JNCCN

National Comprehensive Cancer Network®

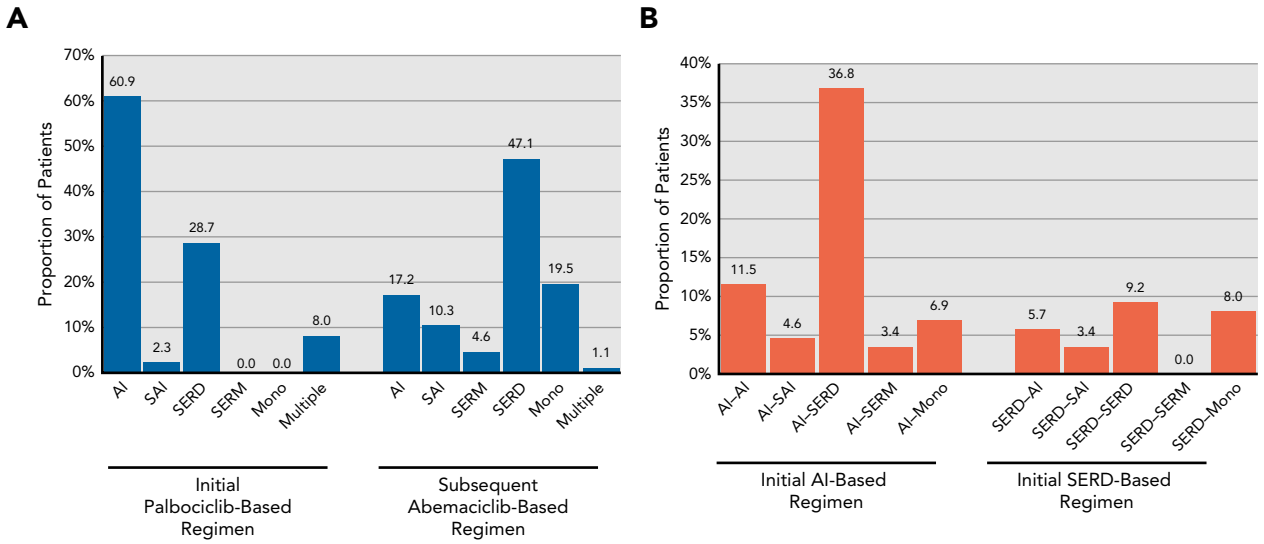
JOURNAL OF THE NATIONAL COMPREHENSIVE CANCER NETWORK

Supplemental online content for:

Clinical Outcomes With CDK4/6 Inhibitor Abemaciclib After Prior CDK4/6 Inhibitor Use in Breast Cancer: A Multicenter Experience

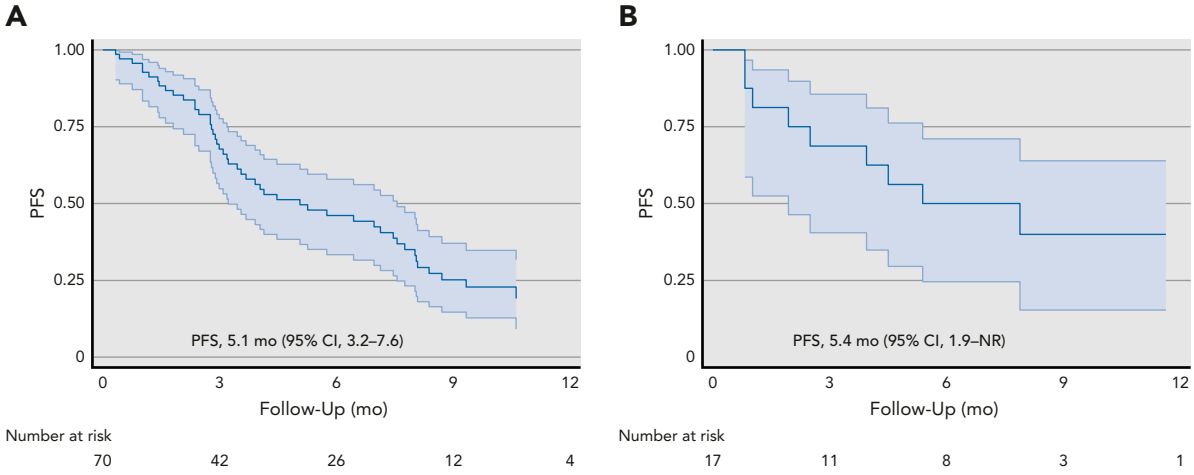
Seth A. Wander, MD, PhD; Hyo S. Han, MD; Mark L. Zangardi, PharmD; Andrzej Niemierko, PhD; Veronica Mariotti, MD; Leslie S.L. Kim, BS; Jing Xi, MD; Apurva Pandey, MD; Siobhan Dunne, BA; Azadeh Nasrazadani, MD, PhD; Avinash Kambadakone, MD; Casey Stein, BS; Maxwell R. Lloyd, BS; Megan Yuen, BS; Laura M. Spring, MD; Dejan Juric, MD; Irene Kuter, MD; Ioannis Sanidas, PhD; Beverly Moy, MD, MPH; Therese Mulvey, MD; Neelima Vidula, MD; Nicholas J. Dyson, PhD; Leif W. Ellisen, MD, PhD; Steven Isakoff, MD, PhD; Nikhil Wagle, MD, PhD; Adam Brufsky, MD, PhD; Kevin Kalinsky, MD; Cynthia X. Ma, MD, PhD; Joyce O'Shaughnessy, MD; and Aditya Bardia, MD, MPH

J Natl Compr Canc Netw, doi: 10.6004/jnccn.2020.7662



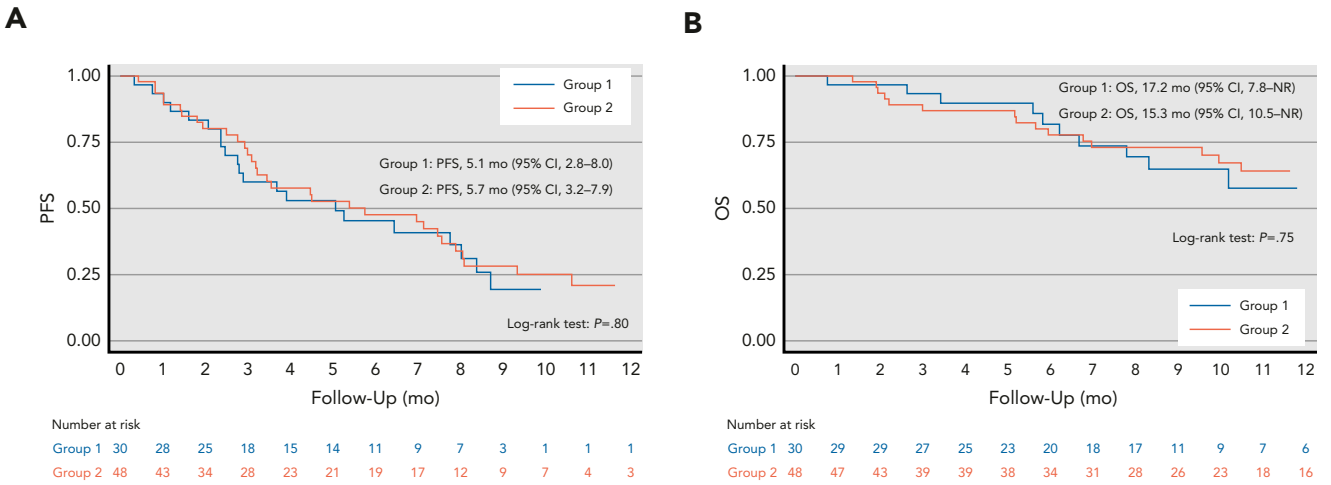
eFigure 1. (A) Proportion of patients receiving the indicated antiestrogen in the initial palbociclib-based regimen and subsequent abemaciclib-based regimen. (B) Proportion of patients with each pattern of antiestrogen transition (between the 2 CDK4/6i regimens) for treatment with palbociclib with an AI or with fulvestrant.

Abbreviations: AI, (nonsteroidal) aromatase inhibitor; CDK4/6i, cyclin-dependent kinase 4 and 6 inhibitor; mono, monotherapy; SAI, steroidal aromatase inhibitor; SERD, selective estrogen receptor degrader (fulvestrant); SERM, selective estrogen receptor modulator (tamoxifen).



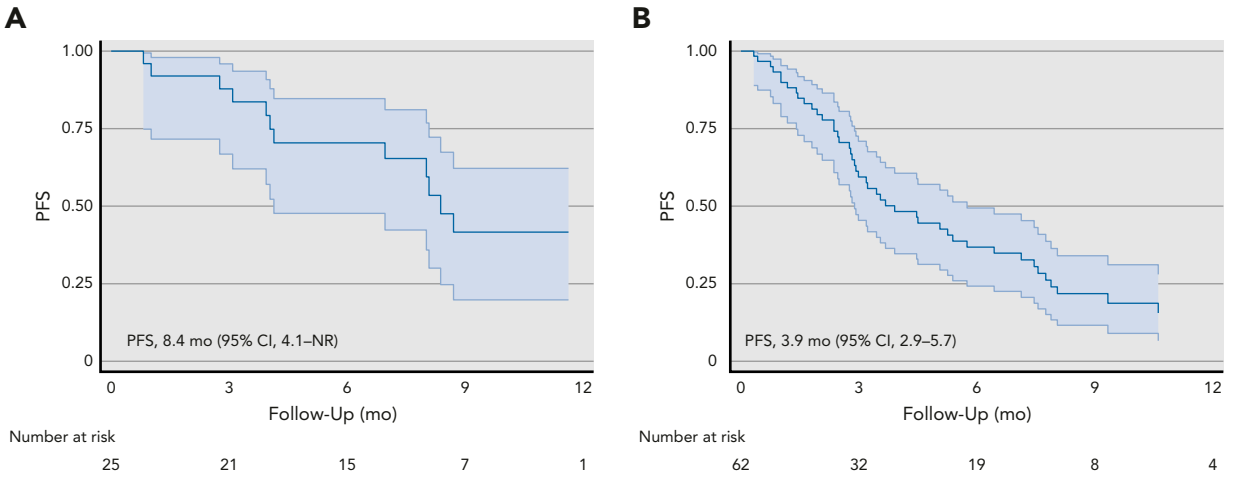
eFigure 2. Clinical outcomes on abemaciclib in patients receiving monotherapy versus hormone therapy. PFS results after stratification based on whether patients received abemaciclib therapy (A) in combination with an antiestrogen or (B) as monotherapy did not demonstrate any meaningful difference.

Abbreviations: mono, monotherapy; NR, not reached; PFS, progression-free survival.



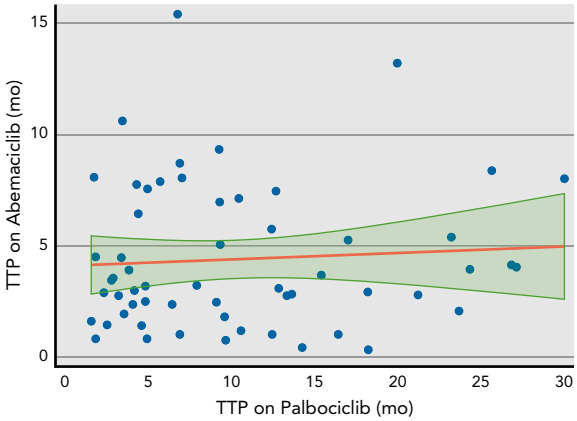
eFigure 3. Clinical outcomes on abemaciclib after change versus no change in antiestrogen backbone. (A) PFS and (B) OS in patients for whom a change in the class of antiestrogen backbone was made when switching from palbociclib to abemaciclib (Group 1) and those who received abemaciclib monotherapy or abemaciclib in combination with an antiestrogen to which they had previously been exposed in the metastatic setting (Group 2).

Abbreviations: NR, not reached; OS, overall survival; PFS, progression-free survival.

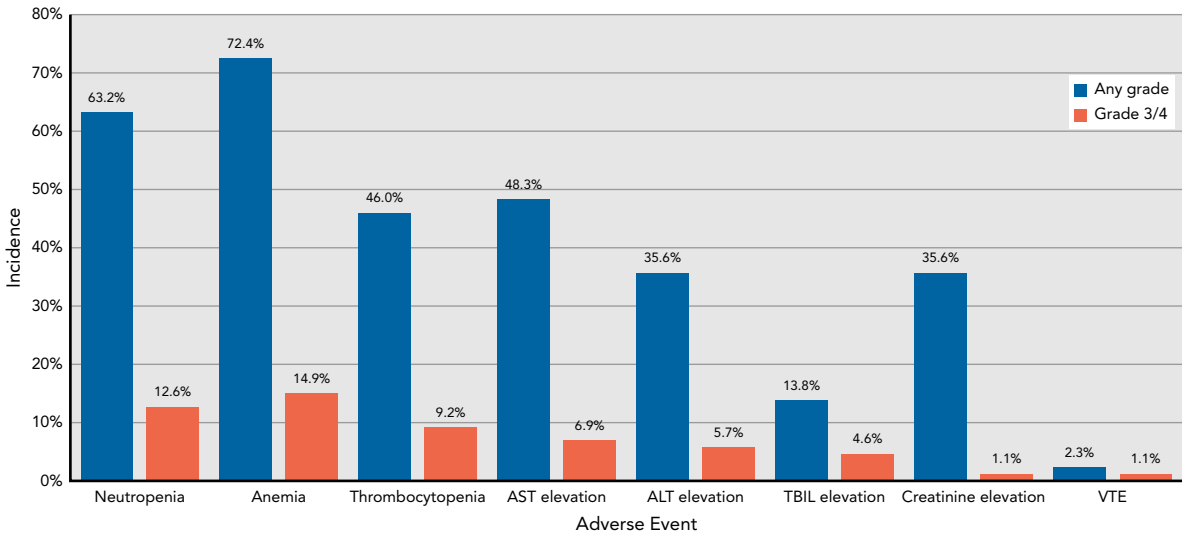


eFigure 4. Median PFS after stratification based on whether patients received CDK4/6i therapy (A) sequentially or (B) nonsequentially suggested that patients receiving sequential therapy derived greater clinical benefit.

Abbreviations: CDK4/6i, cyclin-dependent kinase 4 and 6 inhibitor; NR, not reached; PFS, progression-free survival.



eFigure 5. TTP on palbociclib-based therapy does not correlate with subsequent clinical outcome on abemaciclib.
Abbreviation: TTP, time to progression.



eFigure 6. Incidence of AEs of interest during abemaciclib treatment.
Abbreviations: AE, adverse effect; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBIL, total bilirubin; VTE, venous thromboembolism.

eTable 1. Abemaciclib Dose Reductions

	n
Single dose reduction	31 (35.6%)
Two dose reductions	5 (5.8%)
Indication for dose reduction, per EMR review[a]	
Diarrhea	14
Neutropenia	6
Fatigue	6
Nausea/Vomiting	5
Thrombocytopenia	2
Transaminitis	2
NA	2
Cough	1
Headache	1
Weakness	1

Abbreviations: EMR, electronic medical record; NA, not available.
[a]For some patients, multiple indications for dose reductions were cited.

eAppendix 1. Supplemental Methods

Given that the primary objective was to evaluate the role of abemaciclib-based therapy in patients whose disease had progressed on prior inhibitors of cyclin-dependent kinases 4 and 6 (CDK4/6i; palbociclib or ribociclib) and to maintain homogeneity in the eligible population, we included patients who experienced progression while on the initial course of CDK4/6i but not those who discontinued the initial CDK4/6i because of toxicity or who had received abemaciclib as the initial CDK4/6i. Similarly, patients who received >1 line of CDK4/6i regimen prior to receiving abemaciclib or who received CDK4/6i in the context of a triplet regimen on a clinical trial (such as endocrine therapy with CDK4/6i and an mTOR inhibitor) were also excluded.

Patients were included if they received abemaciclib sequentially (immediately after disease progression on the initial CDK4/6i) or nonsequentially (after at least 1 intervening systemic therapy after progression on the initial CDK4/6i). Abemaciclib could have been administered in combination with an antiestrogen agent or as monotherapy. Patients with HER2-positive or triple-negative disease were excluded.

Dose, schedule, and dose reduction information for both CDK4/6i regimens were captured, along with treatment duration, whether the CDK4/6i regimens were given sequentially or nonsequentially, the number of metastatic therapy regimens given prior to the initiation of abemaciclib, the current status of the abemaciclib-based regimen (on or off treatment), reason for discontinuation (disease progression or toxicity, per medical record and radiology review), date of last follow-up, and survival status.

Medical records (progress notes, laboratory values) for each patient were reviewed to identify select adverse events and laboratory abnormalities associated with abemaciclib.