Late Breaking Abstract for SITC 2021 - AIPAC

Abstract Title:

Final results from AIPAC: A phase IIb comparing eftilagimod alpha (a soluble LAG-3 protein) vs. placebo in combination with weekly paclitaxel in HR^+ HER2- MBC.

Background:

Eftilagimod alpha (efti; IMP321) is a soluble LAG-3 protein (LAG-3Ig) that binds to a subset of MHC class II molecules and mediates activation of antigen-presenting cells followed by CD8 T-cells. Weekly paclitaxel is a standard of care chemo-regimen after failure of endocrine-based therapy for metastatic breast carcinoma (MBC). AIPAC (Active Immunotherapy PAClitaxel) investigated the addition of efti to weekly paclitaxel in these patients (pts).

Methods:

This placebo-controlled, double-blinded, 1:1 randomized phase IIb trial enrolled pts with measurable disease, HR^+ HER2- MBC after endocrine-based therapy. Pts received paclitaxel (80 mg/m² IV on D1, D8, D15) + efti (30 mg) or placebo on D2, D16 (every 2 weeks) for up to 24 weeks following efti/placebo for up to 52 weeks. The primary endpoint (EP) was progression-free survival (RECIST1.1) by BICR. Secondary EPs included overall survival (OS), PFS (local read), overall response rate (ORR), biomarker, quality of life. Exploratory EPs included univariate/multivariate analyses.

Results:

227 pts were randomized (Jan2017-Jul2019). All except 1 received ≥1 treatment and were included in the full analysis set [efti (n=114); placebo (n=112)]. Data cut-off was 14May2021 (min. follow-up= 22 months). Median age was 60 yrs with ECOG 0 in 61.5%. 91.6% had visceral disease. Pts were mostly endocrine resistant (84%) and partially pre-treated with CDK4/6 inhibitors (44.2%). Post-study treatment was similar. Median OS was 20.4 (95% CI: 14.3-25.1) months in the efti group vs. 17.5 (95% CI: 12.9-21.9) in the placebo group. HR was 0.88 (95%CI: 0.64-1.19; p=0.197). In predefined univariate analyses, younger pts, low baseline monocytes and luminal B showed significant/clinically meaningful improvement in OS (Table 1).

Table 1. Overall survival by subgroups at final analysis

OS / population	**Overall**	**<65 yrs of age**	**Low monocytes (<250/µl)**	**Luminal B**
Events % (N/N)	72.5 164 /226	72.8 107/147	70.2 33/47	83.1 69/83
Efti group – median (months); [95% CI]	20.4; [14.3-25.1]	22.3; [15.3-29.6]	32.5; [18.2-NA]	16.8; [9.9-24.9]
Placebo group median (months); [95% CI]	17.5; [12.9-21.9]	14.8; [10.9-18.5]	12.9; [7.5-20.4]	12.6; [10.2-17.3]
HR [95% CI]; p-value	0.88 [0.64-1.19]; 0.197	0.66 [0.45-0.97]; 0.017	0.44 [0.22-0.88]; 0.008	0.67 [0.41-1.08]; 0.049

Efti increased PBMC/T cell (CD4/CD8) count vs. placebo, correlating with improved OS (Spearman Rho=0.6, p=0.02 for CD8 T cells). In a whole population multivariate cox regression model, increasing BMI and prior treatment with CDK4/6 were independent significant poor prognostic markers for PFS and OS.
TEAEs leading to discontinuation were similar at 5.3%(efti) & 6.3%(placebo). PFS (Primary EP) and safety were reported at SABCS 2020 (Abstract#132).

Conclusion:

Efti added to paclitaxel led to a non-significant 2.9 months median OS increase in HR^+ HER2- MBC pts after endocrine-based therapy. Effects were significant in pts <65yrs, with low monocytes and more aggressive disease (luminal B). Efti increased circulating CD4/CD8 T cells, which significantly correlated to improved OS. Weekly paclitaxel + efti should be further investigated in MBC.

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