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LBA18

POSEIDON randomized phase II trial: Tamoxifen (TAM) + taselisib or placebo (PLA) in patients (pts) with hormone receptor positive (HR+)/HER2- metastatic breast cancer (MBC)

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Background

Taselisib is an oral inhibitor of class I α, δ, and Υ isoforms of PI3K that has demonstrated clinical activity in combination with TAM (Baird R et al, CCR 2019).

Methods

POSEIDON is an international, multicenter, randomized (1:1) phase II trial of TAM + taselisib or PLA in pts with HR+/HER2- MBC after prior endocrine treatment (ET). Cross-over was allowed. Primary endpoint: unstratified progression-free survival (PFS; local assessment). Secondary endpoints: safety, RECIST 1.1 overall response rate (ORR; complete response [CR] + partial response [PR]), clinical benefit rate (CBR; CR + PR + stable disease >6 months) and overall survival (OS). 180 pts were required to detect a PFS constant hazard ratio (HR) of 0.64 (ß=90%, 2-sided α=0.2). Accrual closed prematurely due to Covid-19, decreasing the power to 83%.

Results

152 pts (median age 63) enrolled (Table), median follow-up 26.4 months (m). Addition of taselisib to TAM increased median PFS from 3.2 to 4.8m (unstratified HR 0.62, 95%CI 0.43-0.93, p=0.02; stratified HR 0.68, 95%CI 0.4-1.2, p=0.16), independently of *PIK3CA* status. In taselisib arm, ORR 11.8% (95%CI 5.6- 21.3) and CBR 22.4% (95%CI 13.6-33.4); in PLA arm, ORR 2.6% (95%CI 0.3- 9.2) and CBR 14.5% (95%CI 7.5-24.4). Reasons for stopping taselisib / PLA: toxicity 22% / 4%, progressive disease 55% / 67%, other (mainly Covid-19) 23% / 29%. Common adverse events (AEs) in taselisib arm: diarrhea (36%), nausea (35%), hyperglycemia (28%). Common AEs in PLA arm: nausea (21%), fatigue (16%). G3-5 AEs were more common with taselisib (44% vs 5%, p<0.01), mainly diarrhea (11%), hyperglycemia (5%) and transaminitis (5%). OS will be presented.Table: LBA18

Stratification factors, n(%)		
	Taselisib + TAM N=76	PLA + TAM N=76
Post-menopausal	72 (95)	70 (92)
Lobular histology	14 (18)	13 (17)
PIK3CAmut Exon 20 Exon 9 Not detected Not tested	11 (14) 8 (11) 25 (33) 32 (42)	10 (13) 15 (20) 19 (25) 32 (42)
<6m on prior ET for MBC	25 (33)	24 (32)
Prior EVE	25 (33)	19 (25)
0-1 prior CT for MBC	49 (64)	51 (67)

Conclusions

Addition of taselisib to TAM increased PFS in pts with HR+/HER2-neg MBC but the tolerability of the regimen was poor.

Combining ET and PI3K-AKT pathway inhibition using drugs with a better therapeutic index warrants additional study in breast cancer subgroups most likely to benefit.

Clinical trial identification

EudraCT 2013-003947-51; NCT02301988.

Legal entity responsible for the study

The Netherlands Cancer Institute (NKI).

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Disclosure

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