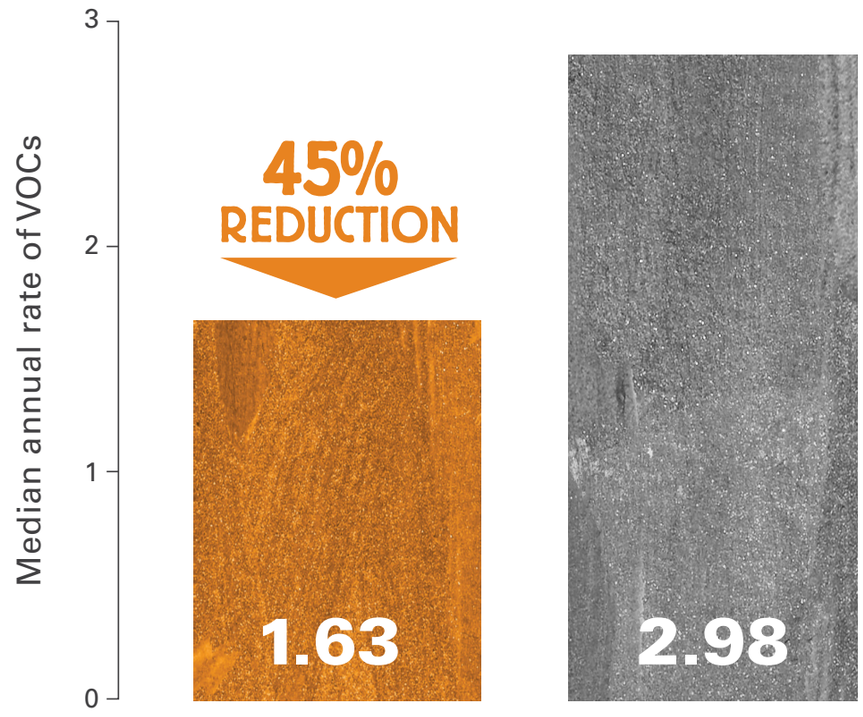
In the 52-week SUSTAIN study

ADAKVEO was proven to reduce the frequency of VOCs[1]

Significant 45% (1.63 vs 2.98) reduction in the median annual rate of VOCs vs placebo[1,2]*

PRIMARY END POINT: MEDIAN ANNUAL RATE OF VOCs (ITT)[1,2†]



The range of VOCs for the ADAKVEO and placebo population was 0 to 24 in each treatment arm[3]

(*P*=.010; HL=-1.01; 95% CI: -2.00, 0.00)

Reduction in the frequency of VOCs was observed regardless of VOC baseline frequency, genotype, or hydroxyurea use[1,2]

In a prespecified, noncomparative subgroup analysis[2,3]

- 32% (2.43 ADAKVEO with HU vs 3.58 placebo with HU) reduction in the median annual rate of VOCs leading to a health care visit was observed for patients already on hydroxyurea who still experienced VOCs in the previous 12 months (HL=-1.01; 95% CI: -2.44, 0.00)
- 50% (1.0 ADAKVEO without HU vs 2.0 placebo without HU) reduction in the median annual rate of VOCs with ADAKVEO vs placebo was observed in patients not on hydroxyurea who experienced VOCs in the previous 12 months (HL=-1.02; 95% CI: -2.00, 0.00)

The subgroup analyses should be interpreted with caution because the data are from a prespecified, noncomparative subgroup analysis of the primary end point and are not powered to detect statistical significance or superiority of ADAKVEO over placebo.[3]

In a prespecified analysis of the per-protocol population[2,3]

- A 52% reduction in VOCs was observed with ADAKVEO® (crizanlizumab-tmca) vs placebo (1.04 vs 2.18; HL=-1.02; 95% CI: -2.00, -0.03)

Per-protocol population is a subset of the ITT patient population who received at least 12 of the 14 planned doses of ADAKVEO (n=40) or placebo (n=41), completed a visit at least 14 days after final dose of study drug, and had no major protocol violations. The per-protocol population was analyzed according to the randomized treatment arm and not powered to show statistical significance.[2]

VOC, vaso-occlusive crisis; ITT, intent to treat; HL, Hodges-Lehmann; CI, confidence interval; SCD, sickle cell disease; ER, emergency room.

*Annual rate of VOCs leading to a health care visit (ER, clinic, hospital, or local physician visit).[1,4]

†The efficacy of ADAKVEO was evaluated based on the annual rate of VOCs in patients (16 to 63 years of age) with SCD in a pivotal, phase 2, 52-week, randomized, multicenter, placebo-controlled, double-blind study. The study included 198 patients evaluated at 60 study centers, the majority of which were located in the United States (51 centers with 151 study patients). Other study sites included: 8 in Brazil (n=40); 1 in Jamaica (n=7). All efficacy analyses were conducted using the ITT population, which included all patients randomized to ADAKVEO 5 mg/kg (n=67) or placebo (n=65). Patients were stratified by hydroxyurea use (Y/N) and number of VOCs in the previous 12 months (2 to 4, 5 to 10).

INDICATION

ADAKVEO® (crizanlizumab-tmca) is indicated to reduce the frequency of vaso-occlusive crises (VOCs) in adults and pediatric patients, aged 16 years and older, with sickle cell disease.

IMPORTANT SAFETY INFORMATION

Infusion-Related Reactions

In the SUSTAIN clinical trial, infusion-related reactions (defined as occurring within 24 hours of infusion) were observed in 2 (3%) patients treated with ADAKVEO 5 mg/kg. Monitor patients for signs and symptoms of infusion-related reactions, which may include fever, chills, nausea, vomiting, fatigue, dizziness, pruritus, urticaria, sweating, or shortness of breath or wheezing. Discontinue ADAKVEO infusion for severe reactions and institute appropriate medical care.

Laboratory Test Interference: Platelet Counts

Interference with automated platelet counts (platelet clumping) has been observed following administration of ADAKVEO, in particular, when blood samples were collected in tubes containing EDTA.

Run blood samples within 4 hours of blood collection or collect blood samples in tubes containing citrate. When needed, estimate platelet count via peripheral blood smear.

Pregnancy

Based on animal data ADAKVEO has the potential to cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. ADAKVEO should only be used during pregnancy if the expected benefit to the patient justifies the potential risk to the fetus.

Most Common Adverse Reactions

The most frequently reported adverse reactions (≥10%) in patients treated with ADAKVEO were nausea (18%), arthralgia (18%), back pain (15%), and pyrexia (11%).

Other Clinically Important Adverse Reactions

Clinically relevant adverse reactions (all grades) that were reported in <10% of patients treated with ADAKVEO included: oropharyngeal pain, abdominal pain (abdominal pain, upper abdominal pain, lower abdominal pain, abdominal discomfort, and abdominal tenderness), diarrhea, vomiting, pruritus (pruritus and vulvovaginal pruritus), musculoskeletal chest pain, myalgia, infusion-site reaction (infusion-site extravasation, infusion-site pain, and infusion-site swelling), and infusion-related reaction.

Please see a representative at this booth for full Prescribing Information.

References: 1. Adakveo [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corp; 2019. **2.** Ataga KI, Kutlar A, Kanter J, et al. Crizanlizumab for the prevention of pain crises in sickle cell disease. *N Engl J Med*. 2017;376(5):429-439. **3.** Data on file. Study NCT01895361. Novartis Pharmaceuticals Corp; 2016. **4.** Data on file. Novartis Pharmaceuticals Corp; July 2013.

NOVARTIS

ADAKVEO-HCP.com

ADAKVEO® crizanlizumab-tmca FOR IV INFUSION • 10 mg/mL

Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936-1080

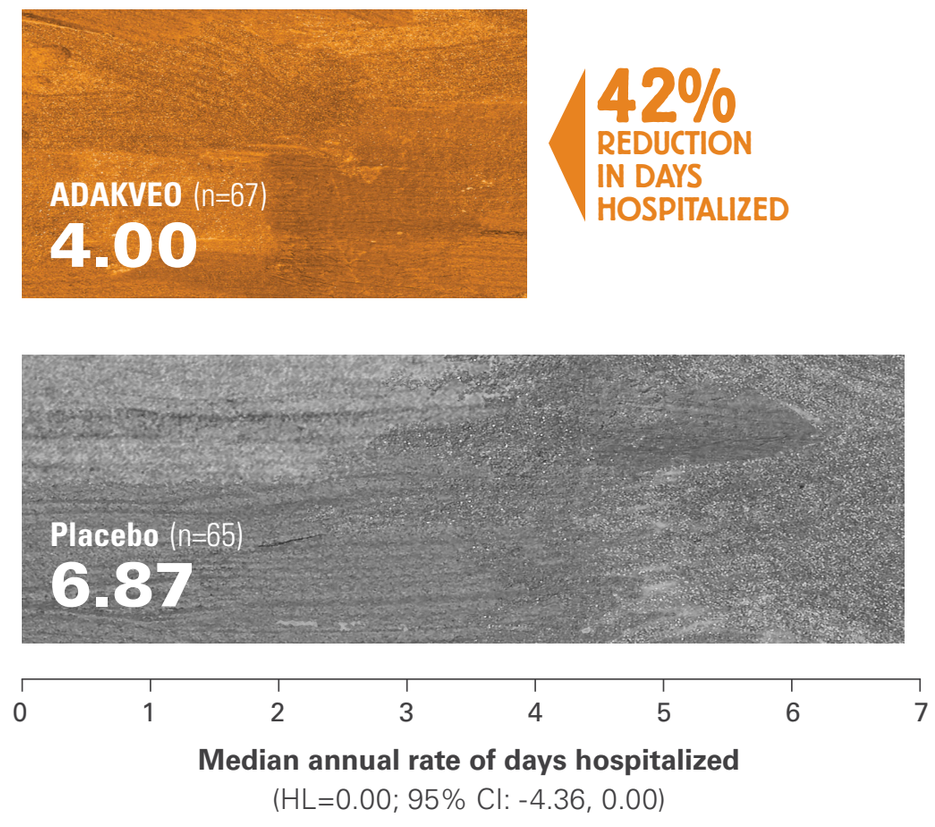
© 2020 Novartis

Key secondary end point

Patients treated with ADAKVEO were hospitalized for fewer days[1]

42% (4.00 vs 6.87) reduction with ADAKVEO® (crizanlizumab-tmca) in the median annual rate of days hospitalized vs placebo[1,2]*

KEY SECONDARY END POINT: MEDIAN ANNUAL RATE OF DAYS HOSPITALIZED[1,3]



42% REDUCTION IN DAYS HOSPITALIZED

The key secondary end point in the SUSTAIN study was defined as the annual rate of days a patient was hospitalized, including those related to VOCs. The range of days hospitalized for the ADAKVEO and placebo population was 0 to 131 days and 0 to 307 days, respectively.[3]

ADAKVEO achieved a clinically meaningful reduction in the median annual rate of days hospitalized[1,2]

>2 times more patients did not experience a VOC with ADAKVEO[1]

36% of patients treated with ADAKVEO did not experience a VOC vs 17% with placebo (24 of 67 vs 11 of 65; OR=2.65; 95% CI: 1.38, 5.09)

- A patient was considered to not have experienced a VOC if the annualized VOC rate was zero, whether or not the patient completed the 12-month treatment period.

VOC, vaso-occlusive crisis; ITT, intent to treat; HL, Hodges-Lehmann; CI, confidence interval.

*The efficacy of ADAKVEO was evaluated based on the annual rate of VOCs in patients (16 to 63 years of age) with SCD in a pivotal, phase 2, 52-week, randomized, multicenter, placebo-controlled, double-blind study. The study included 198 patients evaluated at 60 study centers, the majority of which were located in the United States (51 centers with 151 study patients). Other study sites included: 8 in Brazil (n=40); 1 in Jamaica (n=7). All efficacy analyses were conducted using the ITT population, which included all patients randomized to ADAKVEO 5 mg/kg (n=67) or placebo (n=65). Patients were stratified by hydroxyurea use (Y/N) and number of VOCs in the previous 12 months (2 to 4, 5 to 10).[1-3]

INDICATION

ADAKVEO® (crizanlizumab-tmca) is indicated to reduce the frequency of vaso-occlusive crises (VOCs) in adults and pediatric patients, aged 16 years and older, with sickle cell disease.

IMPORTANT SAFETY INFORMATION

Infusion-Related Reactions

In the SUSTAIN clinical trial, infusion-related reactions (defined as occurring within 24 hours of infusion) were observed in 2 (3%) patients treated with ADAKVEO 5 mg/kg. Monitor patients for signs and symptoms of infusion-related reactions, which may include fever, chills, nausea, vomiting, fatigue, dizziness, pruritus, urticaria, sweating, or shortness of breath or wheezing. Discontinue ADAKVEO infusion for severe reactions and institute appropriate medical care.

Laboratory Test Interference: Platelet Counts

Interference with automated platelet counts (platelet clumping) has been observed following administration of ADAKVEO, in particular, when blood samples were collected in tubes containing EDTA.

Run blood samples within 4 hours of blood collection or collect blood samples in tubes containing citrate. When needed, estimate platelet count via peripheral blood smear.

Pregnancy

Based on animal data ADAKVEO has the potential to cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. ADAKVEO should only be used during pregnancy if the expected benefit to the patient justifies the potential risk to the fetus.

Most Common Adverse Reactions

The most frequently reported adverse reactions (≥10%) in patients treated with ADAKVEO were nausea (18%), arthralgia (18%), back pain (15%), and pyrexia (11%).

Other Clinically Important Adverse Reactions

Clinically relevant adverse reactions (all grades) that were reported in <10% of patients treated with ADAKVEO included: oropharyngeal pain, abdominal pain (abdominal pain, upper abdominal pain, lower abdominal pain, abdominal discomfort, and abdominal tenderness), diarrhea, vomiting, pruritus (pruritus and vulvovaginal pruritus), musculoskeletal chest pain, myalgia, infusion-site reaction (infusion-site extravasation, infusion-site pain, and infusion-site swelling), and infusion-related reaction.

Please see a representative at this booth for full Prescribing Information.

References: 1. Adakveo [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corp; 2019. **2.** Ataga KI, Kutlar A, Kanter J, et al. Crizanlizumab for the prevention of pain crises in sickle cell disease. *N Engl J Med*. 2017;376(5):429-439. **3.** Data on file. Study NCT01895361. Novartis Pharmaceuticals Corp; 2016. **4.** Data on file. Novartis Pharmaceuticals Corp; February 2020.

NOVARTIS

ADAKVEO-HCP.com

ADAKVEO® crizanlizumab-tmca FOR IV INFUSION • 10 mg/mL

Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936-1080

© 2020 Novartis

For your patients with **SICKLE CELL DISEASE**

The Power of VOC Protection



PROTECTION

- Significant 45% (1.63 vs 2.98) reduction with ADAKVEO® (crizanlizumab-tmca) in the median annual rate of VOCs vs placebo* (*P*=.010; HL=-1.01; 95% CI: -2.00, 0.00)[1,2]
- Clinically meaningful reduction in the frequency of VOCs was observed regardless of VOC baseline frequency, genotype, or hydroxyurea use[1,2†]

IMPACT

- 42% (4.00 vs 6.87) reduction with ADAKVEO in the median annual rate of days hospitalized vs placebo (HL=0.00; 95% CI: -4.36, 0.00)[1,3]
- More than one-third of patients did not experience a VOC with ADAKVEO vs placebo (36% vs 17%; OR=2.65; 95% CI: 1.38, 5.09)[2,3]
- >3 times delay in the median time to first VOC from randomization vs placebo (4.1 vs 1.4 months; HR=0.50; 95% CI: 0.33, 0.74)[1,2]

CONFIDENCE

- The once-monthly IV dosing‡ of ADAKVEO gives you the confidence of knowing your patients are receiving their treatment with each infusion[1]
- ADAKVEO is the first and only FDA-approved, once-monthly treatment to reduce the frequency of VOCs in sickle cell disease[1]

Safety Profile[1]

- In the SUSTAIN clinical trial, infusion-related reactions occurring within 24 hours of infusion were observed in 2 (3%) patients treated with ADAKVEO 5 mg/kg. Monitor patients for signs and symptoms. Discontinue ADAKVEO infusion for severe reactions and manage medically
- Lab interference with automated platelet counts (platelet clumping) has been observed following administration of ADAKVEO when samples were collected in tubes containing ethylenediaminetetraacetic acid (EDTA). Run test as soon as possible or use citrate tubes
- The most common adverse reactions (≥10%) were nausea, arthralgia, back pain, and pyrexia

ADAKVEO is the first and only FDA-approved, once-monthly‡ treatment to reduce the frequency of VOCs in sickle cell disease[1]

VOC, vaso-occlusive crisis; HL, Hodges-Lehmann; CI, confidence interval; FDA, US Food and Drug Administration; ER, emergency room; SCD, sickle cell disease; ITT, intent to treat; IV, intravenous.

*Annual rate of VOCs leading to a health care visit (ER, clinic, hospital, or local physician visit).[1,4]

†The efficacy of ADAKVEO was evaluated based on the annual rate of VOCs in patients (16 to 63 years of age) with SCD in a pivotal, phase 2, 52-week, randomized, multicenter, placebo-controlled, double-blind study. The study included 198 patients evaluated at 60 study centers, the majority of which were located in the United States (51 centers with 151 study patients). Other study sites included: 8 in Brazil (n=40); 1 in Jamaica (n=7). All efficacy analyses were conducted using the ITT population, which included all patients randomized to ADAKVEO 5 mg/kg (n=67) or placebo (n=65). Patients were stratified by HU use (Y/N) and number of VOCs in the previous 12 months (2 to 4, 5 to 10).[1,3]

‡ADAKVEO 5 mg/kg is administered by IV infusion over 30 minutes at Weeks 0 and 2, then every 4 weeks.[1]

INDICATION

ADAKVEO® (crizanlizumab-tmca) is indicated to reduce the frequency of vaso-occlusive crises (VOCs) in adults and pediatric patients, aged 16 years and older, with sickle cell disease.

IMPORTANT SAFETY INFORMATION

Infusion-Related Reactions

In the SUSTAIN clinical trial, infusion-related reactions (defined as occurring within 24 hours of infusion) were observed in 2 (3%) patients treated with ADAKVEO 5 mg/kg. Monitor patients for signs and symptoms of infusion-related reactions, which may include fever, chills, nausea, vomiting, fatigue, dizziness, pruritus, urticaria, sweating, or shortness of breath or wheezing. Discontinue ADAKVEO infusion for severe reactions and institute appropriate medical care.

Laboratory Test Interference: Platelet Counts

Interference with automated platelet counts (platelet clumping) has been observed following administration of ADAKVEO, in particular, when blood samples were collected in tubes containing EDTA.

Run blood samples within 4 hours of blood collection or collect blood samples in tubes containing citrate. When needed, estimate platelet count via peripheral blood smear.

Pregnancy

Based on animal data ADAKVEO has the potential to cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. ADAKVEO should only be used during pregnancy if the expected benefit to the patient justifies the potential risk to the fetus.

Most Common Adverse Reactions

The most frequently reported adverse reactions (≥10%) in patients treated with ADAKVEO were nausea (18%), arthralgia (18%), back pain (15%), and pyrexia (11%).

Other Clinically Important Adverse Reactions

Clinically relevant adverse reactions (all grades) that were reported in <10% of patients treated with ADAKVEO included: oropharyngeal pain, abdominal pain (abdominal pain, upper abdominal pain, lower abdominal pain, abdominal discomfort, and abdominal tenderness), diarrhea, vomiting, pruritus (pruritus and vulvovaginal pruritus), musculoskeletal chest pain, myalgia, infusion-site reaction (infusion-site extravasation, infusion-site pain, and infusion-site swelling), and infusion-related reaction.

Please see a representative at this booth for full Prescribing Information.

References: 1. Adakveo [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corp; 2019. **2.** Ataga KI, Kutlar A, Kanter J, et al. Crizanlizumab for the prevention of pain crises in sickle cell disease. *N Engl J Med*. 2017;376(5):429-439. **3.** Data on file. Study NCT01895361. Novartis Pharmaceuticals Corp; 2016. **4.** Data on file. Novartis Pharmaceuticals Corp; July 2013.

NOVARTIS

ADAKVEO-HCP.com

ADAKVEO® crizanlizumab-tmca FOR IV INFUSION • 10 mg/mL

Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936-1080

© 2020 Novartis

7/20

CZB-1228754

ROUND

L09

Job# HH1094634 HPS Job # TBD

Job Title MED-LED-Congress-Panels-ALL

Client/Product HEM ONC Village

PM Frederick Zaretsky CW

AD Elliot Taub Acct Edit

Last Modified By Luis Aley Date/Time 8/12/2020

HAVAS VILLAGE

ROUND KEY

PRINT O=Content Outline C=Concept/Design Options V=Manuscript L=Layout LR=Layout Release M=Mechanical R=Disk Release PP=Printer's Proof

DIGITAL S=Sitemap P=Content Plan U=User Flows W=Wireframes O=Content Outline C=Concept/Design Options V=Manuscript L=Layout D=Development/Staging Link Z=Video

STAFF	REVIEW STAMP	COMMENTS
Account		
Account		
Medical		
Copy		
Copy Creative Lead		
Art		
Art Creative Lead		
Digital Creative Supvsr		
Editorial		
Editorial #2		
Production		
Strategy/ Content Strategist		
UX		
New Media/Art Buyer		

Check Next Steps to Complete:

☐ Initial Cold Read ☐ FC ☐ Check Changes vs _____ ☐ Full Edit

☐ Final Cold Read ☐ Supplemental FC ☐ Proof vs _____

☐ Careful Slug ☐ Consistency Review ☐ **Med/Legal Submission, NO OTHER CHANGES CAN BE MADE**

NOTES/INSTRUCTIONS

smb://us-nyc-srv518.globalservs.com/Oncology Village/Benign Hematology/SEG101 US-SEUS/HH1094634-SEUS-MED LED Congress Panels/Design/HH1094634-MED-LED-Congress-Panels-ALL_L03 Folder