Clinical Efficacy of BG-12 (Dimethyl Fumarate) in Relapsing–Remitting Multiple Sclerosis (RRMS): An Integrated Analysis of the Phase 3 DEFINE and CONFIRM Studies

**INTRODUCTION**

- BG-12 (dimethyl fumarate) is an oral agent in development for relapsing MS.
- Experimental evidence shows that BG-12 may have anti-inflammatory and cytoprotective/anti-oxidative activity via the nucleic factor (erythroid-derived 2-like 1) in iron (Nf2) transcriptional pathway.1,2
- In the Phase 3 DEFINE and CONFIRM, studies, BG-12 significantly reduced the risk of relapse and the annualized relapse rate (ARR) at 2 years compared with placebo in patients with RRMS.1,3
- A pre-specified integrated analysis of data from DEFINE and CONFIRM was conducted to provide a more precise estimate of the therapeutic effect of BG-12 relative to placebo than can be obtained from either study in isolation.

**OBJECTIVE**

- To report a pre-specified integrated analysis of clinical efficacy data from DEFINE and CONFIRM.

**METHODS**

**Study Design**

- Patients were randomized to receive oral BG-12 240 mg twice daily (BID) or three times daily (TID) or matching placebo for 2 years (Figure 1). – DEFINE also included glatiramer acetate (GA) as a reference comparator.
- Clinical efficacy was assessed in the intent-to-treat (ITT) population.

**RESULTS**

- The integrated analysis plan was finalized prior to unblinding of CONFIRM and was to be conducted only if baseline characteristics and treatment effects were homogeneous across the studies.
- **Key Inclusion Criteria**
  - Age 18–55 years.
  - Diagnosis of RRMS (McDonald criteria 2005).3
  - Expanded Disability Status Scale (EDSS) score of 0–5.0.
  - At any time (CONFIRM).
- **Key Exclusion Criteria**
  - Progressive forms of MS.
  - Other significant illness or pre-specified abnormal laboratory parameters.
  - A relapse or corticosteroids within 50 days prior to randomization.
  - Prior treatment with GA: – Within the past 3 months (DEFINE) – At any time (CONFIRM).
- **Clinical Efficacy Endpoints**
  - Proportion of patients relapsed at 2 years (primary endpoint in DEFINE and secondary endpoint in CONFIRM).
  - ARR at 2 years (primary endpoint in CONFIRM and secondary endpoint in DEFINE).
  - Time to 12-week confirmed disability progression on the EDSS at 2 years was a secondary endpoint in both studies and 24-week confirmed disability progression was a sensitivity analysis of this endpoint.

- **Disability Progression**
  - BG-12 BID and TID significantly reduced the risk of 12-week confirmed disability progression at 2 years by 32% and 30%, respectively, compared with placebo (Figure 1).
  - Similarly, both doses of BG-12 significantly reduced the proportion of patients with 24-week confirmed disability progression at 2 years by 29% and 32%, respectively, compared with placebo (Figure 5).

**DISCUSSIONS**

- Both doses of BG-12 demonstrated significant clinical efficacy in this integrated analysis of DEFINE and CONFIRM.
  - Compared with placebo, BG-12 significantly reduced ARR, risk of relapse, and 12- and 24-week confirmed disability progression over 2 years.
  - When considered alongside MRI efficacy1,2 and an acceptable safety profile, the results of this integrated analysis suggest that BG-12 has the potential to become a valuable oral treatment option for patients with relapsing MS.

**REFERENCES**


**DISCLOSURES**

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