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Response to chemotherapy of solitary fibrous tumour: A retrospective study ☆

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Abstract ***Background:*** To report on anthracycline-based chemotherapy in a retrospective case-series analysis of solitary fibrous tumour (SFT) patients treated within the Italian Rare Cancer Network.

Patients and methods: We reviewed a set of SFT treated with chemotherapy since 2002, focusing on anthracycline, administered alone or in combination with ifosfamide. Responses to ifosfamide as a single agent were also evaluated. Pathologic diagnosis was centrally reviewed, distinguishing typical, malignant (MSFT) and dedifferentiated (DSFT) subtypes.

Results: Among 42 SFT patients treated with chemotherapy, we selected 31 cases (mean age: 62 years; locally advanced/metastatic: 13/18; front-line/further line: 25/6; typical/MSFT/DSFT/not assessable: 1/17/12/1) who received anthracycline-based chemotherapy (anthracycline monotherapy: eight; anthracycline + ifosfamide: 23). 30 patients are evaluable for response. Best response by Response Evaluation Criteria in Solid Tumours (RECIST) was: partial response (PR): 6 (20%), stable disease (SD): eight (27%), progressive disease (PD): 16 (53%) cases. Responses were confirmed after 3 months. Median progression-free survival (PFS) was 4 (range 2–15) months, with 20% of patients being progression-free at 6 months. PR was found in 2/18 (11%) MSFT and 4/12 (30%) DSFT, with a median PFS of 3.5 and 5 months in MSFT and DSFT, respectively. 19 patients received high-dose prolonged-infusion

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ifosfamide (front-line/further line: 11/8; typical/MSFT/DSFT: 0/15/4) with two (10%) PR, five (26%) SD, 12 (63%) PD.

Conclusions: This retrospective series suggests that in SFT anthracyclines have a degree of antitumour activity in the range of soft tissue sarcoma chemotherapy. Ifosfamide monotherapy seemed to have lower activity. A higher response rate was observed in DSFT in comparison to MSFT. Studies on targeted therapies are ongoing.

1. Introduction

Solitary fibrous tumour (SFT) is a rare soft tissue sarcoma (STS), with an estimated incidence <0.1/100.000/years.[1] SFT natural history is characterised by a high cure-rate after complete surgery, with a 10–15% risk of metastasis.[2–4]

Three clinical-pathologic variants of SFT can currently be recognised: typical SFT (TSFT), malignant (MSFT) and dedifferentiated (DSFT).[3] TSFT is characterised by bland morphologic appearance and usually a favourable outcome, but unexpected recurrences with aggressive behaviour can be observed rarely.[5] MSFT is characterised by a mitotic index ⩾4/10HPF, coupled with hypercellularity and/or necrosis and/or pleomorphism. DSFT's hallmark is the presence of transition to high-grade morphology mimicking not otherwise specified sarcomas or distinct high-grade sarcoma types. DSFT shows an aggressive behaviour with a higher metastatic potential.[6,7] The high-grade component may be present at tumour onset. With the disease progression this component may become dominant leading to possible under recognised recurrent SFT, if tumour sampling of previously resected primary tumour is not available for comparison.

Standard treatment of SFT is the complete surgical resection but in case of advanced disease a medical treatment is needed. No prospective studies are available on the activity of chemotherapy in SFT. Few retrospective series including <20 patients showed a variable response rate (RR) to doxorubicin-based chemotherapy, ranging from 50% to 0%.[8–11] Objective responses to trabectedin in two SFT patients[12,13] were published, too. Among molecular target agents, the activity of temozolomide and bevacizumab,[14] sorafenib, sunitinib,[15–19] pazopanib[20] and IGF1R inhibitors[18,21] was described in the last years. Responses were non-dimensional in the majority of patients.

We herein report on a retrospective series of 42 advanced SFT treated with chemotherapy at our institution and within the Italian Rare Cancer Network, a collaborative network sharing clinical cases of rare cancers in Italy, focusing on the subgroup of 32 patients treated with anthracycline-based chemotherapy, that is the standard front-line treatment in advanced STS. We also reviewed the data on the activity of ifosfamide as single agent administered in 19 more cases.

2. Patients and methods

2.1. Patients selection

We retrospectively identified 42 patients with locally advanced or metastatic SFT consecutively treated with chemotherapy at Fondazione IRCCS Istituto Nazionale Tumori, Milano (39 patients), and those included in the data-base of the Italian Rare Cancer Network, registered by other three Italian institutions (S. Maria Hospital, Terni, one patient; Ospedali Riuniti, Bergamo, one patient; University Campus Bio-Medico, Roma, one patient), from January 2002 to June 2012. We selected the subgroup of 31 patients who received anthracycline-based chemotherapy and the subgroup of 17 patients treated with ifosfamide monotherapy. The analysis was approved by the Institutional Ethics Committee.

Histological diagnosis was centrally reviewed in all cases by two expert pathologists (Silvana Pilotti and Angelo Paolo Dei Tos). All patients had evidence of progressive disease before starting treatment, Eastern Cooperative Oncology Group performance status (ECOG PS) ⩽ 3 and an adequate bone marrow and organ function. All patients provided a written informed consent to data collection within the network and to the treatment. Data were extracted from individual patient file and analysed.

Tables 1 and 2 show the characteristics of patients treated with anthracycline and with high-dose ifosfamide, respectively. Supplementary Table 1 summarises clinical characteristics of the whole series.

2.2. Pathology

The diagnosis was rendered according to the World Health Organization (WHO) classification[2] and to updated criteria.[6] The tumour specimen evaluated was represented by the primary tumour and the available sample closest to the start of chemotherapy, to better understand the correlation between tumour aggressiveness degree and sensitivity to the medical treatment.

Immunoprofile assessment was performed by using the following antibodies and dilutions: CD34 (NCL-L-END, Leica Microsystems GmbH, Wetzlar, Germany; 1:200), Ki-67 (Mib-1, DAKO, Glostrup, Denmark; 1:200), bcl2 (124, DAKO; 1:500). Antigen retrieval was made at 95 °C with 5 mM pH 6 citrate buffer for