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Licensed monoclonal antibodies and associated challenges

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Abstract.
Monoclonal antibodies (mAbs) are the leading class of targeted therapeutics and remarkably effective in addressing autoimmune diseases, inflammations, infections, and various types of cancer. Several mAbs approved by US food and drug administration (FDA), are available on the market and a number are pending for approval. Luckily, FDA approved mAbs have played a pivotal role in the treatment and prevention of lethal diseases. However, claiming that licensed mAbs are 100% safe is still debatable, because infections, malignancies, anaphylactoid, and anaphylactic reactions are the more frequently associated adverse events. To evaluate benefit to risk ratio of mAbs, it is important for the clinical research staff or physicians to monitor and follow-up the patients who are receiving mAbs dozes. It is recommended that patients, physicians, biopharmaceutical companies, and researchers should keep in touch to highlight and resolve antibody-based adverse events. In this review we underscore the associated challenges of mAbs, approved by FDA from 2007–2014.

Keywords: FDA approved mAbs, adverse events of mAbs, antibody-based therapeutics, safety and risks of mAbs, licensed mAbs and associated challenges

1. Introduction

Kohler and Milstein have inaugurated monoclonal antibodies (mAbs) production technology with their seminal work on hybridoma [1]. Further advancement in the field of genomics and proteomics enabled the researchers to develop mouse, chimeric, humanized, and ultimately fully human mAbs. Variable regions of chimeric and complementarity determining regions (CDRs) of humanized mAbs are derived from murine origin. On the other hand, fully human mAbs are derived purely from human sequences. International nonproprietary (INN) names of mAbs ends with suffixes -ximab, -zumab, and -mumab respectively. Table 1 enlist some of the mAbs approved by US food and drug administration (FDA) from 2007–2014.

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Target specificity and low toxicity have made mAbs fast and growing class of therapeutics and preventive agents. Amino acid sequences of mAbs have been tailored to reduce the antigenicity and enhance the specificity and functionality. Majority of the mAbs available on the market of US and Europe have been produced in murine myeloma cell lines (e.g. SP2/0, NS0), Chinese hamster ovary (CHO) cells, phage display, and *E. coli* cells [2]. Unfortunately, mAbs derived from mammalian cell lines are expensive, which is the remaining foremost obstacle in the development of new biopharmaceuticals. However, fragment antibodies such as scFv, Fab, and diabodies have been easily produced in yeast, phage display, and *E. coli* at reduced cost [3]. Luckily, antibody-based therapeutics, including, conjugated antibodies, intact antibodies and fragment antibodies have also been licensed for marketing [4].

Mechanism of action of mAbs include, antigen crosslinking, activation of apoptosis, and blockade of ligand-receptors interaction or signalling pathways (Fig. 1). Several mAbs, for instance, eculizumab,

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