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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

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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 ≥ 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.

Clinical trial identification

NCT03262935.

Legal entity responsible for the study

Byondis B.V., Nijmegen, The Netherlands.

Funding

Byondis B.V.

Disclosure

C. Saura Manich: Financial Interests, Personal, Advisory Board: AstraZeneca; Financial Interests, Personal, Advisory Board: Daiichi Sankyo; Financial Interests, Personal, Advisory Board: Eisai; Financial Interests, Personal, Advisory Board: Exact Sciences; Financial Interests, Personal, Advisory Board: Exeter Pharma; Financial Interests, Personal, Advisory Board: F. 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