Clinical Trials Complete

**Abstract 948**

**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**

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**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 pretreated 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: 0.64-1.21, p=0.197). In predefined univariate analyses, younger pts, low baseline monocytes and luminal B showed significant/clinically meaningful improvement in OS (table 1).

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.

**Conclusions**

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.

**Trial Registration**

The trial identifiers are IMP321-P011 (code for sponsor), 2015-002541-63 (EudraCT) and NCT02614833 (ClinicalTrials.gov).

**Ethics Approval**

The study was approved by relevant ethics committees and institutional review boards.

http://dx.doi.org/10.1136/jitc-2021-SITC2021.948

**Abstract 948 Table 1**

<table>
<thead>
<tr>
<th>OS / population</th>
<th>Overall</th>
<th>&lt;65 yrs of age</th>
<th>Low monocytes (&lt;250/µl)</th>
<th>Luminal B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events % (N/H)</td>
<td>72.5 (164/226)</td>
<td>72.8 (107/147)</td>
<td>70.2 (31/47)</td>
<td>81.1 (69/83)</td>
</tr>
<tr>
<td>Efti group – median (months) [95% CI]</td>
<td>20.4 [14.2-25.1]</td>
<td>22.3 [15.3-29.4]</td>
<td>32.5 [18.2-44.3]</td>
<td>16.8 [9.9-24.9]</td>
</tr>
<tr>
<td>Placebo group median (months) [95% CI]</td>
<td>17.5 [12.9-21.9]</td>
<td>14.8 [10.0-18.5]</td>
<td>12.9 [7.5-20.4]</td>
<td>12.6 [10.2-17.3]</td>
</tr>
<tr>
<td>hR (95% CI); p-value</td>
<td>0.08 [0.04-0.19]; 0.197</td>
<td>0.06 [0.04-0.07]; 0.017</td>
<td>0.44 [0.22-0.88]; 0.008</td>
<td>0.67 [0.41-1.08]; 0.049</td>
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</tbody>
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