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10th December 2012

Direct Healthcare Professional Communication on Tyverb© (lapatinib)

Comparative data have shown that lapatinib based regimens are less effective than Herceptin© (trastuzumab) based regimens in certain settings.

Dear Healthcare Professional:

Summary

- Two recent trials have shown statistically significant superior efficacy of trastuzumab as compared to lapatinib. This effect was particularly pronounced in the patients who had no prior exposure to trastuzumab.

- Prescribers are reminded that Tyverb should not be prescribed in combination with capecitabine unless patients have progressed on trastuzumab, in accordance with the licensed indication.

The information contained in this letter has been endorsed by the European Medicines Agency and the Medicines Authority.

Further information on the efficacy concern

Recently, there have been results reported from pre-planned interim analyses from two comparative studies of Tyverb© in combination with chemotherapy versus Herceptin© (trastuzumab) in combination with chemotherapy in HER2 positive metastatic breast cancer patients.

- EGF111438/CEREBEL is a randomised Phase III study comparing the effect of lapatinib in combination with capecitabine relative to trastuzumab in combination with capecitabine on the incidence of CNS as site of first relapse in women with HER2 positive metastatic breast cancer. Patients were stratified based on prior trastuzumab treatment (yes versus no) and number of prior treatments for metastatic disease (0 versus ≥1 line).

  The study was stopped early as the interim analysis showed:
  - A low incidence of CNS events
  - Superior efficacy of the trastuzumab plus capecitabine arm in terms of progression-free and overall survival

  The results of the final analysis of Study EGF111438/CEREBEL, including subgroup analysis based on prior trastuzumab treatment, are presented in the table below:

Study EGF111438/CEREBEL: Kaplan-Meier Analyses of Investigator-Assessed Progression-Free Survival and Overall Survival (ITT population, final analysis)

	Investigator-Assessed PFS [b]		Overall Survival	
	Lapatinib+ Capecitabine 2000 mg/m^2/day	Trastuzumab+ Capecitabine 2500 mg/m^2/day	Lapatinib+ Capecitabine 2000 mg/m^2/day	Trastuzumab+ Capecitabine 2500 mg/m^2/day
ITT population (All)				
N	271	269	271	269
Events, n(%)	160 (59)	134 (50)	70 (26)	58 (22)
Censored, ended	25 (9)	40 (15)	16 (6)	20 (7)
Censored, ongoing	86 (32)	95 (35)	185 (68)	191 (71)
Median, mo (95% CI)	6.60 (5.72, 8.11)	8.05 (6.14, 8.9)	22.7 (19.5, -)	27.3 (23.7, -)
HR (95% CI) [a]	1.30 (1.04, 1.64)		1.34 (0.95,1.90)	
Subjects who had received prior trastuzumab				
N	167	159	167	159
Events, n(%)	103 (62)	86 (54)	43 (26)	38 (24)
Censored, ended	15 (9)	25 (16)	8 (5)	11 (7)
Censored, ongoing	49 (29)	48 (30)	116 (69)	110 (69)
Median, mo (95% CI)	6.6 (5.7, 8.3)	6.1 (5.7, 8.0)	22.7 (20.1, -)	27.3 (22.5, 33.6)
HR (95% CI) [a]	1.13 (0.85, 1.50)		1.18 (0.76, 1.83)	
Subjects who had not received prior trastuzumab				
N	104	110	104	110
Events, n(%)	57 (55)	48 (44)	27 (26)	20 (18)
Censored, ended	10 (10)	15 (14)	8 (8)	9 (8)
Censored, ongoing	37 (36)	47 (43)	69 (66)	81 (74)
Median, mo (95% CI)	6.3 (5.6, 8.1)	10.9 (8.3, 15.0)	- (14.6, -)	- (21.6,-)
HR (95% CI) [a]	1.70 (1.15, 2.50)		1.67 (0.94, 2.96)	

Final analysis; based on data from a cut-off date of 11 June 2012.
CI = confidence interval; HR = hazard ratio; mo = months; PFS = progression free survival
a. Pike estimate of the treatment hazard ratio, <1 indicates a lower risk for lapatinib+capecitabine compared with trastuzumab+capecitabine
b. PFS was defined as the time from randomization to the earliest date of disease progression or death from any cause, or to the date of censor

- The second study, EGF108919 (COMPLETE), is a randomised Phase III study comparing the activity of lapatinib plus taxane followed by lapatinib alone versus trastuzumab plus taxane followed by trastuzumab as first line therapy for women with HER2 positive metastatic breast cancer. Tyverb is not approved in combination with a taxane.

  EGF108919 was also stopped early due to superior efficacy of the trastuzumab plus taxane arm in terms of progression-free survival: median PFS was 8.8 months in the lapatinib-containing arm compared to 11.4 months in the trastuzumab-containing arm; HR: 1.33 (95% CI: 1.06, 1.67, p=0.01). The hazard ratio for overall survival was 1.1 (95% CI: 0.75, 1.61; p=0.62), based on 18% (n=115) deaths.

In view of the available data from these studies, and in agreement with the European Medicines Agency (EMA), you are reminded that Tyverb in combination with capecitabine is approved for patients with advanced or metastatic disease with progression following prior therapy, which must have included anthracyclines and taxanes and therapy with trastuzumab in the metastatic setting.

The product information for Tyverb has been updated with information that in certain settings lapatinib based regimens have been shown to be less effective than trastuzumab based regimens.

Call for reporting

Any suspected adverse reaction to Tyverb should be reported to GSK contact details below.

Alternatively any suspected adverse reactions can also be reported to
Medicines Authority Post-licensing Directorate, 203, Level 3, Rue D'Argens, Gżira GŻR 1368, MALTA, or at: http://www.medicinesauthority.gov.mt/pub/adr.doc

Communication Information

Should you have any questions or require additional information please contact the undersigned.

Yours sincerely,

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References

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