Poster No. DXT48

Efficacy of subcutaneous interferon β-1a in patients with a first clinical demyelinating event: REFLEX study – outcomes in patients stratified by 2017 McDonald criteria

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CONCLUSIONS

Both dosing frequencies of subcutaneous interferon beta-1a (sc IFN β-1a) significantly reduced the risk versus placebo of McDonald 2005 multiple sclerosis (MS) and clinically definite MS (CDMS), irrespective of McDonald 2017 status at baseline.

Both dosing frequencies of sc IFN β-1a significantly reduced time to either McDonald 2005 MS or CDMS in patients positive for McDonald 2017 MS at baseline.

Results support the main conclusions of the REFLEX study – sc IFN β-1a reduces the risk of McDonald 2005 MS and CDMS in patients with a first clinical demyelinating event.

INTRODUCTION

- In 2017, the McDonald relapsing–remitting MS criteria were revised to include the presence of cerebrospinal fluid–specific oligoclonal bands, symptomatic magnetic resonance imaging lesions, and cortical lesions.[1]
- The **REFLEX trial** demonstrated that sc IFN β-1a reduced conversion to McDonald 2005 MS and to CDMS versus placebo in patients with a first clinical event suggestive of MS (**Figure 1**).[2]

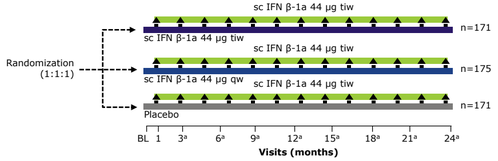
OBJECTIVES

To assess the effects of two dosing frequencies of sc IFN β-1a on time to McDonald 2005–defined MS-related event, CDMS, and annualized relapse rate (ARR) during REFLEX, stratified by retrospective diagnosis at baseline for patients who either meet or do not meet the updated McDonald 2017 criteria for MS.

METHODS

- This retrospective analysis stratified patients randomized to the intention-to-treat population in REFLEX into McDonald 2017–positive (those who retrospectively met the 2010 McDonald criteria for MS at baseline or those with positive oligoclonal bands) and McDonald 2017–negative subgroups (**Tables 1 and 2**).
- Kaplan–Meier curves estimated time to McDonald 2005–defined MS-related event or CDMS by treatment group for each McDonald 2017 subgroup.
- Relapse rates were analyzed using a Poisson regression model with factors for treatment and randomization stratification factors as covariates.

Figure 1. REFLEX trial design



[a]MRI ▲ Conversion to CDMS; switch to open-label treatment – MRI every 6 months ■ sc IFN β-1a 44 µg tiw

BL, baseline; **CDMS**, clinically definite multiple sclerosis; **IFN**, interferon; **MRI**, magnetic resonance imaging; **qw**, once weekly; **sc**, subcutaneous; **tiw**, three times weekly.

RESULTS

Table 1. Patient baseline demographics

Characteristic	Placebo		sc IFN β-1a 44 µg qw		sc IFN β-1a 44 µg tiw		Overall	
	McDonald 2017 positive (n=77)	McDonald 2017 negative (n=94)	McDonald 2017 positive (n=85)	McDonald 2017 negative (n=90)	McDonald 2017 positive (n=73)	McDonald 2017 negative (n=98)	McDonald 2017 positive (N=235)	McDonald 2017 negative (N=282)
Age, mean (SD), years	30.1 (7.4)	31.5 (7.8)	29.4 (7.8)	32.0 (8.3)	28.6 (8.0)	32.2 (8.6)	29.4 (7.7)	31.9 (8.4)
Female, n (%)	54 (70.1)	58 (61.7)	47 (55.3)	59 (65.6)	50 (68.5)	64 (65.3)	151 (64.3)	181 (64.2)
Time since first demyelinating event, mean (SD), days	57.8 (4.5)	57.4 (4.0)	57.8 (3.5)	57.6 (3.4)	57.3 (3.6)	57.8 (3.8)	57.7 (3.9)	57.6 (3.7)
Classification of first clinical demyelinating event as monofocal,[a] n (%)	35 (45.5)	62 (66.0)	50 (58.8)	54 (60.0)	40 (54.8)	59 (60.2)	125 (53.2)	175 (62.1)
Steroid use at first clinical demyelinating event, n (%)	53 (68.8)	68 (72.3)	57 (67.1)	66 (73.3)	53 (72.6)	68 (69.4)	163 (69.4)	202 (71.6)
EDSS score, mean (SD)	1.61 (0.80)	1.54 (0.73)	145 (0.75)	1.66 (0.71)	1.67 (0.84)	1.48 (0.79)	1.57 (0.80)	1.56 (0.75)

[a]According to the investigator. McDonald 2017–positive patients are defined as those previously classified as McDonald 2010 plus having CSF-specific oligoclonal bands (optional and done locally).
CSF, cerebrospinal fluid; **EDSS**, Expanded Disability Status Scale; **IFN**, interferon; **qw**, once weekly; **sc**, subcutaneous; **SD**, standard deviation; **tiw**, three times weekly.

Table 2. Patients in the REFLEX intention-to-treat population classified as McDonald 2017–positive at baseline

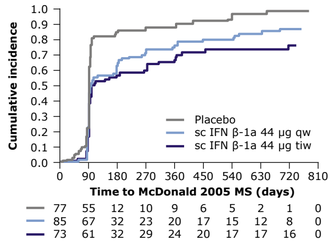
Criteria classification	Placebo (n=171)	sc IFN β-1a 44 µg qw (n=175)	sc IFN β-1a 44 µg tiw (n=171)	Overall (N=517)
McDonald 2017 positive at baseline (McDonald 2010 negative at baseline and CSF positive at baseline), n (%)	10 (5.8)	19 (10.9)	11 (6.4)	40 (7.7)
McDonald 2017 positive at baseline (McDonald 2010 positive at baseline), n (%)	67 (39.2)	66 (37.7)	62 (36.3)	195 (37.7)
McDonald 2017 negative, n (%)	94 (55.0)	90 (51.4)	98 (57.3)	282 (54.5)

McDonald 2017–positive patients are defined as those previously classified as McDonald 2010 plus having CSF-specific oligoclonal bands (optional and done locally).
CSF, cerebrospinal fluid; **IFN**, interferon; **qw**, once weekly; **sc**, subcutaneous; **tiw**, three times weekly.

- In the McDonald 2017–positive subgroup, sc IFN β-1a once weekly (qw) or three times weekly (tiw) significantly delayed time to McDonald 2005 MS versus placebo (**Figure 2a**).
- Treatment with sc IFN β-1a tiw significantly delayed time to McDonald 2005–defined MS-related event versus placebo in the McDonald 2017–negative subgroup (**Figure 2b**).
- In the McDonald 2017–positive subgroup, sc IFN β-1a qw or tiw significantly delayed time to CDMS versus placebo (**Figure 3a**).
- Treatment with sc IFN β-1a tiw significantly delayed time to CDMS versus placebo in McDonald 2017–negative patients at baseline (**Figure 3b**).
- sc IFN β-1a qw and tiw significantly reduced mean ARR versus placebo in McDonald 2017–positive patients (reductions of 59.3% and 69.1%, respectively; p<0.001 for both).

Figure 2. Time to McDonald 2005–defined MS-related event by McDonald 2017 status at baseline (ITT population)

a. McDonald 2017–positive patients

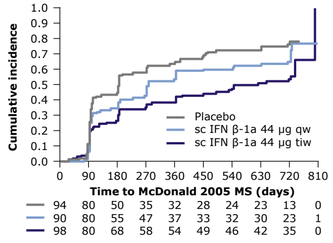


Hazard ratio (95% CI)

sc IFN β-1a 44 µg tiw vs placebo: 0.47 (0.33–0.67) p≤0.001

sc IFN β-1a 44 µg qw vs placebo: 0.58 (0.42–0.82) p=0.002

b. McDonald 2017–negative patients



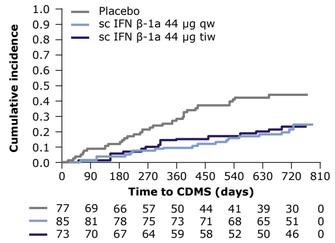
Hazard ratio (95% CI)

sc IFN β-1a 44 µg tiw vs placebo: 0.54 (0.37–0.77) p<0.001

sc IFN β-1a 44 µg qw vs placebo: 0.75 (0.53–1.06) p=0.099

Figure 3. Time to CDMS by McDonald 2017 status at baseline (ITT population)

a. McDonald 2017–positive patients

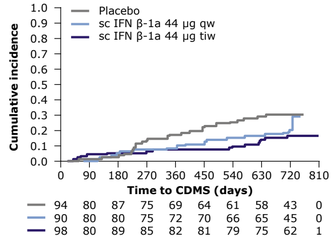


Hazard ratio (95% CI)

sc IFN β-1a 44 µg tiw vs placebo: 0.46 (0.26–0.83) p=0.010

sc IFN β-1a 44 µg qw vs placebo: 0.42 (0.24–0.74) p=0.003

b. McDonald 2017–negative patients



Hazard ratio (95% CI)

sc IFN β-1a 44 µg tiw vs placebo: 0.51 (0.28–0.95) p=0.034

sc IFN β-1a 44 µg qw vs placebo: 0.66 (0.36–1.20) p=0.170

CDMS, clinically definite multiple sclerosis; **CI**, confidence interval; **IFN**, interferon; **ITT**, intention-to-treat; **qw**, once weekly; **sc**, subcutaneous; **tiw**, three times weekly.

REFERENCES
1. Thompson AJ, et al. *Lancet Neurol* 2018;17:162–73; 2. Comi G, et al. *Lancet Neurol* 2012;11:33–41.

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