



# First experience of durable cytoreduction in chronic lymphoid leukemia with $^{177}\text{Lu}$ -DOTATATE

Tijana Savovic<sup>1</sup> · John O. Prior<sup>1</sup> · Marie Nicod-Lalonde<sup>1</sup> · Alberic Bressoud<sup>2</sup> · Stéphane Roux<sup>3</sup> · Niklaus Schaefer<sup>1</sup> · Marie Meyer<sup>1</sup>

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## Abstract

This is the first described case of effective and durable cytoreduction after PRRT with  $^{177}\text{Lu}$ -DOTATATE in a 75-year-old female, with B cell chronic lymphoid leukemia, and well-differentiated metastatic neuroendocrine tumor.

**Keywords** PET/CT ·  $^{177}\text{Lu}$ -DOTATATE · Chronic lymphoid leukemia · Neuroendocrine tumor · PRRT

We report the case of a 75-year-old female, with B cell chronic lymphoid leukemia (CLL) since 2013, and well-differentiated metastatic neuroendocrine tumor of terminal ileum (pT4 pN1 pM1, G1, L1, V1, R0).

The patient did not receive any treatment for the CLL because she was in Binet stage A, with no node or organ enlargement and normal levels of hemoglobin and platelets.

The neuroendocrine tumor of terminal ileum was diagnosed in 2015, with complete resection of both primary lesion and peritoneal implants. The patient relapsed in 2016 with metastatic liver lesions, and was treated with Lanreotide sc 120 mg every four weeks. In 2018, she further progressed with an increase of both number and size of the diffuse liver metastasis. A treatment with  $^{177}\text{Lu}$ -DOTATATE was decided in the multidisciplinary tumor board.

Peptide receptor radionuclide therapy (PRRT) provides a means of delivering targeted radiation with a high therapeutic index to tumors that express somatostatin receptors. Recent studies have shown that PRRT with  $^{177}\text{Lu}$ -DOTATATE is indicated in patients with advanced, progressive, somatostatin-receptor-positive midgut neuroendocrine tumors [1–3].

The pre-treatment images showed multiple metastatic liver lesions with high uptake of  $^{68}\text{Ga}$ -DOTATATE (Fig. 1a–c), and no uptake of  $^{18}\text{F}$ -FDG (Fig. 1d–f). In addition, the scans did not show any adenopathy related to leukemia. The blood count showed increased number of total leukocytes (57.3 G/L) and lymphocytes (50.5 G/L), due to the leukemia, and normal levels of hemoglobin and platelets.

Due to possible hematologic toxicity of the treatment in the context of the CLL, the patient received reduced doses of  $^{177}\text{Lu}$ -DOTATATE with no complication: 3700 MBq at cycle 1, 4500 MBq at cycle 2, and 5400 MBq at cycle 3 (cycle 4 not administered yet). Hematologic toxicity of  $^{177}\text{Lu}$ -DOTATATE is well known, with acute transient side effects (leucopenia, anemia, thrombocytopenia) and delayed side effects such as myelodysplastic syndrome [2, 4–6]. However, serious hematologic toxicity is rare.

The successive post-treatment  $^{177}\text{Lu}$ -DOTATATE SPECT/CT showed a high uptake in  $^{68}\text{Ga}$ -DOTATATE positive liver metastases and a good response to PRRT. Indeed, based on quantitative SPECT/CT (xSPECT/CT), we showed a decrease of the  $^{177}\text{Lu}$ -DOTATATE uptake about 20% at cycle 2, and 30% at cycle 3, in comparison to baseline.

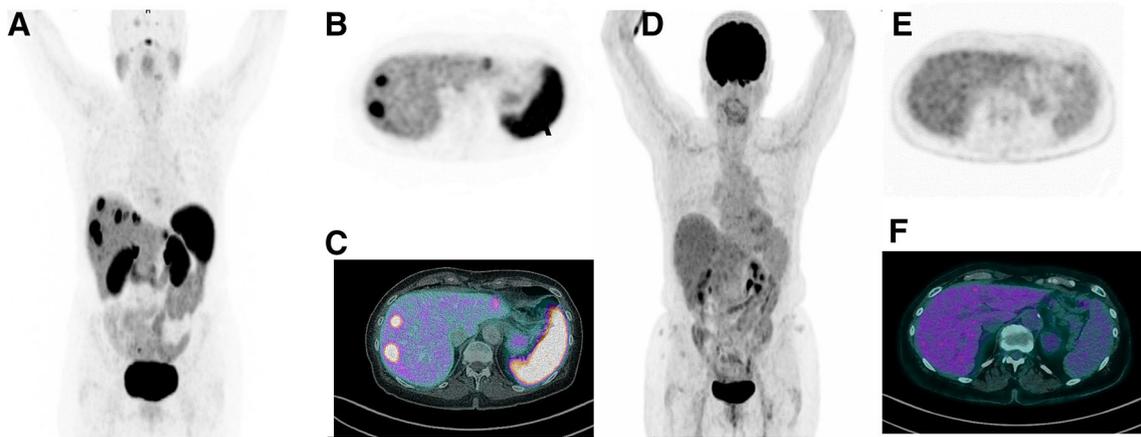
At the same time, one month after the therapy, the blood test showed normalization of total leukocytes (6.3 G/L (N: 3.8–10.7 G/L)) and lymphocytes (2.9 G/L (N: 1.5–4.8 G/L)), and still normal levels of hemoglobin and platelets. This normalization of leukocytes and lymphocytes lasted for at least 6 months, before the third treatment cycle (leukocytes 6 G/L, lymphocytes 1.9 G/L). The first blood count after 2 weeks after the second cycle showed a mild thrombocytopenia (135 G/l) and lymphocytopenia (0.84 G/l) and normal

✉ Niklaus Schaefer  
niklaus.schaefer@chuv.ch

<sup>1</sup> Nuclear Medicine Department and Molecular Imaging, CHUV, Rue du Bugnon 46, 1011 Lausanne, Switzerland

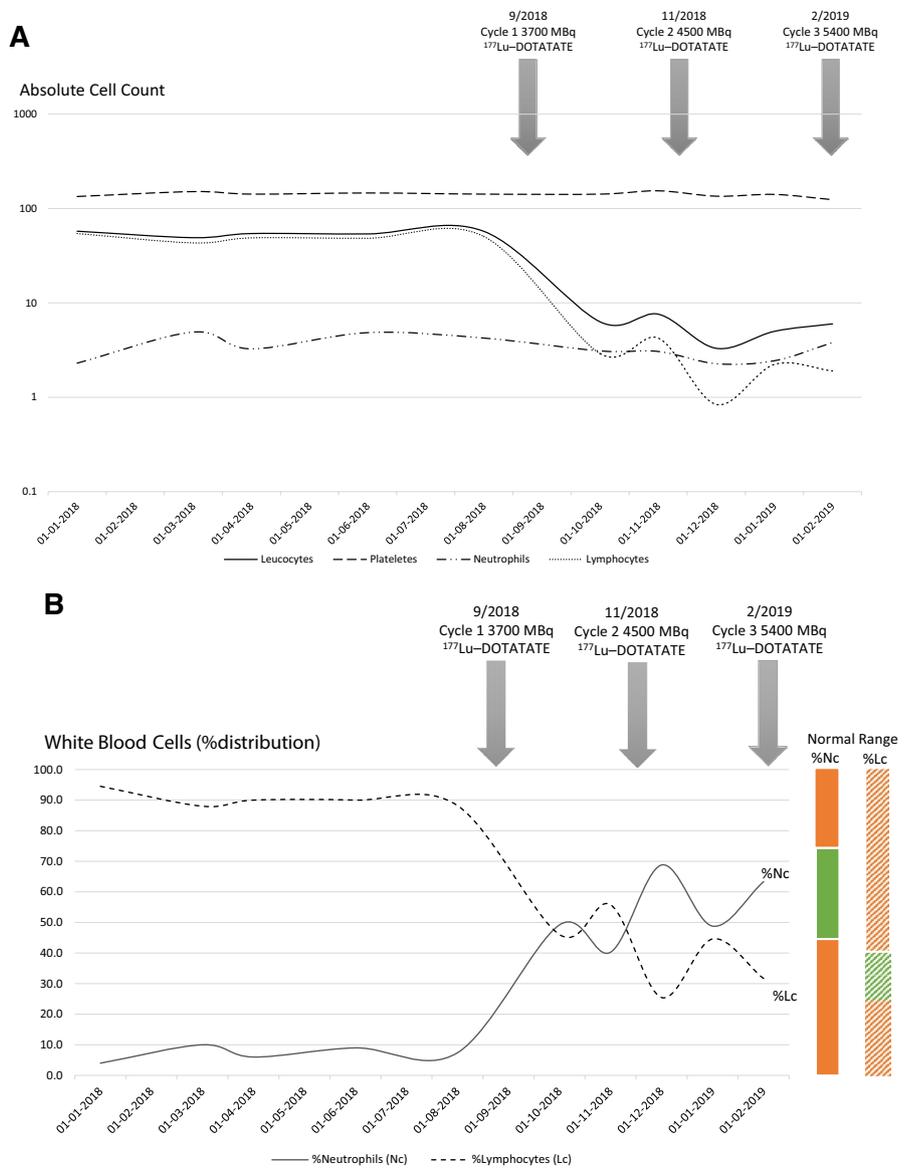
<sup>2</sup> Medical Oncology, Clinique Bois-Cerf, Lausanne, Switzerland

<sup>3</sup> Internal Medicine, Centre Médical du Bouveret, Bouveret, Switzerland



**Fig. 1** Pre-treatment  $^{68}\text{Ga}$ -DOTATATE (a–c) and  $^{18}\text{F}$ -FDG (d–f) PET/CT

**Fig. 2** Absolute cells count (a) and white blood cells distribution (b)



neutrophil (2.27 G/l) and leucocyte count (3.3 G/l) (Fig. 2a). The reversed neutrophil-to-lymphocyte ratio normalized after the second cycle. (Figure 2B). Hemoglobin levels and kidney clearance remained stable.

Previous studies have shown that both human normal lymphocytes and leukemia cells bear receptors for somatostatin [7]. It has further been shown that somatostatin targets specifically CLL cells [8] and has anti-proliferative activity in low-grade NHL including CLL [9]. To our knowledge, this is the first published case of durable cytoreduction in CLL PRRT induced by  $^{177}\text{Lu}$ -DOTATATE monotherapy.

### Compliance with ethical standards

**Conflict of interest** All the authors declared that they have no conflict of interest.

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