touchIME ONCOLOGY®

touchCONGRESS webinar

HR+/HER2- Advanced breast cancer: what are the latest developments in CDK4/6 inhibition?

Dr. Joyce A. O'Shaughnessy, Baylor-Sammons Cancer Center, Texas, USA

Webinar recorded June 2019

This activity is supported by an educational grant from Eli Lilly and Company.

Disclaimer

Unapproved products or unapproved uses of approved products may be discussed by the faculty; these situations may reflect the approval status in one or more jurisdictions.

The presenting faculty have been advised by touchIME to ensure that they disclose any such references made to unlabelled or unapproved use.

No endorsement by touchIME of any unapproved products or unapproved uses is either made or implied by mention of these products or uses in touchIME activities.

touchIME accepts no responsibility for errors or omissions.

touchime
INNOVATION.KNOWLEDGE.OUTCOMES

Disclosures

Received honoraria as a speaker or consultant from:

AbbVie Inc., Agendia, Amgen Biotechnology, AstraZeneca, Bristol-Myers Squibb, Celgene Corporation, Eisai, Genentech, Genomic Health, GRAIL, Immunomedics, Heron Therapeutics, Ipsen Biopharmaceuticals, Jounce Therapeutics, Lilly, Merck, Myriad, Novartis, Odonate Therapeutics, Pfizer, Puma Biotechnology, Roche, Seattle Genetics and Syndax Pharmaceuticals.

Webinar overview

HR+/HER2- advanced breast cancer

- Part 1: Current treatment landscape for CDK4/6 inhibitors
- Part 2: ASCO Annual Meeting 2019 – Recent evidence for CDK4/6 inhibitors
- Part 3: ASCO Annual Meeting 2019 – Identifying predictive biomarkers for CDK4/6 inhibitors: where are we now?
- Part 4: ASCO Annual Meeting 2019 – Next directions for CDK4/6 inhibitors

CDK, cyclin-dependent kinase.

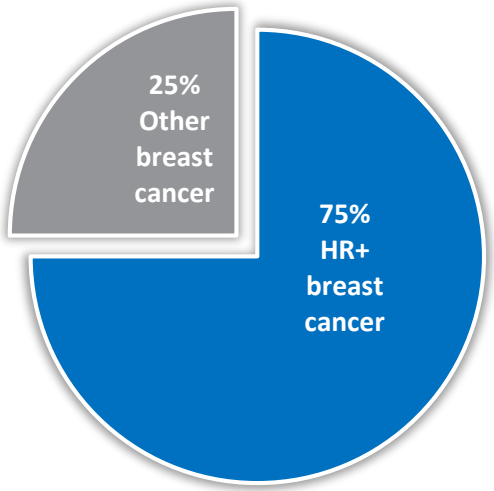
touchime
INNOVATION.KNOWLEDGE.OUTCOMES

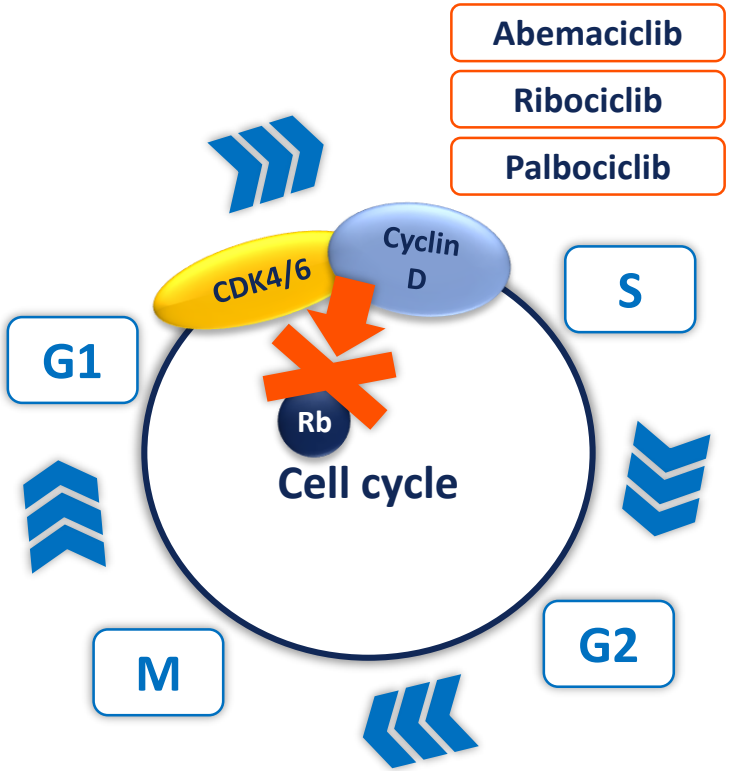
Part 1.
Current treatment landscape for CDK4/6 inhibitors

Focus on CDK4/6 inhibitors for HR+/HER2- advanced breast cancer

CDK, cyclin-dependent kinase; HER2-, human epidermal growth factor receptor 2 negative; HR+, hormone receptor positive.

Breast cancer and CDK4/6 inhibitors





CDK4/6, cyclin-dependent kinase 4/6, Rb, retinoblastoma protein.
Perou CM, Sørlie T, Eisen MB, et al. *Nature*. 2000;406:747–752; Vidula N and Rugo HS. *Clin Breast Cancer* 2016;16(1):8–17.

Key clinical trials of CDK4/6 inhibitors for the treatment of HR+/HER2- advanced breast cancer

First-line/AI-sensitive		
Trial (N)	**Treatment**	**PFS HR (95%CI)**
PALOMA-2 N=666	**Letrozole+palbociclib** Letrozole+placebo	**27.6 vs.14.5 0.56 (0.46–0.69)**
MONALEESA-2 N=668	**Letrozole+ribociclib** Letrozole+placebo	**25.3 vs. 16.0 0.57 (0.46–0.70)**
MONARCH-3 N=493	**AI+abemaciclib** AI+placebo	**28.8 vs. 14.8 0.54 (0.42–0.70)**
MONALEESA-3 N=367	**Fulvestrant+ribociclib** Fulvestrant+placebo	**NR vs. 18.3 0.58 (0.42–0.80)**
MONALEESA-7 N=672	**AI + goserelin +ribociclib** AI + goserelin	**23.8 vs. 13 0·55 (0·44–0·69)**

Second-line/endocrine resistant		
Trial	**Treatment**	**PFS HR (95%CI)**
PALOMA-3 N=521	**Fulvestrant+palbociclib** Fulvestrant+placebo	**11.2 vs. 4.6 0·50 (0·40–0·62)**
MONARCH-2 N=669	**Fulvestrant+abemaciclib** Fulvestrant+placebo	**16.4 vs. 9.3 0.55 (0.45–0.68)**
MONALEESA-3 N=345	**Fulvestrant+ribociclib** Fulvestrant+placebo	**14.6 vs. 9.1 0.57 (0.43–10.74)**

CDK, cyclin-dependent kinase; CI, confidence interval; HER2-, human epidermal growth factor receptor 2 negative; HR, hazard ratio; HR+, hormone receptor positive; PFS, progression-free survival.

Finn, *N Engl J Med* 2016; Rugo H, SABCS 2017; Hortobagyi G, *N Engl J Med* 2016 & *Ann Oncol* 2018; Goezt M, *J Clin Oncol* 2017 & AACR 2018; Tripathy D. *Lancet Oncol.* 2018;19:904–915; Turner N, *N Engl J Med* 2015, updated SABCS 2016; Cristofanilli M, *Lancet Oncol* 2016; Sledge, *J Clin Oncol* 2017; Slamon DJ, ASCO 2018.

Adverse event profiles for CDK4/6 inhibitors in advanced breast cancer

Most common grade 3/4 adverse events

Abemaciclib (MONARCH-3)[1]

Neutropenia	21.1%	vs.	1.2%
Diarrhoea	9.5%	vs.	1.2%
Leukopenia	7.6%	vs.	0.6%
Anaemia	5.8%	vs.	1.2%

Palbociclib (PALOMA-2)[2]

Neutropenia	66.4%	vs.	1.4%
Leukopenia	24.8%	vs.	0%
Anaemia	5.4%	vs.	1.8%
Asthenia	2.3%	vs.	0%

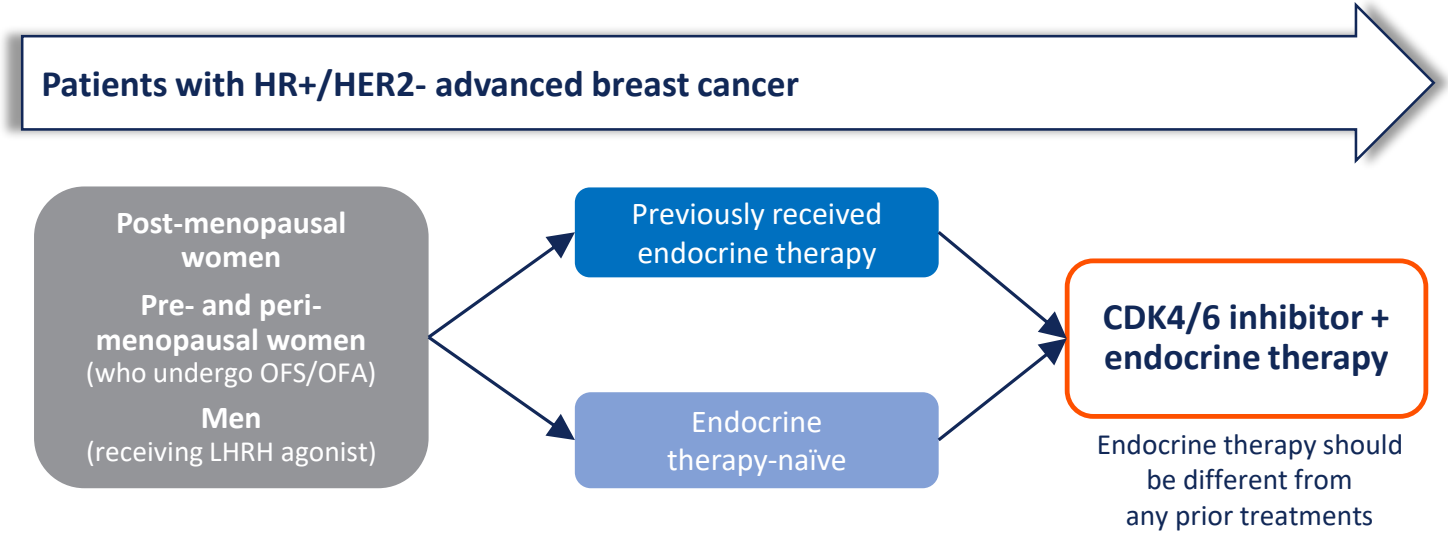
Ribociclib (MONALEESA-2)[3]

Neutropenia	62%	vs.	7%
Leukopenia	21.3%	vs.	0.9%
Abnormal LFTs	10.2%	vs.	2.4%
Vomiting	3.6%	vs.	0.9%

CDK, cyclin-dependent kinase; LFT, liver function test.

1. Goetz MP, et al. *J Clin Oncol.* 2017;35:3638–3646; 2. Finn RS, et al. *N Engl J Med.* 2016;375:1925–1936; 3. Hortobagyi GN, et al. *Ann Oncol.* 2018;29:1541–1547.

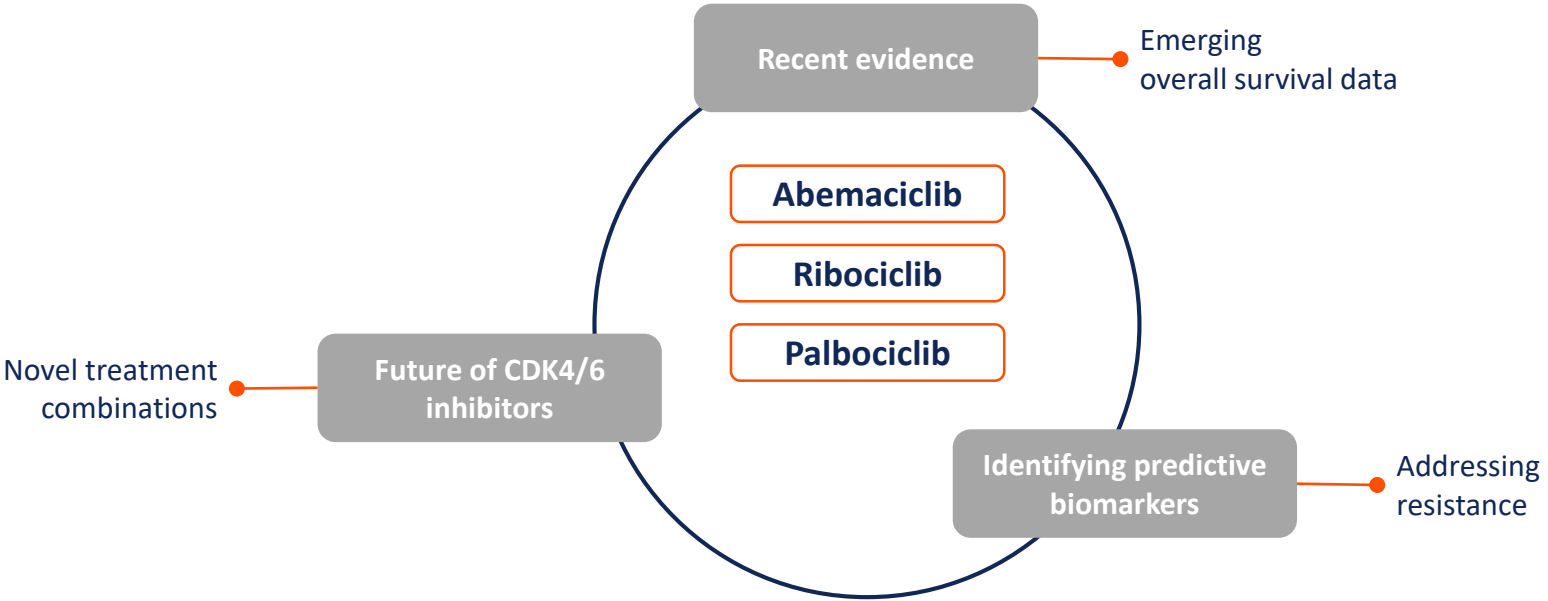
Treatment strategy for advanced breast cancer



CDK, cyclin-dependent kinase; HER2-, human epidermal growth factor receptor 2 negative; HR+, hormone receptor positive; LHRH, luteinizing hormone-releasing hormone; OFA, ovarian function ablation; OFS ovarian function suppression.

Cardoso F, et al. *Ann Oncol*. 2018;29:1634–1657; NCCN Clinical Practice Guidelines Breast Cancer. Version 1.2019. Available at NCCN.org.

CDK4/6 inhibitors: clinical areas of interest



Clinical areas of interest include identifying predictive biomarkers, the optimal treatment sequence for each patient and best management for patients after disease progression on CDK4/6 inhibitors

CDK, cyclin-dependent kinase.
Portman N. *Endocr Relat Cancer* 2019; 26:R15–R30.

touchime
INNOVATION.KNOWLEDGE.OUTCOMES

Part 2.
ASCO Annual Meeting 2019 – Recent evidence for CDK4/6 inhibitors

Focus on CDK4/6 inhibitors for HR+/HER2- advanced breast cancer

CDK, cyclin-dependent kinase; HER2-, human epidermal growth factor receptor 2 negative; HR+, hormone receptor positive.

touchime
INNOVATION.KNOWLEDGE.OUTCOMES

Phase III MONALEESA-7 trial of premenopausal patients with HR+/HER2- ABC therapy treated with endocrine therapy ± ribociclib: OS results

Hurvitz SA, et al.

OS results from MONALEESA-7

Premenopausal patients with HR+/HER2- (N=672)

Median follow-up (months)	34.6	
Number on treatment at data cut-off (N=173)	n=116	n=57
OS evaluated after 192 deaths	n=83	n=109

Prespecified interim analysis: Data cut-off Nov 30, 2018

	RIB + ET	PBO + ET	
OS, months (95% CI)	**Not reached**	40.9	HR, 0.712 (95% CI, 0.54–0.95) p = 0.00973
Estimated OS rates at 42 months	**70.2%**	46%	**~29% relative reduction in risk of death**

- In patients who received an NSAI (n=495) RIB + ET demonstrated a consistent OS improvement vs PBO + ET (HR, 0.699; 95% CI, 0.50-0.98)
- Post-treatment therapy use was balanced between treatment arms (RIB, 69%; PBO, 73%)

RIB + ET demonstrated a clinically and statistically significant longer OS than ET alone in premenopausal patients with HR+/HER2– ABC

ABC, advanced breast cancer; CI, confidence interval; ET, endocrine therapy; HER2- human epidermal receptor 2-negative; HR, hazard ratio; HR+ hormone receptor-positive; NE, not evaluable; NSAI, nonsteroidal aromatase inhibitor; OS, overall survival; PBO, placebo; RIB, ribociclib.

Hurvitz SA, et al. Abstract LBA 1008 Presented at the ASCO Annual Meeting 2019.

touchime
INNOVATION.KNOWLEDGE.OUTCOMES

First-line ribociclib plus letrozole for postmenopausal women with HR+/HER2- ABC: MONALEESA-2 long-term safety results

O'Shaughnessy J, et al.

Long-term safety data from MONALEESA-2

	RIB+LET arm	PBO+LET arm
Data cut-off: October, 2018		
Number on treatment at data cut-off	79 (23.7%) pts	39 (11.7%) pts
Median duration of exposure	20.2 months (range, 0-54)	14.1 months (range, 0-54)
Discontinuations due to AEs	19.2%	4.2%

AEs were the most common reason for RIB dose reductions (56.6%) and interruptions (73.4%)

AEs occurring with first-line ribociclib + letrozole in postmenopausal patients with HR+/HER2- ABC were manageable and the safety profile was comparable to that in the primary report

Exposure-adjusted AESI in the phase III MONALEESA-2 study

Exposure-adjusted AEs, rate per 100 pt Tx years	RIB + LET (n = 334)	PBO + LET (n = 330)
Neutropenia	92.1	3.7
Nausea	56.7	27.1
Fatigue	34.7	31.8
Diarrhoea	33.0	21.8
Alopecia	28.2	12.5
Arthralgia	25.7	33.0
Vomiting	24.5	14.0
Constipation	20.0	16.9

Neutropenia was the most common exposure-adjusted AESI in the RIB + LET arm

ABC, advanced breast cancer; AE. adverse event; AESI, AE of special interest; HER2- human epidermal receptor 2-negative; HR+ hormone receptor-positive; LET, letrozole; PBO , placebo; pt, patient; RIB, ribociclib; Tx, treatment.

O'Shaughnessy J, et al. Abstract 1078 Presented at the ASCO Annual Meeting 2019.

Interim results from the full population of the phase 3b CompLEEment-1 study of ribociclib plus letrozole in the treatment of HR+/HER2- ABC

De Laurentiis M, et al.

Interim safety and efficacy results from CompLEEment-1, a large phase 3b trial evaluating RIB+LET in an expanded patient population

Men and women (N=3,246) with HR+/HER2- ABC, ≤1 line of prior chemotherapy, and no prior ET received RIB+LET

- ↑ alanine (7.3%) and ↑ aspartate (5.3%) aminotransferase were the only non-haematological any-cause grade ≥3 AEs ≥5%
- Treatment-related AEs (any grade) led to discontinuation in 11.4% patients. Of the 51 (1.6%) on-treatment deaths, 26 were due to study indication and 25 to other reasons

Efficacy results: Patients (N=3,246) receiving ≥1 dose of RIB+LET		
Median duration of RIB exposure	8.1 months	Range, 0.0–22.4
Median time to progression	NE	95% CI, 17.1–NE
Overall response rate	20.5%	95% CI, 19.1–21.9
Clinical benefit rate	66.1%	95% CI, 64.4–67.7

This interim analysis demonstrates the safety, tolerability and efficacy of RIBO+LET in a large, diverse cohort of patients with HR+/HER2- ABC who had not previously received ET for ABC, and no new safety signals were observed

ABC, advanced breast cancer; AE. Adverse event; CDK, cyclin-dependent kinase; ET, endocrine therapy; HER2- human epidermal receptor 2-negative; HR+ hormone receptor-positive; LET, letrozole; NE, not estimable; pt, patient; RIB, ribociclib.

De Laurentiis M, et al. Abstract 1041 Presented at the ASCO Annual Meeting 2019.

A multicentre analysis of abemaciclib after progression on palbociclib in patients with HR+/HER2- MBC

Wander SA, et al.

Clinical outcomes of abemaciclib in patients with HR+/HER2- MBC after progressive disease with palbociclib or ribociclib at 4 US academic centres

From February 2015 to January 2019

58 patients with HR+/HER2- MBC received abemaciclib following progression on prior palbociclib

- **20 pts (34%)** received sequential courses of therapy
- **38 pts (66%)** received ≥1 intervening non-CDK4/6 inhibitor regimen
- **14 pts (24%)** received abemaciclib monotherapy
- **44 pts (76%)** received abemaciclib plus an antioestrogen
- **23 pts (40%)** required dose reduction
- **8 pts (14%)** discontinued due to toxicity

At data cut-off, 5th January 2019

15 pts (26%) had early PD (duration <90 days)

25 pts (43%) had treatment duration >6 months; 11 remained on treatment at interim analysis (range 197–460 days)

Median PFS = 5.4 months (95% CI 3.5–8.0)

This multicentre analysis demonstrates that a substantial proportion of patients continue to derive clinical benefit with abemaciclib after prior CDK4/6 inhibitor, highlighting the potential for its use following CDK4/6 blockade.

A second subset had early progression, suggesting cross-resistance to CDK4/6 inhibitor via common pathways

CDK, cyclin-dependent kinase; HER2- human epidermal receptor 2-negative; HR+ hormone receptor-positive; MBC, metastatic breast cancer; PD progressive disease; pt, patient.

Wander SA, et al. Abstract 1057 Presented at the ASCO Annual Meeting 2019.

Summary

- OS data from the MONALEESA-7 trial showed that ribociclib plus ET demonstrated a clinically and statistically significant longer OS than ET alone in premenopausal pts with HR+/HER2− ABC. This is the first report of an OS benefit with a CDK4/6 inhibitor + ET
- Long-term safety data for ribociclib from the MONALEESA-2 trial showed that adverse events were manageable and the safety profile had not changed from the primary report
- Safety and efficacy of ribociclib plus letrozole was also demonstrated for a large and diverse cohort of patients with HR+/HER2- ABC who had not previously received ET
- A multicentre analysis of abemaciclib after previous CDK4/6 inhibitor treatment showed that while there may be a common pathway for CDK4/6 inhibitor cross-resistance, a substantial proportion of patients derived benefit from this therapy, providing some insight into potential treatment sequencing

ABC, advanced breast cancer; CDK, cyclin-dependent kinase; ET, endocrine therapy; HER2- human epidermal receptor 2-negative; HR+ hormone receptor-positive; OS, overall survival.

Part 3.
ASCO Annual Meeting 2019 – Identifying predictive biomarkers for CDK4/6 inhibitors: where are we now?

Focus on HR+/HER2- advanced breast cancer

CDK, cyclin-dependent kinase; HER2-, human epidermal growth factor receptor 2 negative; HR+, hormone receptor positive.

touchime
INNOVATION.KNOWLEDGE.OUTCOMES

In-depth gene expression analysis of premenopausal patients with HR+/HER2- ABC treated with ribociclib containing therapy in the Phase III MONALEESA-7 trial

Lu Y-S, et al.

A gene expression analysis of baseline tumour mRNA from MONALEESA-7

Premenopausal pts with HR+/HER2- ABC

RIB		PBO	
n=185	+ GOS + NSAI or TAM	n=175	+ GOS + NSAI or TAM

- Baseline archival tumour samples were evaluated for **gene expression**
- Patient subgroups were classified as having **low or high mRNA expression**

A trend toward a ↑**PFS benefit with RIB** was observed in pts with:

High vs. low expression of
- *CCND1* (HR 0.38 vs. 0.67)
- *IGF1R* (HR 0.33 vs. 0.77
- *ERBB3* (HR 0.33 vs. 0.76)

Low vs. high expression of
- *CCNE1* (HR 0.38 vs. 0.65)
- *MYC* (HR 0.37 vs. 0.69)

PFS benefit with RIB was similar in pts with:

High vs. low expression of
- *FGFR1* (HR 0.45 vs. 0.61)
- *ESR1* (HR 0.57 vs. 0.57)
- Tumour proliferation genes, such as *MKI67* (HR 0.50 vs. 0.51)

The benefit with RIB was generally consistent across gene expression subgroups, although the magnitude varied in certain subsets. This analysis suggests that there may be unique resistance mechanisms to ET ± CDK4/6 inhibitors in premenopausal pts with ABC, but more studies are needed.

ABC, advanced breast cancer; AE. Adverse event; CDK, cyclin-dependent kinase; ET, endocrine therapy; GOS, goserelin; HER2- human epidermal receptor 2-negative; HR+ hormone receptor-positive; ITT, intent-to-treat; NSAI, nonsteroidal aromatase inhibitor; PBO, placebo; PFS, progression free survival; pt, patient; RIB, ribociclib; TAM, tamoxifen.

Lu Y-S, et al. Abstract 1018 Presented at the ASCO Annual Meeting 2019.

Genomic markers of early progression on fulvestrant with or without palbociclib for ER+ advanced breast cancer in the PALOMA-3 trial

O'Leary B, et al.

Investigation of genomic aberrations in patients treated with fulvestrant, with and without palbociclib, with a circulating tumour DNA analysis of baseline plasma in the PALOMA-3 trial

Patients with HR+/HER2– ABC (N=521)

Randomized 2:1

Palbociclib + fulvestrant

Placebo + fulvestrant

Somatic mutations and copy number aberrations were characterized in 310 patients (203 palbociclib, 107 placebo) using baseline plasma samples

Palbociclib treatment was comparable with the overall trial result (HR 0.43, 95% CI 0.32–0.57, p<0.0001)

Whole cohort multivariable analysis

↑ baseline tumour purity in plasma was associated with ↓ PFS
(HR 1.20, 95% CI 1.09–1.32, p=0.0001, HR/10% ↑ in purity)

Baseline *TP53* mutation was associated with ↓PFS
(HR 1.84, 95% CI 1.27–2.65, p=0.0011)

Baseline *FGFR1* amplification was associated with ↓ PFS
(HR 2.91, 95% CI 1.61–5.25, p=0.0004)

PIK3CA and *ESR1* mutations had no significant association with PFS

TP53 mutations were significantly associated with the number of disease sites, soft tissue/LN and visceral metastases

_TP53_ mutation, _FGFR1_ amplification, and tumour purity in plasma, identified patients at-risk of early progression in PALOMA-3

ABC, advanced breast cancer; CI, confidence interval; HER2- human epidermal receptor 2-negative; HR, hazard ratio; HR+ hormone receptor-positive; PBO, placebo; PFS, progression-free survival.

O'Leary et al. Abstract 1010 Presented at the ASCO Annual Meeting 2019.

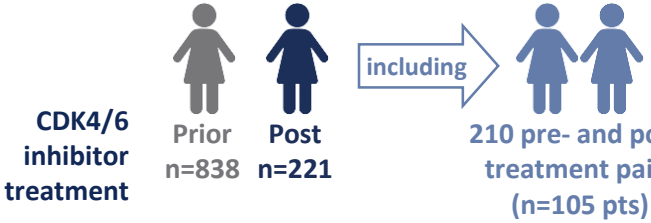
touchime
INNOVATION.KNOWLEDGE.OUTCOMES

Molecular profiling of ER+ metastatic breast cancers to reveal association of genomic alterations with acquired resistance to CDK4/6 inhibitors

Razavi P, et al.

Identify genomic alterations associated with acquired resistance to CDK4/6 inhibitor + anti-oestrogen combinations

Prospective tumour and matched normal sequencing on 1059 samples from 845 patients with MBC



Oncogenic mutations and copy number alterations were compared in samples from patients CDK4/6 inhibitor-naïve, post-CDK4/6 inhibitor treatment, and post-hormone alone therapy

Analysis of genes enriched post-CDK4/6 inhibitor treatment

- Significant enrichment of loss-of-function alterations in *RB1* in the post-CDK4/6i versus CDK4/6 inhibitor-naïve samples (7.9% vs. 2.7%, p=1.5e-5)
- LOH occurred in the majority of the *RB1* mutations in the post-CDK4/6 inhibitor tumours, and was uncommon in the CDK4/6 inhibitor-naïve tumours
- ↑ frequency of multiple alterations in PI3K/AKT signalling effectors (excluding *PIK3CA*), cell cycle (e.g. *CDKN2A* loss) and Hippo signalling, in post-CDK4/6 inhibitor tumours

Analysis identified enrichment of multiple genomic lesions after exposure to CDK4/6 inhibitors, highlighting therapy-related genomic evolution and identifying genomic subsets that might alter the benefit of subsequent lines of therapies

CDK, cyclin-dependent kinase; HR+ hormone receptor-positive; LOH, loss of heterozygosity; MBC, metastatic breast cancer; pts, patients..

Razavi P, et al. Abstract 1009 Presented at the ASCO Annual Meeting 2019.

Summary

- Gene expression analysis in MONALEESA-7 showed that the benefit of ribociclib was consistent across genetic subgroups, although there was some variation in the magnitude of effect
- In the PALOMA-3 trial, TP53 mutation, FGFR1 amplification, and tumour purity in plasma, identified patients at-risk of early progression
- Genetic analysis has also shown that therapy-related genomic evolution may occur following treatment with CDK4/6 inhibitors, which could be used to inform treatment-sequencing decisions

CDK, cyclin-dependent kinase; FGFR, fibroblast growth factor receptor.

Part 4.
ASCO Annual Meeting 2019 – Next directions for CDK4/6 inhibitors

Focus on HR+/HER2- advanced breast cancer

CDK, cyclin-dependent kinase; HER2-, human epidermal growth factor receptor 2 negative; HR+, hormone receptor positive.

touchime
INNOVATION.KNOWLEDGE.OUTCOMES

A phase II study of abemaciclib in patients with brain metastases secondary to HR+/HER2- MBC

Anders CK, et al.

Investigate the intracranial clinical response rates of abemaciclib in patients with BM secondary to HR+/HER2- MBC

Eligible patients

CDK4/6 inhibitor naïve pts with ≥1 new/not previously irradiated BM ≥10 mm or a progressive previously irradiated BM

Abemaciclib was orally administered 200mg BID

Patients (N=58)

- Median of 4 prior systemic therapies, 75.9% had prior chemotherapies and 87.9% had prior systemic therapies in the metastatic setting
- 46.6% of patients had prior whole brain radiotherapy, 34.5% stereotactic radiosurgery and 6.9% surgical resection of BM
- Median time from radiation to study enrolment was 9.4 months

Results

- 3 pts had a confirmed intracranial response (5% OIRR)
- 38% of pts showed a ↓ in the size of their intracranial target lesions
- Intracranial clinical benefit rate (CR+PR+SD persisting for ≥6 months) was 24%
- Median intracranial PFS was 4.9 months (95% CI, 2.9–5.6)
- Safety and tolerability were similar to previous reports for abemaciclib

Abemaciclib demonstrated intracranial clinical benefit in heavily pre-treated HR+/HER2- MBC pts with BM in this study

BID, twice a day; BM, brain metastases; CI, confidence interval; CR, complete response; ET, endocrine therapy; OIRR, objective intracranial response rate; PFS, progression-free survival; PR partial response; pts, patients; SD, stable disease.

Anders CK, et al. Abstract 1017 Presented at the ASCO Annual Meeting 2019.

A randomized phase II study of palbociclib plus exemestane with GNRH agonist versus capecitabine in premenopausal women with hormone receptor-positive metastatic breast cancer (KCSG-BR 15-10, NCT02592746)

Park YH, et al.

Assess the safety and the clinical anti-tumour activity of exemestane plus GNRH agonist in combination with palbociclib versus capecitabine in premenopausal HR+ MBC patients

Patients

Randomized (N=184)

Exemestane + palbociclib with GNHR agonist (n=92)

Capecitabine (n=92)

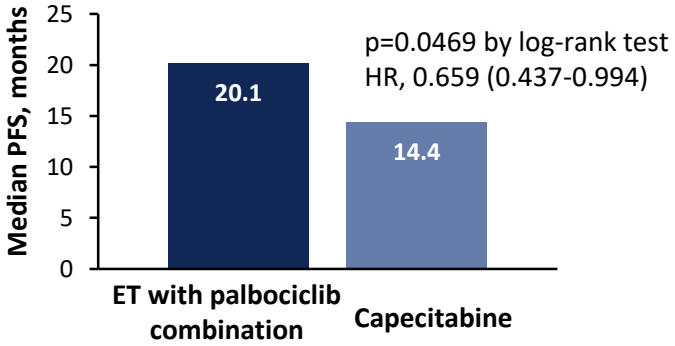
51%

Were treatment naïve in the advanced setting

- ≥ Grade 3 neutropenia was more common with palbociclib than capecitabine (75% vs. 16.3%,)
- Diarrhoea (38.4% vs. 12%) and Hand-Foot syndromes (76.7% vs. 1.1%) were more common with capecitabine than palbociclib

Primary endpoint: PFS

during median 17 months follow up



Exemestane plus palbociclib with ovarian suppression showed clinical benefit in terms of PFS compared with capecitabine in patients with premenopausal HR+ MBC

GnRH, gonadotropin-releasing hormone; HR+ hormone receptor-positive; MBC, metastatic breast cancer.

Park YH, et al. Oral Abstract 1007 Presented at the ASCO Annual Meeting 2019.

Triplet therapy (continuous ribociclib, everolimus, exemestane) in HR+/HER2- advanced breast cancer post progression on a CDK4/6 inhibitor (TRINITI-1): Efficacy, safety, and biomarker results

Bardia A, et al.

First results of the TRINITI-1 trial in the entire patient population who received triplet therapy (continuous ribociclib, everolimus, exemestane) and the correlation of biomarkers with outcomes

Phase I/II, open-label trial of triplet therapy (continuous ribociclib, everolimus, exemestane)

- **Men or postmenopausal women with HR+/HER2– ABC that progressed on prior CDK4/6i and ≤3 lines of therapy**
- **N=95 patients were evaluable (24 October 2018) (ET refractory and post-CDK4/6i) in Phases I (n = 17) and II (n = 78)**

- Most common AEs were neutropenia (all grades, 64.6%); stomatitis (41.7%)
- No grade 3/4 QTc prolongation was noted

Triplet therapy demonstrated clinical benefit at week 24 in 39 patients (41.1%), exceeding the predefined threshold (> 10%)

ORR was 8.4% by investigator assessment

Median PFS was 5.7 months

1-year PFS was 33%

ctDNA genotyping demonstrated tumour alterations, e.g. ESR1, had ↓ median PFS vs. wild-type: 3.5 vs. 6.9 months (HR 1.76, 95% CI 1.01–3.05)

Continuous triplet therapy showed clinical benefit and tolerability in patients with ET-refractory HR+/ HER2– ABC post CDK4/6 inhibitor progression. Tumour genomic profile might impact the clinical outcome with triplet therapy

ABC, advanced breast cancer; AE, Adverse event; CDK, cyclin-dependent kinase; CI, confidence interval; ET, endocrine therapy; HER2- human epidermal receptor 2-negative; HR+ hormone receptor-positive; ORR, overall response rate; PFS, progression-free survival.

Bardia A, et al. Abstract 1016 Presented at the ASCO Annual Meeting 2019.

Alpelisib + endocrine therapy in patients with PIK3CA-mutated hormone HR+/HER2- ABC: First interim BYLieve study results

Rugo HS, et al.

Interim data from the BYLieve study in pts with PIK3CA-mutated ABC and prior CDK inhibitor exposure

FUL cohort

- Pts with prior CDK inhibitor* and AI receive ALP and FUL
- At data cut-off, n= 64

LET cohort

- Pts with prior CDK inhibitor* and FUL receive ALP and LET
- At data cut-off, n=36

- Median duration on study = 7.4 months and 9.5 months in the FUL and LET cohort, respectively
- Median duration of exposure to ALP was similar in the two cohorts (FUL, 3.7 months; LET, 4.0 months)
- Median relative dose intensity of ALP was >85% in both cohorts

Safety and efficacy data†		FUL cohort	LET cohort
Most common grade ≥3 AEs	Hyperglycaemia	38.1%	27.8%
	Rash	4.8%	27.8%
	GI toxicities	9.5%	0
Discontinuation (hyperglycaemia)		n=1	n=1
ORR		15.2%	27.3%
CBR		33.3%	36.4%

In this interim analysis, safety and tolerability of ALP and hormonal therapy in pts with prior CDK inhibitors are consistent with those of SOLAR-1; discontinuation due to toxicity was rare

*Pts are permitted ≤2 prior anticancer therapies and ≤1 prior chemotherapy regimen for ABC. †In pts with centrally confirmed *PIK3CA* mutation, measurable disease and ≥6 months follow-up

AE, adverse event; ALP, alpelisib; CBR, clinical benefit rate; FUL, fulvestrant; GI, gastrointestinal; LET, letrozole; ORR, overall response rate; pts, patients.

Rugo HS, et al. Abstract 1040 Presented at the ASCO Annual Meeting 2019.

Summary

- In patients with HR+/HER2- breast cancer that had metastasized to the brain and who had been heavily pre-treated, abemaciclib demonstrated intracranial clinical benefit
- In pre-menopausal women with HR+ breast cancer, exemestane plus palbociclib with ovarian suppression extended PFS compared with capecitabine
- Continuous triplet therapy showed clinical benefit and tolerability in patients with ET-refractory HR+/ HER2- ABC post CDK4/6 inhibitor progression. Tumour genomic profile might impact the clinical outcome with triplet therapy
- In patients who had previously received a CDK4/6 inhibitor, the safety and tolerability of alpelisib were consistent with the findings from SOLAR-1 and few patients discontinued treatment due to toxicity

CDK, cyclin-dependent kinase; ET, endocrine therapy; HER2- human epidermal receptor 2-negative; HR+ hormone receptor-positive; PFS, progression-free survival.

Thank you for watching this on-demand event

educationzone.touchoncology.com

touchime
INNOVATION.KNOWLEDGE.OUTCOMES

Disclaimer

Unapproved products or unapproved uses of approved products may be discussed by the faculty; these situations may reflect the approval status in one or more jurisdictions.

The presenting faculty have been advised by touchIME to ensure that they disclose any such references made to unlabelled or unapproved use.

No endorsement by touchIME of any unapproved products or unapproved uses is either made or implied by mention of these products or uses in touchIME activities.

touchIME accepts no responsibility for errors or omissions.

touchime
INNOVATION.KNOWLEDGE.OUTCOMES