

Supplementary

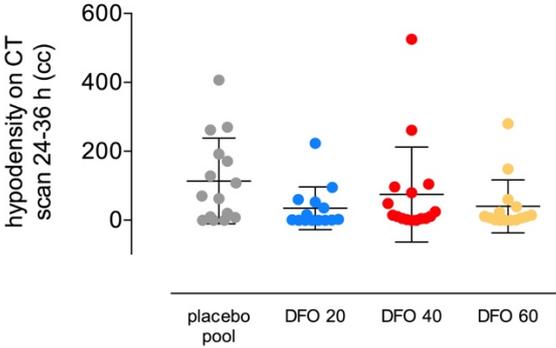


Figure S1. Effect of DFO on CT hypodensity. No effect was observed on hypodensity volume on CT scans during the first 36 h post-stroke onset between placebo and DFO groups.

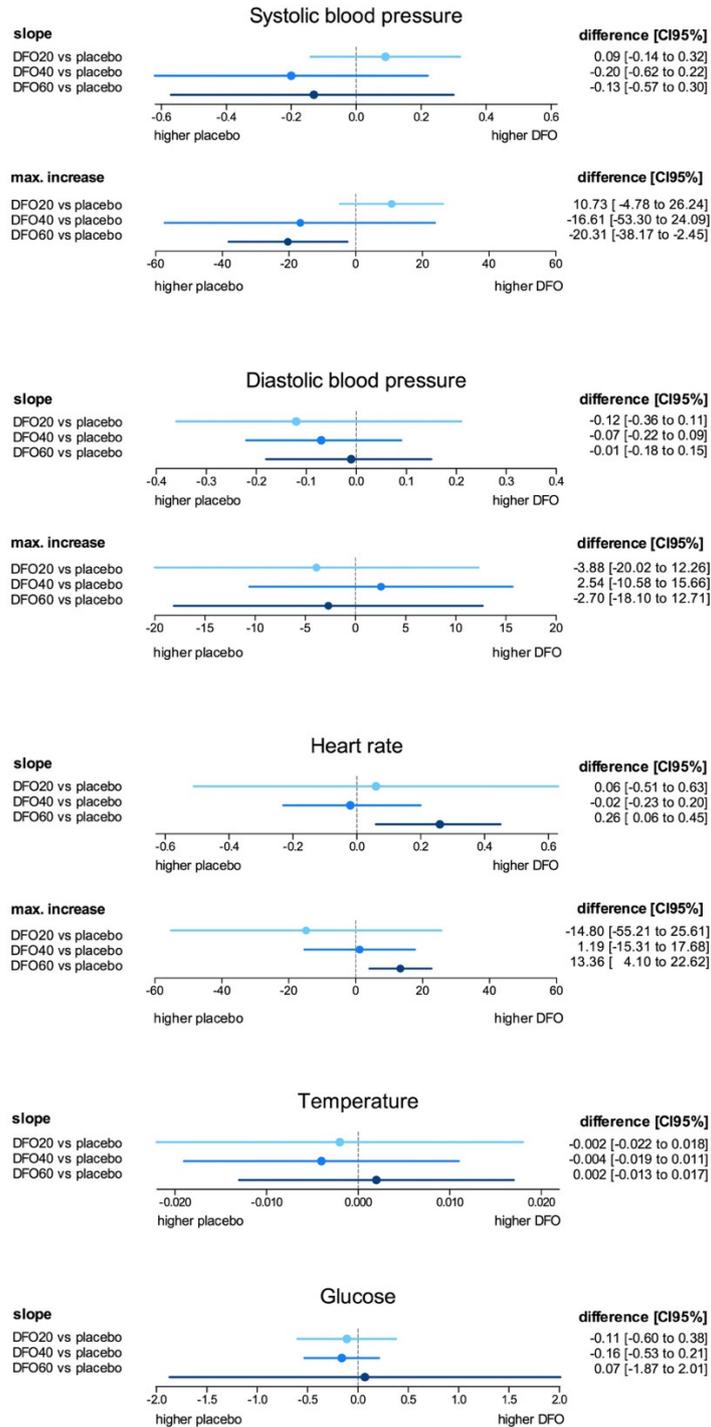


Figure S2. Effect of deferoxamine (DFO) on cardiovascular parameters, body temperature, and blood glucose. Estimated linear regression slope and maximum increase differences for systolic blood pressure, diastolic blood pressure, heart rate, temperature, and blood glucose in each dose tier group of DFO (20, 40 and 60 mg/Kg/day) versus the placebo group (CI 95%). For each patient, a simple linear regression and slope was calculated by plotting in the Y axis values obtained for a given variable at different time points vs time in the X axis. For each patient the maximum increase was calculated as the maximum among the differences between each of the values taken over time and the baseline value.

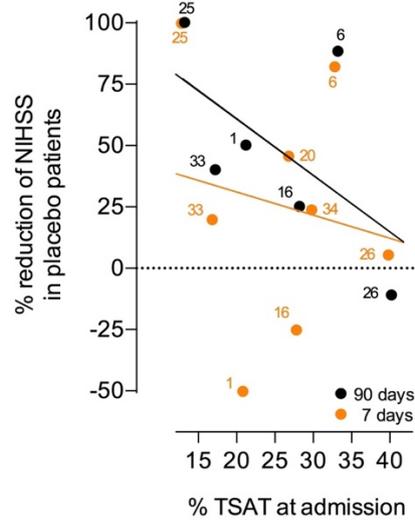


Figure S3. Relationship between % TSAT of each patient in the placebo arm at admission and % reduction of neurological impairment. Serum TSAT was measured at admission and neurological impairment was assessed by an expert neurologist at admission and along the follow-up of the TANDEM-1 clinical trial. Percentage of neurological improvement was calculated at 7 days and at 90 days in the placebo arm using the formula: % reduction of NIHSS in placebo patients= $((\text{NIHSS at admission} - \text{NIHSS at a given time}) \times 100) / \text{NIHSS at admission}$). Lower endogenous TSAT levels in blood samples obtained in patients at admission associated to a higher improvement of neurological symptoms along time. This trend to improvement in the TANDEM-1 placebo patients is very similar to that we previously observed in experimental animals, in which lower TSAT meant less infarct and less neurological impairment.

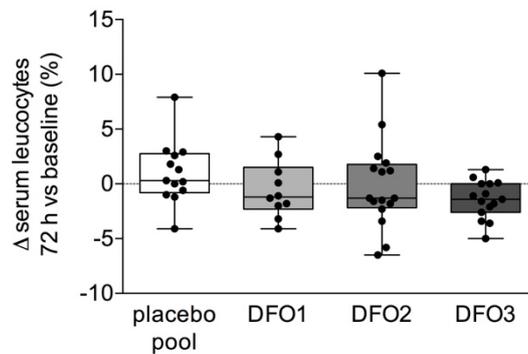


Figure S4. Effect of 72 h treatment with DFO on blood leucocytes. No significant effect of the DFO treatment was observed.

Table S1. Reported serious adverse events in the placebo and DFO group in each DTS

DTS 1		DTS 2		DTS3	
Placebo (n=5)	DFO 20 (n=15)	Placebo (n=5)	DFO 40 (n=16)	Placebo (n=5)	DFO 60 (n=16)
Neurological worsening Not related	sICH- PH2 Not related		Deep venous thrombosis Not related & Stroke recurrence Not related & Neurological worsening- Death Not related	Neurological worsening- Malignant MCA infarct Not related & Urinary infection Not related	Neurological worsening Not related
ENW- Malignant MCA infarct Death Not related	sICH-PH2 Possibly related				ENW- Malignant MCA infarct Death Not related
	Asymptomatic bradycardia Possibly related- Discontinued			Symptomatic hypotension Possibly related- Discontinued	Neurological worsening- Malignant MCA infarct Death Not related & Broncho- aspiration Not related
	Pulmonary neoplasm- Death Not related		ENW- Intracranial hypertension- Death Possibly related- Discontinued		
	Uncontrolled hypertension Not related & ENW- Malignant MCA infarct Death Not related		Colon neoplasm- Death Not related		Anaphylaxis Definitely related- Discontinued #

DTS: dose tier sub-study. DFO: deferoxamine (in mg/Kg/day for 3 days). Serious adverse effects (SAE) types are reported in the table in bold; those considered to be the cause of death are indicated (text in red) and relationship with treatment (not related, possible-related or related) and drug discontinuation are indicated. Cells in white correspond to patients that suffered only one SAE. Cells displaying identical colour in the table indicate SAE recorded in the same patient: 3 patients presented 2 SAE and 2 patients presented 3 SAE. sICH: symptomatic intracranial hemorrhage. PH2: parenchymal hematoma type. ENW: early neurological worsening. #: Although this patient was randomized into DTS3, anaphylaxis was observed during the 10 mg/Kg DFO bolus administration which is common for the DFO arm in all the DTS.