P052

Cladribine Tablets Demonstrate Similar Efficacy in Male and Female Patients with Relapsing-Remitting Multiple Sclerosis in CLARITY

G. Pardo,[1] F. Dangond,[2] J. Aldridge,[2] C. Lemieux,[3] J.D. Bowen[4]

[1]Oklahoma Medical Research Foundation, Oklahoma City, OK, US; [2]EMD Serono, Inc., Billerica, MA, US; [3]EMD Serono, Inc., Mississauga, ON, CAN; [4]Swedish Neuroscience Institute, MS Center, Seattle, WA, US

INTRODUCTION

- In the 96-week, randomized, placebo-controlled Phase 3 CLARITY trial, cladribine tablets improved clinical and magnetic resonance imaging (MRI) outcomes versus placebo in patients with relapsing-remitting multiple sclerosis (RRMS)[1]
- Although MS prevalence and relapse frequency are consistently higher in female than male patients, the rate of disease progression has typically been found to be higher in males[2,3]

OBJECTIVE

- To examine differences in the effects of treatment with placebo or cladribine tablets 10 mg (3.5 mg/kg cumulative dose over 2 years) on clinical and MRI outcomes in male and female patients from the CLARITY study

METHODS

- A *post hoc* analysis of CLARITY[1] data (trial design: **Figure 1**), to retrospectively analyze the following endpoints in male and female subgroups: annualized relapse rate (ARR), 3- or 6-month confirmed disability progression (CDP), occurrence of new T1 gadolinium-enhancing (Gd+) lesions and active T2 lesions, and the No Evidence of Disease Activity (NEDA) composite index, using either 3- or 6-month CDP at Week 96
- All comparisons were cladribine tablets 3.5 mg/kg versus placebo; P<0.05 was considered nominally significant

RESULTS

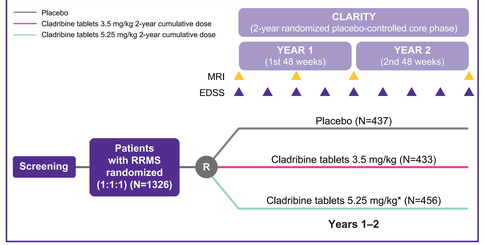
Patients

- Baseline characteristics were generally well balanced between male and female subgroups and between treatment arms (**Table 1**)
  - However, fewer male patients treated with cladribine tablets 3.5 mg/kg compared with placebo had ≥9 T2 lesions (84.3% vs. 91.8%)

Efficacy

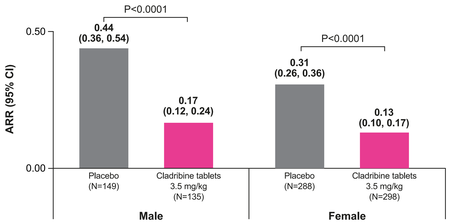
- By Week 96, treatment with cladribine tablets 3.5 mg/kg was associated with greater improvements in clinical and MRI outcomes versus placebo in male and female patient subgroups:
  - Lower ARR with cladribine tablets 3.5 mg/kg versus placebo: males (0.17 vs. 0.44; 60.6% decrease; P<0.0001); females (0.13 vs. 0.31; 56.5% decrease; P<0.0001) (**Figure 2**)
  - Increased probability of remaining free of 3-month CDP for cladribine tablets 3.5 mg/kg compared with placebo in males (85% vs. 70%, 21.4% risk reduction) and females (85% vs. 79%, 7.6% risk reduction) at Week 96 (**Figure 3**)
  - Increased probability of remaining free of 6-month CDP for cladribine tablets 3.5 mg/kg compared with placebo in males (91% vs. 81%, 12.3% risk reduction) and females (91% vs. 85%, 7.1% risk reduction) at Week 96 (please see QR code to the right)
  - Greater percent reduction in the mean cumulative number of new lesions with cladribine tablets 3.5 mg/kg versus placebo
    - T1 Gd+ reduction: males 95.8%; females 86.9%, both P<0.0001 (**Figure 4**)
    - T2 reduction: males 78.4%, females 69.5%, both P<0.0001 (**Figure 5**)
  - Achievement of NEDA (3-month and 6-month CDP) was more likely with cladribine tablets 3.5 mg/kg versus placebo (P<0.0001 in males and females, **Table 2**)

Figure 1. Design of the CLARITY Study



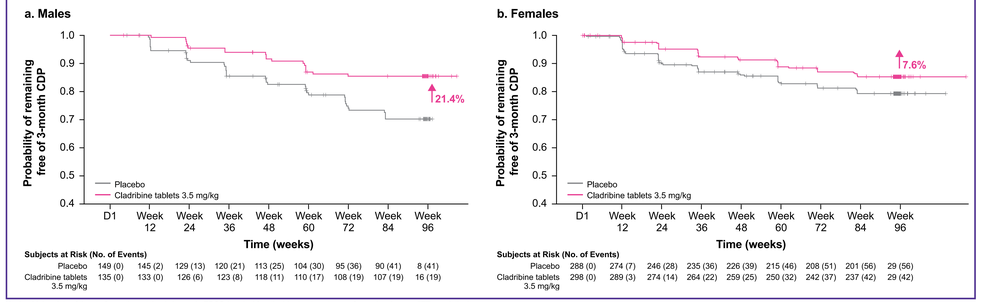
*Cladribine tablets 3.5 mg/kg over 2 years is the only approved dose, and data for Cladribine tablets 5.25 mg/kg are not presented.
EDSS, Expanded Disability Status Scale; **MRI**, magnetic resonance imaging; **RRMS**, relapsing-remitting multiple sclerosis

Figure 2. Annualized Relapse Rate* in Male and Female Patients



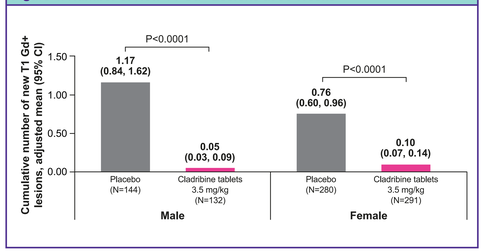
*Estimated using a Poisson regression model of the relapse count as the dependent variable with fixed effect for treatment group and region and the log of time on study as offset.
ARR, annualized relapse rate; **CI**, confidence interval

Figure 3. Time to 3-Month CDP, 96 Weeks



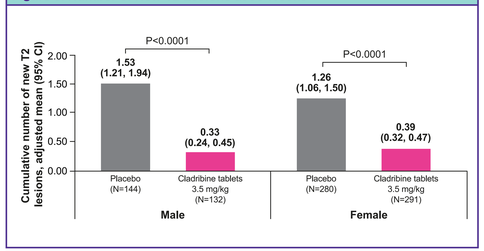
Kaplan-Meier plots of time to 3-month sustained change in EDSS (survival function) by treatment group for each subgroup (ITT population).
CDP, confirmed disability progression; **ITT**, intention-to-treat

Figure 4. Number of New T1 Gd+ Lesions at 96 Weeks



CI, confidence interval; **Gd+**, gadolinium-enhanced

Figure 5. Number of New T2 Lesions at 96 Weeks



CI, confidence interval

Table 1. Patient Demographics and Disease Characteristics at Baseline (ITT Population)

	Males		Females	
Randomized population	**Placebo (N=149)**	**Cladribine tablets 3.5 mg/kg (N=135)**	**Placebo (N=288)**	**Cladribine tablets 3.5 mg/kg (N=298)**
Age (years), mean (SD)	36.9 (9.6)	36.3 (10.4)	39.6 (9.9)	38.7 (10.2)
Disease duration (years), mean (SD)	4.34 (4.5)	3.63 (4.86)	5.62 (5.84)	5.15 (5.73)
Prior use of DMDs, n (%)	45 (30.2)	22 (16.3)	87 (30.2)	88 (29.5)
Relapses in prior 12 months, n (%)				
0	0	0	0	0
1	100 (67.1)	101 (74.8)	206 (71.5)	202 (67.8)
2	42 (28.2)	27 (20.0)	68 (23.6)	78 (26.2)
≥3	7 (4.7)	7 (5.2)	14 (4.9)	18 (6.0)
EDSS score, mean (SD)	2.93 (1.38)	2.93 (1.21)	2.95 (1.28)	2.79 (1.27)
Number of T1 Gd+ lesions, mean (SD)	0.7 (1.5)	0.7 (1.8)	0.9 (2.3)	1.1 (3.0)
Number of T1 Gd+ lesions, n (%)				
0	106 (71.6)	98 (73.1)	201 (70.0)	196 (65.8)
≥1	42 (28.4)	36 (26.9)	86 (30.0)	102 (34.2)
Median number of T2 Gd+ lesions (IQR)	22 (14–36)	19 (12–29)	24 (15–36)	23 (13–35)
Number of T2 lesions, n (%)				
<9	12 (8.2)	21 (15.7)	29 (10.1)	28 (9.4)
≥9	135 (91.8)	113 (84.3)	258 (89.9)	270 (90.6)
Median volume of T2 lesions (IQR), cm³	12.6 (6.1–25.6)	9.7 (4.1–19.2)	9.3 (3.8–17.3)	9.6 (3.6–19.7)

DMD, disease-modifying drug; **EDSS**, Expanded Disability Status Scale; **Gd+**, gadolinium-enhancing; **IQR,** interquartile range; **ITT,** intention-to-treat; **SD**, standard deviation

Table 2. NEDA Status Based on either 3-Month or 6-Month CDP by Week 96 of CLARITY

	Males		Females	
	Placebo (N=149)	**Cladribine tablets 3.5 mg/kg (N=135)**	**Placebo (N=288)**	**Cladribine tablets 3.5 mg/kg (N=298)**
NEDA (using 3-month CDP)				
Achieved, n (%)	13 (8.7)	61 (45.2)	48 (16.7)	116 (38.9)
Failed, n (%)	129 (86.6)	68 (50.4)	226 (78.5)	172 (57.7)
Unknown*, n (%)	7 (4.7)	6 (4.4)	14 (4.9)	10 (3.4)
OR (95% CI)		8.92 (4.56, 17.47)		3.28 (2.21, 4.87)
P value		<0.0001		<0.0001
NEDA (using 6-month CDP)				
Achieved, n (%)	13 (8.7)	62 (45.9)	50 (17.4)	121 (40.6)
Failed, n (%)	128 (85.9)	66 (48.9)	224 (77.8)	166 (55.7)
Unknown*, n (%)	8 (5.4)	7 (5.2)	14 (4.9)	11 (3.7)
OR (95% CI)		9.35 (4.77, 18.34)		3.36 (2.28, 4.96)
P value		<0.0001		<0.0001

NEDA defined as absence of magnetic resonance imaging activity (active T2 and/or new gadolinium-enhanced T1 lesions), relapses and disability progression, using either 3- or 6-month CDP at Week 96.
*Includes patients with NEDA at early withdrawal, NEDA with ≥1 missing component
CDP, confirmed disability progression; **NEDA,** No Evidence of Disease Activity; **OR,** odds ratio

CONCLUSION

- **In this *post hoc* analysis of the CLARITY study, compared with placebo, significant improvements in clinical and MRI outcomes following treatment with cladribine tablets were observed in both male and female patients at 96 weeks**

REFERENCES

1. Giovannoni G, et al. *N Engl J Med*. 2010;362:416–26.
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DISCLOSURES

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