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Impressive response to temsirolimus in a patient with chemotherapy refractory diffuse large B-cell non-Hodgkin's lymphoma

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Impressive response to temsirolimus in a patient with chemotherapy refractory diffuse large B-cell non-Hodgkin's lymphoma

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Philipp Kiewe* and Eckhard Thiel

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Dear Editor,

1
2 Temsirolimus is a selective inhibitor of the cell proliferation promoting intracellular
3
4 protein mTOR (mammalian target of rapamycin). Its activity in lymphatic
5
6 malignancies has first been demonstrated in relapsed mantle-cell lymphoma [1].
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8
9 Further studies confirmed activity in this lymphoma entity and established a weekly
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11 dosage of 75mg as approved treatment regimen [2], although a weekly dose of 25mg
12
13 remains an effective treatment option [3]. Experience with temsirolimus in other
14
15 entities of NHL is limited to a phase II study in recurrent DLCBL, follicular lymphoma
16
17 and chronic lymphocytic leukemia/small lymphocytic lymphoma [4]. In 19 evaluable
18
19 patients with DLCBL and a median of ≥ 2 prior treatment lines, a remarkable overall
20
21 response rate of 42% was observed with a weekly temsirolimus dosage of only
22
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26
27 25mg.

28
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30
31 A 44-year old woman was diagnosed with diffuse-large B-cell Non-Hodgkin's
32
33 lymphoma (NHL) limited to the tongue base (stage IBE) in June 2003. After initial
34
35 treatment with 6 cycles of dose-intensified cyclophosphamide, adriamycin, vincristine,
36
37 etoposide and prednisolone (Hi-CHOEP), a complete response was achieved. The
38
39 patient relapsed in October 2006 with intrathoracic and abdominal manifestations.
40
41
42 Salvage therapy included 3 cycles of rituximab, ifosfamide, carboplatin and etoposide
43
44 (R-ICE) followed by high-dose carmustine, etoposide, cytarabine, melphalan (HD-
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46 BEAM) and autologous stem-cell transplantation resulting in complete response. In
47
48 July 2008, second relapse occurred with cervical and abdominal lymph node
49
50 enlargements. Treatment was initiated with 5 cycles of rituximab and bendamustine
51
52 yielding another complete response. Remission, however, was short-lived, and in
53
54
55 January 2009 disease recurred. Sequential treatment included one cycle of rituximab,
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57
58 dexamethasone, high-dose cytarabine, cisplatin (R-DHAP) and one cycle of
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1 rituximab, high-dose cytarabine, mitoxantrone (dose-modified R-HAM) in reconfirmed
2 CD20-positive disease followed by a second high-dose protocol with ⁹⁰Y-ibritumomab
3
4 tiuxetan, cyclophosphamide, etoposide, carmustine (Z-CVB) and autologous stem-
5
6 cell support. This time, only partial remission was achieved with disease progression
7
8 shortly thereafter in August 2009. Further treatment lines including lenalidomide, two
9
10 cycles each of gemcitabine/mitoxantrone and carboplatin/ifosfamide were ineffective.
11
12 In November 2009 the patient presented with a large intraabdominal tumor-bulk
13
14 resulting in a massively distended abdomen. Lactate dehydrogenase (LDH) had risen
15
16 to 480 U/L (< 247) and bone marrow function was poor with severe tricytopenia,
17
18 predominantly thrombocytopenia of 50 x 10⁹/l (150-400).
19
20
21

22 At this time, weekly monotherapy with 25mg temsirolimus was started. A dramatic
23
24 clinical response was seen after only 5 infusions with normalization of the abdominal
25
26 exam and LDH. No relevant toxicity was noted. The sixth temsirolimus infusion was
27
28 combined with bendamustine after platelet counts had risen to 136 x 10⁹/l. One week
29
30 thereafter, restaging computed tomography (CT) scans confirmed clinical response
31
32 with only minimal residual abdominal lymphoma manifestations compared with pre-
33
34 treatment imaging (Fig 1a+b). Temsirolimus infusions were continued but
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36 unfortunately, tumor progression was observed four weeks later.
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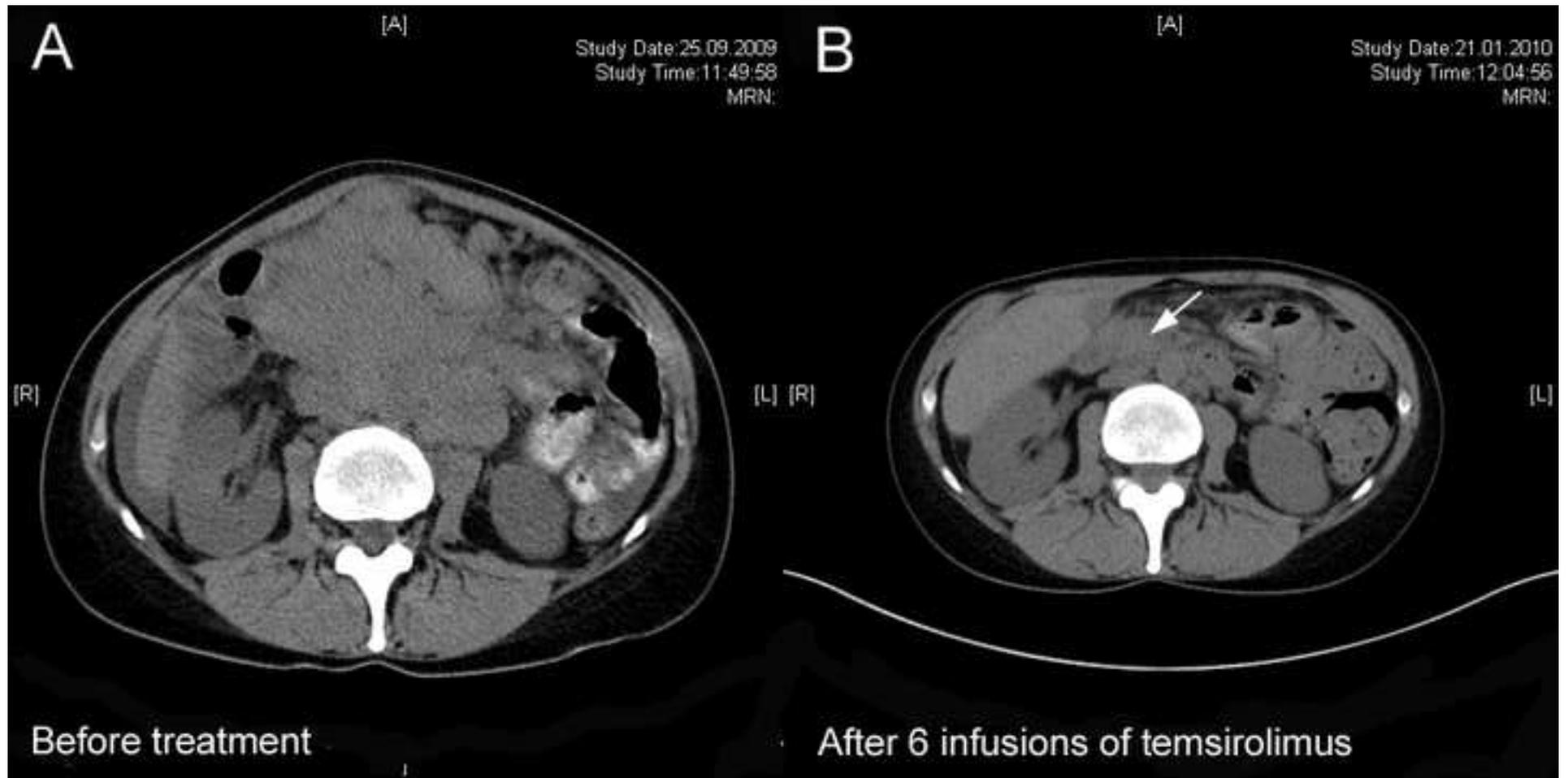
46 The very favourable response in our patient with highly pretreated refractory DLCBL,
47
48 though short-lived, supports the evidence of a high activity of temsirolimus in NHL
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50 including DLCBL. Further investigations are clearly warranted, preferably in less
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52 advanced disease and in combination with chemotherapy. Moreover, the optimal
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54 dosage needs to be defined.
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Figure 1 Abdominal CT scan without intravenous contrast-enhancement before temsirolimus treatment (a) and after six weekly infusions (b) showing only minimal residual lymphoma manifestations (arrow).

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