ינואר 2022

Empliciti (elotuzumab) 300 mg & 400mg

אמפליסיטי (אלוטוזומאב) 300 מ"ג ו-400 מ"ג

Powder for concentrate for solution for infusion

רופא/ה ,רוקח/ת יקר/ה,

חברת בריסטול-מאיירס סקוויב (ישראל) בע"מ מבקשת להודיע על עדכון בעלון לרופא של התכשיר אמפליסיטי (elotuzumab) בישראל.

התוויות התכשיר כפי שאושרו על ידי משרד-הבריאות:

Empliciti is indicated in combination with lenalidomide and dexamethasone for the treatment of multiple myeloma in adult patients who have received at least one prior therapy.

Empliciti is indicated in combination with pomalidomide and dexamethasone for the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least two prior therapies, including lenalidomide and a proteasome inhibitor, and have demonstrated disease progression on the last therapy.

הרכב וחוזק:

Elotuzumab	300mg/vial & 400mg/vial

בפירוט שלהלן כלולים העדכונים המהותיים בלבד (טקסט שנוסף מסומן עם קו תחתון, טקסט שהוסר מסומן עם ~~קו אמצעי חוצה~~, תוספת מידע בטיחות (החמרה) מודגשת בצהוב).

למידע מלא על התרופה יש לעיין בעלון לרופא כפי שאושר על ידי משרד-הבריאות.

העלון לרופא נשלח לפרסום במאגר התרופות שבאתר משרד-הבריאות וניתן לקבלו מודפס על ידי פנייה לבעל הרישום בריסטול- מאיירס סקוויב (ישראל) בע"מ.

בכבוד רב,

ילנה גיטלין
מנהלת רגולציה ורוקחת ממונה
בריסטול-מאיירס סקוויב (ישראל)

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עדכונים מהותיים בעלון לרופא:

4. CLINICAL PARTICULARS

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4.4 Special warnings and precautions for use

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Traceability

In order to improve the traceability of biological medicinal products, the name of the administered product should be clearly recorded. It is recommended to record the batch number as well

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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Table 10: CA204125 Progression-Free Survival and Overall Response ~~Efficacy results~~

	Investigator Assessed		IRC Assessed[f]	
	E-Pd N = 60	**Pd N = 57**	**E-Pd N = 60**	**Pd N = 57**
PFS (ITT)				
Hazard Ratio [95% CI]	0.54 [0.34, 0.86]		0.51 [0.32, 0.82]	
Stratified log-rank test p-value[a]	0.0078		0.0043	
Median PFS in months [95% CI]	10.25 [5.59, NE]	4.67 [2.83, 7.16]	10.25 [6.54, NE]	4.70 [2.83, 7.62]
Response				
Overall Response (ORR)[b] n (%) [95% CI]	32 (53.3) [40.0, 66.3]	15 (26.3) [15.5, 39.7]	35 (58.3) [44.9, 70.9]	14 (24.6) [14.1, 37.8]
p-value[c]	0.0029		0.0002	
Complete Response (CR + sCR)[d] n (%)	5 (8.3)[e]	1 (1.8)	0 (0.0)[e]	0 (0.0)
Very Good Partial Response (VGPR) n (%)	7 (11.7)	4 (7.0)	9 (15.0)	5 (8.8)
Partial Response (RR/PR) n (%)	20 (33.3)	10 (17.5)	26 (43.3)	9 (15.8)
Combined Responses (CR+sCR+VGPR) n (%)	12 (20.0)	5 (8.8)	9 (15.0)	5 (8.8)

[a] p-value based on the log-rank test stratified by stage of disease at study entry (International Staging System I-II vs III) and number of prior lines of therapy (2-3 vs ≥ 4) at randomization.

[b] modified International Myeloma Working Group (IMWG) criteria.

[c] p-value based on the Cochran-Mantel-Haenszel chi-square test stratified by stage of disease at study entry (International Staging System I-II vs III) and number of prior lines of therapy (2-3 vs ≥ 4) at randomization.

[d] Complete response (CR) + stringent complete response (sCR).

[e] Complete response rates in Empliciti group may be underestimated due to interference of elotuzumab monoclonal antibody with immunofixation assay and serum protein electrophoresis assay.

[f] IRC assessment was performed post-hoc. NE: non-estimable

Overall survival (OS) was a key secondary study endpoint. ~~The OS data from the exploratory analysis were not mature at the data cut-off (29 November 2018) with a minimum follow up of 18.3 months. A total of 40 (67%) patients were alive in the E-Pd arm and 29 (51%) in the Pd arm. Median OS was not reached for E-Pd treatment group. The hazard ratio and 95% CI were 0.54 (0.30, 0.96).~~ A pre-planned final OS analysis was performed after at least 78 deaths occurred. The minimum follow-up was 45.0 months. The OS results at final analysis reached statistical significance. A significantly longer OS was observed in patients in the E-Pd arm compared to patients in the Pd arm (HR = 0.59; 95% CI: 0.37, 0.93; p-value 0.0217), representing a 41% reduction in the risk of death. Efficacy results are presented in Table 11 and Figure 4.

Table 11: CA204125 Overall Survival Results

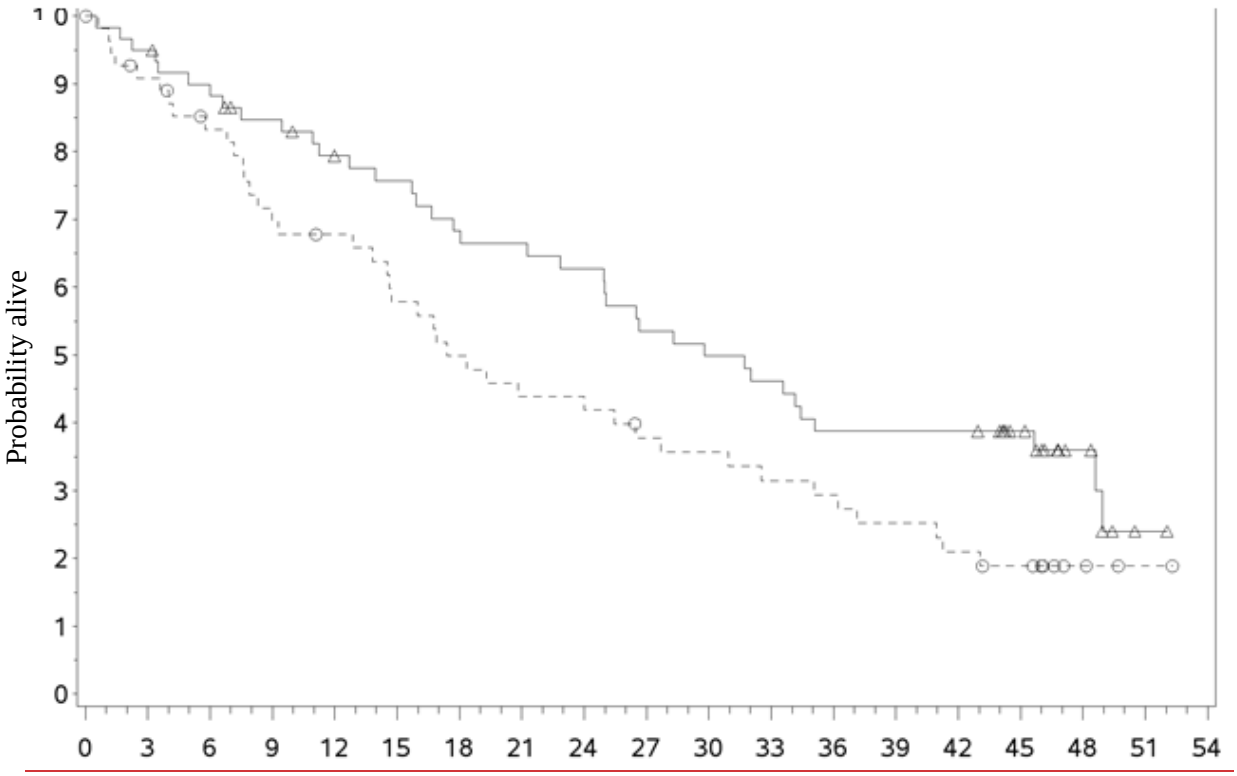
	E-Pd N = 60	Pd N = 57
Overall Survival (OS)**		
Hazard Ratio [95% CI]	0.59 [0.37, 0.93]	
Stratified log-rank test p-value*	0.0217***	
Median OS in months [95% CI]	29.80 [22.87, 45.67]	17.41 [13.83, 27.70]

* p-value based on the log-rank test stratified by stage of disease at study entry (International Staging System I-II vs III) and number of prior lines of therapy (2-3 vs ≥ 4) at randomization

** A pre-specified final analysis for OS was performed based on at least 78 deaths (minimum follow-up time of 45.0 months).

*** The final OS analysis crossed the pre-determined alpha boundary for statistical significance ($p \leq 0.20$) as well as the stringent 0.05 level.

Figure 4: CA204125 Overall Survival



Number of Subjects at Risk

E-Pd	60	57	53	48	43	41	37	36	34	29	27	25	21	21	21	15	7	1	0
Pd	57	49	43	36	34	29	25	22	22	18	17	15	14	12	10	8	3	1	0

—Δ— E-Pd (events: 37/60), median and 95% CI: 29.80 (22.87, 45.67)
- - -O- - - Pd (events: 41/57), median and 95% CI: 17.41 (13.83, 27.70)
E-Pd vs Pd - hazard ratio and 95% CI: 0.59 (0.37, 0.93)
80% CI: 0.59 (0.44, 0.79), p-value: 0.0217

Adjusted alpha level = 0.2.
Symbols represent censored observations.
Stratified by stage of disease at study entry (International Staging System I-II vs III) and number of prior lines of therapy (2-3 vs > = 4) at randomization