Glossary A-Z

Wirkstoffe M

Magrolimab/ anti-CD47 monoclonal antibody Hu5F9-G4

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According to the NCI website, Magrolimab is a humanized monoclonal antibody targeting the human cell surface antigen CD47, with potential immunostimulating and antineoplastic activities. Upon administration, anti-CD47 monoclonal antibody Hu5F9-G4 selectively binds to CD47 expressed on tumor cells and blocks the interaction of CD47 with its ligand signal regulatory protein alpha (SIRPa), a protein expressed on phagocytic cells. This prevents CD47/SIRPa-mediated signaling, allows the activation of macrophages, through the induction of pro-phagocytic signaling mediated by calreticulin, which is specifically expressed on the surface of tumor cells, and results in specific tumor cell phagocytosis. In addition, blocking CD47 signaling activates an anti-tumor T-lymphocyte immune response and T-cell mediated cell killing. CD47, a tumor associated antigen expressed on normal, healthy hematopoietic stem cells (HSC), is overexpressed on the surface of a variety of cancer cells. Expression of CD47, and its interaction with SIRP-alpha, leads to inhibition of macrophages and protects cancer cells from phagocytosis thereby allowing cancer cells to proliferate. Check for active clinical trials using this agent. (NCI Thesaurus)

More Information in English:

Link to Drug Information Portal, a service of the U.S. National Library of Medicine, National Institutes of Health
Link to National Cancer Institute

Margetuximab

According to the NCI website, margetuximab is a Fc-domain optimized IgG monoclonal antibody directed against the human epidermal growth factor receptor 2 (HER2) with potential immunomodulating and antineoplastic activities. After binding to HER2 on the tumor cell surface, margetuximab may induce an antibody-dependent cell-mediated cytotoxicity (ADCC) against tumor cells overexpressing HER2. HER2, a tyrosine kinase receptor, is overexpressed by many cancer cell types. Compared to other anti-HER2 monoclonal antibodies, the Fc domain of MGAH22 is optimized with increased binding to the activating Fcgamma receptor IIIA (CD16A), expressed on cells such as natural killer (NK) cells and macrophages, thereby mediating an enhanced ADCC; the Fc domain also shows decreased binding to the inhibitory Fcgamma receptor IIB (CD32B). Check for active clinical trials using this agent. (NCI Thesaurus)

More Information in English:

Link to Drug Information Portal, a service of the U.S. National Library of Medicine, National Institutes of Health
Link to National Cancer Institute

Wiki

MBG453 - Anti-TIM-3 Monoclonal Antibody

According to the NCI website, MBG453 (Anti-TIM-3 Monoclonal Antibody MBG453) is an inhibitor of the inhibitory T-cell receptor T-cell immunoglobulin and mucin domain-containing protein 3 (TIM-3; hepatitis A virus cellular receptor 2; **HAVCR2**), with potential immune checkpoint inhibitory and antineoplastic activities. Upon administration, the anti-TIM-3 checkpoint inhibitor MBG453 binds to TIM-3 expressed on certain immune cells, including tumor infiltrating lymphocytes (TILs). This abrogates T-cell inhibition, activates antigen-specific T-lymphocytes and enhances cytotoxic T-cell-mediated tumor cell lysis resulting in a reduction in tumor growth. TIM-3, a transmembrane protein expressed on certain T-cells, is associated with tumor-mediated immune suppression.

Link to National Cancer Institute

Wiki

Relationships with other NCI Thesaurus Concepts

MGD013 - anti-PD-1/anti-LAG-3 DART protein

According to the NCI website, MGD013 is an Fc-bearing, humanized antibody-like protein that specifically recognizes the immune checkpoint molecules programmed cell death 1 (PD-1; PD1; PDCD1; CD279; Programmed Death 1) and lymphocyte activation gene-3 (LAG-3; LAG3; CD223), with potential T-lymphocyte immunomodulatory and antineoplastic activities. Upon administration, the anti-PD-1/anti-LAG-3 dual-affinity re-targeting (DART) protein MGD013 specifically binds to both PD-1 and LAG-3, which are both expressed on T cells. The dual blockade of the PD-1 and LAG-3 pathways enables potent activation of a cytotoxic T-lymphocyte (CTL)-mediated immune response against tumor cells. PD-1 and LAG-3 play key roles in suppressing T-cell activation. Check for active clinical trials using this agent. (NCI Thesaurus)

Link to National Cancer Institute

MGD019 bispecific PD-1 x CTLA-4 DART®

According to the NCI website, anti-PD-1/anti-CTLA-4 DART protein MGD019 is a hinge stabilized immunoglobulin G4 (IgG4) tetravalent bispecific antibody-like protein directed against the human negative immunoregulatory checkpoint receptors programmed cell death protein 1 (PD-1; PDCD1; CD279) and cytotoxic T-lymphocyte-associated antigen 4 (CTLA4; CTLA-4), with potential immune checkpoint inhibitory and antineoplastic activities. Upon administration, the anti-PD-1/anti-CTLA4 dual-affinity re-targeting (DART) protein MGD019 specifically binds to both PD-1 and CTLA4 expressed on tumor-infiltrating lymphocytes (TILs) and inhibits the PD-1- and CTLA4-mediated downregulation of T-cell activation and proliferation. Dual blockade of PD1 and CTLA4 pathways provides enhanced activity against PD1+CTLA4+ double positive cells and may increase T-cell activation and proliferation compared to the blockade of either immune checkpoint alone. Check for active clinical trials using this agent. (NCI Thesaurus)

More Information in English:

Inxight: Drugs (NIH)

AdisInsight
Link to National Cancer Institute

Mechlorethamine

According to the NCI the hydrochloride salt of mechlorethamine, is a nitrogen mustard and an analogue of sulfur mustard, with antineoplastic and immunosuppressive activities. Mechlorethamine is metabolized to an unstable, highly reactive ethyleniminium intemediate that alkylates DNA, particularly the 7 nitrogen of guanine residues, resulting in DNA base pair mismatching, DNA interstrand crosslinking, the inhibition of DNA repair and synthesis, cell-cycle arrest, and apoptosis.

Indikationen/Anwendungsmöglichkeiten gemäss Chemocare.com:
As part of combination regimens in treatment of Hodgkin's disease, non-Hodgkin's lymphoma.
As palliative chemotherapy in lung and breast cancers.
As a lotion to skin lesions of mycosis fungoides (cutaneous T-cell lymphoma).

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Zytostatikum

Megestrol

According to the NCI website Mimicking the action of progesterone, megestrol binds to and activates nuclear progesterone receptors (PRs) in the reproductive system and pituitary.

IIndikationen/Anwendungsmöglichkeiten gemäss folgendem Link (Medien Plus):
Megestrol tablets are used to relieve the symptoms and reduce the suffering caused by advanced breast cancer and advanced endometrial cancer (cancer that begins in the lining of the uterus). Megestrol suspension is used to treat loss of appetite, malnutrition, and severe weight loss in patients with acquired immunodeficiency syndrome (AIDS). Megestrol should not be used to prevent loss of appetite and severe weight loss in patients who have not yet developed this condition. Megestrol is a man-made version of the human hormone progesterone. It treats breast cancer and endometrial cancer by affecting female hormones involved in cancer growth. It increases weight gain by increasing appetite.

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MEK 162

According to the NCI website the MEK inhibitor MEK162 isan orally available inhibitor of mitogen-activated protein kinase kinases 1 and 2 (MEK1/2) with potential antineoplastic activity. MEK inhibitor MEK162, noncompetitive with ATP, binds to and inhibits the activity of MEK1/2.

Inhibition of MEK1/2 prevents the activation of MEK1/2-dependent effector proteins and transcription factors, which may result in the inhibition of growth factor-mediated cell signaling. This may eventually lead to an inhibition of tumor cell proliferation and an inhibition in production of various inflammatory cytokines including interleukin-1, -6 and tumor necrosis factor. MEK1 and MEK2 are dual-specificity threonine/tyrosine kinases that play key roles in the activation of the RAS/RAF/MEK/ERK pathway and are often upregulated in a variety of tumor cell types.

Link to Drug Information Portal, a service of the U.S. National Library of Medicine, National Institutes of Health

Link to National Cancer Institute

Mek inhibitors

Melphalan

Alkeran®

Indikationen/Anwendungsmöglichkeiten gemäss Arzneimittel-Kompendium der Schweiz®:

Multiples Myelom.

Fortgeschrittenes Ovarialkarzinom.

Mammakarzinom.

Alkeran kann in Mono- oder Kombinationstherapie beim fortgeschrittenen Mamma-Karzinom eine therapeutische Wirkung haben.

Regionale arterielle Perfusion bei lokalisiertem, malignem Melanom oder Weichteilsarkom der Extremitäten.

Polycythaemia rubra vera: Alkeran hat sich bei einigen Patienten als wirksam erwiesen.

Hochdosiertes Alkeran i.v. als Vorbereitung zur hämopoetischen Stammzell-Transplantation wird

entweder allein oder in Kombination mit Radiotherapie und/oder mit anderen zytostatischen Mitteln angewendet zur Konsolidierung des mit konventioneller Behandlung erreichten Resultates bei Neuroblastom bei Kindern und Jugendlichen und bei Multiplem Myelom.

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Mercaptopurin

According to the NCI mercaptopurine is a thiopurine-derivative antimetabolite with antineoplastic and immunosuppressive activities.

Indikationen/Anwendungsmöglichkeiten gemäss Arzneimittel-Kompendium der Schweiz®:

Zur Behandlung in Kombination mit LHRH Agonisten und Prednison oder Prednisolon bei Patienten mit fortgeschrittenem metastasierenden Prostatakarzinom bei Progredienz nach Behandlung mit Docetaxel.c

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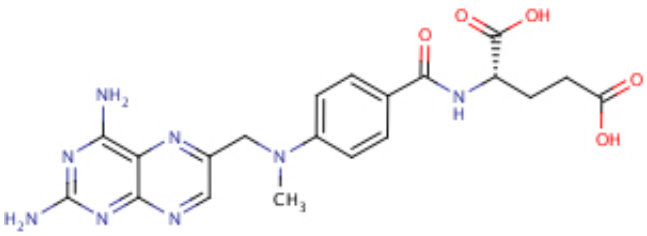
Antimetaboliten

Methotrexate



According to the NCI methotrexate is an antimetabolite and antifolate agent with antineoplastic and immunosuppressant activities. Methotrexate binds to and inhibits the enzyme dihydrofolate reductase, resulting in inhibition of purine nucleotide and thymidylate synthesis and, subsequently, inhibition of DNA and RNA syntheses. Methotrexate also exhibits potent immunosuppressant activity although the mechanism(s) of actions is unclear.

Indikationen/Anwendungsmöglichkeiten gemäss Arzneimittel-Kompendium der Schweiz®:

Behandlung hämatologischer Neoplasien wie akute lymphatische und myeloische Leukämie und Non-Hodgkin-Lymphom sowie solider Tumoren wie Mammakarzinom, Bronchialkarzinom, maligne Kopf- und Halstumoren, Osteosarkom, Chorionkarzinom und andere trophoblastische Tumoren, Blasenkarzinom.
Behandlung von Autoimmunerkrankungen wie z.B. rheumatoide Arthritis.
Behandlung schwerer Fälle unkontrollierbarer Psoriasis, welche gegenüber konventioneller Therapie resistent sind.

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Zytostatikum

Midostaurin

According to the NCI website Midostaurin is a synthetic indolocarbazole multikinase inhibitor with potential antiangiogenic and antineoplastic activities. Midostaurin inhibits protein kinase C alpha **(PKCalpha), vascular endothelial growth factor receptor 2 (VEGFR2), c-kit, platelet-derived growth factor receptor (PDGFR) and FMS-like tyrosine kinase 3 (FLT3) tyrosine kinases, which may result in disruption of the cell cycle, inhibition of proliferation, apoptosis, and inhibition of angiogenesis in susceptible tumors.**

Link to Drug Information Portal, a service of the U.S. National Library of Medicine, National Institutes of Health
Link to National Cancer Institute

The IUPHAR/BPS Guide to PHARMACOLOGY

Link to Wiki

Mek inhibitors

Mirvetuximab soravtansine

According to the NCI website,

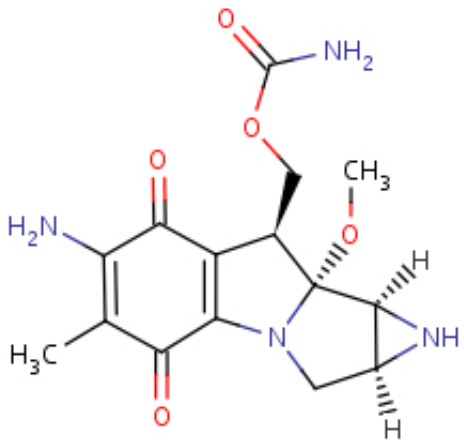
Mirvetuximab soravtansine is an immunoconjugate consisting of the humanized monoclonal antibody M9346A against folate receptor 1 (FOLR1) conjugated, via the disulfide-containing cleavable linker sulfo-SPDB, to the cytotoxic maytansinoid DM4, with potential antineoplastic activity. The anti-FOLR1 monoclonal antibody moiety of mirvetuximab soravtansine targets and binds to the cell surface antigen FOLR1. After antibody-antigen interaction and internalization, the immunoconjugate releases DM4, which binds to tubulin and disrupts microtubule assembly/disassembly dynamics, thereby inhibiting cell division and cell growth of FOLR1-expressing tumor cells. FOLR1, a member of the folate receptor family is overexpressed on a variety of epithelial-derived cancer cells. The sulfo-SPDB linker prevents cleavage in the bloodstream and may improve this agent's efficacy in multidrug resistant tumor cells. Check for active clinical trials using this agent. (NCI Thesaurus)

More Information in English:

Link to Drug Information Portal, a service of the U.S. National Library of Medicine, National Institutes of Health
Link to National Cancer Institute

Wiki
Link to European Medicines Agency (EMEA)

Mitomycin



According to the NCI mitomycin C is a methylazirinopyrroloindoledione antineoplastic antibiotic isolated from the bacterium Streptomyces caespitosus and other Streptomyces bacterial species. Bioreduced mitomycin C generates oxygen radicals, alkylates DNA, and produces interstrand DNA cross-links, thereby inhibiting DNA synthesis. Preferentially toxic to hypoxic cells, mitomycin C also inhibits RNA and protein synthesis at high concentrations.

Indikationen/Anwendungsmöglichkeiten gemäss Medlineplus Druginfo:
This medication is used to treat adenocarcinoma of the stomach and pancreas.

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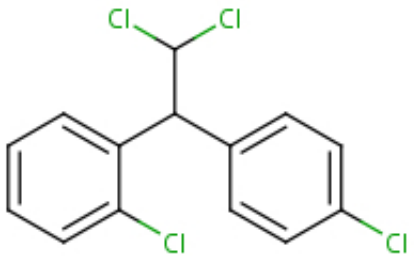
Chemotherapy

Mitotane



Lysodren®; According to the NCI mitotane is a synthetic derivative of the insecticide dichlorodiphenyl trichloroethane (DDT) with anti-adrenocorticoid properties. Following its metabolism in the adrenal cortex to a reactive acyl chloride intermediate, mitotane covalently binds to adrenal proteins, specifically inhibiting adrenal cortical hormone production.

Indikationen/Anwendungsmöglichkeiten gemäss Arzneimittel-Kompendium der Schweiz®:

Symptomatische Behandlung des fortgeschrittenen (nicht-resezierbaren, metastasierenden oder rezidivierenden) Nebennierenrindenkarzinoms.
Die Wirkung von Lysodren bei nicht-funktionellem Nebennierenrindenkarzinom ist nicht belegt.

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Zytostatikum

Mitoxantrone

Mitoxantron Sandoz®, Novantron®; According to the NCI website Mitoxantrone intercalates into and crosslinks DNA, thereby disrupting DNA and RNA replication. This agent also binds to topoisomerase II, resulting in DNA strand breaks and inhibition of DNA repair.

Indikationen/Anwendungsmöglichkeiten gemäss Arzneimittel-Kompendium der Schweiz®:

Metastasierendes Mamma-Karzinom.
Non-Hodgkin-Lymphome.
Akute Leukämie der Erwachsenen.
Blastenschub der chronischen myeloischen Leukämie.
Hepatozelluläres Karzinom.
Palliative Therapie des fortgeschrittenen hormonrefraktären Prostata-Karzinoms mit Schmerzzuständen, in Kombination mit niedrig dosierten Steroiden (Prednison).
Mitoxantron Sandoz ist indiziert für die Behandlung von gehfähigen Patienten mit Multipler Sklerose bei rasch progredientem Verlauf und Versagen oder Unverträglichkeit einer Vortherapie mit Immunmodulatoren. Die rasche Progression kann sich entweder als kontinuierliche Zunahme neurologischer Defizite mit und ohne überlagerte Schübe (sekundär progredienter Verlauf) oder als rasch akkumulierende Defizite aufgrund sich unvollständig zurückbildender Schübe (schubförmiger Verlauf mit Residuen) äussern.

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Zytostatikum

MK 4830

According to the NCI website, the anti-ILT4 monoclonal antibody MK-4830 is a human monoclonal antibody directed against the inhibitory immune checkpoint receptor immunoglobulin-like transcript 4 (ILT4; leukocyte immunoglobulin-like receptor subfamily B member 2; LILRB2; lymphocyte immunoglobulin-like receptor 2; LIR2; monocyte/macrophage immunoglobulin-like receptor 10; MIR-10; CD85d), with potential immunomodulating and antineoplastic activities. Upon administration, anti-ILT4 monoclonal antibody MK-4830 targets and binds to ILT4. This prevents the binding of ILT4 ligands to their receptor and prevents ILT4-mediated signaling. This abrogates the immunosuppressive activities of ILT4 in the tumor microenvironment (TME), activates the expression of pro-inflammatory cytokines, including GM-CSF and tumor necrosis factor alpha (TNFalpha), and enhances a cytotoxic T-lymphocyte (CTL)-mediated anti-tumor immune response. ILT4, plays a key role in tumor immune evasion. ILT4, a transmembrane protein and inhibitory member of the immunoglobulin-like transcript (ILT) family of proteins, is expressed primarily by myeloid cells, including monocytes, macrophages, dendritic cells (DCs) and granulocytes, and certain tumor cells. Check for active clinical trials using this agent. (NCI Thesaurus)

More Information in English:

AdisInsight
Link to National Cancer Institute

MK-6482

AdisInsight