Clinical Trials Complete

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

[1]Hans Wildiers*, [2]Luc Dirix, [3]Anne Armstrong, [4]Eveline De Cuypere, [5]Florence Dalenc, [6]Steven Chan, [7]Frederik Marme, [8]Carolina Pia Schröder, [9]Jens Huober, [10]Peter Vuylsteke, [11]Jean-Philippe Jacquin, [12]Etienne Brain, [13]Sherko Kümmel, [14]Zsuzsanna Pápai, [15]Christian Mueller, [15]Chrystelle Brignone, [15]Frederic Triebel. *[1]University Hospitals Leuven; Department of General Medical Oncology and Multidisciplinary Breast Centre, Leuven, Belgium; [2]GZA Ziekenhuizen campus Sint-Augustin, Oosterveldlaan, Belgium; [3]The Christie NHS Foundation Trust, Manchester, UK; [4]AZ Sint-Jan Brugge-Oostende AV, Ruddershove, Belgium; [5]Institut Claudius Regaud (Institut Claudius regaud- Institut Universitaire du Cancer – Oncopole), Toulouse, France; [6]Nottingham Cancer Clinical Trials Team, Nottingham, UK; [7]National Center for Tumor Diseases (NCT), Heidelberg, Germany; [8]University Medical Center Groningen, Groningen, Netherlands; [9]Universitätsfrauenklinik Ulm, Ulm, Germany; [10]CMSE UCLouvain, CHU UCL NAMUR Site Ste-Elisabeth, AND University of Botswana, Uccle, Belgium; [11]Institut de Cancérologie de la Loire, Saint Priest en Jarez, France; [12]Institut Curie -Hôpital René Huguenin, Saint-Cloud, France; [13]KEM | Evang. Kliniken Essen-Mitte, Essen, Germany; [14]MH Egészségügyi Központ Onkológiai, Budapest, Hungary; [15]Immutep, Berlin, Germany*

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: 0.64-1.19; p=0.197). In predefined univariate analyses, younger pts, low baseline monocytes and luminal B showed significant/clinically meaningful improvement in OS (table 1).

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).

Abstract 948 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

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 ethic committees and institutional review boards.

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