

Company

Epizyme Inc.

Drug or Device Name

TAZVERIK®

Category

Pharmaceutical

Compound/Technical Name

tazemetostat

Trade Name

TAZVERIK®

Date of Approval

01/23/2020

Therapeutic Categories

Date of approval note: January 23, 2020 (epithelioid sarcoma); June 18, 2020 (follicular lymphoma)

Therapeutic Category: Oncology

Indications

TAZVERIK is indicated for the treatment of: - Adults and pediatric patients aged 16 years and older with metastatic or locally advanced epithelioid sarcoma not eligible for complete resection. - Adult patients with relapsed or refractory follicular lymphoma whose tumors are positive for an EZH2 mutation as detected by an FDA-approved test and who have received at least 2 prior systemic therapies. - Adult patients with relapsed or refractory follicular lymphoma who have no satisfactory alternative treatment options. These indications are approved under accelerated approval based on the overall response rate and duration of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Background

The approval of TAZVERIK, a first-in-class oral EZH2 inhibitor, delivers on the promise of epigenetic therapies for patients with cancer. EZH2, an epigenetic modulator of cell proliferation, differentiation, and survival, contributes to tumor pathogenesis when it is dysregulated. Inhibition of EZH2 to treat cancers is mechanistically different than traditional chemotherapy or targeted agents in that it affects gene expression instead of cancerous cells or specific oncogenic mutations. This approach enables the utility of TAZVERIK in diseases as diverse as epithelioid sarcoma and follicular lymphoma – the former, a rare, aggressive, universally fatal soft tissue sarcoma that typically strikes younger adults, and the latter, an indolent yet incurable rare subtype of non-Hodgkin lymphoma that largely affects older individuals. Despite the different populations affected by these cancers, both lacked tolerable, effective therapies that addressed their underlying causes. TAZVERIK was evaluated in the largest prospective

study to date of patients with epithelioid sarcoma, the results of which demonstrated a progression-free survival of 5.5 months, and an overall survival of 19 months. For a disease historically associated with an overall survival of 8 to 12 months, these clinically meaningful results offer hope to a patient population that was largely overlooked. Similarly, results from a clinical trial in patients with follicular lymphoma also provide hope to a population in need of effective, tolerable therapies. Demonstrating a single-agent response rate of up to 69%, TAZVERIK received FDA approval for use in patients with follicular lymphoma only 6 months after its approval for epithelioid sarcoma. Data from both these studies underscore the regulatory role of EZH2 in tumor cell proliferation and survival, and the role of TAZVERIK in the treatment of these cancers.

Development

Epizyme's mission to rewrite treatments for cancer through novel epigenetic medicines began a decade ago with innovative medicinal chemistry and a rigorous biomarker-driven approach that changed the landscape of the field and allowed for the discovery of inhibitors of a previously undrugged class of epigenetic targets. TAZVERIK, the first approved inhibitor of a histone methyltransferase, was discovered using this proprietary approach, marking a shift towards more specific epigenetic inhibitors, and setting a precedence for the rigor needed for successful drug development in this space.

Innovation

TAZVERIK represents a drug class with fundamentally a new mechanism of action directed at specific causes of cancers. Its efficacy and tolerability profile suggests that it has the potential to become a backbone of treatment for epithelioid sarcoma and follicular lymphoma through combinations with other agents with the goal to further improve outcomes. With plans to further explore TAZVERIK as both monotherapy and in combinations across multiple new hematological and solid tumor cancers, TAZVERIK offers a new avenue for others patients affected by prostate cancer, lung cancer, and other hematologic malignancies.

Pubmed

Garber K. Histone-writer cancer drugs enter center stage. *Nat Biotechnol.* 2020;38: 909–912. <https://doi.org/10.1038/s41587-020-0621-1>. <https://pubmed.ncbi.nlm.nih.gov/32760028/> Gounder M, Schöffski P, Jones RL, et al. Tazemetostat in advanced epithelioid sarcoma with loss of INI1/SMARCB1: an international, open-label, phase 2 basket study. *Lancet Onc.* 2020;21(11):1423-1432. doi: 10.1016/S1470-2045(20)30451-4. <https://pubmed.ncbi.nlm.nih.gov/33035459/> Kuntz KW, Campbell JE, Keilhack H, et al. The Importance of Being Me: Magic Methyls, Methyltransferase Inhibitors, and the Discovery of Tazemetostat. *J Med Chem.* 2016;59(4):1556-64. doi: 10.1021/acs.jmedchem.5b01501. <https://pubmed.ncbi.nlm.nih.gov/26769278/> Morschhauser F, Tilly H, Chaidos A, et al. Tazemetostat for patients with relapsed or refractory follicular lymphoma: an open-label, single-arm, multicentre, phase 2 trial. *Lancet Oncol.* 2020;21(11):1433-1442. doi: 10.1016/S1470-2045(20)30441-1. <https://pubmed.ncbi.nlm.nih.gov/33035457/>

Attachments

Submit

