Fingolimod Titration is an Option to Manage Side Effects Effectively, Reduce Patient Treatment Withdrawal and Achieve a Full Therapeutic Dose Regime

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INTRODUCTION

Multiple Sclerosis (MS) is an autoimmune inflammatory demyelinating disease of the central nervous system. Fingolimod was approved by the FDA in 2010 for the first-line treatment of relapsing remitting multiple sclerosis (RRMS). A major Australian tertiary teaching hospital with a large MS clinic anticipated patients commencing Fingolimod. However, initial drug tolerance was poor and many patients requested their medication ceased. To reduce and eliminate treatment side effects, reduce patient treatment withdrawal, and achieve the full therapeutic dose regime, we developed a personalized management titration plan. The aim of this study was to explore whether a titration plan would be effective in reducing and eliminating treatment side effects, reduce patient treatment withdrawal, and achieve the full therapeutic dose regime.

METHODS

In collaboration with the neurologist, MS nurses were engaged to manage side effects, and titrate the Fingolimod dose according to side effects experienced. Patients who chose to withdraw from Fingolimod were given the option of a personalized management plan. No clinical assessment tool was used to grade severity of the adverse event. All supportive care given was based on the patients reported perception of discomfort. The program offered regular monitoring and side effect management for Fingolimod. Gastrointestinal Distress, Headache and a feeling of being generally unwell. Ongoing consultation with the neurologist and MS nursing staff was maintained along with Fingolimod dose adjustments. A variety of supportive medications, although not limited to Paracetamol, Ropinirole, Risperidone, and Loperamide were used. Services were delivered via phone consultation, and MS clinic visits and the patient’s general physician. Although the MS clinic provided a comprehensive supportive service, many patients chose their local pathology facility for blood collection due to location convenience, and travel cost efficiency.

RESULTS

In total 209 patients were treated with Fingolimod (Figure 1). A few patients experienced multiple side effects which contributed to the treatment incidence of 59 (Figure 2). Clinically significant adverse events such as Lymphopenia, Herpes Zoster, Malignancy, Headache, 8 (Figure 1), n=2 (12.5%) patients discontinued treatment due to poor drug tolerability would soon request to cease their medication. From this patient group n=24 (47%) were offered a side effect management and supportive care given was based on the patients reported perception of discomfort. The authors would like to thank Dr Suzanne Hodgkinson, founder and director of the MS clinic Liverpool Hospital; who contributed and supported the MS nursing personalized management titration plan.

DISCUSSION

Historically approved MS treatments offered have been self injectable DTH’s. Although individualised dose adjustment regimes when using numerous types of medication is not a new concept, 1 flu type symptoms that were induced by using the interferons encouraged lesser tolerating by clinicians and patients. Essentially incremental dose facilitating acceptable side effect management. 2,3,4 By employing this strategy, research reinforces that the majority of patients could achieve the full dose prescription.

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Several recent studies, 5-11 have hypothesised that the majority of patients could achieve the full dose prescription. However, a small Japanese study of three patients hypothesised that the majority of patients could achieve the full dose prescription. 12-14 The crude form of data collection provided valuable information and an insight into treatment barriers. All Serious Adverse Events (SAEs) and Medical Events of Interest (MEIs) were officially reported to Novartis locally.

LIMITATIONS

There was no protocol or titration plan constructed as each patient had personalisation recommendations, and time to reach 2mg/day daily administration. A few patients required several dose adjustments over weeks before reaching the desired end-point.

CONCLUSION

Long term data which demonstrates the success of interferon tolerance is encouraging and the same approach should be effective for a select group of patients who struggle tolerating the initial recommended daily Fingolimod dose. Thereby be a role for Fingolimod 0.5mg daily, however the optimal individualised dose of 0.5mg daily is achievable for a few individuals. If side effects and Fingolimod titration is efficiently and effectively managed.

REFERENCES


ACKNOWLEDGEMENTS

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There is no known conflict of interests to be disclosed.