Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Deferasirox

Deferoxamine

Deferiprone

Trial Indication(s)

Chronic iron overload

Protocol Number

CICL670ADE14

Protocol Title

EXCALIBUR. A prospective non-interventional study on iron chelation therapy in patients with chronic iron overload

Clinical Trial Phase

Phase IV

Phase of Drug Development

NA

Study Start/End Dates

Study start date: 15 Sep 2015

Study completion date: 29 Oct 2021

Reason for Termination

NA

Study Design/Methodology

This non-interventional study (NIS) aimed to document the daily clinical practice of iron overload treatment in Germany with all available iron chelators and to describe differences between theses iron chelators.
This study was a prospective, multicenter NIS, meaning that treatment did not follow a pre-defined protocol, but exclusively routine medical practice.

The regular observation period in EXCALIBUR was 24 months for patients without a change of the iron chelator. Follow-up visits could be documented after approximately 1, 3, 6, 9, 12 and 18 months, with a final visit after 24 months or at the end of the observation phase, whichever occurred first. If the product was changed before 31-Oct-2019, the observation period was extended again by 24 months.

Centers

106 centers in Germany

Objectives:

The aim of this NIS was to gain knowledge from daily medical routine of all patients with chronic iron overload who are treated with an approved iron chelator in accordance with the respective SmPC.

Primary objective(s)

- Effectiveness of iron chelation treatment with all approved iron chelating agents in daily medical routine. The serum ferritin value was used to assess the effectiveness of the treatment.

Secondary objective(s)

- Use and application of all approved iron chelators in hemato/oncological practices in Germany according to the respective SmPC. For this purpose, the various preparations, the dose over the course, dose adjustments, side effect management and the reason for treatment were documented.
- Determination of the frequency of switch to a new iron chelator and the reason for switching.
- Determination of the hematological response in patients with myelodysplastic syndromes (MDS) under iron chelation treatment with all available iron chelators in daily medical routine. The hematological response was monitored by documentation of hematological parameters and need for transfusion. The valid International Working Group (IWG) criteria (Cheson BD, Greenberg PL, Bennett JM, et al. Clinical application and proposal for modification of the International Working Group (IWG) response criteria in myelodysplasia. Blood 2006;108(2):419-25) were used for assessment. Hematological response was also determined for patients with myeloproliferative neoplasms (MPN).
- Determination of the safety and tolerability of the prescribed iron chelating agents in daily medical routine and the associated treatment management. The documentation of the safety and tolerability of all approved iron chelators within a NIS enables the detection of possible side effects in a broad patient collective of different ages and with different indications, which no clinical study can depict.
- Presentation and comparison of general satisfaction with all approved iron chelators in everyday life using the treatment satisfaction questionnaire for medication (TSQM-14).

Test Product (s), Dose(s), and Mode(s) of Administration

Not applicable

Statistical Methods

Statistical analyses were purely exploratory and descriptive. The study was not aimed to confirm or reject pre-defined hypotheses. The statistical evaluation was performed using the software package SAS release 9.4.
Continuous data were described by the number of patients in population, non-missing and missing values, mean, standard deviation, median, minimum, maximum as well as lower and upper quartiles and 5 and 95 percentiles.
Categorical data including categories of continuous data were presented in frequency tables containing absolute and relative frequencies.
Data were analyzed for all patients, and separately for patients with MDS and for patients with MPN diagnosis at study inclusion visit. Results were summarized in total and by start treatment or by treatment.
The main analysis set for this NIS was the FAS. All tables, figures and listings (TFL) except for AEs were analyzed for the FAS. All tables for AEs were calculated for the SAF.

Table 9-2 Subgroup analyses

Stratum	Categories
Start treatment	Deferasirox (DT)
	Deferasirox (FCT)
	Deferoxamine
	Deferiprone
Patients with at least one treatment change and with no treatment change	No treatment change
	Any treatment change
Treatment change group	Switch from deferasirox DT to deferasirox FCT
	Switch from deferoxamine to deferasirox FCT
	Other switch combinations

DT: Dispersible tablet, FCT: Film coated tablet.

Study Population: Key Inclusion/Exclusion Criteria

All patients with chronic iron overload who

- had been treated with an iron chelating agent for less than 6 months,
- who had never been treated with an iron chelator before starting current iron chelation treatment, or
- who had discontinued iron chelation treatment more than 6 months ago and started iron chelation treatment again, and
- who signed the informed consent

could be documented in this NIS. The inclusion and exclusion criteria were based on the SmPC of the respective iron chelator.

Patients could not participate in any clinical study in parallel, since such a study does not constitute routine medical practice and is therefore in contrast to the objectives of a NIS. To be documented in this NIS, patients were not allowed to have participated in any other NIS for the same indication or any clinical study for at least 6 months. Pregnant patients were excluded from the documentation.

Participant Flow Table

Table 10-1 Analysis sets

	N (%)
Number of patients included into study database	502 (100.0%)
Number of patients included in the SAF	418 (83.3%)
Number of patients excluded from the SAF	84 (16.7%)
Reasons for exclusion from the the SAF	
No informed consent signed	3 (3.6%)
No dose of the starting prescribed iron chelator given	79 (94.0%)
No follow-up information/AE documented	81 (96.4%)
Number of patients included in the FAS	403 (80.3%)
Number of patients excluded from the FAS	99 (19.7%)
Reasons for exclusion from the the FAS	
No informed consent signed	3 (3.0%)
No dose of the starting prescribed iron chelator given	79 (79.8%)
No follow-up information/AE documented	81 (81.8%)
Age<18 years	0 (0.0%)
Patient included into study erroneously	22 (22.2%)

FAS: Full analysis set, N: Number of patients in analysis set, SAF: Safety analysis set.

Baseline Characteristics

Table 10-3 Demographic characteristics, by start treatment – FAS

Parameter n (%)	Overall N=403	Deferasirox DT N=111	Deferasirox FCT N=267	Deferoxamine N=25
Demographics				
Sex, n (%)				
Female	163 (40.4%)	47 (42.3%)	104 (39.0%)	12 (48.0%)
Male	240 (59.6%)	64 (57.7%)	163 (61.0%)	13 (52.0%)
Age at baseline [years], mean (SD)	72.3 (10.99)	71.5 (11.07)	72.1 (11.21)	78.2 (5.30)
Weight at baseline [kg], mean (SD)	76.8 (17.38)	78.4 (16.96)	76.3 (17.90)	75.1 (12.88)
Height at baseline [cm], mean (SD)	170.2 (9.51)	169.2 (9.49)	171.0 (9.44)	166.8 (9.56)
BMI at baseline [kg/m^2], mean (SD)	26.4 (5.09)	27.2 (4.84)	26.0 (5.23)	26.9 (4.23)
Ethnicity, n (%)				
Caucasian	399 (99.0%)	110 (99.1%)	264 (98.9%)	25 (100.0%)
Asian	3 (0.7%)	0 (0.0%)	3 (1.1%)	0 (0.0%)
African	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other	1 (0.2%)	1 (0.9%)	0 (0.0%)	0 (0.0%)

DT: Dispersible tablet, FAS: Full analysis set, FCT: Film coated tablet, N: Number of patients in analysis set, n: number of patients with observation, SD: Standard deviation.

Table 10-2 Primary diagnosis by start treatment – FAS

Parameter	Overall	Deferasirox DT	Deferasirox FCT	Deferoxamine
n (%)	N=403	N=111	N=267	N=25
MDS	243 (60.3%)	69 (62.2%)	160 (59.9%)	14 (56.0%)
MPN	62 (15.4%)	13 (11.7%)	44 (16.5%)	5 (20.0%)
Leukemia	25 (6.2%)	7 (6.3%)	17 (6.4%)	1 (4.0%)
Lymphoma	21 (5.2%)	8 (7.2%)	9 (3.4%)	4 (16.0%)
Haemoglobinopathies	6 (1.5%)	1 (0.9%)	5 (1.9%)	0 (0.0%)
Other primary diagnosis (pre-specified)	26 (6.5%)	7 (6.3%)	19 (7.1%)	0 (0.0%)
Other (free text entry)	20 (5.0%)	6 (5.4%)	13 (4.9%)	1 (4.0%)

DT: Dispersible tablet, FAS: Full analysis set, FCT: Film coated tablet, MDS: Myelodysplastic syndrome, MPN: Myeloproliferative neoplasm, N: Number of patients in analysis set, n: number of patients with observation.

Table 10-4 Reasons for diagnosis, by start treatment – FAS

Parameter n (%)	Overall N=403	Deferasirox DT N=111	Deferasirox FCT N=267	Deferoxamine N=25
Weakness/ Fatigue	132 (32.8%)	32 (28.8%)	93 (34.8%)	7 (28.0%)
Infections	7 (1.7%)	1 (0.9%)	6 (2.2%)	0 (0.0%)
Bleeding	10 (2.5%)	3 (2.7%)	6 (2.2%)	1 (4.0%)
Cytopenia	279 (69.2%)	70 (63.1%)	191 (71.5%)	18 (72.0%)
Anemia	262 (65.0%)	64 (57.7%)	181 (67.8%)	17 (68.0%)
Thrombocytopenia	65 (16.1%)	18 (16.2%)	41 (15.4%)	6 (24.0%)
Neutropenia	43 (10.7%)	9 (8.1%)	31 (11.6%)	3 (12.0%)
Hereditary predisposition	2 (0.5%)	1 (0.9%)	1 (0.4%)	0 (0.0%)
Other	63 (15.6%)	20 (18.0%)	38 (14.2%)	5 (20.0%)
Unknown	55 (13.6%)	23 (20.7%)	29 (10.9%)	3 (12.0%)

Multiple responses were possible.
DT: Dispersible tablet, FAS: Full analysis set, FCT: Film coated tablet, N: Number of patients in analysis set, n: number of patients with observation.

Primary Outcome Result(s)

Efficiency of iron overload therapy – Serum ferritin change from baseline during start treatment, by start treatment

Table 10-14 Serum ferritin change from baseline during start treatment, by start treatment – FAS

Serum ferritin [µg/l]	N	n	Mean	SD	Median	Min	Max
Overall							
Month 1	367	214	-2.47	1110.377	-54.50	-5535.00	11301.00
Month 3	301	218	-53.24	1010.510	38.55	-6214.00	4840.00
Month 6	234	167	-42.86	1363.440	-16.20	-7140.00	5922.00
Month 9	183	128	-289.49	1439.103	-198.60	-7723.00	3587.00
Month 12	140	105	-271.13	1447.381	-219.00	-7878.00	3428.00
Month 18	101	75	-235.30	1745.478	-339.00	-8860.00	5310.00
Month 24	78	56	-66.67	1511.093	-458.00	-3003.00	5080.00
Last visit	372	251	-30.47	1398.569	-93.00	-8860.00	5638.00
Deferasirox DT							
Month 1	98	49	-88.73	642.722	-67.50	-1513.00	2117.00
Month 3	72	50	-43.92	856.493	61.30	-2119.00	2353.00
Month 6	51	32	96.82	1019.995	32.50	-1845.00	3688.00
Month 9	31	20	-123.82	940.547	-58.50	-1959.00	1827.00
Month 12	17	10	-192.54	1247.089	-335.00	-2120.00	2050.61
Month 18	7	4	-240.82	2027.365	-849.50	-1910.00	2645.71
Month 24	2	2	1342.15	2496.299	1342.15	-423.00	3107.30
Last visit	100	60	-197.17	961.651	-87.85	-2119.00	3107.30

Serum ferritin [µg/l]	N	n	Mean	SD	Median	Min	Max
Deferasirox FCT							
Month 1	246	150	57.81	1251.945	-27.50	-5535.00	11301.00
Month 3	208	151	-77.60	1007.252	30.00	-6214.00	2988.00
Month 6	167	126	-103.97	1356.076	-32.61	-7140.00	5638.00
Month 9	138	99	-321.77	1511.043	-215.00	-7723.00	3587.00
Month 12	116	89	-280.92	1474.373	-227.00	-7878.00	3428.00
Month 18	89	67	-217.77	1751.982	-282.00	-8860.00	5310.00
Month 24	71	50	-114.48	1429.569	-365.50	-3003.00	5080.00
Last visit	249	175	1.89	1476.801	-129.00	-8860.00	5638.00
Deferoxamine							
Month 1	23	15	-323.40	696.663	-100.00	-1949.00	620.00
Month 3	21	17	135.68	1430.818	69.00	-2409.00	4840.00
Month 6	16	9	316.07	2350.925	32.10	-2493.00	5922.00
Month 9	14	9	-302.59	1650.732	-219.30	-2852.00	2030.00
Month 12	7	6	-256.87	1581.779	208.10	-3104.00	1300.00
Month 18	5	4	-523.55	1842.855	-454.10	-2802.00	1616.00
Month 24	5	4	-173.42	2242.507	-709.85	-2274.00	3000.00
Last visit	23	16	240.72	1860.570	110.00	-2605.00	4840.00

DT: Dispersible tablet, FAS: Full analysis set, FCT: Film coated tablet, Min: Minimum, Max: Maximum, N: Number of patients in analysis set, n: number of patients with observation, SD: Standard deviation.

Secondary Outcome Result(s)

Number of patients treated with different iron chelators

Table 10-10 Reason for and purpose of iron chelation treatment, by start treatment – FAS

Parameter	Overall	Deferasirox DT	Deferasirox FCT	Deferoxamine
n (%)	N=403	N=111	N=267	N=25
Reason for iron chelation treatment*				
Transfusion of > 20 units	122 (30.3%)	37 (33.3%)	78 (29.2%)	7 (28.0%)
Serum ferritin >1000 ng/ml	366 (90.8%)	99 (89.2%)	243 (91.0%)	24 (96.0%)
Missing	7 (1.7%)	1 (0.9%)	6 (2.2%)	0 (0.0%)
Purpose of the iron chelation treatment				
Reduction of serum ferritin	374 (92.8%)	104 (93.7%)	247 (92.5%)	23 (92.0%)
Stabilization of serum ferritin	29 (7.2%)	7 (6.3%)	20 (7.5%)	2 (8.0%)

*Multiple responses were possible.
DT: Dispersible tablet, FAS: Full analysis set, FCT: Film coated tablet, N: Number of patients in analysis set, n: number of patients with observation.

Number of patients with therapy switch

Table 10-11 Treatment changes – FAS

	N (%)
Total	403 (100.0%)
Number of patients with one treatment change	48 (11.9%)
deferasirox DT to deferasirox FCT	40 (83.3%)
deferasirox FCT to deferasirox DT	3 (6.3%)
deferasirox FCT to deferoxamine	3 (6.3%)
deferoxamine to deferasirox DT	1 (2.1%)
deferoxamine to deferasirox FCT	1 (2.1%)
Number of patients with two treatment changes	4 (1.0%)
deferasirox DT to deferasirox FCT to deferasirox DT	1 (25.0%)
deferasirox DT to deferasirox FCT to deferoxamine	1 (25.0%)
deferasirox FCT to deferasirox DT to deferasirox FCT	1 (25.0%)
deferasirox FCT to deferoxamine to deferasirox FCT	1 (25.0%)

DT: Dispersible tablet, FAS: Full analysis set, FCT: Film coated tablet, N: Number of patients in analysis set.

Table 10-12 Reason for treatment change and interruption prior to change, by treatment change group – FAS

Parameter	Deferasirox DT to Deferasirox FCT	Deferoxamine to Deferasirox FCT	Other switch combinations
n (%)	N=43	N=2	N=11
Reason for treatment change (multiple response)			
Adverse Event	3 (7.0%)	1 (50.0%)	5 (45.5%)
Chelation too heavy	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chelation too soft	1 (2.3%)	0 (0.0%)	4 (36.4%)
Poor compatibility	1 (2.3%)	0 (0.0%)	2 (18.2%)
Intricate application	21 (48.8%)	1 (50.0%)	0 (0.0%)
Other	19 (44.2%)	0 (0.0%)	2 (18.2%)
Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)
Interruption of iron chelation treatment prior to treatment change			
Yes	4 (9.3%)	0 (0.0%)	2 (18.2%)
No	39 (90.7%)	2 (100.0%)	9 (81.8%)
Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)

DT: Dispersible tablet, FAS: Full analysis set, FCT: Film coated tablet, N: Number of patients in analysis set.

Number of patients with dose adjustments

Table 10-13 Initial and last daily dose of changed treatment [mg/kg], by treatment change group – FAS

Parameter	Deferasirox DT to Deferasirox FCT	Deferoxamine to Deferasirox FCT	Other switch combinations
	N=43	N=2	N=11
Prior treatment			
First daily dose [mg/kg]			
Mean (SD)	10.5 (6.22)	24.1 (1.24)	15.6 (7.34)
Median	9.4	24.1	16.1
Last daily dose [mg/kg]			
Mean (SD)	12.8 (5.89)	24.1 (1.24)	15.6 (8.04)
Median	12.9	24.1	14.6
New treatment			
First daily dose [mg/kg]			
Mean (SD)	14.6 (6.98)	15.9 (13.97)	16.0 (8.12)
Median	15.4	15.9	14.0
Last daily dose [mg/kg]			
Mean (SD)	15.2 (7.21)	17.4 (6.61)	18.4 (10.17)
Median	15.7	17.4	14.3

Daily doses documented for deferasirox FCT were multiplied with the conversion factor 1.43 for comparability.
DT: Dispersible tablet, FAS: Full analysis set, FCT: Film coated tablet, N: Number of patients in analysis set, SD: Standard deviation.

Number of patients with myelodysplastic syndromes or myeloproliferative neoplasms experiencing a hematologic response during an iron chelation therapy - Hematological response in MDS/MPN patients

Table 10-19 Patients fulfilling the response criteria or suffering from a competing event – HRAS

Parameter	MDS	MPN	Total
n	N=223	N=43	N=266
Hemoglobin response / death without response	21 / 46	3 / 9	24 / 55
Platelets response / death without response	8 / 18	4 / 3	12 / 21
Neutrophil response / death without response	6 / 8	0 / 1	6 / 9
Transfusion response / death without response	15 / 30	4 / 5	19 / 35

MDS: Myelodysplastic syndrome, MPN: Myeloproliferative neoplasm, N: Number of patients in analysis set, n: number of patients with observation.

Table 10-20 Cumulative incidences of responses and deaths without responses at 12 months – HRAS

Parameter	MDS	MPN	Total
Cumulative incidences, n [95%-CI]	N=223	N=43	N=266
Response with regard to hemoglobin	11% [7%; 17%]	10% [2%; 24%]	11% [7%; 17%]
Death without response	17% [11%; 24%]	20% [8%; 37%]	17% [12%; 24%]
Response with regard to platelets	18% [8%; 31%]	37% [8%; 67%]	22% [12%; 33%]
Death without response	25% [12%; 41%]	26% [5%; 53%]	26% [14%; 40%]
Response with regard to neutrophils	26% [9%; 47%]	0%	21% [7%; 40%]
Death without response	25% [8%; 46%]	25% [0%; 71%]	24% [9%; 43%]
Response with regard to transfusions	15% [8%; 23%]	17% [4%; 39%]	15% [9%; 23%]
Death without response	20% [12%; 29%]	20% [4%; 44%]	20% [12%; 28%]

CI: Confidence interval, MDS: Myelodysplastic syndrome, MPN: Myeloproliferative neoplasm, N: Number of patients in analysis set, n: number of patients with observation.

Number of patients with AEs and SAE

Table 10-36 Patient based incidences of AEs, by treatment* – SAF

Parameter	Overall	Deferasirox DT	Deferasirox FCT	Deferoxamine
n (%)	N=418	N=122	N=319	N=34
Patients without AEs	31 (7.4%)	21 (17.2%)	25 (7.8%)	3 (8.8%)
Patients with AEs	387 (92.6%)	101 (82.8%)	294 (92.2%)	31 (91.2%)
Patients with nsAEs	256 (61.2%)	66 (54.1%)	188 (58.9%)	20 (58.8%)
Patients with SAEs	270 (64.6%)	65 (53.3%)	201 (63.0%)	25 (73.5%)
Patients with nsADRs	220 (52.6%)	61 (50.0%)	156 (48.9%)	15 (44.1%)
Patients with SADRs	86 (20.6%)	26 (21.3%)	57 (17.9%)	5 (14.7%)

*For patients with treatment change the assignment of treatment to AE corresponds to the physician's specification in EDC. AEs not assigned to treatment are only included in the "Overall" column.
Non-fatal protocol exempted events and non-related AEs documented more than 30 days after treatment discontinuation/ study end were excluded.
AE: Adverse event, DT: Dispersible tablet, EDC: Electronic data capture, FCT: Film coated tablet, N: Number of patients in analysis set, n: number of patients with observation, nsADR: non-serious adverse drug reaction, nsAE: non-serious adverse event, SADR: Serious adverse drug reaction, SAE: Serious adverse event, SAF: Safety analysis set.

Table 10-37 Patient based incidences of AEs for patients with a treatment change– SAF

Parameter	Deferasirox DT to Deferasirox FCT	Deferoxamine to Deferasirox FCT	Other switch combination
n (%)	N=47	N=3	N=13
Patients without AEs	1 (2.1%)	0 (0.0%)	0 (0.0%)
Patients with AEs	46 (97.9%)	3 (100.0%)	13 (100.0%)
Patients with nsAEs	39 (83.0%)	3 (100.0%)	12 (92.3%)
Patients with SAEs	31 (66.0%)	2 (66.7%)	10 (76.9%)
Patients with nsADRs	30 (63.8%)	2 (66.7%)	6 (46.2%)
Patients with SADRs	11 (23.4%)	1 (33.3%)	6 (46.2%)

AE: Adverse event, DT: Dispersible tablet, FCT: Film coated tablet, N: Number of patients in analysis set, n: number of patients with observation, nsADR: non-serious adverse drug reaction, nsAE: non-serious adverse event, SADR: Serious adverse drug reaction, SAE: Serious adverse event, SAF: Safety analysis set.

Number of patients with side effects

Table 10-38 Most common patient based AEs (>5%), by MedDRA SOC and PT, for overall population – SAF

MedDRA SOC/PT n (%)	Total N=418	nsAE N=256	SAE N=270	nsADR N=220	SADR N=86
General disorders and administration site conditions	202 (48.3%)	109 (42.6%)	82 (30.4%)	53 (24.1%)	11 (12.8%)
General physical health deterioration	51 (12.2%)	17 (6.6%)	25 (9.3%)	7 (3.2%)	3 (3.5%)
Fatigue	41 (9.8%)	31 (12.1%)	2 (0.7%)	8 (3.6%)	1 (1.2%)
Pyrexia	36 (8.6%)	16 (6.3%)	18 (6.7%)	4 (1.8%)	0 (0.0%)
Oedema peripheral	23 (5.5%)	17 (6.6%)	2 (0.7%)	4 (1.8%)	0 (0.0%)
Death	19 (4.5%)	0 (0.0%)	16 (5.9%)	0 (0.0%)	3 (3.5%)
Asthenia	17 (4.1%)	15 (5.9%)	3 (1.1%)	1 (0.5%)	0 (0.0%)
Gastrointestinal disorders	187 (44.7%)	80 (31.3%)	44 (16.3%)	113 (51.4%)	16 (18.6%)
Diarrhoea	82 (19.6%)	22 (8.6%)	4 (1.5%)	57 (25.9%)	6 (7.0%)
Nausea	50 (12.0%)	26 (10.2%)	3 (1.1%)	22 (10.0%)	3 (3.5%)
Constipation	28 (6.7%)	12 (4.7%)	1 (0.4%)	14 (6.4%)	1 (1.2%)
Infections and infestations	151 (36.1%)	71 (27.7%)	105 (38.9%)	5 (2.3%)	7 (8.1%)
Pneumonia	34 (8.1%)	0 (0.0%)	34 (12.6%)	0 (0.0%)	0 (0.0%)
Urinary tract infection	26 (6.2%)	12 (4.7%)	17 (6.3%)	0 (0.0%)	0 (0.0%)
Nasopharyngitis	23 (5.5%)	21 (8.2%)	2 (0.7%)	0 (0.0%)	0 (0.0%)

MedDRA SOC/PT n (%)	Total N=418	nsAE N=256	SAE N=270	nsADR N=220	SADR N=86
Investigations	141 (33.7%)	43 (16.8%)	44 (16.3%)	72 (32.7%)	25 (29.1%)
Blood creatinine increased	41 (9.8%)	7 (2.7%)	0 (0.0%)	29 (13.2%)	7 (8.1%)
Haemoglobin decreased	36 (8.6%)	7 (2.7%)	21 (7.8%)	7 (3.2%)	6 (7.0%)
Serum ferritin increased	17 (4.1%)	2 (0.8%)	0 (0.0%)	14 (6.4%)	1 (1.2%)
Respiratory, thoracic and mediastinal disorders	93 (22.2%)	67 (26.2%)	31 (11.5%)	6 (2.7%)	3 (3.5%)
Dyspnoea	32 (7.7%)	25 (9.8%)	7 (2.6%)	1 (0.5%)	0 (0.0%)
Dyspnoea exertional	24 (5.7%)	18 (7.0%)	5 (1.9%)	1 (0.5%)	0 (0.0%)
Epistaxis	17 (4.1%)	13 (5.1%)	5 (1.9%)	0 (0.0%)	0 (0.0%)
Musculoskeletal and connective tissue disorders	74 (17.7%)	52 (20.3%)	15 (5.6%)	11 (5.0%)	0 (0.0%)
Back pain	15 (3.6%)	13 (5.1%)	2 (0.7%)	0 (0.0%)	0 (0.0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	73 (17.5%)	1 (0.4%)	68 (25.2%)	0 (0.0%)	6 (7.0%)
Acute myeloid leukaemia	24 (5.7%)	0 (0.0%)	23 (8.5%)	0 (0.0%)	1 (1.2%)
Myelodysplastic syndrome	24 (5.7%)	0 (0.0%)	20 (7.4%)	0 (0.0%)	4 (4.7%)
Malignant neoplasm progression	19 (4.5%)	0 (0.0%)	17 (6.3%)	0 (0.0%)	2 (2.3%)

MedDRA SOC/PT n (%)	Total N=418	nsAE N=256	SAE N=270	nsADR N=220	SADR N=86
Nervous system disorders	70 (16.7%)	39 (15.2%)	24 (8.9%)	16 (7.3%)	3 (3.5%)
Dizziness	39 (9.3%)	26 (10.2%)	4 (1.5%)	10 (4.5%)	2 (2.3%)
Blood and lymphatic system disorders	66 (15.8%)	15 (5.9%)	43 (15.9%)	6 (2.7%)	12 (14.0%)
Neutropenia	25 (6.0%)	0 (0.0%)	19 (7.0%)	0 (0.0%)	6 (7.0%)
Skin and subcutaneous tissue disorders	60 (14.4%)	30 (11.7%)	6 (2.2%)	22 (10.0%)	7 (8.1%)
Injury, poisoning and procedural complications	50 (12.0%)	21 (8.2%)	22 (8.1%)	10 (4.5%)	2 (2.3%)
Renal and urinary disorders	49 (11.7%)	9 (3.5%)	20 (7.4%)	8 (3.6%)	15 (17.4%)
Renal failure	14 (3.3%)	0 (0.0%)	4 (1.5%)	0 (0.0%)	10 (11.6%)
Cardiac disorders	45 (10.8%)	3 (1.2%)	41 (15.2%)	3 (1.4%)	3 (3.5%)
Metabolism and nutrition disorders	43 (10.3%)	26 (10.2%)	12 (4.4%)	8 (3.6%)	2 (2.3%)
Vascular disorders	36 (8.6%)	20 (7.8%)	17 (6.3%)	2 (0.9%)	0 (0.0%)
Psychiatric disorders	23 (5.5%)	19 (7.4%)	4 (1.5%)	1 (0.5%)	0 (0.0%)
Hepatobiliary disorders	17 (4.1%)	3 (1.2%)	9 (3.3%)	0 (0.0%)	6 (7.0%)

Coding was performed using MedDRA Version 24.1.
Non-fatal protocol exempted events and non-related AEs documented more than 30 days after treatment discontinuation/ study end were excluded.
AE: Adverse event, MedDRA: Medical dictionary for regulatory activities, N: Number of patients in analysis set, n: number of patients with observation, nsADR: non-serious adverse drug reaction, nsAE: non-serious adverse event, PT: Preferred term, SADR: Serious adverse drug reaction, SAE: Serious adverse event, SAF: Safety analysis set, SOC: System organ class.

Treatment Satisfaction Questionnaire to Medication (TSQM) 1.4

Table 10-21 TSQM-14 Subscales during start treatment, overall population – FAS

Parameter	N	n	Mean	SD	Median	Min	Max
Effectiveness							
Month 1	237	220	62.7	22.31	66.7	0.0	100.0
Month 3	191	182	59.3	21.68	61.1	0.0	100.0
Side effects							
Month 1	237	135	68.4	27.56	75.0	0.0	100.0
Month 3	191	112	65.4	25.87	68.8	0.0	100.0
Convenience							
Month 1	237	233	78.0	19.15	77.8	11.1	100.0
Month 3	191	191	77.7	18.81	77.8	16.7	100.0
Overall satisfaction							
Month 1	237	224	65.2	20.89	68.1	0.0	100.0
Month 3	191	181	62.9	22.84	63.9	0.0	100.0

FAS: Full analysis set, Max: Maximum, Min: Minimum, N: Number of patients in analysis set, n: number of patients with observation, SD: Standard deviation, TSQM-14: Treatment satisfaction questionnaire for medication (with 14 questions).

Safety Results

Refer to adverse events tables in the outcomes section

Other Relevant Findings

NA

Conclusion:

This study provided valuable insights into the utilization, effectiveness, safety, and patient's satisfaction in daily medical practice, while additionally documenting change of iron chelator medication. A large proportion of patients switched from deferasirox DT to deferasirox FCT, mainly due to more convenient application. This was also reflected in the TSQM-14 scores. There was a slight tendency towards decreasing scores from month 1 to month 3, and towards increasing scores after treatment change. Deferasirox FCT and deferoxamine were effective in lowering serum ferritin levels, however for deferasirox DT patient numbers at later time points were too small for a meaningful interpretation. The observed ADRs were in line with the known safety profile.

Date of Clinical Study Report

19 Jul 2022