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Real-world effectiveness of fingolimod in Polish group of patients with relapsing-remitting multiple sclerosis

Agata Walczak[a,*], Iwona Kurkowska-Jastrzebska[b], Beata Zakrzewska-Pniewska[c], Malgorzata Dorobek[d], Waldemar Brola[e], Radoslaw Zajdel[f], Halina Bartosik-Psujek[g], Mariusz Stasiolek[a], Alina Kulakowska[h], Stanislaw Rusek[i], Andrzej Tutaj[j], Andrzej Glabinski[k], Agata Wlodek[l], Jan Kochanowski[m], Agnieszka Ciach[a], Malgorzata Siger[a], Katarzyna Kurowska[b], Wojciech Wicha[b], Monika Nojszewska[c], Aleksandra Podlecka-Pietowska[c], Anna Czajka[d], Katarzyna Kapica-Topczewska[h], Bartosz Bielecki[k], Marzena Maciagowska-Terela[n], Adam Stepien[n]

[a] Department of Neurology, Medical University of Lodz, Lodz, Poland
[b] 2nd Department of Neurology, Institute of Psychiatry and Neurology in Warsaw, Poland
[c] Department of Neurology, Medical University of Warsaw, Poland
[d] Department of Neurology, Central Clinical Hospital of the Ministry of Interior, Warsaw, Poland
[e] Department of Neurology, Specialist Hospital in Konskie, Poland
[f] Chair of Informatics in Business, University of Lodz, Poland
[g] Department of Neurology, Clinical Regional Hospital No. 2 in Rzeszow, Rzeszow, Poland
[h] Department of Neurology, Medical University of Bialystok, Bialystok, Poland
[i] Department of Neurology, Specialist Hospital Ludwika Rydygiera in Krakow, Krakow, Poland
[j] Department of Neurology, Voivodeship Specialist Hospital in Olsztyn, Olsztyn, Poland
[k] Department of Neurology and Stroke, Medical University of Lodz, Lodz, Poland
[l] Department of Neurology, Masovian Voivodeship Hospital in Siedlce, Siedlce, Poland
[m] Bielanski Hospital, Warsaw, Poland
[n] Department of Neurology, Military Institute of Medicine in Warsaw, Poland

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ABSTRACT

Objectives: Fingolimod is indicated for the treatment of relapsing-remitting multiple sclerosis (RRMS) patients with highly aggressive disease characterized by frequent relapses and active magnetic resonance imaging. Its efficacy has been demonstrated in three large phase III trials, used in the regulatory submissions throughout the world. Fingolimod in licensed in Europe since 2011 but with a growing number of disease-modifying drugs (DMD) becoming available for RRMS, it is important to gather real-world evidence data regarding long-term effectiveness in treated patients with MS. The aim of this study was to assess fingolimod effectiveness in a real life Polish group of RRMS patients receiving fingolimod as second line treatment.

Patients and methods: The observational study with retrospective data collection was performed at 13 sites that were asked to document eligible patients in consecutive chronological order to avoid selection bias. Demographic and clinical data from 253 adult patients with RRMS treated with fingolimod were analyzed.

Results: Mean treatment time with fingolimod was 42 months. Relapses reduction during 3 years treatment period was observed (2.0 v 0.2) and majority of patients were free of relapses. Mean EDSS score was stable during the time of observation. The proportion of patients who were free from any clinical disease activity, i.e. without relapses and disability progression, was over 70%. During the first and second year of observation significant reduction of new MRI lesions was observed.

Conclusion: In the Polish group of patients with RRMS treated with fingolimod, the majority of them showed freedom from relapses, disability progression and reduction of new MRI lesions. Switching from injectable immunomodulatory drugs to fingolimod is associated with fewer relapses and lower disability progression.

* Corresponding author.
E-mail address: agata.walczak@umed.lodz.pl (A. Walczak).

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1. Introduction

Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system (CNS) [1,2] that affects approximately 2.1 million people worldwide [3]. Importantly, the incidence of multiple sclerosis appear to increase. Relapsing-remitting MS (RRMS) is the most common type of MS and high relapse activity especially at the initial phase of the disease has been associated with poorer long-term prognosis. The exact influence of inflammatory events on the extent and rate of neurodegenerative processes in MS is not fully known. However, it has been assumed that a “therapeutic window” for available anti-inflammatory agents exists early in the clinical course when successful disease stabilization may postpone disability progression [4].

Currently available disease-modifying therapies (DMTs) influence various aspects of immune system function in mechanisms including mainly anti-inflammatory and/or regulatory shift in the immune reaction profile, inhibition of immune cell trafficking into CNS or exchange and renewal of immune system repertoire e.g. in so called immune system reconstitution therapies. The therapeutic effectiveness of particular drugs was demonstrated in large randomized clinical trials showing various degree of inhibition of clinical and radiological disease activity, with predominantly low level influence on progression parameters. Importantly, the clinical trials data also demonstrated substantial differences in the safety profile of particular DMTs.

Fingolimod was the first oral medication approved for the treatment of RRMS [5]. Preclinical studies provided evidence that apart from the effect on lymphocyte trafficking, neural cells might also benefit from sphingosine-1-phosphate receptor modulation, resulting in better oligodendroglial survival and differentiation as well as improved remyelination [6]. Fingolimod is indicated for the treatment of adult patients with relapsing-remitting multiple sclerosis (RRMS) with active disease defined by clinical or imaging features. The indication states that it should generally be reserved for the treatment of patients with RRMS who have had an inadequate response to first line of DMTs or as first line for patients with rapidly evolving severe relapsing remitting multiple sclerosis defined by 2 or more disabling relapses in one year (RES). In three pivotal clinical trials, fingolimod demonstrated high efficacy in reducing relapse rate, progression of disability, accumulation of new brain lesions and progression of brain atrophy as compared with placebo or intramuscular interferon beta-1a [7–10].

Real-world studies usually employ broader inclusion criteria than randomized trials, allowing for better assessment of the effects of a medication administered in a larger patient population [11]. Additionally, patient-reported outcomes (PROs) included in the analysis are able to provide clinicians with greater insight into the influence of treatment on patient’s daily life, and can serve as a complement to traditional clinical trial outcome measures by providing information regarding patients' adherence to therapy and its outcomes.

The aim of the study was to assess clinical effectiveness and retention in fingolimod therapy in real-life settings in Poland. Therapy of patients with RRMS in Poland is reimbursed by the National Health Fund (NFZ), which distinguish the first- and the second-line treatment. First-line treatment is based on interferons, glatiramer acetate (GA), fumaric acid and teriflunomide. When first-line medications become ineffective, the second-line treatment should be implemented (fingolimod and natalizumab). Treatment with fingolimod of rapidly evolving severe (RES) RR MS treatment with fingolimod has been reimbursed in Poland since 2018. Before 2018 only natalizumab could be used in such indication.

The primary objective was to assess the long-term effectiveness of fingolimod in patients with RRMS in terms of freedom from relapses. Secondary endpoints included the collection of disability progression confirmed at 3 months and treatment retention, defined as the proportion of patients who, at a given time, continued to receive fingolimod. Additionally, change from baseline in number of patients with new or active lesions in brain MRI scan was analyzed.

2. Patient and methods

The retrospective observational study was performed at 13 sites across Poland and included patient data obtained between January 2015 and January 2018. A total of 253 male and female patients with RRMS, aged 18–55 years, who had received uninterrupted treatment with fingolimod (0.5 mg, orally, once daily) as second line therapy for at least 6 months, were included in the study. The uninterrupted treatment was defined as treatment with no interruptions lasting longer than 4 weeks. All patients in the study group had previously received other DMTs (interferon beta preparations (IFNb) or glatiramer acetate (GA) within 2 years before the study, and the therapy was switched to fingolimod because of insufficient effectiveness and worsening of disease. As per the observational plan, patients were recruited in a chronological and consecutive manner in order to avoid selection bias. The collected data encompassed medical history before commencement and during fingolimod treatment, and included demography, previous DMT, number of relapses under fingolimod and in the 24 months before starting fingolimod.

We allocated eligible patients aged 18–55 years with relapsing-remitting multiple sclerosis to receive fingolimod 0.5 mg, orally once daily according with recommendation and Polish health care program (National Health Fund, NFZ) from the data and safety monitoring board.

According to NFZ criteria all the patients included in the study had met the criteria of ineffectiveness of the first-line therapy before they could be assigned to the second-line therapeutic program. The lack of response to a complete, minimum one-year period of treatment with IFNb or GA, was defined as the fulfillment of following criteria [12]:

1 The number and severity of relapses: two or more moderate relapses requiring steroids administration (an increase of one to two points in EDSS score or of two points in one or two EDSS functional-system scores), or one severe relapse after five months of treatment (an increase in EDSS score higher than in the definition of a moderate relapse), and:
2 Minimum three new T2-weighted lesions or minimum two Gd + lesions demonstrated in MRI performed after 12 months of therapy.

Clinical effectiveness was evaluated after each 12 months of fingolimod treatment in all patients included in the analysis. Investigated outcomes included change in disability from EDSS score at baseline, annual relapse rate (ARR), and the proportion of patients free from relapses and with 3-month confirmed disability worsening.

Relapses were defined according to the McDonald criteria [13]. A relapse was confirmed when it was accompanied by an increase of at least half a step (0.5) on the EDSS, an increase of 1 point on two different functional systems of the EDSS, or 2 points on one of the functional systems (excluding bowel, bladder, or cerebral functional systems). The annualized relapse rate was calculated as number of relapses divided by the exact (decimal) number of years on fingolimod treatment.

Confirmed disability progression between two assessments was defined as an increase of ≥ 1 points in the Expanded Disability Status Score (EDSS) [14].

Change from baseline to the end of study on MRI measurements of inflammatory disease activity (number and volume of gadolinium-enhancing T1 lesions, number of new or newly enlarged T2 lesions, proportion of patients free of gadolinium-enhanced T1 lesions, proportion of patients free of new or newly enlarged T2 lesions, and proportion of patients free of new inflammatory activity [no gadolinium-enhanced T1 lesions and no new or newly enlarged T2 lesions) was analyzed at the end of every year of observation.

MRI scans were obtained on a 1.5 T scanners. The following MRI sequences were acquired in all participants: axial dual-echo (TR

= 3760 ms, TE = 22/88 ms; 50 slices, thickness = 3 mm, gap = 0.0 mm, matrix 154 × 256 and FOV = 250 mm), axial FLAIR (TR = 9000 ms, IR = 2500 ms; TE = 106 ms, 50 slices, thickness = 3.0, gap = 0.0 mm, FOV = 250 mm), T1-weighted Magnetization Prepared Rapid Gradient Echo (MPRAGE TR = 9.7 ms, TE = 2.9 ms, eff thick 1.5 mm, no partitions 164, matrix 192 × 256) with and without contrast administration.

Analyses were performed for the total sample and stratified according to the duration of treatment with fingolimod and pretreatment history. The study was approved by the respective local ethics committees prior to the start of the study.

3. Statistical analysis

For all kinds of variables, according to descriptive statistics, data are presented as the number of cases and the proportion of cases in each category. Dealing with numerical variables, data are summarized using the mean, SD, and median. Non-parametrical tests were used due to the non-normal distribution. Friedman ANOVA test was used to analyze the multivariable statistics. Wilcoxon matched pairs test was used to assess the statistical significance when pars of variables were in use.

4. Results

4.1. Patient and treatment characteristics

Between January 2015, and March 2018, we enrolled and allocated 253 patients. Baseline demographic characteristics and clinical data from 253 consenting adult patients (159 female and 94 male) with RRMS who had received treatment with fingolimod as a second-line therapy were demonstrated in Table 1. Fingolimod was used as a second-line therapy. The most recent prior DMTs taken by "switchers" prior to study entry were interferon-beta (n = 214, 85%), glatiramer acetate (n = 39, 15%). Mean treatment duration with fingolimod was 42 months (Table 4).

Table 1
Patient characteristics and treatment history in the year before starting fingolimod treatment. Duration of MS since diagnosis till 01.11.2018. Data are n (%) unless otherwise indicated. N = 253. Clinical characteristics (ARR, EDSS) and MRI parameters in the year before starting fingolimod treatment (2 T – 2nd line treatment).

Patients (n)	253
Age (years)	
Mean (± SD)	38.4 ± 9.1
Median	38.0
Gender [n(%)]	
Female	159 (62.9)
Male	94 (37.1)
MS disease duration (years)	
Mean (± SD)	11.1 ± 5.2
Previous MS DMTs [n(%)]	
None	0
IFNs	214 (84.6)
Glatiramer acetate	39 (15.4)
ARR (Mean ± SD)	
Y < 1T (1 year before 1st line treatment)	1.5 ± 0.8
Y < 2T (1 year before 2nd line treatment)	2.0 ± 0.5
EDSS (Mean ± SD)	
Y < 1T	2.4 ± 1.5
Y < 2T	3.2 ± 1.4
Number of patients with > 9 T2 –weighted lesions (MRI) [n(%)]	
Y < 1T	199 (88.1)
Y < 2T	232 (93.2)
Number of patients with 1-9 Gd + lesions (MRI) [n(%)]	
Y < 1 T	82 (36.1)
Y < 2 T	156 (62.9)

MS, multiple sclerosis, DMT, disease modifying therapy, ARR, annualized relapse rate; EDSS, Expanded Disability Status Score.

Table 2
Delay in groups. In the observed group we found the delays between 1 st symptom (1S), MS diagnosis (DIAG), onset of the 1 st line treatment (1 T), termination of 1 T and the onset of 2nd line treatment to vary significantly (very high standard deviations), the mode value revealed, that the most frequent delays between the 1S and DIAG as well as DIAG and 1 T were shorter than one week. The median values were 17 and 36 weeks respectively. The median period of 1 st line treatment was 158 with mode 208 weeks. The median delay between 1 st symptom and starting 2 T was 346 with mode 329 weeks. making duration of 1 T equal app. 7 years. The median delay between To1 T and the onset of 2 T was 4 weeks with mode equal zero.

	Median	Mode	Mean ± SD
Delay between the 1 st symptom and MS diagnosis (weeks)	17	0	73 ± 144
Delay between MS diagnosis and starting 1T. N = 252	36	0	119 ± 189
Delay between 1 st symptom and starting 1T. N = 252	104	0	193 ± 231
Duration of the 1 T. N = 246	158	208	187 ± 141
Delay between 1 st symptom and starting 2T.	346	329	400 ± 261
Delay between Termination of 1T and starting 2T. N = 246	4	0	28 ± 64

Table 3
Mean and (SD) number of lesions in T2 and Gadolinium enhanced (Gd +) MRI.

MRI	Y < 2T	1y2T	2y2T	3y2T	4y2T
$T2_{new}$ *	–	0.5 (1.2)	0.3 (1.9)	0.5 (1.9)	0.5 (0.9)
Gd + ** all	2.2 (2.6)	0.3 (0.7)	0.3 (0.8)	0.4 (1.5)	0.4 (0.9)

* Friedman Chiˆ2 ANOVA p > 0.05.
** Friedman Chiˆ2 ANOVA (N = 55, df = 4) = 78.1 p = 0.000.

In the investigated group of Polish RRMS patients the diagnosis was made quickly – median value: 17 weeks from the first disease symptoms to MS diagnosis. The median value of delay between diagnosis and commencement of the first-line therapy was 36 weeks. However, the range of these parameters was very broad. The median duration of the first-line treatment was 158 with mode 208 weeks. In analyzed group median time from first MS symptoms and disease diagnosis to fingolimod treatment was 346 with mode 329. Median delay in start of the second-line therapy was 4 weeks after termination of the first-one (Table 2).

4.2. Clinical effectiveness

The annualized relapse rate (ARR) during the therapy with fingolimod was significantly lower than in the year preceding the switch to this treatment from the first-line DMTs (Table 1). After 1 year of fingolimod therapy mean AAR value was 0.2 as compared with 2.0 during previous DMTs therapy. The reduction of relapse activity was retained during near 4 years of the observation in the study (Fig. 1).

The majority of patients treated with fingolimod were free from relapses over the entire course of the study. Stratifying patients according to the duration of fingolimod treatment, the proportion of those free from relapses was 87.3%, 874%, 864% and 875% during year 1, 2, 3 and over 3 years of therapy (Table 4).

As measured by the EDSS total scores, patient-reported disability remained stable over the 36 months study (Fig. 1). Mean EDSS scores remained stable from baseline to month 42 and did not increase significantly during any period of the treatment (Fig. 2). EDSS score during the fourth year of the treatment was significantly lower than during the third one (Fig. 1). During the time of observation the proportion of patients with EDSS score lower or equal than prior to study enrollment was near or over 80% (Table 4).

The proportion of patients who were free from any clinical disease activity, i.e. without relapses and disability progression, was 74.9%

Table 4
Cumulative data of fingolimod treatment effectiveness in Polish group of MS patients (NEDA, No Evidence of Disease Activity).

n	Mean (SD) exposure to fingolimod. years	Relapse in year prior to study enrollment (mean. SD)	Period of treatment	ARR (mean, SD)	Proportion of patients free from relapses, %	Proportion of patients with EDSS score lower or equal than prior to study enrollment, %	Cumulative proportion of patients free of clinical disease activity*, %	NEDA 3 n' (%)**
253	3.5 ± 1.4	2.0 ± 0.9	1y2T	0.2 ± 0.5	87.3	84.4	74.9	111 (52.4)
			2y2T	0.1 ± 0.4	87.4	81.0	71.0	91 (57.6)
			3y2T	0.2 ± 0.4	86.4	80.2	70.4	59 (57.3)
			4y2T	0.2 ± 0.4	87.5	77.4	68.8	31 (66.0)

* Cumulative proportion of patients free of clinical disease activity – patients ["$ARR_n = 0$" AND "$EDSS_n <= EDSS_{n-1}$"].
** NEDA 3 is defined as: ($ARR_n = 0 \cap EDSS_n <= EDSS_{n-1} \cap T2_{n\_new} = 0 \cap GEL_n = 0$).

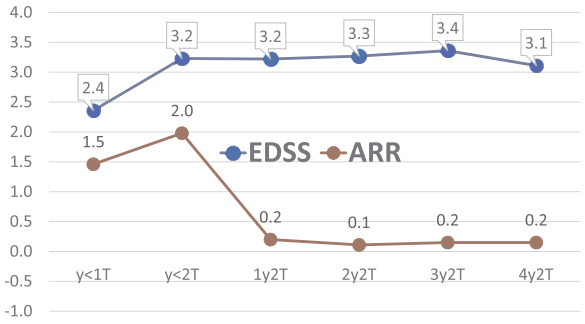

Fig. 1. Change from baseline in Expanded Disability Status Scale (EDSS) scores. The baseline mean value (3.2) was the EDSS score in 12 months before fingolimod treatment (y < 2 T). The consecutive columns are: the 1 st year of 2 T (1y2 T), 2nd year of 2 T (2y2 T), 3rd year of 2 T (3y2 T), 4th year of 2 T (4y2 T). Available amount of data varies between the years: Ny < 2 T = 252, N1y2 T = 224, N2y2 T = 174, N3y2 T = 113, N4y2 T = 53.
The mean Annualized Relapse Rate (ARR) in the 12 months before 1 st line Treatment (y < 1 T), in 12 months before the 2nd line treatment (y < 2 T), in the 1 st year of 2 T (1y2 T), 2nd year of 2 T (2y2 T), 3rd year of 2 T (3y2 T), 4th year of 2 T (4y2 T). Available amount of data varies between the years: Ny < 1 T = 241, Ny < 2 T = 251, N1y2 T = 220, N2y2 T = 183, N3y2 T = 118, N4y2 T = 48. All patients treated with fingolimod.
Friedman ANOVA and Wilcoxon matched pairs tests applied to ARR data suggest, that the Fingolimod introduction to the treatment decreases significantly the ARR value every ongoing year of the treatment, starting the first one (Friedman Chi^2 ANOVA (N = 52, df = 5) = 82.6 p = 0.000; Wilcoxon test respectively: $p_{y < 2T\text{-}1y2T} = 0.000$, $p_{y < 2t\text{-}2y2T} = 0.000$, $p_{y < 2T\text{-}3y2T} = 0.000$, $p_{y < 2T\text{-}4y2T} = 0.000$). The decreases achieved in the first year do not vary significantly in the next four years of treatment ($p > 0.05$).
Friedman ANOVA test suggests, that the Expanded Disability Status Scale (EDSS) varied during the Fingolimod treatment (Chi^2 ANOVA (N = 46, df = 5) = 180.2 p = 0.000), however it revealed that EDSS did not increase during any period of the treatment. Wilcoxon test revealed, that EDSS score tended to decrease between 2y2 T and the 4y2 T year of the treatment ($p_{y < 2T\text{-}2y2T} = 0.055$). EDSS score during the 4th year of the treatment was significantly lower than during the 3rd year ($p_{3y2T < 2t\text{-}4y2T} = 0.023$).

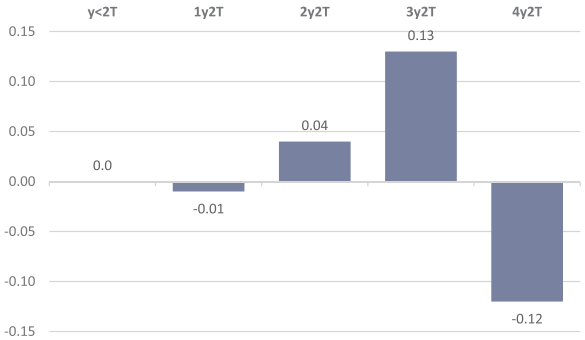

Fig. 2. Change from baseline in Expanded Disability Status Scale (EDSS) scores. The baseline mean value (3.2) was the EDSS score in 12 months before fingolimod treatment (y < 2 T). The consecutive columns are: the 1 st year of 2 T (1y2 T), 2nd year of 2 T (2y2 T), 3rd year of 2 T (3y2 T), 4th year of 2 T (4y2 T). Available amount of data varies between the years: Ny < 2 T = 252, N1y2 T = 224, N2y2 T = 174, N3y2 T = 113, N4y2 T = 53.

after first 1 year of fingolimod treatment and 70.4% after 3 years (Table 4).

4.3. MRI effectiveness

In our study group MRI inflammatory disease activity outcomes were lower during the fingolimod therapy at each year of observation in comparison to the previous two years of other DMTs therapies. The proportion of patients with more than 9 T2-weighted lesions (at first

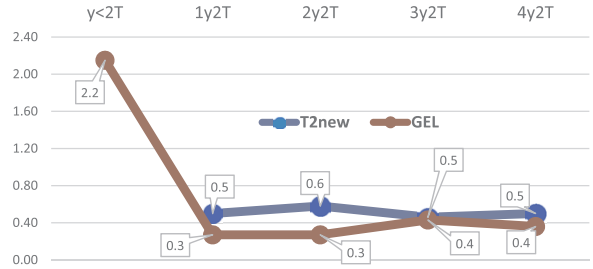

Fig. 3. Friedman ANOVA test suggests, that the number of T2 lesions do not increase significantly during the fingolimod treatment ($p > 0.05$). Both Friedman ANOVA and Wilcoxon matched pairs tests applied to Gd + data suggest, that the fingolimod introduction to the treatment decreases significantly the number of Gd + lesions every ongoing year of the treatment, starting the first one (Friedman ANOVA $p = 0.000$; Wilcoxon test respectively: $p_{1\text{-}2} = 0.000$, $p_{1\text{-}3} = 0.000$, $p_{1\text{-}4} = 0.000$). The decreases achieved in the first year do not vary significantly in the next three years of treatment ($p > 0.05$).

and second year assessed) was significantly lower in the fingolimod group than it was during the therapy with previous DMTs ($p < 0.0001$ at all-time points). The proportion of patients with 1–9 or more than 9 gadolinium (Gd)-enhancing T1 lesions was also lower than in the year before fingolimod treatment (Table 1).

The number of new or enlarged T2-weighted lesions do not increase significantly during the fingolimod treatment ($p > 0.05$) (Table 3). The introduction of fingolimod therapy decreased significantly the number of Gd + lesions every ongoing year of the treatment, starting the first one (Friedman ANOVA $p = 0.000$; Wilcoxon test respectively: $p_{1\text{-}2} = 0.000$, $p_{1\text{-}3} = 0.000$, $p_{1\text{-}4} = 0.000$). The decreases achieved in the first year do not vary significantly in the next three years of treatment ($p > .05$) (Fig. 3).

On the basis of the clinical (EDSS, relapses) and MRI outcomes the proportion of fingolimod-treated patients who fulfilled the NEDA-3 (Non-Evidence of Disease Activity-3: no relapses, no disability progression and no MRI activity) criteria was also assessed. After each year of fingolimod therapy the proportion of patients who achieved NEDA-3 was 52.4%, 57.6%, 57.3% and 66.0% respectively (Fig. 4).

4.4. Safety

The assessed population has not identified any unexpected or new safety signals. In general, the incidence rates for reported events were in line with the known fingolimod safety profile, reported in clinical studies and other RWE studies (e.g. PANGAEA) [17,18]. Practical guidelines for initiating and monitoring treatment have been implemented in Poland, thanks to which it has turned out that bradycardia is a transient, usually asymptomatic event. Currently, over 3 years of treatment with fingolimod is continued by over 85% of patients, about 10% showed ineffectiveness and these were usually patients treated earlier with 2 or 3 DMTs. The most frequent infections reported in the observed group were upper respiratory and urinary tract infections.

5. Discussion

Randomized controlled clinical trials assess the short-term efficacy and safety of DMT in a determined patient population. Real-world evidence (RWE) is defined as data regarding a treatment not collected in a randomized controlled trial [15] and can provide more generalizable details and long-term evidence on various end points such as effectiveness, safety or patient-reported outcomes (PROs).

Short-term RWE studies have been reviewed by Ziemssen et al [16]. PANGEA is a multicenter non-interventional study on disease active RRMS patients whose therapy is switched to fingolimod [17]. In the second phase of this study, 1500 patients who switch to fingolimod as being non-responders to other DMTs are entering a 3-year observation. Interim results of PANGEA provide evidence for sustained effectiveness of fingolimod. ARRs were reduced after 12 months of fingolimod therapy compared with during the 12-month period before PANGEA enrollment [18]. EDSS scores also remained stable and a high proportion of patients were free from relapses and 6-month confirmed disability progression.

The key objectives of our study were to assess the effectiveness of fingolimod 0.5 mg versus previous DMTs in real-world setting in relapsing remitting MS patients. This exploration has shown significant greater reductions in relapse rate, disability progression, MRI disease activity in patients with RRMS than before given first-line therapy. These results are concordant with controlled, double-blind 3 phase extension studies [7].

TRANSFORMS clinical trial compared fingolimod with intramuscular interferon beta-1a. It demonstrated superior efficacy of fingolimod on relapse activity, number of gadolinium-enhancing lesions on MRI, and total lesion burden [19]. A subgroup analysis in the context of previously active disease despite DMT, patients in the IFN beta-1a group who switched treatment to fingolimod also experienced a reduction in ARR [19].

MS is a progressive disease and delay in starting adequate DMT can have long-term consequences. In clinical practice choosing the right drug for an individual patient with established MS should remain in the hands of the treating neurologist, who takes into account the patients' history, their age, the level of disease activity, their comorbidities and, very importantly, patient personal preferences. In the Polish healthcare

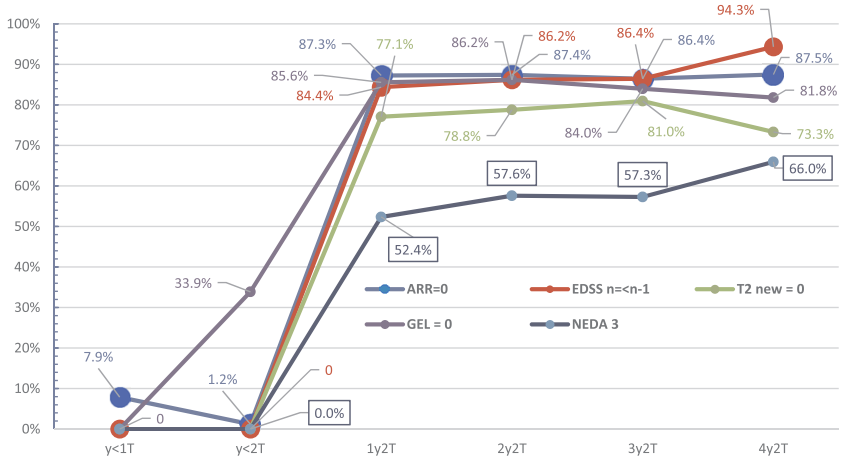

Fig. 4. The percentage of $ARR_n = 0$, $EDSS_n <= EDSS_{n\text{-}1}$, $T2_{n\_new} = 0$, $GEL_n = 0$ and $NEDA3_n$ patients in consecutive years of observation. NEDA 3 is defined as: ($ARR_n = 0 \cap EDSS_n <= EDSS_{n\text{-}1} \cap T2_{n\_new} = 0 \cap GEL_n = 0$).

system the choice of medication depends on internal licensing regulations in which fingolimod may be used after failure of first-line DMT like interferons or glatiramer acetate (or other products with a similar efficacy range) or in RES starting from July 2018.

In Poland, patients could be treated with the second-line medications when new relapses or new lesions on MRI occurr. Our retrospective analysis has showed that switching to fingolimod resulted in improved relapse outcomes (ARR and proportion of patients free from relapses) compared to patients previously experiencing disease activity while treating with interferon beta or glatiramer acetate. The high and constant value of NEDA-3 assessment during the first years of the fingolimod therapy could be good prediction of long-term outcomes.

The safety and tolerability of fingolimod seen in this real-world study was also consistent with that observed in previous phase II and III clinical trials, complementing these trials and providing real-world verification of these observations. For this reason fingolimod as second-line therapy is often preferred. Based on the results obtained in the study, we can conclude that fingolimod treatment achieved the best results when applied immediately after setting the ineffectiveness of treatment with the first-line medications. Delay in the treatment change in such situation will influence the severity of the disease and the patient's disability progression (EDSS).

In conclusion, our data show that under the second-line real life use of fingolimod we observe a high proportion of patients free from relapse and from disability progression over a mean follow-up of 42 months. Similar results were detected from MRI inflammatory disease activity outcomes assessment. It confirms that in case of lack of prior DMT efficacy switch decision should be undertaken early.

Disclosure

Adam Stepien, Halina Bartosik-Psujek, Beata Zakrzewska-Pniewska, Agata Walczak, Mariusz Stasiolek, Malgorzata Dorobek, Iwona Kurkowska-Jastrzebska, Alina Kulakowska, Stanislaw Rusek, Andrzej Tutaj, Andrzej Glabinski, Waldemar Brola, Jan Kochanowski, Malgorzata Siger, Bartosz Bielecki, Monika Nojszewska, Aleksandra Podlecka-Pietowska, Katarzyna Kurowska, Wojciech Wicha, Anna Czajka, Katarzyna Kapica-Topczewska, Marzena Maciagowska-Terela received in the last 3 years honoraria for participation in clinical trials, advisory boards, consultancy fees, speaker fees from Bayer HealthCare, Biogen Idec, Genzyme, Merck, Novartis, Roche, Sanofi, Teva. Agata Wlodek, Radoslaw Zajdel, Agnieszka Ciach: nothing to disclose.

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