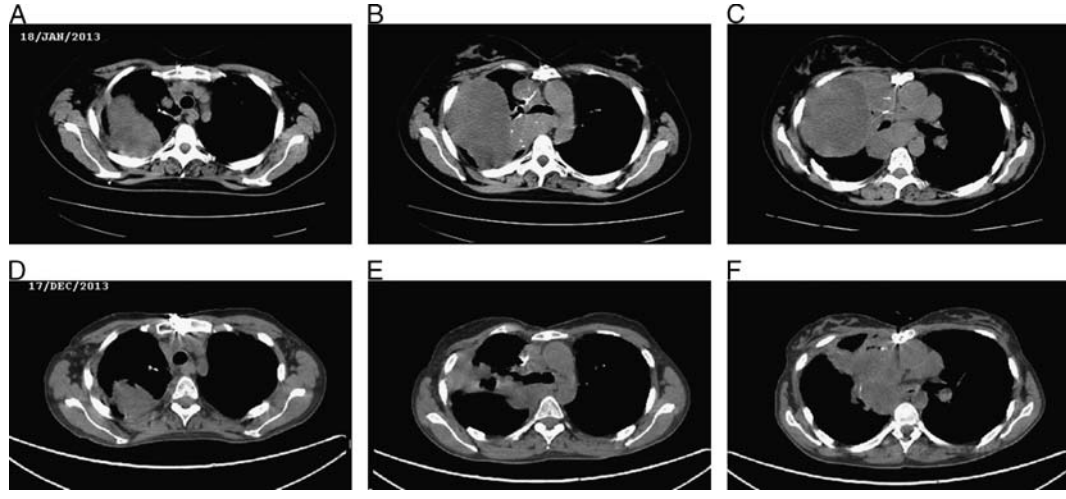

FIGURE 3. Objective partial response based on RECIST criteria (reduction of >50%) was observed after 2 courses of Lutathera. Figure 3 shows baseline thoracic computed tomography scan (**A–C**) and after 11 months (**D–F**). The overall duration of her response (stabilization with cold lanreotide and partial response with Lutathera) exceeded 1 year. The objective reduction made possible a surgical approach in an attempt to reduce the tumor load, and therefore a thoracotomy and debulking was carried out in January 2014. Unfortunately, an accidental rupture of the right atrium with profuse bleeding occurred during surgery. She died in April 2014 after a long stay in the intensive care unit. Lutathera is an investigational medical product in late-stage development.