Risk Perception in Multiple Sclerosis: Reasons for Switching Treatment Between High Efficacy and Non-high Efficacy Disease-modifying Therapies

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Disclosures

James Pike and **Eddie Jones** are employees of Adelphi Real World.
Gustavo Seifer, **Patricia Dominguez-Castro**, **Rainel Sanchez-de la Rosa** and **Simone Hiltl** are employees of Novartis.

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Background

- Multiple sclerosis is a complex chronic disease of the CNS characterized by inflammation and neurodegeneration; it is the most common autoimmune disorder among young adults[1]
- DMTs approved for the treatment of MS include various Non-HETs and HETs[2], and have variable benefit-risk profiles that need to be suitable for each patient's disease severity and personal preference[3]
- Decision to initiate a DMT can be strongly influenced by an individual's risk perception[4]
- Risk perception is dynamic and influenced by personal, emotional, social, and experiential factors of both the patient and the neurologist and might differ from one region to another[4,5]
- HETs are potentially perceived by physicians as having greater safety concerns[6] than Non-HETs and are generally reserved for patients with high disease activity or in cases of suboptimal response[3,7]

CNS, central nervous system; DMT, disease-modifying therapy; HET, high efficacy treatment

1. Wallin MT, et al. The Lancet Neurology. 2019;18(3):269-285. 2. Samjoo IA, et al. *J Comp Eff Res*; 2021;10(6):495–507; 3. Comi G, et al. *Lancet*;2017;389 (1076):1347-56; 4. Cocco E, et al. *Expert Rev Neurother*; 2017;17(2):173-80; 5. Bernanrdi BD, et al. *Arq.NeuroPsiquiatr*;2018;76 (1):6-12; 6. Luna G, et al. *JAMA Neurol.* 2020;77(2):184-191; 7. Rio J, et al. *Curr Opin Neurol*. 2011;24(3):230-237.

Objective and endpoints

To investigate the influence of risk perception on switching treatment decisions that are made by physicians when prescribing Non-HETs and HETs

Primary endpoint

- The proportion of patients who were switched based on risk perception (infections, malignancies, others) in patients previously treated with Non-HET versus HET

Secondary endpoints

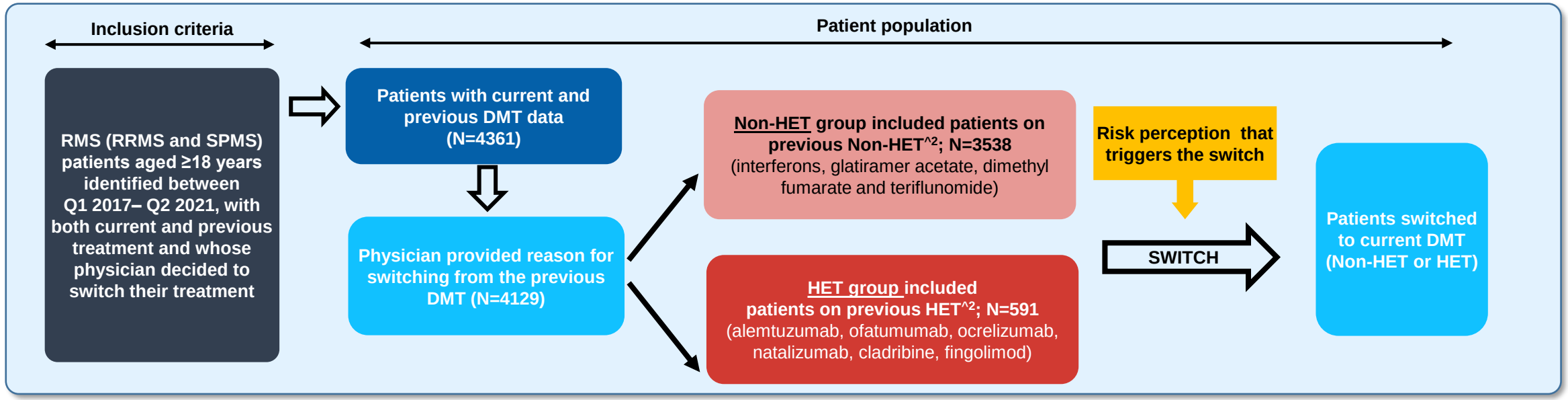
- Reasons for switching treatment in the previous Non-HET and HET groups
- Proportion of patients who switched due to lack of efficacy or due to new or enlarging lesions on MRI, increase in the frequency and/or severity of the relapses, progression in physical disability measured by EDSS or patient compliance issues between the groups
- Proportion of patients who changed treatment group versus patients who continued in the same treatment group

EDSS, Expanded Disability Status Scale; HET, high efficacy treatment; MRI, magnetic resonance imaging

Methods

- Data were drawn from the Adelphi Real-World MS DSP, a retrospective non-interventional cross-sectional, multi-cohort study[1]; the patient selection flow chart is presented in figure
- Descriptive statistics (n, %) and Fisher's Exact test were used to compare risk perception (malignancies/infections), and other reasons for influencing treatment switches

Patient selection flow chart



^The classification of HET and Non-HET is based on Samjoo IA, et al. publication cited below.
DMT, disease-modifying therapy; DSP, Disease-Specific Program; HET, high efficacy treatment; MS, multiple sclerosis; Q, quarter; RMS, relapsing MS; RRMS, relapsing remitting MS; SPMS, secondary progressive MS. 1. Anderson P, et al. *Curr Med Res Opin*; 2008:24 (11);3063–72. 2. Samjoo IA, et al. *J Comp Eff Res*; 2021;10(6):495–507.

Results: Demographics and clinical characteristics

- Of 4361 patients with data available for current and previous DMT, the reason for switching from previous DMT was provided by physicians for 4129 (Non-HET, N=3538; HETs, N=591) patients
- Patients in the previous HET group had longer time since initial MS diagnosis (9.5 vs 7.9 years), higher current EDSS score (mean: 3.5 vs 2.7), lower proportion of patients with RRMS (72.0% vs 86.1%) and higher proportion of patients with rapid deterioration (3.9% vs. 1.5%) versus Non-HET group

Variable	Overall (N=4361)	Previous Non-HET (N=3768)	Previous HET (N=593)
Age, mean (SD)	42.1 (11)	42.0 (11.1)	42.5 (10.4)
Female (%)	65.5	64.8	69.8
Time since initial MS diagnosis (years), mean (SD)	8.1 (6.1)	7.9 (6.0)	9.5 (6.4)
Current diagnosis: RRMS (%)	84.2	86.1	72.0
Current diagnosis: SPMS (%)	15.8	13.9	28.0
Current EDSS, mean (SD)	2.8 (1.8)	2.7 (1.7)	3.5 (1.9)
Working full time (%)	47.7	49.0	39.4
Unemployed (%)	8.3	7.9	10.9
Patients improving (%)	6.9	7.1	5.1
Patients deteriorating rapidly (%)	1.8	1.5	3.9
Duration of previous treatment (years), mean (SD)	3.3 (3.2)	3.3 (3.3)	3.0 (2.4)

DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; HET, high efficacy treatment; MS, multiple sclerosis; RRMS, relapsing remitting MS; SD, standard deviation; SPMS, secondary progressive MS

Results: Common current DMTs switched to from previous DMT

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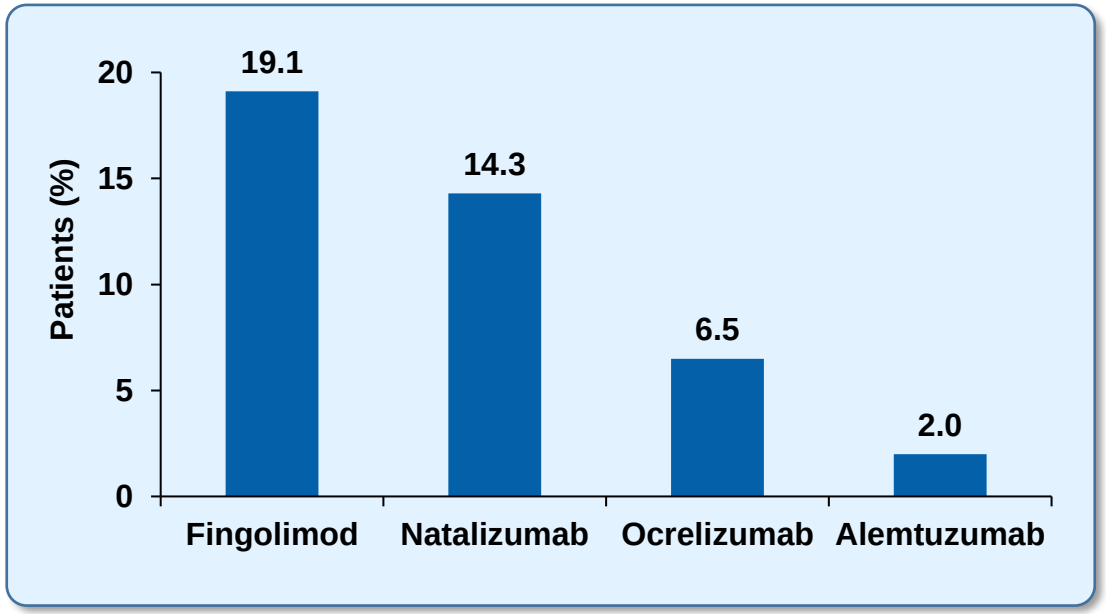
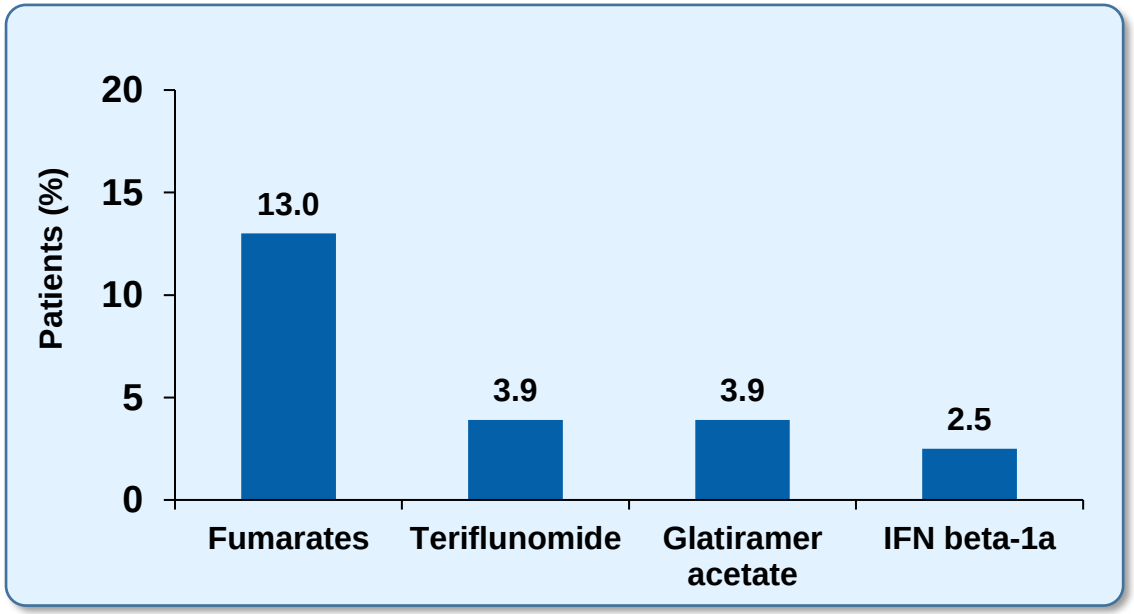
Non-HET → HET (45.4%)
54.6% patients continued in the Non-HET group

HET → Non-HET (28.7%)
71.3% patients continued in the HET group

Switch from previous Non-HET to HET



Switch from previous HET to Non-HET

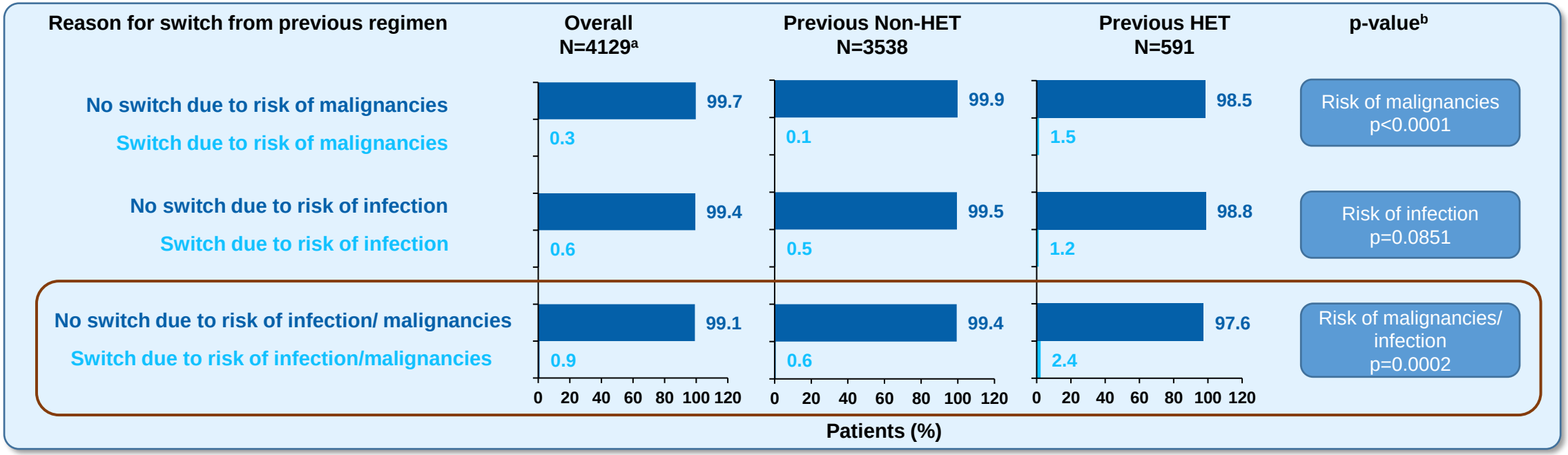


The most common current DMTs (HET/Non-HET) switched to from previous DMT are presented in figure.
DMT, disease-modifying therapy; HET, high efficacy treatment

Results: Physicians' risk perception of malignancies/infections

- Switch due to any risk of infections or malignancies was rare irrespective of switching from HET or Non-HET
- Although the overall combined perceived risk of malignancy/infection was significantly higher in the previous HET versus previous Non-HET, very few patients switched treatment for risk of malignancies/infections versus those switched for no risk of malignancies/infections (0.9% vs 99.1%)
- Risk perception of infection was low and not significantly higher in patients with previous HET versus previous Non-HET

Physicians' risk perception of malignancies and infections as a reason for switching therapies



a4129 patients for whom the reason for switch from previous DMT was provided by the physician were included for the analysis; of those, 3538 switched from Non-HET and 591 from HETs
bDerived from Fisher's exact test
DMT, disease-modifying therapy; HET, high efficacy treatment

Results: Reasons for switching the treatment

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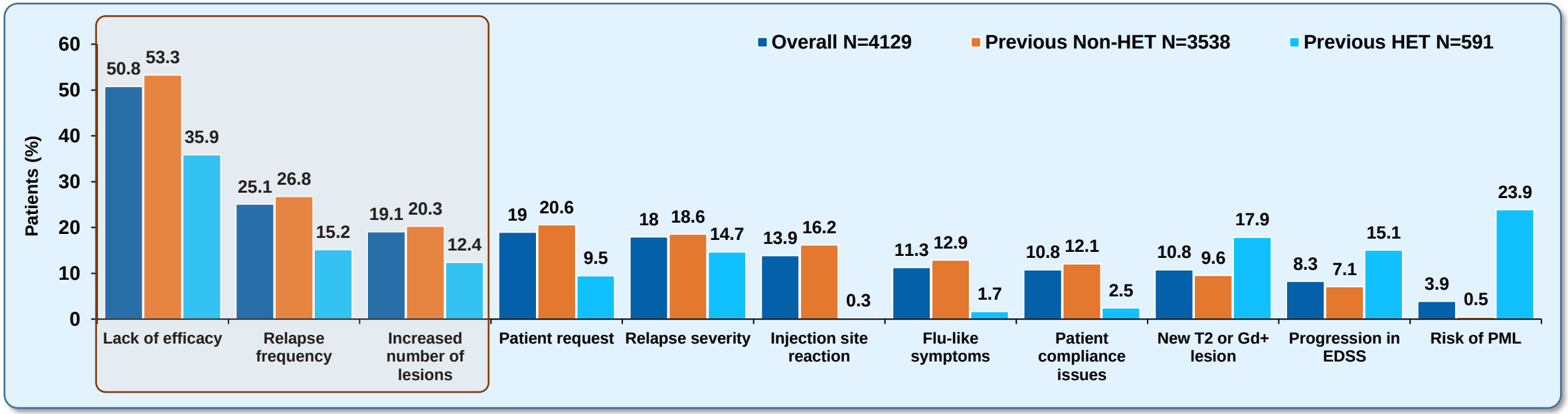
- The top 3 reasons for switching the treatment in the overall group were lack of efficacy (50.8%), relapse frequency (25.1%) and increased number of lesions (19.1%)
  - **Non-HET group**: **Lack of efficacy** (53.3%), relapse frequency (26.8%), and patient request (20.6%)
  - **HET group**: **Lack of efficacy** (35.9%), risk of PML[a] (23.9%), and new T2 or Gd+ T1 lesion (17.9%)

Most common (>10% in any group) reasons for switching treatment



[a]Largely contributed by Natalizumab
EDSS, Expanded Disability Status Scale; Gd+, gadolinium-enhancing; HET, high efficacy treatment; PML, progressive multifocal leukoencephalopathy

Results: Reasons for switching the treatment

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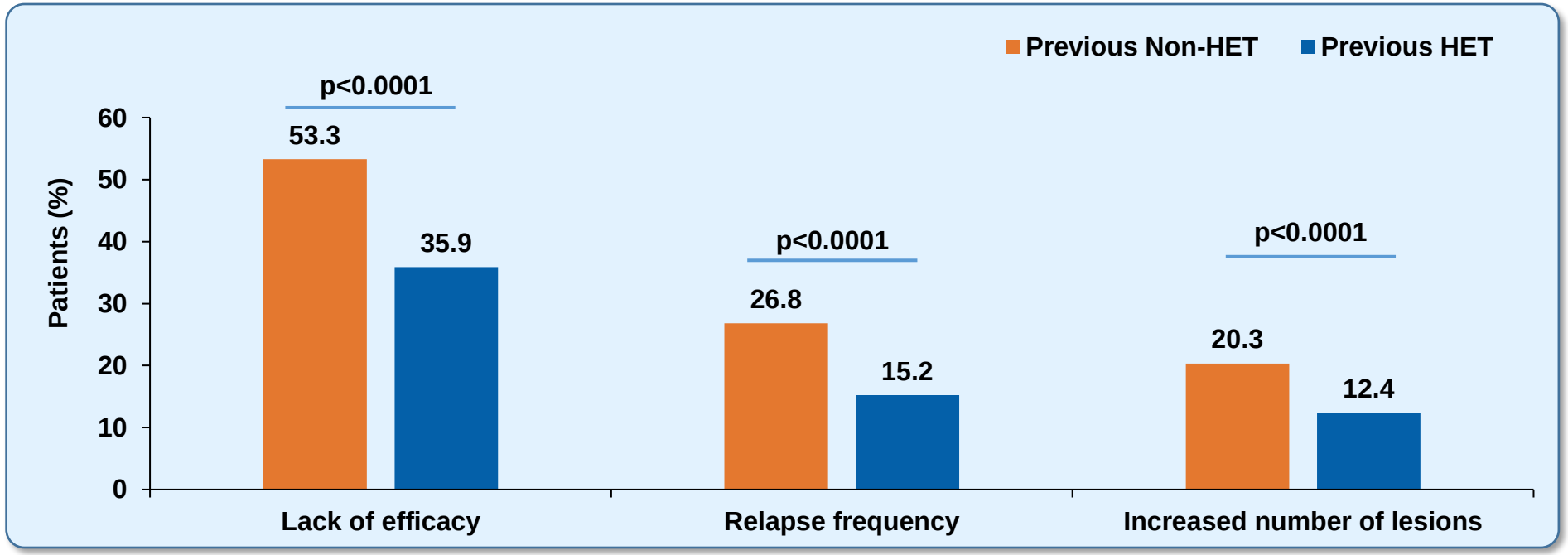
- Lack of efficacy, relapse frequency and increased number of lesions are the main factors influencing treatment switching, especially in the case of previous Non-HETs

Patients switching treatment due to lack of efficacy, relapse frequency and increased lesions



HET, high efficacy treatment

Conclusions

- Physicians' risk perception of malignancies and infection is not a leading factor when switching from high efficacy treatments (HETs) or Non-HETs
- Lack of efficacy, including relapse frequency, increased lesions and relapse severity are the main factors influencing treatment switching, especially in Non-HETs
- Patients in the previous HET group already had more progressive disease prior to initiation of the HETs which might be indicative of a widespread escalation approach
- Our findings suggest early initiation of HET in treating MS and underscore the need for evaluation of the current approach of escalation therapy
- The choice of treatment should be made based on the benefit-risk profile of the specific treatment