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CD123: a paradigmatic target for immunotherapeutic treatment modalities

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Abstracts

CD123: a paradigmatic target for immunotherapeutic treatment modalities

This report describes and evaluates the competitive landscape of CD123-targeted immunotherapeutics based on different treatment modalities. CD123, or the interleukin-3 receptor alpha subunit (IL-3R?) is differentially and significantly overexpressed in a large proportion (up to 93 %) of patients with acute myeloid leukemia (AML) and has been identified as a marker of quiescent leukemic stem cells with very low or negligible expression in normal CD34+ progenitor cells. However, CD123 is normally expressed at low levels on some endothelial cells, monocytes, plasmocytoid dendritic cells (pDC), basophils, and myeloid progenitors. This expression profile makes CD123 an attractive surface target for novel antileukemic therapies.

Clinical experience showed that the simple blockade of interleukin-3 signalling by a naked antibody was an insufficient therapeutic strategy which opened the way for generation and devleopment of empowered anti-CD123 immunotherapeutics using emerging novel treatment modalities including:

Fc-engineered antibodies;

Immunotoxins;

Antibody-drug conjugates;

T-cell redirecting bispecific antibodies;

Chimeric Antigen Receptor (CAR) engineered T-cells.

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This report describes the profiles of 16 different anti-CD123 immunotherapeutics based on different treatment modalities. The FDA recently acknowledged the anti-CD123 treatment approach by granting Breakthrough Therapy designation to the immunotoxin SL-401 for the treatment of blastic plasmacytoid dendritic cell neoplasm (BPDCN). SL-401 is the most advanced of 15 different anti-CD123 immunotherapeutis, seven of them are in earlier clinical develoment and further four are being prepared for clinical evaluation.

This report describes and analyzes the

Target Background & Scientific Rationale

Preclinical Proof-of-Concept of Anti-CD123 Immunotherapeutics

Clinical Experience with CD123-Targeted Treatment Modalities

Target and Treatment Modality Safety Concerns of anti-CD123 Immunotherapeutics

Competitive Landscape

Profiles of Anti-CD123 Immunotherapeutics

Company Profiles

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