Fingolimod for the treatment of Relapsing-Remitting Multiple Sclerosis

Renato Turrini
*Medical Head Franchise Neurosciences*

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What is RWE?

- Real-world data are observations of treatment effects where the researcher has no control over subsequent medical management of the patient beyond observing the outcomes.

- The ISPOR task force defines RWE as:

  Data used for clinical, coverage and payment decision-making that are not collected in conventional randomised controlled trials.

ISPOR, International Society for Pharmacoeconomics and Outcomes Research; RWE, real-world evidence
Garrison LP Jr et al. Value Health 2007
Why do we need RWE?

- Payers, healthcare decision-makers and regulatory authorities are increasingly asking for post-launch evidence of therapies in a real-world setting.
Multiple sclerosis: worldwide incidence

Global prevalence of MS per 100,000 population

<table>
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<tr>
<th>Incidence</th>
<th>MS global incidence 2.5 cases/100,000 population per year²</th>
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<tr>
<td>Prevalence</td>
<td>MS global median prevalence of 33 patients/100,000 population, 10% with PPMS¹</td>
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2. 2. World Health Organization. MS resources in the world 2008.
Multiple sclerosis: disease burden

* Calculated using EuroQol 5-Dimensions questionnaire. EDSS = Extended Disability Status Scale; MS = multiple sclerosis.

Clinical impact of focal and diffuse damage in multiple sclerosis

MRI = magnetic resonance imaging; MS = multiple sclerosis.
Fingolimod EU indication

Gilenya is indicated as single disease modifying therapy in highly active relapsing remitting multiple sclerosis for the following adult patient groups:

- **Patients with highly active disease despite a full and adequate course of treatment with at least one disease modifying therapy**

Or

- **Patients with rapidly evolving severe relapsing remitting multiple sclerosis defined by 2 or more disabling relapses in 1 year, and with 1 or more Gadolinium-enhancing lesions on brain MRI or a significant increase in T2 lesion load as compared to a previous recent MRI**

Indication reimbursed in Italy

- **Patients with high disease activity despite treatment with at least one disease modifying therapy (for exceptions and information about washout periods see sections 4.4 and 5.1).**
  These patients may be defined as those who have failed to respond to a full and adequate course (normally at least one year of treatment) of at least one disease modifying therapy. Patients should have had at least 1 relapse in the previous year while on therapy, and have at least 9 T2-hyperintense lesions in cranial MRI or at least 1 Gadolinium-enhancing lesion. A “non-responder” could also be defined as a patient with an unchanged or increased relapse rate or ongoing severe relapses, as compared to the previous year

Or

- **Patients with rapidly evolving severe relapsing-remitting multiple sclerosis defined by 2 or more disabling relapses in one year, and with 1 or more Gadolinium enhancing lesions on brain MRI or a significant increase in T2 lesion load as compared to a previous recent MRI**
Fingolimod has an innovative and unique mechanism of action

Targeting S1P receptors in the immune system and in the central nervous system\textsuperscript{9,10,11}

- Fingolimod’s main effect in the immune system:
  - reversible and selective retention of circulating lymphocytes in the lymph nodes
  - post-treatment: recovery to lymphocyte normal levels within weeks, since lymphocytes are not destroyed

- Fingolimod’s potential effect in the CNS:
  - fingolimod enters into the CNS
  - glial cells and neurons express S1P receptors known to modulate neuropathological processes relevant to MS

Worldwide fingolimod exposure

Cumulative worldwide exposure in clinical trials and from marketing experience. Data cut-off 28-02-2017\textsuperscript{14,15}

Global fingolimod MS patient exposure

\(~204,000\) patients
\(~424,000\) patient-years

\textsuperscript{15.} Novartis data on file
RWE publications with fingolimod

- Even if limited to 2015 and 2016, 170 RWE publications from 25 Countries with fingolimod have been issued

- Main topics:
  - Brain volume loss
  - Relapses
  - Disability
  - No evidence of disease activity
  - Persistence/adherence
  - Patient Reported Outcomes (PRO)
  - Safety
  - Health care resources
  - Magnetic Resonances Imaging (MRI)
Main RWE fingolimod publications
Some key RWE fingolimod data

**Impact of fingolimod on relapse rate and disability progression vs DMTs**

- He A et al. JAMA Neurol 2015;
- Ziemssen T et al. Poster P21144 presented at EAN 2016;
- Ziemssen T et al. Poster P21144 presented at EAN 2016;

**Effect of switching to fingolimod on ARR for up to 4 years in an observational study**

**EDSS change in the first 4 years of fingolimod treatment in an observational study**

**Impact of fingolimod on brain volume: MS-MRIUS study results**

Fingolimod RWE in the Italian practice

Observational study on 366 patients treated for 2 years at San Raffaele Hospital

19. Esposito F. et al. ECTRIMS 2016 P 735