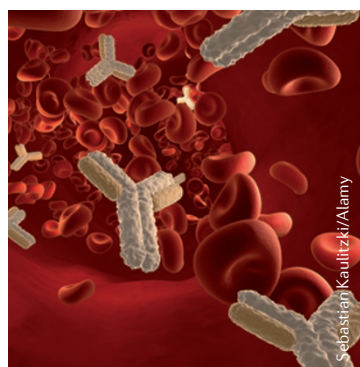


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B iologics account for almost a third of the novel drugs currently in clinical trials and a growing number of new drug approvals. However, despite the greater target specificity and resulting generally superior safety profiles of biologics compared with small molecules, adverse reactions continue to pose a challenge. In their Review, Park and colleagues discuss serious side effects that have been associated with immunomodulatory biologics, such as increased risk for infection, malignancy, cytokine release syndrome and immunogenicity. They assess the currently available models and tools that may be used to predict such adverse reactions and consider approaches to mitigate them. Animal models are important tools in the discovery and development of therapies for rare diseases, particularly given the limited numbers of patients available for enrolment in clinical trials. In their Review, Sepodes and colleagues from the European Medicines Agency's Committee for Orphan Medicinal Products assess the advantages and limitations of animal models for metabolic, neuromuscular and ophthalmological rare diseases, with the aim of identifying which models are most appropriate for the preclinical evaluation of therapeutic candidates. Although numerous clinical trials testing adenosine-receptor targeted drugs in various indications have been initiated, only one agent — the adenosine A_{2A} receptor agonist regadenoson, a coronary vasodilator used for myocardial perfusion imaging — has so far gained approval from the US Food and Drug Administration. In their Review, Fredholm and colleagues focus on the biological challenges hampering the development of compounds targeting adenosine signalling and highlight those that are currently undergoing clinical investigation for the treatment of pathologies including Parkinson's disease, chronic heart failure, inflammatory and autoimmune disorders.

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