Siponimod for Secondary Progressive Multiple Sclerosis (SPMS) in NHS Lothian – are we up to standard?

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Introduction

Siponimod (Mayzent) is a sphingosine-1-phosphate receptor (S1P) modulator, approved by Scottish Medicines Consortium (SMC) for the treatment of active SPMS in October 2021. Siponimod prevents lymphocyte egress to the CNS from the lymphatic tissue and slows disability progression. Siponimod treatment presents a range of potential risks and side effects, including lymphopenia, macular oedema, basal cell carcinoma and cardiac arrhythmias. Each patient should undergo appropriate screening, including genotying, to ensure safe initiation of treatment, and should be monitored closely during the duration of treatment in accordance with guidelines and best practice. In NHS Lothian, patient selection, screening, consent, and monitoring is managed in a specialist clinic run by the MS Clinical Team (Consultant Neurologist and the MS Specialist Nurses) using the approved NHS Lothian Siponimod Protocol.

Objectives and aims

Primary aim:

- Ensure care delivered is in accordance with best practice and measure compliance with the NHS Lothian Siponimod Protocol

Secondary aims:

- Assess 'real world' clinical effectiveness of siponimod
- Discern reasons for stopping siponimod treatment
- Highlight areas for improvements

Method

Using the audit cycle, the MS clinical team derived seven standards of care to benchmark siponimod care against. A retrospective case note audit of NHS Lothian patients who were prescribed siponimod between 2021-2024 was completed. 42 patients were identified for inclusion in the audit. Information was gathered from the NHS Lothian TRAK system between December 2024 - January 2025.

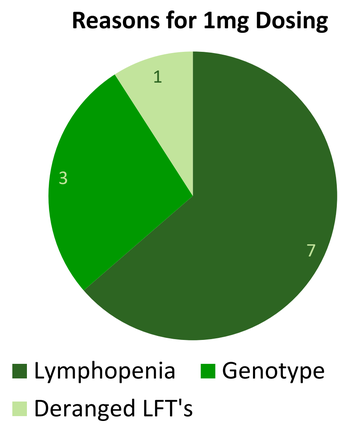
Results: Primary Aim

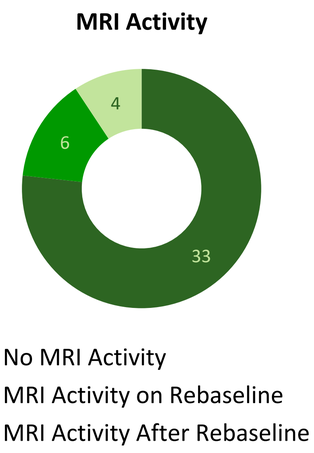
The audit included 42 patients consisting of 15 males (36%) and 27 females (64%). The mean age of the patient was 57 years, with an age range of 37 to 73 years. Extended Disability Status Scale (EDSS) ranging from 2.5 - 8 (mean EDSS 6) at time of commencing siponimod. Mean time since diagnosis to commencing siponimod was 16.25 years.

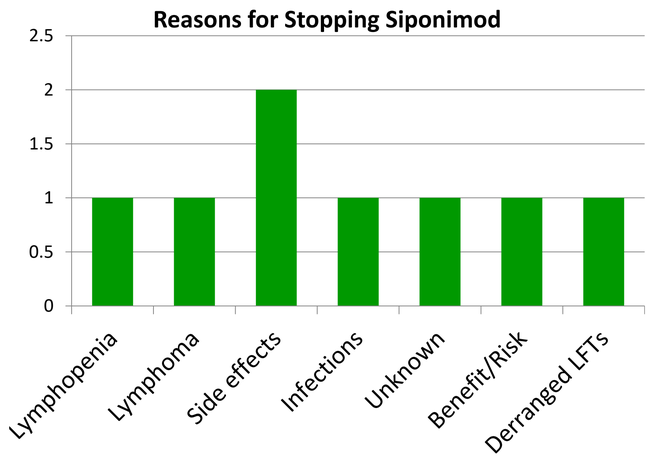
	STANDARD OF CARE	COMPLIANCE WITH STANDARD
1	All patients should meet the SMC criteria/ indication for prescribing siponimod, to include MRI imaging	90.47%
2	All patients should have genotyping performed prior to starting siponimod.	100%
3	All patients should have baseline measures documented in their medical records prior to starting	90.48%
4	All patients should have a documented risk benefit discussion prior to commencing siponimod	92.94%
5	All patients should have ophthalmic screening performed 3-4 months after starting siponimod.	88%
6	All patients should have bloods monitoring performed month 1, 3, 6 and 6 monthly after starting siponimod.	64.28% *
7	All patients should have BP checked regularly whilst taking siponimod.	50%

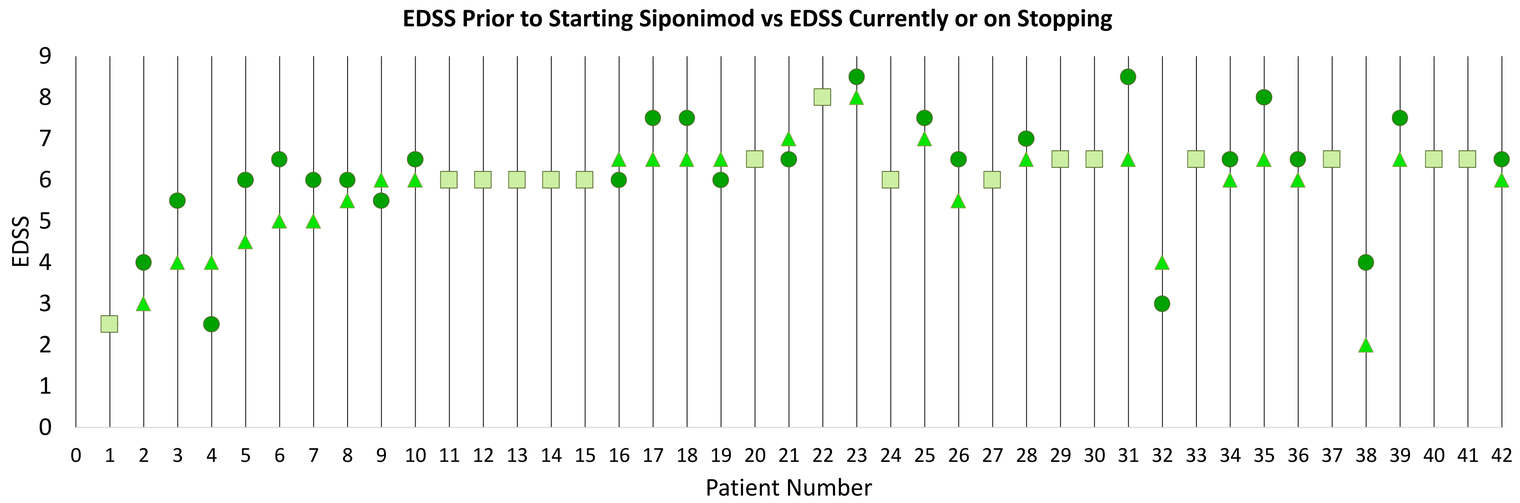
*while 35.72% of patients did not meet this standard, 33.33% of these had regular bloods monitored but these were not strictly to time.

Results: Secondary Aim









Discussion

- The audit revealed typical gender and age pattern among SPMS participants, however, these differ from the EXPAND[1] trial, where the inclusion range was 18-60 years.
- Compliance with the standards was variable. Poorer compliance with blood monitoring monitoring was due to missed appointments and pressures upon the service. Compliance with bloods pressure monitoring was poor (50%), however, the summary of product characteristics (SPC)[2] only specifies that this should be monitored regularly on treatment.
- Patients who continued to have radiological activity despite treatment with siponimod (4/42) remained on treatment due to lack of alternative licensed treatments for SPMS.
- While 90.47% of patients met SMC criteria for being prescribed siponimod having had clinical or radiological activity, the remaining 9.53% were switched from other disease modifying therapies due phenotype reclassification.
- While only 1% of participants in the EXPAND trial[1] experienced lymphopenia, 19.04% of our patients discontinued or reduced their dose of siponimod due to lymphopenia. Lymphopenia is associated with older age[3] and this difference may reflect the difference in age groups (mean age of EXPAND[1] participants was 48.1, and out mean age was 57 years old).
- 6 of 42(14.28%) patients were hospitalised for infection while on Siponimod, 2 of these were for Covid-19, 2 for sepsis (1 unknown source, 1 from a pressure sore), 1 was admitted with Influenza A and 1 for aspiration pneumonia. Only one of these patient discontinued siponimod due to infections.

Limitations

- EDSS scores are approximate as they were calculated retrospectively from clinic letters where an official EDSS has not been noted by the patient's consultant.
- Some documentation was poor or incomplete making data difficult to collect.

Recommendations and Changes to Practice

- Creation of an electronic siponimod initiation/ review template on our electronic system that promotes a consistent approach between clinicians to improve compliance with the standards.
- In collaboration with business intelligence colleagues, we established an electronic daily alert notifying the MS Nursing Team of all non-elective admissions with an ICD-10 diagnostic code of G35(MS), which has resulted improved communication between acute medicine and MS Services, leading to improved co-ordination, optimal management during the admission and a more streamlined discharge from hospital.
- Creation of a medical support worker post to improve compliance with blood monitoring and to perform regular subjective measurements of disability progression i.e. 9 hole peg test, EDSS.
- We propose a re-audit of siponimod use in 12 months to ensure standards being met/maintained

References
1. Siponimod versus placebo in secondary progressive multiple sclerosis (EXPAND): a double-blind, randomised, phase 3 study
Prof Ludwig Kappos, MD[a] ludwig.kappos@usb.ch · Prof Amit Bar-Or, MD[b,c] · Prof Bruce A C Cree, MD[d] · Robert J Fox, MD[e] · Prof Gavin Giovannoni, MD[f] · Prof Ralf Gold, MD[g] · Prof Patrick Vermersch, MD[h] · Prof Douglas L Arnold, MD[i,j] · Sophie Arnould, MSc[k] · Tatiana Scherz, MD[k] · Christian Wolf, MD[l] · Erik Wallström, MD[k] · Frank Dahlke, MD[k] for the EXPAND Clinical Investigators
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