

18420
Efficacy and safety of atirmociclib (ATI) + fulvestrant (FUL) in patients (pts) with HR+/HER2– advanced/metastatic breast cancer (mBC) who progressed on prior CDK4/6 inhibitor (CDK4/6i) in a randomized phase 2 study (FOURLIGHT-1)

A. Giordano¹, B. Xu², Y.H. Park³, C-S. Huang⁴, G.L. Lerzo⁵, H. Li⁶, A. Shai⁷, G. Garnica Jaliffe⁸, M. Ito⁹, A. Williams¹⁰, S. Goel¹¹, S-A. Im¹², P.W. Cobb¹³, M. Golmakani¹⁴, F. Liu¹⁵, J. Gong¹⁶, A. Vana¹⁵, M. Ignatiadis¹⁷, T. Yoshinami¹⁸, H.S. Rugo¹⁹

¹ Department of Medical Oncology, Dana–Farber Cancer Institute, Harvard Medical School, Boston, United States of America, ² Department of Medical Oncology, Chinese Academy of Medical Science - National Cancer Center, Cancer Hospital, Beijing, China, ³ Department of Haemato-Oncology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea, ⁴ Department of Surgery, National Taiwan University Hospital, Taipei City, Taiwan, ⁵ Department of Oncology, LUCEN Centro Médico - Oncología, Buenos Aires, Argentina, ⁶ Department of Breast Medical Oncology, Peking University Cancer Hospital & Institute, Beijing, China, ⁷ Oncology Department, Rambam Health Care Campus, Haifa, Israel, ⁸ Medical Oncology Department, Hospital General de Mexico Dr. Eduardo Liceaga SSA, Ciudad De Mexico, Mexico, ⁹ Hiroshima City Hiroshima Citizens Hospital, Hiroshima, Japan, ¹⁰ Sarah Cannon Research Institute, London, United Kingdom, ¹¹ Department of Cancer Research, Peter MacCallum Cancer Centre, Melbourne, Australia, ¹² Internal Medicine Department, Seoul National University Hospital, Seoul, Republic of Korea, ¹³ St. Vincent Cancer Centers of Montana, Billings, United States of America, ¹⁴ Department of Oncology Biostatistics, Pfizer Inc., San Diego, United States of America, ¹⁵ Department of Oncology Late Stage Development, Pfizer Inc., San Diego, United States of America, ¹⁶ Department of Oncology Late Stage Development, Pfizer Inc., New York, United States of America, ¹⁷ Department of Medical Oncology, Institut Jules Bordet, Hôpital Universitaire de Bruxelles, Université Libre de Bruxelles, Anderlecht, Belgium, ¹⁸ Department of Breast and Endocrine Surgery, Graduate School of Medicine, The University of Osaka, Suita, Japan ¹⁹ Department of Medical Oncology and Therapeutics Research, City of Hope Comprehensive Cancer Center, Duarte, United States of America

Background

CDK4/6i + endocrine therapy (ET) is the standard-of-care 1L treatment of HR+/HER2– mBC for nearly a decade, yet durable disease control remains elusive. ATI (PF-07220060) is a next-generation cell cycle inhibitor that is highly selective for CDK4. In a phase 1/2a study, ATI + ET (letrozole [LET] or FUL) was well tolerated and showed encouraging antitumor activity in pts with HR+/HER2– mBC. We present results from the first randomized study of ATI + FUL vs investigator’s choice of standard therapy (ICT) in pts with HR+/HER2– mBC who progressed on prior adjuvant or 1L CDK4/6i.

Methods

FOURLIGHT-1 (NCT06105632) is an open-label, multicenter phase 2 study; pts were randomized 1:1 to ATI (300 mg PO BID) + FUL or ICT (FUL alone or everolimus [EVE] + exemestane [EXE]). Pts were stratified by disease site (visceral vs nonvisceral) and prior CDK4/6i duration (<12 vs ≥12 mos). Primary endpoint was investigator-assessed PFS. Secondary endpoints included OS, ORR, DOR, CBR, and safety.

Results

At data cutoff (12 January 2026), 263 pts were enrolled (ATI, n=126; ICT, n=137). Median age was 57 y; as the immediate prior therapy, 94.3% of pts received 1L CDK4/6i and 3.8% received adjuvant CDK4/6i. PFS was significantly improved with ATI vs ICT (Table). A consistent PFS benefit was observed across most prespecified subgroups. OS is not yet mature; Table shows ORR, DOR, and CBR. The most common TRAEs in the ATI arm were neutropenia (46.4%) and leukopenia (32.8%); 4.0% of pts discontinued ATI due to TRAEs.

Conclusions

ATI (+ FUL) is the first next-generation CDKi to show significant and clinically meaningful PFS improvement in pts who progressed on prior CDK4/6i, while maintaining a manageable safety profile. These data support continued development in earlier lines, including an ongoing phase 3 study of ATI vs CDK4/6i (+ LET) in 1L HR+/HER2– mBC. Table: 18420

	ATI + FUL (n=126)	ICT (n=137 [FUL alone, n=79; EVE + EXE, n=58])
Median follow-up duration (95% CI), mos	13.7 (11.6–13.8)	13.6 (11.1–14.0)
PFS		
Median (95% CI), mos	9.4 (7.3–13.6)	6.6 (3.8–7.8)
HR (95% CI)	0.60 (0.440–0.825)	
1-sided P value	0.0007	

	ATI + FUL (n=126)	ICT (n=137 [FUL alone, n=79; EVE + EXE, n=58])
ORR		
Measurable disease, n	109	115
ORR ^a , % (95% CI)	19.3 (13.0–27.7)	11.3 (6.7–18.4)
Odds ratio (95% CI)	1.914 (0.849–4.366)	
1-sided <i>P</i> value	0.0451	
DOR		
Confirmed CR or PR, n	21	13
Median (95% CI), mos	14.8 (7.4–NE)	9.3 (5.5–NE)
CBR		
CBR ^b , % (95% CI)	61.9 (53.2–69.9)	46.0 (37.9–54.3)
Odds ratio (95% CI)	1.972 (1.154–3.382)	
1-sided <i>P</i> value	0.0041	

^aConfirmed CR or PR. ^bConfirmed CR, PR, or SD/non-CR/non-PD (for pt/s with nonmeasurable disease) ≥24 wks.

Clinical trial identification

NCT06105632.

Editorial acknowledgement

Medical writing support was provided by Diana Avery, PhD, of Oxford PharmaGenesis Inc., Wilmington, DE, USA, and was funded by Pfizer Inc.

Legal entity responsible for the study

Pfizer Inc.

Funding

Pfizer Inc.

Disclosure

A. Giordano: Financial Interests, Personal, Advisory Board: Pfizer, Novartis; Financial Interests, Personal, Advisory Board, Singapore ESMO ASIA: Pfizer; Financial Interests, Personal, Other, Travel grant - ESMO ASIA: Pfizer; Financial Interests, Personal, Advisory Board, PIK3CA AD board: Lilly; Financial Interests, Personal, Advisory Board, ctDNA ad board: Guardant Health; Financial Interests, Personal, Other, travel ESMO annual meeting 2025: Lilly; Financial Interests, Personal, Advisory Board, Vepdeg: Arvinas; Financial Interests, Personal, Other, Travel - ESMO TAT 2026: Totus Medicine; Financial Interests, Institutional, Funding, Sponsor funds IST: Cardiff Oncology. B. Xu: Financial Interests, Personal, Financially compensated role: Novartis, AstraZeneca. Y.H. Park: Financial Interests, Personal, Advisory Board: AstraZeneca, Pfizer, Roche, Novartis, MSD, Daiichi Sankyo, Helsinn, Voronoi, Aimer Blo, BeOne, Gilead, ALX Oncology; Financial Interests, Personal, Invited Speaker: AstraZeneca, Pfizer, Roche, Novartis, MSD, Daiichi Sankyo, Relay Therapeutics; Financial Interests, Institutional, Other, Research Grant: AstraZeneca, Pfizer, Roche, MSD, Novartis; Financial Interests, Personal, Writing Engagement: Lilly; Non-Financial Interests, , Principal Investigator: AstraZeneca, Pfizer, Novartis, MSD, Lilly, Roche, Daiichi Sankyo; Non-Financial Interests, , Member of Board of Directors: Menarini-Stemline; Non-Financial Interests, , Advisory Role: OnKure, Daewoong, Inocras, ALX Oncology, Relay Therapeutics. C. Huang: Financial Interests, Personal, Invited Speaker, Speakers bureaus: Daiichi Sankyo; Financial Interests, Personal, Invited Speaker, speakers bureaus: Astra Zeneca, Pfizer, Novartis, Roche, Eli Lilly, Gilead; Financial Interests, Personal, Advisory Board, Advisory Role: Daiichi Sankyo, Astra Zeneca, Eli Lilly, Pfizer, Novartis, Roche, Gilead, EirGenix; Financial Interests, Institutional, Research Grant, research grants to institution: Daiichi Sankyo; Financial Interests, Institutional, Research Grant, Research grants to institution.: Astra Zeneca, EirGenix, Eli Lilly, MSD, OBI Pharma, Pfizer, Roche, Novartis, Seagen, Gilead, Aston Sci, Stemline Therapeutics. A. Shai: Financial Interests, Personal, Speaker, Consultant, Advisor: Eli Lilly, Roche, Novartis, Gilead; Financial Interests, Personal, Advisory Board: Eli Lilly, Roche, Novartis, Gilead; Financial Interests, Personal, Speaker’s Bureau: Roche; Financial Interests, Personal, Other, Travel Support: Roche, AstraZeneca. A. Williams: Financial Interests, Personal, Advisory Board: Ellipses Pharma; Financial Interests, Personal, Full or part-time Employment, I work for SCRI as a Medical Oncologist: HCA Healthcare UK, Sarah Cannon Research Institute. S. Goel: Financial Interests, Personal, Research Grant: Eli Lilly, Incyclix Bio, G1 Therapeutics; Financial Interests, Personal, Research Grant, (GNT1177357): National Health and Medical Research Council of Australia; Financial Interests, Personal, Research Grant, (Grant No. SF2020-47): Snow Medical Research Foundation; Financial Interests, Personal, Financially compensated role: Incyclix Bio, Novartis, Pfizer, Belharra Therapeutics. S. Im: Financial Interests, Personal, Advisory Board, no payment: AstraZeneca, Novartis, Eisai, Roche, Pfizer, Lilly, MSD, Daiichi-Sankyo, SK Biopharmaceuticals Co., Ltd., Gilead Sciences; Financial Interests, Institutional, Research Grant: AstraZeneca, Pfizer, Roche, Eisai; Financial Interests, Institutional, Local PI,

Clinical Trial Budget: AstraZeneca, Novartis, Roche, Pfizer, Daiichi-Sankyo, MSD, Lilly; Financial Interests, Institutional, Coordinating PI, Clinical Trial Budget: Eisai; Financial Interests, Institutional, Research Grant, Clinical Trial Budget: Boryung Pharm. P.W. Cobb: Financial Interests, Personal, Research Funding: GTx. M. Golmakani: Financial Interests, Personal, Full or part-time Employment: Pfizer Inc.; Financial Interests, Personal, Stocks/Shares: Pfizer Inc. F. Liu: Financial Interests, Personal, Full or part-time Employment: Pfizer Inc.; Financial Interests, Personal, Stocks/Shares: Pfizer Inc. J. Gong: Financial Interests, Personal, Full or part-time Employment: Pfizer Inc.; Financial Interests, , Stocks/Shares: Pfizer Inc. A. Vana: Financial Interests, Personal, Full or part-time Employment: Pfizer Inc.; Financial Interests, Personal, Stocks/Shares: Pfizer Inc. M. Ignatiadis: Financial Interests, Institutional, Other, Consultant: Novartis, Daichi, Menarini Group; Financial Interests, Institutional, Other, Independent monitoring committee: Seattle Genetics; Financial Interests, Institutional, Other, consultant: Rejuveron Senescence Therapeutics; Financial Interests, Institutional, Other, travel grants: Astra Zeneca; Financial Interests, Institutional, Other, Travel grant: Gilead, Roche, Daiichi Sankyo, Novartis; Financial Interests, Institutional, Coordinating PI: Roche, Natera, Inivata Inc; Financial Interests, Institutional, Coordinating PI, Real world study: Gilead; Non-Financial Interests, , Officer: EORTC. T. Yoshinami: Financial Interests, Personal, Other, payment/honoraria: Eli Lilly Japan, AstraZeneca, Chugai Pharmaceutical, Kyowa Kirin, Pfizer, MSD, Eisai, Daiichi Sankyo. H.S. Rugo: Financial Interests, Personal, Advisory Board, Consultancy/advisory support: Napo; Financial Interests, Personal, Other, Advisory/Consultant: Bristol Myers Squibb; Financial Interests, Personal, Other, Consulting/Advisory Role: Helsinn, Biontech Rna Pharmaceuticals GMBH; Financial Interests, Institutional, Research Grant: Novartis, Lilly, Pfizer, F. Hoffmann-La Roche/Genentech, Inc., Daiichi Sankyo, Astra Zeneca, Gilead Sciences, Inc., Stemline Therapeutics, Ambryx, Bicycle Therapeutics, PhoenixMD, Relay Therapeutics, ALX Oncology, Mabwell; Financial Interests, Institutional, Coordinating PI: Merck. All other authors have declared no conflicts of interest.