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יוני 2024

SARCLISA

CONCENTRATE FOR SOLUTION FOR INFUSION

ISATUXIMAB 20 MG / 1 ML :חומר פעיל

התוויות התכשיר:

- in combination with pomalidomide and dexamethasone, for the treatment of adult patients with multiple myeloma (MM) who have received at least two prior therapies including lenalidomide and a proteasome inhibitor (PI).

- in combination with carfilzomib and dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least one prior therapy.

חברת סאנופי מבקשת להודיע על עדכון העלונים לצרכן ולרופא.

העדכונים העיקריים הינם:

בעלון לרופא:

4.4. Special warnings and precautions for use

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Second primary malignancies

In ICARIA-MM, second primary malignancies (SPMs) were reported at a median follow-up time of 52.44 months in 10 patients (6.6%) treated with Isa-Pd and in 3 patients (2%) treated with Pd. SPM were skin cancer in 6 patients treated with Isa-Pd and in 3 patients treated with Pd, solid tumours other than skin cancer in 3 patients treated with Isa-Pd (one patient also had a skin cancer), and haematological malignancy (myelodysplastic syndrome) in 1 patient treated with Isa-Pd (see section 4.8). Patients continued treatment after resection of the new malignancy, except two patients treated with Isa-Pd. One patient developed metastatic melanoma and the other developed myelodysplastic syndrome. ~~The overall benefit of Isa-Pd remains favourable (see section 5.1). In ongoing~~ In IKEMA study, at a median follow-up time of ~~20.73~~56.61 months, SPMs were reported in 18 patients (10.2%) treated with Isa-Kd and in 10 patients (8.2%) treated with Kd. SPMs were skin cancers in 13 patients (7.3%) treated with Isa-Kd and in ~~6 patients (4.9%) treated with Kd. SPMs were skin cancers in 9 patients (5.1%) treated with Isa-Kd and in 3~~ 4 patients (~~2.5~~3.3%) treated with Kd, ~~and~~ were solid tumours other than skin cancer in ~~5~~ 7 patients (~~2.8~~4.0%) treated with Isa-Kd and in 6 patients (4.9%) treated with Kd, and ~~in 4 patients (3.3%) treated with Kd. One~~ heamatological malignancy (acute myeloid

leukaemia) in 1 patient (0.8%) in the Kd group. For 1 patient (0.6%) in the Isa-Kd group, the aetiology of the SPM was unknown. Two patients (1.1%) in the Isa-Kd group and one patient (0.8%) in the Kd group had both skin cancer and solid tumours other than skin cancer (see section 4.8). Patients with skin cancer continued treatment after resection of the skin cancer. Solid tumours other than skin cancer were diagnosed within 3 months after treatment initiation in 3 patients (1.7%) treated with Isa-Kd and in 2 patients (1.6%) treated with Kd. The overall incidence of SPMs in all the SARCLISA-exposed patients is 4.~~1~~3%. Physicians should carefully evaluate patients before and during treatment as per IMWG guidelines for occurrence of SPM and initiate treatment as indicated.

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Interference with serological testing (indirect antiglobulin test)

Isatuximab binds to CD38 on red blood cells (RBCs) and may result in a false positive indirect antiglobulin test (indirect Coombs test). This interference with the indirect Coombs test may persist for at least 6 months after the last infusion of SARCLISA. To avoid potential problems with RBC transfusion, patients being treated with SARCLISA should have blood type and screen tests performed prior to the first infusion. Phenotyping may be considered prior to starting SARCLISA treatment as per local practice.
If treatment with SARCLISA has already started, the blood bank should be informed. Patients should be monitored for theoretical risk of haemolysis. If an emergency transfusion is required,
non- cross- matched ABO/Rh-compatible RBCs can be given as per local blood bank practices (see section 4.5). ~~There is currently no available information with regards to how long the interference with the indirect Coombs test may persist after the last infusion of SARCLISA. Based on the half-life of isatuximab, it is anticipated that isatuximab mediated positive indirect Coombs test may persist for approximately 6 months after the last infusion.~~

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4.8. Undesirable effects

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The adverse reactions were reported ~~from the 152 patients who received Isa-Pd with a median duration of exposure of 41 weeks~~ in clinical trials ~~ICARIA-MM study~~ (see section 5.1) and post-market settings.

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Table 3[a]: Adverse reactions reported in patients with multiple myeloma treated with isatuximabin combination with pomalidomide and low-dose dexamethasone (ICARIA-MM)[b]

System Organ Class Preferred Term	Adverse reaction	Frequency	Incidence (%) (N=152)	
			Any Grade	Grade ≥3
Infections and infestations	Pneumonia [c,d,a,b]	Very common	34.8%47 (30.9)	27.9%40 (26.3)
	Upper respiratory tractinfection*	Very common	43 (28.3)40.2%	5 (3.3)%
	Bronchitis*	Very common	36 (23.7)20.9%	5 (3.3)7%
	Herpes zoster	Common	2.5%—7 (4.6)	1 (0.7)4%
Neoplasms benign, malignant and unspecified (incl cystsand polyps)[e,c]	Skin cancer	Common	6 (3.9)4.9%	4 (2.6) 1.6%
	Solid tumour (non-skin cancer)	Common	3 (2.0) 2.9%	2 (1.3) 1.6%
	Haematology malignancy	Uncommon	1 (0.7) 0.4%	1 (0.7)0.4%
Blood and lymphatic system disorders	Neutropenia[f]	Very common	71 (46.7)52.5%	70 (46.1)51.6 %
	Thrombocytopenia	Very common	12.7%	11.9%
	Febrile neutropenia	CVery common	18 (11.8)7.4%	18 (11.8)7.4%
	Anaemia	Common	6.1%	4.5%
	Lymphopenia [d]	Not known	-----	-----
Immune system disorders	Anaphylactic reaction[g]	Uncommon	5 (0.3%)	5 (0.3%)
Metabolism and nutrition disorders	Decreased appetite*	CommonVery common	—15	2

			(9.9)11.5%	(1.3)1.2%
Cardiac disorders	Atrial fibrillation	Common	7 (4.6)5.7%	3 (2.0)2.5%
Respiratory, thoracic and mediastinal disorders	Dyspnoea*	Very common	23 (15.1)25.8%	6 (3.9)5.7%
Gastrointestinal disorders	Diarrhoea*	Very common	39 (25.7)34.0%	3 (2.0)2.5%
	Nausea*	Very common	23 (15.1)22.1%	0%
	Vomiting*	Very common	18 (11.8)14.8%	2 (1.3)0.8%
Investigations	Weight decreased*	Common	10 (6.6)4.9%	0%
Injury, poisoning and procedural complications	Infusion reaction [b]	Very common	58 (38.2)39.3%	4 (2.6)2.0%

[a] Only TEAEs are reported in Table 3. The haematology laboratory values are reported in Table 5.

[b] Cut-off date of 11 Oct 2018. Median follow-up time=11.60 months.

[e-a] The term pneumonia is a grouping of the following terms: atypical pneumonia, bronchopulmonary aspergillosis, pneumonia, pneumonia haemophilus, pneumonia influenzainfluenzal, pneumonia pneumococcal, pneumoniastreptococcal, pneumonia viral, , pneumonia bacterial, haemophilus infection, lung infection, pneumonia fungal and pneumocystis jirovecii pneumonia.

[d-b] See "Description of selected adverse reactions".

[e] Cut-off date of 14 Mar 2022. Median follow-up time=52.44 months. [c] Based on second primary malignancies reported during study treatment period and during post-treatment period.

[f] Haematology laboratory values were recorded as TEAEs only if they led to treatment discontinuation and/ordose modification and/or fulfilled a serious criterion and/or were defined as an AESI.

[g-d] Based on post-marketingmultiple myeloma clinical trials.

* No grade 4

The adverse reactions were reported from the 177 patients who received Isa-Kd with a median duration of exposure of 80.0 weeks in IKEMA study (see section 5.1).

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Table 4[a]: Adverse reactions reported in patients with multiple myeloma treated with isatuximab in combination with carfilzomib and dexamethasone[a]~~dexamethasone (IKEMA)~~

System Organ Class Preferred Term	Adverse reaction	Frequency	Incidence ~~(%)~~ (N=177)	
			Any Grade	Grade ≥3
Infections and infestations	Pneumonia[b c]	Very common	28.8%	20.9%
	Upper respiratory tract infection*	Very common	36.2%	3.4%
	Bronchitis*	Very common	22.6%	2.3%
	Herpes zoster	Common	2.3%	0.6%
Vascular disorders	Hypertension*	Very common	36.7%	20.3%
Neoplasms benign, malignant and unspecified (incl cysts and polyps)[d]	Skin cancers*	Common	~~5.1~~7.3%	~~0.6~~1.7%
	Solid tumours ~~other than~~(-non-skin cancers)	Common	~~3.4~~4.0%	~~1.7~~3.4%
Blood and lymphatic system disorders	Anaemia	Common	5.1%	4.5%
	Neutropenia[d]	Common	4.5%	4.0%
	Thrombocytopenia	Common	2.8%	2.3%
	Lymphopenia[e]	Not known	-----	-----
Immune system disorders	Anaphylactic ~~reaction~~[e]reaction[g]	Uncommon	5 (0.3%)	5 (0.3%)
Respiratory, thoracic and mediastinal disorders	Dyspnoea*	Very common	27.7%	5.1%
	Cough*	Very common	19.8%	0%
Gastrointestinal disorders	Diarrhoea*	Very common	36.2%	2.8%
	Vomiting*	Very common	15.3%	1.1%

General disorders and administration site conditions	Fatigue*	Very common	28.2%	3.4%
Injury, poisoning and procedural complications	Infusion reaction[c]*	Very common	45.8%	0.6%

[a] Cut-off date of 07-Feb-2020. Median follow-up time=20.73 months.
~~[a] Only TEAEs are reported in Table 4. The haematology laboratory values are reported in Table 6.~~
[b] The term pneumonia is a grouping of the following terms: atypical pneumonia, pneumocystis jirovecii pneumonia, pneumonia, pneumonia influenza~~influenzal~~, pneumonia legionella, pneumonia streptococcal, pneumonia viral, and pulmonary sepsis.
[c] See "Description of selected adverse reactions".
~~[d] Haematology laboratory values were recorded as TEAEs only if they led to treatment discontinuation and/or dose modification or fulfilled a serious criterion.~~
[d] Cut-off date of 07-Feb-2023. Median follow-up time=56.61 months. Based on second primary malignancies reported during study treatment period and during post-treatment period.
[e] Based on post-marketing adverse reactions~~multiple myeloma clinical trials~~
~~* No grade 4 or 5~~.

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5.1. Pharmacodynamic properties

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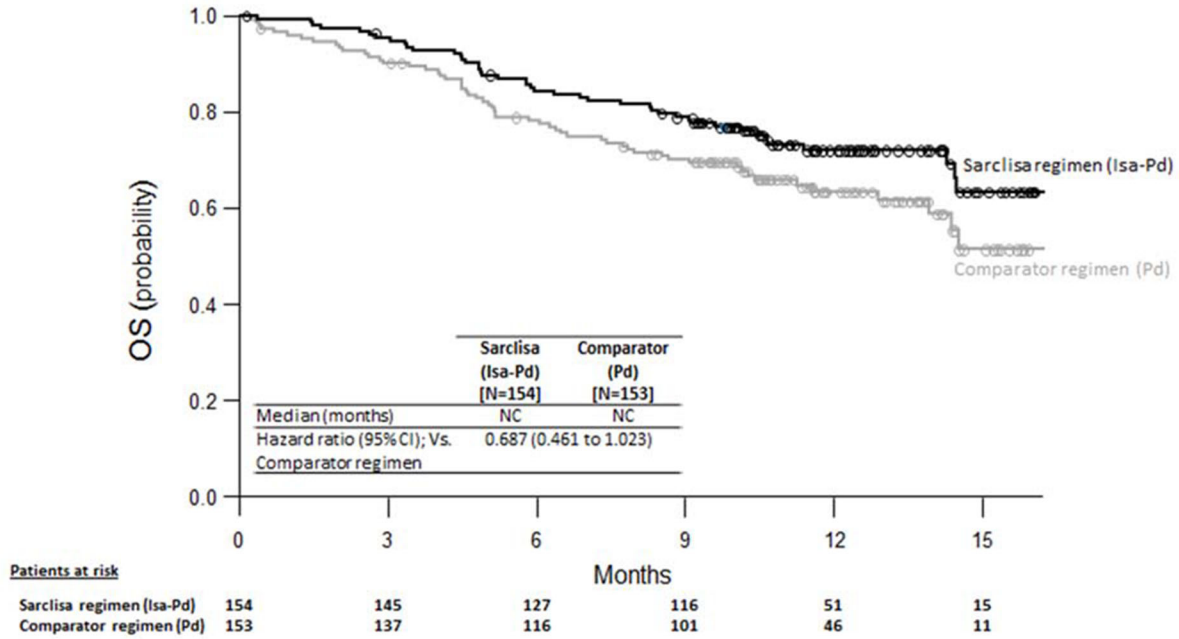

Cutoff date = 07 February 2023~~11 October 2018~~

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Efficacy results are presented in Table 8 and Kaplan-Meier curves for PFS and OS are provided in the Figures 3 and 4:

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The median time to first response was 1.08 months in the Isa-Kd group and 1.12 months in the Kd group. ~~With a~~The median ~~follow-up~~ time to next anti-myeloma treatment was 43.99~~of 20.73~~ months~~, 17.3% patients~~ in the Isa-Kd ~~arm~~ group and 25.00 months in the Kd group (HR=0.583; 95% CI: 0.429 to 0.792).

~~20.3% patients in the Kd arm had died.~~

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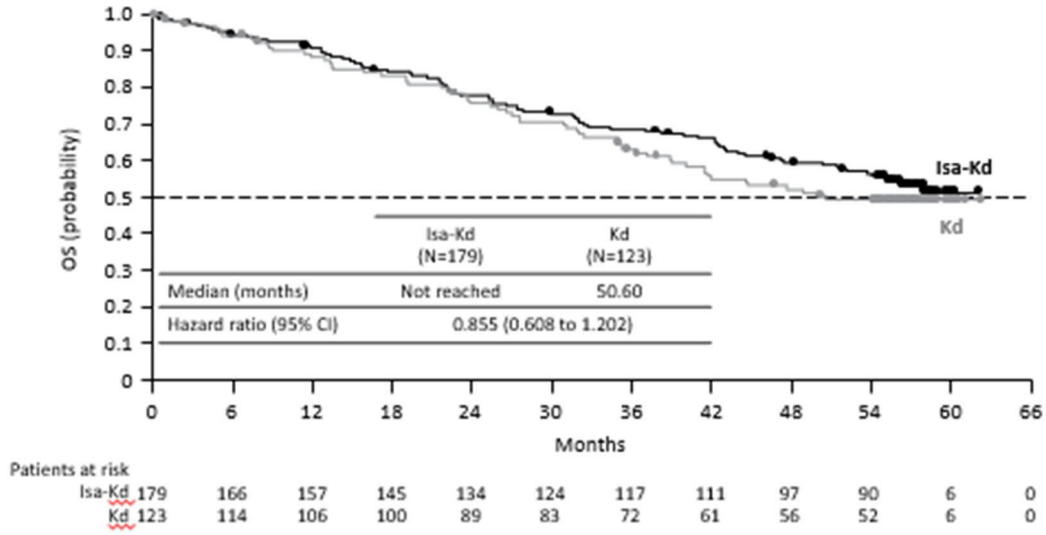
Figure 4: Kaplan-Meier Curves of OS – ITT population – IKEMA



Cut-off date = 07 February 2023

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At a median follow-up time of 56.61 months, median overall survival was not reached in the Isa-Kd group (95% CI: 52.172 to NR) and was 50.60 months in Kd group (95% CI: 38.932 to NR) (HR=0.855; 95% CI: 0.608 to 1.202).

בעלון לצרכן:

2. לפני השימוש בתרופה

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עירוי דם

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אמור לאדם שמבצע את בדיקת הדם שאתה מטופל בסרקליסה, מכיוון שהיא ~~יכולה~~ עשויה להשפיע על התוצאות של בדיקת דם זו למשך לפחות שישה חודשים לאחר נטילת המנה האחרונה של סרקליסה.

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היריון, הנקה ופוריות

התייעצי עם הרופא, האחות או הרוקח שלך לפני לקיחת כל תרופה.

~~הודיעי לרופא שלך אם הנך בהיריון, חושבת שהנך בהיריון, מתכננת היריון או מניקה.~~

היריון

שימוש בסרקליסה אינו מומלץ במהלך ההיריון~~, מכיוון שאין מספיק מידע בנוגע לשימוש בתרופה בנשים בהריון~~. אם את בהיריון, חושבת שאת בהיריון או מתכננת ~~להיות ב~~היריון, שוחחי עם הרופא שלך על השימוש בסרקליסה.

לקבלת מידע על היריון בהקשר של תרופות אחרות הנלקחות עם סרקליסה, אנא עייני בעלונים של תכשירים אלו.

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4. תופעות לוואי

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תופעות לוואי שכיחות מאד (יכולות להופיע אצל~~להשפיע על~~ יותר מ-1 מתוך 10 אנשים):

- ~~מספר נמוך של כדוריות דם אדומות (אנמיה)~~
- מספר נמוך של תאי דם לבנים מסוימים (נויטרופילים ~~או לימפוציטים~~) החשובים במלחמה בזיהום
- .....

תופעות לוואי שכיחות (יכולות להופיע אצל~~להשפיע על~~ עד 1 מתוך 10 אנשים):

- .....
- מספר נמוך של כדוריות דם אדומות (אנמיה)
- .....

תופעות לוואי בשכיחות לא ידועה (לא ניתן להעריך מהנתונים הקיימים):

- מספר נמוך של תאי דם לבנים מסוימים (לימפוציטים) החשובים במלחמה בזיהום

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העלונים המעודכנים נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות וניתן לקבלם מודפסים על ידי פנייה לבעל הרישום - סאנופי ישראל בע"מ, Greenwork Park, מתחם העסקים בקיבוץ יקום, בניין E (קומה 1), 6097600, יקום או בטלפון: 09-8633081.

להלן הקישור לאתר משרד הבריאות: https://israeldrugs.health.gov.il/#!/byDrug

בברכה,
חברת סאנופי ישראל בע"מ