Direct Healthcare Professional Communication (DHPC)

9 March 2023

ADAKVEO (crizanlizumab): Phase III study (CSEG101A2301) shows no superiority of crizanlizumab over placebo

Dear Healthcare Professional,

Novartis in agreement with SFDA would like to inform you of the following:

Summary

- Preliminary results from the phase III study CSEG101A2301 (STAND) did not show a difference between crizanlizumab and placebo in annualized rates of vaso-occlusive crises leading to a healthcare visit over the first-year post randomization.
- The preliminary results do not suggest new safety concerns with crizanlizumab. However, higher rates for grade ≥3 treatment-related adverse events were reported for crizanlizumab compared to placebo.
- Physicians should consider the individual benefit and risks when making therapeutic decisions regarding the use of crizanlizumab.

Background Information

Adakveo® is indicated to reduce the frequency of vasoocclusive crises (VOCs) in adults and pediatric patients aged 16 years and older with sickle cell disease. It can be given as an add on therapy to hydroxyurea/hydroxycarbamide (HU/HC) or as monotherapy in patients for whom HU/HC is inappropriate or inadequate. Adakveo is currently approved for use at the dose of 5.0 mg/kg.

The initial analysis of the confirmatory trial CSEG101A2301 (STAND[1]) was conducted on data from 252 participants enrolled in this study from initiation in 2019 to the data cut-off of 31 August 2022. The results did not confirm the statistical superiority of crizanlizumab over placebo in reducing VOCs leading to a healthcare visit over the first year post randomization.

For the primary endpoint, the adjusted annualized rates of VOC leading to healthcare visit over the first year post randomization estimated via negative binomial regression were 2.49, 95% CI: (1.90, 3.26) in the crizanlizumab 5.0 mg/kg arm versus 2.30, 95% CI: (1.75, 3.01) in the placebo arm. Rate ratio was 1.08, 95% CI: (0.76, 1.55) in crizanlizumab 5.0 mg/kg versus placebo.

For the key secondary endpoint, the adjusted annualized rates of VOC leading to healthcare visit and treated at home estimated via negative binomial regression was 4.70, 95% CI: (3.60, 6.14) in crizanlizumab 5.0 mg/kg arm versus 3.87, 95% CI: (3.00, 5.01) in the placebo arm. Rate ratio was 1.21, 95% CI: (0.87, 1.70) in crizanlizumab 5.0 mg/kg versus placebo.

No new safety concerns were identified at this point. However, there were higher rates for grade ≥3 treatment related adverse events for crizanlizumab compared to placebo. Similar results were observed

in the 7.5 mg/kg arm. This dose is currently not authorised.

While further assessment of the study data is ongoing, physicians should consider the individual benefit and risks when making therapeutic decisions regarding the use of crizanlizumab in SCD.

Call for reporting

Please report any suspected adverse reactions associated with the use of crizanlizumab in accordance with the national requirements via the national spontaneous reporting system, to:

Novartis Pharma AG Patient Safety Department - Saudi Arabia -.
Toll Free Number: 8001240078
Phone: +966112658100
Fax: +966112658107
Email: adverse.events@novartis.com
Or by online: https://report.novartis.com/

Saudi Food and Drug Authority National Pharmacovigilance Center
Unified Contact Center: 19999
Email: npc.drug@sfda.gov.sa
Or by online: https://ade.sfda.gov.sa

Company contacts point

Should you need any further information, please do not hesitate to contact us:
Hajer Mohammed AlSaleh, Patient Safety Manager and Risk Management Plan Manager
Novartis Patient Safety - GDD, Riyadh, Saudi Arabia
Phone (+966) 11 265 8100
Email :Hager.alsaleh@novartis.com or adverse.events@novartis.com
Or by online: www.novartis.com

This letter is not intended as a complete description of the benefits and risks related to the use of ADAKVEO ®. Please refer the full SPC (prescribing information).

Sincerely,

Hajer Alsaleh

Country Patient Safety Manager / Novartis QPPV

Alsaleh Hager

Digitally signed by Alsaleh Hager
DN: dc=com, dc=novartis, ou=people, ou=GD, serialNumber=2495984, cn=Alsaleh Hager
Reason: I am approving this document
Date: 2023.03.21 15:07:17 +03'00'

Annexes

[1] SUSTAIN Study to Assess Safety and Impact of SelG1 with or Without Hydroxyurea Therapy in Sickle Cell Disease Patients With Pain Crises (NCT01895361)

[1] STAND Study of Two Doses of Crizanlizumab Versus Placebo in Adolescent and Adult Sickle Cell Disease Patients (NCT03814746)