Safety Profile of Daclizumab for the Treatment of Relapsing-Remitting Multiple Sclerosis: A Systematic Review and Meta Analysis

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INTRODUCTION

- Multiple sclerosis (MS) is a chronic, autoimmune, inflammatory neurological disease of the central nervous system (CNS).
- MS destroys the myelin and the axons in various myelinated CNS nerves to varying degrees.
- The course of MS is unpredictable: in most patients, initial episodes of reversible neurological deficits are often followed by progressive neurological deterioration.
- The four clinical categories of MS are:
  - Relapsing-remitting MS (RRMS): the most common form, affecting about 85% of MS patients.
  - Secondary progressive MS (SPMS): may develop in some patients with RRMS.
  - Primary progressive MS (PPMS): affects approximately 10% of MS patients.
  - Progressive-relapsing MS (PRMS): a rare form, affecting fewer than 5% of patients.
- Daclizumab has been approved by the US FDA for the treatment of RRMS in May 2016.

OBJECTIVE

- To analyze the safety of Daclizumab in the treatment of relapsing-remitting multiple sclerosis (RRMS).

MATERIALS AND METHODS

- Literature search was conducted in Cochrane library and Clinicaltrials.gov databases from inception.
- An initial search using the MeSH Terms “dacituzumab”, “multiple sclerosis”, and “Randomized Controlled Trials” was followed by a search of related citations.
- All randomized controlled trials (RCTs) comparing daclizumab with placebo for the treatment of RRMS were included.
- In addition, references of the included studies were screened for additional studies.
- Four authors independently screened titles, abstracts, and subsequently the full texts of all the potentially relevant studies. The same four authors extracted data and assessed risk of bias using the modified Jadad scale.
- The main outcome was safety in terms of various adverse events at 52 weeks.

RESULTS

- A total of four RCTs involving 3286 RRMS patients were included in this meta-analysis.
- RRMS patients received 150 mg or 300 mg Daclizumab via subcutaneous route.
- Overall, the risk of bias of included trials was low.
- Daclizumab was associated with increased risk of infections when compared to placebo (RR 1.16, 95% CI 1.04 to 1.30; three RCTs).
- The pooled results indicated no significant difference between Daclizumab and placebo for any adverse event (Risk Ratio 0.96, 95% CI 0.92 to 1.03; three RCTs).

DISCUSSION

- Currently, the US FDA has approved ten medications for the treatment of MS, and several are in various stages of development.
- Each of these medications has their own unique profile in terms of efficacy, tolerability, adverse event profile, advantages and disadvantages.
- The earliest approved treatments were various formulations of interferon beta and glatiramer acetate. Other drugs include Mitoxantrone, fingolimod, teriflunomide and dimethyl fumarate.
- The monoclonal antibodies approved for MS include Natalizumab, Alemtuzumab, and more recently, Daclizumab.
- Daclizumab is a humanized monoclonal antibody targeting the a subunit (CD25) of the interleukin 2 (IL-2) receptor (IL-2R)
- It is said to have the potential to reduce the homoeostasis between autotolerance and autoreactivity that is a feature of MS.
- Daclizumab may reduce disease activity and the incidence of relapse.
- It is associated with the risk of developing infection and disease activity monitoring by MRI, and risk of confirmed disability worsening in many pivotal RCTs.
- Daclizumab was approved for use in the US and the European Union as a once-monthly subcutaneous (SC) injection for the treatment of RRMS in May & July 2016.
- The mechanism of action of Daclizumab is thought to be the following: it reduces the expansion of proinflammatory activated T lymphocytes, simultaneously promotes autotolerance through the expansion of CD25+ natural killer (NK) cells, and partially preserves the regulatory T cell (T[reg]) population and function.
- Daclizumab was associated with modest increases in mild-to-moderate severity hepatic disorders, cutaneous events, and infections; these were manageable with routine medical care, and did not appear to increase with extended treatment.

CONCLUSION

- Our findings demonstrated that incidence of any adverse event with Daclizumab was comparable with placebo.
- However, Daclizumab was associated with more infections and cutaneous events during the treatment of RRMS, when compared with placebo.
- Further high quality trials are needed to establish the safety of Daclizumab in RRMS.

REFERENCES


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