Category : **Hematology: Other**

A158 - *Impact of cefiderocol treatment on iron homeostasis and anaemia in critically ill patients with carbapenem-resistant infections in the credible-cr study*

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Introduction:

We studied whether cefiderocol (CFDC) treatment had an adverse effect on iron homeostasis or led to anaemia in critically ill patients enrolled into the open-label, pathogen-focused, Phase 3 CREDIBLE-CR study [1]. CFDC is an iron-chelator, siderophore cephalosporin developed for the treatment of infections caused by carbapenem-resistant (CR) Gram-negative bacteria, including Enterobacterales and non-fermenter species, in adult patients with limited treatment options.

Methods:

Patients with serious CR infections were randomised 2:1 to receive intravenous CFDC, 2 g, q8h, or best available therapy (BAT; ≤3 antibiotics with Gram-negative activity) for 7–14 days [1]. Haemoglobin levels were measured in protocol-defined routine laboratory analyses. Specific iron homeostasis-related laboratory tests were performed at randomisation and test of cure [TOC; end of treatment +7 days) to determine serum levels of total iron, hepcidin, total iron binding capacity (TIBC) and transferrin saturation (TS%). Normal iron level ranges were defined as 59–178 µg/mL (males) and 37–173 µg/mL (females).

Results:

Of 150 randomised patients (CFDC 101, BAT 49), 71 (47.3%) had anaemia in their medical history (CFDC 44.6% [45/101], BAT 53.1% [26/49]) and 134 (CFDC 91, BAT 43) had serum iron data available at baseline. Most patients had iron levels below the lower limit of normal (CFDC 76.2% [77/101], BAT 57.1% [28/49]), and fewer patients had iron levels in the normal range (CFDC 13.9% [14/101], BAT 30.6% [15/49]). Between baseline and TOC, mean haemoglobin level increased from 9.6 to 9.9 g/dL in the CFDC arm and from 9.0 to 9.5 g/dL in the BAT arm (Figure 1). Changes in all four specific iron homeostasis parameters between baseline and TOC were similar between treatment arms (Figure 1).
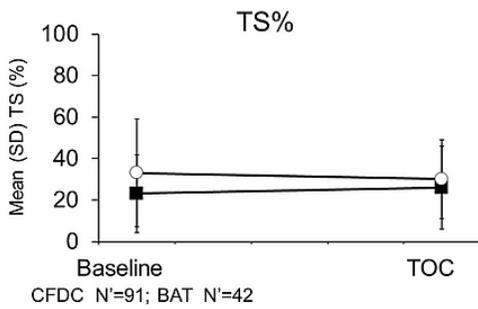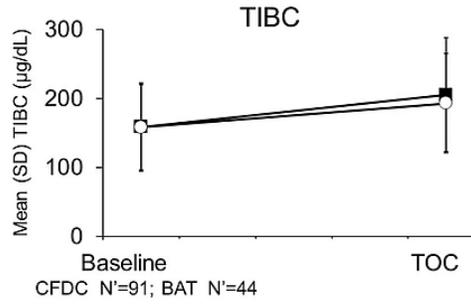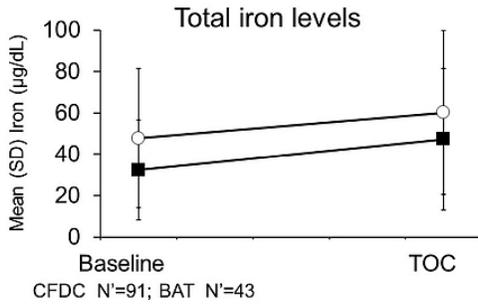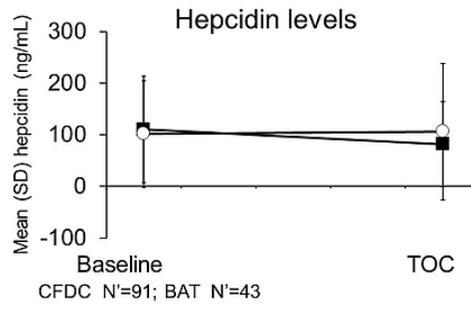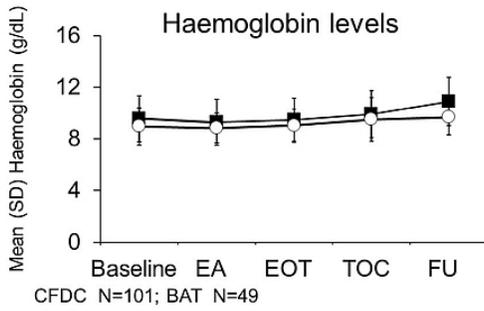
Conclusion:

CFDC therapy did not lead to increased anaemia or reduced serum iron level in patients with serious CR infections.

References:

1. Bassetti M et al. Lancet Infect Dis 21(2):226–240, 2021.

Image :

Haemoglobin levels

Mean (SD) Haemoglobin (g/dL)

16 — 12 — 8 — 4 — 0

Baseline EA EOT TOC FU

CFDC N=101; BAT N=49

Hepcidin levels

Mean (SD) hepcidin (ng/mL)

300 — 200 — 100 — 0 — -100

Baseline TOC

CFDC N'=91; BAT N'=43

Total iron levels

Mean (SD) Iron (µg/dL)

100 — 80 — 60 — 40 — 20 — 0

Baseline TOC

CFDC N'=91; BAT N'=43

TIBC

Mean (SD) TIBC (µg/dL)

300 — 200 — 100 — 0

Baseline TOC

CFDC N'=91; BAT N'=44

TS%

Mean (SD) TS (%)

100 — 80 — 60 — 40 — 20 — 0

Baseline TOC

CFDC N'=91; BAT N'=42

■— Cefiderocol (CFDC)
○— Best available therapy (BAT)

EA, early assessment (Day 3–4); EOT, end of treatment; FU, follow-up (EOT +14 days); TIBC, total iron-binding capacity; TOC, test of cure (EOT +7 days); TS%, transferrin saturation N': number of patients with non-missing values.

Changes in iron homeostasis parameters in the CREDIBLE-CR study.