PALBOCICLIB: EARLY NEUTROPENIA AS A PHARMACODYNAMIC MARKER IN A REAL WORLD SETTING?

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Background and importance

The most frequent adverse effect of palbociclib is neutropenia resulting in dose reductions and treatment interruptions. Recently, it has been reported that early palbociclib-related neutropenia is associated with prolonged PFS (progression-free survival)1. However, there is no analysis data based in the real-world setting, outside the context of clinical trials.

Aim and objectives

To determine whether early neutropenia in our cohort of patients is associated with disease response to palbociclib combined with fulvestrant or aromatase inhibitor.

Material and methods

Retrospective study including all patients who started treatment with palbociclib between December 2016-January 2020. Demographic and clinical data were obtained from the electronic clinical records. Primary endpoints included both PFS and OS (overall survival). Early neutropenia was defined as the nadir absolute neutrophil count (ANC) during the first 2 cycles of treatment.

PFS and OS were analyzed through Kaplan–Meier survival curves comparing neutropenia grades using log-rank test to check differences between survival curves. Multivariate Cox proportional hazard regression model was also used to predict OS.

Results

A total of 61 patients were included. Demographic and clinical characteristics are shown in Table 1.

Twenty-eight patients (45.9%) stopped the treatment and 24 (85.7%) discontinued due to progression. Twenty-five patients (41.0%) required ≥ 1 dose reduction. In the first two cycles, 54 patients (88.5%) experienced grade 1–4 neutropenia.

Patients who experience grade 2-4 neutropenia in the first two cycles were associated with significantly prolonged median OS (log-rank p=0.019) (Figure 1). However, there was no significantly association with prolonged median PFS (log-rank p=0.572) (Figure 2).

After adjusting for potential cofounders (baseline ACN, age and weight), grade 2-4 neutropenia remained significantly and independently associated with prolonged OS (HR 0.26, 95% CI 0.09–0.77, p=0.015).

Table 1. Patients' characteristics.

	Total patients (n=61)
Age in years, mean±SD	61±11.8
Female, N(%)	60(98.4%)
Weight in kg, mean±SD	65.8±14.5
Baseline ECOG PS 0-1, N(%)	56(91.8%)
Line of therapy, N(%)	
1	41(67.2%)
2	14(23.0%)
≥3	6(9.8%)
Concomitant drug, N(%)	
Fulvestrant	25(41.7%)
Aromatase inhibitor	36(59.0%)
Baseline ANC , mean±SD	5.0±2.6

Figure 1. Kaplan-Meier overall survival (OS) by cycle 1-2 grade 2-4 neutropenia

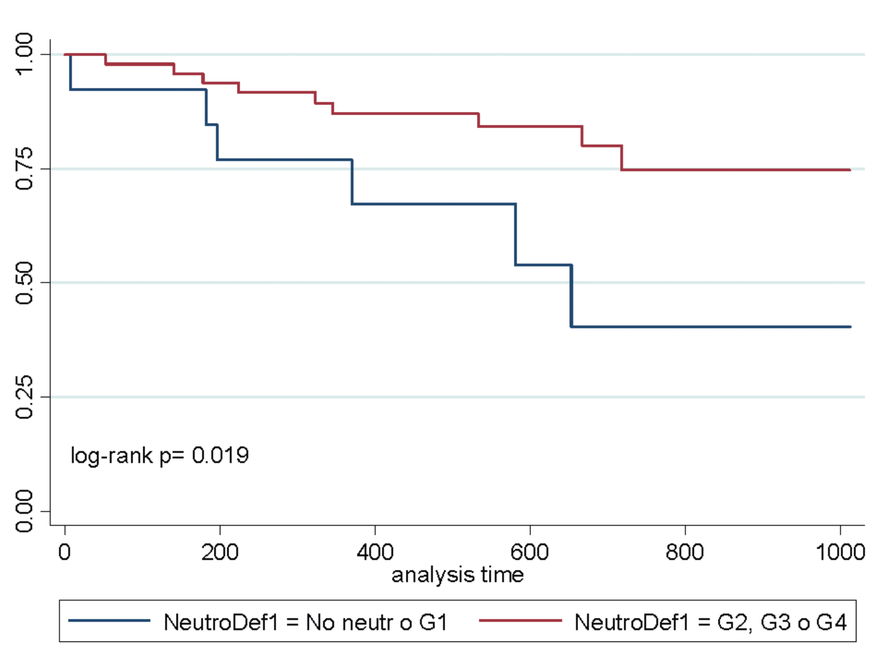
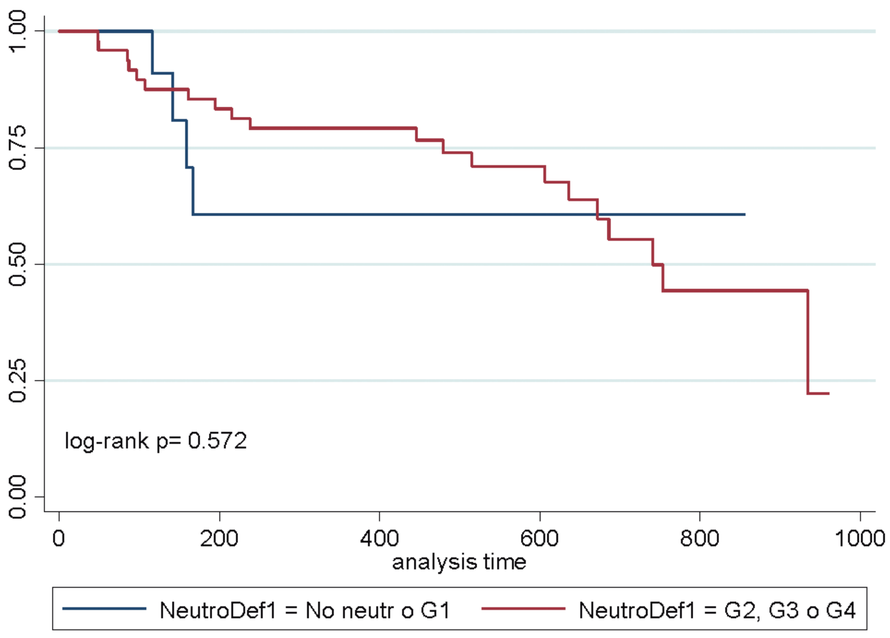


Figure 2. Kaplan-Meier progression-free survival (PFS) by cycle 1-2 grade 2-4 neutropenia



Conclusion and relevance

Early neutropenia was significantly associated with a prolonged OS, supporting the suggestion that neutropenia could be a pharmacodynamic marker for palbociclib dosing.

References: 1. McAndrew NP, *et al. Br J Cancer* 2020;123:912–918

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