CDK4/6 inhibitors treatment use in women treated for advanced breast cancer: Integrating ASCO/NCODA patient-centered standards in a community pharmacy

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Abstract

Outpatients treated with oral anti-cancer drugs, including CDK4/6 inhibitors, may benefit from a **pharmacy practice setting adapted to support proper oral anti-cancer drug monitoring**. This real-world study aimed to characterize patient-centered pharmacy practice **aligned with ASCO/NCODA standards** and to describe its impact on CDK4/6i treatment use. An average of **7 pharmaceutical care activities per patient per treatment cycle** was documented. The **mean proportion of days covered was 89.6%. The median time-to-treatment discontinuation was estimated at 44.2 months in patients treated with CDK4/6i + letrozole and 17.0 months in patients treated with CDK4/6i + fulvestrant**. A structured patient-centered pharmacy practice model integrating the ASCO/NCODA patient-centered standards and ongoing communication with patients and healthcare providers ensure timely refills, close monitoring, and allows patients to achieve high adherence and persistence rates comparable to those reported in clinical trials.

Background

The addition of cyclin-dependent kinase 4/6 inhibitors (CDK4/6i) to endocrine therapy has led to substantial progression-free survival (PFS) and overall survival (OS) in the first- and second-line advanced breast cancer (ABC), making CDK4/6i therapy (palbociclib, ribociclib, or abemaciclib) plus standard endocrine therapy the treatment of choice in these contexts.[1-4]

The pharmacy delivery of oral anticancer drugs (OACDs), such as CDK4/6i, to outpatients represents a more convenient approach compared to intravenous chemotherapy, with only periodic visits to cancer care centers being necessary. However, patients must assume greater responsibility for their own care, which may lead to numerous challenges for clinicians including medication adherence, drug reimbursement, toxicity recognition and management, and suboptimal treatment outcomes.[5]

Larivière et Massicotte Pharmaciennes Inc. (LMP), **is a community pharmacy** in Canada dedicated to the dispensing of specialty medicines for over 14 years, and has adapted its practice model to circumvent many of these challenges. LMP structured and standardized its workflow to offer continuing support to patients and to ensure ongoing communication and collaboration with hospital teams as well as with community pharmacists that dispense patients' general medication. These are **in line with recent guidelines** related to the dispensing and follow-up of patients treated with OACDs published collaboratively by the **ASCO/NCODA**.[6]

The **objectives** of this project were to **characterize the practice processes at LMP** for patients dispensed with CDK4/6i for the treatment of ABC, namely **by measuring the frequency of pharmacists' clinical and administrative activities** based on ASCO/NCODA standards and **analyzing the impact on patients' use of CDK4/6i.**

Methods

This retrospective study included women

- with locally advanced or metastatic breast cancer
- hormone receptor-positive (ER+)/human epidermal growth factor 2 negative (HER2-)
- treated with either palbociclib, abemaciclib or ribociclib
- combined with letrozole or fulvestrant.

Following recruitment, pharmacists collected patient characteristics, clinical activities, and treatment patterns using data from the pharmacy chart.

CDK4/6i treatment adherence rates were estimated based on medication claims data. Time-to-treatment discontinuation, a proxy for time-to-event, was assessed using the Kaplan-Meier estimate.

Results

65 patients gave consent and were included in the study (Table 1). Most (90%) had a metastatic disease. CDK4/6i were generally combined with either letrozole (68%) in a first-line setting or fulvestrant (29%) as a second-line treatment or beyond.

The number of clinical interventions and administrative activities required to dispense CDK4/6i are presented in (Table 2). There was an average of 7 activities per 28-day cycle. Communication with patients and laboratory result verification accounted for 70% of these activities.

Table 1. Patient and disease baseline characteristics at the time of CDK4/6 inhibitor treatment initiation

Characteristic	Patients (n=65)
Age	
Median - yr (range)	66 (39-94)
<65 years - no. (%)	30 (46)
≥65 years - no. (%)	35 (54)
Menopausal status - no. (%)	
Pre- or perimenopause	4 (6)
Post-menopause	**61 (94)**
CDK4/6 inhibitor used - no. (%)	
Palbociclib	**51(78)**
Abemaciclib	**14 (22)**
Ribociclib	0 (0)
Concurrent hormonal therapy - no. (%)	
Letrozole	**44 (68)**
Fulvestrant	**19 (29)**
None	2 (3)
Line of treatment in ABC, MBC setting - no. (%)	
First	**37 (57)**
Second or more	**20 (31)**
Unknown	8 (12)
Tumor involvement - no. (%)	
Metastatic	**59 (90)**
Locally advanced	3 (5)
Unknown	3 (5)

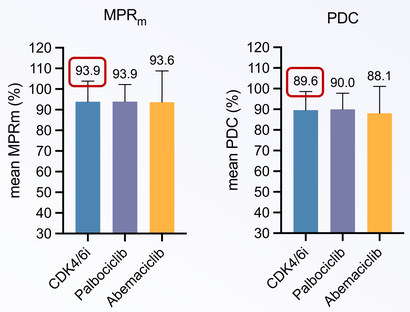
Table 2. Clinical and administrative activities related to patients treated with CDK4/6i

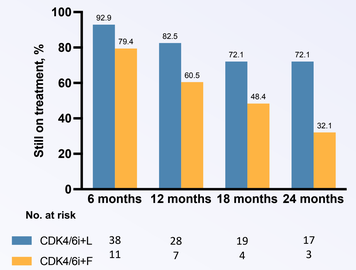
Activity	Total mean/cycle (range)	Cycles 1-3 mean/cycle (range)	Cycles ≥ 4 mean/cycle (range)
Total activities per cycle	**7.1 (2.8-21.7)**	11 (4.7-26.7)	5.2 (1.5-17)
Communications with patients	**3.1 (1.4-8)**	4.5 (2-10)	2.4 (1-9)
Verification of laboratory test results	1.9 (0.8-4.2)	2.4 (1-5.7)	1.6 (0.5-4.5)
Communications with community pharmacists	0.3 (0-1.3)	0,7 (0-3.3)	0.2 (0-1)
Communications with other healthcare professionals	0.6 (0-3.7)	1.1 (0-5.3)	0.3 (0-2)
Follow-up with payers	1.2 (0-8)	2.2 (0.3-13)	0.7 (0-2.5)

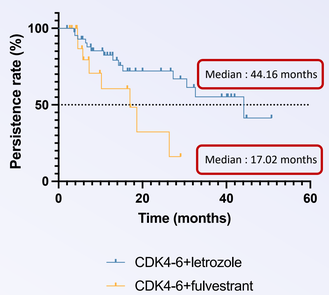
Table 3. Treatment modifications of CDK4/6i

Treatment modification	CDK4/6i (n=65)	Palbociclib (n=51)	Abemaciclib (n=14)
Interruptions - no. (%)			
Cycles 1-3	32 (49)	24 (47)	8 (57)
Total	**41 (63)**	32 (63)	9 (64)
Reductions - no. (%)			
Cycles 1-3	14 (22)	8 (16)	6 (43)
Total	**27 (42)**	17 (33)	10 (71)
Duration of follow-up			
median (IQR), months	13.6 (7.0-26.6)	13.9 (6.4-29.0)	12.4 (7.3-16.5)
mean (range), months	17.3 (3.2-50.8)	18.5 (3.2-50.8)	13.2 (3.8-40.3)

Structured and systematic clinical approaches that follow ASCO/NCODA standards translate into high adherence rates (e.g. MPRm, PDC) and persistence rates (e.g. Time-to-Treatment Discontinuation).







Conclusion

This RWE study used CDK4/6i as an archetype of the evergrowing OACD class to describe how patients' adherence and clinical outcomes can be optimized through an evolved pharmacy workflow integrating ASCO/NCODA standards of practice.

Implementing such a structured approach and adapting the pharmacy workflow may represent a considerable level of effort, but it contributes positively to patient relevant outcomes, including:

- High adherence rates
- Continuous insurance eligibility
- Treatment use comparable to clinical trials :
  - Dose reduction
  - Dose interruption
  - Duration of treatment

Similar pharmaceutical care evaluations should be performed regularly, as they drive continuous improvement.

References

1. N Engl J Med. 2016 Nov 17;375(20):1925-1936.
2. Lancet Oncol. 2016 Apr;17(4):425-439.
3. J Clin Oncol. 2017 Nov 10;35(32):3638-3646
4. J Clin Oncol.2017 Sep 1;35(25):2875-2884
5. Br J Clin Pharmacol. 2015 Dec;80(6):1289-302.
6. J Clin Oncol. 2020 Feb 20;38(6):633-644.

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