נובמבר 2024

Caprelsa 100 mg

חומר פעיל:

Vandetanib 100 mg

ההתוויה המאושרת:

Caprelsa is indicated for the treatment of aggressive and symptomatic medullary thyroid cancer (MTC) in patients with unresectable locally advanced or metastatic disease.

For patients in whom Rearranged during Transfection (RET) mutation is not known or is negative, a possible lower benefit should be taken into account before individual treatment decision (see important information in sections 4.4 and 5.1).

חברת סאנופי מבקשת להודיע על עדכון העלונים לרופא ולצרכן, העדכון כולל את צמצום ההתוויה, ועדכון העלונים בהתאם.

להלן ההתוויה המעודכנת:

Caprelsa is indicated for the treatment of aggressive and symptomatic Rearranged during Transfection (RET) mutant medullary thyroid cancer (MTC) in patients with unresectable locally advanced or metastatic disease.

העדכונים העיקריים הם:

בעלון לרופא:

4.1 Therapeutic indications

Caprelsa is indicated for the treatment of aggressive and symptomatic Rearranged during Transfection (RET) mutant medullary thyroid cancer (MTC) in patients with unresectable locally advanced or metastatic disease.

~~For patients in whom Rearranged during Transfection (RET) mutation is not known or is negative, a possible lower benefit should be taken into account before individual treatment decision (see important information in sections 4.4 and 5.1).~~

4.2 Posology and method of administration

Treatment should be initiated and supervised by a physician experienced in treatment of MTC and in the use of anticancer medicinal products and experienced in the assessment of electrocardiogram (ECG).

Rearranged during transfection (RET) status

Since the activity of Caprelsa, based on available data, is considered insufficient in patients with no identified RET mutation, the presence of a RET mutation should be determined by a validated test prior to initiation of treatment with Caprelsa. When establishing RET mutation status, tissue samples should be obtained if possible at the time of initiation of treatment rather than at the time of diagnosis.

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4.4 Special warnings and precautions for use

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~~Rearranged during transfection (RET) status~~

~~Patients without RET mutation may have a decreased benefit from vandetanib treatment and the benefit/risk balance for this group of patients may therefore differ from that of the group with RET mutations. For patients whose RET mutation status could be negative, a possible lower benefit should be taken into account before individual treatment decisions and the use of vandetanib should be carefully considered because of the treatment related risks. Therefore RET mutation testing is recommended. When establishing RET mutation status, tissue samples should be obtained if possible at the time of initiation of treatment rather than at the time of diagnosis (see sections 4.1 and 5.1).~~

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5.1 Pharmacodynamic properties

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RET mutation status reanalysis in Study 58

In Study 58, RET mutation testing was performed by using the polymerase chain reaction (PCR) based Amplification Refractory Mutation System (ARMS) assay for the M918T mutation, and direct sequencing of DNA for mutations in exons 10, 11, 13, 14, 15 and 16 (site of M918T mutation) on all sporadic patients where DNA was available (297/298). For reanalysis of samples lacking M918T mutation, the RET sequences were enriched using a custom Agilent SureSelect reagent and sequenced on an Illumina sequencer. Data processing and automated calling of RET variants were carried out using the Broad Genome Analysis ToolKit (GATK) pipeline with manual curation of any difficult cases using Broad Integrative Genomics Viewer (IGV).

Initially, 79 patients had no M918T mutation identified. Of these 79 patients, 69 had enough tissue sample to allow a post-hoc reanalysis of RET mutation status based on new available assays. Most patients were reclassified as RET mutant (52/69) and 17/69 patients had no RET mutation (M918T or other) detected (11 with vandetanib and 6 with a placebo). Patients reclassified as RET mutant (N = 52) were pooled with those 187 patients initially identified as RET mutant, leading to a total number of 239 RET mutant patients (172 treated with vandetanib and 67 treated with a placebo). Results were based on a blinded central review of imaging.

~~However, RET status could not be tested in a large proportion of patients (mainly because of unavailable results for direct sequencing of DNA) and response rate was somewhat lower in the patients with unknown RET status compared with RET mutation positive status: 51.8% vs. 35.9 % respectively. In the blinded comparison of vandetanib vs. placebo, only 2 patients known to be RET negative at all 6 exons received vandetanib and none demonstrated responses.~~

~~A post-hoc subgroup analysis of RET negative status based on absence of M918T mutation of the pivotal study 58 was performed. A patient was considered to have a RET mutation if either an M918T mutation by the ARMS assay, or a RET mutation in any exons sequenced was present in the tumour. Actually 79 patients were identified by absence of an M918T mutation and no RET mutation identified at any of the other 6 exons tested but in 71 of such~~

patients sequencing of the 6 exons was incomplete. M918T mutation is the most frequent mutation observed in patients with sporadic MTC; however it cannot be ruled out that some patients tested RET negative for M918T mutation might be positive for mutation on other exons.

Results according to RET status (positive, unknown and RET M918T mutation negative definition) are presented in Table 3.

Table 3: Efficacy end-points in RET mutant patients Summary of efficacy findings in a segment of patients according to RET mutation status

Efficacy end-point (Vandetanib vs placebo)	Patients with documented RET mutation (n=187239)	Patients with no M918T mutation and other mutations not tested or negative (n=79)*
Objective response rate (vandetanib arm)	52% 51.7% vs 14.9%	35%
Efficacy endpoint PFS HR (95%) confidence interval	0.465 (0.296, 0.748)	0.57 (0.29, 1.13)
2-year PFS rate	55.7% vs 40.1%	

*RET mutation status was obtained at the time of diagnosis in a majority of patients and could have changed since.

בעלון לצרכן:

1. למה מיועדת התרופה?

קפרלסה מיועדת לטיפול בסוג של סרטן גרורתי לשדי מודולרי של בבלוטת התריס שמאופיין במוטציה בגן RET (Rearranged during Transfection), סרטן שלא ושאינו ניתן להסרה בניתוח או שהתפשט לחלקים אחרים בגוף.

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2. לפני השימוש בתרופה

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יש לקבוע את סטטוס ה- RET של הסרטן, לפני התחלת טיפול בקפרלסה.

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העלונים המעדכנים נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות וניתן לקבלו מודפס 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

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