



## PhD Lenka Besse

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### Bereiche

Medizinische Onkologie und Hämatologie

## Publikationen (26)

Purde M, Cupovic J, Palmowski Y, Makky A, Schmidt S, Rochwarger A, Hartmann F, Stemeseder F, Lercher A, Abdou M, Bomze D, Besse L, Berner F, Tüting T, Hözel M, Bergthaler A, Kochanek S, Ludewig B, Lauterbach H, Orlinger K, Bald T, Schlieter A, Schürch C, Ring S, Flatz L. A replicating LCMV-based vaccine for the treatment of solid tumors. *Mol Ther* 2023

Mendez Lopez M, Besse A, Besse L, Kraus M, Driessen C (2023). Targeting IGF1R/Insr Pathway with Approved ALK-Inhibitors Overcomes Proteasome Inhibitor Resistance in Multiple Myeloma.

Bandini C, Mereu E, Paradzik T, Labrador M, Maccagno M, Cumerlato M, Oreglia F, Prever L, Manicardi V, Taiana E, Ronchetti D, D'Agostino M, Gay F, Larocca A, Besse L, Merlo G, Hirsch E, Ciarrocchi A, Inghirami G, Neri A, Piva R. Lysin (K)-specific demethylase 1 inhibition enhances proteasome inhibitor response and overcomes drug resistance in multiple myeloma. *Exp Hematol Oncol* 2023; 12:71.

Zhou X, Besse A, Peter J, Steinhardt M, Vogt C, Nerreter S, Teufel E, Stanojkovska E, Xiao X, Hornburger H, Haertle L, Mendez Lopez M, Munawar U, Riedel A, Han S, Maurits E, Overkleeft H, Florea B, Einsele H, Kortüm K, Driessen C, Besse L, Rasche L. High-dose carfilzomib achieves superior anti-tumor activity over low-dose and recaptures response in relapsed/refractory multiple myeloma resistant to lowdose carfilzomib by co-inhibiting the  $\beta 2$  and  $\beta 1$  subunits of the proteasome complex. *Haematologica* 2023; 108:1628–1639.

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Ferguson I, Patiño-Escobar B, Tuomivaara S, Lin Y, Nix M, Leung K, Kasap C, Ramos E, Nieves Vasquez W, Talbot A, Hale M, Naik A, Kishishita A, Choudhry P, Lopez-Girona A, Miao W, Wong S, Wolf J, Martin T, Shah N, Vandenberg S, Prakash S, Besse L, Driessen C, Posey A, Mullins R, Eyquem J, Wells J, Wiita A. The surfaceome of multiple myeloma cells suggests potential immunotherapeutic strategies and protein markers of drug resistance. *Nat Commun* 2022; 13:4121.

Schwestermann J, Besse A, Driessen C, Besse L. Contribution of the Tumor Microenvironment to Metabolic Changes Triggering Resistance of Multiple Myeloma to Proteasome Inhibitors. *Front Oncol* 2022; 12:899272.

Besse A, Kraus M, Mendez Lopez M, Maurits E, Overkleeft H, Driessen C, Besse L. Immunoproteasome Activity in Chronic Lymphocytic Leukemia as a Target of the Immunoproteasome-Selective Inhibitors. *Cells* 2022; 11

Bolomsky A, Caers J, Hübl W, Schreder M, Zojer N, Driessen C, Tang J, Besse L, Heckman C, Kubicek S, Hannich J, Miettinen J, Malyutina A, Besse A, Huber J, Fellinger S, Breid H, Parsons A, Klavins K, Ludwig H. Heterogeneous modulation of Bcl-2 family members and drug efflux mediate MCL-1 inhibitor resistance in multiple myeloma. *Blood Adv* 2021; 5:4125–4139.

Besse L, Besse A, Kraus M, Maurits E, Overkleeft H, Bornhauser B, Bourquin J, Driessen C. High Immunoproteasome Activity and sXBP1 in Pediatric Precursor B-ALL Predicts Sensitivity towards Proteasome Inhibitors. *Cells* 2021; 10

Mendez Lopez M, Besse A, Florea B, Zuppinger C, Overkleeft H, Besse L, Driessen C (2021). Carfilzomib-induced acute cardiotoxicity is mediated through angiotensin and caused by cardiomyocyte energy depletion.

Besse L, Bolomsky A, Ludwig H, Hannich J, Loguinov A, Everts B, Berkers C, Pilon M, Farhan H, Vulpe C, Overkleeft H, Huber J, Ståhlman M, Borén J, Besse A, Stolze S, Sobh A, Zaai E, van der Ham A, Ruiz M, Phuyal S, Büchler L, Sathianathan M, Florea B, Driessen C. Treatment with HIV-Protease Inhibitor Nelfinavir Identifies Membrane Lipid Composition and Fluidity as a Therapeutic Target in Advanced Multiple Myeloma. *Cancer Res* 2021; 81:4581-4593.

Byrgazov K, Besse A, Kraus M, Slipcevic A, Lehmann F, Driessen C, Besse L. Novel Peptide-drug Conjugate Melflufen Efficiently Eradicates Bortezomib-resistant Multiple Myeloma Cells Including Tumor-initiating Myeloma Progenitor Cells. *Hemasphere* 2021; 5:e602.

Byrgazov K, Kraus M, Besse A, Slipcevic A, Lehmann F, Driessen C, Besse L. Up-regulation of multidrug resistance protein MDR1/ABCB1 in carfilzomib-resistant multiple myeloma differentially affects efficacy of anti-myeloma drugs. *Leuk Res* 2020; 101:106499.

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Vrabel D, Sevcikova S, Pour L, Stork M, Sandecka V, Jelinek T, Plonkova H, Jarkovsky J, Brožová L, Kubaczkova V, Almasi M, Bezdekova R, Rihova L, Besse L, Sedlarikova L, Hájek R. Dynamics of tumor-specific cfDNA in response to therapy in multiple myeloma patients. *Eur J Haematol* 2019

Mendez Lopez M, Sutter T, Driessen C, Besse L. HIV protease inhibitors for the treatment of multiple myeloma. *Clin Adv Hematol Oncol* 2019; 17:615-623.

Hitz F, Driessen C, Mey U, Samaras P, Vilei S, Stüdeli S, Rondeau S, Seipel K, Novak U, Silzle T, Besse L, Hess D, Pabst T, Kraus M, Swiss Group for Clinical Cancer Research SAKK. Nelfinavir and lenalidomide/dexamethasone in patients with lenalidomide-refractory multiple myeloma. A phase I/II Trial (SAKK 39/10). *Blood Cancer J* 2019; 9:70.

Besse L, Besse A, Mendez Lopez M, Vasickova K, Sedlackova M, Vanhara P, Kraus M, Bader J, Ferreira R, Castellano R, Law B, Driessen C. A metabolic switch in proteasome inhibitor-resistant multiple myeloma ensures higher mitochondrial metabolism, protein folding and sphingomyelin synthesis. *Haematologica* 2019; 104:e415-e419.

Besse A, Besse L, Kraus M, Mendez Lopez M, Bader J, Xin B, de Bruin G, Maurits E, Overkleeft H, Driessen C. Proteasome Inhibition in Multiple Myeloma: Head-to-Head Comparison of Currently Available Proteasome Inhibitors. *Cell Chem Biol* 2019; 26:340-351.e3.

Driessen C, Pabst T, Hitz F, Hawle H, Rondeau S, Berset C, Besse A, Besse L, Ribi K, Samaras P, Mey U, Rüfer A, Mach N, Betticher D, Cantoni N, Novak U, Müller R, Zander T. Promising activity of nelfinavir-bortezomib-dexamethasone (NeVd) in proteasome inhibitor-refractory multiple myeloma. *Blood* 2018

Krupkova O, Cambria E, Besse L, Besse A, Bowles R, Wuertz-Kozak K. The potential of CRISPR/Cas9 genome editing for the study and treatment of intervertebral disc pathologies. *JOR Spine* 2018; 1:e1003.

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Besse L, Kraus M, Besse A, Bader J, Silzle T, Mehrling T, Driessen C. The first-in-class alkylating HDAC inhibitor EDO-S101 is highly synergistic with proteasome inhibition against multiple myeloma through activation of multiple pathways. *Blood Cancer J* 2017; 7:e589.

Besse A, Besse L, Overkleeft H, Bader J, Kraus M, Morgan G, Weinhold N, Rasche L, Stolze S, Driessen C. Carfilzomib resistance due to ABCB1/MDR1 overexpression is overcome by nelfinavir and lopinavir in multiple myeloma. Leukemia 2017; 32:391-401.

Kraus J, Kraus M, Liu N, Besse L, Bader J, Geurink P, de Bruin G, Kisselov A, Overkleeft H, Driessen C. The novel  $\beta$ 2-selective proteasome inhibitor LU-102 decreases phosphorylation of I kappa B and induces highly synergistic cytotoxicity in combination with ibrutinib in multiple myeloma cells. Cancer Chemother Pharmacol 2015; 76:383-96.

## Projekte (12)

### **Targeting des Immunoproteasoms in vivo**

*Grundlagenforschung - 01.08.2023 - 31.12.2023*

*Automatisch geschlossen*

### **Genetic contributors of multiple myeloma cells involved in their homing and escape from T-cell recognition**

*Grundlagenforschung - 01.07.2022 - 30.06.2023*

*Automatisch geschlossen*

### **ALK-Inhibitoren als potentielle Therapie bei Proteasom-Inhibitor-resistentem Multiplen Myelom**

*Grundlagenforschung - 01.10.2021 - 30.09.2023*

*Automatisch geschlossen*

### **Immunoproteasome activity as a predictive marker and therapeutic target in hematological malignancies**

*Grundlagenforschung - 01.07.2021 - 31.12.2021*

*Automatisch geschlossen*

### **Towards identification of novel therapeutic targets: Assessment of proteasome-related alterations in MM patients' datasets**

*Grundlagenforschung - 01.01.2021 - 31.12.2021*

*Automatisch geschlossen*

### **The molecular landscape of proteasome inhibitor resistance of multiple myeloma in vivo**

*Grundlagenforschung - 01.07.2020 - 31.12.2023*

*Automatisch geschlossen*

### **Revealing molecular basis of cardiotoxicity of carfilzomib towards its safer use in the patients with multiple myeloma**

*Grundlagenforschung - 01.03.2020 - 28.02.2021*

*Automatisch geschlossen*

### **The „seed and soil“-based pathogenesis of proteasome inhibitor resistance in multiple myeloma**

*Grundlagenforschung - 01.01.2019 - 31.12.2019*

*Automatisch geschlossen*

### **Identifying and targeting the “Achilles’ heel” in proteasome inhibitor-resistant multiple myeloma**

*Grundlagenforschung - 01.10.2018 - 31.12.2021*

*Automatisch geschlossen*

**Preclinical investigation of cardiotoxicity as a clinically important side effect of proteasome inhibitor-based therapy**

*Grundlagenforschung - 01.07.2017 - 30.06.2018*

*Automatisch geschlossen*

**HIV-Proteaseinhibitoren als Basis für Krebstherapie: Verständnis des Mechanismus, Identifikation der Targets, Entwicklung wirksamerer Substanzen**

*Grundlagenforschung - 01.11.2016 - 31.10.2018*

*Automatisch geschlossen*

**Proteasominhibitor-resistenter Multiples Myelom: Biologie und Therapieoptionen**

*Grundlagenforschung - 05.01.2015 - 31.12.2015*

*Automatisch geschlossen*

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