Bioorganic Chemistry
Volume 153, December 2024, 107803

Review Article

Clinical and preclinical advances in PSMA-Directed Antibody-Drug conjugates (ADCs): Current status and hope for the future

Yousef Mirzaei [a], Ali Hussein Mer [b], Bahia fattah Maran [c], Leila Omidvar [d], Fatemeh Misamogooe [e], Zahra Amirkhani [e], Nafiseh Javaheri Haghighi [e], Nader Bagheri [f], Zahra Keshtkaran [g], Behzad Rezaei [h], Farshad Bargrizaneh [i], Saeed Jahandideh [j], Nesa Barpour [k], Hosein Shahsavarani [l m], Ahmadreza Bazyari [n] ✉, Meghdad Abdollahpour-Alitappeh [o] ✉

Abstract

Prostate-specific membrane antigen (PSMA) is a type II membrane glycoprotein overexpressed in a variety of tumors, especially in nearly all prostate cancers, which makes it a potentially attractive antigen for targeted cancer therapies. More importantly, PSMA, due to no shedding into circulation and efficient internalization after antibody binding, becomes a potential target for antibody-drug conjugates (ADCs), a valid and emerging paradigm of cancer treatment. Four and eight PSMA-directed ADCs have been or are currently being investigated in clinical trials (three of which failed to confirm the promising results while one is currently being evaluated in an ongoing clinical study) and preclinical studies, respectively, for the treatment of PSMA-positive solid tumors, especially prostate cancer. The present study aims to completely review clinical- and preclinical-stage PSMA-directed ADCs.

Graphical abstract

Prostate-specific membrane antigen (PSMA)-directed antibody drug conjugates (ADCs)