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LBA15 Primary outcome of the phase III SYD985.002/TULIP trial comparing [vic-]trastuzumab duocarmazine to physician's choice treatment in patients with pre-treated HER2-positive locally advanced or metastatic breast cancer

C. Saura Manich[1], J. O'Shaughnessy[2], P.G. Aftimos[3], E. van den Tweel[4], M. Oesterholt[4], S.I. Escrivá-de-Romaní[1], N. Quenel Tueux[5], T.J. Tan[6], J.S. Lim[7], S. Ladoire[8], A. Armstrong[9], T. Crook[10], A. Stradella[11], G. Bianchi[12], R. Mulder[4], N. Koper[4], N. Turner[13]

[1]Department of Medical Oncology, Vall d'Hebron Institute of Oncology (VHIO), Hospital Universitari Vall d'Hebron, Barcelona, Spain; [2]Breast Oncology, Baylor University Medical Center Texas Oncology, Dallas, TX, USA; [3]Clinical Trials Conduct Unit, Institut Jules Bordet - Université Libre de Bruxelles, Brussels, Belgium; [4]Clinical Development, Byondis B.V., Nijmegen, Netherlands; [5]Medical Oncology, Institut Bergonie, Bordeaux, France; [6]Division of Medical Oncology, National Cancer Centre Singapore, Singapore; [7]Department of Hemato-Oncology, National University Cancer Institute, Singapore; [8]Oncology, Centre Georges-François Leclerc (Dijon), Dijon, France; [9]The Christie Clinic - Medical Oncology, The Christie NHS Foundation Trust, Manchester, UK; [10]Medical Oncology, Sarah Cannon Research Institute, London, UK; [11]Medical Oncology, Institut Català d'Oncologia - Hospitalet, Barcelona, Spain; [12]Oncologia Medica 1, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [13]Breast Oncology, The Royal Marsden Hospital ICR, London, UK

Background: [vic-]Trastuzumab duocarmazine (SYD985, Byondis B.V., NL) is a novel HER2-targeting antibody—drug conjugate comprised of trastuzumab bound to a linker drug containing duocarmycin. TULIP assessed the efficacy of SYD985 in advanced HER2-positive breast cancer.

Methods: The TULIP trial (NCT03262935) randomly assigned HER2-positive locally advanced or metastatic breast cancer (MBC) patients with $\geq$ 2 previous MBC regimens or previous MBC treatment with T-DM1, 2:1 between SYD985 (1.2 mg/kg q three weeks) and physician's choice (PC) chemotherapy. The primary endpoint was progression-free survival (PFS) by blinded central review. The trial was powered to detect a Hazard Ratio (HR) of 0.65 at the $P < 0.05$ significance level. Secondary endpoints were investigator-assessed PFS, overall survival (OS), objective response rate (ORR), and health-related quality of life (HRQoL).

Results: 437 patients from 11 countries were randomized to SYD985 (n=291) or PC (n=146). Median age was 56 years, median number of prior MBC treatments was 4 [range 1-16]. Centrally reviewed median PFS was 7.0 months [95% CI 5.4-7.2] for SYD985 and 4.9 mo [4.0-5.5] for PC (HR 0.64 [0.49-0.84]; $p = 0.002$). Investigator-assessed PFS was also significantly improved (6.9 mo [6.0-7.2] vs 4.6 mo [4.0-5.6]; HR 0.60 [0.47-0.77]; $p < 0.001$). In this first analysis of OS the HR was 0.83 [0.62-1.09]; $p = 0.153$. No significant differences were observed in ORR or HRQoL. The most frequently reported adverse events for SYD985 were conjunctivitis (38.2%), keratitis (38.2%) and fatigue (33.3%), for PC these were diarrhoea (35.8%), nausea (31.4%) and fatigue (29.9%). Interstitial lung disease / pneumonitis was reported for 7.6% (5.2% grade 1-2) of patients treated with SYD985, including two grade 5 events. Adverse events leading to discontinuation (SYD985 35.4%, PC 10.2%) in the SYD985 group were mainly related to eye disorders (20.8%) or respiratory disorders (6.3%).

Conclusions: Treatment with SYD985 significantly improved PFS in comparison with standard PC and may provide a new treatment option for patients with pre-treated locally advanced or metastatic HER2-positive MBC.

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J. O'Shaughnessy: Financial Interests, Personal, Advisory Board: AbbVie Inc; Financial Interests, Personal, Advisory Board: Agendia; Financial Interests, Personal, Advisory Board: Aptitude Health; Financial Interests, Personal, Advisory Board: AstraZeneca; Financial Interests, Personal, Advisory Board: Bayer; Financial Interests, Personal, Advisory Board: Bristol Myers Squibb; Financial Interests, Personal, Advisory Board: Celgene Corporation; Financial Interests, Personal, Advisory Board: Clovis Oncology; Financial Interests, Personal, Advisory Board: Daiichi Sankyo; Financial Interests, Personal, Advisory Board: Eisai; Financial Interests, Personal, Advisory Board: G1 Therapeutics; Financial Interests, Personal, Advisory Board: Genentech; Financial Interests, Personal, Advisory Board: Gilead Sciences; Financial Interests, Personal, Advisory Board: GRAIL; Financial Interests, Personal, Advisory Board: Halozyme Therapeutics; Financial Interests, Personal, Advisory Board: Heron Therapeutics; Financial Interests, Personal, Advisory Board: Immunomedics; Financial Interests, Personal, Advisory Board: Ipsen Biopharmaceuticals; Financial Interests, Personal, Advisory Board: Lilly; Financial Interests, Personal, Advisory Board: Merck; Financial Interests, Personal, Advisory Board: Myriad; Financial Interests, Personal, Advisory Board: Nektar Therapeutics; Financial Interests, Personal, Advisory Board: Novartis; Financial Interests, Personal, Advisory Board: Ontada; Financial Interests, Personal, Advisory Board: Pfizer; Financial Interests, Personal, Advisory Board: Pharmacyclics; Financial Interests, Personal, Advisory Board: Pierre Fabre Pharmaceuticals; Financial Interests, Personal, Advisory Board: Puma Biotechnology; Financial Interests, Personal, Advisory Board: Prime Oncology; Financial Interests, Personal, Advisory Board: Roche; Financial Interests, Personal, Advisory Board: Samsung Bioepis; Financial Interests, Personal, Advisory Board: Sanofi; Financial Interests, Personal, Advisory Board: Seagen; Financial Interests, Personal, Advisory Board: Syndax Pharmaceuticals; Financial Interests, Personal, Advisory Board: Taiho Oncology; Financial Interests, Personal, Advisory Board: Takeda; Financial Interests, Personal, Advisory Board: Synthon B.V.; Financial Interests, Personal, Advisory Board: Byondis B.V. P.G. Aftimos: Financial Interests, Personal, Advisory Board: Boehringer Ingelheim; Financial Interests, Personal, Advisory Board: Macrogenics; Financial Interests, Personal, Advisory Board: Roche; Financial Interests, Personal, Advisory Board: Novartis; Financial Interests, Personal, Advisory Board: Amcure; Financial Interests, Personal, Advisory Board: Servier; Financial Interests, Personal, Advisory Board: G1 Therapeutics; Financial Interests, Personal, Advisory Board: Radius; Financial Interests, Personal, Advisory Board: Deloitte; Financial Interests, Personal, Advisory Board: Menarini; Financial Interests, Personal, Advisory Board: Synthon; Financial Interests, Personal, Advisory Board: Byondis; Financial Interests, Personal, Advisory Board: Amgen; Financial Interests, Personal, Advisory Role: Gilead; Non-Financial Interests, Personal, Other, Travel grant: MSD; Non-Financial Interests, Personal, Other, Travel grant: Pfizer; Financial Interests, Institutional, Funding: Roche; Financial Interests, Personal, Advisory Board: Sanofi-Aventis; Non-Financial Interests, Personal, Other, Travel grant: Roche; Non-Financial Interests, Personal, Other, Travel grant: Amgen; Non-Financial Interests, Personal, Other, Member of the scientific committee: IBCSG. E. van den Tweel: Financial Interests, Personal, Full or part-time Employment: Byondis B.V.; Non-Financial Interests, Personal, Member: ESMO; Non-Financial Interests, Personal, Member: ASCO. M. Oesterholt: Financial Interests, Personal, Full or part-time Employment: Byondis B.V. S.I. Escrivá-de-Romaní: Financial Interests, Personal, Invited Speaker, Advisory board, Travel grants: Roche; Financial Interests, Institutional, Research Grant: Roche; Financial Interests, Personal, Advisory Board, Invited speaker, travel grants: Daiichi Sankyo; Financial Interests, Personal, Advisory Board, Invited speaker, travel grant: Pierre Fabre; Financial Interests, Personal, Invited Speaker: Eisai; Financial Interests, Personal, Invited Speaker: Pfizer; Financial Interests, Institutional, Research Grant: Zymeworks; Financial Interests, Institutional, Research Grant: Synthon B.V.; Financial Interests, Institutional, Research Grant: Byondis B.V.; Financial Interests, Personal, Advisory Board: Seagen. N. Quenel Tueux: Financial Interests, Institutional, Principal Investigator: Byondis B.V. T.J. Tan: Financial Interests, Personal and Institutional, Advisory Board, Invited speaker, Board & Principal Investigator: Novartis; Financial Interests, Personal and Institutional, Advisory Board, Principal Investigator: Roche; Financial Interests, Personal, Speaker's Bureau, Advisory board: DKSH; Financial Interests, Personal, Advisory Board: Pfizer; Financial Interests, Personal, Invited Speaker, Advisory board: MSD; Financial Interests, Personal and Institutional, Invited Speaker, Advisory board, Principal Investigator, Research grant: AstraZeneca; Non-Financial Interests, Institutional, Principal Investigator: Seagen. J.S. Lim: Financial Interests, Personal, Invited Speaker, Advisory board: AstraZeneca; Financial Interests, Personal, Advisory Board, Invited speaker: DKSH; Financial Interests, Personal, Advisory Board: Novartis; Financial Interests, Personal, Advisory Board: Pfizer; Financial Interests, Personal, Invited Speaker: Pierre Fabre; Financial Interests, Personal, Invited Speaker: Roche; Non-Financial Interests, Institutional, Funding: CTI Biopharma; Non-Financial Interests, Institutional, Principal Investigator: Daiichi Sankyo; Non-Financial Interests, Institutional, Principal Investigator: Byondis B.V.; Non-Financial Interests, Institutional, Principal Investigator: Synthon B.V.; Non-Financial Interests, Institutional, Principal Investigator: Taiho Pharmaceuticals. S. Ladoire: Financial Interests, Institutional, Principal Investigator: Byondis B.V. A. Armstrong: Financial Interests, Institutional, Principal Investigator: Byondis B.V. T. Crook: Financial Interests, Institutional, Principal Investigator: Byondis B.V.; Financial Interests, Personal, Invited Speaker: Eli Lilly; Financial Interests, Personal, Advisory Board: Eli Lilly; Financial Interests, Personal, Advisory Board: Daiichi Sankyo. A. Stradella: Financial Interests, Institutional, Principal Investigator: Byondis B.V.; Financial Interests, Personal, Invited Speaker: Pierre Fabre; Financial Interests, Personal, Invited Speaker: Novartis; Financial Interests, Personal, Invited Speaker: Eisai; Financial Interests, Personal and Institutional, Expert Testimony: Seagen. G. Bianchi: Financial Interests, Institutional, Principal Investigator: Byondis B.V.; Financial Interests, Personal, Advisory Board: Eli Lilly; Financial Interests, Personal, Advisory Board: Novartis; Financial Interests, Personal, Advisory Board: Roche. R. Mulder: Financial Interests, Personal, Full or part-time Employment: Byondis B.V. N. Koper: Financial Interests, Personal, Full or part-time Employment: Byondis B.V. N. Turner: Financial Interests, Institutional, Principal Investigator: Byondis B.V.; Financial Interests, Personal, Advisory Board: AstraZeneca; Financial Interests, Personal, Advisory Board: Bristol Myers Squibb; Financial Interests, Personal, Advisory Board: Lilly; Financial Interests, Personal, Advisory Board: Merck Sharpe and Dohme; Financial Interests, Personal, Advisory Board: Novartis; Financial Interests, Personal, Advisory Board: Pfizer; Financial Interests, Personal, Advisory Board: Roche/Genentech; Financial Interests, Personal, Advisory Board: Bicycle Therapeutics; Financial Interests, Personal, Advisory Board: Taiho; Financial Interests, Personal, Advisory Board: Zeno Phamraceuticals; Financial Interests, Personal, Advisory Board: Repare therapeutics; Financial Interests, Institutional, Funding: AstraZeneca; Financial Interests, Institutional, Funding: BioRad; Financial Interests, Institutional, Funding: Pfizer; Financial Interests, Institutional, Funding: Roche/Genentech; Financial Interests, Institutional, Funding: Clovis; Financial Interests, Institutional, Funding: MSD; Financial Interests, Institutional, Funding: Guardant Health; Non-Financial Interests, Personal, Advisory Board: Byondis B.V.

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