

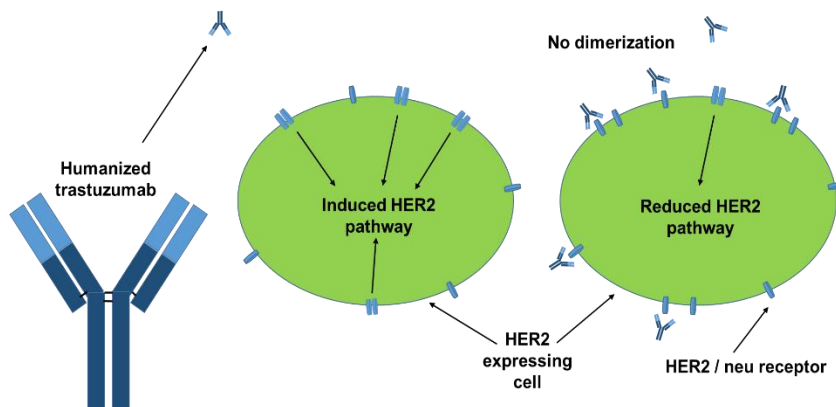
Trastuzumab – Fact Sheet

Molecule

Trastuzumab (Herceptin®) is a humanized monoclonal IgG1 antibody comprised of a tetramer of two heavy and two light chains with one N-glycosylation site per heavy chain.

Mode of Action

The human epidermal growth factor 2 (HER2) pathway promotes cell growth and cell division via HER2 receptor. When HER2 is over-induced and dimerized, cell growth accelerates, which can lead to tumor formation. Trastuzumab binds to domain IV of the extracellular segment of HER2 receptor preventing it from dimerization and activation of its signaling pathways.



Indication

Herceptin® is indicated for the treatment of HER2-positive metastatic breast cancer patients. It is also approved for adjuvant treatment of HER2 over-expressing breast cancer and metastatic gastric cancer.

Patent Situation

Primary patents for Herceptin® expired in 2014 in EU and will expire in US in 2019. Further patents related to dosage and composition of the drug are under litigation and already invalidated in some countries.

Market and Competitive Field

Roche's Herceptin®, the originator product, was approved by FDA in 1998 and by EMA in 2000. Herceptin® had worldwide sales of 6.28 billion € in 2018. Several biosimilars are approved or submitted for approval at FDA and EMA.

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| | | Trastuzumab |
| | | Herceptin® |
| | | Herzuma®, Kanjinti™, Ogivri™, Ontruzant® Trazimera™ |
| | Clone selection/ comparability | |
| HPLC | Separation based on size (SE-HPLC) | |
| | Separation based on hydrophobicity (RP-HPLC) | |
| | Detection of charge variants (CEX-HPLC) | |
| Binding | Binding to cell surface expressed target (Flow cytometry) | |
| | Binding to soluble target (ELISA) | |
| | Binding to specific antibody or antigen (SPR-BIACORE, ELISA) | |
| | Affinity/ kinetic to recombinant target (SPR-BIACORE) | |
| Effector function | Binding to C1q, ¹CDC surrogate (ELISA) | |
| | Affinity to recombinant Fc-receptors (SPR-BIACORE) | |
| | Reporter gene assays, ²ADCC surrogate (Luminescence) | |
| | ¹CDC (Flow cytometry) | |
| | ²ADCC (DELFI, Fluorescence) | |
| | Additional bioassays (Luminescence, fluorescence) | Anti-proliferation |
| Gly | Glyco-pattern with Lectin Microarray (45 different lectins) | |
| | (Pre)clinical application | |
| Clinics | Pharmacokinetics – PK (ECL, ELISA) | |
| | Pharmacodynamics – PD (ECL, ELISA, flow cytometry, bioassay) | |
| | Immunogenicity - ³ADAs (ECL, Biacore, ELISA, neutr. assay) | |

¹CDC = Complement Dependent Cytotoxicity
²ADCC = Antibody Dependent Cellular Cytotoxicity
³ADA = Anti-Drug Antibody

VelaLabs portfolio