Emerging Landscape of Adoptive Cell Therapy in Hematologic and Solid Tumors

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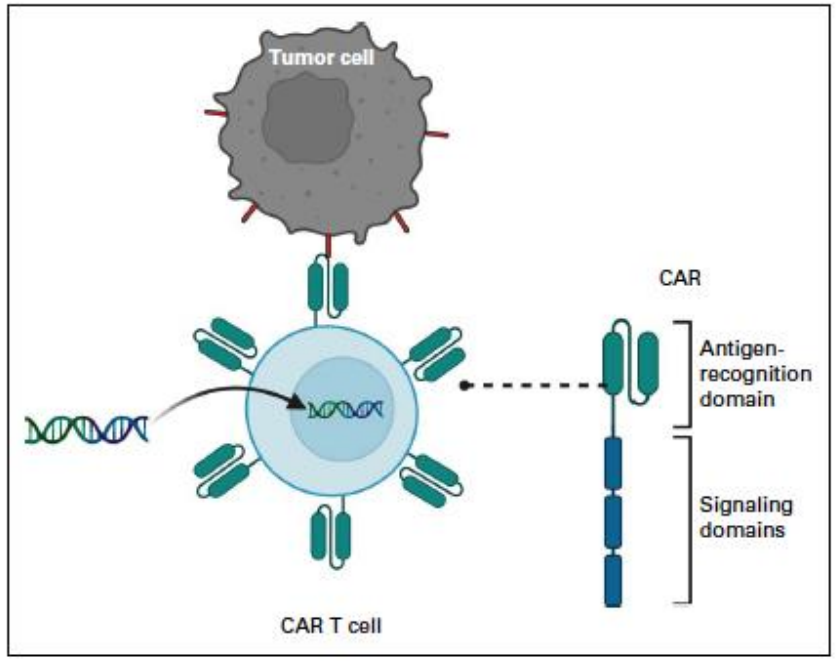
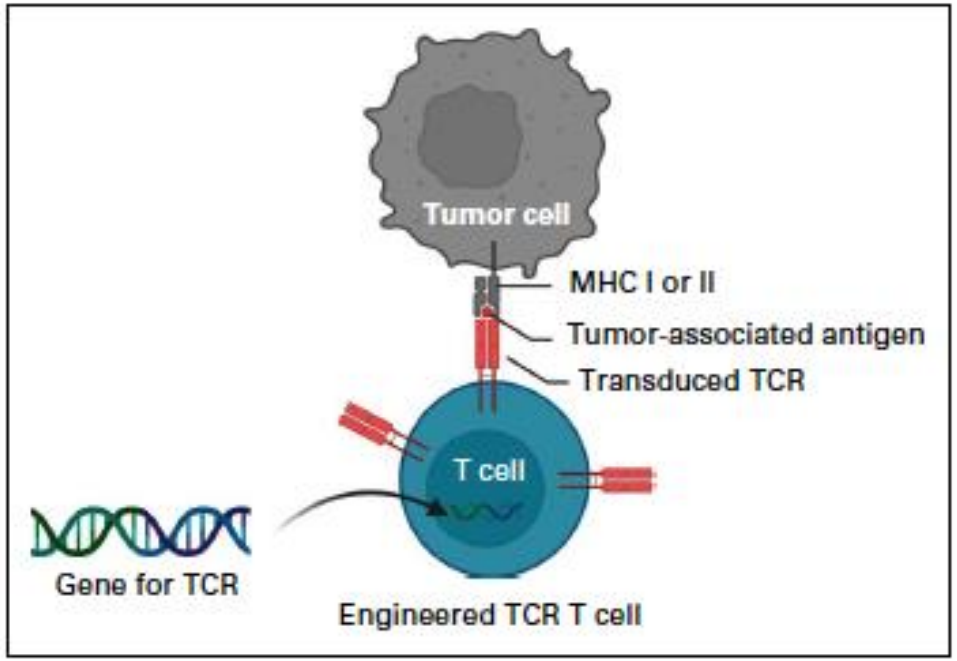
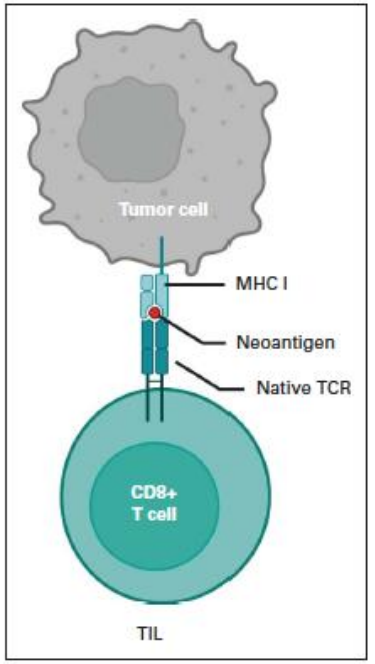
CAR T Cells, TCR T Cells, and TILs

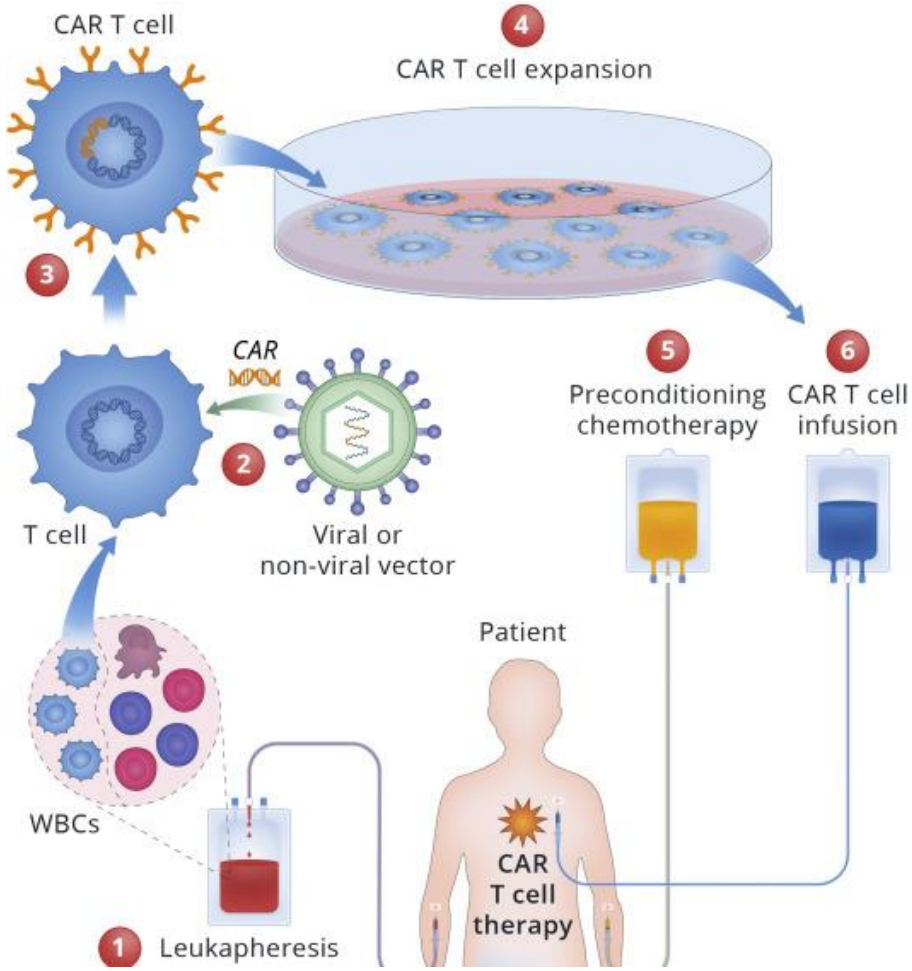






(Olson & Odunsi *J Clin Oncol* 2023)

Overview of the CAR T Cell Process



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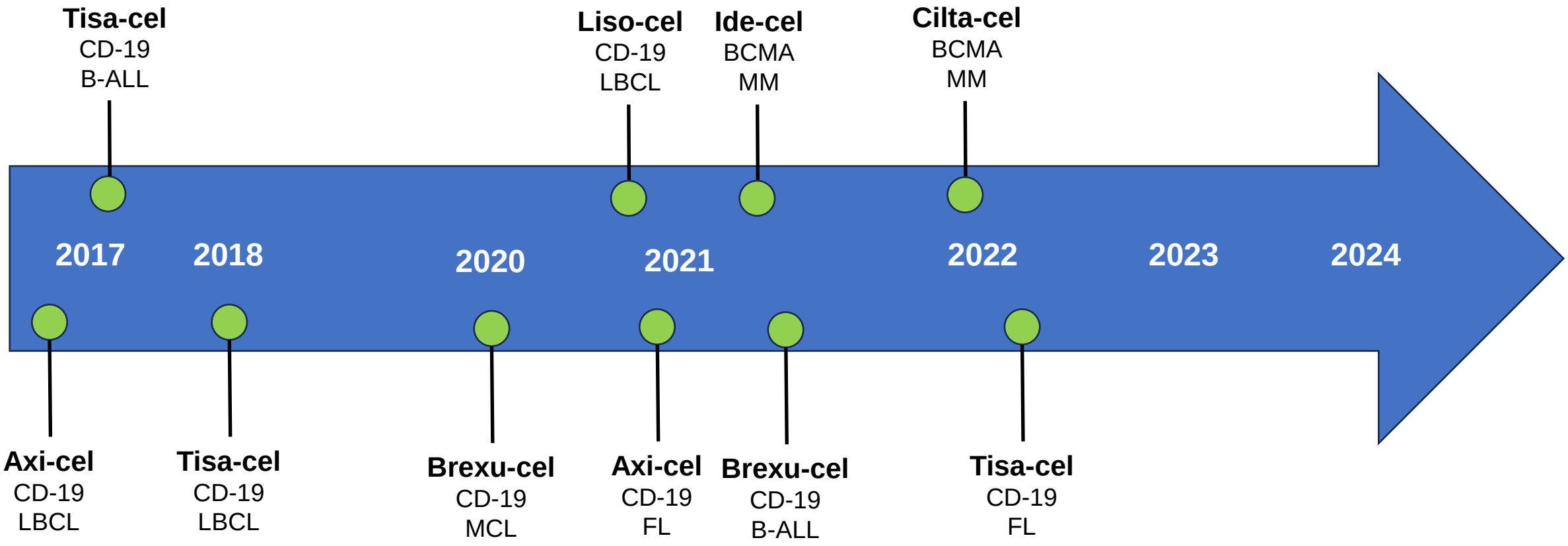
(Ganatra S et al. *JACC* 2019)

CAR T Cells for Hematologic Malignancies



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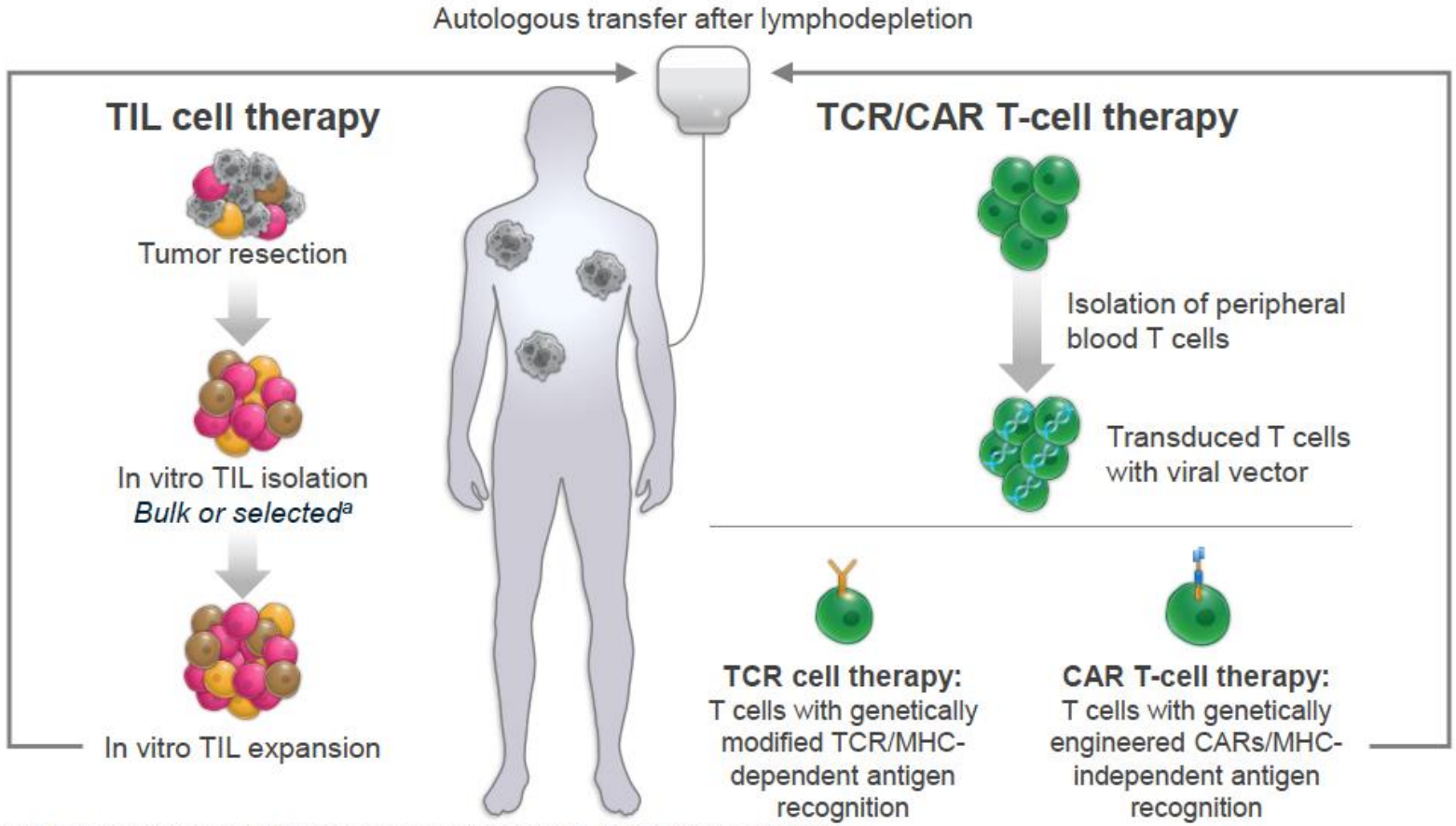
Adoptive T Cell Therapy Approaches



CAR, chimeric antigen receptor; MHC, major histocompatibility complex; TCR, T-cell receptor; TIL, tumor-infiltrating lymphocyte.
[a] Bulk TIL refers to non-selected TILs; selected TILs refers to TILs selected against specific antigens.
Rohaan MW, et al. *Virchows Arch*. 2019;474:449.

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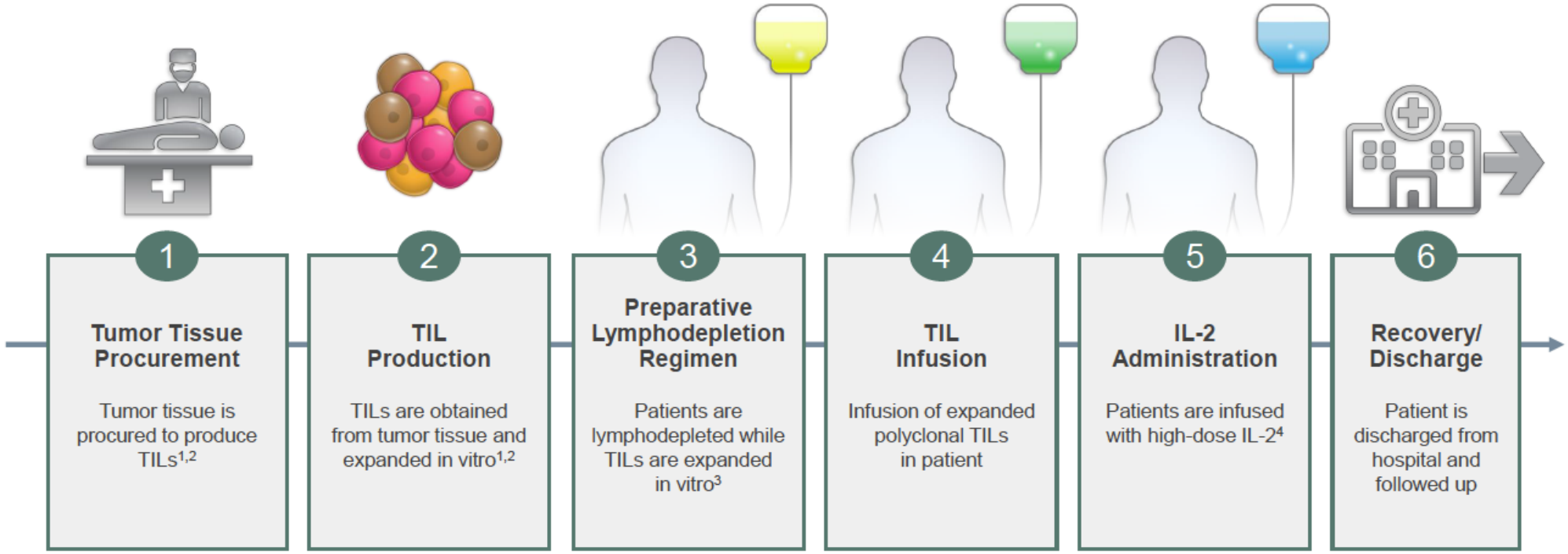
(www.tilworkinggroup.com)

Overview of TIL Therapy



IL, interleukin; TIL, tumor-infiltrating lymphocyte.

1. Itzhaki O, et al. *J Immunother*. 2011;34:212. 2. Dudley ME, et al. *J Immunother*. 2003;26:332. 3. Dudley ME, et al. *J Clin Oncol*. 2008;26:5233. 4. Atkins MB, et al. *J Clin Oncol*. 1999;17:2105.

TIL CELL THERAPY WORKING GROUP

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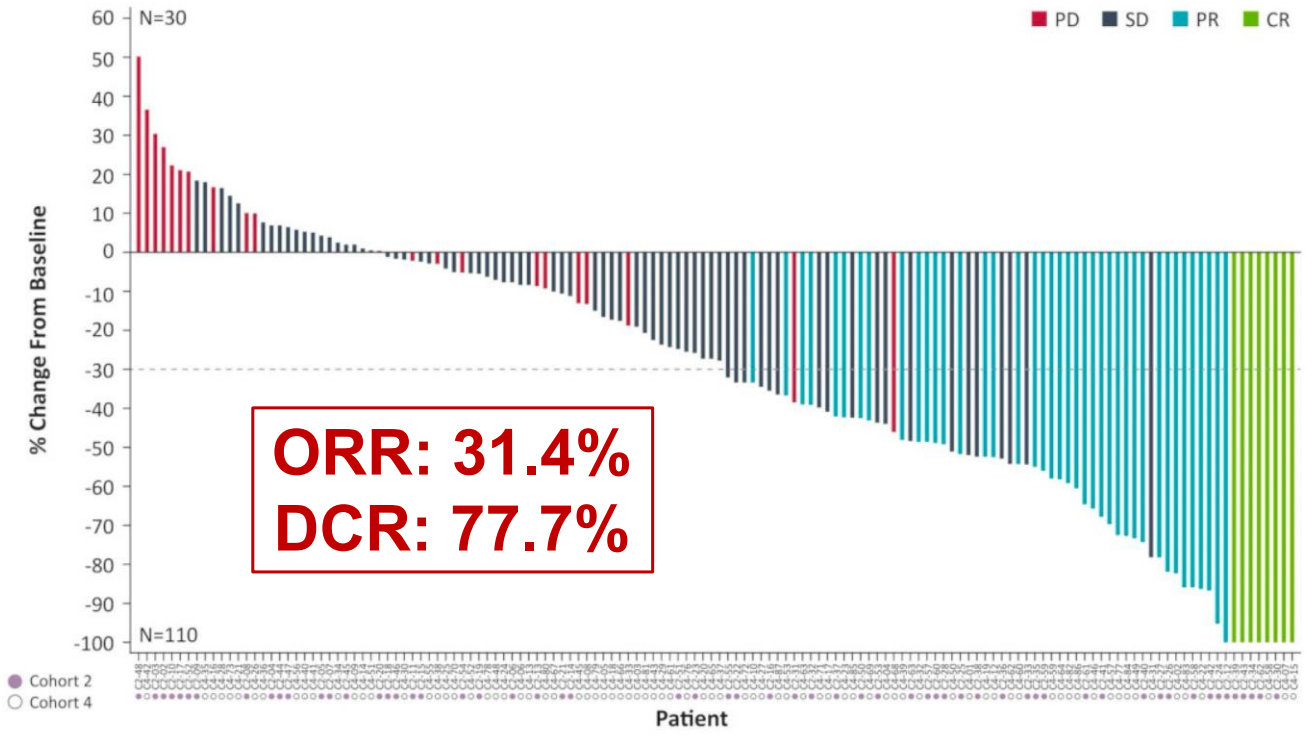
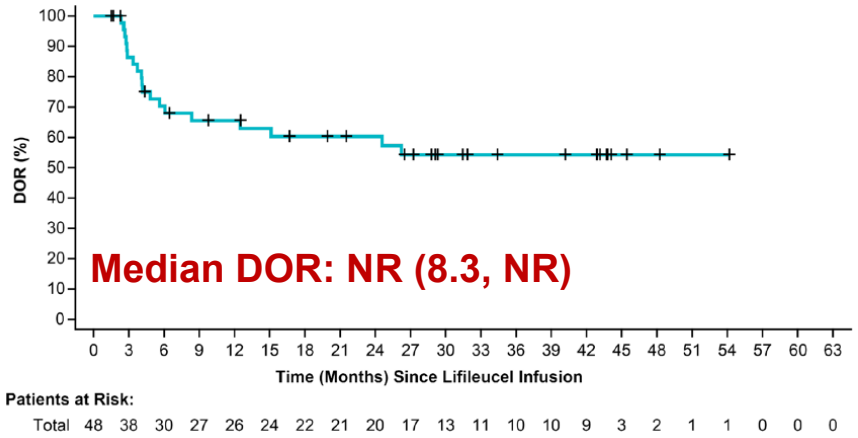
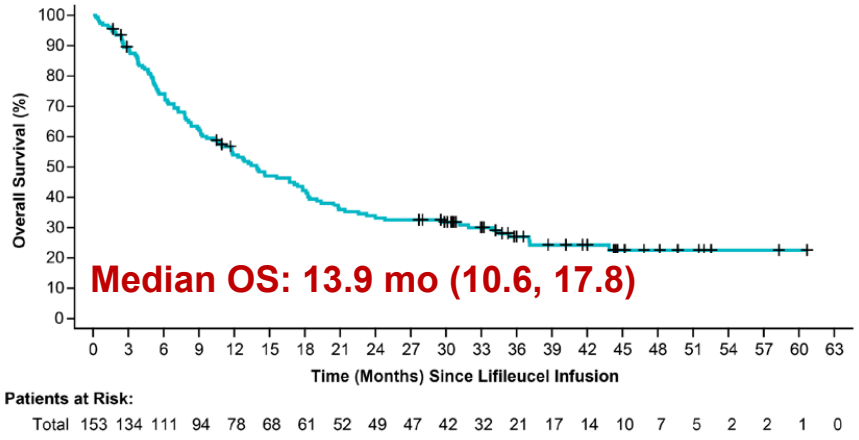
Lifileucel for PD-1 Refractory Melanoma







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(Chesney et al. *JITC* 2022)

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Cell Therapy for Solid Tumors is Here!

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FDA NEWS RELEASE

FDA Approves First Cellular Therapy to Treat Patients with Unresectable or Metastatic Melanoma

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For Immediate Release: February 16, 2024

Today, the U.S. Food and Drug Administration approved Amtagvi (lifileucel), the first cellular therapy indicated for the treatment of adult patients with a type of skin cancer (melanoma) that is unable to be removed with surgery (unresectable) or has spread to other parts of the body (metastatic) that previously has been treated with other therapies (a PD-1 blocking antibody, and if *BRAF* V600 mutation positive, a *BRAF* inhibitor with or without a MEK inhibitor).

Content current as of: 02/16/2024

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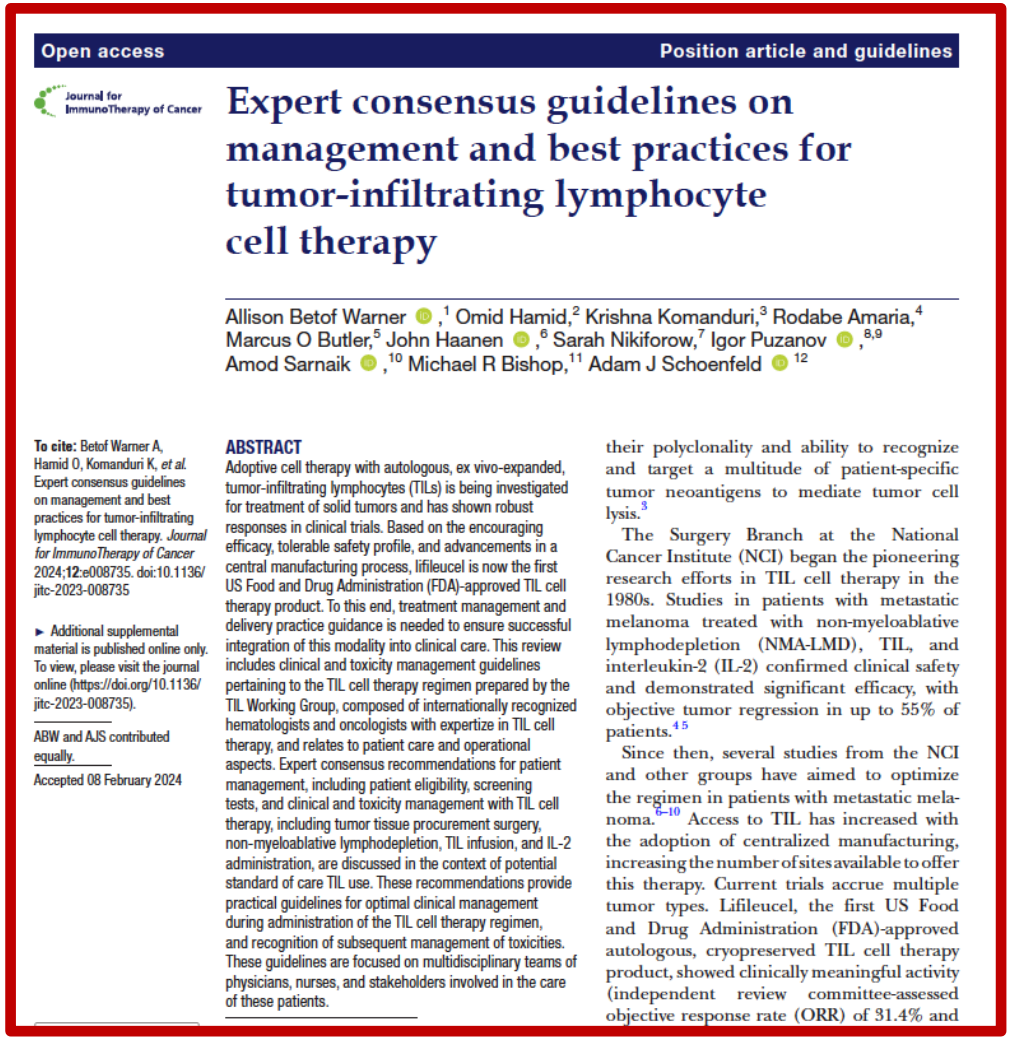

Open access Position article and guidelines

Journal for ImmunoTherapy of Cancer

Expert consensus guidelines on management and best practices for tumor-infiltrating lymphocyte cell therapy

Allison Betof Warner ,[1] Omid Hamid,[2] Krishna Komanduri,[3] Rodabe Amaria,[4] Marcus O Butler,[5] John Haanen ,[6] Sarah Nikiforow,[7] Igor Puzanov ,[8,9] Amod Sarnaik ,[10] Michael R Bishop,[11] Adam J Schoenfeld [12]

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► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/jitc-2023-008735).

ABW and AJS contributed equally.

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ABSTRACT

Adoptive cell therapy with autologous, ex vivo-expanded, tumor-infiltrating lymphocytes (TILs) is being investigated for treatment of solid tumors and has shown robust responses in clinical trials. Based on the encouraging efficacy, tolerable safety profile, and advancements in a central manufacturing process, lifileucel is now the first US Food and Drug Administration (FDA)-approved TIL cell therapy product. To this end, treatment management and delivery practice guidance is needed to ensure successful integration of this modality into clinical care. This review includes clinical and toxicity management guidelines pertaining to the TIL cell therapy regimen prepared by the TIL Working Group, composed of internationally recognized hematologists and oncologists with expertize in TIL cell therapy, and relates to patient care and operational aspects. Expert consensus recommendations for patient management, including patient eligibility, screening tests, and clinical and toxicity management with TIL cell therapy, including tumor tissue procurement surgery, non-myeloablative lymphodepletion, TIL infusion, and IL-2 administration, are discussed in the context of potential standard of care TIL use. These recommendations provide practical guidelines for optimal clinical management during administration of the TIL cell therapy regimen, and recognition of subsequent management of toxicities. These guidelines are focused on multidisciplinary teams of physicians, nurses, and stakeholders involved in the care of these patients.

their polyclonality and ability to recognize and target a multitude of patient-specific tumor neoantigens to mediate tumor cell lysis.[3]

The Surgery Branch at the National Cancer Institute (NCI) began the pioneering research efforts in TIL cell therapy in the 1980s. Studies in patients with metastatic melanoma treated with non-myeloablative lymphodepletion (NMA-LMD), TIL, and interleukin-2 (IL-2) confirmed clinical safety and demonstrated significant efficacy, with objective tumor regression in up to 55% of patients.[4 5]

Since then, several studies from the NCI and other groups have aimed to optimize the regimen in patients with metastatic melanoma.[6–10] Access to TIL has increased with the adoption of centralized manufacturing, increasing the number of sites available to offer this therapy. Current trials accrue multiple tumor types. Lifileucel, the first US Food and Drug Administration (FDA)-approved autologous, cryopreserved TIL cell therapy product, showed clinically meaningful activity (independent review committee-assessed objective response rate (ORR) of 31.4% and

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