

Hautkrebs:

Tumorinfiltrierende-Lymphozyten(TIL)-Therapie beim malignen Melanom (S. 16–22)

H. Läubli, A. Zippelius

1. Larkin J et al. Five-Year Survival with Combined Nivolumab and Ipilimumab in Advanced Melanoma. *N Engl J Med* 2019; 381: 1535–46
2. Schadendorf D et al. Melanoma. *Lancet* 2018; 392: 971–84
3. Rohaan MW et al. Adoptive transfer of tumor-infiltrating lymphocytes in melanoma: a viable treatment option. *J Immunother Cancer* 2018; 6: 102
4. Rosenberg SA, Restifo NP. Adoptive cell transfer as personalized immunotherapy for human cancer. *Science* 2015; 348: 62–8
5. June CH, Riddell SR, Schumacher TN. Adoptive cellular therapy: a race to the finish line. *Sci Transl Med* 2015; 7: 280ps7
6. Kradin RL et al. Tumour-infiltrating lymphocytes and interleukin-2 in treatment of advanced cancer. *Lancet* 1989; 1: 577–80
7. Goedegebuure PS et al. Adoptive immunotherapy with tumor-infiltrating lymphocytes and interleukin-2 in patients with metastatic malignant melanoma and renal cell carcinoma: a pilot study. *J Clin Oncol* 1995; 13: 1939–49
8. Rosenberg SA et al. Treatment of patients with metastatic melanoma with autologous tumor-infiltrating lymphocytes and interleukin 2. *J Natl Cancer Inst* 1994; 86: 1159–66
9. Dudley ME et al. Cancer regression and autoimmunity in patients after clonal repopulation with antitumor lymphocytes. *Science* 2002; 298: 850–54
10. Krishna S et al. Stem-like CD8 T cells mediate response of adoptive cell immunotherapy against human cancer. *Science* 2020; 370: 1328–34
11. Rosenberg SA et al. Durable complete responses in heavily pretreated patients with metastatic melanoma using T-cell transfer immunotherapy. *Clin Cancer Res* 2011; 17: 4550–57
12. Wu R et al. Adoptive T-cell therapy using autologous tumorinfiltrating lymphocytes for metastatic melanoma: current status and future outlook. *Cancer J* 2012; 18: 160–75
13. Forget M-A et al. Prospective Analysis of Adoptive TIL Therapy in Patients with Metastatic Melanoma: Response, Impact of Anti-CTLA4, and Biomarkers to Predict Clinical Outcome. *Clin Cancer Res* 2018; 24: 4416–28
14. Saint-Jean M et al. Adoptive Cell Therapy with Tumor-Infiltrating Lymphocytes in Advanced Melanoma Patients. *J Immunol Res* 2018; 2018:3530148
15. Besser MJ et al. Comprehensive single institute experience with melanoma TIL: Long term clinical results, toxicity profile, and prognostic factors of response. *Mol Carcinog* 2020; 59: 736–44
16. van den Berg JH et al. Tumor infiltrating lymphocytes (TIL) therapy in metastatic melanoma: boosting of neoantigen-specific T cell reactivity and long-term followup. *J Immunother Cancer* 2020; 8:e000848
17. Orcurto A et al. Guillain-Barré syndrome after adoptive cell therapy with tumor-infiltrating lymphocytes. *J Immunother Cancer* 2020; 8:e001155
18. Borch TH et al. Future role for adoptive T-cell therapy in checkpoint inhibitor-resistant metastatic melanoma. *J Immunother Cancer* 2020; 8:e000668

19. Sarnaik A et al. Long-term follow up of lifileucel (LN-144) cryopreserved autologous tumor infiltrating lymphocyte therapy in patients with advanced melanoma progressed on multiple prior therapies. *J Clin Oncol* 2020; 38 (Suppl): 10006
20. Goff SL et al. Randomized, Prospective Evaluation Comparing Intensity of Lymphodepletion Before Adoptive Transfer of Tumor-Infiltrating Lymphocytes for Patients With Metastatic Melanoma. *J Clin Oncol* 2016; 34: 2389–97
21. Dafni U et al. Efficacy of adoptive therapy with tumorinfiltrating lymphocytes and recombinant interleukin-2 in advanced cutaneous melanoma: a systematic review and metaanalysis. *Ann Oncol* 2019; 30: 1902–13
22. Nguyen LT et al. Phase II clinical trial of adoptive cell therapy for patients with metastatic melanoma with autologous tumor-infiltrating lymphocytes and low-dose interleukin-2. *Cancer Immunol Immunother* 2019; 68: 773–85
23. Stevanović S et al. Complete regression of metastatic cervical cancer after treatment with human papillomavirustargeted tumor-infiltrating T cells. *J Clin Oncol* 2015; 33: 1543–50
24. Feldman SA et al. Adoptive Cell Therapy – Tumor-Infiltrating Lymphocytes, T-Cell Receptors, and Chimeric Antigen Receptors. *Semin Oncol* 2015; 42: 626–39
25. Andersen R et al. Tumor infiltrating lymphocyte therapy for ovarian cancer and renal cell carcinoma. *Hum Vaccin Immunother* 2015; 11: 2790–95
26. Bouet-Toussaint F et al. Interleukin-2 expanded lymphocytes from lymph node and tumor biopsies of human renal cell carcinoma, breast and ovarian cancer. *Eur Cytokine Netw* 2000; 11: 217–24
27. Hamaidi I et al. Sirt2 Inhibition Enhances Metabolic Fitness and Effector Functions of Tumor-Reactive T Cells. *Cell Metab* 2020; 32: 420–436.e12
28. Ben-Avi R et al. Establishment of adoptive cell therapy with tumor infiltrating lymphocytes for non-small cell lung cancer patients. *Cancer Immunol Immunother* 2018; 67: 1221–30
29. Merlo A et al. Adoptive cell therapy against EBV-related malignancies: a survey of clinical results. *Expert Opin Biol Ther* 2008; 8: 1265–94
30. Itzhaki O et al. Establishment and large-scale expansion of minimally cultured „young“ tumor infiltrating lymphocytes for adoptive transfer therapy. *J Immunother* 2011; 34: 212–20
31. Dudley ME et al. CD8+ enriched „young“ tumor infiltrating lymphocytes can mediate regression of metastatic melanoma. *Clin Cancer Res* 2010; 16: 6122–31
32. Tran E , et al. Cancer immunotherapy based on mutation-specific CD4+ T cells in a patient with epithelial cancer. *Science* 2014; 344: 641–45
33. Zacharakis N et al. Immune recognition of somatic mutations leading to complete durable regression in metastatic breast cancer. *Nat Med* 2018; 24: 724–30
34. Bianchi V, Harari A, Coukos G. Neoantigen-Specific Adoptive Cell Therapies for Cancer: Making T-Cell Products More Personal. *Front Immunol* 2020; 11: 1215
35. Bobisse S et al. Sensitive and frequent identification of high avidity neo-epitope specific CD8+ T cells in immunotherapy-naïve ovarian cancer. *Nat Commun* 2018; 9: 1092
36. Thommen DS et al. A transcriptionally and functionally distinct PD-1+ CD8+ T cell pool with predictive potential in non-small cell lung cancer treated with PD-1 blockade. *Nat Med* 2018; 24: 994–1004
37. Radvanyi LG et al. Specific lymphocyte subsets predict response to adoptive cell therapy using expanded autologous tumorinfiltrating lymphocytes in metastatic melanoma patients. *Clin Cancer Res* 2012; 18: 6758–70

38. Dudley ME et al. Randomized selection design trial evaluating CD8+-enriched versus unselected tumor-infiltrating lymphocytes for adoptive cell therapy for patients with melanoma. *J Clin Oncol* 2013; 31: 2152–59
 39. Beane JD et al. Clinical Scale Zinc Finger Nuclease-mediated Gene Editing of PD-1 in Tumor Infiltrating Lymphocytes for the Treatment of Metastatic Melanoma. *Mol Ther* 2015; 23: 1380–90
 40. Forget M-A et al. A Novel Method to Generate and Expand Clinical-Grade, Genetically Modified, Tumor-Infiltrating Lymphocytes. *Front Immunol* 2017; 8: 908
 41. Mullard A. Restoring IL-2 to its cancer immunotherapy glory. *Nat Rev Drug Discov* 2021; 20: 163–5
 42. Diab A et al. Bempegaldesleukin (NKTR-214) plus Nivolumab in Patients with Advanced Solid Tumors: Phase I Dose-Escalation Study of Safety, Efficacy, and Immune Activation (PIVOT-02). *Cancer Discov* 2020; 10: 1158–73
 43. Deniger DC et al. A Pilot Trial of the Combination of Vemurafenib with Adoptive Cell Therapy in Patients with Metastatic Melanoma. *Clin Cancer Res* 2017; 23: 351–62
 44. Donia M et al. PD-1+ Polyfunctional T Cells Dominate the Periphery after Tumor-Infiltrating Lymphocyte Therapy for Cancer. *Clin Cancer Res* 2017; 23: 5779–88
 45. Mullinax JE et al. Combination of Ipilimumab and Adoptive Cell Therapy with Tumor-Infiltrating Lymphocytes for Patients with Metastatic Melanoma. *Front Oncol* 2018; 8: 44
-

Interview mit Dr. K. Lübke:

Hormonsensitiver Brustkrebs im Frühstadium:

„Der Recurrence Score sollte bereits im Tumorboard vorliegen“ (S. 35)

1. Kalinsky K et al., mündliche Präsentation: [GS2-07]. San Antonio Breast Cancer Symposium (SABCS); Dezember 2021
2. Kalinsky K et al. *New Engl J Med* 2021
3. Sparano et al. *New Engl J Med* 2018
4. Verweis mit Genehmigung von NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer, V.3.2021©National Comprehensive Cancer Network, Inc. 2021. Alle Rechte vorbehalten. Zugriff am 17. Mai 2021. Die aktuelle und vollständige Version der Leitlinien finden Sie unter: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf