P017

Delayed-Release Dimethyl Fumarate in Relapsing Multiple Sclerosis after Suboptimal Response to Glatiramer Acetate: *RESPOND 6-month Interim Analysis*

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INTRODUCTION

- Delayed-release dimethyl fumarate (DMF; also known as gastro-resistant DMF) demonstrated significant efficacy and a favorable benefit-risk profile vs. placebo in patients with relapsing-remitting multiple sclerosis in 2 Phase 3 trials.[1,2]
- In an integrated analysis of the DEFINE and CONFIRM studies, patients treated with DMF showed improved health-related quality of life vs. placebo as assessed by patient-reported outcomes (PROs), including the Physical and Mental Component Summaries (PCS and MCS, respectively) of the 36-Item Short-Form Health Survey (SF-36), the global assessment of well-being visual analog scale (VAS), and the EuroQoL 5-Dimensions (EQ-5D) VAS.[3]
- RESPOND is an ongoing study evaluating the effectiveness of DMF on clinical outcomes and PROs in patients with relapsing multiple sclerosis (RMS) who switched from glatiramer acetate (GA) to DMF after suboptimal response to GA in real-world clinical practice.

OBJECTIVES

- To present 6-month interim analysis results from the RESPOND study.

METHODS

- RESPOND is a Phase 4, prospective, multicenter, open-label, single-arm, 12-month observational study in the United States (ClinicalTrials.gov identifier, NCT01903291).
- Eligibility criteria include:
  - Age ≥18 years
  - Relapsing form of MS
  - Ongoing treatment with and suboptimal response to (e.g., suboptimal efficacy, intolerance, or poor adherence) GA or discontinuation of GA as a result of suboptimal response within 30 days of enrollment
  - Pre-enrollment decision to initiate DMF treatment.
- DMF treatment is initiated within 60 days after enrollment and administered per the US prescribing information.[4]
- Relapse data are collected from medical records.
- PROs completed by patients before DMF initiation and at 6 and 12 months post initiation include:
  - Fourteen-item Treatment Satisfaction Questionnaire for Medication (TSQM-14)
  - SF-36 version 1, standard recall
  - Five-item Modified Fatigue Impact Scale (MFIS-5)
  - Seven-item Beck Depression Inventory (BDI-7)
  - Work Productivity and Impairment Questionnaire: Multiple Sclerosis (WPAI-MS)
  - Eight-item Morisky Medication Adherence Scale (MMAS-8)
  - Patient-Reported Expanded Disability Status Scale (PREDSS).
- The variability of unadjusted annualized relapse rate (ARR) was based on robust SE from a Poisson regression model.
- The change from Baseline to 6 months in PROs was assessed using a Wilcoxon signed-rank test.
- RESPOND was not designed to accommodate a formal statistical inferential comparison at interim analysis; therefore, no adjustment for significance level was performed.
- RESPOND is ongoing; results of the 6-month interim analysis are reported.
- The final analysis will include individual components of the SF-36 PCS and MCS, WPAI-MS, MMAS-8, and PREDSS.

RESULTS

Patients

- As of June 12, 2015, 333 patients were enrolled in RESPOND, 318 received ≥1 dose of DMF and did not have any major protocol deviations; 168 completed the study, 61 discontinued treatment, and 20 withdrew from the study. Reasons for DMF treatment discontinuation included adverse events, efficacy reasons, lost to follow-up, investigator decision, and death (1 death was reported; the cause was not related to DMF treatment).
- Baseline characteristics are presented in Table 1.
- Notably, there was a higher percentage of older patients in RESPOND compared with the Phase 3 clinical trials:
  - Mean (SD) age of patients was 47.6 (10.89) in RESPOND vs. 37.9 (9.2) in DEFINE/CONFIRM integrated analysis.[1,2]
  - In RESPOND, 26% of patients were ≤39 years of age vs. 55% in DEFINE and 58% in CONFIRM[1,2]
  - And 45% of patients were ≥50 years of age in RESPOND vs. 12% in DEFINE and 13% in CONFIRM.[1,2]
- Additionally, there was a greater percentage of black or African American patients and a much lower percentage of Asian patients in RESPOND compared with the Phase 3 clinical trials:
  - In RESPOND, 8.2% of patients were black or African American vs. 2% in DEFINE and <1% in CONFIRM[1,2]
  - And 0.3% of patients were Asian in RESPOND vs. 9% in DEFINE and 8% in CONFIRM.[1,2]
- Reasons for treatment discontinuation of most recent GA are presented in Table 2.

Table 1. Patient baseline characteristics

Characteristic	N=318
Mean (SD) age, years	**47.6 (10.9)**
Age category, n (%)	
18–19 years	1 (0.3)
20–29 years	14 (4.4)
30–39 years	67 (21.1)
40–49 years	93 (29.2)
50–59 years	94 (29.6)
≥60 years	49 (15.4)
Female, n (%)	**263 (82.7)**
Race, n (%)	
White	290 (91.2)
Black or African American	26 (8.2)
Asian	1 (0.3)
Other	1 (0.3)
Mean (SD) time since diagnosis of MS, years	**8.8 (7.9) n=263**
Mean (SD) time since most recent prestudy relapse, months	**17.0 (21.0) n=106**
Prior MS medication, n (%)	
GA[a]	318 (100)
Interferon beta-1a	72 (22.6)
Interferon beta-1b	20 (6.3)
Natalizumab	13 (4.1)
Other[b]	12 (3.8)

[a]The branded version (Copaxone) was administered daily or 3 times per week
[b]Dexamethasone, 0.3%; fampridine, 0.3%; fingolimod hydrochloride, 1.3%; methylprednisolone sodium succinate, 0.9%; mitoxantrone hydrochloride, 0.3%; prednisone, 0.3%; teriflunomide, 0.3%

Table 2. Reasons for most recent GA[a,b] treatment discontinuation

Reason for discontinuation, n (%)	N=318
Efficacy	161 (50.6)
Tolerability	144 (45.3)
Patient preference	119 (37.4)
Lack of adherence	16 (5.0)
Safety	15 (4.7)

[a]Most recent GA treatment before DMF treatment initiation
[b]Patients may indicate >1 reason for discontinuation

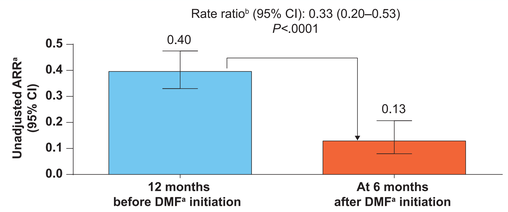
Relapses

- ARR at 6 months of DMF treatment was significantly lower than the ARR during the 12 months before treatment initiation (Figure 1).
- The majority of patients (95%) were relapse free at 6 months of DMF treatment compared with 65% during the 12 months before treatment initiation.

PRO Measures

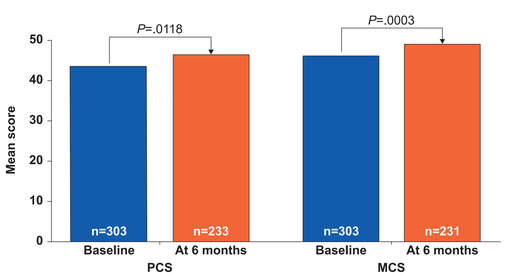
- At 6 months, several PRO measures improved significantly from Baseline.
  - PCS and MCS scores improved significantly (*P*=.0118 and *P*=.0003, respectively; Figure 2).
  - Patient treatment satisfaction level increased significantly as indicated by higher TSQM-14 scores (Figure 3).
  - Fatigue impact (MFIS-5) and depression symptom (BDI-7) scores also improved significantly.

Figure 1. ARR at 6 months of DMF[a] treatment vs. during the 12 months before treatment initiation



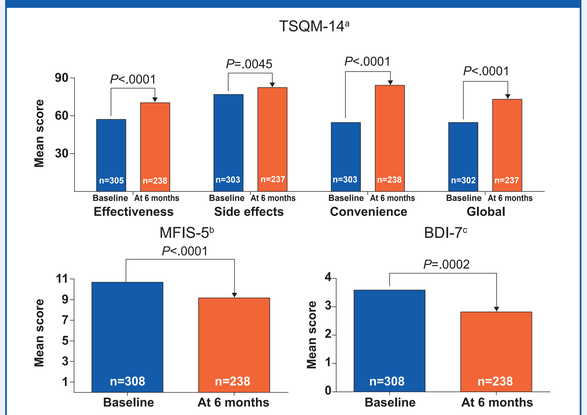
[a]DMF; delayed-release DMF (also known as gastro-resistant DMF)
[b]95% CI is based on empirical (robust) SE from a generalized estimating equation using an unadjusted Poisson regression model; N=318

Figure 2. SF-36[a,b] PCS and MCS at 6 months



N=318; PCS =Physical component summary; MCS=Mental component summary
[a]Higher score indicates improved functioning; range, 0–100; *P* values based on a Wilcoxon signed-rank test
[b]Only patients with no major protocol deviations and no missing data were included

Figure 3. TSQM-14, MFIS-5, and BDI-7 6-month interim results



N=318
[a]TSQM-14; Treatment Satisfaction Questionnaire for Medication: Higher score indicates higher satisfaction; range 0 - 100
[b]MFIS-5; Modified Fatigue Impact Scale: Lower score indicates improved functioning; range 0 - 20
[c]BDI-7; Beck Depression Inventory: Lower score indicates less severe depressive symptoms; range 0 - 21

CONCLUSIONS

- The 6-month interim analysis of RESPOND suggests that DMF was associated with lower ARR and improvement on PROs in patients with RMS switching to DMF after suboptimal response to GA.
- ARR at 6 months of DMF treatment was lower than the ARR at 12 months before treatment initiation.
- The majority of patients (95%) experienced no relapses after 6 months of DMF treatment.
- Statistically significant improvements from Baseline at 6 months were observed for SF-36 PCS and MCS, TSQM-14, BDI-7, and MFIS-5 scores.
- RESPOND is ongoing; data collection is projected to be completed in mid-2016.

References

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Disclosures

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