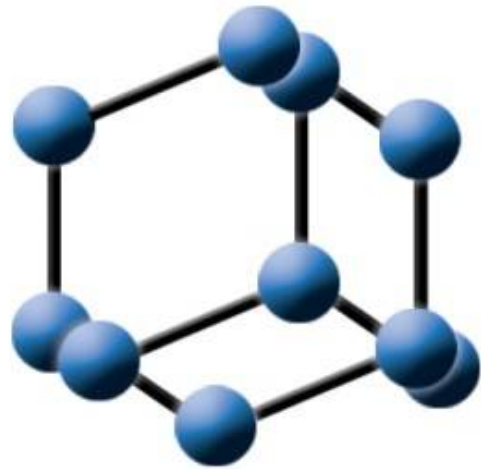


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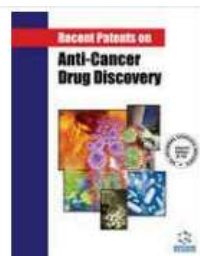
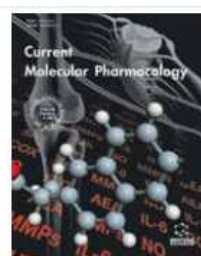
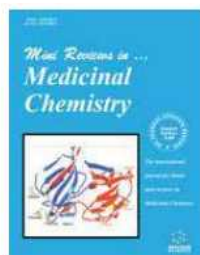
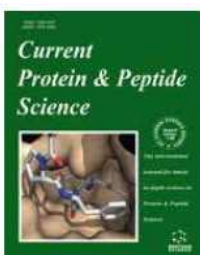
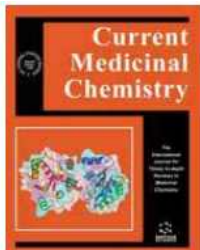
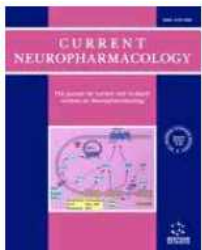
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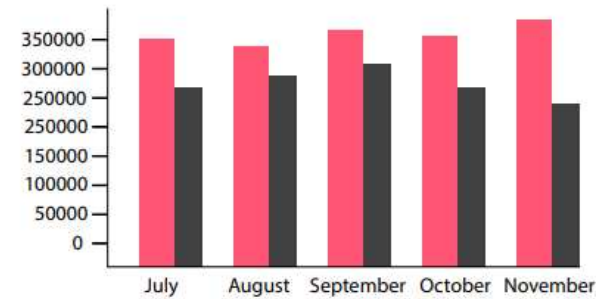
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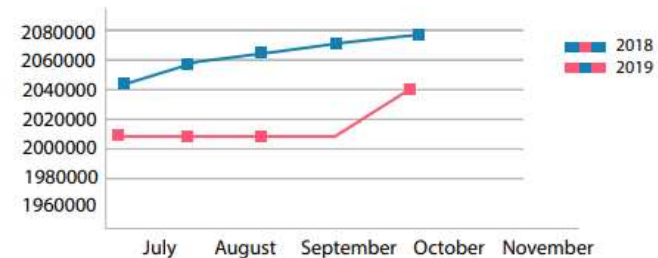


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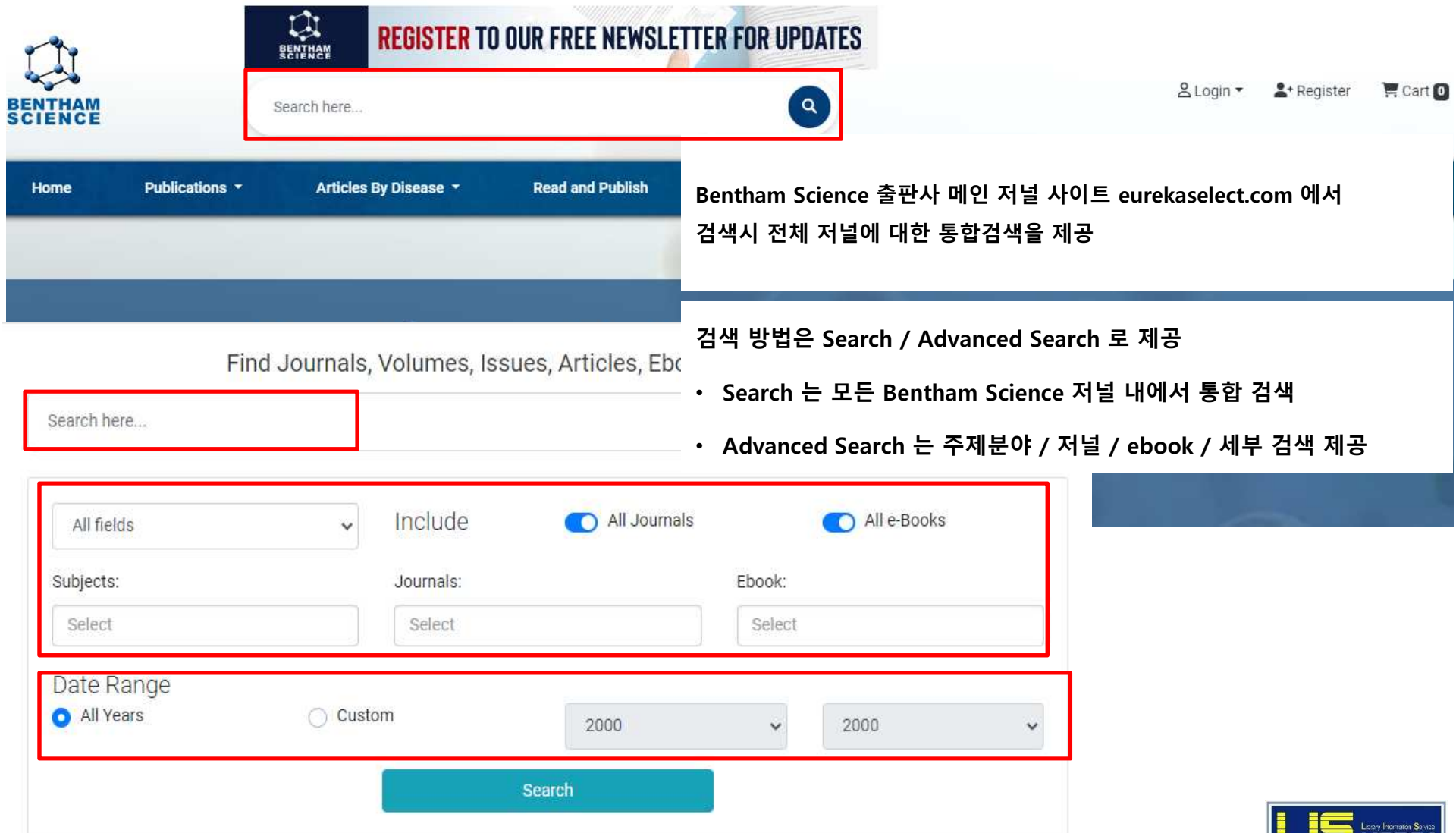
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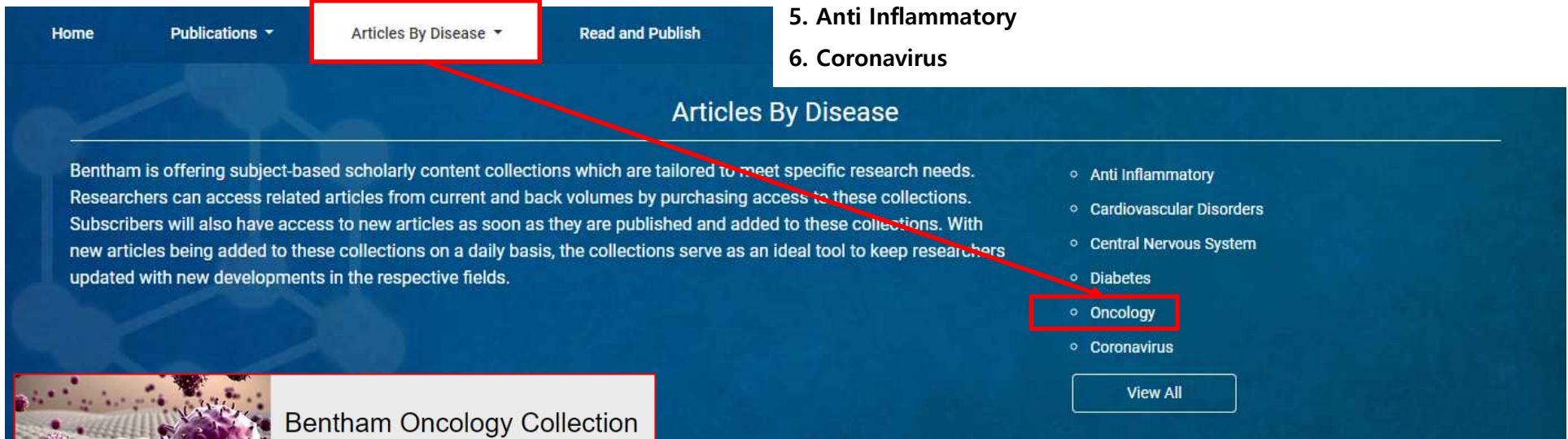
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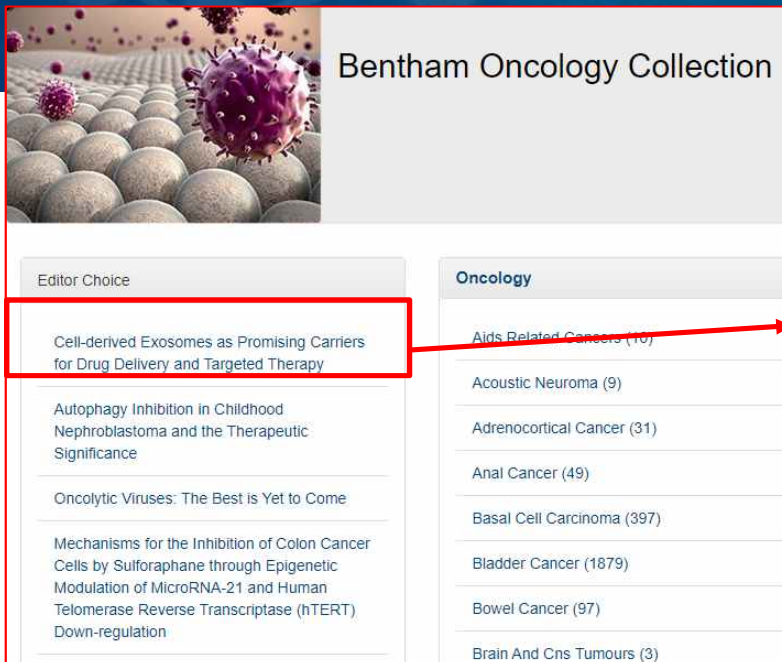
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Cell-derived Exosomes as Promising Carriers for Drug Delivery and Targeted Therapy

Author(s): Xinyi Wang, Haiyang Zhang, Haiou Yang, Ming Bai, Tao Ning, Shuang Li, Jialu Li, Ting Deng, Guoguang Ying*, Yi Ba*

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SYSTEMATIC REVIEW ARTICLE

Optimal Dose of Erenumab for Preventive Treatment of Episodic Migraine: A Systematic Review and Meta-Analysis

Yanbo Yang^{1,2*}, Mingjia Chen^{3*}, Da Wu⁴, Yue Sun⁵, Fan Jiang⁶, Zhouqing Chen^{7*} and Zhong Wang^{8*}

¹Department of Neurosurgery & Brain and Nerve Research Laboratory, The First Affiliated Hospital of Soochow University, Suzhou, Jiangsu Province, 215006, China; ²Department of Neurology and National Research Center for Aging and Medicine, Huashan Hospital, Fudan University, Shanghai 200040, China; ³Department of Neurosurgery, Chino-Japan Friendship Hospital, Beijing, 100020, China; ⁴Department of Neurosurgery, Xijing People's Hospital, Xijing 214200, China; ⁵School of Biology and Basic Medical Science of Soochow University, Suzhou, Jiangsu Province, 215006, China

Abstract: Background: Erenumab is a novel monoclonal calcitonin gene-related peptide receptor antibody that is used for the preventive treatment of migraine.
Objective: This study aimed to evaluate the overall safety, efficacy, and dose-response relationship of erenumab in patients with episodic migraine and patients with prior migraine treatment failures.
Methods: We searched randomized clinical trials on PubMed, Embase database, and Cochrane Library database. A pair-wise meta-analysis and Bayesian network analysis were performed.
Results: For efficacy outcomes, the network meta-analysis suggests that in comparison to erenumab 70 mg, participants who received erenumab 140 mg reported a significant decrease in monthly acute Migraine-Specific Medication Days (MSMD) and 50% increase in response rate, and erenumab was more likely to be ranked first for Monthly Migraine Days (MMD), MSMD, and 50% response rate. For safety outcomes, the network meta-analysis has found no significant difference between the 70 mg group and the 140 mg group measured by adverse events and serious adverse events. In the 140 mg erenumab group, a significant decrease in MMD and MSMD and 50% and 75% increase in response rate were reported in patients with ≥ 2 treatment failures compared to placebo. For safety outcomes, no significant difference was found between the 140 mg erenumab group and the placebo group.
Conclusion: Erenumab was effective in patients with episodic migraine. A total of 140 mg erenumab was associated with better efficacy outcomes without any increased risk for developing adverse events compared to 70 mg erenumab. Furthermore, 140 mg erenumab was effective in patients with prior migraine treatment failures.

Keywords: Calcitonin gene-related peptide receptor antagonist, erenumab, migraine, network meta-analysis, MSMD, MMD

1. INTRODUCTION

Migraine is one of the most common neurological disorders, with an estimated global prevalence of 15% [1]. It is manifested with recurrent attacks of unilateral, pulsatile headache that could be triggered by daily activities. A migraine attack usually lasts for 4 to 72 hours and is frequently accompanied by nausea, vomiting, photophobia, and phonophobia. Thus, patients may suffer from significant disabling pain and impaired quality of life.

In the past decade, multiple targets have been identified for migraine therapy. Among them, Calcitonin Gene-Related Peptide (CGRP) is considered one of the most promising targets [2]. CGRP is a 37-amino acid peptide produced through alternative RNA processing of the calcitonin gene, located in the neuronal tissue, especially C sensory fibers [3]. It has two forms, αCGRP and βCGRP. αCGRP is mainly expressed in the central and peripheral nervous system, while βCGRP is primarily found in the enteric nervous system [4]. Dimerization of Calcitonin Receptor-Like Protein (CLR) and Receptor Activity-Modifying Protein (RAMP) creates CGRP receptors [4], which are located in the trigeminal neurons, peripheral autonomic vascular smooth muscle cells, the brainstem, and the dura mater [5].

*Address correspondence to these authors at the Department of Neurosurgery, The First Affiliated Hospital of Soochow University, 155 Shou Street, Suzhou 215006, China. E-mails: yangyb163@163.com
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SYSTEMATIC REVIEW ARTICLE

Optimal Dose of Erenumab for Preventive Treatment of Episodic Migraine: A Systematic Review and Meta-Analysis

Yanbo Yang^{1,2*}, Mingjia Chen^{3*}, Da Wu⁴, Yue Sun⁵, Fan Jiang⁶, Zhouqing Chen^{7*} and Zhong Wang^{8*}

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Abstract: Background: Erenumab is a novel monoclonal calcitonin gene-related peptide receptor antibody that is used for the preventive treatment of migraine.
Objective: This study aimed to evaluate the overall safety, efficacy, and dose-response relationship of erenumab in patients with episodic migraine and patients with prior migraine treatment failures.
Methods: We searched randomized clinical trials on PubMed, Embase database, and Cochrane Library database. A pair-wise meta-analysis and Bayesian network analysis were performed.
Results: For efficacy outcomes, the network meta-analysis suggests that in comparison to erenumab 70 mg, participants who received erenumab 140 mg reported a significant decrease in monthly acute Migraine-Specific Medication Days (MSMD) and 50% increase in response rate, and erenumab was more likely to be ranked first for Monthly Migraine Days (MMD), MSMD, and 50% response rate. For safety outcomes, the network meta-analysis has found no significant difference between the 70 mg group and the 140 mg group measured by adverse events and serious adverse events. In the 140 mg erenumab group, a significant decrease in MMD and MSMD and 50% and 75% increase in response rate were reported in patients with ≥ 2 treatment failures compared to placebo. For safety outcomes, no significant difference was found between the 140 mg erenumab group and the placebo group.
Conclusion: Erenumab was effective in patients with episodic migraine. A total of 140 mg erenumab was associated with better efficacy outcomes without any increased risk for developing adverse events compared to 70 mg erenumab. Furthermore, 140 mg erenumab was effective in patients with prior migraine treatment failures.

Keywords: Calcitonin gene-related peptide receptor antagonist, erenumab, migraine, network meta-analysis, MSMD, MMD

1. INTRODUCTION

Migraine is one of the most common neurological disorders, with an estimated global prevalence of 15% [1]. It is manifested with recurrent attacks of unilateral, pulsatile headache that could be triggered by daily activities. A migraine attack usually lasts for 4 to 72 hours and is frequently accompanied by nausea, vomiting, photophobia, and phonophobia. Thus, patients may suffer from significant disabling pain and impaired quality of life.

In the past decade, multiple targets have been identified for migraine therapy. Among them, Calcitonin Gene-Related Peptide (CGRP) is considered one of the most promising targets [2]. CGRP is a 37-amino acid peptide produced through alternative RNA processing of the calcitonin gene, located in the neuronal tissue, especially C sensory fibers [3]. It has two forms, αCGRP and βCGRP. αCGRP is mainly expressed in the central and peripheral nervous system, while βCGRP is primarily found in the enteric nervous system [4]. Dimerization of Calcitonin Receptor-Like Protein (CLR) and Receptor Activity-Modifying Protein (RAMP) creates CGRP receptors [4], which are located in the trigeminal neurons, peripheral autonomic vascular smooth muscle cells, the brainstem, and the dura mater [5].

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