BERLIN 2025 ESMO congress

LBA20

Primary results from ASCENT-03: A randomized phase III study of sacituzumab govitecan (SG) vs chemotherapy (chemo) in patients (pts) with previously untreated advanced triple-negative breast cancer (TNBC) who are unable to receive PD-(L)1 inhibitors (PD-[L]1i)

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Background

Significant PFS benefit was observed with SG vs chemo in pretreated metastatic (m)TNBC (ASCENT) and with SG + pembrolizumab vs chemo + pembrolizumab in first-line (1L) PD-L1+ mTNBC (ASCENT-04). For pts with mTNBC who cannot receive PD-(L)1i, treatment options are limited. We report primary results from the randomized phase 3 ASCENT-03 study (NCT05382299) of 1L SG vs chemo in pts with locally advanced unresectable or mTNBC who are unable to receive a PD-(L)1i.

Methods

Pts had centrally confirmed PD-L1– mTNBC (defined as combined positive score [CPS] < 10) or PD-L1+ mTNBC (CPS ≥ 10) but were unable to receive PD-(L)1i due to a comorbidity or prior use in the curative setting. Randomization (1:1) to SG (10 mg/kg IV, days 1 & 8 in 21-day cycles) or chemo (paclitaxel, nab-paclitaxel, or gemcitabine + carboplatin) was stratified by disease status and geography. The primary end point was PFS by BICR. Key secondary end points included overall survival (OS), ORR and DOR by BICR, and safety.

Results

558 pts (279 in each group) with mTNBC were randomized. With a median follow-up of 13.2 mo, SG showed a significant improvement in median PFS vs chemo (9.7 vs 6.9 mo; HR, 0.62; 95% CI, 0.50-0.78; $P < .0001$); median DOR was 12.2 mo vs 7.2 mo (Table). OS data were immature. The most frequent grade ≥ 3 TEAEs were neutropenia (43%) and diarrhea (9%) with SG and neutropenia (41%) and anemia (16%) with chemo.

Conclusions

SG led to a statistically significant and clinically meaningful improvement in PFS and more durable responses vs chemo in 1L mTNBC. The safety profile of SG was manageable and consistent with its known profile; treatment discontinuation rate due to TEAEs was lower with SG vs chemo. These data support SG as a potential new standard of care for pts with previously untreated mTNBC who are unable to receive a PD-(L)1i.Table: LBA20

Efficacy: Intent-to-treat	SG (n = 279)	Chemo (n = 279)

Efficacy: Intent-to-treat	SG (n = 279)	Chemo (n = 279)
Median PFS per BICR (95% CI), mo	9.7 (8.2-11.1)	6.9 (5.6-8.3)
HR (95% CI); adjusted two-sided *P*-value	0.62 (0.50-0.78);*P* < .0001	
ORR (95% CI), %	48.4 (42.4-54.4)	45.5 (39.6-51.6)
Median DOR (95% CI), mo	12.2 (9.7-13.8)	7.2 (5.7-8.4)
Safety: All treated	n = 275	n = 276
TEAEs, n (%) Any gradeGrade ≥ 3Led to dose reductionLed to treatment discontinuation	273 (99)181 (66)101 (37)10 (4)	269 (97)171 (62)124 (45)33 (12)

BICR, blinded independent central review; DOR, duration of response; HR, hazard ratio; ORR, objective response rate; PFS, progression-free survival; TEAE, treatment-emergent adverse event.

Clinical trial identification

NCT05382299.

Editorial acknowledgement

Editorial assistance was provided by Peggy Robinet, PharmD, PhD, and Sonal S. Joshi, PhD, of Parexel, and funded by Gilead Sciences, Inc.

Legal entity responsible for the study

Gilead Sciences, Inc.

Funding

Gilead Sciences, Inc.

Disclosure

J.C. Cortés: Financial Interests, Personal, Advisory Board, consulting/advisor: Roche, AstraZeneca, Seattle Genetics, Daiichi Sankyo, Lilly, Merck Sharpe & Dohme, Leuko, Bioasis, Clovis oncology, Boehringer Ingelheim, Ellipses, Hibercell, BioInvent, Gemoab, Gilead, Menarini, Zymeworks, Reveal Genomics, Expres2ion Biotechnologies, Jazz Pharmaceuticals, AbbVie, Scorpion Therapeutics, Bridgebio, Biocon, Biontech, Circle Pharma, Delcath Systems, Hexagon Bio; Financial Interests, Personal, Invited Speaker: Roche, Novartis, Eisai, Pfizer, Lilly, MERCK SHARP& DOHME, Daiichi Sankyo, AstraZeneca, Gilead, Steamline Therapeutics; Financial Interests, Personal, Stocks/Shares: MAJ3 Capital; Financial Interests, Personal, Stocks/Shares, (relative): Leuko; Financial Interests, Institutional, Research Grant: Roche, Ariad Pharmaceuticals, AstraZeneca, Baxalta GMBH/Servier Affaires, Bayer healthcare, Eisai, Guardanth health, Merck Sharp&Dohme, Pfizer, Piqur Therapeutics, Queen Mary University of London, Iqvia; Other, Travel cost and expenses: Roche, Novartis, Eisai, Daiichi Sankyo, Pfizer, Gilead, AstraZeneca, Steamline Therapeutics; Other, travel cost and expenses: Merck Sharp&Dhome. A. Bardia: Financial Interests, Personal, Advisory Board: Pfizer, Novartis, Genentech, Merck, Sanofi, Eisai, Lilly, Mersana, AstraZeneca/Daiichi, Menarini, Gilead; Financial Interests, Personal, Royalties: UpToDate; Financial Interests, Institutional, Coordinating PI: Genentech, Novartis, Pfizer, Merck, Sanofi, Gilead, Daiichi Pharma/AstraZeneca, Eli Lilly, Menarini; Non-Financial Interests, Principal Investigator: Gilead, Mersana, AstraZeneca/Daiichi, Novartis, Pfizer, Genentech, Lilly, Merck, Sanofi. K. Punie: Financial Interests, Personal, Other, Consultancy: Gilead, Novartis, MSD, Roche; Financial Interests, Personal, Invited Speaker: Sanofi, AstraZeneca, Exact Sciences, Focus Patient, Pfizer, Gilead Sciences, Eli Lilly, Eli Lilly, Medimix, Menarini-Stemline; Financial Interests, Personal, Advisory Board: Seagen, AstraZeneca, Pfizer, NordicPharma, Menarini-Stemline; Financial Interests, Personal, Other, External Advisor: National Reimbursement Committee; Financial Interests, Personal, Other, External Scientific Advisor: EMA; Non-Financial Interests, Leadership Role, Vice President: Belgian Society of Medical Oncology BSMO; Non-Financial Interests, Leadership Role: EORTC Breast Cancer Task Force Steering Committee Member; Non-Financial Interests, Advisory Role: Commission personalized medecine Federal Government Belgium; Non-Financial Interests, Advisory Role, External Scientific Advisor: European Medicine Agency. C.H.E. Barrios: Financial Interests, Personal, Advisory Board, Consulting scientific presentations: Novartis, Pfizer, Roche, Msd, AstraZeneca, Lilly; Financial Interests, Personal, Advisory Board, Scientific Presentations Consulting AD Board: Daiichi Sankyo; Financial Interests, Personal, Invited Speaker, Consulting Scientific presentations: GILEAD; Financial Interests, Personal, Ownership Interest, APP: THUMMI; Financial Interests, Personal, Ownership Interest, CLINICAL research company: MEDSIR; Financial Interests, Personal, Ownership Interest, Clinical Research Company: Centro de Pesquisa em Oncologia - CPO; Financial Interests, Institutional, Research Grant, research funding to the institution: Pfizer, Amgem, GSK, Lilly, Sanofi, Merk, BMS, Exelixis, Merck KGAA, Pharmamar; Financial Interests, Institutional, Research Grant, research funding to the institution Steering Committee: Novartis, AstraZeneca, Daiichi; Financial Interests, Institutional, Research Grant, Research funding to the institution Steering committee: Roche; Financial Interests, Institutional, Local PI, Research funding to the institution: Janssen, OBI Pharma, Seagen, Novocure, Aveo Oncology, Takeda, TRIO, PPD, Syneos health, Labcorp, IQIVIA, Parexel, Nuvisan, PSI, Medplace; Financial Interests, Institutional, Research Grant, Research grant to the institution: Fortrea, Toolbar, Worldwide; Financial Interests, Institutional, Research Grant, Research Grant to the Institution: Dizal Pharma; Financial Interests, Institutional, Research Grant, Research Grant to the institution: Stemline, Samsung, Icon, Biontech, Taiho; Non-Financial Interests, Leadership Role, Latin American

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All other authors have declared no conflicts of interest.