

Immunotherapy with dendritic cells (DCT)

Fighting cancer with the immune system, a century-old dream of medicine, which has come a considerable step closer since the discovery of immunotherapy using dendritic cells at the end of the 1990s.

For this, the "father of modern immunotherapy" Professor Ralph Steinmann was honored with the Nobel Prize for Medicine - the highest distinction for a scientist - in 2011.

In countless research and therapy facilities around the world, people are increasingly turning to dendritic cell therapy, more than 7,000 scientific papers have been published on the subject and in some modern countries, such as the USA, this therapy has already been approved.

The effectiveness of dendritic cell therapy

Who can benefit from dendritic cell treatment?



Dendritic cells are processed in a highly specialized laboratory

The effectiveness of dendritic cell therapy has been proven for all types of cancer except for blood cancer. It has been shown to be particularly effective for skin, kidney, breast, colon, pancreas, and prostate cancer. Patients with ovarian cancer have also been shown to benefit from treatment with dendritic cells.

However, since there are standard therapies for most types of cancer, some of which have been developed over decades, it is advisable to use these therapies and to carry out immunotherapy to support them. Today we know that tumour cells that have already been damaged by chemotherapy or radiation can be destroyed much better by immune cells than undamaged tumour cells.

Treatment with dendritic cells is often also used when conventional therapies have not been successful.

This has been shown in renal cell carcinoma and malignant melanoma. However, vaccination with dendritic cells is most promising when only small amounts of tumour cells are present. It is now known that the immune system often functions much better in patients with a low tumour mass than in patients with a high tumour load.

As with chemo- and radiotherapy, the earlier the therapy with dendritic cells is started, the more successful it is

Cancer and the immune system

Can the immune system protect against cancer?



Our immune system is protecting us every day

The immune system is our body's own defense system against damaging pathogens such as bacteria, fungi and viruses, but also against cells that are degenerate and divide uncontrollably. Every day in our lives, about eight malignant cell proliferations occur in the body.

Nevertheless, only 1 cancer develops on average over 200 years of life. This shows that the human immune system recognizes and destroys almost all cells that show changes that could develop into cancer.

This question has been investigated by scientists.

In 3625 healthy people who were over 40 years old, they examined the function of the immune system over a long period of 11 years. People with a normal or even above-average functioning immune system had an approximately 40% lower risk of developing cancer.

A well-functioning immune system is therefore important to protect against cancer.

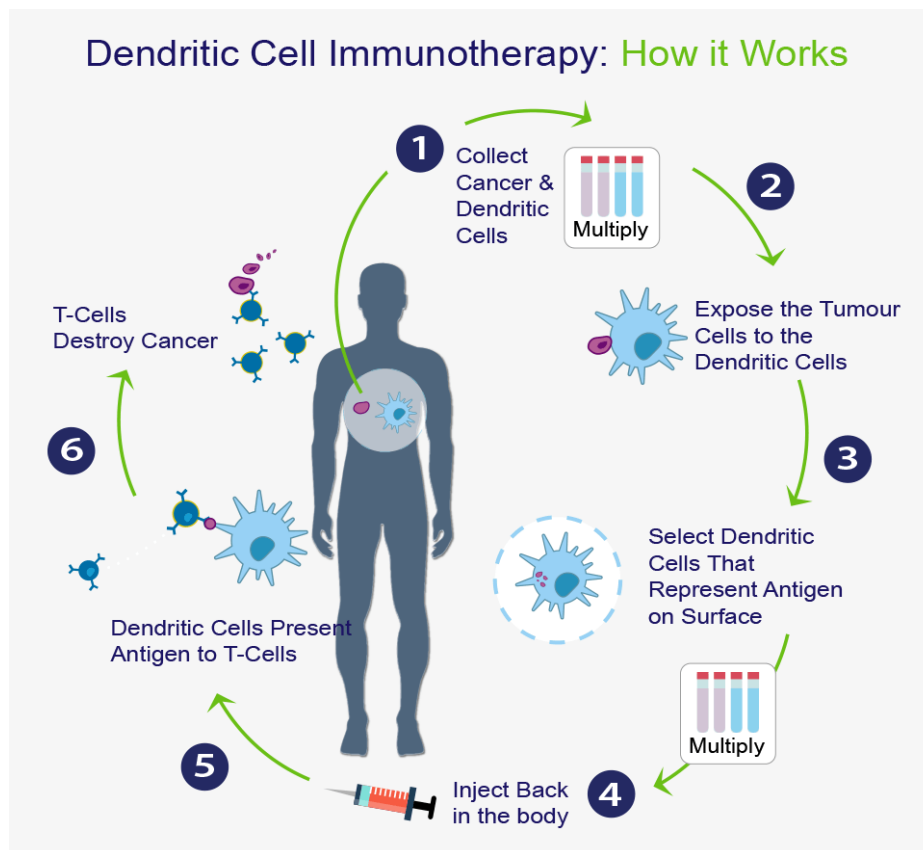
Nevertheless, it can happen that our immune system does not recognize these cells precisely because of their changes. In addition, tumours above a certain size can produce messenger substances that lead to a weakening of the immune system. Therefore, the immune system is weakened in most patients with cancer.

Because of this and based on this knowledge, doctors are trying to strengthen the immune system of cancer patients by means of drugs, vitamins and supplements, but also by using complementary medical treatments.

Through intensive research, knowledge of the immune system, the individual factors and cell types that play a decisive role in the defense against harmful pathogens or cells have grown considerably in recent years.

Today we understand much more about the cells of the immune system than 10 years ago. Among other things, it is now known that dendritic cells play a very special role in the fight against cancer.

The principle of therapy



Using a special procedure, precursor cells can be isolated from the blood, which have the potential to become dendritic cells. This ability is enhanced by means of certain messenger substances to which the cells are exposed in the test tube.

■ ■ While the precursor cells are in the maturing phase, they can take up proteins (e.g. tumour antigens from the patient's own plasma) into their interior.

■ ■ Progenitor cells that are not yet fully mature can also take up these proteins outside the body under highly purified laboratory conditions.

■ ■ Once the cells have taken up tumour antigens, they convert them and present them on their surface. Thus, the characteristic features of these antigens are later more easily recognizable for other immune cells. During this process, the precursor cells mature into fully developed dendritic cells, which carry the characteristic features of harmful structures of tumour cells in connection with a special signaling sign on their surface. The immune cells can recognize this signal and identify it as harmful

■ ■ If the now fully developed dendritic cells are now injected under the skin, they migrate from there into the lymph nodes and activate different types of extender cells (so-called cytotoxic T-lymphocytes), which are capable of killing degenerate cells.

■ ■ The activated extender cells "remember" the foreign structural features. They enter the blood vessel system, spread throughout the entire body and search the various tissues for cells that carry precisely these characteristics.

■ ■ If the extensor cells encounter corresponding cells (in this case tumour cells) during their search, they destroy them and send out messenger substances that alert other defense cells.

Always a dream of mankind

Dendritic cells can also be cultivated outside the body



To fight cancer with the help of one's own immune system is an old dream of mankind. This dream was brought a little closer in the 1990s by the possibility of breeding dendritic cells.

Dendritic cells are cells that patrol the body tissue and detect foreign structures. These structures are taken up by the cells and broken down into smaller components that are displayed on the cell surface.

With this "display" dendritic cells then migrate from the tissue into the lymph nodes. There, the foreign structures are offered to special executor cells (cytotoxic T lymphocytes), which then become active and set off to destroy cells with precisely these structural features.

In addition, the dendritic cells can also activate other cells, so-called T-helper cells, which then also reach the site via the bloodstream and produce substances that have a supporting effect on the cytotoxic T-cells.

Through the interaction of the dendritic cells with the T-helper cells, antibody-producing cells, such as B-cells, are also stimulated to grow and produce corresponding antibodies.

How are dendritic cells produced?



To isolate dendritic precursor cells, 200 ml of blood is taken from the patient, transported under stable temperature conditions and immediately stored and processed in a clean room laboratory, certified according to EU-GMP guidelines. After centrifugation, the blood is separated into different fractions to separate the white blood cells from the red blood cells and the non-specific defense cells, the granulocytes.

The fraction with the red blood cells and the granulocytes is discarded.

The lymphocyte fraction contains the cells from which dendritic cells will later develop. After several purification steps, the isolated cells are placed in nutrient solution. These cells, including the precursor cells of dendritic cells, settle down. Optimal maturation in the cell incubator is promoted by a nutrient solution and special growth factors. Autologous (endogenous) tumour antigens from the patient's own plasma are added to the precursor cells at the beginning of the maturation process.

The dendritic cells are cultured for 7 days in the incubator and monitored microscopically. These cells, which are very conspicuous in their shape, differ from other cells by their thin, hair-like extensions.

Before the cells are harvested on day 7, the surface characteristics, the number of cells and their vitality are specified in the flow cytometer. Afterwards, the cells are harvested, cleaned several times and placed in two small syringes.

Immunization with dendritic cells is performed subcutaneously by the treating physician in the patient's groin region, after which the patient receives high-dose vitamin C infusions and can then leave the clinic.

The therapy with dendritic cells is a gentle therapy

Vaccination with dendritic cells is rather a complementary therapy besides the standard therapies to date.

In contrast to other forms of therapy, such as chemotherapy or radiation in which foreign substances or harmful radiation are used to fight the tumour, treatment with dendritic cells uses the body's own immune system to fight the cancer.

In comparison to other forms of therapy, side effects after vaccination with dendritic cells are very rare. If at all, they are very small, subside quickly after a short period of time and have little or no effect on the patient. Therefore, a hospital stay is not necessary for the treatment, but the therapy can be performed on an outpatient basis.

For these reasons, vaccination with dendritic cells can also be carried out in addition to other therapies. However, care should be taken to ensure that the various treatments are coordinated in time. Although the number of studies on the therapeutic benefit of dendritic cells in tumour treatment is constantly growing, standard therapies should not be abandoned under any circumstances. These forms of therapy have already largely proven their effectiveness in extensive studies and represent the basic therapy for a whole range of diseases.

What side effects can occur

Although the therapy is carried out with the body's own cells, side effects occur. These side effects can occur because the body's immune response, like an infection, releases inflammatory messengers that cause mild fever and tiredness. A reaction to the vaccination can also be noticeable through swelling lymph nodes. Occasionally, redness may occur at the injection site. However, all these symptoms are harmless.

FAQ's

1. how do I know whether the DCT is suitable for me?

All cancers that form a solid tumour or carcinoma can be fought with dendritic cells, even if metastases have already formed.

2. who is not suitable for the Therapy?

Some types of leukemia don't respond to dendritic cells.

A blood sample should be taken not less than 7 days after a blood transfusion.

3. Will my family doctor recommend this therapy?

Most specialists are aware of this therapy, although it is not yet widely used in treatment protocols. As with all new treatments, it takes time to convince most of the medical profession. The advantage of this therapy is that no damage is done to the body and there is a higher success rate.

4. I really do not want chemotherapy

Dendritic cell therapy as a non-invasive and pollutant-free treatment gives the chance to avoid chemotherapy. But every patient is different, and your Doctor will know if and when chemotherapy will be needed. Often a low-dose chemo can be used instead of a full one.

5. what is the right time to receive a DCT?

The DCT cannot be used as a cancer prevention tool, even though the term "vaccine" might suggest it. Dendritic cells must be loaded with information from cancerous material (antigens). This is only present in an affected body. The earlier the therapy is given, the easier it is for the immune system to fight the cancer. Nevertheless, amazing results have been documented even in the final stages.

In palliative treatment, the DCT can relieve pain and improve quality of life, even if full recovery is no longer expected.

6 How can I verify the expected success rates?

You can find more information at: www.iaso-cancer.com

Contact Mr. Bruno Rosset. He will discuss everything else with you. He has access to a database of studies on many cancers. The best thing is to talk to him, please call him. He will also arrange an appointment for you at the best located clinic that offers DCT

7. when will the first results be seen?

Patients report a better feeling of well-being a few days after the vaccination, recognizable results of the effect on the tumor are expected about 3 months.

8. what are the costs - and who covers them?

Depending on the chosen program, the costs are about 16.500 Euro.

In some countries, private insurances cover the costs partially or completely. Otherwise, the costs can also be financed through some banks if necessary. Foundations also grant subsidies.

9 How can I further contribute in my own recovery?

The development of cancer is determined by long-term factors. Some of them are determined by genetic factors, possibly by environmental ones - or just bad luck. Others are based on our own circumstances, our lifestyle or habits. The clinics Bruno Rosset works with promote a self-confident, holistic approach to personal health and show the way back to health - not only the way away from the disease.

10. Where can I get the therapy?

The treatment takes place in a private clinic in Germany under specialist medical supervision, -



11. If I have any further questions, who can I ask

Contact Mr. Bruno Rosset. He will discuss everything else with you and make an appointment in the clinic:



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Rosset Consulting: aims to be a leader in providing alternative, scientifically proven cancer therapies to improve the lives and survival of cancer patients.

Important note

The contents of this information are for general information and should under no circumstances be used without the advice of a specialist who is familiar with the medical method of dendritic cell therapy and who knows the personal medical situation and history of the patient in order to recommend the correct form of treatment.

Literature list DC therapies

Allgemein

1. Banchereau J, Steinman RM: Dendritic cells and the control of immunity. *Nature* 1998, 392:245–252.
2. Fernandez NC, Flament C, Crepineau F, *et al.*: Dendritic cells (DC) promote natural killer (NK) cell functions: dynamics of the human DC/NK cell cross talk. *Eur Cytokine Netw* 2002, 13:17–27.

3. Gerosa F, Baldani-Guerra B, Nisii C, *et al.*: Reciprocal activating interaction between natural killer cells and dendritic cells. *J Exp Med* 2002, 195:327–333.
4. Mailliard RB, Son YI, Redlinger R, *et al.*: Dendritic cells mediate NK cell help for Th1 and CTL responses: two-signal requirement for the induction of NK cell helper function. *J Immunol* 2003, 171:2366–2373.
5. Munz C, Dao T, Ferlazzo G, *et al.*: Mature myeloid dendritic cell subsets have distinct roles for activation and viability of circulating human natural killer cells. *Blood* 2005, 105:266–273.
6. Piccioli D, Sbrana S, Melandri E, *et al.*: Contact-dependent stimulation and inhibition of dendritic cells by natural killer cells. *J Exp Med* 2002, 195:335–341.
7. Banchereau J, Briere F, Caux C, *et al.*: Immunobiology of dendritic cells. *Annu Rev Immunol* 2000, 18:767–811.
8. Figdor CG, de Vries IJ, Lesterhuis WJ, *et al.*: Dendritic cell immunotherapy: mapping the way. *Nat Med* 2004, 10:475–480.
9. Steinman RM, Banchereau J: Taking dendritic cells into medicine. *Nature* 2007, 449:419–426.
10. Fong L, Engleman EG: Dendritic cells in cancer immunotherapy. *Annu Rev Immunol* 2000, 18:245–273.
11. Schuler G, Schuler-Thurner B, Steinman RM: The use of dendritic cells in cancer immunotherapy. *Curr Opin Immunol* 2003, 15:138–147.
12. Nestle FO, Banchereau J, Hart D: Dendritic cells: On the move from bench to bedside. *Nat Med* 2001, 7:761–765.
13. Berinstein NL. Strategies to enhance the therapeutic activity of cancer vaccines: using melanoma as a model. *Ann. N. Y. Acad. Sci.* 2009;1174:107-117.
14. Van Poppel H, Joniau S, Van Gool SW. Vaccine therapy in patients with renal cell carcinoma. *Eur. Urol.* 2009;55(6):1333-1342.
15. Eggermont AMM, Schadendorf D. Melanoma and immunotherapy. *Hematol. Oncol. Clin. North Am.* 2009;23(3):547-564
16. Harzstark AL, Small EJ. Immunotherapeutics in development for prostate cancer. *Oncologist.* 2009;14(4):391-398.
17. Xu Z, Zhu X, Lu P, u. a. Activation of tumor-infiltrating antigen presenting cells by high intensity focused ultrasound ablation of human breast cancer. *Ultrasound Med Biol.* 2009;35(1):50-57.
18. Braly P, Nicodemus CF, Chu C, u. a. The Immune adjuvant properties of front-line carboplatin-paclitaxel: a randomized phase 2 study of alternative schedules of intravenous oregovomab chemoimmunotherapy in advanced ovarian cancer. *J. Immunother.* 2009;32(1):54-65.
19. Lesterhuis WJ, Aarntzen EHJG, De Vries IJM, u. a. Dendritic cell vaccines in melanoma: from promise to proof? *Crit. Rev. Oncol. Hematol.* 2008;66(2):118-134.
20. Dai S, Wei D, Wu Z, u. a. Phase I clinical trial of autologous ascites-derived exosomes combined with GM-CSF for colorectal cancer. *Mol. Ther.* 2008;16(4):782-790.
21. Carrasco J, Van Pel A, Neyns B, u. a. Vaccination of a melanoma patient with mature dendritic cells pulsed with MAGE-3 peptides triggers the activity of nonvaccine anti-tumor cells. *J. Immunol.* 2008;180(5):3585-3593.
22. Sonpavde G, Spencer DM, Slawin KM. Vaccine therapy for prostate cancer. *Urol. Oncol.* 2007;25(6):451-459.
23. Marble DJ, Gordon KB, Nickoloff BJ. Targeting TNFalpha rapidly reduces density of dendritic cells and macrophages in psoriatic plaques with restoration of epidermal keratinocyte differentiation. *J. Dermatol. Sci.* 2007;48(2):87-101.
24. O'Rourke MGE, Johnson MK, Lanagan CM, u. a. Dendritic cell immunotherapy for stage IV melanoma. *Melanoma Res.* 2007;17(5):316-322.
25. Celis E. Overlapping human leukocyte antigen class I/II binding peptide vaccine for the treatment of patients with stage IV melanoma: evidence of systemic immune dysfunction. *Cancer.* 2007;110(1):203-214.

26. Lee S, Neelapu SS, Kwak LW. Therapeutic vaccine for lymphoma. *Yonsei Med. J.* 2007;48(1):1-10.
27. Lin AM, Hershberg RM, Small EJ. Immunotherapy for prostate cancer using prostatic acid phosphatase loaded antigen presenting cells. *Urol. Oncol.* 2006;24(5):434-441.
28. Tan G, Wang Z, Wang X, Cheng L, Yin S. [Immunotherapeutic effects of beta-elemene combined with interleukin-23 gene-modified dendritic cells on murine pancreatic carcinoma]. *Ai Zheng.* 2006;25(9):1082-1086.
29. Srivastava PK. Therapeutic cancer vaccines. *Curr. Opin. Immunol.* 2006;18(2):201-205.
30. Schadendorf D, Ugurel S, Schuler-Thurner B, u. a. Dacarbazine (DTIC) versus vaccination with autologous peptide-pulsed dendritic cells (DC) in first-line treatment of patients with metastatic melanoma: a randomized phase III trial of the DC study group of the DeCOG. *Ann. Oncol.* 2006;17(4):563-570.
31. Loveland BE, Zhao A, White S, u. a. Mannan-MUC1-pulsed dendritic cell immunotherapy: a phase I trial in patients with adenocarcinoma. *Clin. Cancer Res.* 2006;12(3 Pt 1):869-877.
32. Ooi T, Barnetson RS, Zhuang L, u. a. Imiquimod-induced regression of actinic keratosis is associated with infiltration by T lymphocytes and dendritic cells: a randomized controlled trial. *Br. J. Dermatol.* 2006;154(1):72-78.
33. Lou E, Marshall J, Aklilu M, u. a. A phase II study of active immunotherapy with PANVAC or autologous, cultured dendritic cells infected with PANVAC after complete resection of hepatic metastases of colorectal carcinoma. *Clin Colorectal Cancer.* 2006;5(5):368-371.
34. Slingluff CL, Chianese-Bullock KA, Bullock TNJ, u. a. Immunity to melanoma antigens: from self-tolerance to immunotherapy. *Adv. Immunol.* 2006;90:243-295.
35. Oosterling SJ, Mels AK, Geijtenbeek TBH, u. a. Preoperative granulocyte/macrophage colony-stimulating factor (GM-CSF) increases hepatic dendritic cell numbers and clustering with lymphocytes in colorectal cancer patients. *Immunobiology.* 2006;211(6-8):641-649.
36. Hamuro J. [Anticancer immunotherapy with perorally effective lentinan]. *Gan To Kagaku Ryoho.* 2005;32(8):1209-1215.
37. Reinartz S, Wagner U. Current approaches in ovarian cancer vaccines. *Minerva Ginecol.* 2004;56(6):515-527.
38. Lonial S, Hicks M, Rosenthal H, u. a. A randomized trial comparing the combination of granulocyte-macrophage colony-stimulating factor plus granulocyte colony-stimulating factor versus granulocyte colony-stimulating factor for mobilization of dendritic cell subsets in hematopoietic progenitor cell products. *Biol. Blood Marrow Transplant.* 2004;10(12):848-857.
39. Rini B. Recent clinical development of dendritic cell-based immunotherapy for prostate cancer. *Expert Opin Biol Ther.* 2004;4(11):1729-1734.
40. Arellano M, K Waller E. Granulocyte-macrophage-colony-stimulating factor and other cytokines: as adjuncts to cancer immunotherapy, stem cell transplantation, and vaccines. *Curr. Hematol. Rep.* 2004;3(6):424-431.
41. Parkhurst MR, Riley JP, Igarashi T, u. a. Immunization of patients with the hTERT:540-548 peptide induces peptide-reactive T lymphocytes that do not recognize tumors endogenously expressing telomerase. *Clin. Cancer Res.* 2004;10(14):4688-4698.
42. Campoli M, Ferrone S. T-cell-based immunotherapy of melanoma: what have we learned and how can we improve? *Expert Rev Vaccines.* 2004;3(2):171-187.
43. Higano CS, Vogelzang NJ, Sosman JA, u. a. Safety and biological activity of repeated doses of recombinant human Flt3 ligand in patients with bone scan-negative hormone-refractory prostate cancer. *Clin. Cancer Res.* 2004;10(4):1219-1225.
44. Freedman RS, Vadhan-Raj S, Butts C, u. a. Pilot study of Flt3 ligand comparing intraperitoneal with subcutaneous routes on hematologic and immunologic responses in patients with peritoneal carcinomatosis and mesotheliomas. *Clin. Cancer Res.* 2003;9(14):5228-5237.

45. Bedrosian I, Mick R, Xu S, et al. Intranodal administration of peptide-pulsed mature dendritic cell vaccines results in superior CD8+ T-cell function in melanoma patients. *J. Clin. Oncol.* 2003;21(20):3826-3835.
46. Coughlin CM, Vonderheide RH. Targeting adult and pediatric cancers via cell-based vaccines and the prospect of activated B lymphocytes as a novel modality. *Cancer Biol. Ther.* 2003;2(5):466-470.
47. Quillien V, Lesimple T, Toujas L. [Vaccinal cell therapy in melanoma]. *Bull Cancer.* 2003;90(8-9):722-733.
48. Kwak LW. Translational development of active immunotherapy for hematologic malignancies. *Semin. Oncol.* 2003;30(3 Suppl 8):17-22.
49. Waller EK, Ernstoff MS. Modulation of antitumor immune responses by hematopoietic cytokines. *Cancer.* 2003;97(7):1797-1809.
50. Kadison AS, Morton DL. Immunotherapy of malignant melanoma. *Surg. Clin. North Am.* 2003;83(2):343-370.
51. Lissoni P, Mengo S, Bucovec R, et al. Clinical and biological effects of interleukin-2 with or without a concomitant administration of granulocyte-macrophage colony-stimulating factor in metastatic cancer patients. *In Vivo.* 2003;17(1):73-75.
52. McNeel DG, Knutson KL, Schiffman K, et al. Pilot study of an HLA-A2 peptide vaccine using flt3 ligand as a systemic vaccine adjuvant. *J. Clin. Immunol.* 2003;23(1):62-72.
53. Volk J, Sel S, Ganser A, Schöffski P. Tumor cell-based vaccination in renal cell carcinoma: rationale, approaches, and recent clinical development. *Curr Drug Targets.* 2002;3(5):401-408.
54. Wysocki PJ, Karczewska A, Mackiewicz A. [Gene modified tumor vaccines in therapy of malignant melanoma]. *Otolaryngol Pol.* 2002;56(2):147-153.
55. Gansauge F, Poch B, Kleef R, Schwarz M. Effectivity of long antigen exposition dendritic cell therapy (LANEX-DC®) in the palliative treatment of pancreatic cancer. *Curr Med Chem* 2013; 20, 4827-4835.
56. Drake, C.G. Prostate cancer as a model for tumour immunotherapy. *Nat. Rev. Immunol.* 2010, 10, 580–593.
57. Saad, F.; Miller, K. Current and Emerging Immunotherapies for Castration-resistant Prostate Cancer. *Urology* 2015, 85, 976–986.
58. Aalamian-Matheis, M.; Chatta, G.S.; Shurin, M.R.; Huland, E.; Huland, H.; Shurin, G.V. Inhibition of dendritic cell generation and function by serum from prostate cancer patients: Correlation with serum-free PSA. *Adv. Exp. Med. Biol.* 2007, 601, 173–182.
59. Ostrand-Rosenberg, S.; Sinha, P.; Beury, D.W.; Clements, V.K. Cross-talk between myeloid-derived suppressor cells (MDSC), macrophages, and dendritic cells enhances tumor-induced immune suppression. *Semin. Cancer Biol.* 2012, 22, 275–281.
60. Sharma, P.; Wagner, K.; Wolchok, J.D.; Allison, J.P. Novel cancer immunotherapy agents with survival benefit: Recent successes and next steps. *Nat. Rev. Cancer* 2011, 11, 805–812.
61. Weber, J.S. Current perspectives on immunotherapy. *Semin. Oncol.* 2014, 41, 14–29.
62. Melero, I.; Berman, D.M.; Aznar, M.A.; Korman, A.J.; Pérez Gracia, J.L.; Haanen, J. Evolving synergistic combinations of targeted immunotherapies to combat cancer. *Nat. Rev. Cancer* 2015, 15, 457–472.
63. Melero, I.; Gaudernack, G.; Gerritsen, W.; Huber, C.; Parmiani, G.; Scholl, S.; Thatcher, N.; Wagstaff, J.; Zielinski, C.; Faulkner, I.; et al. Therapeutic vaccines for cancer: An overview of clinical trials. *Nat. Rev. Clin. Oncol.* 2014, 11, 509–524.
64. Obeid, J.; Hu, Y.; Slingluff, C.L., Jr. Vaccines, Adjuvants, and dendritic cell activators-current status and future challenges. *Semin. Oncol.* 2015, 42, 549–561.
65. Joniau, S.; Abrahamsson, P.A.; Bellmunt, J.; Figdor, C.; Hamdy, F.; Verhagen, P.; Vogelzang, N.J.; Wirth, M.; van Poppel, H.; Osanto, S. Current vaccination strategies for prostate cancer. *Eur. Urol.* 2012, 61, 290–306.

66. Fernandez-Garcia, E.M.; Vera-Badillo, F.E.; Perez-Valderrama, B.; Matos-Pita, A.S.; Duran, I. Immunotherapy in prostate cancer: Review of the current evidence. *Clin. Transl. Oncol.* 2014, 17, 339–357.
67. Wei, X.X.; Fong, L.; Small, E.J. Prostate cancer immunotherapy with sipuleucel-t: Current standards and future directions. *Expert Rev. Vaccines* 2015, 14, 1529–1541.
68. Sims, R.B. Development of sipuleucel-T: Autologous cellular immunotherapy for the treatment of metastatic castrate resistant prostate cancer. *Vaccine* 2012, 30, 4394–4397.
69. Matera, L. The choice of the antigen in the dendritic cell-based vaccine therapy for prostate cancer. *Cancer Treat. Rev.* 2010, 36, 131–141.
70. Johnson, L.E.; Frye, T.P.; Arnot, A.R.; Marquette, C.; Couture, L.A.; Gendron-Fitzpatrick, A.; McNeel, D.G. Safety and immunological efficacy of a prostate cancer plasmid DNA vaccine encoding prostatic acid phosphatase (PAP). *Vaccine* 2006, 24, 293–303.
71. Small, E.J.; Schellhammer, P.F.; Higano, C.S.; Redfern, C.H.; Nemunaitis, J.J.; Valone, F.H.; Verjee, S.S.; Jones, L.A.; Hershberg, R.M. Placebo-controlled phase III trial of immunologic therapy with Sipuleucel-T (APC8015) in patients with metastatic, asymptomatic hormone refractory prostate cancer. *J. Clin. Oncol.* 2006, 24, 3089–3094.
72. Tse, B.W.; Jovanovic, L.; Nelson, C.C.; de Souza, P.; Power, C.A.; Russell, P.J. From bench to bedside: Immunotherapy for prostate cancer. *Biomed. Res. Int.* 2014, 2014, 1–11.
73. Small, E.J.; Fratesi, P.; Reese, D.M.; Strang, G.; Laus, R.; Peshwa, M.V.; Valone, F.H. Immunotherapy of hormone-refractory prostate cancer with antigen-loaded dendritic cells. *J. Clin. Oncol.* 2000, 18, 3894–3903.
74. Burch, P.A.; Breen, J.K.; Buckner, J.C.; Gastineau, D.A.; Kaur, J.A.; Laus, R.L.; Padley, D.J.; Peshwa, M.V.; Pitot, H.C.; Richardson, R.L.; et al. Priming tissue specific cellular immunity in a phase I trial of autologous dendritic cells for prostate cancer. *Clin. Cancer Res.* 2000, 6, 2175–2182.
75. Higano, C.S.; Schellhammer, P.F.; Small, E.J.; Burch, P.A.; Nemunaitis, J.; Yuh, L.; Provost, N.; Frohlich, M.W. Integrated data from 2 randomized, double-blind, placebo-controlled, phase 3 trials of active cellular immunotherapy with sipuleucel-T in advanced prostate cancer. *Cancer* 2009, 115, 3670–3679.
76. Kantoff, P.W.; Higano, C.S.; Shore, N.D.; Berger, E.R.; Small, E.J.; Penson, D.F.; Redfern, C.H.; Ferrari, A.C.; Dreicer, R.; Sims, R.B.; et al. Sipuleucel-T immunotherapy for castration-resistant prostate cancer. *N. Engl. J. Med.* 2010, 363, 411–422.
77. Schellhammer, P.F.; Chodak, G.; Whitmore, J.B.; Sims, R.; Frohlich, M.W.; Kantoff, P.W. Lower baseline prostate-specific antigen is associated with a greater overall survival benefit from sipuleucel-T in the Immunotherapy for Prostate Adenocarcinoma Treatment (IMPACT) trial. *Urology* 2013, 81, 1297–1302.
78. Wesley, J.D.; Whitmore, J.; Trager, J.; Sheikh, N. An overview of sipuleucel-T: Autologous cellular immunotherapy for prostate cancer. *Hum. Vaccines Immunother.* 2012, 8, 520–527.
79. Wgarwal, N.; Padmanabh, S.; Vogelzang, N.J. Development of novel immune interventions for prostate cancer. *Clin. Genitourin. Cancer* 2012, 10, 84–92.
80. Pieczonka, C.M.; Telonis, D.; Mouraviev, V.; Albala, D. Sipuleucel-T for the treatment of patients with metastatic castrate-resistant prostate cancer: Considerations for clinical practice. *Rev. Urol.* 2015, 17, 203–210.
81. Small, E.J.; Lance, R.S.; Gardner, T.A.; Karsh, L.I.; Fong, L.; McCoy, C.; DeVries, T.; Sheikh, N.A.; GuhaThakurta, D.; Chang, N.; et al. Randomized phase II trial of sipuleucel-T with concurrent versus sequential abiraterone acetate plus prednisone in metastatic castration-resistant prostate cancer. *Clin. Cancer Res.* 2015, 21, 3862–3869.
82. Graff, J.N.; Drake, C.G.; Beer, T.M. Complete biochemical (prostate-specific antigen) response to sipuleucel-T with enzalutamide in castration-resistant prostate cancer: A case report with implications for future research. *Urology* 2013, 81, 381–383.
83. Podrazil, M.; Horvath, R.; Becht, E.; Rozkova, D.; Bilkova, P.; Sochorova, K.; Hromadkova, H.; Kayserova, J.; Vavrova, K.; Lastovicka, J.; et al. Phase I/II clinical trial of dendritic-cell based immunotherapy (DCVAC/PCa) combined with chemotherapy in patients with metastatic, castration-resistant prostate cancer. *Oncotarget* 2015, 6, 18192–18205.

84. Prue, R.L.; Vari, F.; Radford, K.; Tong, H.; Hardy, M.Y.; D'Rozario, R.; Waterhouse, N.J.; Rossetti, T.; Coleman, R.; Tracey, C.; et al. A phase I clinical trial of CD1c (BDCA-1)+ dendritic cells pulsed with HLA-A*0201 peptides for immunotherapy of metastatic hormone refractory prostate cancer. *J. Immunother.* 2015, 38, 71–76

Glioblastom

1. Gene expression profile correlates with T-cell infiltration and relative survival in glioblastoma patients vaccinated with dendritic cell immunotherapy. Prins RM, Soto H, Konkankit V, Odesa SK, Eskin A, Yong WH, Nelson SF, Liao LM. *Clin Cancer Res.* 2011 Mar 15;17(6):1603-15. doi: 10.1158/1078-0432.CCR-10-2563. Epub 2010 Dec 6.
2. Active dendritic cell immunotherapy for glioblastoma: Current status and challenges. Polyzoidis S, Tuazon J, Brazil L, Beaney R, Al-Sarraj ST, Doey L, Logan J, Hurwitz V, Jarosz J, Bhangoo R, Gullan R, Mijovic A, Richardson M, Farzaneh F, Ashkan K. *Br J Neurosurg.* 2015 Apr;29(2):197-205. doi: 10.3109/02688697.2014.994473. Epub 2014 Dec 26. Review.
3. Cellular-based immunotherapies for patients with glioblastoma multiforme. Xu X, Stockhammer F, Schmitt M. *Clin Dev Immunol.* 2012;2012:764213. doi: 10.1155/2012/764213. Epub 2012 Feb 28. Review.
4. Perspectives for immunotherapy in glioblastoma treatment. Finocchiaro G, Pellegatta S. *Curr Opin Oncol.* 2014 Nov;26(6):608-14. doi: 10.1097/CCO.000000000000135. Review.
5. Vaccine therapies for patients with glioblastoma. Sayegh ET, Oh T, Fakurnejad S, Bloch O, Parsa AT. *J Neurooncol.* 2014 Sep;119(3):531-46. doi: 10.1007/s11060-014-1502-6. Epub 2014 Aug 28. Review.
6. Dendritic cell immunotherapy for solid tumors: evaluation of the DCVax® platform in the treatment of glioblastoma multiforme. Hdeib A, Sloan AE. *CNS Oncol.* 2015;4(2):63-9. doi: 10.2217/cns.14.54. Review.
7. An update on vaccine therapy and other immunotherapeutic approaches for glioblastoma. Reardon DA, Wucherpennig KW, Freeman G, Wu CJ, Chiocca EA, Wen PY, Curry WT Jr, Mitchell DA, Fecci PE, Sampson JH, Dranoff G. *Expert Rev Vaccines.* 2013 Jun;12(6):597-615. doi: 10.1586/erv.13.41. Review.
8. Dendritic Cell-Based Immunotherapy Treatment for Glioblastoma Multiforme. Yang L, Guo G, Niu XY, Liu J. *Biomed Res Int.* 2015;2015:717530. doi: 10.1155/2015/717530. Epub 2015 Jun 17. Review.
9. Brain Tumor Immunotherapy: What have We Learned so Far? Van Gool SW. *Front Oncol.* 2015 Jun 17;5:98. doi: 10.3389/fonc.2015.00098. eCollection 2015. Review.
10. Immunotherapy advances for glioblastoma. Reardon DA, Freeman G, Wu C, Chiocca EA, Wucherpennig KW, Wen PY, Fritsch EF, Curry WT Jr, Sampson JH, Dranoff G. *Neuro Oncol.* 2014 Nov;16(11):1441-58. doi: 10.1093/neuonc/nou212. Epub 2014 Sep 4. Review
11. Treatment of intracranial gliomas with bone marrow-derived dendritic cells pulsed with tumor antigens. Liao LM, Black KL, Prins RM, Sykes SN, DiPatre PL, Cloughesy TF, Becker DP, Bronstein JM. *J Neurosurg.* 1999 Jun;90(6):1115-24.
12. Dendritic cell vaccination in glioblastoma patients induces systemic and intracranial T-cell responses modulated by the local central nervous system tumor microenvironment. Liao LM, Prins RM, Kiertscher SM, Odesa SK, Kremen TJ, Giovannone AJ, Lin JW, Chute DJ, Mischel PS, Cloughesy TF, Roth MD. *Clin Cancer Res.* 2005 Aug 1;11(15):5515-25.
13. Cellular immunity and immunotherapy of brain tumors. Prins RM, Liao LM. *Front Biosci.* 2004 Sep 1;9:3124-36. Review.

14. Cytomegalovirus immunity after vaccination with autologous glioblastoma lysate. Prins RM, Cloughesy TF, Liao LM. *N Engl J Med.* 2008 Jul 31;359(5):539-41.

Colorektales Ca

1. Xiang B., Snook A. E., Magee M. S., Waldman S. A.; *Colorectal Cancer Immunotherapy*; Discovery Medicine; 2013; 15(84):301-308.
2. Nagorsen, D., Thiel, E.; *Clinical and immunologic responses to active specific cancer vaccines in human colorectal cancer*; *Clinical Cancer Research*; 2006, 12(10): 3064-3069
3. Mocellin S., Rossi C. R., Lise M., Nitti D.; *Colorectal cancer vaccines: principles, results, and perspectives*; *Gastroenterology*; 2004; 127(6):1821-1837
4. Rahma O. E., Myint Z. W., Estfan B.; *Dendritic Cell Cancer Vaccines for Treatment of Colon Cancer*; *Current Colorectal Cancer Reports*; 2014; 10(4):470-476.
5. Burgdorf S. K., Fischer A., Claesson M. H., Kirkin A. F.; Dzhandzhugazyan K. N., Rosenberg J.; *Vaccination with melanoma lysate-pulsed dendritic cells, of patients with advanced colorectal carcinoma: report from a phase I study*; *Journal of Experimental & Clinical Cancer Research*; 2006; 25(2):201-206
6. Burgdorf S. K., Fischer A., Myschetzky P. S., Munksgaard S. B., Zocca M. B., Claesson M. H., Rosenberg J.; *Clinical responses in patients with advanced colorectal cancer to a dendritic cell based vaccine*; *Oncology Reports*; 2008; 20(6):1305-1311.
7. Itoh T., Ueda Y., Kawashima I., Nukaya I., Fujiwara H., Fuji N., Yamashita T., Yoshimura T., Okugawa K., Iwasaki T., Ideno M., Takesako K., Mitsuhashi M., Orita K., Yamagishi H.; *Immunotherapy of solid cancer using dendritic cells pulsed with the HLA-A24-restricted peptide of carcinoembryonic antigen*; *Cancer Immunology, Immunotherapy*; 2002; 51(2):99-106.
8. Lesterhuis W. J., de Vries I. J. M., Schuurhuis D. H., Boullart A. C. I., Jacobs J. F. M., de Boer A. J., Scharenborg N. M., Brouwer H. M. H., van de Rakt M. W. M. M., Figdor C. G., Ruers T. J., Adema G. J., Punt C. J. A.; *Vaccination of colorectal cancer patients with CEA-loaded dendritic cells: antigen-specific T cell responses in DTH skin tests*; *Annals of Oncology*; 2006; 17(6):974-980.
9. Kavanagh B., Ko A., Venook A., Margolin K., Zeh H., Lotze M., Schillinger B., Liu W., Lu Y., Mitsky P., Schilling M., Bercovici N., Loudovaris M., Guillermo R., Lee S. M., Bender J., Mills B., Fong L.; *Vaccination of metastatic colorectal cancer patients with matured dendritic cells loaded with multiple major histocompatibility complex class I peptides*; *Journal of Immunotherapy*; 2007; 30(7):762-772.
10. Nair S. K., Morse M., Boczkowski D., Ian Cumming R., Vasovic L., Gilboa E., Kim Lyerly H.; *Induction of tumor-specific cytotoxic T lymphocytes in cancer patients by autologous tumor RNA-transfected dendritic cells*; *Annals of Surgery*; 2002; 235(4):540-549.
11. Morse M. A., Nair S. K., Mosca P. J., Hobeika A. C., Clay T. M., Deng Y., Boczkowski D., Proia A., Neidzwiecki D., Clavien P.-A., Hurwitz H. I., Schlom J., Gilboa E., Kim Lyerly H.; *Immunotherapy with autologous, human dendritic cells transfected with carcinoembryonic antigen mRNA*; *Cancer Investigation*; 2003; 21(3):341-349.
12. Burgdorf S. K., Claesson M. H., Nielsen H. J., Rosenberg J.; *Changes in cytokine and biomarker blood levels in patients with colorectal cancer during dendritic cell-based vaccination*; *Acta Oncologica*; 2009; 48(8):1157-1164.

Prostata-Ca

1. Drake, C.G. Prostate cancer as a model for tumour immunotherapy. *Nat. Rev. Immunol.* 2010, 10, 580–593.
2. Saad, F.; Miller, K. Current and Emerging Immunotherapies for Castration-resistant Prostate Cancer. *Urology* 2015, 85, 976–986.
3. Aalamian-Matheis, M.; Chatta, G.S.; Shurin, M.R.; Huland, E.; Huland, H.; Shurin, G.V. Inhibition of dendritic cell generation and function by serum from prostate cancer patients: Correlation with serum-free PSA. *Adv. Exp. Med. Biol.* 2007, 601, 173–182.

4. Ostrand-Rosenberg, S.; Sinha, P.; Beury, D.W.; Clements, V.K. Cross-talk between myeloid-derived suppressor cells (MDSC), macrophages, and dendritic cells enhances tumor-induced immune suppression. *Semin. Cancer Biol.* 2012, 22, 275–281.
5. Sharma, P.; Wagner, K.; Wolchok, J.D.; Allison, J.P. Novel cancer immunotherapy agents with survival benefit: Recent successes and next steps. *Nat. Rev. Cancer* 2011, 11, 805–812.
6. Weber, J.S. Current perspectives on immunotherapy. *Semin. Oncol.* 2014, 41, 14–29.
7. Melero, I.; Berman, D.M.; Aznar, M.A.; Korman, A.J.; Pérez Gracia, J.L.; Haanen, J. Evolving synergistic combinations of targeted immunotherapies to combat cancer. *Nat. Rev. Cancer* 2015, 15, 457–472.
8. Melero, I.; Gaudernack, G.; Gerritsen, W.; Huber, C.; Parmiani, G.; Scholl, S.; Thatcher, N.; Wagstaff, J.; Zielinski, C.; Faulkner, I.; et al. Therapeutic vaccines for cancer: An overview of clinical trials. *Nat. Rev. Clin. Oncol.* 2014, 11, 509–524.
9. Obeid, J.; Hu, Y.; Slingluff, C.L., Jr. Vaccines, Adjuvants, and dendritic cell activators-current status and future challenges. *Semin. Oncol.* 2015, 42, 549–561.
10. Joniau, S.; Abrahamsson, P.A.; Bellmunt, J.; Figdor, C.; Hamdy, F.; Verhagen, P.; Vogelzang, N.J.; Wirth, M.; van Poppel, H.; Osanto, S. Current vaccination strategies for prostate cancer. *Eur. Urol.* 2012, 61, 290–306.
11. Fernandez-Garcia, E.M.; Vera-Badillo, F.E.; Perez-Valderrama, B.; Matos-Pita, A.S.; Duran, I. Immunotherapy in prostate cancer: Review of the current evidence. *Clin. Transl. Oncol.* 2014, 17, 339–357.
12. Wei, X.X.; Fong, L.; Small, E.J. Prostate cancer immunotherapy with sipuleucel-t: Current standards and future directions. *Expert Rev. Vaccines* 2015, 14, 1529–1541.
13. Sims, R.B. Development of sipuleucel-T: Autologous cellular immunotherapy for the treatment of metastatic castrate resistant prostate cancer. *Vaccine* 2012, 30, 4394–4397.
14. Matera, L. The choice of the antigen in the dendritic cell-based vaccine therapy for prostate cancer. *Cancer Treat. Rev.* 2010, 36, 131–141.
15. Johnson, L.E.; Frye, T.P.; Arnot, A.R.; Marquette, C.; Couture, L.A.; Gendron-Fitzpatrick, A.; McNeel, D.G. Safety and immunological efficacy of a prostate cancer plasmid DNA vaccine encoding prostatic acid phosphatase (PAP). *Vaccine* 2006, 24, 293–303.
16. Small, E.J.; Schellhammer, P.F.; Higano, C.S.; Redfern, C.H.; Nemunaitis, J.J.; Valone, F.H.; Verjee, S.S.; Jones, L.A.; Hershberg, R.M. Placebo-controlled phase III trial of immunologic therapy with Sipuleucel-T (APC8015) in patients with metastatic, asymptomatic hormone refractory prostate cancer. *J. Clin. Oncol.* 2006, 24, 3089–3094.
17. Tse, B.W.; Jovanovic, L.; Nelson, C.C.; de Souza, P.; Power, C.A.; Russell, P.J. From bench to bedside: Immunotherapy for prostate cancer. *Biomed. Res. Int.* 2014, 2014, 1–11.
18. Small, E.J.; Fratesi, P.; Reese, D.M.; Strang, G.; Laus, R.; Peshwa, M.V.; Valone, F.H. Immunotherapy of hormone-refractory prostate cancer with antigen-loaded dendritic cells. *J. Clin. Oncol.* 2000, 18, 3894–3903.
19. Burch, P.A.; Breen, J.K.; Buckner, J.C.; Gastineau, D.A.; Kaur, J.A.; Laus, R.L.; Padley, D.J.; Peshwa, M.V.; Pitot, H.C.; Richardson, R.L.; et al. Priming tissue specific cellular immunity in a phase I trial of autologous dendritic cells for prostate cancer. *Clin. Cancer Res.* 2000, 6, 2175–2182.
20. Higano, C.S.; Schellhammer, P.F.; Small, E.J.; Burch, P.A.; Nemunaitis, J.; Yuh, L.; Provost, N.; Frohlich, M.W. Integrated data from 2 randomized, double-blind, placebo-controlled, phase 3 trials of active cellular immunotherapy with sipuleucel-T in advanced prostate cancer. *Cancer* 2009, 115, 3670–3679.
21. Kantoff, P.W.; Higano, C.S.; Shore, N.D.; Berger, E.R.; Small, E.J.; Penson, D.F.; Redfern, C.H.; Ferrari, A.C.; Dreicer, R.; Sims, R.B.; et al. Sipuleucel-T immunotherapy for castration-resistant prostate cancer. *N. Engl. J. Med.* 2010, 363, 411–422.
22. Schellhammer, P.F.; Chodak, G.; Whitmore, J.B.; Sims, R.; Frohlich, M.W.; Kantoff, P.W. Lower baseline prostate-specific antigen is associated with a greater overall survival benefit from sipuleucel-T in the Immunotherapy for Prostate Adenocarcinoma Treatment (IMPACT) trial. *Urology* 2013, 81, 1297–1302.
23. Wesley, J.D.; Whitmore, J.; Trager, J.; Sheikh, N. An overview of sipuleucel-T: Autologous cellular immunotherapy for prostate cancer. *Hum. Vaccines Immunother.* 2012, 8, 520–527

24. Wgarwal, N.; Padmanabh, S.; Vogelzang, N.J. Development of novel immune interventions for prostate cancer. *Clin. Genitourin. Cancer* 2012, 10, 84–92
25. Pieczonka, C.M.; Telonis, D.; Mouraviev, V.; Albala, D. Sipuleucel-T for the treatment of patients with metastatic castrate-resistant prostate cancer: Considerations for clinical practice. *Rev. Urol.* 2015, 17, 203–210.
26. Small, E.J.; Lance, R.S.; Gardner, T.A.; Karsh, L.I.; Fong, L.; McCoy, C.; DeVries, T.; Sheikh, N.A.; GuhaThakurta, D.; Chang, N.; et al. Randomized phase II trial of sipuleucel-T with concurrent versus sequential abiraterone acetate plus prednisone in metastatic castration-resistant prostate cancer. *Clin. Cancer Res.* 2015, 21, 3862–3869
27. Graff, J.N.; Drake, C.G.; Beer, T.M. Complete biochemical (prostate-specific antigen) response to sipuleucel-T with enzalutamide in castration-resistant prostate cancer: A case report with implications for future research. *Urology* 2013, 81, 381–383.
28. Podrazil, M.; Horvath, R.; Becht, E.; Rozkova, D.; Bilkova, P.; Sochorova, K.; Hromadkova, H.; Kayserova, J.; Vavrova, K.; Lastovicka, J.; et al. Phase I/II clinical trial of dendritic-cell based immunotherapy (DCVAC/PCa) combined with chemotherapy in patients with metastatic, castration-resistant prostate cancer. *Oncotarget* 2015, 6, 18192–18205.
29. Prue, R.L.; Vari, F.; Radford, K.; Tong, H.; Hardy, M.Y.; D’Rozario, R.; Waterhouse, N.J.; Rossetti, T.; Coleman, R.; Tracey, C.; et al. A phase I clinical trial of CD1c (BDCA-1)+ dendritic cells pulsed with HLA-A*0201 peptides for immunotherapy of metastatic hormone refractory prostate cancer. *J. Immunother.* 2015, 38, 71–76
30. Tewari M., Sahai S., Mishra R. R., Shukla S. K., Shukla H. S.; Dendritic cell therapy in advanced gastric cancer: A promising new hope?; *Surgical Oncology* 2012; 21:164-171
31. Kobayashi M., Sakabe T., Chiba A., Nakajima A., Okamoto M., Shimodaira S., Yonemitsu Y., Shibamoto Y., Suzuki N., Nagaya M.; *Therapeutic effect of intratumoral injections of dendritic cells for locally recurrent gastric cancer: a case report*; *World Journal of Surgical Oncology*; 2014; 12(390).
32. Kanazawa M., Yoshihara K., Abe H., Iwadate M, Watanabe K., Suzuki S., Endoh Y., Ohki S., Takita K., Sekikawa K., Takenoshita S., Takagi T., Irisawa A., Sato Y., Ogata T., Ohto H.; *Case report on intra-tumor injection therapy of dendritic cells in advanced gastric cancer*; *Gan To Kagaku Ryoho*; 2004; 31(11):1773-1776.
33. Kono K., Takahashi A., Sugai H., Fujii H., Choudhury A. R., Kiessling R., Matsumoto Y.; Dendritic cells pulsed with HER-2/neu-derived peptides can induce specific T-cell responses in patients with gastric cancer; *Clinical Cancer Research*; 2002; 8(11):3394-3400.
34. Sadanaga N., Nagashima H., Mashino K., Tahara K., Yamaguchi H., Ohta M., Fujie T., Tanaka F., Onoue H., Takesako K., Akiyoshi T., Mori M.; Dendritic cell vaccination with MAGE peptide is a novel therapeutic approach for gastrointestinal carcinomas; *Clinical Cancer Research*; 2001, 7(8):22277-2284.
35. Galetto A., Contarini M., Sapino A., Cassoni P., Consalvo E., Forno S, Pezzi C., Barnaba V., Mussa A., Matera L.; *In vivo Host Response to Gastrointestinal Cancer Cells Presented by Autologous Dendritic Cells*; *Journal of Surgical Research*; 2001, 100:32-38.

Mamma-Ca

1. *Curigliano G, Criscitiello C, Esposito A et al.* Developing an effective breast cancer vaccine: challenges to achieving sterile immunity versus resetting equilibrium. *Breast* 22(Suppl. 2), S96–S99(2013).
2. *Gelao L, Criscitiello C, Esposito A et al.* Dendritic cell-based vaccines: clinical applications in breast cancer. *Immunotherapy* 6(3), 349–360 (2014).
3. *Dunn GP, Old LJ, Schreiber RD.* The three Es of cancer immunoediting. *Annu. Rev. Immunol.* 22, 329–360 (2004).
4. *Mahmoud SM, Paish EC, Powe DG et al.* Tumor-infiltrating CD⁸⁺ lymphocytes predict clinical outcome in breast cancer. *J. Clin. Oncol.* 29(15), 1949–1955 (2011).
5. *DeNardo DG, Coussens LM.* Inflammation and breast cancer. Balancing immune response: crosstalk between adaptive and innate immune cells during breast cancer progression. *Breast Cancer Res.* 9(4), 212 (2007).

6. Schirmmacher V, Feuerer M, Beckhove P, Ahlert T, Umansky V. T cell memory, anergy and immunotherapy in breast cancer. *J. Mammary Gland Biol. Neoplasia* 7, 201–208 (2002).
7. Feuerer M, Rocha M, Bai L et al. Enrichment of memory T cells and other profound immunological changes in the bone marrow from untreated breast cancer patients. *Int. J. Cancer* 92, 96–105(2001).
8. Sommerfeld N, Schütz F, Sohn C et al. The shaping of a polyvalent and highly individual T-cell repertoire in the bone marrow of breast cancer patients. *Cancer Res.* 66, 8258–8265 (2006).
9. Bai L, Koopmann J, Fiola C et al. Dendritic cells pulsed with viral oncolysate potently stimulate autologous T cells from cancer patients. *Int. J. Oncol.* 21(4), 685–694 (2002).
10. Lien Vandenberg, Jochen Belmans, Matthias Van Woensel, Matteo Riva, Stefaan W. Van Gool. (2016) Exploiting the Immunogenic Potential of Cancer Cells for Improved Dendritic Cell Vaccines. *Frontiers in Immunology* 6. Online publication date: 14-Jan-2016.
11. Volker Schirmmacher. (2015) Cancer-reactive memory T cells from bone marrow: Spontaneous induction and therapeutic potential (Review). *International Journal of Oncology*. Online publication date: 12-Oct-2015.
12. Czerniecki BJ, Koski GK, Koldovsky U, Xu S, Cohen PA, Mick R, Nisenbaum H, Pasha T, Xu M, Fox KR, Weinstein S, Orel SG, Vonderheide R, Coukos G, DeMichele A, Araujo L, Spitz FR, Rosen M, Levine BL, June C, Zhang PJ. Targeting HER-2/neu in early breast cancer development using dendritic cells with staged IL-12 burst secretion. *Cancer Res* 67:1842-1853 2007.
13. Roses R, Xu M, Xu S, Koldovsky U, Son G, Koski GK, Czerniecki BJ. Working towards the development of cancer vaccines for the treatment and prevention of early breast cancer. *Current Cancer Therapy Reviews* 3:97-107 2007.
14. Czerniecki BJ, Roses R, Koski GK. Development of vaccines for high risk ductal carcinoma in situ of the breast. *Cancer Res* 67: 6531-6534 2007.
15. Soyoung Baek, Choung-Soo Kim, Sung-Bae Kim, Yong-man Kim, Seog-Woon Kwon, YongMan Kim, HyunSoo Kim, Hyunah Lee. Combination therapy of renal cell carcinoma or breast cancer patients with dendritic cell vaccine and IL-2: results from a phase I/II trial. *Journal of Translational Medicine* 2011 9:178

Ovarial-Ca

1. Coosemans A., Vergote I., Van Gool S. W.; *Dendritic cell-based immunotherapy in ovarian cancer*; *Oncoimmunology*; 2013; 2(12):e27059.
2. Bouria A. B., Zamarin D.; *Immunotherapy: New Strategies for the Treatment of Gynecologic Malignancies*; *Oncology*; 2016; 30(1): 59-66, 69.
3. Drakes M. L., Stiff P. J.; *Understanding dendritic cell immunotherapy in ovarian cancer*; *Expert Review of Anticancer Therapy*; 2016; 16(6): 643-652.
4. Coosemans A., Baert T., Vergote I.; *A view on dendritic cell immunotherapy in ovarian cancer: how far have we come?*; *Facts, Views & Vision IN OBGYN*; 2015; 7(1):73-78
5. Brossart P., Wirths S., Stuhler G., Reichhardt V. L., Kanz L., Brugger W.; *Induction of cytotoxic T-lymphocyte responses in vivo after vaccinations with peptide-pulsed dendritic cells*; *Blood*; 2000; 96(9):3102-3108.
6. Hernando J. J., Park T. W., Kübler K., Offergeld R., Schlebusch H., Bauknecht T.; *Vaccination with autologous tumor antigen-pulsed dendritic cells in advanced gynaecological malignancies: clinical and immunological evaluation of a phase I trial*; *Cancer, Immunology & Immunotherapy*; 2002; 51(1):45-52
7. Loveland B. E., Zhao A., White S., Gan H., Hamilton K., Xing P. X., Pietersz G. A., Apostolopoulos V., Vaughan H., Karanikas V., Kyriakou P., McKenzie I. F., Mitchell P. L.; *Mannan-MUC1-pulsed dendritic cell immunotherapy: a phase I trial in patients with adenocarcinoma*; *Clinical Cancer Research*; 2006; 12(3 Pt 1):869-877.
8. Homma S., Sagawa Y., Ito M., Ohno T., Toda G.; *Cancer immunotherapy using dendritic/tumor-fusion vaccine induces elevation of serum anti-nuclear antibody with better clinical responses*; *Clinical & Experimental Immunology*; 2006; 144(1):41-47.

9. Hernando J. J., Park T. W., Fischer H. P., Zivanovic O., Braun M., Pölcher M., Grün U., Leutner C., Pöttsch B., Kuhn W.; *Vaccination with dendritic cells transfected with mRNA-encoded folate-receptor- α for relapsed metastatic ovarian cancer*; *The Lancet Oncology*; 2007; 8(5):451-454.
10. Peethambaram P. P., Melisko M. E., Rinn K. J., Alberts S. R., Provost N. M., Jones L. A., Sims R. B., Lin L. R., Frohlich M. W., Park J. W.; *A phase I trial of immunotherapy with lapuleucel-T (APC8024) in patients with refractory metastatic tumors that express HER-2/neu*; *Clinical Cancer Research*; 2009; 15(18):5937-5944.
11. Chu C. S., Boyer J., Schullery D. S., Gimotty P. A., Gamerman V., Bender J., Levine B. L., Coukos G., Rubin S. C., Morgan M. A., Vonderheide R. H., June C. H.; *Phase I/II randomized trial of dendritic cell vaccination with or without cyclophosphamide for consolidation therapy of advanced ovarian cancer in first or second remission*; *Cancer, Immunology & Immunotherapy*; 2012; 61(5):629-641.
12. Rahma O. E., Ashtar E., Czystowska M., Szajnik M. E., Wiechowski E., Berstein S., Herrin V. E., Shams M. A., Steinberg S. M., Merino M., Gooding W., Visus C., Deleo A. B., Wolf J. K., Bell J. G., Berzofsky J. A., Whiteside T. L., Khleif S. N.; *A gynecologic oncology group phase II trial of two p53 peptide vaccine approaches: subcutaneous injection and intravenous pulsed dendritic cells in high recurrence risk ovarian cancer patients*; *Cancer, Immunology & Immunotherapy*; 2012; 61(3):373-384.
13. Kandalaf L. E., Powell D. J. Jr., Chiang C. L., Tanyi J., Kim S., Bosch M., Montone K., Mick R., Levine B. L., Torigian D. A., June C. H., Coukos G.; *Autologous lysate-pulsed dendritic cell vaccination followed by adoptive transfer of vaccine-primed ex vivo co-stimulated T cells in recurrent ovarian cancer*; *Oncoimmunology*; 2013; 2(1):e22664
14. Cooseman A., Vanderstraeten A., Tuyaerts S., Verschuere T., Moerman P., Berneman Z., Vergote I., Amant F., Van Gool S. W.; *Immunological response after WT1 mRNA-loaded dendritic cell immunotherapy in ovarian carcinoma and carcinosarcoma*; *Anticancer Research*; 2013; 33(9):3855-3859.
15. Mitchell P. L., Quinn M. A., Grant P. T., Allen D. G., Jobling T. W., White S. C., Zhao A., Karanikas V., Vaughan H., Pietersz G., McKenzie I. F., Gargosky S. E., Loveland B. E.; *A phase 2, single-arm study of an autologous dendritic cell treatment against mucin 1 in patients with advanced epithelial ovarian cancer*; *Journal for ImmunoTherapy of Cancer*; 2014; 18(2):16.
16. Kobayashi M., Chiba A., Izawa H., Yanagida E., Okamoto M., Shimodaira S., Yonemitsu Y., Shibamoto Y., Suzuki N., Nagaya M.; *The feasibility and clinical effects of dendritic cell-based immunotherapy targeting synthesized peptides for recurrent ovarian cancer*; *Journal of Ovarian Research*; 2014; 7:48.
17. Bapsy P. P., Sharan B., Kumar C., Das R. P., Rangarajan B., Jain M., Suresh Attili V. S., Subramanian S., Aggarwal S., Srivastava M., Vaid A.; *Open-label, multi-center, non-randomized, single-arm study to evaluate the safety and efficacy of dendritic cell immunotherapy in patients with refractory solid malignancies, on supportive care*; *Cytotherapy*; 2014; 16(2) 234-244.
18. Gray H. J., Benigno B., Berek J., Chang J., Mason J., Mileskin L., Mitchell P., Moradi M., Recio F. O., Michener C. M., Alvarez Secord A., Tchabo N. E., Chan J. K., Young J., Kohrt H., Gargosky S. E., Goh J. C.; *Progression-free and overall survival in ovarian cancer patients treated with CVac, a mucin 1 dendritic cell therapy in a randomized phase 2 trial*; *Journal for ImmunoTherapy of Cancer*; 2016; 4:34.

Pankreas-Ca

1. Gansauge F, Poch B, Kleef R, Schwarz M. Effectivity of long antigen exposition dendritic cell therapy (LANEX-DC®) in the palliative treatment of pancreatic cancer. *Curr Med Chem* 2013; 20, 4827-4835.

Melanom

Table 1: Kopiert aus Anguille S. et al.; Clinical use of dendritic cells for cancer therapy

Author	Year		Evidence level	Overall survival	DC group (months)	Control group (months)	% change
Thurner et al.	1999	N = 11	III-3		9.3	4.0	+133%
Dillman et al.	2004/2009/2012	N = 54	III.1		64	31	+107 %
Trefzer et al.	2004	N = 17	III.3		22.4	9.0	+180 %
Vilella	2004	N = 11	III-3		7.3	4.0	+83 %
Kyte et al.	2006	N = 16/22	III-2		12.3	5.8	+112 %
Nakai et al.	2006/2008	N = 20	III-3		8.6	4.0	+ 115 %
Hersey et al.	2008	N = 34	III-3		18.5	11.6	+60 %
Ellebaek et al.	2012	N = 28	III-3		9.4	5.1	+ 84 %
Oshita	2012	N = 24	III-3		13.6	7.3	+86 %
Aarntzen et al.	2013	N = 29	III-3		15.0	8.3	+81 %
Tel et al.	2013	N = 15	III-3		22.0	7.6	+189%

1. Mukherji B., Chakraborty N. G., Yamasaki S., Okino T., Yamase H., Sport J. R.; Kurtzman S. K., Ergin M. T., Ozols J., Meehan J., Mauri F.; Induction of antigen-specific cytolytic T cells in situ in human melanoma by immunization with synthetic peptide-pulsed autologous antigen presenting cells; *Proceedings of the National Academy of Sciences*; 1995 (92):8078-8082
2. Wimmers F., Aarntzen E. H., Duiveman-deBoer T., Figdor C. G., Jacobs J. F., Tel J., de Vries I. J.; Long-lasting multifunctional CD8+ T cell responses in end-stage melanoma patients can be induced by dendritic cell vaccination; *Oncoimmunology*; 2015; 5(1): e1067745 (13 pages)
3. Anguille S, Smits E. L., Lion E., van Tendeloo V. F., Berneman Z. N.; Clinical use of dendritic cells for cancer therapy; *The Lancet Oncology*; 2014; 15:e257-267
4. Thurner B., Haendle I., Röder C., Dieckmann D., Keikavoussi P., Jonuleit H., Bender A., Maczek C., Schreiner D., von den Driesch P., Bröcker E. B., Steinman R. M., Enk A., Kämpgen E., Schuler G.; Vaccination with mage-3A1 peptide-pulsed mature, monocyte-derived dendritic cells expands specific cytotoxic T cells and induces regression of some metastases in advanced stage IV melanoma; *The Journal of Experimental Medicine*; 1999; 190 (11):1669-1678.
5. Slingluff C. L. Jr., Petrone G. R., Yamshchikov G. V., Barnd D. L., Eastham S., Galavotti H., Patterson J. W., Deacon D. H., Hibbitts S., Teates D., Neese P. Y., Grosh W. W., Chianese-Bullock K. A., Woodson E. M., Wiernasz C. J., Merrill P., Gibson J., Ross M., Engelhard V. H.; Clinical and immunologic results of a randomized phase II trial of vaccination using four melanoma peptides either administered in granulocyte-macrophage colony-stimulating factor in adjuvant or pulsed on dendritic cells; *Journal of Clinical Oncology*; 2003; 21(21):4016-4026
6. Trefzer U., Herberth G., Wohlan K., Milling A., Thiemann M., Sherev T., Sparbier K., Sterry W., Walden P.; Vaccination with hybrids of tumor and dendritic cells induces tumor-specific T-cell and clinical responses in melanoma stage III and IV patients; *International Journal of Cancer*; 2004; 110(5):730-740
7. Vilella R., Benítez D., Millà J., Lozano M., Vilana R., Pomes J., Tomas X., Costa J., Vilalta A., Malveyh J., Puig S., Mellado B., Martí R., Castel T.; Pilot study of treatment of biochemotherapy-refractory stage IV melanoma patients with autologous dendritic cells pulsed with a heterologous melanoma cell line lysate; *Cancer Immunology, Immunotherapy*; 2004; 53(7):651-658
8. Kyte J. A., Mu L., Aamdal S., Kvalheim G., Dueland S., Hauser M., Gullestad H. P., Ryder T., Lislerud K., Hammerstad H., Gaudernack G.; Phase I/II trial of melanoma therapy with dendritic cells transfected with autologous tumor-mRNA; *Cancer Gene Therapy*; 2006; 10:905-918

9. Nakai N., Asai J., Ueda E., Takenaka H., Katoh N., Kishimoto S.; Vaccination of Japanese patients with advanced melanoma with peptide, tumor lysate or both peptide and tumor lysate-pulsed mature, monocyte-derived dendritic cells; *The Journal of Dermatology*; 2006; 33(7):462-472
10. Nakai N., Katoh N., Kitagawa T., Ueda E., Takenaka H., Kishimoto S.; Evaluation of survival in Japanese stage IV melanoma patients treated with melanoma antigen-pulsed mature monocyte-derived dendritic cells; *The Journal of Dermatology*; 2008; 35(12):801-803
11. Schadendorf D., Ugurel S., Schuler-Thumer B., Nestle F. O., Enk A., Bröcker E. B., Grabbe S., Rittgen W., Edler L., Sucker A., Zimpfer-Rechner C., Berger T., Kamarashev J., Burg G., Jonuleit H., Tüttenberg A., Becker J. C., Keikavoussi P., Kämpgen E., Schuler G., DC study group of the DeCOG; Dacarbazine (DTIC) versus vaccination with autologous peptide-pulsed dendritic cells (DC) in first-line treatment of patients with metastatic melanoma: a randomized phase III trial of the DC study group of the DeCOG; *Annals of Oncology*; 2006; 17(4):563-570
12. Hersey P., Halliday G. M., Farrelly M. L., DeSilva C., Lett M., Menzies S. W.; Phase I/II study of treatment with matured dendritic cells with or without low dose IL-2 in patients with disseminated melanoma; *Cancer Immunology, Immunotherapy*; 2008; 57(7):1039-1051
13. Ellebaek E., Engell-Noerregaard L., Iversen T. Z., Froesig T. M., Munir S., Hadrup S. R., Andersen M. H., Svane I. M.; Metastatic melanoma patients treated with dendritic cell vaccination, Interleukin-2 and metronomic cyclophosphamide: results from a phase II trial; *Cancer Immunology Immunotherapy*; 2012; 61(10):1791-1804
14. Oshita C., Takikawa M., Kume A., Miyata H., Ashizawa T., Iizuka A., Kiyohara Y., Yoshikawa S., Tanosaki R., Yamazaki N., Yamamoto A., Takesako K., Yamaguchi K., Akiyama Y.; Dendritic cell-based vaccination in metastatic melanoma patients: phase II clinical trial; *Oncology reports*; 2012; 28(4):1131-1138
15. Thurner B., Haendle I., Röder C., Dieckmann D., Keikavoussi P., Jonuleit H., Bender A., Maczek C., Schreiner D., von den Driesch P., Bröcker E. B., Steinman R. M., Enk A., Kämpgen E., Schuler G.; Vaccination with mage-3A1 peptide-pulsed mature, monocyte-derived dendritic cells expands specific cytotoxic T cells and induces regression of some metastases in advanced stage IV melanoma; *The Journal of Experimental Medicine*; 1999; 190 (11):1669-1678.
16. Slingluff C. L. Jr., Petrone G. R., Yamshchikov G. V., Barnd D. L., Eastham S., Galavotti H., Patterson J. W., Deacon D. H., Hibbitts S., Teates D., Neese P. Y., Grosh W. W., Chianese-Bullock K. A., Woodson E. M., Wiernasz C. J., Merrill P., Gibson J., Ross M., Engelhard V. H.; Clinical and immunologic results of a randomized phase II trial of vaccination using four melanoma peptides either administered in granulocyte-macrophage colony-stimulating factor in adjuvant or pulsed on dendritic cells; *Journal of Clinical Oncology*; 2003; 21(21):4016-4026
17. Dillman R., Selvan S., Schiltz P., Peterson C., Allen K., Depriest C., McClay E., Barth N., Sheehy P., de Leon C., Beutel L.; Phase I/II trial of melanoma patient-specific vaccine of proliferating autologous tumor cells, dendritic cells and GM-CSF: planned interim analysis; *Cancer Biotherapy and Radiopharmaceuticals*; 2004; 19(5):658-665
18. Dillman R. O., Selvan S. R., Schiltz P. M., McClay E.F., Barth N. M., DePriest C., de Leon C., Myorga C., Cornforth A. N., Allen K.; Phase II trial of dendritic cells loaded with antigens from self-renewing, proliferating autologous tumor cells as patient-specific antitumor vaccines in patients with metastatic melanoma: final report; *Cancer Biotherapy and Radiopharmaceuticals*; 2009; 24(3):311-319
19. Dillman R. O., Cornforth A. N., Depriest C., McClay E. F., Amatruda T. T., de Leon C., Ellis R. E., Mayorga C., Carbonell D., Cubellis J. M.; Tumor stem cell antigens as consolidative active specific immunotherapy: a randomized phase II trial of dendritic cells versus tumor cells in patients with metastatic melanoma; *Journal of Immunotherapy*; 2012; 35(8):641-649
20. Dillman R. O., McClay E. F., Barth N. M., Amatruda T. T., Schwartzberg L. S., Mahdavi K., de Leon C., Ellis R. E., DePriest C.; Dendritic Versus Tumor Cell Presentation of Autologous Tumor Antigens for Active Specific Immunotherapy in Metastatic Melanoma: Impact on Long-Term Survival by Extent of Disease at the Time of Treatment; *Cancer Biotherapy and Radiopharmaceuticals*; 2015; 30(5): 187-194.
21. Nakai N., Asai J., Ueda E., Takenaka H., Katoh N., Kishimoto S.; Vaccination of Japanese patients with advanced melanoma with peptide, tumor lysate or both peptide and tumor lysate-

pulsed mature, monocyte-derived dendritic cells; *The Journal of Dermatology*; 2006; 33(7):462-472

22. Aarntzen E. H., De Vries I. J., Lesterhuis W. J., Schuurhuis D., Jacobs J. F., Bol K., Schreiber G., Mus R., De Wilt J. H., Haanen J. B., Schadendorf D., Croockewit A., Blokx W. A., Van Rossum M. M., Kwok W. W., Adema G. J., Figdor C. G.; Targeting CD4(+) T-helper cells improves the induction of antitumor responses in dendritic cell-based vaccination; *Cancer Research*; 2013; 73(1):19-29
23. Tel J., Aarntzen E. H., Baba T., Schreiber G., Schulte B. M., Benitez-Ribas D., Boerman O. C., Croockewit S., Oyen W. J., van Rossum M., Winkels G., Coulie P. G., Punt C. J., Figdor C. G., de Vries I. J.; Natural human plasmacytoid dendritic cells induce antigen-specific T-cell responses in melanoma patients; *Cancer Research*; 2013; 73(3):1063-1075
24. Bol K. F., Aarntzen E. H. J. G., in't Hout F. E. M., Schreiber G., Creemers J. H. A., Lesterhuis W. J., Gerritsen W. R., Grunhagen D. J., Verhoef C., Punt C. J. A., Bonenkamp J. J., de Wilt J. H. W., Figdor C. G., de Vries J. M.; Favorable overall survival in stage III melanoma patients after adjuvant dendritic cell vaccination; *Oncoimmunology*; 2016; 5(1): e1057673