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Deferasirox in MDS patients with transfusion-caused iron overload—a phase-II study

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Abstract Blood transfusions represent a main component of supportive care in myelodysplastic syndromes (MDS). To avoid organ damage caused by transfusion-dependent iron overload, an adequate iron chelation therapy is required. Recently, a new oral iron chelator deferasirox (ICL670, Exjade®) has become available. A study was conducted to demonstrate the efficacy and tolerability of deferasirox in transfusion-dependent iron-overloaded patients with MDS. The efficacy of deferasirox was monitored by changes in serum ferritin, bone marrow iron, and liver iron concentration (LIC), as determined by T2*-weighted magnetic resonance imaging. Twelve patients with MDS of different subtypes (median age 76 years, range 53–91) were enrolled. Deferasirox administered in a

once-daily dose of 20–30 mg/kg for 12 months was effective in reducing median ferritin concentration from 1,515 µg/L (range 665–6,900) to 413 µg/L (range 105–3,052). Within the first 4 weeks of treatment before the continuous decline of ferritin levels, the values markedly rose in eight of 12 patients. The median LIC declined from 315 to 230 µmol/g ($p=0.02$) at the end of study, accompanied by a reduction of bone marrow siderosis. The most common adverse events were mild and transient gastrointestinal disturbances, skin rash, nonprogressive transient increases in serum creatinine and urine β 2-microglobulin, and a temporary reduction of the creatinine clearance. The renal parameters normalized after end of treatment. No hematologic toxicities were observed. Deferasirox proved to be effective in transfusion-dependent iron overload in MDS by mobilizing iron deposits in liver and at least stabilizing iron stores in bone marrow.

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LIC assessment by MRI

Abbreviations

MDS	myelodysplastic syndromes
LIC	liver iron concentration
MRI	magnetic resonance imaging
RA	refractory anemia
RARS	refractory anemia with ringed sideroblasts
RCMD	refractory cytopenia with multilineage dysplasia
RAEB-I	refractory anemia with excess of blasts
RBC	red blood cells
AML	acute myeloid leukemia
ALAT	alanine aminotransferase

Introduction

The myelodysplastic syndromes (MDS) are clonal disorders of hematopoiesis which are characterized by dysplasia in one or more cell lineages and peripheral cytopenia. For the management of MDS patients, blood transfusions represent the main component of supportive care. Ninety percent of all MDS patients with permanent anemia become dependent on blood transfusions to maintain their quality of life and to survive. With every unit of transfused blood, the patients receive approximately 200 to 250 mg iron [1]. As there is no physiological mechanism to remove an excess of body iron, regular blood transfusions inevitably lead to an accumulation of iron in various tissues in these individuals. If untreated, iron overload may cause damages in liver, heart, pancreas, brain, joints, and endocrine tissues [2–4], increasing morbidity and the risk of early death [1]. As phlebotomy is not an option in MDS, the only way to remove toxic iron and to prevent complications of transfusion-dependent iron overload is, to date, rigorous iron chelation therapy [5].

The current standard in iron chelation therapy is deferoxamine mesylate (Desferal®). Long-term data collected since the drug was introduced in the early 1960s have demonstrated its safety and high efficacy in reducing stored iron and the complications of iron burden, resulting in decreased mortality in iron-overloaded subjects [6, 7]. Unfortunately, deferoxamine has a short plasma half-life and an insufficient oral bioavailability. These features require an intravenous or subcutaneous application of the drug over a period of 8 to 12 h, usually five to seven times a week. Alternatively, deferoxamine can be administered as a subcutaneous bolus injection [8]. As a consequence of the cumbersome administration, the compliance of the deferoxamine therapy is often poor, resulting in limited efficacy. In MDS patients, the applicability of deferoxamine is further limited by the fact that the anemia is often associated with severe thrombocytopenia and neutropenia in these individuals.

Due to the risk of bleeding and infection, orally applicable iron chelators are of particular interest in transfused MDS patients. The first oral iron chelator deferiprone (Ferriprox®), introduced already 20 years ago, did not fulfill the expectations. The license of the drug remained limited to second-line therapy of patients with thalassemia major, bearing the risk of neutropenia and agranulocytosis in a frequency of about 0.5–1% [9–11].

Deferasirox (ICL670, Exjade®) is a once-a-day orally active iron chelator formulated as a dispersible tablet with high iron-binding potency and iron selectivity [12–14]. Deferasirox binds iron in a 2:1 ratio before being excreted primarily in the bile [15]. A series of studies have demonstrated its efficacy and safety in patients with thalassemia major in a daily dose ranging between 20 and

30 mg/kg [12, 16–21]. So far, experiences regarding treatment with deferasirox in individuals with diseases other than thalassemia are only limited [20–22].

The aim of the present study was to investigate the efficacy and tolerability of deferasirox in transfusion-dependent iron-overloaded patients with MDS.

Patients and methods

The phase-II study was carried out between March 2004 and November 2006 in the III. Medizinische Universitätsklinik, Mannheim, Germany. The aim of the study was to investigate the tolerability and effectiveness of deferasirox (ICL670, Exjade®) in MDS patients with transfusion-induced iron overload. The efficacy of deferasirox was monitored by changes in serum ferritin, bone marrow iron, and liver iron concentration (LIC), the latter parameter determined quantitatively by magnetic resonance imaging (MRI).

MDS patients who received at least 20 blood transfusions and who had a ferritin concentration >500 µg/L were enrolled into the study, irrespective of prior chelation therapy, age, and MDS subtype. Reasons for exclusion were: alanine aminotransferase (ALAT) >250 U/L, increased serum creatinine concentration (>1.3 mg/dL), proteinuria >1,000 mg/day, acute or chronic viral hepatitis, HIV, prolonged corrected QT interval, AV block II–III°, a history of ocular toxicity related to iron chelation therapy, gastrointestinal conditions preventing absorption of an oral medication, alcohol abuse, or chemotherapy. The diagnosis of MDS was performed according to the World Health Organization (WHO) recommendations [23] by morphological evaluations of a May–Grünwald–Giemsa-stained peripheral blood and bone marrow smears, Prussian blue staining of bone marrow, immunotyping, and cytogenetic analysis.

Treatment with deferasirox was started in all patients at a dose of 20-mg/kg body weight. The drug was given once daily each morning as a suspension in water, half an hour before breakfast. The dose was escalated for 5 mg/kg every 3 months if the ferritin level decreased less than 10% during this period. The maximal allowed dose was 30 mg/kg. The therapy was discontinued when ferritin decreased below 350 µg/L and reinstated at 20 mg/kg when ferritin concentration exceeded 500 µg/L again. Treatment was scheduled for 12 months but could be extended at the physicians' discretion when patients had achieved a reduction of iron overload. Clinical response was defined as a reduction of ferritin concentration of at least 10% as compared to baseline values. Blood transfusions were regularly administered during the study period according to the patient's requirement.

Assessments for safety and efficacy were performed at baseline, weekly in the first month after study initiation and

after each dose escalation and at monthly intervals afterwards. The check included physical examination and extended laboratory testing including complete blood cell count, serum analysis of electrolytes, zinc, copper, liver enzymes, creatinine, β 2-microglobulin, and urine analysis of protein, creatinine, and β 2-microglobulin. Iron parameters tested included the serum analysis for ferritin, iron, transferrin, transferrin saturation, and soluble transferrin receptor. The serum ferritin concentration (normal value 35–310 μ g/L for men, 25–210 μ g/L for women) was measured by an enzyme immunoassay (Access Ferritin immunoassay, Beckmann-Coulter, Krefeld, Germany) based on enhanced luminescence. Electrocardiograms and ophthalmologic and auditory examinations were performed every 3 months.

Iron stores were monitored by assessment of the iron content in the bone marrow, liver, and heart at baseline and every 3 months during the study. Bone marrow iron stores were assessed semiquantitatively on Prussian-blue-stained marrow smears according to the following scale: grade 0=absent; 1=decreased; 2=normal; 3=increased; 4=markedly increased; 5=massively increased. LIC was determined quantitatively by T2*-weighted MRI as described previously [24–26]. An LIC >35- μ mol/g liver tissue was considered as iron overload. The changes in myocardial siderosis were quantified by myocardial T2* MRI [27, 28]. The lower the T2* value in milliseconds (ms), the greater the myocardial iron load (normal value >35 ms; pathologic <25 ms, standard deviation \pm 20) [29, 30].

All statistical analyses were performed using the GraphPad Prism (Version 4.0) statistical package for Windows. Testing for statistical significance between baseline and end-of-study values was performed using the Wilcoxon matched pairs test, *p* values <0.05 were considered to be statistically significant. Correlation coefficients were determined by Pearson's correlation test.

The study was approved by the local ethics committee and followed the Helsinki Declaration of 1975, as revised in 1983. Written informed consent was given by all patients.

Results

Twelve MDS patients (RA=4, RARS=1, RCMD=2, RAEB-1=1, 5q⁻syndrome=4) with transfusion-dependent iron overload were enrolled in this study. The median age of the patients (four males, eight females) was 76 years (range 53–91); nine patients (75%) were older than 70 years. All patients were in a stable-disease phase when entering the study. Median time from diagnosis of MDS to study entry was 15.5 months (range 2–182). From time of diagnosis to study entry, the patients received a median of 36 units (range 20–214) of red blood cells (RBC).

Patient characteristics are shown in Table 1. The individual values of serum ferritin concentration, number of RBC transfusions, dose of deferasirox, LIC, and bone marrow iron in the course of the study are demonstrated in Fig. 1.

Seven patients (nos. 1–7) were treated for 12 months with deferasirox. In the remaining five patients, the study had to be stopped after a median time of 4.7 months (range 1.0–7.5) due to reasons most probably not related to deferasirox therapy. A 54-year-old patient (no. 8) was withdrawn from the study 7.5 months after start of the therapy for allogeneic stem cell transplantation. Another patient (no. 9) developed acute myeloid leukemia 4.9 months after start of the treatment. An 80-year-old woman (no. 10) died from pneumonia 1 month after start with deferasirox. Two patients (nos. 11 and no. 12) died 4.7 and 2.2 months after initiation of the study from fatal bleeding. The bleeding was the result of a nonprogressive thrombocytopenia in one case; the other patient, a 91-year-old male patient (no. 11), died from gastrointestinal bleeding caused by sigma diverticulosis with normal platelet counts. None of the fatal cases was considered as study-drug-related.

In three of the seven patients who completed the study, the deferasirox medication had to be discontinued for adverse events. In one case (no. 1), treatment was interrupted due to pneumonia for 2 weeks. In another patient (no. 5), study medication was stopped for 1 week because of a mild skin rash, which resolved spontaneously. In another case (no. 7), deferasirox was withdrawn after 10 months as this patient developed a severe persistent osteomyelitis of the humerus following an osteosynthesis 1 year before study entry. In the remaining patients, no clinically apparent infection were observed.

Adverse events observed were infrequent and of mild intensity. Nausea was seen in two patients; two patients developed diarrhea occurring early after start of treatment or dose escalation. These symptoms resolved spontaneously without dose interruption in all cases. One patient developed a self-limiting atrial tachycardia after 2 months of treatment at a daily deferasirox dose of 20 mg/kg. Two patients developed a mild hyperbilirubinemia (1.26 and 1.87 mg/dL) which resolved without discontinuation of the study medication. One patient showed a progressive elevation in transaminase levels (ALAT maximal 426 U/L), which lasted for 2 weeks. No abnormalities in serum concentrations of potassium, sodium, or calcium were observed. Serum copper and zinc levels fluctuated during study without decreasing markedly. Hematological parameters were not significantly changed during the study period.

Increased serum creatinine levels (normal 0.7–1.3 mg/dL) were detected in seven patients during the study period,

Table 1 Clinical and laboratory characteristics of all study participants ($n=12$). Values are presented as median (range)

Patient characteristics	
Median age (years)	76 (53–91)
Gender (female; male)	8; 4
Units of RBC transfusions prior to study	36 (20 – 214)
Units of RBC transfusions during study	23 (6 – 50)
Serum ferritin ($\mu\text{g/L}$)	
Baseline	1,575 (665–6,900)
Week 4	1,483 (455–6,975)
Month 3	1,449 (105–6,634)
Month 6	1,544 (689–4,968)
Month 9	1,108 (646–2,211)
Month 12	528 (327–3,052)
LIC (micromole iron per gram liver tissue, normal<35)	
Baseline	315 (189–350)
Month 3	270 (190–350)
Month 6	230 (80–310)
Month 9	160 (56–270)
Month 12	230 (0–350)
Myocardial iron (normal>35 ms)	
Baseline	26 (15–35)
Month 3	31 (21–43)
Month 6	33 (21–46)
Month 9	28 (22–34)
Month 12	29 (19–38)
Bone marrow iron (scale 0–5)	
Baseline	5 (4–5)
Month 6	4 (1–5)
Month 12	3 (1–5)
Adverse effects (number of patients)	
Increase of serum creatinine (>1.3 mg/L)	7/12
Rise of β 2-microglobuline in urine (>300 $\mu\text{g/L}$)	11/12
Decrease of creatinine clearance (<60 ml/min)	7/12
Increased transaminases (>2 \times normal value)	1/12
Hyperbilirubinemia	2/12
Diarrhea	2/12
Nausea	2/12

with a maximum of 1.56 mg/dL occurring 1 to 20 weeks after start of treatment at a dose of deferasirox of 20 mg/kg ($n=5$) and 25 mg/kg ($n=2$), respectively. Three of these patients were the only study participants with a pretherapeutic decreased creatinine clearance below 60 mL/min (nos. 5, 11 and 12). The observed creatinine increase was dose independent and transient without requiring any dose adjustment. Eight of 12 patients had a serum creatinine clearance below 100 mL/min at the start of study. During the study period, all patients showed a serum creatinine clearance below 100 mL/min at least at one laboratory check, seven patients a value below 60 mL/min. In all cases, the creatinine clearance returned to at least pretherapeutic values at one of the subsequent reevaluation under continued deferasirox treatment.

Eleven patients showed an increase of urine β 2-microglobulin at least once in the course of the study. In eight patients, the increase persisted during the whole study. The

values observed in the individual patients showed an enormous variability even with unchanged deferasirox dose and normalized in all patients within a few weeks after the study medication was terminated. The median β 2-microglobulin concentration in the urine obtained 3 months after study initiation was significantly higher when compared to the baseline value (2,605 vs. 200 mg/L; $p=0.02$).

The median serum ferritin concentration of all patients at start of study was 1,575 $\mu\text{g/L}$ (range 665–6,900). Within the first 4 weeks, in eight of 12 patients (67%), an increase of the ferritin concentration was observed from a median of 1,382 $\mu\text{g/L}$ (range 665–6,900) to a median of 1,834 $\mu\text{g/L}$ (range 1,093–6,975; $p=0.4$). In six of these individuals, the increase was detected already at the first control after 1 week of treatment. The highest ferritin levels were measured 4 weeks after the initiation of treatment, being increased by 26.4% (range 8.4–165) when compared to the pretreatment values.

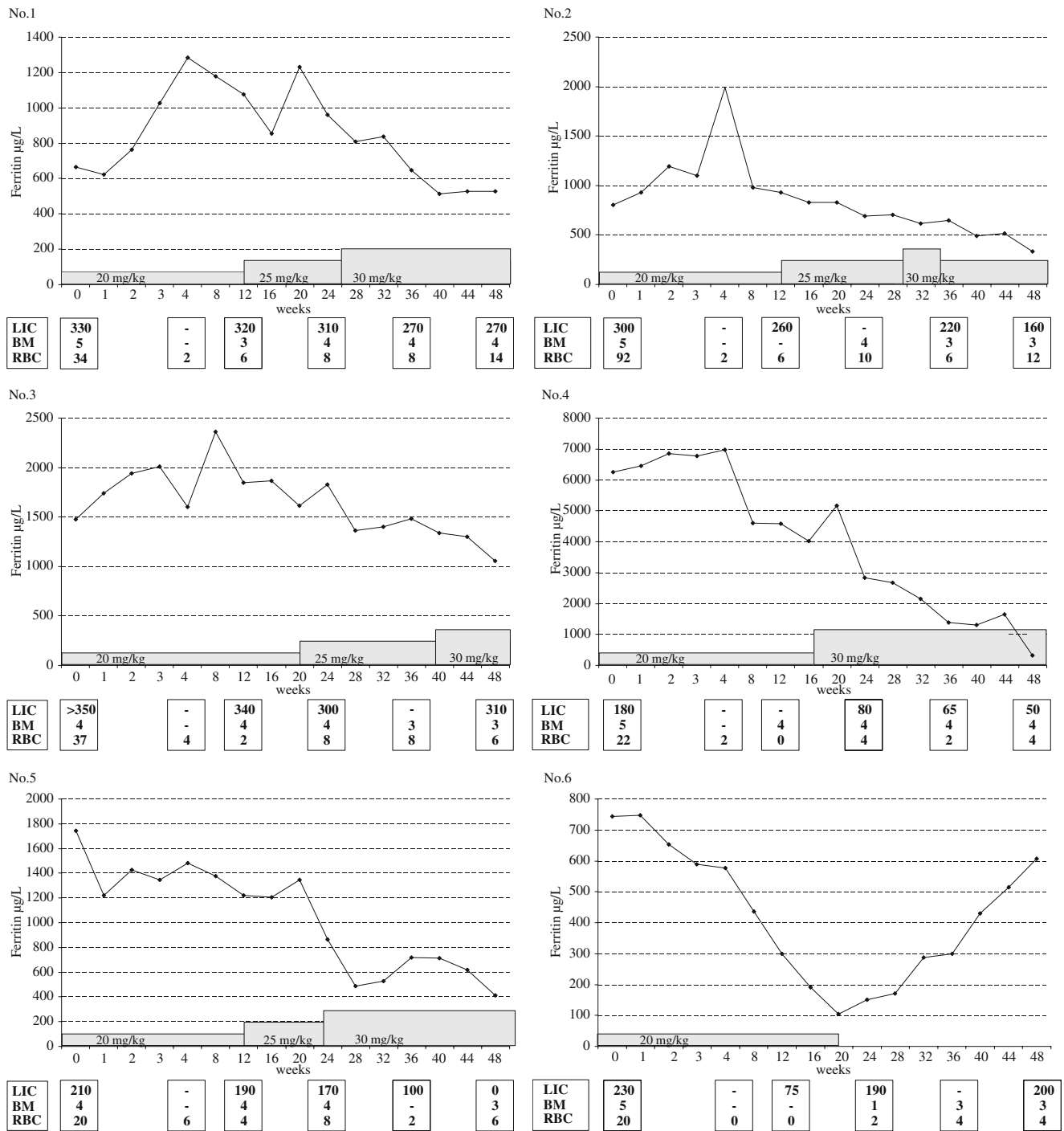


Fig. 1 Serum ferritin (µg/L), LIC (micromole iron per gram liver tissue; normal<35), bone marrow iron (scale: grade 0=absent; 1=decreased; 2=normal; 3=increased; 4=markedly increased; 5=massively increased), and number of transfused RBC units during iron chelation with deferasirox in individual patients over a period of

12 months. Abbreviations: *BM* bone marrow storage iron; *LIC* liver iron concentration; *RBC* number of transfused red blood cell units; *PSCT* peripheral stem cell transplantation; *sAML* secondary acute myeloid leukemia. *Shadowed areas*: deferasirox treatment, dosage per day

In the seven patients receiving deferasirox for 12 months, the median ferritin values decreased by a median of 67.5% (range 20.0–94.7) from 1,575 µg/L (range 665–6,900) to 413 µg/L (range 105–3,052). The observed reduction was not significant due to the rise of ferritin within the first

4 weeks of treatment. However, when comparing the baseline values with the ferritin values obtained after the first 4 weeks of treatment, the difference became significant (1,483 µg/L, range 577–6,975; *p*=0.017). There were no consistent changes in the levels of other iron tests such as

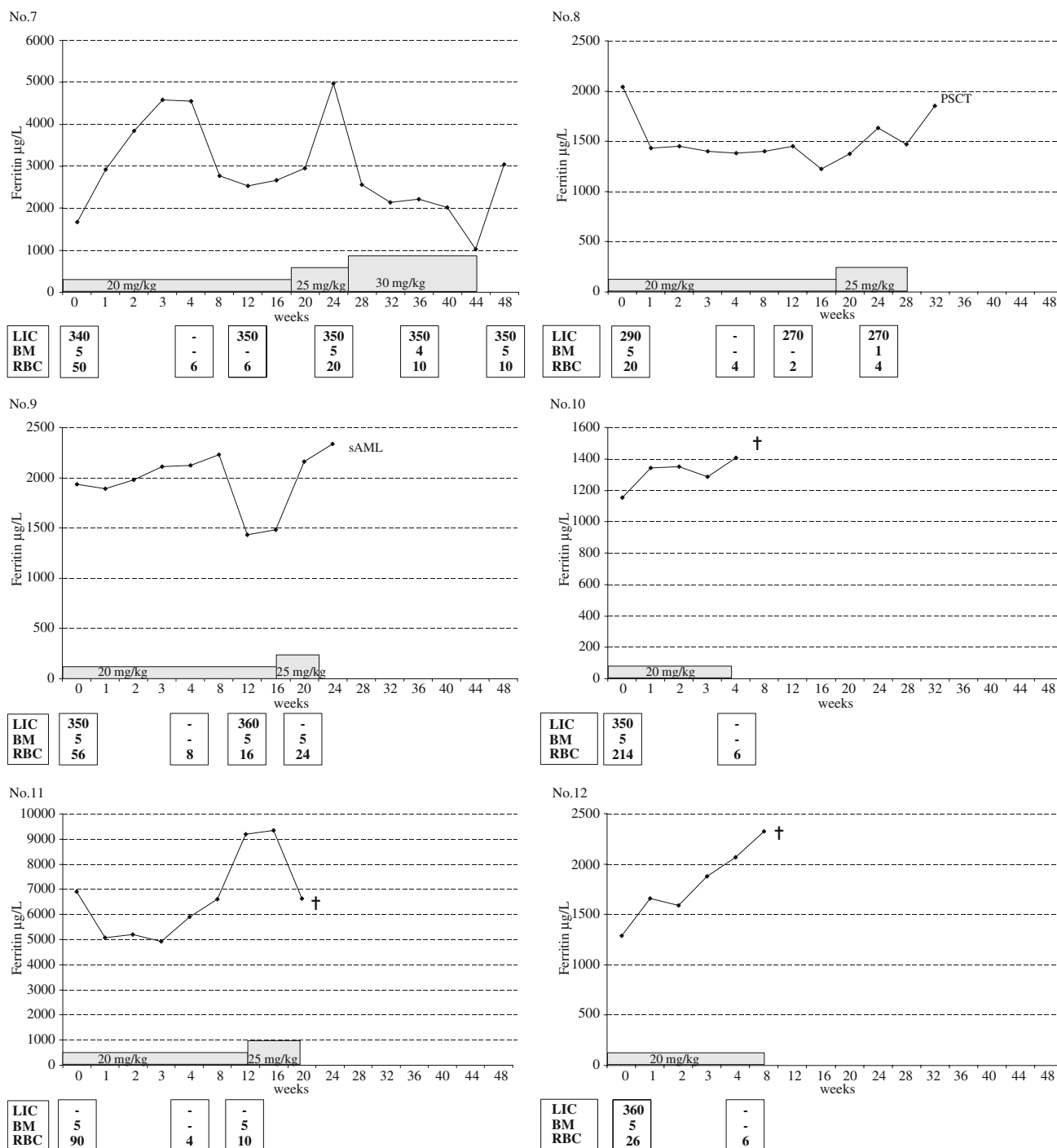


Fig. 1 (continued)

serum iron, transferrin, transferrin saturation, or soluble transferrin receptor.

Treatment had to be discontinued after 4.7 months in one patient (no. 6) who showed an excellent response to deferasirox at a dose of 20 mg/kg, with a decrease of ferritin to 190 µg/L. After withdrawal of the chelation therapy due to iron depletion, the serum ferritin rose subsequently to

515 µg/L. This process was paralleled by an increase of iron deposits in bone marrow and liver (Table 1 and Fig. 1).

Bone marrow storage quantified by Prussian blue staining showed a continuing reduction from the median scale of grade 5 (range 4–5) to 3 (range 1–5, $p=0.002$) at month 12. A decrease of hemosiderin was observed in six of seven patients who received deferasirox for 12 months

and in one other case who received chelation therapy for 6 months.

LIC as determined by T2*-weighted MRI fell significantly from pretreatment values of 315- $\mu\text{mol/g}$ liver tissue (range 180–350) to 230- $\mu\text{mol/g}$ liver tissue (range 0–350; $p=0.015$) at month 12. Within the first 6 months, LIC decreased by an average of 13% (range 0–55%). There was no correlation found between serum ferritin levels and the LIC.

In six of eight patients with available cardiac data, the T2* relaxation time increased as a marker of improvement in myocardial iron loading. In two of these patients, values even normalized (T2* relaxation time >35 ms) within 12 months. The lowest cardiac iron concentration was observed after 6 months of the treatment.

Discussion

The presented results show that deferasirox is an effective oral alternative for iron chelation therapy in MDS patients with secondary hemosiderosis. This is obvious from dynamics of serum ferritin and LIC in the individual patients.

Serum ferritin concentration mirrors the total body iron load and is a well-established test to monitor the effect of chelation therapy in transfusional iron overload. In all but one of our MDS patients who finished the study as planned and were treated with deferasirox for 12 months, ferritin concentrations at the end of the study were below baseline values. There was, however, a surprising phenomenon observed during the initiation of treatment: instead of a decrease, there was rather an increase of ferritin observed in about 70% of the patients during the first 4 weeks of deferasirox therapy. The rise was mostly detectable already 1 week after the medication was initiated. The highest ferritin values were measured after 4 weeks, being increased by 26.4% on average when compared to the pretreatment values. A continuous decline of the ferritin right from the start of study without an intermittent rise was observed only in one patient with a low iron load, as demonstrated by a low initial ferritin of 743 mg/L, only moderately increased LIC of 230 $\mu\text{mol/g}$, and the lack of transfusion requirement during the first 3 months of study.

The initial increase of ferritin observed in our study is of general interest for the management of patients with iron chelation therapy—at least for those receiving deferasirox. Normally, an increase of ferritin in serum leads to dose escalation as it is interpreted as a lack of efficacy. This was also the case in our study design, where the deferasirox dose had to be escalated when the ferritin levels did not decline by at least 10% compared to the ferritin levels obtained at the previously administered dose. Based on our

results, which showed a continuous decline of ferritin in responders not before 6–8 weeks after start of treatment, we recommend dose adjustment not until the third month of treatment. This does not only apply for the initial therapy but also for dose escalations later on.

The measurement of LIC by highly T2*-weighted MRI was demonstrated to correlate well with the iron content assessed by invasive liver biopsy [24, 27, 31]. Iron determination by MRI is a reproducible, sensitive, and noninvasive method that can reduce the need for liver biopsies to assess liver iron content especially in thrombocytopenic patients. The changes of LIC during the course of our study confirm the high efficacy of deferasirox to mobilize iron deposits from liver tissue [12, 32, 33]. Given the fact that the primary goal of chelation therapy is to reduce iron deposits, LIC assessment by MRI seems to be the ideal tool to monitor the efficacy of chelation. In contrast to ferritin, which only indirectly reflects the iron stores and which is influenced by inflammation and liver disorders and obviously also by the chelation therapy itself, the MRI reliably allows a direct control of LIC. Regarding our results which show a LIC decline in responders already after 3–6 months, it is obviously possible to check the success of treatment by this method as early as 3–6 months after start of chelation therapy. From the clinical point of view, before escalating the dose of deferasirox, it may be recommendable to reevaluate body iron by LIC instead of relying on the course of ferritin only.

MRI is not only of interest to determine LIC. A number of studies have demonstrated that by measurement of T2* relaxation time MRI may also be eligible to measure iron overload in the heart, the most critical organ in this respect [28, 34, 35]. Deferasirox is assumed to be inferior to deferoxamine and deferiprone for the removal of excess cardiac iron [36–38], but there are no comparative data that exist in this regard. Removal of cardiac iron was shown experimentally in animals with high doses of deferasirox (100 mg/kg daily) but not in patients at doses of 10–40 mg/kg [37, 38]. In our study, six out of eight patients with available cardiac data showed a decline of myocardial iron by the end of study. Interestingly, the lowest cardiac iron values were observed at month 6. At this time, seven of the eight patients improved when compared to baseline; in four patients, the iron amount even normalized. The reason for an increase of cardiac iron concentration in most cases during the second half of our study despite dose escalation of deferasirox remains unclear.

The most frequent adverse events with suspected relationship to repeated administration of deferasirox consisted of transient WHO grades I–II gastrointestinal symptoms such as nausea and diarrhea, similarly found in other studies [18, 21, 39, 40]. These common side effects may be partly caused by the presence of lactose in the

formulation of deferasirox [33] and did not require treatment discontinuation in our patients.

Infectious complications observed in our study were most probably not related to the study drug but rather the result of the bone marrow suppression in MDS. Previous studies on thalassemia patients have demonstrated that infections were similarly frequent in iron chelation therapy with deferasirox and deferoxamine [33]. The induction of infections through iron chelation therapy would be rather surprising, as a withdrawal of iron is considered as a nonspecific defense mechanism and a common response to systemic infections or generalized inflammatory disorders [41].

Preclinical trials indicated that the kidney would be the organ at risk for deferasirox toxicity. The main toxic effects described were changes of renal tubular cells. The nephrotoxicity was regarded to be caused by decompartmentalization of chelated iron and had been observed in animals that were not heavily iron-overloaded [15]. Based on these observations, a creatinine clearance of <60 mL/min was determined as an exclusion criterion for deferasirox treatment as recommended by the manufacturer. This is no problem in the cases of young thalassemia patients but of concern in patients with MDS, which is primarily a disease of the elderly, with a median age of 65–75 years [42]. The creatinine clearance is mostly reduced due to a physiological reduction of kidney weight and a reduced number of glomerula. Several studies have shown that the creatinine clearance allows only a poor estimation of renal function in older individuals. Renal function is often underestimated by this parameter [43–45] due to erroneous urine sampling, reduced muscle mass because of reduced physical activity, and low calorie intake in elderly people.

In concordance with studies on patients with thalassemia [13, 16–19, 21, 39], we have shown that the renal function is not permanently affected by deferasirox even in elderly patients with MDS. This was the case in patients both with normal renal function and with initially reduced creatinine clearance. Even in patients with a creatinine clearance of <60 mL/h at baseline, further impairment of the renal parameters was only transitional, with parameters at the end of the study being comparable to pretherapeutic values.

The determination of the β 2-microglobulin levels in the urine, considered to be a sign of tubular damage, proved to be especially problematic in this context. Increased values were found in almost all study participants, showing an enormous day-to-day variability with the same deferasirox doses. At the end of the study, the concentrations normalized. Thus, the value of the β 2-microglobulin measurement as a sign of tubular damage during deferasirox therapy remains debatable.

Which is the optimal deferasirox dose for treatment of iron overload in patients with MDS? The required dose

obviously depends primarily on the number of transfusions required to maintain a stable hemoglobin level. As our results show, a deferasirox dose of 20 mg/kg daily can reduce LIC in many patients who need up to four RBC units per month. There is no reason not to start chelation therapy with this low dose to minimize costs and possible side effects. An increase of the dose by 5 mg/kg is justifiable only after a period of 3 months as described above. The maximum dose of 30 mg/kg as recommended by the manufacturer should not be exceeded, as the use of higher doses in our experience is not necessary.

In contrast to other studies [5], we could not observe any significant changes in hemoglobin levels and RBC requirements, no patient became transfusion independent. The lack of improvement of the erythropoietic activity is possibly explained by the relatively low number of patients in our study. Furthermore, the relatively short period of chelation treatment may also contribute to this result, as the hematological improvement was reported to become evident mostly after 12 months [5].

The question of which patients should receive chelation therapy is a matter of debate, which is of course influenced by clinical and economical aspects [46]. Since iron overload has no positive effect but impairs organ functions, chelation therapy has to be considered necessary for all patients whose life expectancy is longer than the time period required for a measurable decrease in tissue iron overload. In light of our data, which show a significant reduction of LIC after 1 year of chelating therapy, there is no reason why patients with a life expectancy of more than 1 year should be deprived of iron chelators beside economical considerations. The consensus conference of Nagasaki [47] recommends chelation therapy for all patients with ferritin levels exceeding 1,000–2,000 μ g/L.

In summary, deferasirox is an oral alternative for iron chelation in MDS patients. The drug is well tolerated and effective in decreasing iron overload and in mobilizing iron deposits from liver tissue. The starting dose is 20 mg/kg; dose escalation should be considered not before 3 months of treatment. Suitable parameters of treatment efficacy are serum ferritin and assessment of liver iron by MRI.

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