

The Medical Letter[®]

on Drugs and Therapeutics

Volume 66

Published online October 14, 2024

Online
Article

IN THIS ISSUE

In Brief: Afamitresgene autoleucel (*Tecelra*) for Synovial Sarcoma

Important Copyright Message

FORWARDING OR COPYING IS A VIOLATION OF U.S. AND INTERNATIONAL COPYRIGHT LAWS

The Medical Letter, Inc. publications are protected by U.S. and international copyright laws. Forwarding, copying, or any distribution of this material without permission to a nonsubscriber is prohibited.

Sharing a password with a nonsubscriber or otherwise making the contents of this site available to third parties is prohibited.

By accessing and reading the attached content I agree to comply with U.S. and international copyright laws and these terms and conditions of The Medical Letter, Inc.

For further information click: [Subscriptions](#), [Site Licenses](#), [Reprints](#)
or call customer service at: 800-211-2769

The Medical Letter®

on Drugs and Therapeutics

Volume 66

Published online October 14, 2024

Online
Article

IN THIS ISSUE

In Brief: Afamitresgene Autoleucel (*Tecelra*) for Synovial Sarcoma

IN BRIEF

Afamitresgene Autoleucel (*Tecelra*) for Synovial Sarcoma

Afamitresgene autoleucel (*Tecelra* – Adaptimmune), a melanoma-associated antigen A4 (MAGE-A4)-directed genetically modified autologous T-cell immunotherapy, has received accelerated approval from the FDA for one-time treatment of adults with unresectable or metastatic synovial sarcoma who received prior chemotherapy and are HLA-A*02:01P, -A*02:02P, -A*02:03P, or -A*02:06P positive and whose tumor expresses the MAGE-A4 antigen. It is the first gene therapy to be approved in the US for treatment of synovial sarcoma. Accelerated approval of the immunotherapy was based on the overall response rate and duration of response.

Pronunciation Key

Afamitresgene autoleucel: af' am it ras jeen au toe loo' sel
Tecelra: te cell' ra

THE PRODUCT – *Tecelra* is prepared from autologous peripheral blood mononuclear cells obtained by leukapheresis. The cells are sent to a commercial laboratory where they are enriched for T cells and then transduced with a replication-incompetent lentiviral vector containing the MAGE-A4 TCR transgene. *Tecelra* is formulated as a cell suspension containing 2.68×10^9 to 10×10^9 MAGE-A4 TCR positive T cells. *Tecelra* contains dimethyl sulfoxide (DMSO), which can cause serious hypersensitivity reactions.

MECHANISM OF ACTION – MAGE-A4 peptide is an intracellular cancer-testis antigen that is expressed in synovial sarcoma. The autologous T-cell immunotherapy recognizes an HLA-A*02 restricted MAGE-A4 peptide expressed on the cell surface. Activation of *Tecelra* results in T cell proliferation,

Key Points: Afamitresgene Autoleucel (*Tecelra*)

- ▶ **Description:** A melanoma-associated antigen A4 (MAGE-A4)-directed genetically modified autologous T-cell immunotherapy.
- ▶ **Indication:** Treatment of adults with unresectable or metastatic synovial sarcoma who received prior chemotherapy and are HLA-A*02:01P, -A*02:02P, -A*02:03P, or -A*02:06P positive and whose tumor expresses the MAGE-A4 antigen.
- ▶ **Efficacy:** A single infusion of the immunotherapy produced an overall response rate of 39%.
- ▶ **Adverse Effects:** Cytokine release syndrome, immune effector cell-associated neurotoxicity, prolonged severe cytopenias, severe infection, and secondary malignancies can occur.
- ▶ **Dosage:** A single IV infusion of 2.68×10^9 to 10×10^9 MAGE-A4 TCR positive T cells.
- ▶ **Cost:** One dose costs \$727,000.
- ▶ **Conclusion:** About 40% of patients with previously treated unresectable or metastatic synovial sarcoma who received a single infusion of *Tecelra* achieved a response.

cytokine secretion, and death of MAGE-A4/HLA-A*02-expressing synovial sarcoma cells.

CLINICAL STUDIES – FDA approval of afamitresgene autoleucel was based on the results of an open-label trial (SPEARHEAD-1) in 44 HLA-A*02:01-03 and 06 allele-positive patients with inoperable or metastatic synovial sarcoma who received prior systemic chemotherapy (doxorubicin and/or ifosfamide) and whose tumor expressed the MAGE-A4 antigen. All patients received a single infusion of afamitresgene autoleucel. After a median follow-up of 32.6 months, the overall response rate was 39%.¹

ADVERSE EFFECTS – The *Tecelra* label includes a boxed warning about the risk of cytokine release syndrome (CRS), which can cause hypotension, pulmonary edema, coagulopathy, multiorgan failure, and death. Nausea, vomiting, fatigue, pyrexia, constipation, dyspnea, abdominal pain, decreased appetite, tachycardia, back pain, hypotension, diarrhea, and edema can occur. Immune effector cell-associated neurotoxicity syndrome (ICANS),

prolonged severe cytopenias, severe infection, and secondary malignancies have been reported. Patients should avoid driving or engaging in hazardous occupations or activities for at least 4 weeks after receiving *Tecelra*. The immunotherapy is contraindicated in patients who are heterozygous or homozygous for HLA-A*02:05P.

DOSAGE, ADMINISTRATION, AND COST – Patients should receive lymphodepleting chemotherapy (cyclophosphamide and fludarabine) starting the seventh day before the *Tecelra* infusion. Acetaminophen and an H₁-antihistamine should be given about 30-60 minutes before the *Tecelra* infusion. Administration of a granulocyte-colony stimulating factor (G-CSF) can be considered

for patients with neutropenia. Patients should be monitored at the treatment facility for at least 7 days after receiving *Tecelra* and stay near the treatment facility for at least 4 weeks. One dose of *Tecelra* costs \$727,000.² ■

1. SP D'Angelo et al. Afamitresgene autoleucel for advanced synovial sarcoma and myxoid round cell liposarcoma (SPEARHEAD-1): an international, open-label, phase 2 trial. *Lancet* 2024; 403:1460.
2. Approximate WAC. WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. September 5, 2024. Reprinted with permission by First Databank, Inc. All rights reserved. ©2023. www.fdbhealth.com/policies/drug-pricing-policy.

PRESIDENT: Mark Abramowicz, M.D.; **VICE PRESIDENT, EDITOR IN CHIEF:** Jean-Marie Pflomm, Pharm.D.; **ASSOCIATE EDITORS:** Susan M. Daron, Pharm.D., Amy Faucard, MLS, Michael P. Viscusi, Pharm.D. **CONSULTING EDITORS:** Joanna Esterow, PA-C, Mordechai Sacks, DMSc, PA-C, Brinda M. Shah, Pharm.D., F. Peter Swanson, M.D.

CONTRIBUTING EDITORS: Carl W. Bazil, M.D., Ph.D., Columbia University College of Physicians and Surgeons; Ericka L. Crouse, Pharm.D., B.C.P.P., C.G.P., F.A.S.H.P., F.A.S.C.P., Virginia Commonwealth University; Vanessa K. Dalton, M.D., M.P.H., University of Michigan Medical School; Eric J. Epstein, M.D., Albert Einstein College of Medicine; David N. Juurlink, BPhm, M.D., Ph.D., Sunnybrook Health Sciences Centre; Richard B. Kim, M.D., University of Western Ontario; Sandip K. Mukherjee, M.D., F.A.C.C., Yale School of Medicine; Dan M. Roden, M.D., Vanderbilt University School of Medicine; Esperance A.K. Schaefer, M.D., M.P.H., Harvard Medical School; Arthur M. F. Yee, M.D., Ph.D., F.A.C.R., Weill Medical College of Cornell University

MANAGING EDITOR AND DIRECTOR OF CONTENT OPERATIONS: Susie Wong; **EDITORIAL ASSISTANT:** Karrie Ferrara

FULFILLMENT AND SYSTEMS MANAGER: Cristine Romatowski; **EXECUTIVE DIRECTOR OF SALES:** Elaine Reaney-Tomaselli

EXECUTIVE DIRECTOR OF MARKETING AND COMMUNICATIONS: Joanne F. Valentino; **INTERIM PUBLISHER:** Jean-Marie Pflomm, Pharm.D.

Founded in 1959 by Arthur Kallet and Harold Aaron, M.D.

Copyright and Disclaimer. The Medical Letter, Inc. is an independent nonprofit organization that provides healthcare professionals with unbiased drug prescribing recommendations. The editorial process used for its publications relies on a review of published and unpublished literature, with an emphasis on controlled clinical trials, and on the opinions of its consultants. The Medical Letter, Inc. does not sell advertising or receive any commercial support. No part of the material may be reproduced or transmitted by any process in whole or in part without prior permission in writing. The Medical Letter, Inc. does not warrant that all the material in this publication is accurate and complete in every respect. The Medical Letter, Inc. and its editors shall not be held responsible for any damage resulting from any error, inaccuracy, or omission.

Subscription Services

Address:

The Medical Letter, Inc.
145 Huguenot St. Ste. 312
New Rochelle, NY 10801-7537
www.medicalletter.org

Customer Service:

Call: 800-211-2769 or 914-235-0500
Fax: 914-632-1733
E-mail: custserv@medicalletter.org

Permissions:


To reproduce any portion of this issue, please e-mail your request to: permissions@medicalletter.org

Subscriptions (US):

1 year - \$159; \$65 per year for students, interns, residents, and fellows in the US and Canada. Reprints - \$45 per issue or article

Site License Inquiries:

E-mail: SubQuote@medicalletter.org
Call: 800-211-2769
Special rates available for bulk subscriptions.

Get Connected:   

Copyright 2024. ISSN 0025-732X

The Medical Letter