פברואר 2020

Empliciti (elotuzumab) 300 mg & 400mg
Powder for concentrate for solution for infusion

רופא/ה ,רוקח/ת יקר/ה,

ברצוננו להודיעך על עדכון בעלון לרופא של התכשיר **אמפליסיטי** (elotuzumab) בישראל.

התוויות התכשיר כפי שאושרו ע"י משה"ב:

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.

בפירוט שלהלן כלולים העדכונים המהותיים בלבד (טקסט שנוסף מסומן בצבע אדום ובקו תחתון,טקסט שהוסר מסומן בצבע אדום ~~ובקו אמצעי~~).

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,
שירן קלאורה,
רוקחת ממונה

689IL2000731-02

עדכונים מהותיים בעלון לרופא:

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5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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Clinical efficacy and safety

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The primary endpoints of this study, progression-free survival (PFS), as assessed by hazard ratio, and overall response rate (ORR) were determined based on assessments made by a blinded Independent Review Committee (IRC). Efficacy results are presented in Table 8 and Figure 1. The median number of treatment cycles was 19 for the Empliciti arm and 14 for the comparator arm.

Overall survival (OS) was a secondary endpoint with the pre-planned final OS analysis to occur after at least 427 deaths.

Table 8: CA204004 Efficacy results

	E-Ld N = 321	Ld N = 325
PFS (ITT)		
Hazard Ratio [97.61% CI]	0.68 [0.55, 0.85]	
Stratified log-rank test p-value[a]	0.0001	
1-Year PFS rate (%) [95% CI]	68 [63, 73]	56 [50, 61]
2-Year PFS rate (%) [95% CI]	39 [34, 45]	26 [21, 31]
3-Year PFS rate[b] (%) [95% CI]	23 [18, 28]	15 [10, 20]
Median PFS in months [95% CI]	18.5 [16.5, 21.4]	14.3 [12.0, 16.0]
Response		
Overall Response (ORR)[c] n (%) [95% CI]	252 (78.5) [73.6, 82.9]	213 (65.5) [60.1, 70.7]
p-value[d]	0.0002	
Complete Response (CR + sCR)e n (%)	14 (4.4)[f]	24 (7.4)
Very Good Partial Response (VGPR) n (%)	91 (28.3)	67 (20.6)
Partial Response (RR/PR) n (%)	147 (45.8)	122 (37.5)
Combined Responses (CR+sCR+VGPR) n (%)	105 (32.7)	91 (28.0)
Overall Survival[g]		
Hazard Ratio [95.4% CI]	0.820.77 [0.680.61, 1.000.97]	
Stratified log-rank test p-value	0.04080.0257[h]	
Median OS in months [95% CI]	48.30 43.7 [40.34, 51.94NE]	39.62 [33.25, 45.27NE]

a p-value based on the log-rank test stratified by B2 microglobulins (<3.5 mg/L versus ≥ 3.5 mg/L), number of prior lines of therapy (1 versus 2 or 3), and prior immunomodulatory therapy (no versus prior thalidomide only versus other).

b A pre-specified analysis for 3-year PFS rate was performed based on a minimum follow-up time of 33 months.

c European Group for Blood and Marrow Transplantation (EBMT) criteria.

d p-value based on the Cochran-Mantel-Haenszel chi-square test stratified by B2 microglobulins (<3.5 mg/L versus ≥ 3.5 mg/L), number of prior lines of therapy (1 versus 2 or 3), and prior immunomodulatory therapy (no versus prior thalidomide only versus other).

e Complete response (CR) + stringent complete response (sCR).

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

g A pre-specified final~~interim~~ analysis for OS was performed based on at least 427 deaths with a minimum follow-up time of 70.6~~35.4~~ months.

h The final~~interim~~ OS analysis met~~did not meet~~ the protocol-specified ~~early stopping~~ boundary for statistical significance~~OS~~ (p ≤ 0.046~~≤ 0.014~~).

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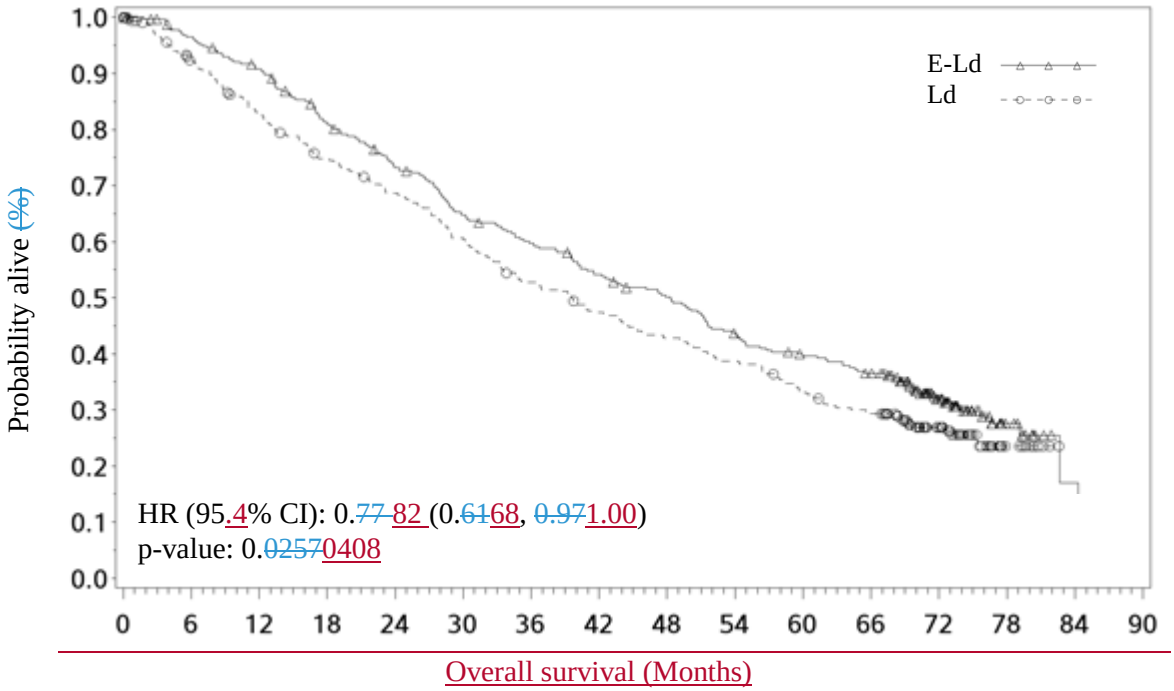
The 1-, 2- ,~~and~~ 3-, 4- and 5 -year rates of overall survival for Empliciti in combination with lenalidomide and dexamethasone treatment were 91%, 73%, ~~and~~ 60%, 50% and 40% respectively, compared with 83%, 69%, ~~and~~ 53%, 43% and 33% respectively, for lenalidomide and dexamethasone treatment (See Figure 2).

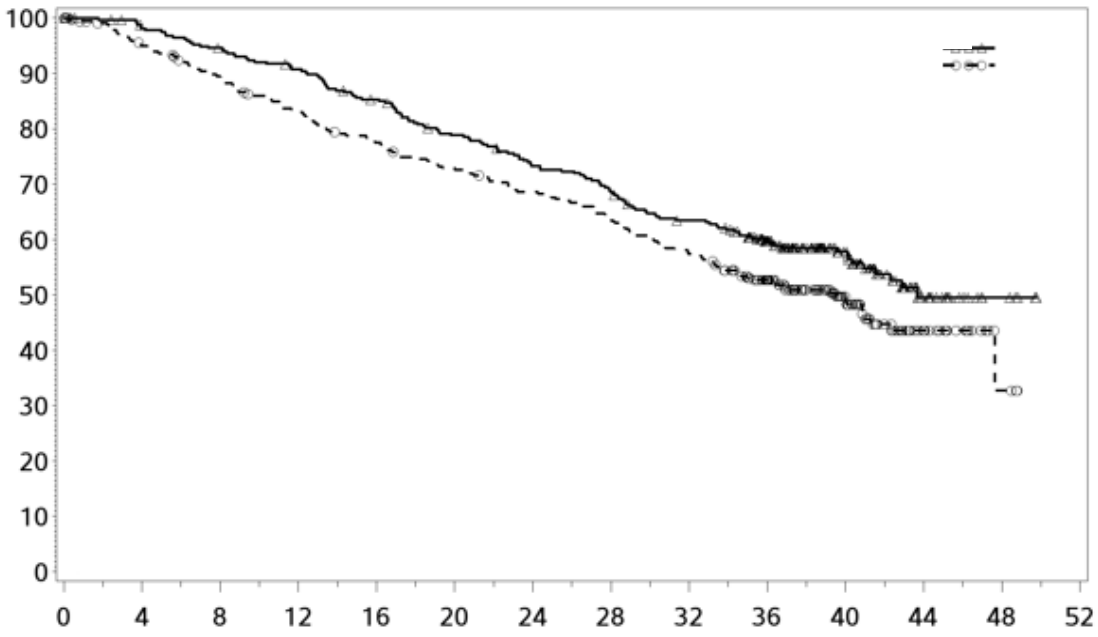
The pre-planned final OS analysis was performed after 212 deaths in the E-Ld arm and 225 deaths in the Ld arm. The minimum follow-up was 70.6 months. A statistically significant advantage in OS was observed in patients in the E-Ld arm compared to patients in the Ld arm. The median OS in the E-Ld arm was 48.30 months compared with 39.62 months in the Ld arm. Patients in the E-Ld arm had an 18% reduction in the risk of death compared with those in the Ld arm (HR = 0.82; 95.4% CI: 0.68, 1.00; p-value = 0.0408). See Table 8 and Figure 2.

Figure 2: CA204004 Overall survival



Number of subjects at risk

E-Ld	321	303	283	250	224	197	181	163	149	129	115	105	57	15	2
Ld	325	287	255	228	208	184	159	142	128	116	98	86	47	9	



Overall survival (Months)

Number of subjects at risk

E-Ld	321	308	296	283	264	242	224	210	191	152	84	23	5
Ld	325	298	278	255	237	222	208	193	174	134	69	22	3