MADRID 2026 ESMO congress

LBA23

Final results of TALENT: A neoadjuvant trial of T-DXd with or without anastrozole, or in sequence with chemotherapy for HER2-low, HR+ early-stage breast cancer

S.A. Hurvitz[1], N.P. McAndrew[2], D. Chan[3], L. Wang[4], V. Phan[5], T. Lomis[6], N.M. Lamble[1], J. Tiulim[3], B. DiCarlo[2], D. Villa[2], N.E. Abdulla[5], G. Patel[7], A. Master[2], S. Sikaria[3], S. Dakhil[8], V. Nair[1], M.F. Press[9], D. Rimm[10], C-H. Tseng[2], A. Bardia[2]

[1] Department of Medicine, Division of Haemato-Oncology, University of Washington, Seattle, United States of America, [2] Hematology/Oncology, Jonsson Comprehensive Cancer Center at UCLA, Los Angeles, United States of America, [3] Hematology/Oncology, Torrance Memorial Physician Network (TMPN)/Cancer Care, Torrance, United States of America, [4] Hematology/Oncology, PIH Health Whittier, Whittier, United States of America, [5] Hematology Oncology, Cancer & Blood Specialty Clinic, Los Alamitos, United States of America, [6] Surgery, Valley Breast Care and Women's Health Center, Van Nuys, United States of America, [7] Department of Hematology Oncology, St Jude Crosson Cancer Institute/Providence Medical Foundation, Fullerton, United States of America, [8] Hematology/Oncology, Cancer Center of Kansas, Wichita, United States of America, [9] Pathology, USC Norris Comprehensive Cancer Center Department of Pathology, Los Angeles, United States of America[10] Departments of Pathology and Medicine, Yale University School of Medicine - Yale Cancer Center, New Haven, United States of America

Background

Pathologic complete response (pCR) in HR+/HER2-negative breast cancer (BC) is uncommon. T-DXd, a HER2-targeted antibody drug conjugate, improves progression-free and overall survival vs chemotherapy in metastatic HER2-low BC. TALENT (NCT04553770) is a phase II, 2-stage neoadjuvant study evaluating T-DXd + endocrine therapy or in sequence with chemotherapy in pts with HR+/HER2-low early BC.

Methods

Pts with untreated, operable invasive early HR+/HER2-low BC were randomized 1:1 to receive 6 cy of T-DXd (5.4 mg/kg q21d) alone (Arm A) or with anastrozole (1 mg PO QD) (Arm B). An arm was expanded if ≥2 pCR (RCB0) were observed. After 29 pts enrolled, subsequent pts received 8 cy. After Arms A/B, Arm C was added to evaluate 4 cy T-DXd → 4 cy docetaxel 75 mg/m^2 + cyclophosphamide 600 mg/m^2 (TC) in <58 pts. Biopsies were taken at baseline, pre-cy2 & surgery. Imaging/biomarkers were assessed at baseline, cy 2 & surgery. Endpoints: Residual Cancer Burden (RCB), safety, overall response rate (ORR) & biomarkers. Ki67, HER2, ER & PR were evaluated centrally, and TROP2 & HER2 levels were quantified (quant) by TROPLEX for Arms A & B.

Results

From 11/2020 - 02/2026, 132 pts were enrolled. Pts in Arm C were more likely to have node+ disease (81%) vs. Arms A/B (53%, 55%). Overall rates of pCR/near-pCR (RCB 0/1) were 16% (Arm A), 17% (Arm B), and 17% (10/58 Arm C). HER2 levels were higher in pts with RCB0 (2691 & 1221 amol/mm^2) vs RCB1/2/3 (715-947 & 440-608 amol/mm^2) at Baseline & cy 2, respectively.Table: LBA23

	Arm A (N=45) n (%)		Arm B (N=29) n (%)	Arm C (N=58) n (%)
Baseline characteristics				
Stage I/II/III	0/32 (71)/13 (29)	0/26 (90)/3 (10)	2 (3)/43 (74)/13 (22)	
Node+	24 (53)	16 (55)	47 (81)	
Grade III	19 (42)	11 (38)	29 (50)	
Ki67>20% (central)	33 (73)	24 (83)	43 (74)	
Antigen quant (med amol/mm^2) Baseline→Cy2→Surgery				
HER2	707→334→150	778→331→83	-	
TROP2	1097→1371→1001	1001→952→925	-	
Results: Evaluable				
RCB0	3/42 (7)	1/29 (3)	5/55 (9)	
ORR	28/42 (67)	19/29 (66)	37/57 (65)	

	Arm A (N=45) n (%)		Arm B (N=29) n (%)	Arm C (N=58) n (%)	
Results ITT	6 cycles (N=15)	8 cycles (N=30)	6 cycles (N=14)	8 cycles (N=15)	8 cycles (N=58)
RCB0	0	3 (10)	0	1 (7)	5 (9)
RCB1	2 (13)	2 (7)	1 (7)	3 (20)	5 (9)
Gr >3 Treatment Emergent AE	3 (20)	8 (27)	3 (21)	2 (13)	16 (28)
Interstitial Lung Disease (all Gr 2)	0	0	1 (7)	0	2 (3)

Conclusions

In this first study to report outcomes with neoadjuvant T-DXd in HR+/HER2-low BC, T-DXd–based therapy was associated with low pCR rates. ILD was rare. HER2 was higher in tumors with RCB0 versus RCB1/2/3, suggesting HER2 level may correlate with treatment outcome. HER2 levels declined significantly on treatment, whereas TROP2 expression remained stable. ER, PR, & Ki67 analyses will be presented.

Clinical trial identification

NCT04553770.

Legal entity responsible for the study

Translational Research In Oncology - US (TRIO-US).

Funding

Daiichi Sankyo, Inc.

Disclosure

S.A. Hurvitz: Financial Interests, Personal, Invited Speaker: AICME, Aptitude, AstraZeneca, At the Limits, Breast Cancer Foundation, New Zealand, CEA, Clinical Care Options, Curio, Efficient CME, Gilead Therapeutics, ICHE, Imedex, MD Outlook, MJH Associates, Med Learning Group, MedLive, Medical Educator Consortium (MEC), OncLive, Outcomes for Me, PER, Peer Education, Peer Voice, PlatformQ, Prime Oncology, Primo, Projects in Knowledge, Prova Education, Reach MD, Reach MD/MedIQ, Research to Practice, Ultimate Medical Academy, Vaniam, WebMD, axis medical, eScientiq; Financial Interests, Institutional, Advisory Board: ALX oncology, Akari, BMS, Bayer, BeiGene/BeOne, Blueprint Medicines, Boundless Bio, BridgeBio, Daiichi Sankyo, Eli Lilly, Gilead Sciences, Jazz Pharmaceuticals, Luminate, Luminate, Myricx, Prelude Therapeutics, Roche – Genentech; Financial Interests, Personal, Other, DSMB: Alliance Foundation, Atossa, Quantum Leap; Financial Interests, Institutional, Other, DSMB: Roche; Financial Interests, Personal, Stocks/Shares, spouse owns: ROM Tech; Financial Interests, Personal, Royalties, author medical book: McGraw; Financial Interests, Personal, Royalties: Elsevier, Springer, Sage, Wolters Kluwer, Wiley; Financial Interests, Institutional, Local PI: AstraZeneca, Novartis, Stemline; Financial Interests, Institutional, Coordinating PI: Boehringer Ingelheim, Briacell, Daiichi Sankyo; Financial Interests, Coordinating PI: Celcuity; Financial Interests, Trial Chair: Genentech/Roche; Financial Interests, Institutional, Steering Committee Member: Jazz/Zymeworks; Financial Interests, Steering Committee Member: Novartis, Stemline, Genentech/Roche, Seagen/Pfizer, Eli Lilly, Gilead Sciences; Non-Financial Interests, Advisory Role: Novartis; Non-Financial Interests, Member: ASCO, AACR; Non-Financial Interests, Other, speaker: National Breast Cancer Coalition. N.P. McAndrew: Financial Interests, Personal and Institutional, Research Funding: Novartis, Mersana; Financial Interests, Institutional, Research Funding: Daiichi Sankyo, Seattle Genetics, Dizal, Loxo, Arvinas, Eisai, Avenzo, Merck, Lilly; Financial Interests, Personal and Institutional, Advisory Board, Advisory board honorarium: Novartis, Daiichi Sankyo, Mersana; Financial Interests, Personal, Advisory Board, Advisory board honorarium: Biotheranostics, Genomic Health, Ataraxis; Financial Interests, Personal and Institutional, Speaker, Consultant, Advisor, Consulting honorarium: Novartis, Daiichi Sankyo; Financial Interests, Personal, Speaker, Consultant, Advisor, Consulting honorarium: AstraZeneca, GoodRx, Ataraxis; Financial Interests, Personal, Other, Travel accommodation: TRIO; Financial Interests, Personal and Institutional, Other, Travel accommodation: Daiichi Sankyo, Novartis; Financial Interests, Personal and Institutional, Speaker, Consultant, Advisor, Speaking honorarium: Novartis. A. Master: Financial Interests, Personal, Speaker's Bureau: Gilead, Menarini Stemline; Financial Interests, Institutional, Research Funding: Greenwich LifeSciences. V. Nair: Financial Interests, Institutional, Research Funding: Kuni Foundation, BeOne, Novartis; Financial Interests, Personal, Speaker, Consultant, Advisor, Consulting: Gilead, Medscape Oncology. M.F. Press: Financial Interests, Personal, Other, Affiliations or financial relationships: Novartis Pharmaceuticals Corp., TORL BioTherapeutics LLC., Jazz Pharmaceuticals, TRIO-US, Iambic Therapeutics; Financial Interests, Personal, Speaker, Consultant, Advisor, Consultant: Novartis Pharmaceuticals Corp; Financial Interests, Personal, Ownership Interest: TORL BioTherapeutics LLC.; Financial Interests, Personal, Financially compensated role, Fee-for-service agreement: Novartis Pharmaceuticals Corp., TORL BioTherapeutics LLC., Jazz Pharmaceuticals, TRIO-US, Iambic Therapeutics; Financial Interests, Institutional, Research Grant: Breast Cancer Research Foundation, Dr. Miriam & Sheldon Adelson Medical Research Foundation; Financial Interests, Institutional, Other, Holds the Harold E. Lee Chair in Cancer Research at the University of Southern California: Holds the Harold E. Lee Chair in Cancer Research at the University of Southern California. D. Rimm: Financial Interests, Personal and Institutional, Speaker, Consultant, Advisor, Advisor: AstraZeneca, Cepheid; Financial Interests, Personal, Speaker, Consultant, Advisor, Advisor: Cell Signaling

Technology, Daiichi Sankyo, Danaher, Halda Therapeutics, Incendia, Nucleai, PAIGE.AI, Sanofi; Financial Interests, Personal and Institutional, Research Funding: AstraZeneca, Cepheid; Financial Interests, Institutional, Research Funding: Konica Minolta, Leica, NavigateBP, NextCure, Nanostring, Lilly. A. Bardia: Financial Interests, Personal and Institutional, Speaker, Consultant, Advisor, Consultant: Pfizer; Financial Interests, Personal, Speaker, Consultant, Advisor, Consultant: Novartis, Merck, Genentech, AstraZeneca/Daiichi Sankyo, Alyssum, Menarini, Vyome, BMS, Gilead, Eli Lilly; Other, Personal and Institutional, Other, Support to institution: Pfizer, Novartis, Merck, Genentech, AstraZeneca/Daiichi Sankyo, Menarini, Gilead, Eli Lilly; Other, Institutional, Other, Support to institution: Onkure. All other authors have declared no conflicts of interest.

© European Society for Medical Oncology