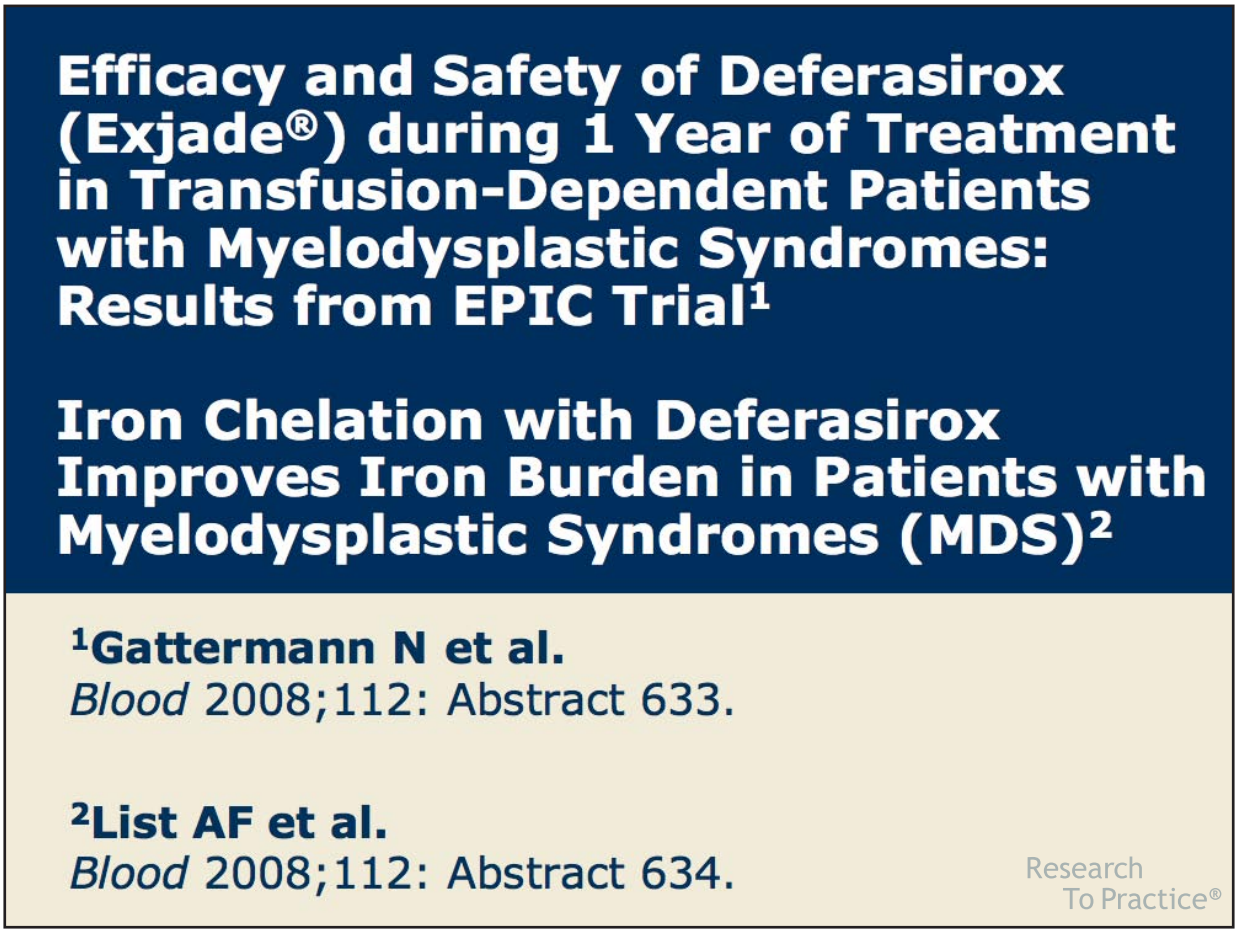
Studies on the Efficacy and Safety of Deferasirox for Iron Chelation in Patients with MDS: EPIC and US03

Presentations discussed in this issue:

Gattermann N et al. **Efficacy and safety of deferasirox (Exjade®) during 1 year of treatment in transfusion-dependent patients with myelodysplastic syndromes: Results from EPIC trial.** *Blood* 2008;112;**Abstract 633**.

List AF et al. **Iron chelation with deferasirox (Exjade®) improves iron burden in patients with myelodysplastic syndromes (MDS).** *Blood* 2008;112;**Abstract 634**.

Slides from presentations at ASH 2008



Introduction

- Many patients with myelodysplastic syndromes (MDS) are susceptible to iron overload from ongoing blood transfusions and increased dietary iron absorption.
- Deferasirox has demonstrated efficacy in maintaining or reducing body iron in patients with MDS.
- The EPIC[1] and US03[2] studies evaluated efficacy and safety of deferasirox in patients with MDS:
  - Primary endpoint: change in serum ferritin (SF) from baseline at 12 months
  - Safety was assessed by laboratory parameters and adverse events monitoring

Source: [1]Gattermann N et al. *Blood* 2008;112:Abstract 633; [2]List AF et al. *Blood* 2008;112:Abstract 634.

EPIC: Multicenter, Open-Label, Single-Arm Study of Deferasirox in Patients with Anemia, including MDS

Eligibility

- Transfusion-dependent MDS; serum ferritin (SF) ≥ 1000 ng/ml or < 1000 ng/ml and requiring >20 transfusions or 100 mL/kg blood;
- MRI-confirmed liver iron concentration >2 mg Fe/g dry weight

↓

Treatment (n=341)

- Initial dose: deferasirox, 10-30 mg/Kg/day for 12 months
- SF assessed q mo; dose adjusted according to protocol specifications in 5-10 mg/kg/d steps q 3 mo based on SF trends and safety markers

Source: Gattermann N et al. *Blood* 2008;112:Abstract 633.

US03: Multicenter, Open-Label Study of Deferasirox in Patients with MDS

Eligibility

- Transfusion-dependent Low- or Int-1 IPSS-risk MDS; serum ferritin (SF) ≥ 1000 ng/ml and requiring >20 units RBC transfusions;
- Serum creatinine (SCr) ≤ 2 x upper limit of normal (ULN)

↓

Treatment (n=176)

- Initial dose: deferasirox, 20 mg/Kg/day, increased to 40 mg/Kg/day based on tolerability and response
- SF assessed q mo and labile plasma iron (LPI) assessed quarterly

Source: List AF et al. *Blood* 2008;112:Abstract 634.

Deferasirox for MDS: Reduction in Serum Ferritin (SF) from Baseline Over 1 Year

Month	Median SF (ng/mL)	
	EPIC[1] (n=341)	US03[2] (n=176)
0 (baseline)	2730	3397
3	2358	3057
6	2210	2802
9	2076	2635
12	1904	2501

[1]EPIC: Change in median SF over one year by last observation carried forward with all patients included: -253 ng/mL (p=0.0019)
[2]US03: At 3 mos, sustained suppression of labile plasma iron (LPI) to within normal range was achieved in patients with ↑baseline levels (41% of patients had elevated LPI at baseline)

Source: [1]Gattermann N et al. *Blood* 2008;112:Abstract 633; [2]List AF et al. *Blood* 2008;112:Abstract 634.

Deferasirox for MDS: Most Common Drug-Related Adverse Events

Adverse Events (AE)	Patients, n (%)	
	EPIC[1] (n=341)	US03[2,3] (n=165)
Diarrhea	110 (32%)	71 (43%)
Nausea	45 (13%)	29 (18%)
Vomiting	26 (8%)	not reported
Abdominal pain[1]/distension[3]	51 (15%)	9 (6%)
Serum creatinine >ULN for ≥2 values	36 (10.6%)	26* (18%)
Rash	23 (7%)	14 (9%)
Constipation	21 (6%)	not reported

*Patients with normal baseline creatinine (n=147)

Discontinuation of drug due to drug-related AEs: 13%(EPIC)[1], 10% (US03)[2]

Source: [1]Gattermann N et al. *Blood* 2008;112:Abstract 633; [2]List AF et al. *Blood* 2008;112:Abstract 634; [3]Sekeres MA. Oncology Congress 2009 Presentation HM107.

Conclusions

- Deferasirox provided significant reduction in SF levels over 1-year of treatment with appropriate dose adjustments based on SF trends and safety markers
  - Primary Reduction in mean SF (EPIC[1]): -253 ng/mL, p=0.0019
  - Reduction in LPI levels after 3 months to normal range (US03[2])
- The adverse events reported were mild to moderate and consistent with previously reported deferasirox data in patients with MDS
  - Diarrhea (32 - 43%)
  - Increase in creatinine to >ULN for at least 2 values (EPIC[1]:10.6%; US03[2]:18%)

Source: [1]Gattermann N et al. *Blood* 2008;112:Abstract 633; [2]List AF et al. *Blood* 2008;112:Abstract 634.