probability of relapse in glatiramer acetate (OR=27.27; 95%CI= 9.15,81.29; p<0.01), dimethyl-fumarate (OR=10.60; 95%CI= 3.49,32.17; p<0.01), fingolimod (OR=16.28; 95%CI=5.35,49.52; p<0.01), and natalizumab (OR=17.20; 95%CI=5.66,52.29; p<0.01), compared with ocrelizumab. EDSS more likely increased in glatiramer acetate (OR=1.34; 95%CI=1.19,1.51; p<0.01), dimethyl-fumarate (OR=1.26; 95%CI=1.12,1.43; p<0.01), fingolimod (OR=1.59; 95%CI=1.41,1.80; p<0.01), and natalizumab (OR=1.86; 95%CI=1.63,2.12; p<0.01), compared with ocrelizumab. The probability of new/Gd-enhancing lesions was higher in glatiramer acetate (OR=4.02; 95%CI =1.74,9.27; p<0.01), compared with ocrelizumab, while no differences were found for dimethyl-fumarate (p=0.42), fingolimod (p=0.87), and natalizumab (p=0.11). On propensity score-adjusted Cox regression models, NEDA-3 status was achieved by 90.23% of patients treated with ocrelizumab, and, less so, glatiramer acetate (44.24%; HR=12.52; 95%CI=9.55,16.42; p<0.01), dimethyl-fumarate (62.08%; HR=1.66; 95%CI=1.30,2.11; p<0.01), fingolimod (54.16%; HR=2.98; 95%CI=2.35,3.77; p<0.01), and natalizumab (57.72%; HR=1.71; 95%CI=1.32,2.21; p<0.01).

Discussion: Ocrelizumab proved superior to other DMTs in achieving NEDA-3 status and reducing EDSS worsening, using propensity score adjustment. The less striking results on MRI lesions could be due to the limited sample size analysed. Further analyses on more MRI outcomes and in a larger group of patients is ongoing.

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O019

Comparative effectiveness of autologous haematopoietic stem cell transplantation vs. fingolimod, ocrelizumab and natalizumab in relapsing-remitting MS

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Introduction: Chemotherapy followed by autologous hematopoietic stem cell transplantation (AHSCT) is occasionally used in patients with aggressive multiple sclerosis (MS). Single-arm observational cohorts have demonstrated its remarkable effect on stabilising highly active inflammatory disease phenotypes. Information about its comparative effectiveness relative to other highly efficacious disease modifying agents is scarce.

Aim: This study emulated a series of pairwise trials of comparative effectiveness of AHSCT vs. fingolimod, ocrelizumab and natalizumab.

Methods: Patients with relapsing-remitting MS from 6 AHSCT MS centres in Ottawa, Uppsala, Sheffield, Bergen, Sydney and Melbourne were combined with patients from MSBase. Patients were included if they were treated with AHSCT or one of the study therapies and had sufficient information recorded before and after the start of the therapy (baseline). They were matched in pairwise comparisons on a propensity score derived from sex, age, disability score (EDSS), number of relapses 12 and 24 months before baseline, time from MS onset, the most effective prior therapy and country. The pairwise-censored groups were compared on annualised relapse rates (ARR) and freedom from relapses and 6-month confirmed EDSS worsening and improvement.

Results: The matched patients had high mean disease activity (>0.9 relapses in the prior year) and mean EDSS 3-4.In comparison to fingolimod (n=612), matched AHSCT (n=120) experienced less relapses (ARR: mean±SD 0.20±0.43 vs. 0.11±0.36; risk of relapses: hazard ratio 0.55, 95%CI 0.37-0.91), similar risk of EDSS worsening (hazard ratio 0.49, 95%CI 0.16-1.54) and higher chance of disability improvement (hazard ratio 2.62, 95%CI 1.46-4.72). Ocrelizumab (303) and AHSCT (91) were associated with similar ARR (0.10±0.39 vs. 0.08±0.33), risk of relapses (0.85, 0.46-1.56), EDSS worsening (0.41, 0.09-1.90) and EDSS improvement (2.31, 0.63-8.48). Natalizumab (n=606) and AHSCT (n=116) were associated with similar ARR (0.12±0.37 vs. 0.09±0.30), risk of relapses (0.78, 0.40-1.52) and EDSS worsening (0.50, 0.09-2.61). EDSS improvement was more common after AHSCT (1.82, 1.19-2.78).

Conclusion: Among patients with highly active MS with moderate disability, AHSCT is superior to fingolimod and comparable with ocrelizumab and natalizumab in preventing relapses. AHSCT is associated with higher rate of recovery from disability then natalizumab, a therapy that is known for reduction of disability in trials.

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IR served on scientific advisory boards/steering committees for Novartis and Merck and received conference travel support and/or speaker honoraria from Roche, Novartis, Biogen, Teva, Sanofi-Genzyme and Merck

JM served on scientific advisory board for Roche, received conference travel support and/or speaker honoraria from Novartis, Biogen, Roche and Merck

RM received compensation for traveling, conference fees and consulting fees from Merck, Teva, Sanofi Genzyme, Biogen Idec, Novartis, Roche, BMS, Celgene

OT received speaker honoraria from and served on scientific advisory boards for Biogen, Sanofi-Aventis, Merck and Novartis

LB received speaker honoraria from Novartis, and consultant fees from Viatris

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MT received honoraria from Janssen, Gilead Sciences, Bristol-Myers Squibb, Takeda, Amgen, Abbvie, Roche, MorphoSys, Novartis, served as an advisor to Takeda, Bristol-Myers Squibb, Incyte, Abbvie, Amgen, Roche, Gilead Sciences, Janssen,

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AV served on advisory boards and receives unrestricted research grants from Novartis, Biogen, Merck and Roche She received speaker's honoraria and travel support from Novartis, Roche, and Merck She receives grant support from the National Health and Medical Research Council of Australia and MS Research Australia

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BV received research and rravel grants, honoraria for MS-Expert advisor and Speaker fees from Bayer-Schering, Biogen, Sanofi Genzyme, Merck, Novartis, Roche and Teva

KB received honoraria and consulting fees from Biogen, Teva, Novartis, Genzyme-Sanofi, Roche, Merck, CSL and Grifols

JLS travel compensation from Novartis, Biogen, Roche and Merck. Her institution receives the honoraria for talks and advisory board commitment as well as research grants from Biogen, Merck, Roche, TEVA and Novartis

MB served on scientific advisory boards for Biogen, Novartis and Genzyme and received conference travel support from Biogen and Novartis. He serves on steering committees for trials conducted by Novartis. His institution received research support from Biogen, Merck and Novartis

PC received honoraria and consulting fees from Novartis, Bayer Schering and Sanofi and travel grants from Novartis, Biogen and Bayer Schering

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GI received speaking honoraria from Biogen, Novartis, Sanofi, Merck, Roche, Almirall and Teva

SE received speaker honoraria and consultant fees from Biogen Idec, Novartis, Merck, Bayer, Sanofi Genzyme, Roche and Teva

CB received conference travel support from Biogen, Novartis, Bayer-Schering, Merck andTeva; participated in clinical trials by Sanofi Aventis, Roche and Novartis

FP received speaker honoraria and advisory board fees from Almirall, Bayer, Biogen, Celgene, Merck, Novartis, Roche, Sanofi-Genzyme and TEVA. He received research funding from Biogen, Merck, FISM (Fondazione Italiana Sclerosi Multipla), Reload Onlus Association and University of Catania

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MG received consulting fees from Teva Canada Innovation, Biogen, Novartis and Genzyme Sanofi; lecture payments from Teva Canada Innovation, Novartis and EMD He also received a research grant from Canadian Institutes of Health Research

PD served on editorial boards and been supported to attend meetings by EMD, Biogen, Novartis, Genzyme, and TEVA Neuroscience He holds grants from the CIHR and the MS Society of Canada and received funding for investigator-initiated trials from Biogen, Novartis, and Genzyme

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AL received personal compensation for consulting, serving on a scientific advisory board, speaking or other activities from Biogen, Merck Serono, Mylan, Novartis, Roche, Sanofi/Genzyme, Teva. Her institutions have received research grants from Novartis and Sanofi

MS participated in, but not received honoraria for, advisory board activity for Biogen, Merck, Bayer Schering, Sanofi Aventis and Novartis

JP accepted travel compensation from Novartis, Biogen, Genzyme, Teva, and speaking honoraria from Biogen, Novartis, Genzyme and Teva

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DM received speaker honoraria for Advisory Board and travel grants from Almirall, Biogen, Merck, Novartis, Roche, Sanofi-Genzyme, and Teva

VV received travel grants from Merck, Biogen, Sanofi, Celgene, Almirall and Roche. His institution received research grants and consultancy fees from Roche, Biogen, Sanofi, Celgene, Merck and Novartis Pharma

GL received travel and/or consultancy compensation from Sanofi-Genzyme, Roche, Teva, Merck, Novartis, Celgene, Biogen

CT received research funding, compensation for travel or speaker honoraria from Biogen, Novartis, Genzyme and Almirall

DS received honoraria as a consultant on scientific advisory boards by Bayer-Schering, Novartis and Sanofi-Aventis and compensation for travel from Novartis, Biogen, Sanofi Aventis, Teva and Merck

TC received speaker honoraria/ conference travel support from Bayer Schering, Biogen, Merck, Novartis, Roche, Sanofi-Aventis and Teva

MPA received honoraria as consultant on scientific advisory boards by Biogen, Bayer-Schering, Merck, Teva and Sanofi-Aventis; received research grants by Biogen, Bayer-Schering, Merck, Teva and Novartis

CS served on scientific advisory boards for Merck, Genzyme, Almirall,and Biogen; received honoraria and travel grants from Sanofi Aventis, Novartis, Biogen, Merck, Genzyme and Teva

TCT received speaking/consulting fees and/or travel funding from Bayer, Biogen, Merck, Novartis, Roche, Sanofi-Genzyme and Teva

JLSM accepted travel compensation from Novartis, Merck and Biogen, speaking honoraria from Biogen, Novartis, Sanofi, Merck, Almirall, Bayer and Teva and participated in clinical trials by Biogen, Merck and Roche
BT received funding for travel and speaker honoraria from Bayer Schering Pharma, CSL Australia, Biogen and Novartis, and served on advisory boards for Biogen, Novartis, Roche and CSL Australia
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RFB received speaking honoraria from Biogen, Novartis, Merckand Teva
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JS declares honoraria for educational events from Jazz, Gilead, Janssen, for advisory board membership from Medac, and for trial IDMC membership from Kiadis Pharma
BS: nothing to disclose
CG: nothing to disclose
KD: nothing to disclose
EAM: nothing to disclose
YB: nothing to disclose
AA: nothing to disclose
BWG: nothing to disclose
JG: nothing to disclose
YG: nothing to disclose
RG: nothing to disclose
LV: nothing to disclose
RK: nothing to disclose
OG: nothing to disclose
MJS: nothing to disclose
VS: nothing to disclose
EB: nothing to disclose
RT: nothing to disclose
BY: nothing to disclose
SJK: nothing to disclose
AS: nothing to disclose
AP: nothing to disclose
JK: nothing to disclose
SO: nothing to disclose
EC: nothing to disclose
BW: nothing to disclose
OS: nothing to disclose
EK: nothing to disclose
AK: nothing to disclose
AG: nothing to disclose
MF: nothing to disclose
HA: nothing to disclose
JB: nothing to disclose
IS: nothing to disclose
BW: nothing to disclose
SS: nothing to disclose
T Kozak: nothing to disclose
RM: nothing to disclose
MO: nothing to disclose

O020

Precision medicine in an unlikely future of multiple sclerosis treatment

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Background: The concept of precision medicine is a common vision of the future of health care, in contrast to the previous paradigm of evidence-based medicine based on RCTs, often criticized as "treatment of the average patient". Although treatment decisions in medicine have always been individualized, progress in the molecular diagnosis of cancers and rare hereditary disorders have fueled expectations of similar advances for other diseases. For multiple sclerosis (MS), the variable outcome is commonly assumed to signify pathogenetic heterogeneity. However, after the departure of NMO/MOGAD from the MS disease spectrum, progress has been limited in defining meaningful subgroups within MS. In addition, MS genetics has failed to identify strongly expressed risks even in rare families of seemingly genetic MS.
Methods: We hypothesized that a heterogenous pathogenesis within the entity of MS, should be reflected in a heterogenous response to disease modifying treatments (DMTs), among which almost a dozen different mechanisms of action are represented. Contrary, a homogenous response to DMTs would indicate that MS is a rather homogenous condition. We therefore analyzed the distribution of new MRI T2 lesions in 48,659 MRI investigations among 10,662 MS patients from the Swedish MS registry to look for deviations from an expected distribution of lesions under a hypothesis of homogenous responses.
Results: For all 12 studied DMTs (Interferon 1b and 1a, glatiramer, natalizumab, fingolimod, dimethyl fumarate, teriflunomide, ocrelizumab, rituximab, alemtuzumab, cladribine) the distribution of new T2 lesions adhered to the expected negative binominal distribution. For all DMTs, an expected number of patients deviated by showing numbers of new T2 lesions outside of the 95th percentile of the distribution.
Conclusion: We interpret our data to indicate that although DMTs differ quantitatively in their ability to suppress the focal inflammation that is the hallmark of early MS, few if any patients appear to be biologically non-responsive to any drug. This suggests that MS is largely pathogenetically homogenous and indicates that precision medicine may have limited prospects in the treatment of MS.

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