Glasdegib (PF-04449913) Fact Sheet

Glasdegib is an investigational agent and has not been approved for marketing by any regulatory agency at this time.

ABOUT GLASDEGIB

Glasdegib (PF-04449913) is being evaluated as an oral therapy for select hematologic malignancies and solid tumors that inhibits the smoothened (SMO) receptor, thereby disrupting the Hedgehog (Hh) pathway.[1,2]

SMO inhibition of Hh signaling disrupts the regulation of cancer stem cell (CSC) survival.[3] This may inhibit development of drug resistance and prevent relapse.

Glasdegib is currently under investigation for select solid tumors and hematologic malignancies, including acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS).

ABOUT AML & MDS

Acute myeloid leukemia (AML) is one of the most common forms of leukemia in adults, accounting for approximately one third of all leukemias worldwide.[4]

- It is estimated that in 2018 there will be about 19,520 new cases of AML and about 10,670 deaths from AML. Most will be in adults.[5]
- In patients with AML, the overall 5-year survival rate is approximately 26%.[6]
- Despite recent advancements, additional treatment options that reduce incidence of disease progression and relapse are still needed, especially for patients who are unable to receive intensive chemotherapy.[7-9]

Myelodysplastic syndromes (MDS) is a group of hematologic disorders characterized by the poor production of myeloid cells due to hematopoietic stem cell dysfunction.[10]

- MDS affects approximately 13,000 people in the U.S. annually, and the median age at diagnosis is 76 years.[11,12]
- The 3-year survival rate for patients with MDS is 35%.[12]

CLINICAL STUDIES

Clinical studies evaluating the safety and efficacy of glasdegib include:

Phase 2

Data from a Phase 2 trial of glasdegib in combination with low-dose cytarabine (LDAC) in patients with AML or high-risk MDS were presented at the American Society of Hematology (ASH) Annual Meeting in December 2016.

- Results showed the addition of glasdegib to LDAC significantly increased overall survival (OS) when compared to LDAC alone in patients with AML and MDS.

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CLINICAL STUDIES (CONT'D)

- Patients were followed for up to four years, and at the time of data cut-off, median OS for patients with AML and MDS who received glasdegib plus LDAC (n=88) was 8.8 months (80% CI: 6.9, 9.9) compared to 4.9 months (80% CI: 3.5, 6.0) for patients taking LDAC only (n=44) (HR: 0.501, 80% CI: 0.384, 0.654, one-sided log rank p-value 0.0003).
- Low blood counts and gastrointestinal toxicities occurred more frequently among patients treated with glasdegib plus LDAC than those treated with LDAC alone. Blood infections were less among patients treated with glasdegib plus LDAC (3.6%) compared to LDAC alone (12.2%). Patients in the glasdegib plus LDAC group experienced increased distortion of taste (23.8%), muscle spasms (20.2%) and thinning or loss of hair (10.2%). Serious AEs of febrile neutropenia were also more frequent in patients taking glasdegib plus LDAC (36.9%) compared to LDAC alone (26.8%). The most common cause of death in both arms was disease progression.

Phase 3

BRIGHT AML1019 consists of two prospective randomized (1:1), double-blind, multi-center, placebo controlled trials evaluating glasdegib with or without intensive chemotherapy in patients with newly-diagnosed AML or azacitidine with or without glasdegib in patients with previously untreated AML.

- In the first study, 400 patients with AML suitable for intensive chemotherapy will be randomized to receive glasdegib plus cytarabine and daunorubicin or placebo plus cytarabine and daunorubicin.
- In the second study, 320 AML patients not suitable for intensive chemotherapy will be randomized to receive glasdegib plus azacitidine or placebo plus azacitidine.

CONTACT & ADDITIONAL INFORMATION

Pfizer Media Relations Contact

Jessica Smith – Pfizer Oncology Media Relations
jessica.m.smith@pfizer.com
Phone: 212-733-6213
Mobile: 646-899-3178

For more information and a complete listing of glasdegib (PF-04449913) clinical trials, please visit www.clinicaltrials.gov.

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