

Paclitaxel poliglumex
[PPX; CT-2103; OPAXIO™ (formerly branded as XYOTAX)] Bibliography

Publications

- (1) Albain K, Belani C, Bonomi P, et al. PIONEER: a phase III randomized trial of paclitaxel poliglumex versus paclitaxel in chemotherapy-naïve women with advanced-stage non-small-cell lung cancer performance status of 2. *Clin Lung Cancer*. 2006 May;7(6):417-19.
- (2) Auzenne E, Donato NJ, Li C, et al. Superior therapeutic profile of poly-L-glutamic acid-paclitaxel copolymer compared with taxol in xenogeneic compartmental models of human ovarian carcinoma. *Clin Cancer Res*. 2002 Feb;8(2):573-81.
- (3) Belani CP. Emerging advances in the management of lung cancer. *Clin Lung Cancer*. 2004 Dec; 6 Suppl 2:S60.
- (4) Boddy AV, Plummer ER, Todd R, et al. A phase I and pharmacokinetic study of paclitaxel poliglumex (XYOTAX), investigating both 3-weekly and 2-weekly schedules. *Clin Cancer Res*. 2005 Nov 1;11(21):7834-40.
- (5) Bonomi P. Paclitaxel poliglumex (PPX, CT-2103): macromolecular medicine for advanced non-small cell lung cancer. *Expert Rev Anticancer Ther*. 2007 Apr;7(4):415-22 [Review]
- (6) Chipman S, Oldham F, Pezzoni G, et al. Biological and clinical characterization of paclitaxel poliglumex (PPX, CT-2103), a macromolecular polymer-drug conjugate. *Int J Nanomed*. 2006;1:375-83.
- (7) Dipetrillo T, Milas L, Evans D, et al. Paclitaxel poliglumex (PPX-Xyotax) and concurrent radiation for esophageal and gastric cancer: a phase I study. *Am J Clin Oncol*. 2006 Aug;29(4):376-9.
- (8) Edelman MJ. Novel cytotoxic agents for non-small cell lung cancer. *J Thorac Oncol*. 2006 Sep;1(7):752-5 [Review]
- (9) Garfield D. New form of paclitaxel shows promise. *Lancet Oncol*. 2001 Apr;2(4):192.
- (10) Govinden R, Garfield DH. Treatment approaches in patients with advanced non-small cell lung cancer and poor performance status. *Semin Oncol*. 2004 Dec;31(6 Suppl 11):27-31 [Review]
- (11) Hede K. Lung cancer may be different for men and women, but researchers ponder what to do? *J Natl Cancer Inst*. 2007 Dec19;99(24):1830-2.
- (12) Ke S, Milas L, Charnsangavej C, et al. Potentiation of radioresponse by polymer-drug conjugates. *J Control Release*. 2001 Jul 6;74(1-3):237-242.
- (13) Kumar A, Wakelee H. Second- and third-line treatments in non-small cell lung cancer. *Curr Treat Options Oncol*. 2006 Jan;7(1):37-49 [Review]
- (14) Langer CJ. CT-2103: a novel macromolecular taxane with potential advantages compared with conventional taxanes. *Clin Lung Cancer*. 2004 Dec;6 Suppl 2:S85-8. [Review]

Paclitaxel poliglumex (PPX; CT-2103; XYOTAX™) Bibliography

- (15) Langer CJ. CT-2103: emerging utility and therapy for solid tumors. *Expert Opin Investig Drugs*. 2004 Nov;13(11):1501-8. [Review]

Publications, continued.

- (16) Langer CJ. Dilemmas in management: the controversial role of chemotherapy in PS 2 advanced NSCLC and the potential role of CT-2103 (Xyotax™). *Oncologist*. 2004;9(4):398-405. [Review]
- (17) Li C, Ke S, Wu Q, et al. Tumor irradiation enhances the tumor-specific distribution of poly(L-glutamic acid)-conjugated paclitaxel and its antitumor efficacy. *Clin Cancer Res*. 2000 Jul;6(7):2829-34.
- (18) Li C, Newman RA, Wu QP, et al. Biodistribution of paclitaxel and poly(L-glutamic acid)-paclitaxel conjugate in mice with ovarian OCa-1 tumor. *Cancer Chemother Pharmacol*. 2000;46(5):416-22.
- (19) Li C, Price JE, Milas L, et al. Antitumor activity of poly(L-glutamic acid)-paclitaxel on syngeneic and xenografted tumors. *Clin Cancer Res*. 1999 Apr;5 (4):891-7.
- (20) Li C, Yu DF, Newman RA, et al. Complete regression of well-established tumors using a novel water-soluble poly(L-glutamic acid)-paclitaxel conjugate. *Cancer Res*. 1998 Jun;58(11):2404-9.
- (21) Li C, Ke S, Wu Q, Tansey W, Hunter N, Buchmiller LM et al. Potentiation of ovarian OCa-1 tumor radioresponse by poly (L-glutamic acid)-paclitaxel conjugate. *Int J Radiat Oncol Biol Phys*. 2000 Nov; 48(4):1119-1126.
- (22) Li C, Newman RA, Wallace S. Reformulating Paclitaxel. *Science & Medicine* 1999 Feb; 6(1):38-41.
- (23) Li C, Yu DF, Inoue T, Yang DJ, Milas L, Hunter N et al. Synthesis and evaluation of water-soluble polyethylene glycol-paclitaxel conjugate as a paclitaxel prodrug. *Anticancer Drugs*. 1996;7:642-48.
- (24) Lin NU, Parker LM, Come SE, et al. Phase II study of CT-2103 as first- or second-line chemotherapy in patients with metastatic breast cancer: unexpected incidence of hypersensitivity reactions. *Invest New Drugs*. 2007 Aug;25(4):369-75.
- (25) Man M, Rugo H. Paclitaxel poliglumex (Cell Therapeutics/Chugai Pharmaceutical). *IDrugs*. 2005 Sep;8(9):739-54. [Review]
- (26) Markman M. Improving the toxicity profile of chemotherapy for advanced ovarian cancer: a potential role for CT-2103. *J Exp Ther Oncol*. 2004 Jul;4(2):131-6. [Review]
- (27) McCormick-Thomson LA, Duncan R. Poly(amino acid) copolymers as a potential soluble drug delivery system. 1. pinocytic uptake and lysosomal degradation measured in vitro. *J Bioactive and Compatible Polymers*. 1989;4:242-51.
- (28) Nemunaitis J, Cunningham C, Senzer N, et al. Phase I study of CT-2103, a polymer-conjugated paclitaxel, and carboplatin in patients with advanced solid tumors. *Cancer Invest*. 2005;23(8):671-6.
- (29) Oldham E, Li C, Ke S, et al. Comparison of action of paclitaxel and poly(L-glutamic acid)-paclitaxel conjugate in human breast cancer cells. *Int J Oncol*. 2000 Jan;16(1):125-32.

Paclitaxel poliglumex (PPX; CT-2103; XYOTAX™) Bibliography

- (30) Ozols RF. Systemic therapy for ovarian cancer: current status and new treatments. *Semin Oncol.* 2006 Apr;33(2 Suppl 6):S3-11 [Review]

Publications, continued.

- (31) Perez EA. Novel enhanced delivery taxanes: an update. *Semin Oncol.* 2007 Jun;34(3):suppl 1-5. [Review]
- (32) Reddy GK. Paclitaxel poliglumex/carboplatin is similar to paclitaxel/carboplatin as first-line treatment in elderly patients with advanced non-small cell lung cancer and a poor performance status. *Clin Lung Cancer.* 2005 Jul;7(1):20-22.
- (33) Richards DA, Richards P, Bodkin D, et al. Efficacy and safety of paclitaxel poliglumex as first-line chemotherapy in patients at high risk with advanced-stage non-small-cell lung cancer: results of a phase II study. *Clin Lung Cancer.* 2005 Nov;7(3):215-20.
- (34) Rowinsky EK, Calvo E. Novel agents that target tubulin and related elements. *Semin Oncol.* 2006 Aug;33(4):421-35. [Review]
- (35) Sabbatini P, Aghajanian C, Dizon D, et al. Phase II study of CT-2103 in patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal carcinoma. *J Clin Oncol.* 2004 Nov 15;22(22):4523-31.
- (36) Shaffer S, Baker-Lee C, Kennedy J, et al. In vitro and in vivo metabolism of paclitaxel poliglumex: identification of metabolites and active proteases. *Cancer Chemother Pharmacol.* 2007 Mar;59(4):537-48.
- (37) Singer JW. Paclitaxel poliglumex (XYOTAX™, CT-2103) a macromolecular taxane. *J Control Release.* 2005 Dec 5;109(1-3):120-6. [Review]
- (38) Singer JW, Shaffer S, Baker B, et al. Paclitaxel poliglumex (XYOTAX; CT-2103): an intracellularly targeted taxane. *Anti-Cancer Drugs.* 2005 Mar;16(3):243-54. [Review]
- (39) Singer JW, Baker B, De Vries P, et al. Poly-(L)-glutamic acid-paclitaxel (CT-2103) [XYOTAX], a biodegradable polymeric drug conjugate: characterization, preclinical pharmacology, and preliminary clinical data. *Adv Exp Med Biol.* 2003; 519:81-99. [Review]
- (40) Tishler RB. Polymer-conjugated paclitaxel as a radiosensitizing agent – a big step forward for combined modality therapy? *Int J Radiat Oncol Biol Phys.* 2003 Mar 1;55(3):563-64.
- (41) Vereronesi ML, Flaherty K, Kramer A, et al. Phase I study of the novel taxane CT-2103 in patients with advanced solid tumors. *Cancer Chemother Pharmacol.* 2005 May;55(5):497-501.

Paclitaxel poliglumex (PPX; CT-2103; XYOTAX™) Bibliography

Abstracts

- (1) Allievi C, Strepponi I, Bastrup U, et al. Biodistribution of paclitaxel poliglumex (PPX) in lung: Analysis of gender-related alterations in a preclinical model. *J Clin Oncol*, 2006 ASCO Annual Meeting Proceedings Part I. Vol 24, No. 18S (June 20 Supplement), 2006: Abstract 17003.
- (2) Amato RJ. Phase II study of xyotax (ppx) for androgen independent prostate cancer (aipc). American Society of Clinical Oncology (ASCO) 2008 Genitourinary Cancers Symposium: Abstract 163.
- (3) Amato RJ, Khan M, Mohammad T. A phase II study of paclitaxel poliglumex (PPX) for androgen independent prostate cancer (AIPC). American Society of Clinical Oncology (ASCO) 2007 Prostate Cancer Symposium: Abstract 243.
- (4) Amato RJ, Sharef S, Khan M. A phase II study of paclitaxel poliglumex (PPX) for androgen independent prostate cancer (AIPC). American Society of Clinical Oncology (ASCO) 2006 Prostate Cancer Symposium: Abstract 263.
- (5) Barbieri P, Oldham F, Holman J, et al. Improved safety profile of a macromolecular taxane: an integrated safety summary of XYOTAX™ (paclitaxel poliglumex; CT-2103) phase 1-2 and phase 2 trials. ESMO 2004 Abstract Book. *Ann Oncol* 15 (Supplement 3), iii106 (397P).
- (6) Bernareggi A, Allievi C, Danese A, et al. Paclitaxel poliglumex (PPX) modulates paclitaxel pharmacokinetics (PK) and accumulates in tumor. 46° Simposio L'Associazione Farmaceutici dell'Industria. June 15, 2006. Rimini, Italy.
- (7) Bernareggi A, Allievi C, Pezzoni G, et al. Gender effect and role of estrogens on pharmacokinetics (PK) and clinical efficacy of paclitaxel poliglumex (PPX). 46° Simposio L'Associazione Farmaceutici dell'Industria. June 15, 2006. Rimini, Italy.
- (8) Bernareggi A, Oldham F, Baker B, et al. XYOTAX™ (paclitaxel poliglumex, PPX): tumor accumulation and prolonged exposure to paclitaxel. American Association for Cancer Research (AACR) Annual Meeting. 2005. Anaheim, CA. Abstract 1408.
- (9) Bolton MG, Cassidy J, Calvert H. Phase I studies of PG-Paclitaxel (CT-2103) as a single agent and in combination with cisplatin. International Symposium on Polymer Therapeutics, 2002. Cardiff, United Kingdom.
- (10) Bonomi P, Langer C, O'Brien M, et al. Analysis of prognostic factors in patients with advanced relapsed /refractory NSCLC: Cox regression analysis of a randomized phase III trial comparing docetaxel and paclitaxel poliglumex (PPX). *J Clin Oncol*, 2006 ASCO Annual Meeting Proceedings Part I. Vol 24, No. 18S (June 20 Supplement), 2006: Abstract 7040.
- (11) Bonomi P, Villaflor VM, Oldham FB, et al. Single-agent compared to combination first-line chemotherapy in patients with advanced non-small cell lung cancer (NSCLC) and a performance status (PS) of 2. *J Clin Oncol*, 2007 ASCO Annual Meeting Proceedings Part I. Vol 25, No. 18S (June 20 Supplement), 2007: Abstract 7637.

Paclitaxel poliglumex (PPX; CT-2103; XYOTAX™) Bibliography

Abstracts, continued.

- (12) Burris H, Shipley D, Greco A, et al. Phase 1 studies of CT-2103 in patients with non small cell lung cancer and with advanced malignancies. *Eur J Cancer* 2003; 1(5):S168.
- (13) Chipman S, Rosler R, Bonham L, et al. Energy dependent uptake of paclitaxel poliglumex by human NSCLC tumor and murine macrophage-like cell lines. EORTC-NCI-AACR 2006. *Eur J Cancer. Supplements, Volume 4, No.12, Pg 194: Abstract 643.*
- (14) de Vries P, Kumar A, Heasley E, Stone I, Singer J. CT-2103: A water soluble poly-L-glutamic acid (PG)-Paclitaxel (TXL) conjugate has enhanced efficacy on MDR-1+ human colon carcinoma cell line xenografts compared to free TXL. Proceedings of the American Association of Cancer Research, 42, 462. 2001. New Orleans, LA.
- (15) de Vries P, Kumar A, Bellamy G, Nudelman E, Brannan M, Lewis RA et al. Pharmacokinetics (PK) and biodistribution of poly-(L)-glutamic acid (PG) paclitaxel (TXL) (CT-2103) in mice with subcutaneous B-16 melanomas. Proceedings of the 11th AACR-NCI-EORTC Symposium, 555. 2000. Amsterdam, Netherlands.
- (16) de Vries P, Kumar A, Heasley E, et al. Optimization of the anti-tumor activity of water-soluble poly L-glutamic acid (PG)-paclitaxel (TXL) conjugates. Proceedings of the 10th AACR-NCI-EORTC Symposium, 451. 1999. Washington, DC.
- (17) Di Giovine S, De Feudis P, Torriani D, et al. Effect of estrogen on cathepsin B activity and antitumor efficacy of paclitaxel poliglumex in human tumor xenografts. EORTC-NCI-AACR 2006. *Eur J Cancer. Supplements, Volume 4, No.12, Pg 191: Abstract 633.*
- (18) Dipetrillo T, Evans D, Akerman P, et al. Paclitaxel poliglumex (PPX), cisplatin and concurrent radiation for esophageal and gastric cancer: A phase I study. *J Clin Oncol*, 2007 ASCO Annual Meeting Proceedings Part I. Vol 25, No. 18S (June 20 Supplement), 2007: Abstract 15130.
- (19) Fornasier M, Bergottini R, Radaelli E, et al. Paclitaxel poliglumex cellular uptake by normal tissues and human tumor xenograft: an IHC study in nude mice. EORTC-NCI-AACR 2006. *Eur J Cancer. Supplements, Volume 4, No.12, Pg 192: Abstract 637.*
- (20) Herzog T, Barret RJ, Edwards R, et al. Phase II study of paclitaxel poliglumex (PPX)/carboplatin (C) for 1st line induction and maintenance therapy of stage III/IV ovarian or primary peritoneal carcinoma. *J Clin Oncol*, 2005 ASCO Annual Meeting Proceedings Part I of II. Vol 23, No. 16S (June 1 Supplement), 2005: Abstract 5012.
- (21) Khan M, Sharef S, Amato R. Phase II study of XYOTAX™ (PPX) for androgen independent prostate cancer (AIPC). *J Clin Oncol*, 2006 ASCO Annual Meeting Proceedings Part I. Vol 24, No. 18S (June 20 Supplement), 2006: Abstract 14624.
- (22) Ke S, Charnsangavej C, Wallace S, Li C. Elevated serum VEGF as a prognosis marker in combined radiation and PG-TXL (CT-2103) therapy in mice with murine ovarian OCa-1 tumor. Proceedings of the American Association of Cancer Research 42, 3873. 2001. New Orleans, LA.

Paclitaxel poliglumex (PPX; CT-2103; XYOTAX™) Bibliography

Abstracts, continued.

- (23) Ke S, Oldham E, Milas L, Hunter NR, Tansey W, Charnsangavej C et al. Schedule-independent radiosensitization of a murine ovarian OCa-1 tumor by PG-TXL. Proceedings of the American Association of Cancer Research 40, 4223. 1999. Philadelphia, PA
- (24) Li C, Ke E, Oldham L, et al. Enhancement of tumor radioresponse of a murine ovarian carcinoma by Poly(L-Glutamic Acid)-Paclitaxel [PG-TXL] conjugate. 3rd International Symposium on Frontiers in Biomedical Polymers. 1999. Shiga, Japan.
- (25) Li C, Price JE, Milas L, Hunter NR, Ke S, Yu DF et al. Antitumor activity of Poly(L-glutamic acid)-Paclitaxel on syngeneic and xenografted tumors. Proceedings of the American Association of Cancer Research 40, 1909. 1999. Philadelphia, PA.
- (26) Mason KA, Hunter N, Wallace S, Milas L. Poly (L-glutamic Acid)-paclitaxel dramatically enhances the anti-tumor efficacy of radiotherapy. AACR-NCI-EORTC, 397. 2001. Miami Beach, FL.
- (27) O'Brien M, Bonomi P, Langer C, et al. Analysis of prognostic factors in chemo-naive patients with advanced NSCLC and poor performance status (PS2): Cox regression analysis of two randomized phase III trials. *J Clin Oncol*, 2006 ASCO Annual Meeting Proceedings Part I. Vol 24, No. 18S (June 20 Supplement), 2006: Abstract 7113.
- (28) O'Byrne K, Singer J, Oldham F, et al. Effect of estrogen on outcome in two randomized phase III studies of paclitaxel poliglumex (PPX) in advanced non-small cell lung cancer NSCLC. EORTC-NCI-AACR 2006. *Eur J Cancer*. Supplements, Volume 4, No.12, Pg 194: Abstract 645.
- (29) O'Byrne K, Bonomi P, Paz-Ares L, et al. Paclitaxel poliglumex vs. docetaxel for second-line treatment of non-small cell lung cancer (NSCLC): the STELLAR 2 phase III study. *Eur J Cancer*. 2005;(Suppl)3:14. Abstract PS13.
- (30) Oldham FB, Anastassopoulos KP, O'Byrne K, et al. Medical resource utilization (MRU) and costs associated with paclitaxel poliglumex (PPX) compared to gemcitabine (Gem) or vinorelbine (Vin) in non-small cell lung cancer (NSCLC) patients. *J Clin Oncol*, 2007 ASCO Annual Meeting Proceedings Part I. Vol 25, No. 18S (June 20 Supplement), 2007: Abstract 18172.
- (31) Redfern C, Schulz J, Burris, H, et al. Phase 2 study of CT-2103 in patients with colorectal cancer having recurrent disease after treatment with a 5-fluorouracil-containing regimen. *Eur J Cancer* 2003; 1(5):S84-5.
- (32) Ross H, Oldham F, Bandstra B, et al. Serum free estradiol (E2) levels are prognostic in men with chemotherapy-naïve advanced non-small cell lung cancer (NSCLC) and performance status (PS) of 2. *J Clin Oncol*, 2007 ASCO Annual Meeting Proceedings Part I. Vol 25, No. 18S (June 20 Supplement), 2007: Abstract 7683.

Paclitaxel poliglumex (PPX; CT-2103; XYOTAX™) Bibliography

Abstracts, continued.

- (33) Ross H, Bonomi P, Langer C, et al. Effect of gender on outcome in two randomized phase III trials of paclitaxel poliglumex (PPX) in chemo-naïve pts with advanced NSCLC and poor performance status (PS2). *J Clin Oncol*, 2006 ASCO Annual Meeting Proceedings Part I. Vol 24, No. 18S (June 20 Supplement), 2006: Abstract 7039.
- (34) Sabbatini P, Soignet S, Aghajanian C, et al. Early findings in a phase I study of PG-paclitaxel (CT-2103) in recurrent ovarian and/or peritoneal cancer. *Clin Cancer Res* 7[11 (Suppl)], 470. 2001.
- (35) Shaffer SA, Baker Lee C, Nudelman E, et al. Metabolism of poly-L-glutamic acid (PG) paclitaxel (CT-2103); proteolysis by lysosomal cathepsin B and identification of intermediate metabolites. Proceedings of the American Association of Cancer Research 43, 416. 2002. San Francisco, CA.
- (36) Shaffer S, Baker Lee C, de Vries P, et al. *In vivo* identification of monoglutamyl paclitaxel metabolite from poly-L-glutamic acid-paclitaxel (CT-2103) in tumor bearing mice. ASMS Conference on Mass Spectrometry and Allied Topics. 2001. Chicago, IL. Abstract A010970.
- (37) Singer JW, Oldham FB, Bandstra B, et al. Serum cathepsin B (CB) levels are prognostic in chemotherapy-naïve patients (pts) with advanced non-small cell lung cancer (NSCLC) and performance status (PS) of 2. *J Clin Oncol*, 2007 ASCO Annual Meeting Proceedings Part I. Vol 25, No. 18S (June 20 Supplement), 2007: Abstract 18036.
- (38) Singer JW, de Vries P, Kumar A, et al. Poly-L-Glutamic Acid Paclitaxel Conjugate (PG-TXL): A water-soluble biodegradable conjugate with decreased toxicity and enhanced efficacy. International Symposium on Polymer Therapeutics. 2000. Nara, Japan.
- (39) Skubitz KM, Verschraegen A, Daud A, et al. A phase I study of paclitaxel poliglumex (PPX) in combination with cisplatin (CIS) for patients (pts) with advanced cancer. *J Clin Oncol*. 2005;23:157s.
- (40) Sludden J, Boddy AV, Griffin MJ, et al. Phase I and pharmacological study of CT-2103, a poly(L-glutamic acid)-paclitaxel conjugate. Proceedings of the American Association of Cancer Research 42, 535. 2002. San Francisco, CA.
- (41) Takimoto C, Schwartz G, Romero O, et al. Phase I evaluation of paclitaxel poliglumex (PPX) administered weekly for patients with advanced cancer. AACR-NCI-EORTC. November 2005. Philadelphia, PA.
- (42) Todd R, Sludden J, Boddy AV, et al. Phase I and pharmacological study of CT-2103, a poly (L-glutamic Acid)-paclitaxel conjugate. Proceedings of Am Soc Clin Oncol 20: 2001. Abstract 439.
- (43) Verrill MW, Boddy AV, Todd R, et al. Phase I pharmacokinetic (PK) study of CT-2103 given Q2 or Q3 weeks in patients with solid tumors. *J Clin Oncol* 2003;20. Abstract 533.
- (44) Wen X, Li C, Wu Q, et al. Potentiation of Antitumor Activity of PG-TXL with Anti-EGFR Monoclonal Antibody C225 in MDA-MB-468 Human Breast Cancer Xenograft. Proceedings of the American Association of Cancer Research 41, 2052. 2000. San Francisco, CA.