Kantonsspital St.Gallen

Prof. Christoph Driessen

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research profile

academic status	Oberarzt mbF/Oberärztin mbF
department	Interdisziplinäre Medizinische Dienste
faculty	Clinical Trials Unit
position	Head Clinical Trials Unit Oberarzt mbF Oncology/Hematology
fields of research	Design and application of small-molecule protease inhibitors as a) research tools to dissect the biology of protease networks (functional proteomics) b) potential therapeutic agents in cancer and autoimmunity (combinatorial chemisty-approach, high-throughput screening)

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research profile

former positions	01/96 - 06/96: Clinical Resident (Assistenzarzt), Department of Rheumatology and Clinical Immunology, University of Freiburg i.Br., Medical Center, Prof. H.H. Peter 07/96 - 04/98 and 05/00 - 12/05: Clinical Resident (Assistenzarzt, Facharzt) Department of Hematology/Oncology/Immunology/Rheumatology, University of Tübingen Medical Center 04/98 - 05/00: Research Fellow, Harvard Medical School, Immunology and Protease Biology, Prof. Hidde Ploegh 12/04: Board-certified in Internal Medicine (Facharzt Innere Medizin) (Zusatzbezeichnung Hämatologie/Onkologie) 12/05: Hability of Internal Medicine 01/06: Consulting Hematologist/Oncologist (Oberarzt), Associate Professor, Department of Hematology/Oncology/Immunology, University of Tübingen Medical Center (Head: Prof. L. Kanz) 10/06: Board-certified for Haematology/Oncology 06/00 - present: Head of Laboratory for Immunology and Protease Biology Since 11/06: Department of Oncology/Hematology Kantonsspital St.Gallen (KSSG) Since 07/08: Head of Clinical Trials Unit Kantonsspital St.Gallen (KSSG), Senior mbf
affiliations	German Society for Immunbiology American Society for Hämatology
awards	2008: Nycomed Research Award

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publications

	title
journal paper/ review	Kraus M, Bader J, Geurink P P, Weyburne E S, Mirabella A C, Silzle T, Shabaneh T B, van der Linden W A, de Bruin G, Haile S, van Rooden E, Appenzeller C, Li N, Kisselev A F, Overkleeft H, Driessen C. The novel β2-selective proteasome inhibitor LU-102 synergizes with bortezomib and carfilzomib to overcome proteasome inhibitor resistance of myeloma cells. Haematologica 2015; 100:1350-60.
	de Bruin G, Huber E M, Xin B T, van Rooden E J, Al-Ayed K, Kim K B, Kisselev A F, Driessen C, van der Stelt M, van der Marel G A, Groll M, Overkleeft H S. Structure-based design of β1i or β5i specific inhibitors of human immunoproteasomes. J Med Chem 2014; 57:6197-209.
	Tornatore L, Sandomenico A, Raimondo D, Low C, Rocci A, Tralau-Stewart C, Capece D, D'Andrea D, Bua M, Boyle E, van Duin M, Zoppoli P, Jaxa-Chamiec A, Thotakura A K, Dyson J, Walker B A, Leonardi A, Chambery A, Driessen C, Sonneveld P, Morgan G, Palumbo A, Tramontano A, Rahemtulla A, Ruvo M, Franzoso G. Cancer-Selective Targeting of the NF-κB Survival Pathway with GADD45β/MKK7 Inhibitors. Cancer Cell 2014; 26:495-508.
	Engelhardt M, Terpos E, Kleber M, Gay F, Wäsch R, Morgan G, Cavo M, van de Donk N, Beilhack A, Bruno B, Johnsen H E, Hájek R, Driessen C, Ludwig H, Beksac M, Boccadoro M, Straka C, Brighen S, Gramatzki M, Larocca A, Lokhorst H, Magarotto V, Morabito F, Dimopoulos M A, Einsele H, Sonneveld P, Palumbo A, European Myeloma Network . European Myeloma Network recommendations on the evaluation and treatment of newly diagnosed patients with multiple myeloma. Haematologica 2014; 99:232-42.
	Kraus M, Bader J, Overkleeft H, Driessen C. Nelfinavir augments proteasome inhibition by bortezomib in myeloma cells and overcomes bortezomib and carfilzomib resistance. Blood Cancer J 2013; 3:e103.

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publications

	title
journal paper/ review	Kraus M, Müller-Ide H, Rückrich T, Bader J, Overkleeft H, Driessen C. Ritonavir, nelfinavir, saquinavir and lopinavir induce proteotoxic stress in acute myeloid leukemia cells and sensitize them for proteasome inhibitor treatment at low micromolar drug concentrations. Leuk Res 2013; 38:383-92.
	Gallerani E, Zucchetti M, Brunelli D, Marangon E, Noberasco C, Hess U, Delmonte A, Martinelli G, Böhm S, Driessen C, De Braud F, Marsoni S, Cereda R, Sala F, D'Incalci M, Sessa C. A first in human phase I study of the proteasome inhibitor CEP-18770 in patients with advanced solid tumours and multiple myeloma. Eur J Cancer 2012; 49:290-6.
	Hundsberger T, Cogliatti S B, Kleger G R, Fretz C, Gähler A, Anliker M D, Fournier J Y, von Moos R, Tettenborn B, Driessen C. Intravascular lymphoma mimicking cerebral stroke: report of two cases. Case Rep Neurol 2011; 3:278-283.
	Engelhardt M, Udi J, Kleber M, Spencer A, Rocci A, Knop S, Bruno B, Bringhen S, Pérez-Simón J A, Zweegman S, Driessen C, Patriarca F, Gramatzki M, Terpos E, Sezer O, Kropff M, Straka C, Johnsen H E, Waage A, Boegsted M, Lokhorst H, Hájek R, Morgan G, Boccadoro M, Ludwig H, Cavo M, Polliack A, Sonneveld P, Einsele H, Palumbo A. European Myeloma Network: the 3rd Trialist Forum Consensus Statement from the European experts meeting on multiple myeloma. Leuk Lymphoma 2010; 51:2006-11.
	Hillaert U, Verdoes M, Florea B I, Saragliadis A, Saragliadis A, Habets K L L, Kuiper J, Van Calenbergh S, Ossendorp F, van der Marel G A, Driessen C, Overkleeft H S. Receptor-mediated targeting of cathepsins in professional antigen presenting cells. Angewandte Chemie (International ed. in English) 2009; 48:1629-32.

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publications

	title
journal paper/ review	Clerc J, Florea B I, Kraus M, Groll M, Huber R, Bachmann A S, Dudler R, Driessen C, Overkleeft H S, Kaiser M. Syringolin A selectively labels the 20 S proteasome in murine EL4 and wild-type and bortezomib-adapted leukaemic cell lines. Chembiochem : a European journal of chemical biology 2009; 10:2638-43.
	Harman A N, Kraus M, Bye C R, Byth K, Turville S G, Tang O, Mercier S K, Nasr N, Stern J L, Slobedman B, Driessen C, Cunningham A L. HIV-1-infected dendritic cells show 2 phases of gene expression changes, with lysosomal enzyme activity decreased during the second phase. Blood 2009; 114:85-94.
	Rückrich T, Kraus M, Gogel J, Beck A, Ovaa H, Verdoes M, Overkleeft H S, Kalbacher H, Driessen C. Characterization of the ubiquitin-proteasome system in bortezomib-adapted cells. Leukemia : official journal of the Leukemia Society of America, Leukemia Research Fund, U.K 2009; 23:1098-105.
	Schulz H, Rehwald U, Morschhauser F, Elter T, Driessen C, Rüdiger T, Borchmann P, Schnell R, Diehl V, Engert A, Reiser M. Rituximab in relapsed lymphocyte-predominant Hodgkin lymphoma: long-term results of a phase 2 trial by the German Hodgkin Lymphoma Study Group (GHSG). Blood 2008; 111:109-11.
	Busse A, Kraus M, Na I K, Rietz A, Scheibenbogen C, Driessen C, Blau I W, Thiel E, Keilholz U. Sensitivity of tumor cells to proteasome inhibitors is associated with expression levels and composition of proteasome subunits. Cancer 2008; 112:659-70.

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publications

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journal paper/ review	Kessler T, Reich M, Jahn G, Tolosa E, Beck A, Kalbacher H, Overkleeft H, Schempp S, Driessen C. Human cytomegalovirus infection interferes with major histocompatibility complex type II maturation and endocytic proteases in dendritic cells at multiple levels. The Journal of general virology 2008; 89:2427-36.
	Kraus M, Malenke E, Gogel J, Müller H, Rückrich T, Overkleeft H, Ovaa H, Koscielniak E, Hartmann J T, Driessen C. Ritonavir induces endoplasmic reticulum stress and sensitizes sarcoma cells toward bortezomib-induced apoptosis. Molecular cancer therapeutics 2008; 7:1940-8.
	Horger M, Pereira P, Claussen C D, Kanz L, Vonthein R, Denecke B, Driessen C. Hyperattenuating bone marrow abnormalities in myeloma patients using whole-body non-enhanced low-dose MDCT: correlation with haematological parameters. The British journal of radiology 2008; 81:386-96.
	Fissolo N, Kraus M, Reich M, Ayturan M, Overkleeft H, Driessen C, Weissert R. Dual inhibition of proteasomal and lysosomal proteolysis ameliorates autoimmune central nervous system inflammation. European journal of immunology 2008; 38:2401-11.
	Kraus M, Rückrich T, Reich M, Gogel J, Beck A, Kammer W, Berkers C R, Burg D, Overkleeft H, Ovaa H, Driessen C. Activity patterns of proteasome subunits reflect bortezomib sensitivity of hematologic malignancies and are variable in primary human leukemia cells. Leukemia : official journal of the Leukemia Society of America, Leukemia Research Fund, U.K 2007; 21:84-92.

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publications

	title
journal paper/ review	Burster T, Marin-Esteban V, Boehm B O, Dunn S, Rotzschke O, Falk K, Weber E, Verhelst S H L, Kalbacher H, Driessen C. Design of protease-resistant myelin basic protein-derived peptides by cleavage site directed amino acid substitutions. Biochemical pharmacology 2007; 74:1514-23.
	Zaidi N, Burster T, Sommandas V, Herrmann T, Boehm B O, Driessen C, Voelter W, Kalbacher H. A novel cell penetrating aspartic protease inhibitor blocks processing and presentation of tetanus toxoid more efficiently than pepstatin A. Biochemical and biophysical research communications 2007; 364:243-9.
	Reich M, van Swieten P F, Sommandas V, Kraus M, Fischer R, Weber E, Kalbacher H, Overkleeft H S, Driessen C. Endocytosis targets exogenous material selectively to cathepsin S in live human dendritic cells, while cell-penetrating peptides mediate nonselective transport to cysteine cathepsins. Journal of leukocyte biology 2007; 81:990-1001.
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	Zaidi N, Herrmann T, Baechle D, Schleicher S, Gogel J, Driessen C, Voelter W, Kalbacher H. A new approach for distinguishing cathepsin E and D activity in antigen-processing organelles. The FEBS journal 2007; 274:3138-49.

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journal paper/ review	Horger M, Kanz L, Denecke B, Vonthein R, Pereira P, Claussen C D, Driessen C. The benefit of using whole-body, low-dose, nonenhanced, multidetector computed tomography for follow-up and therapy response monitoring in patients with multiple myeloma. Cancer 2007; 109:1617-26.
	Horger M, Brodoefel H, Driessen C. [Extramedullary myeloma manifestations: imaging findings]. RöFo : Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin 2006; 178:747-51.
	van Zutphen S, Kraus M, Driessen C, van der Marel G A, Overkleeft H S, Reedijk J. Probing the potential of platinum(II) complexes for the inhibition of thiol-dependent enzymatic activity. Journal of inorganic biochemistry 2005; 99:1384-9.
	Baechle D, Cansier A, Fischer R, Brandenburg J, Burster T, Driessen C, Kalbacher H. Biotinylated fluorescent peptide substrates for the sensitive and specific determination of cathepsin D activity. Journal of peptide science : an official publication of the European Peptide Society 2005; 11:166-74.
	Dengjel J, Schoor O, Fischer R, Reich M, Kraus M, Müller M, Kreymborg K, Altenberend F, Brandenburg J, Kalbacher H, Brock R, Driessen C, Rammensee H G, Stevanovic S. Autophagy promotes MHC class II presentation of peptides from intracellular source proteins. Proceedings of the National Academy of Sciences of the United States of America 2005; 102:7922-7.
	Burster T, Beck A, Tolosa E, Schnorrer P, Weissert R, Reich M, Kraus M, Kalbacher H, Häring H U, Weber E, Overkleeft H, Driessen C. Differential processing of autoantigens in lysosomes from human monocyte-derived and peripheral blood dendritic cells. Journal of immunology (Baltimore, Md. : 1950) 2005; 175:5940-9.

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publications

	title
journal paper/ review	Burster T, Beck A, Tolosa E, Marin-Esteban V, Rötzschke O, Falk K, Lautwein A, Reich M, Brandenburg J, Schwarz G, Wiendl H, Melms A, Lehmann R, Stevanovic S, Kalbacher H, Driessen C. Cathepsin G, and not the asparagine-specific endoprotease, controls the processing of myelin basic protein in lysosomes from human B lymphocytes. Journal of immunology (Baltimore, Md. : 1950) 2004; 172:5495-503.
	van Swieten P F, Maehr R, van den Nieuwendijk A M C H, Kessler B M, Reich M, Wong C S, Kalbacher H, Leeuwenburgh M A, Driessen C, van der Marel G A, Ploegh H L, Overkleeft H S. Development of an isotope-coded activity-based probe for the quantitative profiling of cysteine proteases. Bioorganic & medicinal chemistry letters 2004; 14:3131-4.
	Lautwein A, Kraus M, Reich M, Burster T, Brandenburg J, Overkleeft H S, Schwarz G, Kammer W, Weber E, Kalbacher H, Nordheim A, Driessen C. Human B lymphoblastoid cells contain distinct patterns of cathepsin activity in endocytic compartments and regulate MHC class II transport in a cathepsin S-independent manner. Journal of leukocyte biology 2004; 75:844-55.
	Rehwald U, Schulz H, Reiser M, Sieber M, Staak J O, Morschhauser F, Driessen C, Rudiger T, Muller-Hermelink K, Diehl V, Engert A, German Hodgkin Lymphoma Study Group (GHSG) . Treatment of relapsed CD20+ Hodgkin lymphoma with the monoclonal antibody rituximab is effective and well tolerated: results of a phase 2 trial of the German Hodgkin Lymphoma Study Group. Blood 2003; 101:420-4.
	Greiner A, Lautwein A, Overkleeft H S, Weber E, Driessen C. Activity and subcellular distribution of cathepsins in primary human monocytes. Journal of leukocyte biology 2003; 73:235-42.

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publications

	title
journal paper/ review	Tolosa E, Li W, Yasuda Y, Wienhold W, Denzin L K, Lautwein A, Driessen C, Schnorrer P, Weber E, Stevanovic S, Kurek R, Melms A, Bromme D. Cathepsin V is involved in the degradation of invariant chain in human thymus and is overexpressed in myasthenia gravis. The Journal of clinical investigation 2003; 112:517-26.
	Wiendl H, Lautwein A, Mitsdörffer M, Krause S, Erfurth S, Wienhold W, Morgalla M, Weber E, Overkleeft H S, Lochmüller H, Melms A, Tolosa E, Driessen C. Antigen processing and presentation in human muscle: cathepsin S is critical for MHC class II expression and upregulated in inflammatory myopathies. Journal of neuroimmunology 2003; 138:132-43.
	Schwarz G, Brandenburg J, Reich M, Burster T, Driessen C, Kalbacher H. Characterization of legumain. Biological chemistry 2002; 383:1813-6.
	Plüger E B E, Boes M, Alfonso C, Schröter C J, Kalbacher H, Ploegh H L, Driessen C. Specific role for cathepsin S in the generation of antigenic peptides in vivo. European journal of immunology 2002; 32:467-76.
	Scheding S, Bergmann M, Shimosaka A, Wolff P, Driessen C, Rathke G, Jaschonek K, Brugger W, Kanz L. Human plasma thrombopoietin levels are regulated by binding to platelet thrombopoietin receptors in vivo. Transfusion 2002; 42:321-7.
	Lautwein A, Burster T, Lennon-Duménil A M, Overkleeft H S, Weber E, Kalbacher H, Driessen C. Inflammatory stimuli recruit cathepsin activity to late endosomal compartments in human dendritic cells. European journal of immunology 2002; 32:3348-57.

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publications

	title
journal paper/ review	Lennon-Duménil A M, Roberts R A, Valentijn K, Driessen C, Overkleeft H S, Erickson A, Peters P J, Bikoff E, Ploegh H L, Wolf Bryant P. The p41 isoform of invariant chain is a chaperone for cathepsin L. The EMBO journal 2001; 20:4055-64.
	Beck H, Schwarz G, Schröter C J, Deeg M, Baier D, Stevanovic S, Weber E, Driessen C, Kalbacher H. Cathepsin S and an asparagine-specific endoprotease dominate the proteolytic processing of human myelin basic protein in vitro. European journal of immunology 2001; 31:3726-36.
	Riese R J, Shi G P, Villadangos J, Stetson D, Driessen C, Lennon-Dumenil A M, Chu C L, Naumov Y, Behar S M, Ploegh H, Locksley R, Chapman H A. Regulation of CD1 function and NK1.1(+) T cell selection and maturation by cathepsin S. Immunity 2001; 15:909-19.
	Driessen C, Lennon-Duménil A M, Ploegh H L. Individual cathepsins degrade immune complexes internalized by antigen-presenting cells via Fcgamma receptors. European journal of immunology 2001; 31:1592-601.
	Villadangos J A, Driessen C, Shi G P, Chapman H A, Ploegh H L. Early endosomal maturation of MHC class II molecules independently of cysteine proteases and H-2DM. The EMBO journal 2000; 19:882-91.
	Shi G P, Bryant R A, Riese R, Verhelst S, Driessen C, Li Z, Bromme D, Ploegh H L, Chapman H A. Role for cathepsin F in invariant chain processing and major histocompatibility complex class II peptide loading by macrophages. The Journal of experimental medicine 2000; 191:1177-86.

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publications

	title
journal paper/ review	Driessen C, Bryant R A, Lennon-Duménil A M, Villadangos J A, Bryant P W, Shi G P, Chapman H A, Ploegh H L. Cathepsin S controls the trafficking and maturation of MHC class II molecules in dendritic cells. The Journal of cell biology 1999; 147:775-90.
	Villadangos J A, Bryant R A, Deussing J, Driessen C, Lennon-Duménil A M, Riese R J, Roth W, Saftig P, Shi G P, Chapman H A, Peters C, Ploegh H L. Proteases involved in MHC class II antigen presentation. Immunological reviews 1999; 172:109-20.
	Wellinghausen N, Driessen C, Rink L. Stimulation of human peripheral blood mononuclear cells by zinc and related cations. Cytokine 1996; 8:767-71.
	Driessen C, Hirv K, Wellinghausen N, Kirchner H, Rink L. Influence of serum on zinc, toxic shock syndrome toxin-1, and lipopolysaccharide-induced production of IFN-gamma and IL-1 beta by human mononuclear cells. Journal of leukocyte biology 1995; 57:904-8.
	Driessen C, Hirv K, Kirchner H, Rink L. Zinc regulates cytokine induction by superantigens and lipopolysaccharide. Immunology 1995; 84:272-7.
	Driessen C, Hirv K, Kirchner H, Rink L. Divergent effects of zinc on different bacterial pathogenic agents. The Journal of infectious diseases 1995; 171:486-9.
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publications

	title
journal paper/ review	Rückrich T, Brandenburg J, Cansier A, Müller M, Stevanovi? S, Schilling K, Wiederanders B, Beck A, Melms A, Reich M, Driessen C, Kalbacher H. Specificity of human cathepsin S determined by processing of peptide substrates and MHC class II-associated invariant chain. Biological chemistry 387:1503-11.
	Schmid H, Sauerbrei R, Schwarz G, Weber E, Kalbacher H, Driessen C. Modulation of the endosomal and lysosomal distribution of cathepsins B, L and S in human monocytes/macrophages. Biological chemistry 383:1277-83.

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projects

title	status
Klinische Phase-I-Studie zur Beurteilung der Sicherheit, der pharmakokinetischen Profile sowie der Wirksamkeit von EDO-S101, einem First-in-Class alkylierenden HDA-Ci-Fusionsmolekül, bei rezidivierenden/refraktären hämatologischen Malignitäten	ongoing - follow up
Combination of ibrutinib and bortezomib followed by ibrutinib maintenance to treat patients with relapsed and refractory mantle cell lymphoma; a multicenter Phase I/II trial	ongoing - follow up
Improving the activity of proteasome inhibitors for potential treatment of	ongoing - follow up
HOVON 103 / SAKK 30/10 protocol Tosedostat	scheduled
Etablierung eines humanisierten Maus-Myelom-Modells	ongoing - follow up
In vitro proteotoxic synergism of nelfinavir and carfilzomib in solid cancer cell lines	ongoing - follow up
In vitro proteotoxic synergism of nelfinavir and carfilzomib in solid cancer cell lines	ongoing - follow up

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projects

title	status
Development and preclinical characterization of third-generation proteasome inhibitors	ongoing - follow up

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projects

title	status
An open, multicentric phase II trial to evaluate the efficacy and safety of Bendamustine, Lenalidomide (Revlimid®) and Dexamethasone (BRd) as 2nd-line therapy for patients with relapsed or refractory multiple myeloma	automatically closed
Praeklinische Charakterisierung neuer Einsatzmöglichkeiten von Proteasominhibitoren zur Vorbereitung innovativer klinischer Investigator-initiierter Studien in der Onkologie	automatically closed

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projects

title	status
Master Protokoll: A Program of randomized phase II multicenter sudies to assess the tolerability and efficacy of the addition of new drugs to standard induction chemotherapy in AML and RAEB ≥ 66 years and cery poor risk AML ≥ years	ongoing - follow up
SAKK 39/10	automat-ically closed
Development of third-generation proteasome inhibitors for clinical applications	ongoing - follow up
Randomized study with a run-in feasibility phase to assess the added value of Clofarabine in combination with standard remission-induction chemotherapy in patients aged 18-65 years with previously untreated acute myeloid leukemia (AML) or myelodysplasia (MDS) RAEB with IPSS (grösser gleich 1.5) A multicenter phase III trial	ongoing - follow up
Phase I trial of nelfinavir and bortezomib in advanced hematologic malignancies	ongoing - follow up

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projects

title	status
Phase III trial of combined immunochemotherapy with Fludarabine, Cyclophosphamide and Rituximab (FCR) versus Bendamustine and Rituximab (BR) in patients with previously untreated chronic lymphocytic leukaemia	automatically closed
Rituximab, bendamustine and lenalidomide in patients with relapsed or refractory aggressive B-cell lymphoma not eligible for high dose chemotherapy. A phase I/II trial	automatically closed
In vitro Untersuchung der Proteasen-Aktivität und der Wirkung von Proteasen-Inhibitoren bei hämatolgischen Neoplasien	ongoing - follow up
An open-label, multi-centre, dose escalating, phase I/II study to investigate the safety and tolerability of RO5072759 given as monotherapy in patients with CD 20+ malignant disease	automatically closed

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projects

title	status
Prospective evaluation of the predictive value of PET in patients with diffuse large B-cell-lymphoma under R-CHOP-14. A multicenter study	ongoing - follow up
Protocole multicentrique de traitement	ongoing - follow up