18 לינואר 2021

רופא/ה נכבד/ה
רוקח/ת נכבד/ה שלום רב,

<u>פרסום עדכון בעלון התכשיר :</u>
<u>TAGRISSO 40mg film-coated tablets</u>
<u>TAGRISSO 80mg film-coated tablets</u>

הרכב:

TAGRISSO 40 mg tablets

Each tablet contains osimertinib 40mg (equivalent to 47.7mg of osimertinib mesylate)

TAGRISSO 80 mg tablets

Each tablet contains osimertinib 80mg (equivalent to 95.4mg of osimertinib mesylate)

התוויה:

Tagrisso as monotherapy is indicated for:

- the first-line treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with activating epidermal growth factor receptor (EGFR) mutations.
- the treatment of adult patients with locally advanced or metastatic EGFR T790M mutation-positive NSCLC.

חברת אסטרהזניקה ישראל מבקשת להודיע על עדכון עלון בהתאם להוראות משרד הבריאות בתאריך **ינואר 2021.**

העדכון העיקרי בעלון לרופא הוא:

4.8 Undesirable effects

Table 2. Adverse reactions reported in FLAURA and AURA studies[a]

MedDRA SOC	MedDRA term	CIOMS descriptor/ overall frequency (allCTCAE grades) [b]	Frequency of CTCAE grade 3 or higher
Respiratory, thoracic and mediastinal disorders	Interstitial lung disease[c]	Common (3.9%)[d]	1.5%
Gastrointestinal disorders	Diarrhoea	Very common (49%)	1.2%
	Stomatitis	Very common (20%)	0.2%
Eye disorders	Keratitis[e]	Uncommon (0.7%)	0.1%
Skin and subcutaneous tissue disorders	Rash[f]	Very common (47%)	0.9%
	Dry skin[g]	Very common (33%)	0.1%
	Paronychia[h]	Very common (31%)	0.3%
	Pruritus[i]	Very common (17%)	0.1%
	Erythema multiforme[j]	Uncommon (0.35%)	0%
	Stevens-Johnson syndrome[k]	Rare (0.02%)	
	Cutaneous Vasculitis[l]	Uncommon (0.26%)	

5.1 Pharmacodynamic properties

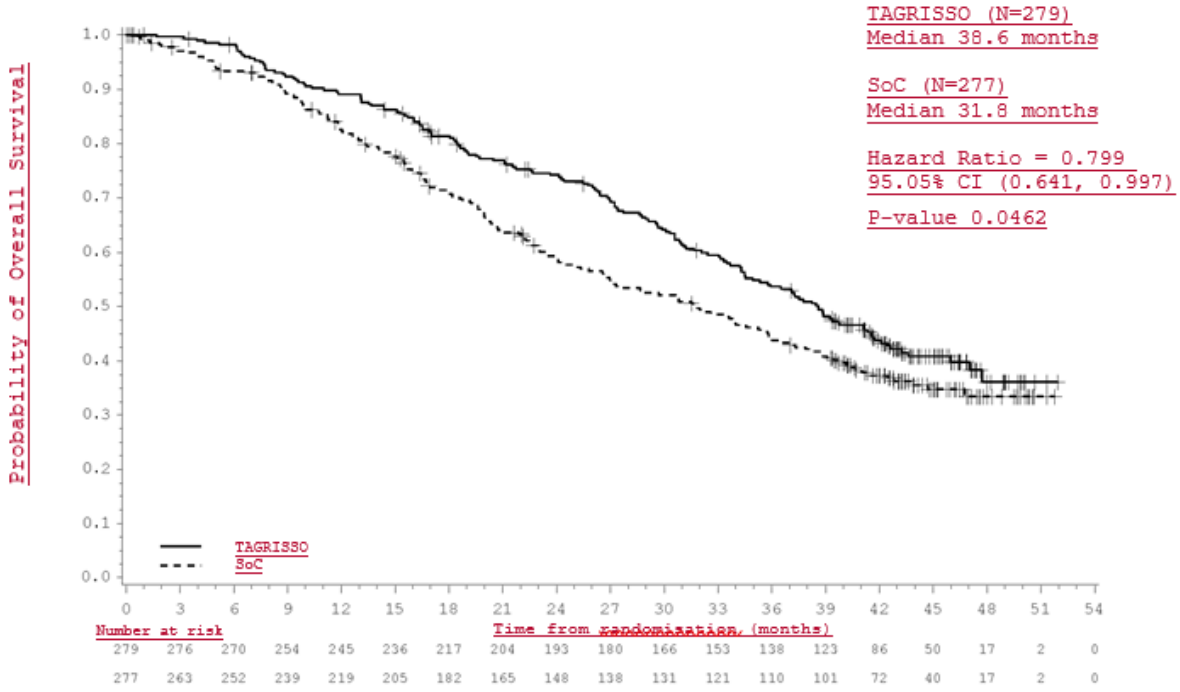
Clinical efficacy and safety

Efficacy results from FLAURA by investigator assessment are summarised in Table 3, and the Kaplan-Meier curve for PFS is shown in Figure 1. ~~At the time of the interim~~, ~~-~~the final analysis of overall survival (OS, 58~~25~~% maturity), demonstrated a statistically significant improvement with an HR of 0.799~~63 favoured TAGRISSO~~ (95.05% CI: 0.641~~45~~, 0.~~88; P = 0.0068), which did not reach formal statistical significance~~ 997) and a clinically meaningful longer median survival time in patients randomized to TAGRISSO compared to EGFR TKI comparator (Table 3 and Figure 2). A greater proportion of patients treated with TAGRISSO were alive at 12 ~~months and~~, 18, 24 and 36 months (89%, 81%, 74% and 54~~83~~%, respectively) compared to patients treated with EGFR TKI comparator (83~~% and~~ %, 71%, 59% and 44% respectively). Analysis of post-progression end–points demonstrated that the PFS benefit was preserved through subsequent lines of therapy.

Table 3. Efficacy results from FLAURA by investigator assessment

Efficacy Parameter	TAGRISSO (N=279)	EGFR TKI comparator (gefitinib or erlotinib) (N=277)
Progression-Free Survival		
Number of Events (62% maturity)	136 (49)	206 (74)
Median, Months (95% CI)	18.9 (15.2, 21.4)	10.2 (9.6, 11.1)
HR (95% CI) ; P-value	0.46 (0.37, 0.57); P < 0.0001	
Overall Survival		
Number of deaths, (5825% maturity)	~~58 (21)~~ 155 (56)	~~83 (30)~~ 166 (60)
Median OS in months (95% CI)	~~NC~~ 38.6 (34.5, 41.8)	~~NC~~ 31.8 (26.6, 36.0)
HR (95.05% CI); P-value	0.~~63~~799 (0.~~45~~641, 0.~~88~~997); P=0.~~0068 (NS)~~0462 †	

Figure 2. Kaplan-Meier Curves of Overall Survival in FLAURA



+ Censored patients.
The values at the base of the figure indicate number of subjects at risk.

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Pre-treated T790M positive NSCLC patients-AURA3

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Table 5. Efficacy results from AURA3 by investigator assessment

Efficacy Parameter	TAGRISSO (N=279)	Chemotherapy (Pemetrexed/Cisplatin or Pemetrexed/Carboplatin) (N=140)
Progression-Free Survival		
Number of Events (% maturity)	140 (50)	110 (79)
Median, Months (95% CI)	10.1 (8.3, 12.3)	4.4 (4.2, 5.6)
HR (95% CI); P-value	0.30 (0.23,0.41); P-~~value~~ <0.001	
Overall Survival[1] (OS)		
Number of Deaths (% maturity)	~~69 (24.7)~~ 188 (67.4)	~~40 (28.6)~~ 93 (66.4)
Median OS, Months (95% CI)	~~NC (20~~26.8 (23.5, ~~NC~~ 31.5)	~~NC~~ 22.5(20.~~6, NC~~ 2. 28.8)
HR (95.56% CI); P-value	0.~~72~~87 (0.~~48~~67, 1.~~09~~13); P-~~value~~ = 0-~~121~~277	
Objective Response Rate[2]		
Number of responses, Response Rate (95% CI)	197 71% (65, 76)	44 31% (24, 40)
Odds ratio (95% CI); P-value	5.4 (3.5, 8.5); P-~~value~~ <0.001	
Duration of Response (DoR)[2]		
Median, Months (95% CI)	9.7 (8.3, 11.6)	4.1 (3.0, 5.6)

העדכון העיקרי בעלון לצרכן הוא:

4. תופעות לוואי

- תופעות לוואי שאינן שכיחות (תופעות שמופיעות ב 1-10 משתמשים מתוך 1000):

דלקת בכלי הדם בעור. יתכן שיראה כחבורה או כתמים של פריחה על העור (non-blanching rash)

תוספות לעלון מסומנות בקו תחתון וטקסט שנמחק מסומן בקו חוצה.

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

בכבוד רב,

אורה סטוליק
רוקחת ממונה
אסטרהזניקה (ישראל) בע"מ

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