

# Dose Reduction of Preoperative Radiotherapy in Myxoid Liposarcoma A Nonrandomized Controlled Trial

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**IMPORTANCE** Currently, preoperative radiotherapy for all soft-tissue sarcomas is identical at a 50-Gy dose level, which can be associated with morbidity, particularly wound complications. The observed clinical radiosensitivity of the myxoid liposarcoma subtype might offer the possibility to reduce morbidity.

**OBJECTIVE** To assess whether a dose reduction of preoperative radiotherapy for myxoid liposarcoma would result in comparable oncological outcome with less morbidity.

**DESIGN, SETTING, AND PARTICIPANTS** The Dose Reduction of Preoperative Radiotherapy in Myxoid Liposarcomas (DOREMY) trial is a prospective, single-group, phase 2 nonrandomized controlled trial being conducted in 9 tertiary sarcoma centers in Europe and the US. Participants include adults with nonmetastatic, biopsy-proven and translocation-confirmed myxoid liposarcoma of the extremity or trunk who were enrolled between November 24, 2010, and August 1, 2019. Data analyses, using both per-protocol and intention-to-treat approaches, were conducted from November 24, 2010, to January 31, 2020.

**INTERVENTIONS** The experimental preoperative radiotherapy regimen consisted of 36 Gy in once-daily 2-Gy fractions, with subsequent definitive surgical resection after an interval of 4 or more weeks.

**MAIN OUTCOMES AND MEASURES** As a short-term evaluable surrogate for local control, the primary end point was centrally reviewed pathologic treatment response. The experimental regimen was regarded as a success when 70% or more of the resection specimens showed extensive treatment response, defined as 50% or greater of the tumor volume containing treatment effects. Morbidity outcomes consisted of wound complications and late toxic effects.

**RESULTS** Among the 79 eligible patients, 44 (56%) were men and the median (interquartile range) age was 45 (39-56) years. Two patients did not undergo surgical resection because of intercurrent metastatic disease. Extensive pathological treatment response was observed in 70 of 77 patients (91%; posterior mean, 90.4%; 95% highest probability density interval, 83.8%-96.4%). The local control rate was 100%. The rate of wound complication requiring intervention was 17%, and the rate of grade 2 or higher toxic effects was 14%.

**CONCLUSIONS AND RELEVANCE** The findings of the DOREMY nonrandomized clinical trial suggest that deintensification of preoperative radiotherapy dose is effective and oncologically safe and is associated with less morbidity than historical controls, although differences in radiotherapy techniques and follow-up should be considered. A 36-Gy dose delivered in once-daily 2-Gy fractions is proposed as a dose-fractionation approach for myxoid liposarcoma, given that phase 3 trials are logistically impossible to execute in rare cancers.

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**M**yxoid liposarcoma is a rare cancer with an incidence of 2 per million person-years,<sup>1</sup> representing approximately 5% of soft-tissue sarcoma (STS) in adults worldwide.<sup>2</sup> The predominant tumor location is the extremity, although the cancer can also present primarily in the trunk or head and neck region. Myxoid liposarcoma occurs in a relatively young patient population, with a peak incidence in the fifth decade of life,<sup>2</sup> which implies that survivors could experience late-treatment toxic effects for a long time.

The standard of care for most intermediate- and high-grade STS, including myxoid liposarcoma, is surgical resection with radiotherapy,<sup>3,4</sup> resulting in more favorable local control than surgical resection alone.<sup>5-8</sup> With respect to timing, preoperative radiotherapy is associated with fewer late adverse effects, such as fibrosis, joint stiffness, and edema, compared with postoperative radiotherapy.<sup>9</sup> However, with an incidence of 35%, wound complications are observed more frequently after preoperative radiotherapy.<sup>8,10</sup> A shift toward preoperative radiotherapy has been observed within the past decade,<sup>11</sup> given the temporary nature of wound complications weighted against the permanent nature of fibrosis, stiffness, and edema.<sup>10</sup> However, wound complications, albeit temporary, have an adverse effect on patient quality of life, functional outcome, and health care costs.<sup>12-16</sup>

Data suggest that myxoid liposarcoma is more sensitive to radiotherapy than other STS histological subtypes.<sup>7,17-25</sup> During and continuing after radiotherapy until the date of surgical resection, myxoid liposarcoma frequently exhibits a marked tumor volume reduction, in sharp contrast to other subtypes of STS in which the volumes, as a rule, remain fairly constant.<sup>17-19</sup> In addition, unique to myxoid liposarcoma, in 78% to 100% of the resected specimens, 50% or greater pathological response is observed after a standard dose of 50 Gy preoperative radiotherapy delivered using 25 fractions, each of 2 Gy.<sup>20-23</sup> In addition to these remarkable histological responses, local control after standard preoperative radiotherapy and surgical intervention is exceptionally high, with reported 5-year local control rates of 96% to 98% in a large retrospective series.<sup>7,24,25</sup>

Given the enhanced radiosensitivity demonstrated by tumor volume reduction, pathological complete response, and excellent local control, we hypothesized that deintensification of preoperative radiotherapy for myxoid liposarcoma would not compromise the outcome. We initiated the Dose Reduction of Preoperative Radiotherapy in Myxoid Liposarcomas (DOREMY) trial to evaluate the oncological safety of decreasing the preoperative radiotherapy dose from 50 Gy to 36 Gy for myxoid liposarcoma. In addition to maintaining an excellent local control rate, this dose reduction may decrease wound complication rates and other toxic effects.

## Methods

### Design and Participants

DOREMY is a prospective, multicenter, single-group, phase 2 nonrandomized controlled trial being conducted at 9 tertiary sarcoma centers in Europe and the US. The trial opened to ac-

## Key Points

**Question** Given the radiosensitivity of myxoid liposarcoma, is it possible to reduce preoperative radiotherapy dose for this histological subtype without jeopardizing oncological outcome?

**Findings** In this nonrandomized controlled trial of 79 adults with myxoid liposarcoma of the extremity or trunk, 77 of whom underwent surgical resection, extensive pathological treatment response was found in the surgical specimens of 91% of patients along with a local control rate of 100% and a median follow-up of 25 months.

**Meaning** Findings of this trial suggest that a dose reduction is effective and oncologically safe, and thus 36 Gy is proposed as an acceptable alternative preoperative radiotherapy dose for myxoid liposarcoma.

crual on November 24, 2010. All eligible patients provided written informed consent before enrollment, and the conduct of the trial has complied with the Declaration of Helsinki<sup>26</sup> and all other applicable laws. The trial protocol ([Supplement 1](#)) and all amendments to it were approved by the institutional review board or research ethics committee of each of the 9 participating sarcoma centers. We followed the Transparent Reporting of Evaluations With Nonrandomized Designs ([TREND](#)) reporting guideline.

Eligible patients were adults ( $\geq 18$  years) with nonmetastatic and biopsy-proven myxoid liposarcoma of the extremity or trunk. Molecular confirmation of the diagnosis was mandatory. Exclusion criteria were pregnancy, Eastern Cooperative Oncology Group Performance Status score higher than 2, and previous radiotherapy to the target area.

### Procedures

The staging procedures consisted of magnetic resonance imaging (MRI) scans of the primary site followed by image-guided biopsies and computed tomography scans of the chest, abdomen, and pelvis.<sup>3,4</sup> The radiotherapy protocol, which conforms to the International Commission on Radiation Units and Measurements 50 and 62 guidelines,<sup>27,28</sup> required standardized target volume delineation. The gross tumor volume was defined by using gadolinium-enhanced, T1-weighted MRI. The clinical target volume (CTV) was constructed by expanding the gross tumor volume by 3 cm in the longitudinal axis and 1.5 cm in all other directions. Subsequently, if applicable, the CTV was manually edited to encompass any T2-weighted MRI-identified peritumoral edema in the CTV. The planning target volume was produced by expanding the CTV by 1 cm isotropically in all directions.<sup>29</sup> The treatment planning technique was intensity-modulated radiation therapy (IMRT). The total prescribed dose was 36 Gy, given in once-daily fractions of 2 Gy, 5 fractions per week. Definitive surgical resection according to local guidelines was performed a minimum of 4 weeks after the final fraction of radiotherapy, preferably after repeated preoperative MRI scans. The resection specimens were processed routinely. Diagnostic biopsies and the resection specimens were scanned using microscope slides (ScanScope; Aperio) and then uploaded on Slide Score.<sup>30</sup>

Central pathology review was performed by 3 of us, who are sarcoma pathologists (J.V.M.G.B., H.V.B., K.T.). Diagnostic biopsies were examined, and the percentage of the round cell component was estimated. For every resection specimen, all available sections were reviewed and the percentages of vital tumor cells,<sup>31</sup> hyalinization,<sup>32</sup> fatty maturation, and necrosis in the specimen were scored systematically, together adding up to 100%. Seventeen cases were independently reviewed by 2 of us (J.V.M.G.B., H.V.B.), and the concordance was 100%. The remaining 53 cases were divided among the expert pathologists for central pathology review. For 7 cases, sections from the resection specimens were not evaluable for central pathology review, and the judgment of the local pathologist was used as a surrogate to determine histological response.

### End Points

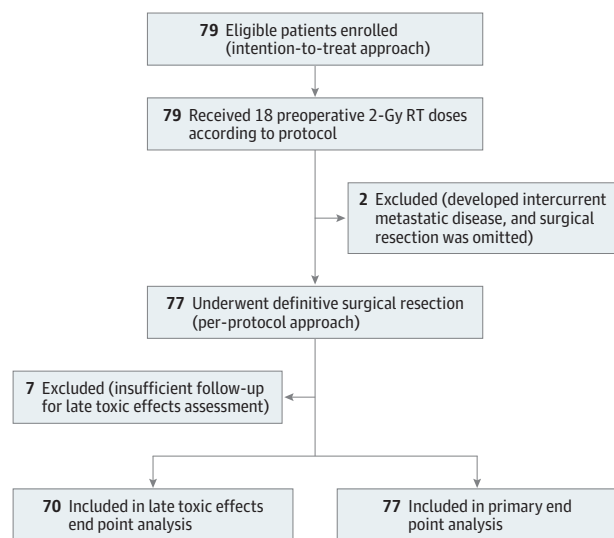
The primary end point of the trial was extensive treatment response in the definitive resection specimen (thus containing <50% of vital tumor cells). The definition of an extensive treatment response was a resection specimen containing 50% or greater of any histological treatment effect, including hyalinization, fatty maturation, and necrosis. The dose reduction was regarded as a success if 70% or more of the patients achieved an extensive treatment response. At the time the trial was conceptualized, the study group hypothesized that this rate of treatment responses would not jeopardize local control because definitive surgical resection was still to follow after radiotherapy.

Secondary end points included local control, wound complication rate, late toxic effect, progression-free survival, disease-specific survival, and overall survival. Wound complications were classified as minor, requiring no intervention or noninvasive intervention without readmission; moderate, requiring secondary wound management without secondary operation; or major, requiring secondary operation (eTable 1 in Supplement 2).<sup>8</sup> Late toxic effect was scored at the time of follow-up visits according to the Radiation Therapy Oncology Group toxicity criteria<sup>33</sup> and, in the case of edema, according to the Stern Rating Scale for Edema. Follow-up visits were scheduled every 3 months in years 1 and 2; every 6 months in years 3, 4, and 5; and annually thereafter. At these follow-up visits, the decision to perform appropriate imaging to detect metastases and to repeat the MRI scans of the primary site was left to the discretion of the local investigator.

### Statistical Analysis

A bayesian statistical design was used to provide a stopping rule for inefficacy of the decreased dose. The observed pathological response was a binary variable indicating either a 50% or greater response in the treated tumor (success, with probability  $P$ ) or a less than 50% response (failure). Jeffreys prior was used: a  $\beta$  distribution with parameters of  $\alpha = .50$  and  $\beta = 0.50$ . The posterior mean of the success probability  $P$  was calculated, and the 95% highest probability density interval (HPDI) was reported. The final conclusion of the trial will be based on the 95% HPDI and whether it excludes 70% of patients. The trial would have stopped for inefficacy if the posterior probability of  $P \geq .70$  were  $P < .05$  at any time. In the case

Figure 1. CONSORT Study Flowchart



RT indicates radiotherapy.

of potentially reaching the stopping rule, the trial would have been put on temporary hold until the observation period of the previous case was completed. At the time of the cutoff date (August 1, 2019), the minimum required number of responders to preclude the activation of the stopping rule was reached for the maximum sample size of 100 participants.

To assess the differences in baseline characteristics between responders and nonresponders, Mann-Whitney test was performed for continuous variables and Fisher exact test was performed for categorical variables. Differences in baseline presentation and type of surgical intervention were not tested, as these variables were not considered meaningful given the small numbers of patients in 1 or more of the subgroups.

The primary end point was analyzed by both per-protocol and intention-to-treat approaches (Figure 1). Local control and morbidity data were analyzed per protocol. Survival end points were measured from the date of the baseline visit and were analyzed by intention to treat using the Kaplan-Meier method. The level of statistical significance was a 2-sided  $P \leq .05$  in all tests. Statistical analyses were conducted from November 24, 2010, to January 31, 2020, with SPSS Statistics, version 25 (IBM).

## Results

A total of 79 patients were enrolled in the DOREMY trial by August 1, 2019; of these patients, 44 (56%) were men and 35 (44%) were women, with a median (interquartile range [IQR]) age of 45 (39-56) years (Table 1). All patients were treated according to the radiotherapy protocol and received a preoperative dose of 36 Gy in once-daily 2-Gy fractions, with a median (IQR) overall treatment time of 23 (23-23) days and median (IQR) follow-up time of 25 (13-38) months. The median (IQR) interval between completion of radiotherapy and surgical resection was

Table 1. Baseline Characteristics

Characteristic	No. (%)			P value
	Total (n = 79)	≥50% (n = 70)	<50% (n = 7)	
Follow-up, median (IQR), mo	25 (13-38)	25 (13-38)	35 (8-51)	NS
Age, median (IQR), y	45 (39-56)	46 (41-55)	43 (40-67)	NS
Sex				NS
Female	35 (44)	30 (43)	4 (43)	
Male	44 (56)	40 (57)	3 (57)	
Presentation				NA <sup>b</sup>
Primary	77 (98)	70 (100)	6 (86)	
Recurrence	2 (2)	0	1 (14)	
Tumor location				NS <sup>c</sup>
Lower extremity				
Proximal	62 (78)	57 (81)	3 (42)	
Distal	10 (13)	8 (11)	2 (29)	
Upper extremity	2 (3)	1 (1)	1 (14)	
Trunk	5 (6)	4 (6)	1 (14)	
Tumor diameter, median (IQR), cm	9.9 (7.3-15.9)	10.4 (8.0-16.2)	6.4 (4.3-7.8)	.003
Round cell component				NS
0%-5%	61 (77)	54 (77)	5 (71)	
>5%	15 (19)	13 (19)	2 (29)	
Unknown	3 (4)	3 (4)	0	
Type of surgical intervention				NA <sup>b</sup>
Limb sparing or other	76 (96)	69 (99)	7 (100)	
Amputation	1 (1)	1 (1)	0	
None	2 (3)	0	0	
Surgical margins				.004
Negative	72 (94)	68 (97)	4 (57)	
Positive	5 (6)	2 (3)	3 (43)	

Abbreviations: IQR, interquartile range; NA, not assessed; NS, not significant.

<sup>a</sup> The cumulative values in the ≥50% and <50% pathological treatment effect columns do not match the total value because 2 patients did not undergo surgical intervention and therefore did not have resection specimens available for analysis.

<sup>b</sup> No statistic testing was performed because of the small number of participants in (at least 1 of) the subgroups.

<sup>c</sup> Fisher exact test of proximal lower extremity and distal lower extremity was performed.

44 (39-53) days, with 90% of patients undergoing resection within 8 weeks. Surgical margins were negative in 72 of 77 patients (94%) and microscopically positive in 5 of 77 patients (6%) (Table 1).

One patient received an additional postoperative 30-Gy dose because of the presence of only 20% pathological treatment effect and multiple positive surgical margins. One patient refused a free flap reconstruction and underwent a limb amputation because of the absence of a volumetric response in a large mass in the distal lower extremity. However, despite the lack of a volumetric response, this tumor showed 80% pathological treatment effect. In 2 patients, surgical resection was omitted because of the development of intercurrent metastatic disease. The first of these 2 patients died from progressive disease 5 months after diagnosis. The second patient continued follow-up at 8 months after diagnosis, without clinical tumor progression of the irradiated primary lesion.

### Pathological Response and Local Control

Overall, resection specimens from 70 of 77 patients (91%) showed extensive pathological response. The posterior mean was 90.4% (95% HPDI, 83.8%-96.4%), which demonstrates that the percentage with extensive pathological response was 70% or greater. In addition, when responses from the 2 patients with intercurrent metastatic disease were considered as failures, the

posterior mean was 88.1% (95% HPDI, 81.0%-94.7%). An overview of patient, tumor, and treatment characteristics stratified by 50% or greater or less than 50% pathological response status is presented in Table 1. Patients who met the primary end point of extensive pathological response (≥50%) vs those in the other group (<50%) had larger tumors (median [IQR] tumor diameter: 10.4 [8.0-16.2] cm vs 6.4 [4.3-7.8] cm;  $P = .003$ ) and more frequent negative surgical margins (68 [97%] vs 4 [57%];  $P = .004$ ). After a median (IQR) follow-up time of 25 (13-38) months among the patients who underwent a limb-sparing operation, the local control rate was 100% for all patients regardless of the extent of pathological response.

### Survival and Morbidity

Progression-free survival at year 1 was 97% and at year 3 was 93%. Disease-specific survival at year 1 was 99% and at year 3 was 96%. Overall survival rates were 99% at year 1 and 95% at year 3 (Figure 2).

Wound complications of any severity were observed in 17 of 77 patients (22%), with 4 patients (5%) having minor complications, 8 patients (10%) having moderate complications, and 5 (6%) having major complications (Table 2). Of these moderate or major complications, 13 (17%) needed any intervention. Incidences of any grade 1 late toxic effects were 40% (28 of 70 patients) and of any grade 2 late toxic effects were 11%

(8 of 70 patients) (eTable 2 in Supplement 2). Grade 3 late toxic effects (edema) were observed in only 2 of 70 patients (3%). No grade 4 or 5 toxic effects were found. When patients with less than 2 years of follow-up were excluded, the incidence was 7% for grade 2 or higher fibrosis, 0% for joints stiffness, and 5% for edema (eTable 2 in Supplement 2).

## Discussion

In the DOREMY trial, we found that decreasing the dose of preoperative radiotherapy for myxoid liposarcoma from 50 Gy to 36 Gy was oncologically safe. An extensive pathological treatment response was observed in 91% of patients, which met the primary end point. After a median follow-up time of 25 months, no local relapses occurred. The wound complication rate that required intervention was only 17%, and any grade 2 or higher late toxic effects were found in 14% of patients.

Figure 2. Kaplan-Meier Survival Analysis of the Intention-to-Treat Population

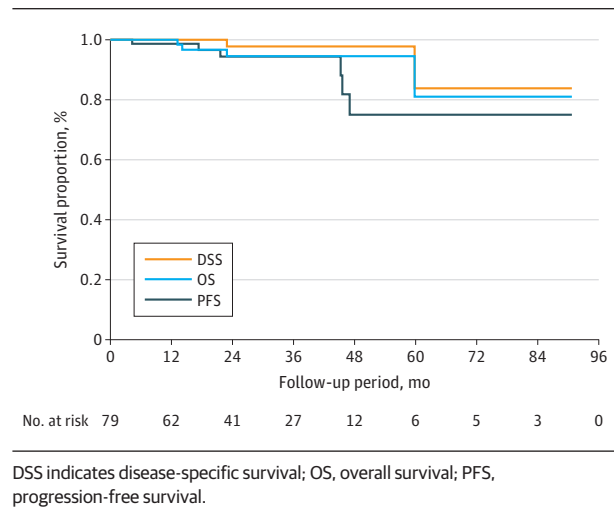


Table 2. Wound Complication Overview<sup>a</sup>

Wound complication type	No. (%)				
	Total	Lower extremity		Upper extremity	Other tumor location
		Proximal	Distal		
Wound complication					
None	60 (78)	48 (80)	8 (80)	1 (50)	3 (60)
Any	17 (22)	12 (20)	2 (20)	1 (50)	2 (40)
Minor	4 (5)	1 (2)	1 (10)	1 (50)	1 (20)
Moderate	8 (10)	7 (12)	1 (10)	0	0
Major	5 (6)	4 (7)	0	0	1 (20)
Wound complication necessitating any intervention (moderate/major)	13 (17)	11 (18)	1 (10)	0	1 (20)
Total surgical cases	77 (100)	60 (78)	10 (13)	2 (3)	5 (7)

<sup>a</sup> Wound complication data were available for all 77 patients, stratified by tumor location.

Table 3. Overview of the Most Relevant Studies on Morbidity and Local Control After Preoperative Radiotherapy in Soft-Tissue Sarcomas

Source	No. of patients	Design	Subgroup	Preoperative RT regimen	Rate, %				Follow-up, y
					Grade $\geq 2$ toxic effect	RO	WC	LC	
DOREMY trial	77 <sup>a</sup>	Prospective	All	18 × 2 Gy	14	94	17	100	2.1
O'Sullivan et al, <sup>8</sup> 2002; Davis et al, <sup>9</sup> 2005	88 <sup>a</sup>	Prospective	Preoperative group, various histological subtypes	25 × 2 Gy	37	84	35	92 <sup>b</sup>	3.3
Lansu et al, <sup>10</sup> 2019	32 <sup>c</sup>	Retrospective	Myxoid liposarcoma subgroup	25 × 2 Gy	NA	91	38	97	5
Chung et al, <sup>7</sup> 2009	88 <sup>d</sup>	Retrospective	Myxoid liposarcoma subgroup	25 × 2 Gy	NA	81	NA	98	5
O'Sullivan et al, <sup>34</sup> 2013	59 <sup>e</sup>	Prospective	All, various histological subtypes	25 × 2 Gy	24	93	31	93 <sup>b</sup>	4
Wang et al, <sup>35</sup> 2015 (RTOG-0630 trial)	57 <sup>f</sup>	Prospective	All, various histological subtypes	25 × 2 Gy	11	76	36	89	2

Abbreviations: DOREMY, Dose Reduction of Preoperative Radiotherapy in Myxoid Liposarcomas; LC, local control; NA, not applicable; RT, radiotherapy; RO, radical resection; WC, wound complication.

<sup>a</sup> The number of patients in the per-protocol analysis, which is relevant for wound complications.

<sup>b</sup> Most patients in the SR2 trial had other histological subtypes than myxoid liposarcoma, so a comparison with LC rates is not applicable.

<sup>c</sup> All patients with schedules other than 25 × 2 Gy preoperative RT dose were excluded. In Lansu et al,<sup>10</sup> the definition of a WC was slightly stricter in

comparison to the definition in the SR2 trial (definition: a single seroma aspiration did not meet the criteria for WC).

<sup>d</sup> Only 47% of patients underwent preoperative RT; the remaining patients received postoperative RT dose of 33 × 2 Gy (43%) or preoperative RT dose of 25 × 2 Gy and postoperative RT dose of 8 × 2 Gy (10%).

<sup>e</sup> This cohort included only lower extremity localizations, which is associated with a higher WC risk.

<sup>f</sup> The use of 3-cm craniocaudal and 1-cm radial gross tumor volume-clinical target volume expansions resulted in decreased target volumes.



Comparing the experimental preoperative radiotherapy regimen of 36 Gy with historical data of a conventional 50-Gy regimen, we observed similar outcomes and a more favorable toxic effect profile. The dose reduction did not compromise the quality of surgical technique and local control, as reported in previous studies on myxoid liposarcoma with conventional radiotherapy doses.<sup>7,24,25</sup> The observed wound complication rate of 17% was substantially lower than the 35% in the preoperative radiotherapy group in the randomized clinical trial by O'Sullivan et al,<sup>8</sup> using identical wound complication definitions (Table 3 and eTable 2 in Supplement 2). Furthermore, when patients with less than 2 years of follow-up were not taken into account, the late toxic effect rates seemed to be at least 3-fold lower.<sup>9</sup> Some of these differences could be explained by the use of 3-dimensional radiotherapy by O'Sullivan et al,<sup>8</sup> whereas the current trial used IMRT. This difference is underscored by the more favorable morbidity rates reported in subsequent single-group phase 2 trials of the value of modern radiotherapy planning techniques.<sup>34,35</sup> Although 1 of these trials (RTOG-0630<sup>35</sup>) reported a similar grade 2 or higher late toxic effects rate (11%), from the use of image-guided IMRT and decreased target volumes, the grade 2 or higher late toxic effects rate in the other study (24%)<sup>34</sup> and the wound complication rates in both studies (31% and 36%)<sup>34,35</sup> were clinically relevant and higher compared with the rates in the current trial. Although we recognize the potential biases that complicate these comparisons, in the setting of rare diseases, we also believe these data from other trials are the most robust available and help put the DOREMY trial findings in perspective.

The pragmatically chosen bayesian statistical design facilitates the best level of evidence possible in rare diseases.<sup>36</sup> With a primary end point being a short-term evaluable predictor of outcome,<sup>37-40</sup> continuous reconsideration of trial continuation provides optimal safety for the trial patients (eTable 3 in Supplement 2). This design maximizes the sample size of the experimental treatment. Although the use of external controls is prone to bias, it does not hamper the introduction of new treatment strategies in rare cancers.<sup>41,42</sup>

We propose the use of 36 Gy in once-daily 2-Gy fractions as an alternative dose-fractionation approach of preoperative radiotherapy for myxoid liposarcoma. This approach may be feasible for resource-limited or high-acuity centers during the ongoing coronavirus disease 2019 pandemic. Demonstrating the noninferiority of this regimen in a conventional phase 3 trial is practically impossible. Therefore, we invite the international sarcoma community to participate in a registry to confirm the findings of the DOREMY trial in daily practice.

### Limitations

This trial has several limitations. First, the primary end point may be subject to discussion, with regard to the optimal pathological response evaluation in STS in general and in myxoid liposarcoma in particular.<sup>32</sup> Second, in the DOREMY cohort, the median follow-up of 25 months is relatively short. However, in the largest previous series, the median time to local recurrence was reported to be 21 months,<sup>43</sup> suggesting that at least half of the potential local recurrences should have occurred by now in this cohort, but we have observed none. Third, we did not assess the potential advantages in quality of life, patient-reported outcomes, and health care costs resulting from the lower overall treatment time, fewer readmissions and reoperations for wound complications, and favorable toxic effect profile.

### Conclusions

The DOREMY trial found that a dose reduction of preoperative radiotherapy in myxoid liposarcoma was effective and oncologically safe. Furthermore, the morbidity of the decreased dose regimen appeared to be lower than the rate of the conventional dose regimen. Therefore, we propose the use of 36 Gy in once-daily 2-Gy fractions as an alternative dose-fractionation approach of preoperative radiotherapy for myxoid liposarcoma. This approach could be reasonable for resource-limited or high-acuity centers particularly during the coronavirus disease 2019 pandemic.

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*Other - Inclusion of patients:* van den Ende.  
*Other - National coordinator/PI for Norway:* Jebesen.

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