

# INPLASY PROTOCOL

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None declared.

## Ixazomib combined with autologous stem cell transplantation for POEMS syndrome: a case report and meta-analysis

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**Review question / Objective:** POEMS syndrome is a rare monoclonal plasma cell proliferation disorder. At present, there is no unified treatment for POEMS syndrome. Here, we describe one case with POEMS syndrome. And we made a metaanalysis to assess the efficacy of treatment strategies in recent ten years.

**Search strategy:** We searched relevant articles in PubMed, Embase and MEDLINE database for the period up to July 2021. The search strategy included the keywords: POEMS, Therapy, Drug Therapy, Biological Therapy, Combined Modality Therapy, Hematopoietic Stem Cell Transplantation, Immunotherapy, Molecular Targeted Therapy, Chemoradiotherapy, Salvage Therapy, Controlled Clinical Trial, Randomized Controlled Trial et al. In addition, we checked all the references of eligible articles that our search retrieved to identify potentially eligible papers.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 11 July 2022 and was last updated on 11 July 2022 (registration number INPLASY202270061).

assess the efficacy of treatment strategies in recent ten years.

**Rationale:** POEMS syndrome is a rare monoclonal plasma cell proliferation disorder. The patient had multiple organ dysfunction, such as polyneuropathy, organomegaly, endocrinopathy, increased Mprotein, and skin lesions [1]. Current

### INTRODUCTION

**Review question / Objective:** POEMS syndrome is a rare monoclonal plasma cell proliferation disorder. At present, there is no unified treatment for POEMS syndrome. Here, we describe one case with POEMS syndrome. And we made a metaanalysis to

treatment of patients with POEMS includes anthracycline, immunomodulators, proteasome inhibitors, and ASCT for patients in remission. Lenalidomide has immunomodulatory, anti-angiogenesis and cytotoxic effects. It had achieved revolutionary results in the treatment of B-cell nonHodgkin's lymphoma and multiple myeloma (MM) and was often used in the treatment of POEMS syndrome. Its safety and efficacy were confirmed by multiple studies [2-6]. As a proteasome inhibitor, bortezomib exerts antitumor effects by selectively inhibiting the ubiquitin-proteasome pathway [7,8]. And bortezomib was mainly used in the treatment of MM, which can improve the survival rate of patients [9]. In recent years, it has also been tried for the treatment of POEMS syndrome [10-12]. Autologous stem cell transplantation (ASCT) can not only obviously improve the clinical symptoms of patients with POEMS syndrome but also has significant advantages in improving patients' overall survival (OS) and progression-free survival (PFS) [13-15]. The current treatment options are mainly derived from limited clinical trial data and non-clinical trial studies (cohort studies, case reports, case series). It is unclear which one is the best firstline treatment for POEMS syndrome. We report a case diagnosed with POEMS syndrome and got complete response (CR) after being treated with ixazomib and ACST. In the present study, we conduct a metaanalysis containing 6 clinical trials and 14 non-clinical trials to summarize, compare and get favorable consequences for treatment recommendations.

**Condition being studied:** POEMS syndrome is a rare monoclonal plasma cell proliferation disorder. The patient had multiple organ dysfunction, such as polyneuropathy, organomegaly, endocrinopathy, increased M protein, and skin lesions. Current treatment of patients with POEMS includes anthracycline, immunomodulators, proteasome inhibitors, and ASCT for patients in remission. Lenalidomide has immunomodulatory, anti-angiogenesis and cytotoxic effects. It had achieved revolutionary results in the

treatment of B cell nonHodgkin's lymphoma and multiple myeloma (MM) and was often used in the treatment of POEMS syndrome. Its safety and efficacy were confirmed by multiple studies. As a proteasome inhibitor, bortezomib exerts antitumor effects by selectively inhibiting the ubiquitinproteasome pathway. And bortezomib was mainly used in the treatment of MM, which can improve the survival rate of patients. In recent years, it has also been tried for the treatment of POEMS syndrome. Autologous stem cell transplantation (ASCT) can not only obviously improve the clinical symptoms of patients with POEMS syndrome but also has significant advantages in improving patients' overall survival (OS) and progression-free survival (PFS). The current treatment options are mainly derived from limited clinical trial data and non-clinical trial studies (cohort studies, case reports, case series). It is unclear which one is the best firstline treatment for POEMS syndrome. We report a case diagnosed with POEMS syndrome and got complete response (CR) after being treated with ixazomib and ACST. In the present study, we conduct a meta-analysis containing 6 clinical trials and 14 nonclinical trials to summarize, compare and get favorable consequences for treatment recommendations.

## METHODS

**Search strategy:** We searched relevant articles in PubMed, Embase and MEDLINE database for the period up to July 2021. The search strategy included the keywords: POEMS, Therapy, Drug Therapy, Biological Therapy, Combined Modality Therapy, Hematopoietic Stem Cell Transplantation, Immunotherapy, Molecular Targeted Therapy, Chemoradiotherapy, Salvage Therapy, Controlled Clinical Trial, Randomized Controlled Trial et al. In addition, we checked all the references of eligible articles that our search retrieved to identify potentially eligible papers.

**Participant or population:** Patients with POEMS syndrome. The search strategy retrieved 221 articles. Of these articles, 6

were reviews, 47 were excluded due to language restrictions (articles in non-English), 119 were excluded due to incomplete POEMS diagnosis, 30 were excluded due to inadequate sample size (with fewer than 5 patients), and finally, 19 were eligible for inclusion in this systematic review. After examining all references to relevant checks and eligible articles, one more study was deemed suitable for inclusion. Hence, overall, 20 articles were included in this pooled analysis.

**Intervention:** This meta-analysis included 6 clinical trials and 14 retrospective studies, 936 patients (28 cases were relapsed or refractory patients, the rest were newly diagnosed patients). There were two clinical trials with 196 patients and six retrospective studies with 440 patients whose treatment plan was ASCT. Three clinical trials with 64 patients and three retrospective studies with 132 patients whose treatment plan was lenalidomide plus dexamethasone. And only one retrospective study with 17 patients whose treatment plans were bortezomib.

**Comparator:** There were two clinical trials with 196 patients and six retrospective studies with 440 patients whose treatment plan was ASCT. Three clinical trials with 64 patients and three retrospective studies with 132 patients whose treatment plan was lenalidomide plus dexamethasone. And only one retrospective study with 17 patients whose treatment plans were bortezomib.

**Study designs to be included:** The search strategy included the keywords: POEMS, Therapy, Drug Therapy, Biological Therapy, Combined Modality Therapy, Hematopoietic Stem Cell Transplantation, Immunotherapy, Molecular Targeted Therapy, Chemoradiotherapy, Salvage Therapy, Controlled Clinical Trial, Randomized Controlled Trial et al. In addition, we checked all the references of eligible articles that our search retrieved to identify potentially eligible papers. Articles with fewer than 5 patients were considered to have insufficient sample size.

**Eligibility criteria:** Meet the diagnostic criteria for POEMS syndrome and have patient survival data.

**Information sources:** Pubmed database.

**Main outcome(s):** Overall, 20 articles consist of 6 clinical trials, 14 retrospective studies, and 936 patients were included in this meta-analysis. There was no significant difference in complete hematologic response rate between people who underwent ASCT and those who did not. However, ASCT might have a better survival rate.

**Quality assessment / Risk of bias analysis:** Risk of bias assessment using R language software.

**Strategy of data synthesis:** Combine statistical patient survival data.

**Subgroup analysis:** Subgroup analysis by treatment regimen.

**Sensitivity analysis:** Heterogeneity existed between studies, which may influence the results of meta-analysis. Therefore, we searched for inter-study heterogeneity and evaluated the stability of meta-analysis results through sensitivity analysis.

**Language:** English.

**Country(ies) involved:** China, Department of Hematology, Shengli Oilfield Central Hospital.

**Keywords:** POEMS syndrome, Autologous stem cell transplantation (ASCT), Ixazomib, Metaanalysis.

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