

PERIFOSINE

Publications – Clinical and non clinical data

Paul G. Richardson, Jeff Wolf, Andrzej Jakubowiak, Jeff Zonder, Sagar Lonial, David Irwin, John Densmore, Amrita Krishnan, Noopur Raje, Michael Bar, Tom Martin, Robert Schlossman, Irene M. Ghobrial, Nikhil Munshi, Jacob Laubach, Jeff Allerton, Teru Hideshima, Kathleen Colson, Enrique Poradosu, Lesa Gardner, Peter Sportelli, and Kenneth C. Anderson. **Perifosine Plus Bortezomib and Dexamethasone in Patients With Relapsed/Refractory Multiple Myeloma Previously Treated With Bortezomib: Results of a Multicenter Phase I/II Trial.** *Journal of Clinical Oncology*, October 11, 2011.

Johanna C. Bendell, John Nemunaitis, Sasha J. Vukelja, Christopher Hagenstad, Luis T. Campos, Robert C. Hermann, Peter Sportelli, Lesa Gardner, and Donald A. Richards. **Randomized Placebo-Controlled Phase 2 Trial of Perifosine Plus Capecitabine as Second- or Third-Line Therapy in Patients with Metastatic Colorectal Cancer.** *Journal of Clinical Oncology*, October 3, 2011.

Martin Schmidt-Hieber, Robert Dabrowski, Babette Aicher, Philipp Lohneis, Antonia Busse, Carola Tietze-Buerger, Birgit Reufi, Eckhard Thiel and Igor Wolfgang Blau. **In vitro effects of perifosine, bortezomib and lenalidomide against hematopoietic progenitor cells from healthy donors.** *Investigational New Drugs*, July 2011.

Li Z, Tan F, Liewehr DJ, Steinberg SM, Thiele CJ. **In vitro and in vivo inhibition of neuroblastoma tumor cell growth by AKT inhibitor perifosine.** *J Natl Cancer Inst.* 2010 Jun 2;102(11):758-70. Epub 2010 May 12.

Dr. Irene Ghobrial, *et al.*, **Clinical and Translational Studies of a Phase II Trial of the Novel Oral Akt Inhibitor Perifosine in Relapsed or Relapsed/Refractory Waldenstrom's Macroglobulinemia.** *The Journal of clinical Cancer Research*, February 1, 2010.

Camillo Porta, Robert A. Figlin, **Phosphatidylinositol-3-Kinase/Akt Signaling Pathway and Kidney Cancer, and the Therapeutic Potential of Phosphatidylinositol-3-Kinase/Akt Inhibitors,** *The Journal of Urology*, December 2009 (Vol. 182, Issue 6, Pages 2569-2577).

Zerp SF, Vink SR, Ruiter GA, Koolwijk P, Peters E, van der Luit AH, de Jong D, Budde M, Bartelink H, van Blitterswijk WJ, Verheij M. **Alkylphospholipids inhibit capillary-like endothelial tube formation in vitro: antiangiogenic properties of a new class of antitumor agents.** *Anticancer Drugs*. 2008;19(1):65-75.

Papa V, Tazzari PL, Chiarini F, Cappellini A, Ricci F, Billi AM, Evangelisti C, Ottaviani E, Martinelli G, Testoni N, McCubrey JA, Martelli AM. **Proapoptotic activity and chemosensitizing effect of the novel Akt inhibitor perifosine in acute myelogenous leukemia cells.** *Leukemia*. 2008;22 (1):147-160.

Huston A, Leleu X, Jia X, Moreau AS, Ngo HT, Runnels J, Anderson J, Alsayed Y, Roccaro A, Vallet S, Hatjiharissi E, Tai YT, Sportelli P, Munshi N, Richardson P, Hideshima T, Roodman DG, Anderson KC, Ghobrial IM. **Targeting Akt and heat shock protein 90 produces synergistic multiple myeloma cell cytotoxicity in the bone marrow microenvironment.** *Clin Cancer Res* 2008;14(3):865-74.

Leleu X, Eeckhoutte J, Jia X, Roccaro AM, Moreau AS, Farag M, Sacco A, Ngo HT, Runnels J, Melhem MR, Burwick N, Azab A, Azab F, Hunter Z, Hatjiharissi E, Carrasco DR, Treon SP, Witzig TE, Hideshima T, Brown M, Anderson KC, Ghobrial IM. **Targeting NF-kappaB in Waldenstrom macroglobulinemia.** *Blood*. 2008;111(10):5068-5077.

Hennessy BT, Lu Y, Poradosu E, Yu Q, Yu S, Hall H, Carey MS, Ravoori M, Gonzalez-Angulo AM, Birch R, Henderson IC, Kundra V, Mills GB. **Pharmacodynamic markers of perifosine efficacy.** *Clin Cancer Research*. 2007;13(24):7421-7431.

Vink SR, van Blitterswijk WJ, Schellens JH, Verheij M. **Rationale and clinical application of alkylphospholipid analogues in combination with radiotherapy.** *Cancer Treat Rev*. 2007.

Gajate C, Mollinedo F. **Edelfosine and perifosine induce selective apoptosis in multiple myeloma by recruitment of death receptors and downstream signaling molecules into lipid rafts.** Blood 2007;109:711-719.

Mollinedo, Faustino. **Antitumour ether lipids: proapoptotic agents with multiple therapeutic indications.** Expert Opinion on Therapeutic Patents 2007;17(4):385-405.

R Donald Harvey & Sagar Lonial. **PI3 kinase/AKT pathway as a therapeutic target in multiple myeloma.** Future Oncology 2007;3(6):639-647.

Younes H, Leleu X, Hatjiharissi E, Moreau AS, Hideshima T, Richardson P, Anderson KC, Ghobrial IM. **Targeting the phosphatidylinositol 3-kinase pathway in multiple myeloma.** Clin Cancer Res. 2007;13(13):3771-3775.

Vink, Stefan R.; Schellens, Jan H. M.; Beijnen, Jos H.; Sindermann, Herbert; Engel, Juergen; Dubbelman, Ria; Moppi, Gemi; Hillebrand, Michel J. X.; Bartelink, Harry; Verheij, Marcel. **Phase I and pharmacokinetic study of combined treatment with perifosine and radiation in patients with advanced solid tumours.** Radiotherapy and Oncology 2006;80(2):207-213.

Vink SR, Lagerwerf S, Mesman E, Schellens JHM, Begg AC, van Blitterswijk WJ, Verheij M. **Radiosensitization of Squamous Cell Carcinoma by the Alkylphospholipid Perifosine in Cell Culture and Xenografts.** Clin Cancer Res 2006;12(5):1615-1622.

Hideshima T, Catley L, Yasui H et al. **Perifosine, an oral bioactive novel alkylphospholipid, inhibits Akt and induces *in vitro* and *in vivo* cytotoxicity in human multiple myeloma cells.** Blood. 2006;107:4053-62.

Vink SR, Schellens JHM, Wim J van Blitterwijk et al. **Tumor and normal tissue pharmacokinetics of perifosine, an oral anti-cancer alkylphospholipid.** Invest New Drug 2005;23:279-286.

Chee KG, Lara PN, Longmate J, Twardowski P, Quinn DI, Chatta G, Gandara DR. **The AKT Inhibitor perifosine in Biochemically Recurrent, Hormone-Sensitive Prostate Cancer (HSPC). A Phase II California Cancer Consortium Trial.** Proc Am Soc Clin Oncol 2005;23(16S) part I of II: 413s (abstract #4642).

Hedley D, Moore MJ, Hirte H, Siu L, Vincent M, Jonker D, Mwang H, Nagai J, Dancey J. **A Phase II trial of perifosine as second line therapy for advanced pancreatic cancer. A study of the Princess Margaret Hospital [PMH] Phase II Consortium.** Proc Am Soc Clin Oncol 2005;23(16S) part I of II: 349s (abstract #4166).

Belka C, Jendrossek, V, Pruschy M, Vink S, Verheij M, Budach W. **Apoptosis modulating drugs in combination with radiotherapy – current status and outlook.** Int J Radiat Oncol Biol Phys 2004;58(2):542-554.

Van Ummersen L, Binger K, Volkman J et al. **A Phase I trial of perifosine (NSC 639966) on a loading dose/maintenance dose schedule in patients with advanced cancer.** Clin Cancer Res 2004;10:7450-456.

Ruiter GA, Zerp SF, Bartelink H et al. **Anti-cancer alkyl-phospholipids inhibit the phosphatidylinositol 3-kinase-Akt/PKB survival pathway.** Cancer Drugs 2003;14:167-173.

Crul M, Rosing H, de Klerk GJ, et al. **Phase I and pharmacological study of daily oral administration of perifosine (D-21266) in patients with advanced solid tumours.** Eur J Cancer 2002;38:1615-1621.

Monga M, Messmann RA, Headlee D, Woo EW, Figg WD, Murgo A, and Sausville EA. **A Phase I trial of oral perifosine in patients with refractory neoplasms.** Proc Am Soc Clin Oncol 2002;21 (part 2 of 2):7b (abstract #1837).

- Patel V, Lahusen T, Sy E, Sausville EA, Gutkind JS, Senderowicz AM. **Perifosine, a novel alkylphospholipid, induces p21WAF1 expression in squamous carcinoma cells through p53-independent pathway, leading to loss in cyclin-dependent kinase activity and cell cycle arrest.** *Cancer Res* 2002;62:1401-1409.
- Ruiter GA, Verheij M, Zerp SF, van Blitterswijk. **Alkyl-lysophospholipids as anti-cancer agents and enhancers of radiation-induced apoptosis.** *Int J Radiat Oncol Biol Phys* 2001;49:415-419.
- Kim AH, Khursigara G, Sun X, et al. **Akt phosphorylates and negatively regulates apoptosis signal-regulating kinase 1.** *Mol Cell Biol* 2001;21:893-901.
- Knebel NG, Grieb S, Winkler M, Locher M, van der Vlis E, Verheij ER. **Quantification of perifosine, an alkylphosphocholine anti-tumor agent, in plasma by pneumatically assisted electrospray tandem mass spectrometry coupled with high-performance liquid chromatography.** *J Chromatogr B Biomed Sci Appl* 1999;721:257-269.
- Brunet A, Bonni A, Zigmond MJ et al. **Akt promotes cell survival by phosphorylating and inhibiting a Forkhead transcription factor.** *Cell* 1999;96:857-868.
- Ruiter GA, Zerp SF, Bartelink H, et al. **Alkyl-lysophospholipids activate the SAPK/JNK pathway and enhance radiation-induced apoptosis.** *Cancer Res* 1999;59:2457-463.
- Knebel NG, Locher M. **Quantification of an alkylphosphocholine antitumor agent, in plasma by pneumatically assisted electrospray: Tandem mass spectrometry coupled with high-performance liquid chromatography.** *Drugs of Today* 1998;34:141-152.
- Downward J. **Mechanisms and consequences of activation of protein kinase B/Akt.** *Curr Opin Cell Biol* 1998;10:262-267.
- Berkovic D, Gründel O, Berkovic K, et al. **Synergistic cytotoxic effects of ether phospholipid analogues and ionizing radiation in human carcinoma cells.** *Radiother Oncol* 1997;43:293-301.
- Hilgard P, Klenner T, Stekar J, Nössner G, Kutscher B, and Engel J. **D-21266, a new heterocyclic alkylphospholipid with antitumor activity.** *Eur J Cancer* 1997;33(3):442-446.
- Grunicke HH, Maly K, Überall F, Schubert C, Kindler E, Stekar J, and Brachwitz H. **Cellular signaling as a target in cancer chemotherapy. Phospholipid analogues as inhibitors of mitogenic signal transduction.** *Adv Enzyme Regul* 1996;36:385-407.
- Hilgard P, Stekar J, Klenner T, Nössner G, Kutscher B, and Engel J. **Heterocyclic alkylphospholipids with an improved therapeutic range. In Platelet-activating factor and related lipid mediators 2.** Nigram et al (eds), Plenum Press, New York 1996;157-164.
- Zeisig R, Shimada K, Hirota S, and Arndt D. **Effect of sterical stabilisation on macrophage uptake *in vitro* and on thickness of the fixed aqueous layer of liposomes made from alkylphosphocholines.** *Biochim. Biophys Acta* 1996;1285:237-245.
- Maly K, Überall F, Schubert C, Kindler E, Stekar J, Brachwitz H, and Grunicke HH. **Interference of new alkylphospholipid analogues with mitogenic signal transduction.** *Anticancer Drug Des* 1995;10(5):411-425.
- Rosen O, Schymanietz C, and Hölzel F. **Antiproliferative, cytotoxic and recovery effects in tumor cell cultures treated with synthetic phospholipids.** *Int J Oncology* 1994;5:517-523.
- Principe P, Sidoti C, Coulomb H et al. **Tumor cell kinetic following long-term treatment with antineoplastic ether phospholipids.** *Cancer Detec Prev* 1994;18:393-400.

Presentations

I. Seipelt, E. Guenther, L. Blumenstein, G. Mueller, P. Schmidt, B. Aicher, M. Teifel and M. Gerlach. **A highly selective Erk1/2 inhibitor with in vivo antitumor potency.** American Association for Cancer Research Annual Meeting. Abstract #3563. Tuesday, April 5, 2011.

Tae Soo Kim, Hyo Song Kim, Bo Ram Kwan, Chan Hee Park, Hei-Cheul Jeung, Woo Ick Jang, Juergen Engel, Hyun Cheol Chung, Jae Kyung Roh, Sun Young Rha, (Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Korea). **Antitumor activity of novel Akt inhibitor, perifosine in gastric cell lines.** 102nd annual meeting of the American Association for Cancer Research. Poster #1965. April 4, 2011.

Arianna Giacomini, Silvia L. Locatelli, Marco Righi, Loredana Cleris, Paolo D. Longoni, Marco Milanese, Maura Francolini, Michele Magni, Massimo Di Nicola, Alessandro M. Gianni, Carmelo Carlo-Stella (Medical Oncology, Fondazione IRCCS Istituto Nazionale Tumori Milano and University of Milan, Milan, Italy). **The Akt inhibitor Perifosine strongly enhances the antitumor and antivascular activity of CD34+ cells engineered to express membrane-bound tumor necrosis factor-related apoptosis-inducing ligand (TRAIL).** 102nd annual meeting of the American Association for Cancer Research. Poster #640. April 4, 2011.

A. Giacomini, S. L. Locatelli, M. Righi, L. Cleris, P.D. Longoni, M. Milanese, M. Francolini, M. Magni, M. Di Nicola, A. M. Gianni, C. Carlo-Stella. **The Akt inhibitor Perifosine strongly enhances the antitumor and antivascular activity of CD34+ cells engineered to express membrane-bound tumor necrosis factor-related apoptosis-inducing ligand (TRAIL).** American Association for Cancer Research Annual Meeting. Abstract #640, Sunday, April 3, 2011.

Daphne R. Friedman, MD, Duke University Medical Center, Durham, NC. **Pre-Clinical and Interim Results of a Phase II Trial of Perifosine in Patients with Relapsed or Refractory Chronic Lymphocytic Leukemia (CLL).** ASH meeting, Orlando, FLA. December 4, 2010, 5:30-7:30 p.m. Abstract #1842, Poster Board: I-822.

Carmelo Carlo-Stella, MD, Fondazione IRCCS Istituto Nazionale Tumori and University of Milano, Milano, Italy. **Clinical Activity and Safety of the Combined Therapy with the Akt Inhibitor Perifosine and the Multikinase Inhibitor Sorafenib in Heavily Pretreated Patients with Relapsed/Refractory Lymphomas: Preliminary Results of a Phase II Trial.** ASH meeting, Orlando, FLA. December 5, 2010, 6:00 PM-8:00 PM. Abstract #2861, Poster Board: II-741.

Andrzej Jakubowiak, MD, University of Michigan Comprehensive Cancer Center, Ann Arbor, MI. **Final Phase I Results of Perifosine in Combination with Lenalidomide and Dexamethasone in Patients with Relapsed or Refractory Multiple Myeloma (MM).** ASH meeting, Orlando, FLA. December 5, 2010, 6:00 PM-8:00 PM. Abstract #3064, Poster Board: II-944.

Weihua Song, MD, Dana-Farber Cancer Institute, Boston, MA. **Perifosine Affects Phenotype and Function of Human Myeloid Dendritic Cells.** ASH meeting, Orlando, FLA. December 6, 2010, 6:00 PM-8:00 PM. Abstract #3911.

B. Aicher, P. Schmidt, M. Teifel, J. Engel, E. G. Günther. **Perifosine in combination with antimetabolites induces synergistic effects on cytotoxicity and apoptosis in human colon, multiple myeloma, breast, renal, and liver tumor cell lines.** 22nd EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics, November 17, 2010. Abstract #203.

Paulo Hoff, *et al.*, **Subset Analysis of 5-FU Refractory Patients from a Randomized Ph II Study of Perifosine + Capecitabine (P-CAP) vs. Placebo + Capecitabine (CAP) in Patients with 2nd or 3rd Line Metastatic CRC.** 12th World Congress on Gastrointestinal Cancer, Barcelona, Spain, June 30 - July 2, 2010. Poster.

D Richards, *et al.*, **Final results of a randomized phase II study of perifosine in combination with capecitabine (P-CAP) vs. placebo plus capecitabine (CAP) in patients (pts) with second or third line metastatic colorectal cancer (mCRC)**. ASCO meeting, June 2010, Abstract 3531.

Oren J. Becher, *et al.*, **Phase 1 Study of Single Agent Perifosine for Recurrent Pediatric Solid Tumors**. American Society of Clinical Oncology (ASCO) Annual Meeting, June 2010. Abstract #9540.

Zhijie Li, Carol J. Thiele, Cell & Molecular Biology Section, POB/NCI/NIH, Bethesda, MD. **Neuroblastoma tumors with different ALK mutations are sensitive to Perifosine**. AACR 2010, April 20, 2010. Abstract # 5248.

Johanna Bendel, *et al.*, **Randomized Phase II study of perifosine in combination with capecitabine (P-CAP) versus capecitabine plus placebo (CAP) in patients with second- or third-line metastatic colon cancer (mCRC): Updated results**. 2010 ASCO, Gastrointestinal Cancers Symposium. January, 24, 2010.

Paul Richardson, **Perifosine in Combination with Bortezomib and Dexamethasone Extends Progression-Free Survival and Overall Survival in Relapsed/Refractory Multiple Myeloma Patients Previously Treated with Bortezomib: Updated Phase 1/2 Trial Results**, American Society of Hematology (ASH), December 5, 2009.

Hutson TE, et al **Phase II study of perifosine in aptients with metastatic RCC progression after prior therapy with both a VEGF receptor inhibitor and an mTOR inhibitor** KCA 2009; Final program.

Vukelja S, Richards D, Campos LT, Bedell C, Hagenstad C, Hyman W, Letzer J, Gardner L, Sportelli P, Nemunaitis J. **Randomized Phase 2 study of perifosine in combination with capecitabine versus capecitabine alone in patients with second- or third-line metastatic colon cancer**. ASCO 2009. Abstract 4081. J Clin. Oncol. 2009;27:15s

Conley AP, Araujo D, Ludwig J, Ravi V, Samuels BL, Choi H, Thall PF, Patel S, Benjamin R, Trent J. **A randomized Phase II study of perifosine plus imatinib for patients with imatinib-resistant gastrointestinal stromal tumor (GIST)**. ASCO 2009. Abstract 10563. J. Clin. Oncol 27;15s.

Cho DC, Figlin RA, Flaherty KT, Michaelson D, Sosman JA, Ghebremichael M, Bowers ME, Mier JW, Atkins MB, McDermott DF. **A Phase II trial or perifosine in patients with advanced renal cell carcinoma (RCC) who have failed tyrosine kinase inhibitors (TKI)**. ASCO 2009. Abstract 5101. J. Clin. Oncol 27;15s.

Vogelzang NJ, Hutson TE, Samlowski W, Somer B, Richey S, Alemany C, Loesch D, Richards P, Gardner L, Sportelli P. **Phase 2 study of perifosine in metastatic renal cell carcinoma (RCC) progressing after prior therapy with a VEGF receptor inhibitor**. ASCO 2009. Abstract 5034. J. Clin. Oncol 27;15s.

Andrzej Jakubowiak A, Richardson P, Zimmerman TM, Alsina M, Kaufman JL, Harvey C, Brozo C, Kendall T, McAllister A, Hideshima T, Sportelli P, Gardner L, Anderson KC, Giusti. **Phase I Results of Perifosine (KRX-0401) in Combination with Lenalidomide and Dexamethasone in Patients with Relapsed or Refractory Multiple Myeloma**. ASH 2008. Abstract 3691.

Paul Richardson, Jeffrey Wol, Andrzej Jakubowiak, Jeffrey Zonder, Sagar Lonial, David H Irwin, John Densmore, Amrita Krishnan, Noopur Raje, Michael H. Bar, Jeffrey P. Allerton, Robert Schlossman, Irene M. Ghobrial, Nikhil C. Munshi, Thomas Martin, Jacob Laubach, Kathy Colson, Sarah Dean, Deanna Tocco, Elizabeth Steinfield, Tara Kendall, Kimberly O'Riley, Teru Hideshima, Peter Sportelli, Lesa Gardner, and Kenneth C. Anderson. **Phase I/II Results of a Multicenter Trial of Perifosine (KRX-0401) + Bortezomib in Patients with Relapsed or Relapsed / Refractory Multiple Myeloma Who Were Previously Relapsed from or Refractory to Bortezomib**. ASH 2008. Abstract 870.

Ghobrial IM, Leleu X, Rubin N, Xie W, Hong F, Chuma S, Leduc R, Nelson M, O'Connor K, Sam A, Harris B, Warren D, Sportelli P, Treon SP, Weller E, Anderson KC, and Richardson PG. **Final Results of a Phase II Trial of the Novel Oral Akt Inhibitor Perifosine in Relapsed and/or Refractory Waldenstrom Macroglobulinemia.** ASH 2008. Abstract 1010.

Tazzari PL, Papa V, Ricci F, Chiarini F, Evangelisti C, Martinelli G, Bontadini A, McCubrey J, and Martelli AM. **Synergistic Proapoptotic Activity of Recombinant TRAIL Plus the Akt Inhibitor Perifosine in Acute Myelogenous Leukemia Cells—a Novel Therapeutic Approach for Leukemia Displaying Elevated Akt signalling.** ASH 2008. Abstract 957.

Song W, Hideshima T, Tai YT, Anderson KC, Munshi NC. **Phenotypic and Functional Effects of Novel Akt Inhibitor Perifosine on Immune system.** ASH 2008. Abstract 1555.

Cirstea D, Hideshima T, Pozzi S, Vallet S, Ikeda H, Santo L, Rodig S, Vaghela N, Currie T, Okawa Y, Chhetri G, Patel CG, Perrone G, Gorgun G, Calabrese E, Trieu V, Desai N, Sportelli P, Munshi NC, Anderson KC, Raje N. **Combination of Nab-Rapamycin and Perifosine Induces Synergistic Cytotoxicity and Antitumor Activity Via Autophagy and Apoptosis in Multiple Myeloma.** ASH 2008.

Jakubowiak A, Richardson P, Zimmerman T, Alsina M, Kaufman J, Brozo C, Kendall T, McAllister A, Leister C, Harvey C, Hari M, Dean S, Colson K, Mitchell M, Mintz M, Smith R, Hideshima T, Sportelli P, Gardner L, Giusti K, and Anderson KC. **A Multiple Myeloma Research Consortium (MMRC) Multicenter Phase I results of perifosine (KRX-0401) in combination with lenalidomide and dexamethasone in patient with relapsed or refractory multiple myeloma.** ASH 2008.

Ghobrial IM, Leleu X, Rubin, Leduc R, Chuma S, Nelson M, O'Connor K, Sportelli P, Sam A, Treon SP, Anderson KC, Richardson P. **Phase II Trial of the novel oral Akt inhibitor Perifosine in Relapsed and/or Refractory Waldenström Macroglobulinemia.** ASCO 2008.

Richardson PG, Lonial S, Jakubowiak A, Krishnan A, Wolf J, Densmore J, Singhal S, Ghobrial I, Stephenson J, Colson K, Francis D, Kendall T, Obadike N, Sullivan K, Martin J, Hideshima T, Lai L, Sportelli P, Gardner L, Birch R, Henderson IC. **Multi-center Phase II Study of Perifosine (KRX-0401) Alone and in Combination with Dexamethasone for Patients with Relapsed or Relapsed/Refractory Multiple Myeloma: Promising Activity as Combination Therapy with Manageable Toxicity.** ASH 2007.

Jakubowiak A, Zimmerman T, Alsina M, Richardson PG, Kaufman J, Brozo C, Kendall T, McAllister A, Leister C, Hideshima T, Sportelli P, Gardner L, Birch R, Henderson IC, Giusti K, Anderson K. **A Multiple Myeloma Research Consortium (MMRC) Multicenter Phase I Trial of Perifosine (KRX-0401) in Combination with Lenalidomide and Dexamethasone in Patients with Relapsed or Refractory Multiple Myeloma: Updated Results.** ASH 2007.

Richardson PG, Jakubowiak A, Wolf J, Allerton J, Zonder J, Lonial S, Krishnan A, Densmore J, Colson K, Kendall T, Leister C, Martineau B, Hideshima T, Sportelli P, Gardner L, Birch R, Henderson IC, Facon T, and Anderson KC. **Phase I/II Report from a Multicenter Trial of Perifosine (KRX-0401) + Bortezomib in Patients with Relapsed or Relapsed / Refractory Multiple Myeloma Previously Treated with Bortezomib.** ASH 2007.

Leleu X, Eeckhoutte J, Jia X, Moreau AS, Roccaro AM, Farag M, Sacco A, Hatjiharissi E, Ngo HT, Runnels J, Azab A, Azab F, Hunter Z, Sportelli P, Treon SP, Hideshima T, Anderson KC, Irene M, Ghobrial. **Targeting NF- κ B by Perifosine, Bortezomib and Rituximab in Waldenstrom Macroglobulinemia.** ASH 2007.

Song W, Hideshima T, Tai YT, Anderson KC, Munshi N. **Phenotype and Functional Effect of Perifosine on Dendritic cells.** ASH 2007.

Richardson PG, Lonial S, Jakubowiak A, Krishnan A, Wolf J, Singhal S, Densmore J, Ghobrial I, Stephenson J, Colson K, Harris J, Kendall T, Obadike N, Martineau B, Vickrey E, Sullivan K, Hideshima T, Lai L, Sportelli P, Gardner L, Birch R, Henderson IC, Anderson KC. **Perifosine (KRX-0401) + low**

dose dexamethasone is active in patients with relapsed and refractory multiple myeloma (MM): perifosine MM investigator group Phase II multicenter study update. XI International Workshop on Multiple Myeloma. June 2007.

Jakubowiak A, Richardson PG, Zimmerman T, Alsina M, Lonial S, Kendall T, Hideshima T, Sportelli P, Birch R, Henderson IC, Giusti K, Anderson K. **A multicenter Phase I trial of perifosine (KRX-0401) in combination with lenalidomide and dexamethasone in patients with relapsed or refractory multiple myeloma: preliminary results. Multiple Myeloma Research Consortium (MMRC) trial.** XI International Workshop on Multiple Myeloma. June 2007.

Richardson PG, Jakubowiak A, Wolf J, Krishnan A, Lonial S, Ghobrial I, Facon T, Colson K, Kendall T, Leister C, Martineau B, Hideshima T, Sportelli P, Birch R, Henderson IC, Anderson K. **A multicenter Phase I/II trial of perifosine (KRX-0401) + Bortezomib in relapsed and refractory multiple myeloma patients previously treated with Bortezomib: preliminary results.** XI International Workshop on Multiple Myeloma. June 2007.

Huston A, Leleu X, Jia X, Anderson J, Alsayed Y, Vallet S, Roccaro A, Moreau AS, Runnels J, Ngo H, Hatjiharissi E, Roodman D, Tai YT, Sportelli P, Hideshima T, Richardson P, Anderson K and Ghobrial I. **Combination of the AKT Inhibitor Perifosine with the HSP90 Inhibitor 17-(Dimethylaminoethylamino)-17-Demethoxygeldanamycin (17-DMAG) Has Synergistic Activity in tumor cell and its microenvironment in Multiple Myeloma.** XI International Workshop on Multiple Myeloma. June 2007.

Leleu X, Jia X, Moreau AS, Ngo H, Runnels J, Roccaro A, Kiziltepe T, Ciccarelli B, Hatjiharissi E, Hunter Z, Adamia S, Sportelli P, Treon S, Anderson K, and Ghobrial I. **The combination of Perifosine with Bortezomib and Rituximab provides synergistic anti-tumor activity in Waldenström's Macroglobulinemia.** Fourth International Workshop on Waldenström Macroglobulinemia. June 2007.

Ghobrial IM, Leleu X, Treon SP, Toolan E, Nelson MB, Leduc R, Warren D, Soumerai J, Ngo H, Sportelli P, Birch R, Henderson IC, Richardson P, and Anderson K. **Phase II trial of perifosine (KRX-0401) in relapsed and/or refractory Waldenström Macroglobulinemia: preliminary results.** Fourth International Workshop on Waldenström Macroglobulinemia. June 2007.

Weiss S, Nemunaitis JJ, Diaz-Lacayo M, Birch R, Ebrahimi B, Berdeaux DH, Allerton JP, Gardner LR, Henderson IC. **A Phase 1 study of daily oral perifosine and weekly gemcitabine.** ASCO 2007.

Birch R, Chawla S, Nemunaitis J, Savage P, Kaiser P, Spira A, Cervera A, Middleman E, Sausville E, Knowling M, Henderson I. **Perifosine an active agent in the treatment of patients with advanced sarcoma.** ASCO 2007.

Stephenson J, Schreeder M, Waples J, Hargis J, Campos L, Birch R, Henderson I; **Perifosine, active as a single agent for renal cell carcinoma (RCC), now in phase I trials combined with tyrosine kinase inhibitors (TKI's).** ASCO 2007.

Henderson IC, Schwartzberg L, Richards D, Vukelja S, Kapur D, Keaton M, Ebrahimi M, Rao H, Hermann R, Barve M, Bernhardt B; **A randomized, placebo (Plac) controlled, double blind exploratory trial of single agent chemotherapy with or without perifosine (P).** ASCO 2007.

Campos LT, Stephenson J, Swan F, Richards D, Birch R, Henderson I; **Daily dose of perifosine less toxic than weekly and active in patients with hepatocellular carcinoma (HCC).** ASCO 2007.

Steinert D, Henderson C, Chawla S, Staddon A, Schuetze S, Ryan C. **A Phase II Trial of perifosine in patients with chemo-insensitive sarcomas: preliminary results. A Sarcoma Alliance for Research through collaboration (SARC) study.** Connective Tissue Oncology Society (CTOS) 2007.

Leighl NB, Warr D, Vandenberg T, Dent S, Tannock IF, Crump M, Tozer R, Dancy J, Moore MJ. **Phase II study of perifosine in metastatic or advanced breast cancer.** 28th Annual San Antonio Breast Cancer Symposium 2004. Abstract #1077.

AEZS-108

Publications

Emons G, Sindermann H, Engel J, Schally AV, Gründker C. **Luteinizing hormone-releasing hormone receptor-targeted chemotherapy using AN-152.** Neuroendocrinology. 2009;90(1):15-8.

Engel JB, Schally AV, Dietl J, Rieger L, Hönig A. **Targeted therapy of breast and gynecological cancers with cytotoxic analogues of peptide hormones.** Mol Pharm. 2007;4(5):652-8.

Engel JB, Keller G, Schally AV, Nagy A, Chism DD, Halmos G. **Effective treatment of experimental human endometrial cancers with targeted cytotoxic luteinizing hormone-releasing hormone analogues AN-152 and AN-207.** Fertil Steril. 2005 ;83 Suppl 1:1125-33.

Nagy A, Schally AV. **Targeting of cytotoxic conjugates of somatostatin, luteinizing hormone-releasing hormone and bombesin to cancers expressing their receptors: a “smarter” chemotherapy.** Curr Pharm Des 2005;11(9):1167-1180.

Günther AR, Gründker C, Bongertz T, Schlott T, Nagy A, Schally AV, and Emons G. **Internalization of cytotoxic analog AN-152 of luteinizing hormone-releasing hormone induces apoptosis in human endometrial and ovarian cancer cell lines independent of multidrug resistance-1 (MDR-1) system.** Am J Obstet Gynecol. 2004;191:1164-1172.

Günther AR, Gründker C, Bongertz T, Nagy A, Schally AV, and Emons G. **Induction of apoptosis by AN-152, a cytotoxic analog of luteinizing hormone-releasing hormone (LHRH), in LHRH-R positive human breast cancer cells is independent of multidrug resistance-1 (MDR-1) system.** Breast Cancer Res Treat. 2004;87:255-264.

Letsch M, Schally AV, Szepeshazi K, Halmos G, and Nagy A. **Preclinical evaluation of targeted cytotoxic luteinizing hormone-releasing hormone analogue AN-152 in androgen-sensitive and insensitive prostate cancers.** Clin Cancer Res 2003;9:4505-4513.

Bajo AM, Schally AV, Halmos G, Nagy A. **Targeted doxorubicin-containing luteinizing hormone-releasing hormone analogue AN-152 inhibits the growth of doxorubicin-resistant MX-1 human breast cancers.** Clin Cancer Res. 2003;9:3742-8.

Nagy A, Schally AV. **Cytotoxic analogs of luteinizing hormone-releasing hormone (LH-RH): A new approach to targeted chemotherapy.** Drugs of the future 2002;27:359-370.

Gründker C, Völker P, Griesinger F, Ramaswamy A, Nagy A, Schally AV, and Emons G. **Antitumor effects of the cytotoxic luteinizing hormone-releasing hormone analog AN-152 on human endometrial and ovarian cancers xenografted into nude mice.** Am J Obstet Gynecol 2002;187:528-537.

Westphalen S, Kotulla G, Kaiser F, Krauss W, Werning G, Elsasser HP, Nagy A, Schulz KD, Grundker C, Schally AV, Emons G. **Receptor mediated antiproliferative effects of the cytotoxic LHRH agonist AN-152 in human ovarian and endometrial cancer cell lines.** Int J Oncol. 2000;17(5):1063-9.

Szepeshazi K, Schally AV, Nagy A. **Effective treatment of advanced estrogen-independent MXT mouse mammary cancers with targeted cytotoxic LH-RH analogs.** Breast Cancer Res Treat. 1999;56(3):267-76.

Miyazaki M, Nagy A, Schally AV, Lamharzi N, Halmos G, Szepeshazi K, Groot K, Armatas P. **Growth Inhibition of Human Ovarian Cancers by Cytotoxic Analogues of Luteinizing Hormone-Releasing Hormone.** J Natl Cancer Inst.1997;89(23):1803-1809.

Presentations

S. V. Liu, A. V. Schally, T. Dorff, S. Groshen, D. Hawes, D. Quinn, Y.C. Tai, N. L. Block, J. Engel, and J. Pinski. **A Phase I/II Trial of AEZS-108 (AN-152) in Castration-and Taxane-Resistant Prostate Cancer.** European Society of Medical Oncology Congress. Abstract #294. September 24, 2011. Stockholm, Sweden.

Wimberger P., Gorchev G., Hanker L., Stähle A., Hristamian A., Beckmann M.W., Dall P., Gründker C., Hilpert F., Sehouli J., Harter P., Taskova V., Emons G., AGO Study Group, Germany. **AGO-GYN 5 - (Phase II) study with AEZS-108, a targeted cytotoxic LHRH analog in patients with LHRH receptor positive endometrial cancer.** Abstract #247. September 14, 2011, Milan, Italy.

G. Emons, S. Tomov, P. Harter, J. Sehouli, P. Wimberger, A. Staehle, LC. Hanker, F. Hilpert, P. Dall, C. Gruendker. **Phase 2 study of AEZS-108 (AN-152), a targeted cytotoxic LHRH analog, in patients with LHRH receptor positive endometrial cancer.** 22nd EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics, November 18, 2010. Abstract #378.

G. Emons, S. Tomov, P. Harter, J. Sehouli, P. Wimberger, A. Staehle, L. C. Hanker, F. Hilpert, P. Dall, and C. Gruendker. **Phase 2 study of AEZS-108, a targeted cytotoxic LHRH analog, in patients with LHRH receptor positive platinum resistant ovarian cancer.** American Society of Clinical Oncology (ASCO) Annual Meeting, June 2010. Abstract #5035.

S. Liu, A. V. Schally, S. Xiong, R. Cote, D. Hawes, L. Fazli, M. Gleave, J. Cai, F. Brands, J. Engel, J. Pinski. **Expression of LHRH receptors in prostate cancer cells prior to therapy, following castration, or following treatment with LHRH agonists.** ASCO 2009. Poster #5163.

G. Emons, A.V. Schally, H. Sindermann, J. Engel. **AEZS-108 (AN-152): A new targeted treatment for GnRH receptor positive tumors.** The 9th International Symposium on GnRH. Feb 2008.

G. Emons, M. Kaufmann, A. Günthert, C. Gründker, S. Loibl, V.I. Tzekova, M.T. Velikova, S. Tomov, H. Sindermann, J. Engel and A.V. Schally. **Phase 1 study of ZEN-008 (AN-152), a targeted cytotoxic LHRH analog, in female patients with cancers expressing LHRH receptors.** ASCO 2007. Poster #3571.

Teifel M, Engel JB, Paulini K, Guenther E, Schally AV. **Targeting doxorubicin to LHRH-receptor positive tumors by the cytotoxic hybrid ZEN-008 (AN-152).** ENA-EORTC 2006. Poster 525.

Emons G, Kaufmann M, Günthert AR, Hamid-Werner M, Gründker C, Loibl S, and Schally AV. **Phase I study of ZEN-008 (AN-152), a targeted cytotoxic LHRH analog, in female patients with cancers expressing LHRH receptors.** ASCO 2006.

Engel JB, Teifel M, Schally AV. **Targeted Therapy of gynecological tumors with cytotoxic peptide analogs.** AACR 2006.

AEZS-112

Publication

Engel JB, Schönhals T, Weidler C, Häusler S, Krockenberger M, Rieger L, Dietl J, Wischhusen J, Honig A. **Tubulin inhibitor AEZS 112 inhibits the growth of experimental human ovarian and endometrial cancers irrespective of caspase inhibition.** Oncol Rep. 2009 Aug;22(2):361-7.

Presentations

Northfelt DW, Griffin P, Block H, Sindermann H, Teifel M, Von Hoff D, Mendelson D. **Phase I dose-escalation, safety, and pharmacokinetic study on weekly oral AEZS-112, a small molecule anti-cancer agent in patients with advanced cancer and lymphoma.** AACR 2009. Poster #5567.

Engel, J. Gerlach, M., Teifel, M., Baasner, S., Schmidt, P. and Guenther, E.G. **ZEN-012 – A novel highly potent orally active multi-target cytotoxic compound with inhibitory effects on tubulin polymerization, topoisomerase II and angiogenesis.** Joint conference of the AACR and JCA 2007. Abstract #5399.

Aicher B, Gerlach M, Schmidt P, Blumenstein L, Teifel M, Schuster T, Engel J, and Guenther E. **Highly potent cytotoxic compounds with inhibitory effects on Tubulin polymerization and Topoisomerase II.** ENA 2007. Poster #801.

Engel, J. Gerlach, M., Teifel, M., Baasner, S., Schmidt, P. and Guenther, E.G. **AEZS-112 – A novel highly potent orally active multi-target cytotoxic compound with inhibitory effects on tubulin polymerization, topoisomerase II and angiogenesis.** European School of Haematology (ESH) 2007.

Gerlach M, Teifel M, Baasner S, Schmidt P, and Guenther EG. **ZEN-017 (ZEN-012) – A new highly potent orally active multi-target cytotoxic compound with inhibitory effects on tubulin polymerization, topoisomerase II and angiogenesis.** AACR 2006. Abstract #499.

AEZS-126, 129, 131, 132 (Erk-PI3K inhibitors)

Publication

N/A

Presentations

M. Gerlach, I. Seipelt, G. Mueller, T. Schuster, L. Blumenstein, B. Aicher, E. Guenther and M. Teifel. **Novel Pyrido[2,3-b]pyrazines as orally active ERK inhibitors.** American Chemical Society's National Meeting. Poster #17068. Monday, August 29, 2011, Colorado Convention Center

Irene Seipelt, Eckhard Guenther, Lars Blumenstein, Gilbert Mueller, Peter Schmidt, Babette Aicher, Michael Teifel and Matthias Gerlach (Aeterna Zentaris GmbH). **A highly selective Erk 1/2 inhibitor with *in-vivo* anti tumor potency.** American Association for Cancer Research Annual Meeting. Poster #3563. April 5, 2011

I. Seipelt, E. Guenther, S. Baasner, L. Blumenstein, G. Mueller, J. Fensterle, J. Engel, M. Teifel, M. Gerlach. **AEZS-129, an orally active PI3K inhibitor in preclinical development.** 22nd EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics, November 17, 2010. Abstract #98

I. Seipelt, M. Gerlach, S. Baasner, L. Blumenstein, G. Mueller, B. Aicher, J. Engel, E. Guenther, M. Teifel. **AEZS-132, a new orally bioavailable PI3K/Erk inhibitor with antitumor effects.** 22nd EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics. November 2010. Abstract #197.

M.Teifel, I. Seipelt, L. Blumenstein, S. Baasner, G. Mueller, B. Aicher, E. Guenther and M. Gerlach. **A highly selective Erk-Inhibitor with anti-proliferative activity and the potential for combination therapy with modulators of the PI3K pathway.** Poster and oral presentation. Cambridge Healthtech Institute's 8th International "Discovery on Target" Conference, November 2, 2010.

I. Seipelt, L. Blumenstein, S. Baasner, G. Mueller, B. Aicher, M.Teifel, E. Guenther, M. Gerlach. **A highly selective Erk-inhibitor with antiproliferative efficacy and the potential for combination therapy with modulators of the PI3K pathway,** Oral Presentation. AACR 2010, April 20, 2010. Abstract #3856.

I. Seipelt, M. Gerlach, S. Baasner, L. Blumenstein, G. Mueller, B. Aicher, E. Guenther, M.I Teifel. **Dual inhibitors for PI3K and Erk induce growth inhibition of tumor cells**, Poster Presentation. AACR 2010, April 20. Abstract #4474.

Seipelt I, Gerlach M, Blumenstein L, Mueller G, Teifel M, Polymeropoulos E, and Guenther E. ***In vitro* profiling of the potent and selective PI3K inhibitor, AEZS-126**. AACR 2009. Poster #3706.

Seipelt I, Baasner S, Gerlach M, Teifel M, Fensterle J, Blumenstein L, Mueller G and Guenther E. **AEZS-126, a new orally bioavailable PI3K inhibitor with antitumor effects**. AACR 2009. Poster #3705.

Seipelt I, Claus E, Schuster T, Polymeropoulos E, Teifel M, and Guenther E. **New Generation of Anilino-Substituted Pyridopyrazine-Urea Derivatives Show Highly Selective PI3K-Inhibition**. AACR 2007. Poster #2379

AEZS-130 (MACIMORELIN)

Publications

Biller, Beverly M.K., M.D., K.C.J. Yuen, V. Bonert, M. Chen, A. Dobs, J.M. Garcia, M. Kipnes, M. Molitch, R. Swerdloff, C. Wang, D. Cook, I.R. Altomose, G.R. Merriam, **AEZS-130 (Macimorelin, Solorel™) an Oral Ghrelin Mimetic GH Secretagogue, as a Potential Diagnostic Test for Adult GH Deficiency**, 5th International Congress of the GRS-IGF Society, October 2010, poster #3.

Babette Aicher, Peter Schmidt, Elena Bresciani, Vittorio Locatelli, Daniel Perrissoud, Michael Teifel, **Pharmacological and Toxicological Evaluation of AEZS-130/Ghrelin Receptor Agonist, a Novel, Oral Synthetic Growth Hormone Secretagogue for the Diagnosis of Growth Hormone Deficiency**, 92nd Annual Endocrine Society (ENDO), June 2010, poster #851112.

MacLean CM, Casanova AT, Baselgia-Jeker L, Neave N, Larsen F, Skillern L, Drewe J, Beglinger C. **Effect of food on the pharmacokinetics and pharmacodynamics of an oral ghrelin agonist (ARD-07) in healthy subjects**. J Clin Pharmacol. 2009;49(5):553-9

Piccoli F, Degen L, MacLean C, Peter S, Baselgia L, Larsen F, Beglinger C, Drewe J. **Pharmacokinetics and pharmacodynamic effects of an oral ghrelin agonist in healthy subjects**. J Clin Endocrinol Metab. 2007;92(5):1814-20

Guerlavais JV, Boeglin D, Mousseaux D, Oiry C, Heitz A, Deghenghi R, Locatelli V, Torsello A, Ghè C, Catapano F, Muccioli G, Galleyrand JC, Fehrentz JA and Martinez. **New active series of growth hormone secretagogues**. J. Med. Chem. 46:1191-1203, 2003

Broglio F, Boutignon F, Benso A, Gottero C, Prodam F, Arvat E, Ghè C, Catapano F, Torsello A, Locatelli V, Muccioli G, Boeglin D, Guerlavais V, Fehrentz JA, Martinez J, Ghigo E, Deghenghi R. **EP1572: a novel peptido-mimetic GH secretagogue with potent and selective GH-releasing activity in man**. J Endocrinol Invest. 2002;25(8):RC26-8.

Presentations

Merriam G.R., Yuen K., Bonert V., Dobs A, Garcia J., Kipnes M., Molitch M., Swerdloff R., Wang C., Cook d., Altomose I. and Biller B. **Use of the Orally Active Ghrelin Mimetic AEZS-130 as a Simple Test for the Diagnosis of Growth Hormone (GH) Deficiency (GHD) in adults (AGHD)**. International Congress of Neuroendocrinology, Rouen en France. July 14, 2010. Poster P2-98.

Merriam GR, Yuen KJC, Asberry P, Bonert V, Dobs A, Garcia JM, Kipnes M, Kletke M, Molitch M, Swerdloff R, Wang C, Cook D, and Biller BMK. **Use of an Oral Ghrelin-Mimetic GH Secretagogue as a Simple Diagnostic Test for Adult GH Deficiency**. ENDO 2009. Poster P2-749

GHRELIN (AEZS-123)

Publications

Jerlhaga E, Egecioglu E, Landgrena S, Salome N, Heilig M, Moechars D, Datta R, Perrissoud D, Dickson SL, and Engel JA. **Requirement of central ghrelin signaling for alcohol reward.** PNAS 2009;106:11318-11323.

Salomé N, Haage D, Perrissoud D, Moulin A, Demange L, Egecioglu E, Fehrentz JA, Martinez J, and Dickson SL. **Anorexic and electrophysiological actions of novel ghrelin receptor antagonists in rats.** Eur. J. Pharmacol. 2009;612:167-173

Moulin A, Demange L, Ryan J, Mousseaux D, Sanchez P, Bergé G, Gagne D, Perrissoud D, Locatelli V, Torsello A, Galleyrand JC, Fehrentz JA, Martinez J. **New trisubstituted 1, 2, 4-triazole derivatives as potent ghrelin receptor antagonists. Synthesis and pharmacological in vitro and in vivo evaluations** J. Med. Chem. 51 (3): 689-693 2008.

Demange L, Boeglin D, Moulin A, Mousseaux D, Ryan R, Bergé G, Gagne D, Heitz A, Perrissoud D, Locatelli V, Torsello A, Galleyrand JC, Fehrentz JA, Martinez J. **Synthesis and pharmacological in vitro and in vivo evaluations of novel triazole derivatives as ligands of the ghrelin receptor** J. Med. Chem 50 (8): 1939-57 2007

Moulin A, Demange L, Bergé G, Gagne D, Ryan J, Mousseaux D, Heitz A, Perrissoud D, Locatelli V, Torsello A, Galleyrand JC, Fehrentz JA, Martinez J. **Toward potent ghrelin receptor ligands based on trisubstituted 1, 2, 4 – triazole structure. Synthesis and pharmacological in vitro and in vivo evaluations** J. Med Chem. 50 (23): 5790-806 2007

Presentations

Mulumba M, Jossart C, Perrissoud D., Proulx LI, Servant M, Marleau S, Ong H. **JMV2959 (AEZS-123), a triazole derivative ghrelin receptor antagonist, inhibits the antilipolytic effect of ghrelin but not that of unacylated ghrelin in 3T3-L1 cells.** ENDO 2009.

Roy MC, Paradis E, Samson P, Fehrentz JA, Martinez J, Proulx LI, Perrissoud D, Richard D. **Effect of a non-peptide growth hormone secretagogue ligand, JMV2959, on energy balance in rats fed a high-fat diet.** ENDO 2008.

Mulumba M, Jossart C, Escher E, Servant M, Marleau S, and Ong H. **Modulatory effect of QRFP on the signalling pathway of lipolysis induced by isoproterenol in 3T3-adipocytes.** ENDO 2008.

Salomé N, Gustafsson L, Taube M, Hansson C, Karlsson L, Fehrentz JA, Martinez J, Perrissoud D, and Dickson SL. **Chronic central infusion of a ghrelin receptor (GHS-R1A) antagonist to rats: impact on ICV ghrelin-induced food intake and altered body composition.** ECE 2008.

Torsello A, Bresciani E, Tamiazzo L, Bulgarelli I, Caporali S, Fehrentz JA, Martinez J, Perrissoud D and Locatelli V. **Novel potent and selective non-peptide ligands of ghrelin receptor : characterization of endocrine and extraendocrine actions.** ECE 2008.

Salomé N, Haage D, Perrissoud D, and Dickson SL. **Interrupted central ghrelin signalling by GHS-R1A antagonists in rats: impact on food intake and electrical activity of arcuate nucleus cells.** Keystone Symposium – Molecular Control of. Adipogenesis and Obesity. 2008

Perrissoud D, Fehrentz JA, Galleyrand JC, Martinez J, Torsello A and Locatelli V. **Novel non-peptide ghrelin receptor ligands inhibit food intake in rats without alteration of growth hormone secretion.** ENDO 2007.

Mulumba M, Jossart C, Latterich M, Escher E, Clement JF, Servant M, Marleau S, Ong H. **Inhibition of isoproterenol-induced lipolysis by QRFP via a GPR103B pathway in 3T3-L1 adipocytes.** ENDO 2007.

Roy MC, Paradis E, Samson P, Thiboutot-Gagnon N, Marcotte M, Lachance Y, Perrissoud D, Richard D. **Long term treatment with non-peptide ghrelin receptor ligands affect energy balance in mice fed a high-fat diet.** ENDO 2007.

CETRORELIX (AEZS-102)

Publications

Debruyne F, Gres AA, Arustamov DL. **Placebo-controlled dose-ranging phase 2 study of subcutaneously administered LHRH antagonist cetorelix in patients with symptomatic benign prostatic hyperplasia.** Eur Urol. 2008;54(1):170-7.

Ficarra V, Novara G. **Editorial comment on: placebo-controlled dose-ranging phase 2 study of subcutaneously administered LHRH antagonist cetorelix in patients with symptomatic benign prostatic hyperplasia.** Eur Urol. 2008;54(1):178.

Bastian PJ. **Editorial comment on: placebo-controlled dose-ranging phase 2 study of subcutaneously administered LHRH antagonist cetorelix in patients with symptomatic benign prostatic hyperplasia.** Eur Urol. 2008;54(1):179-80.

Drewa T, Chlosta P. **Comment on : Placebo-controlled dose-ranging phase 2 study of subcutaneously administered LHRH antagonist Cetorelix in patients with symptomatic benign prostatic hyperplasia.** Eur Urol. 2009 ;55(2):e36-7; author reply e38-9.

Engel JB, Rieger L, Dietl J, and Hönig A. **The GnRH antagonist cetorelix: established indications and future potential.** Expert Review of Obstetrics & Gynecology. 2007;2(4):431-440.

Engel JB, Schally AV. **Drug Insight: clinical use of agonists and antagonists of luteinizing-hormone-releasing hormone.** Nat. Clin. Pract. Endocrinol. Metab.2007;3:157-167.

Lepor H. **The role of gonadotropin-releasing hormone antagonists for the treatment of benign prostatic hyperplasia.** Rev Urol. 2006; 8(4):183-9.

Reissmann T, Schally AV, Bouchard P, Riethmiiller H, Engel J. **The LHRH antagonist cetorelix: a review.** Hum Reprod Update. 2000;6(4):322-31.

Endometriosis

Altintas D, Kokcu A, Tosun M, Cetinkaya MB, and Kandemir B. **Comparison of the effects of cetorelix, a GnRH antagonist, and leuprolide, a GnRH agonist, on experimental endometriosis.** J Obstet Gynaecol Res. 2008;34(6):1014-1019.

Presentations

J.Engel. Cetorelix: **A new treatment for BPH.** 9th International Symposium on GnRH. Feb. 2008.

FMJ Debruyne, A.A. Gres, A. Bantshev, M. Tzvetkov, K. Grdovic. **“LHRH antagonist cetorelix for symptomatic BPH: Prolonged improvement beyond end of treatment in placebo-controlled trials.”** European Urology Supplements, 2008;7(3):171. EAU 2008.

Engel J, Rozsa B, Schally AV, et al. **Luteinizing hormone-releasing hormone (LHRH) receptors in BPH as potential molecular targets for therapy with Cetrorelix.** AUA 2008. Abstract 1310. J Urol. 2008;179:449.

Debruyne, FMJ., Tzvetkov, M., Medverec, Z., Altarac, S., Peukert, M., Engel, J., **Cetrorelix pamoate, an LHRH antagonist, in the treatment of BPH: randomized, placebo-controlled multicenter study.** SIU 2006.

Debruyne FMJ, Gres AA, Bantshev A, Tzvetkov M, Grdovic K. **LHRH antagonist cetrorelix in the treatment of BPH: results from two randomized, placebo-controlled multicenter trials.** 8th International Symposium on GnRH Analogues. 2005.

Lepor, H., Dixon, C., Crawford, D., Steidi, C., Oesterling, J.A. **Randomized double-blind placebo controlled Phase 2 study of the safety and efficacy of cetrorelix in men with BPH.** AUA 1997. J. Urol. 1997;157 (4 suppl):136.

OZARELIX

Publications

Schally AV. **LHRH analogs: their impact on the control of tumorigenesis.** Peptides. 1999;20:1247-1262.

Kutscher B, Bernd M, Beckers T et al. **Chemistry and molecular biology in the search for new LH-RH antagonist.** Angewandte Chemie 1997;109:2240-2254.

Presentations

Debruyne FMJ. **The efficacy and safety of ozarelix, a novel GNRH antagonist, in men with lower urinary tract symptoms (LUTS) due to benign prostatic hyperplasia (BPH).** AUA 2007. Abstract 1552. J Urol. 2007;177(4 suppl):512.

Denes BS, Reddy G. **The efficacy and safety of Ozarelix in men with BPH.** The 9th International Symposium on GnRH. Feb 2008.

Debruyne FMJ, Neykov K, Taskova VD, Stratev S, Bantchev A, Karanikilov SS, Chawla S, Lenaz G, Peukert M, and Engel J. **Phase II dose-finding study of ozarelix, an LHRH antagonist, in patients with inoperable prostate cancer.** SIU 2006.

Goerres U, Bernd M, Zugmaier G, Reissmann T. **Pharmalogical characteristics of D-63153 (ozarelix), a new potent GnRH antagonist.** EORTC-NCI-AACR 2002. Poster #92.