**אוגוסט 2019**

**רופא/ה נכבד/ה**
**רוקח/ת נכבד/ה שלום רב,**

**<u>פרסום עדכון בעלון התכשיר :</u>**
**<u>Imfinzi® 120 mg/2.4 ml solution for infusion</u>**
**<u>Imfinzi® 500 mg/10 ml solution for infusion</u>**

**הרכב:**

Durvalumab 120 mg, 500 mg.

**התוויה:**

**Urothelial Carcinoma**

IMFINZI is indicated for the treatment of patients with PD-L1 high (Tumor cell ≥ 25% or IC ≥ 25%) locally advanced or metastatic urothelial carcinoma who:

- have disease progression during or following platinum-containing chemotherapy.
- have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum containing chemotherapy.

**Non-Small Cell Lung Cancer**

IMFINZI is indicated for the treatment of patients with unresectable Stage III non-small cell lung cancer (NSCLC) whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy.

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חברת אסטרהזניקה ישראל מבקשת להודיע על עדכון עלון בהתאם להוראות משרד הבריאות בתאריך **אוגוסט 2019.**

**העדכון העיקרי בעלון לרופא הוא:**

**14.2 Non-Small Cell Lung Cancer (NSCLC)**

The efficacy of IMFINZI was evaluated in the PACIFIC study (NCT02125461), a multicenter, randomized, double-blind, placebo-controlled study in patients with unresectable Stage III NSCLC who completed at least 2 cycles of concurrent platinum-based chemotherapy and definitive radiation within 42 days prior to initiation of the study drug and had a WHO performance status of 0 or 1. The study excluded patients who had

progressed following concurrent chemoradiation, patients with active or prior documented autoimmune disease within 2 years of initiation of the study or patients with medical conditions that required systemic immunosuppression. Randomization was stratified by sex, age (<65 years vs. ≥ 65 years) and smoking history (smoker vs. non-smoker). Patients were randomized 2:1 to receive IMFINZI 10 mg/kg or placebo intravenously every 2 weeks for up to 12 months or until unacceptable toxicity or confirmed RECIST 1.1-defined progression. Assessment of tumor status was performed every 8 weeks. The major efficacy outcome measures were progression-free survival (PFS) as assessed by a BICR RECIST 1.1 and overall survival (OS). Additional efficacy outcome measures included ORR and DoR assessed by BICR.

A total of 713 patients were randomized: 476 patients to the IMFINZI arm and 237 to the placebo arm. The study population characteristics were: median age of 64 years (range: 23 to 90); 70% male; 69% White and 27% Asian; 16% current smokers, 75% former smokers and 9% never smokers; 51% WHO performance status of 1; 53% with Stage IIIA and 45% were Stage IIIB; 46% with squamous and 54% with non-squamous histology. All patients received definitive radiotherapy as per protocol, of which 92% received a total radiation dose of 54 Gy to 66 Gy; 99% of patients received concomitant platinum-based chemotherapy (55% cisplatin-based, 42% carboplatin-based chemotherapy and 2% switched between cisplatin and carboplatin).

~~The pre-specified interim PFS analysis based on 371 events (81% of total planned events) demonstrated a statistically significant improvement in PFS in patients randomized to IMFINZI compared to placebo. Results are presented in Table 7 and Figure 1. OS data were not mature at the time of the interim PFS analysis.~~

At a pre-specified interim analysis for OS based on 299 events (61% of total planned events), the study demonstrated a statistically significant improvement in OS in patients randomized to IMFINZI compared to placebo. The pre-specified interim analysis of PFS based on 371 events (81% of total planned events) demonstrated a statistically significant improvement in PFS in patients randomized to IMFINZI compared to placebo. Table 7 and Figure 1 summarizes the efficacy results for PACIFIC

**~~Table 7. Efficacy Results for the PACIFIC Study~~**

| Endpoint | IMFINZI (N=476)[1] | Placebo (N=237)[1] |
|---|---|---|
| **Progression-Free Survival (PFS)**[2] | | |
| Number (%) of patients with event | 214 (45%) | 157 (66%) |
| Median in months (95% CI) | 16.8 (13, 18.1) | 5.6 (4.6, 7.8) |
| Hazard Ratio (95% CI)[3,4] | 0.52 (0.42, 0.65) | |
| p-value (log-rank)[3,5] | <0.0001 | |
| **Overall Response Rate (ORR)** | | |
| ORR (95% CI) | 26% (23, 31) | 14% (10, 19) |
| Complete Response | 1% | 0 |
| Partial Response | 25% | 14% |

1 Among the ITT population, 7% in the IMFINZI arm and 10% in the placebo arm had non-measurable disease as assessed by BICR according to RECIST v1.1

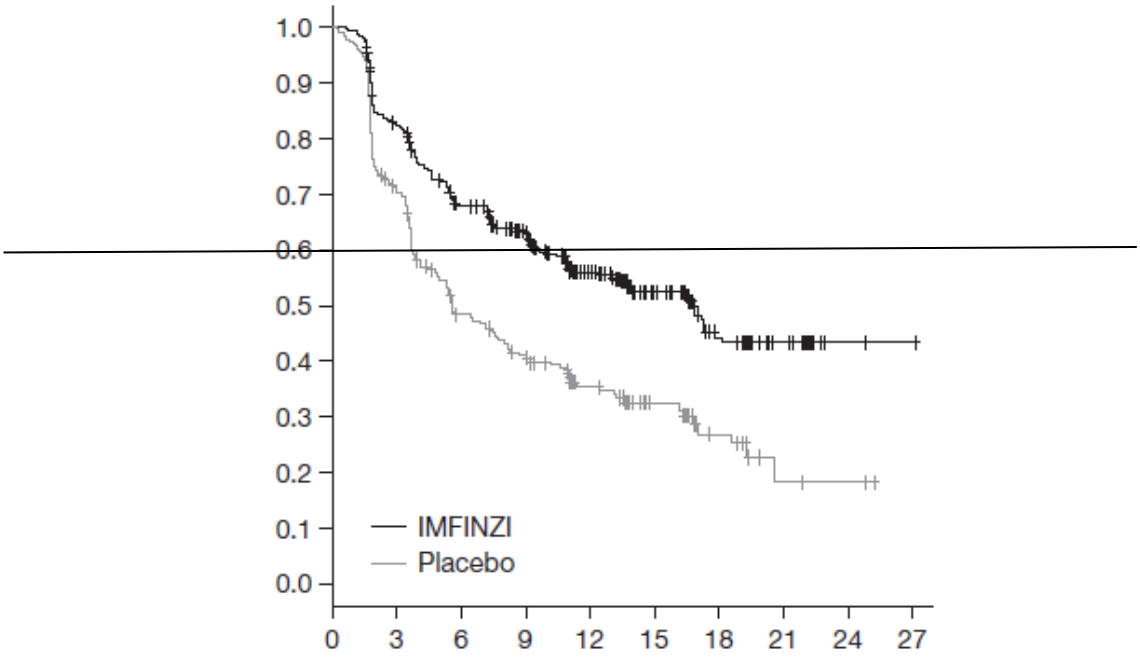
2 Blinded Independent Central Review

3 Stratified by sex, age, and smoking history

4 Pike estimator

5 Compared with allocated α of 0.0104 (Lan DeMets spending function approximating O'Brien Fleming boundary) for interim analysis

**Figure 1 Kaplan-Meier Curves of Progression-Free Survival in the PACIFIC Study**



IMFINZI 476 377 301 264 159 86 44 21 4 1

Placebo 237 163 106 87 52 28 15 4 3 0 Number of patients at risk

**Table 7. Efficacy Results for the PACIFIC Study**

| Endpoint | IMFINZI (N = 476)[1] | Placebo (N = 237)[1] |
|---|---|---|
| **Overall Survival (OS)[2]** | | |
| Number of deaths | 183 (38%) | 116 (49%) |
| Median in months (95% CI) | NR (34.7, NR) | 28.7 (22.9, NR) |
| Hazard Ratio (95% CI)[3] | 0.68 (0.53, 0.87) | |
| p-value[3,4] | 0.0025 | |
| **Progression-Free Survival (PFS)[5,6]** | | |
| Number (%) of patients with event | 214 (45%) | 157 (66%) |
| Median in months (95% CI) | 16.8 (13.0, 18.1) | 5.6 (4.6, 7.8) |
| Hazard Ratio (95% CI)[3,7] | 0.52 (0.42, 0.65) | |
| p-value[3,8] | < 0.0001 | |

[1] Among the ITT population, 7% in the IMFINZI arm and 10% in the placebo arm had non-measurable disease as assessed by BICR according to RECIST v1.1

[2] OS results are based on the interim OS analysis conducted at 299 OS events which occurred 46 months after study initiation

[3] Two-sided p-value based on a log-rank test stratified by sex, age, and smoking history

[4] Compared with allocated α of 0.00274 (Lan DeMets spending function approximating O'Brien Fleming boundary) for interim analysis

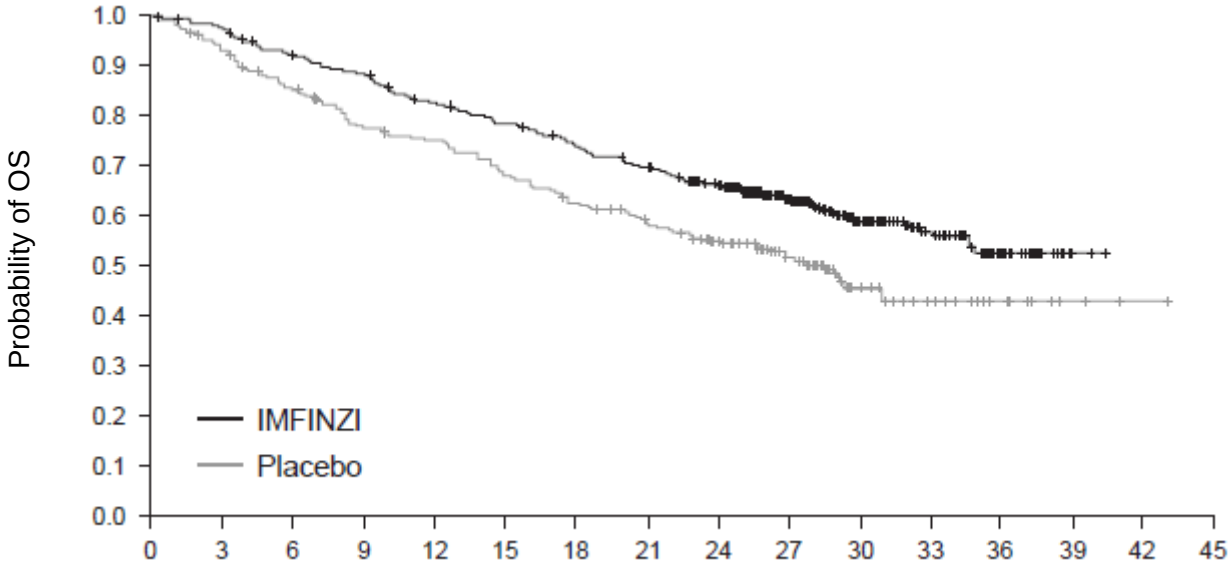
[5] As assessed by BICR RECIST v1.1

[6] PFS results are based on the interim PFS analysis conducted at 371 PFS events which occurred 33 months after study initiation

[7] Pike estimator

[8] Compared with allocated α of 0.011035 (Lan DeMets spending function approximating O'Brien Fleming boundary) for interim analysis

**Figure 1 Kaplan-Meier Curves of Overall Survival in the PACIFIC Study**




| Number of patients at risk | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Month | 0 | 3 | 6 | 9 | 12 | 15 | 18 | 21 | 24 | 27 | 30 | 33 | 36 | 39 | 42 | 45 |
| IMFINZI | 476 | 464 | 431 | 415 | 385 | 364 | 343 | 319 | 274 | 210 | 115 | 57 | 23 | 2 | 0 | 0 |
| Placebo | 237 | 220 | 198 | 178 | 170 | 155 | 141 | 130 | 117 | 78 | 42 | 21 | 9 | 3 | 1 | 0 |

העלונים מפורסמים במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלם מודפסים על ידי פניה לבעל הרישום.

בכבוד רב,

אורה סטוליק
רוקחת ממונה
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