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Chemotherapy of Soft Tissue Sarcoma

A Clinical Evaluation of Treatment over Ten Years

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The aim of the study was to evaluate the effect of palliative chemotherapy on soft tissue sarcomas given outside controlled trials. Therapy and response rates of 77 patients with non-resectable sarcoma treated with different regimens between 1991 and 2000 were reviewed. Thirty-six patients were treated with first-line chemotherapy comprising cyclophosphamide+vincristine+doxorubicin+dacarbazine (CYVADIC), with a response rate of 28% (median response duration 5.5 months). Etoposide and ifosfamide (IVP, or VIG, which also includes granulocyte colony-stimulating factor (G-CSF)) were used in the treatment of 18 patients. The response rate was 22% (median response duration 4.5 months); Nineteen patients were treated with doxorubicin+ifosfamide and one patient responded. Four patients received other first-line treatments. Thirty-eight patients were given second-line chemotherapy and 4 (10%) patients responded. Thirteen patients were given third-line treatment and 5 patients received fourth-line treatment, but without any response. Disease progression was the dominant reason for discontinuation of therapy. The response rate in the present study was lower than the best published results, probably due to the fact that our soft tissue sarcoma patient material was unselected. Treatment with CYVADIC yields at least as high a response rate as the more recently described doxorubicin+ifosfamide combination, but third- and fourth-line therapy is not beneficial. Clinical trials with more active drugs are needed, as are more predictive and prognostic tests and a better selection of patient groups suited for different treatment options for soft tissue sarcomas.

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Soft tissue sarcomas (STSs) are a heterogeneous group of mesenchymal tumors that comprise approximately 1% of all malignancies. In Sweden, the incidence of these tumors is about 25 cases/million/year and the male: female ratio is 1.3:1. At the time of diagnosis, about 50% of patients are over than 60 years of age, with the exception of rhabdomyosarcoma, synovial sarcoma and epithelioid sarcoma, which are more common in children and young adults (1).

There are about 30 different histogenetic types of STS (2). Malignant fibrous histiocytoma (MFH), the most common type, accounts for approximately 30% of all cases. Other common types are liposarcoma, leiomyosarcoma and synovial sarcoma. STSs are usually disseminated hematogenously and are associated with a considerable risk of mortality. About 50% of patients with high-grade lesions die of disseminated disease.

The principal STS treatment is radical surgery. When surgery and radiotherapy are combined, better local control can be achieved. Despite local control, 40–60% of patients with high-grade sarcomas will die of metastatic disease (3).

As a group, STSs respond poorly to chemotherapy. Only a few cytotoxic agents have relevant activity against these tumors. Chemotherapy has been used both in adjuvant situations and in locally advanced or metastatic disease. Agents with the most documented cytotoxic effect are doxorubicin, dacarbazine, ifosfamide, cyclophosphamide, etoposide, vincristine and methotrexate (4).

In a review article by Antman, doxorubicin is described as the most active single agent for patients with STS, inducing overall response rates (RRs) of 15–35% (4). Gherlinzoni et al. showed a therapeutic benefit of doxorubicin therapy given in an adjuvant situation for high-grade extremity STS (5). By contrast, in an adjuvant multicenter study published by Alvegård et al. (1989), doxorubicin did not confer a significant clinical benefit in high-grade STS (6). Consequently, the Scandinavian Sarcoma Group (SSG) decided not to treat patients with adjuvant chemotherapy after radical surgery (SSG I protocol).

During the past few decades, there has been increasing use of combination chemotherapy. In their review article, Gottlieb et al. suggest that the effect of combination therapy with doxorubicin+dacarbazine is superior to doxorubicin given on its own (7). Yap et al. treated 125

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advanced STS patients with a combination of doxorubicin, dacarbazine, cyclophosphamide, and vincristine, the so-called 'CYVADIC regimen', with a reported RR of 50% (8). In 1976–1979, in a randomized study by the Southwest Oncology Group (SWOG) comprising 112 patients, three treatment combinations were compared, i.e., doxorubicin + dacarbazine vs. doxorubicin + dacarbazine + cyclophosphamide vs. doxorubicin + dacarbazine + actinomycin D, but no statistically significant differences in RR were found (33%, 34%, and 24%) (9). In a randomized study comprising 663 patients with advanced STS conducted by the European Organization for Research and Treatment of Cancer (EORTC), it was concluded that single-agent doxorubicin should be the standard treatment. The more toxic CYVADIC was not superior to doxorubicin alone (the RR for CYVADIC was 28.4%, while the RR for doxorubicin was 23.3%) (10). In an EORTC study of 317 patients treated either with CYVADIC or with no adjuvant therapy (controls), CYVADIC resulted in a higher relapse-free survival (56% vs. 43%), and local recurrence was also significantly reduced (17% vs. 31%). The occurrence of distant metastases (32% vs. 36%) and overall survival (63% vs. 56%) did not differ significantly between the treatment groups (11).

A combination of ifosfamide + etoposide was used by Saeter et al. in a pilot study at the Norwegian Radium Hospital, with an RR of 50% but with considerable hematological toxicity. Another study with the addition of granulocyte colony-stimulating factor (G-CSF) and dose escalation gave an RR of 42% (12). Other combinations of ifosfamide + etoposide in various doses and forms of administration have given an RR of 10–42% (13–16).

The SSG XIII protocol used a combination of doxorubicin + ifosfamide in a non-randomized adjuvant study. We used this combination also for advanced disease. A similar type of treatment has been reported to give an RR of 35–45% in studies elsewhere (17,18). The same combination was also used in the study by Santoro et al. (10), but with no significant clinical benefit over that derived from doxorubicin alone (RR 25.2% vs. 21.3%).

The purpose of this retrospective study was to evaluate different chemotherapy regimens implemented outside clinical trials for STSs during the period 1991–2000 at the Department of Oncology, Linköping University Hospital, Linköping, Sweden, and to compare the results with the published data.

MATERIAL AND METHODS

During the period 1991–2000, a total of 77 patients (47 men and 30 women) were treated with different kinds of cytostatic chemotherapy drugs at the Department of Oncology of Linköping University Hospital. The median age was 59 years (range 15–77 years) (Table 1). Data were collected from the patients' files.

For 21 patients (27%), the localization of the primary tumor was in the extremities. Eight patients (10%) had tumors in the head and neck region, and 47 (61%) had primary tumors in the trunk. One patient at the time of diagnosis had bone metastases from STS, but the primary site of the tumor was unknown.

To classify the tumors, we used the grading system described by Angervall et al. (2). In total, 59 patients (77%) had tumors considered to have a higher grade of malignancy (grades '2–3', 3, '3–4', and 4). Eight patients (10%) had a low malignancy grade (grade 1–2) and in 10 patients (13%), no grading was reported (2). At the time of chemotherapy, 69 patients (90%) had metastatic disease, while eight (10%) had localized, non-resectable disease. The sites of metastases were; lungs n = 37 patients, liver n = 20, abdomen n = 17, retroperitoneal lymph nodes n = 9, trunk wall n = 4, pelvis n = 7, pleura n = 5, bone n = 8, local lymph nodes n = 1, mediastinal lymph nodes n = 4, cardia n = 1 and the brain in one patient. Several metastatic sites could occur in the same patient.

The principal aim for giving chemotherapy in this tumor group was to achieve at least stable disease (SD), recorded at an evaluation performed approximately every third month. In the case of progressive disease, the chemotherapy was either terminated or exchanged for another drug combination if the patient continued to have a good performance status. The method for evaluation of response was based on the WHO criteria (Geneva, 1979). During the period studied, the criteria for selection of drug regimens was based on reported results and more informal discussions within the frame of the SSG meetings.

Half of the sarcomas were histologically classified as leiomyosarcoma and MFH. The different first-line treatment regimens together with the histology of the sarcomas are presented in Table 2. CYVADIC was the most commonly used treatment combination. The doses used in this combination were: cyclophosphamide 600 mg/m^2, on day 1; vincristine 1 mg/m^2 (max 2 mg), day 1+8; doxorubicin 30 mg/m^2 day 2+8; dacarbazine 250 mg/m^2 days 1–3. The doses in the IVP regimen were: ifosfamide 2 000 mg/m^2 days 1–3; etoposide 100 mg/m^2 days 1–3; mesna 400 mg/m^2 days 1–3. The VIG regimen included etoposide 600 mg/m^2 72-h infusion; ifosfamide 1 500 mg/m^2, day 1; mesna 20% of the daily ifosfamide dose at 0, 4; and 8 h and G-CSF 5 g/kg, days 5–16. The third major treatment group used in this study was the combination of doxorubicin 50 mg/m^2, 4-h infusion, day 1; ifosfamide 5 000 mg/m^2, 24-h infusion, day 1; and mesna 5 000 mg/m^2, day 1.

RESULTS

As first-line treatment, CYVADIC was given to 36 patients and resulted in an RR of 28% (two complete responses (CRs) and eight partial responses (PRs)). Eight patients (28%) had SD. The duration of response to CYVADIC

Table 1

Gender, age and regimen during first-line chemotherapy for soft tissue sarcoma

	CYVADIC	IVP/VIG	Doxo.+Ifosf.	Other
Female	20	3	5	2
Male	16	15	14	2
Total	36	18	19	4
Median age (yrs)	60	63.5	53	48
Age range (yrs)	19–77	22–73	28–69	15–75

Abbreviations: CYVADIC = cyclophosphamide+vincristine+doxorubicin+dacarbazine; IVP = etoposide and ifosfamide; VIG = etoposide and ifosfamide administered at different doses, and with granulocyte colony-stimulating factor (G-CSF) given in addition; Doxo.+Ifosf. = doxorubicin+ifosfamide.

varied from 2 to 13 months. Survival time ranged from < 1 month to 63 months after start of treatment (Table 3). The treatment results for the different sarcoma subtypes were almost similar. Responders did not have a longer survival time than the group in total.

Altogether, 18 patients were treated with the ifosfamide+etoposide (IVP) and VIG, which includes the same drugs, but at different doses and with the addition of G-CSF as first-line chemotherapy for STS. Four patients (22%) had an objective response (1 CR, 3 PRs), and 7 (39%) had SD. The survival of these patients varied from < 1 month to 75+ months. Four patients are still alive, but none was a responder. This treatment group had a shorter median survival time than did the patients given CYVADIC as first-line treatment (9.5 months vs. 16 months). In this group, patients who responded had a somewhat better median survival time (16 months) than this group as a whole (11 months) (Table 4).

Table 5 shows the results of the combination with doxorubicin+ifosfamide for treatment of STS. The regimen was administered in accordance with the SSG XIII protocol, worked out for adjuvant treatment of high-risk STS. This combination has been used in this department since September 1998 and also for 19 patients with advanced STS. The RR for this combination was 5% (one PR), with an estimated response duration of 2+ months. Seven patients (37%) had SD for between 2 and 19+ months at the time of follow-up.

For 13 patients treated first with IVP, VIG, or, in one case, trofosfamide, CYVADIC was used as second-line therapy and resulted in an RR of 15% (one CR, one PR). Five patients (38%) had SD. The patient with a CR had MFH and metastases in the axillary lymph nodes and lungs, which had progressed during first-line IVP treatment. The patient was given CYVADIC as second-line treatment and had a complete remission for at least 49 months (this patient was still alive at the last study follow-up, on 30 January 2002).

Twenty-five patients treated with CYVADIC were given IVP or VIG as second-line treatment and had an RR of 8% (two PRs) and 6 (24%) had SD. The median duration of response was higher for patients treated with CYVADIC as second-line treatment than for those given IVP/VIG (12.5 months vs. 5 months) as second-line treatment. However, there was no major difference in median survival time between these two groups (14 months vs. 12 months). The other results of the second-line treatment are summarized in Table 6.

Table 2

Different soft tissue sarcoma subgroups and first-line treatment regimens given in 1991–2000

STS subgroup	Number (%)	CYVADIC (n)	IVP/VIG (n)	Doxo.+ifosf. (n)	Other regimens (n)
Leiomyosarcoma	25 (32)	15	5	5	0
MFH	14 (18)	6	4	3	1 (trofosfamide)
Malignant schwannoma	4 (5)	2	1	0	1 (doxorubicin)
Liposarcoma	5 (7)	3	0	2	0
Angiosarcoma	4 (5)	1	2	1	0
Epithelioid sarcoma	4 (5)	1	2	0	1 (VAI-PAI-VAI)
Neurofibrosarcoma	2 (3)	1	1	0	0
Synovial sarcoma	3 (4)	2	0	1	0
Alveolar rhabdomyosarcoma	2 (3)	1	0	0	1 (EVAIA)
Sarcoma NOS	14 (18)	4	3	7	0
Total	77 (100)	36 (47%)	18 (23%)	19 (25%)	4 (5%)

Abbreviations: STS = soft tissue sarcoma; MFH = malignant fibrous histiocytoma; NOS = not otherwise specified; CYVADIC = cyclophosphamide+vincristine+doxorubicin+dacarbazine; IVP = etoposide and ifosfamide; VIG = etoposide and ifosfamide and granulocyte colony-stimulating factor (G-CSF); Doxo.+Ifosf. = doxorubicin+ifosfamide; VAI-PAI-VAI = vincristine+doxorubicin+ifosfamide-cisplatin+doxorubicin+ifosfamide-vincristine+doxorubicin+ifosfamide; EVAIA = etoposide+vincristine+doxorubicin+ifosfamide+dactinomycin.

Table 3

Results for CYVADIC as first-line treatment for soft tissue sarcoma

Sarcoma subtype	Best response (n)	Response duration (months) for each response group	Median survival (months) for each sarcoma subtype
Leiomyosarcoma, n = 15	CR (1) PR (3) SD (2) NE (2) PD (7)	7 3, 4, 9 2, 4 – –	13
MFH, n = 6	PR (1) SD (2) NE (2) PD (1)	13 7, 8 – –	16
Other, n = 15	CR (1) PR (4) SD (4) PD (6)	3 2, 3, 7, 8 1, 2, 2, 2 –	15
Total, n = 36	CR + PR (10) (28%) SD (8) (22%) NE (4) PD (14)	Median = 5.5 (Range = 2–13) Median = 2 (Range = 1–8) – –	Responders: 17.5 (Range = 8–63) Non-responders: 16 (Range = 1–49) Total: 16 (Range = 1–63)

Number of courses administered: median 4 (range = 1–20).
Abbreviations: CYVADIC = cyclophosphamide + vincristine + doxorubicin + dacarbazine; MFH = malignant fibrous histiocytoma; CR = complete response; PR = partial response; SD = stable disease; NE = not evaluable; PD = progressive disease.

As third-line chemotherapy, seven patients received high-dose methotrexate (> 1 g/m^2) for one to four cycles, but none of the patients showed a response. For third-line treatment, six patients were treated with high-dose ifosfamide, or high-dose methotrexate/cisplatinum, or DTIC/introna and IVP. Again, none of the patients responded. Fourth-line therapy given to five patients did not result in any response.

The reason for discontinuing therapy was progressive disease in 31 patients (86%) treated with CYVADIC as first-line therapy, 12 patients (67%) in the IVP/VIG group, and 14 patients (74%) in the doxorubicin + ifosfamide group.

Table 4

Results for IVP and VIG as first-line treatment for soft tissue sarcoma

Sarcoma subtype	Best response (n)	Response duration (months) for every patient in each response group	Median survival (months) for each sarcoma subtype
Leiomyosarcoma, n = 5	PR (1) PD (2) NE (2)	6 – –	7
MFH, n = 4	PR (1) SD (1) PD (2)	1 6 –	11.5
Other, n = 9	CR (1) PR (1) SD (6) PD (1)	11 3 1, 1, 1, 2, 3, 5 –	10
Total, n = 18	CR + PR (4) (22%) SD (7) (39%) PD (5) NE (2)	1, 3, 6, 11 (Median = 4.5 months) 1, 1, 1, 2, 3, 5, 6 – –	Responders: 16 (Range = 6–36) Non-responders: 11 (Range = 0–75+) Total: 9.5 (Range = 0–75+)

Number of courses administered: median 3 (range = 1–14).
Abbreviations: IVP = etoposide and ifosfamide; VIG = etoposide and ifosfamide administered at different doses, and with granulocyte colony-stimulating factor (G-CSF) given in addition; MFH = malignant fibrous histiocytoma; CR = complete response; PR = partial response; SD = stable disease; NE = not evaluable; PD = progressive disease.

Table 5

Results for doxorubicin+ifosfamide as first-line treatment for soft tissue sarcoma

Sarcoma subtype	Best response (n)	Response duration (months) for every patient in each response group	Survival (months) for every patient in each response group
Leiomyosarcoma, n = 5	SD (3)	2, 8, 7	27+, 14, 25+
	PD (1)	–	4
	NE (1)	–	1
MFH, n = 3	SD (3)	3, 12, 18	12, 27+, 22+
Other, n = 11	PR (1)	2	10
	SD (1)	19+	35+
	PD (8)	–	4, 5, 6, 6, 8, 9, 9, 14
	NE (1)	–	3
Total, n = 19	PR (1) (5%)	2+	Total:
	SD (7) (37%)	2, 3, 7, 8, 12, 18, 19+	Median 9
	PD (9)	–	(Range = 1–26+)
	NE (2)	–	

Number of courses administered: median 4 (range = 1–13).
Abbreviations: MFH = malignant fibrous histiocytoma; PR = partial response; SD = stable disease; NE = not evaluable; PD = progressive disease.

Two patients (6%) in the CYVADIC group could not continue their treatment because of side effects (cardiac failure and septicemia, respectively). In the group treated with IVP/VIG, six patients (33%) had to interrupt their therapy because of one or several side effects as infections (n = 2), thromboembolism (n = 2), fatigue (n = 1) or cerebral toxicity related to ifosfamide (n = 1). In the group treated with doxorubicin+ifosfamide, one patient, interrupted the therapy because of renal failure, probably related to the treatment. Besides progressive disease and side effects associated with the therapy, 3 patients (8%) in the CYVADIC group and 4 (21%) in the doxorubicin+ifosfamide group discontinued their treatment for other reasons.

Thirteen patients were treated with CYVADIC as a second-line therapy. In this situation, progressive disease was the reason for discontinuation of therapy in 4 patients (31%), and side effects (infections, anemia, stomatitis, cystitis, and impairment of performance status) in 6 patients (46%). Three patients (23%) discontinued the therapy for other reasons. Out of a total of 25 patients who received IVP/VIG as second-line treatment, 21 (84%) could not continue the treatment because of progression of the disease, 3 (12%) because of side effects (pneumonia, leucopenia, confusion, cystitis and impairment of performance status) and one patient, for other reasons.

DISCUSSION

The results reported on palliative cytotoxic treatment of STS have so far been disappointing. This is also the case in this retrospective study. In Sweden, the majority of patients who are treated for advanced STS are given chemotherapy

Table 6

Results of second-line chemotherapy for soft tissue sarcoma

First-line chemotherapy (n)	Second-line chemotherapy (n)	Best response (n)	Duration of response (months)	Survival (months)
IVP n = 9	CYVADIC	CR (1)	11	56+
VIG n = 3		PR (1)	14	57+
trofosfamide		SD (5) (38%)	4, 2, 3, 8, 17	6, 10, 5, 67+, 49+
n = 1		PD (3)	0	14, 19, 3
		NE (3)	0	1, 3, 4
		RR: 15%	Median: 12.5	14 (range = 1–67+)
CYVADIC	IVP n = 24	PR (2)	2, 8	8, 16
	VIG n = 1	SD (6) (24%)	2, 2, 2, 4, 5, 7	11, 24, 29, 45, 12, 13
		PD (15)	0	2, 3, 5, 6, 6, 7, 9, 11, 12, 13, 14, 14, 16, 20, 21
		NE (2)	0	0, 13
		RR: 8%	Median: 5	12 (range = 0–45)

Abbreviations: CYVADIC = cyclophosphamide+vincristine+doxorubicin+dacarbazine; IVP = etoposide and ifosfamide; VIG = etoposide and ifosfamide administered at different doses, and with granulocyte colony-stimulating factor (G-CSF) given in addition; CR = complete response; PR = partial response; SD = stable disease; NE = not evaluable; PD = progressive disease.

Table 7

Comparison of results from this study with published data about similar chemotherapy regimens for soft tissue sarcoma

Regimen	CR+PR (%) (this study)	CR+PR (%) (reported in the literature)	SD (%) (this study)	SD (%) (reported in the literature)	Duration of response (months) (this study)	Duration of response (months) (reported in the literature)	Work cited
CYVADIC n = 36	6+22	17+33	22 (8)	31	5.5	8	Yap et al. (8) n = 125
		8+18		38		11	Santoro et al. (10) n = 142
IVP/VIG n = 18	5+17	2+14 (IVP)	39	–	4.5	2.3	Edmonson et al. (15) n = 44
		2+10 (IVP)		43		1.9	Stuart-Harris et al. (14) n = 51
		11+31 (VIG)		25	–	10	Saeter et al. (12) n = 86
Doxo.+Ifosf. n = 19	0+5	5+20.2	37	–	2	10.2	Santoro et al. (10) n = 258
		9+26		47		12.5	Schütte et al. (17) n = 175

Abbreviations: CYVADIC = cyclophosphamide+vincristine+doxorubicin+dacarbazine; IVP = etoposide and ifosfamide; VIG = etoposide and ifosfamide administered at different doses, and with granulocyte colony-stimulating factor (G-CSF) given in addition; Doxo.+Ifosf. = doxorubicin+ifosfamide; CR = complete response; PR = partial response; SD = stable disease.

not based on study protocols but 'according to local routines'. Consequently, there is a risk that valuable information on treatment results will never be collected and published. This may lead to inadequate local treatment routines. The process of decision-making concerning selection of therapy strategies is not always rational. A single publication with positive results (even if it is a small study) can have a great impact on clinical routines for unselected patient materials. This general assumption is probably also relevant in this particular study material.

Any comparison between different regimens given over a long period (in this study, 10 years) should be made with precaution, but may provide some information on possible treatment progress. In this study, we chose not to review the pathologic-anatomical diagnosis, but rather, to use the original reports, since the treatment decision at the time was based on these reports.

In some cases, the tumors were classified as grade '2–3' or '3–4' malignancies. To simplify our analyses, this type of grading was translated to the higher of the two grades of STS given, so that '2–3' was registered as grade 3 malignancy, and '3–4' as grade 4. In comparison with the reviewed literature on STSs, our study population did not differ greatly in the frequency of histologic subgroups; however, there were fewer liposarcomas (5%) than is reported in the literature (about 10%).

Although most of the patients were evaluated according to the response grade achieved, it was not always possible to confirm response duration in accordance with the standard criteria. This means that in cases with a short response duration, patients may have not reached the reported response by definition.

We are well aware of the difficulties related to analyzing retrospective material and therefore no traditional statistical analyses were performed. However, some obvious data can be discussed. The present evaluation shows that the latest drug combination, doxorubicin+ifosfamide, was not superior to CYVADIC, which in Sweden was previously considered the standard combination. In our study, the RR for doxorubicin+ifosfamide was inferior to the RR for CYVADIC (5% vs. 28%). Patients treated with IVP as first-line therapy were by selection criteria slightly older than patients in the CYVADIC group, which may account for the higher frequency of side effects among this group.

In the case of therapy failure after first- and second-line treatments, further therapy with cytotoxic drugs resulted in no responses. The low tolerability and the minimal chance of patients deriving any benefit from third- and fourth-line treatments should be reason enough for discontinuing chemotherapy after two lines. Efforts should instead focus on good palliative care.

The RR achieved for CYVADIC was very similar to that reported by other investigators. However, the RR from treatment with doxorubicin+ifosfamide at our hospital did not reach the expected level (Table 7). Further conclusions about choice of the most effective chemotherapy regimens cannot be drawn, owing to the limited size of the study population and to the study design (i.e. retrospective, non-randomized). Furthermore, conclusions from patient's case reports regarding details about relief from symptoms or

improvement in quality of life were difficult to draw. The impression is, however, that even toxic chemotherapy is inadequate in helping the majority of STS patients. According to a recent study from the Swedish Council on Technology Assessment in Health care (SBU), only about 10% of patients treated with chemotherapy with different cancer types participated in clinical trials (19). In some common tumor types, treatments were sometimes given according to regional guidelines, but treatments were not infrequently given according to local routines, as in this study. In the same survey, Glimelius et al. state that some tumor types with limited sensitivity to chemotherapy, have anti-tumor effects that are well documented in randomized trials (20). STSs belong to the group of tumors with limited sensitivity but the effects are not well documented. However, the question of whether the effects are sufficient for routine use must be discussed. Our study illustrates that statements and definitive recommendations on the treatment of STS can only be vague. First-line chemotherapy in STS has to be further evaluated in randomized studies, including analyses of side effects, costs and quality of life issues, to find better therapies than are presently available. Meanwhile, the use of second- and further treatment lines should be avoided as a routine.

Better prognostic and predictive tests and better selection of patient groups suited for different treatment options are needed. As recent results from imatinib mesylate (Glivec, STI-571) for the treatment of gastrointestinal stromal tumors (GISTs) (21) are so positive, there is, however, hope for improved results for systemic therapies and also for STSs as a group.

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