

1 RESULTS: EFFICACY

5.1.1 Effect of study treatment on cell proliferation

Tumour Ki67 expression decreased in 93.4% of patients over the course of the study treatment from baseline to day 15 (Figure 3 & 4); in 9 patients Ki67 expression numerically increased, including 5 patients in the anastrozole group (10.9% of all patients treated with anastrozole) and 4 patients in the combination group (4.4%). More patients in the combination group (87.8%) had an EOT Ki67 expression of <10% compared to anastrozole alone (71.7%).

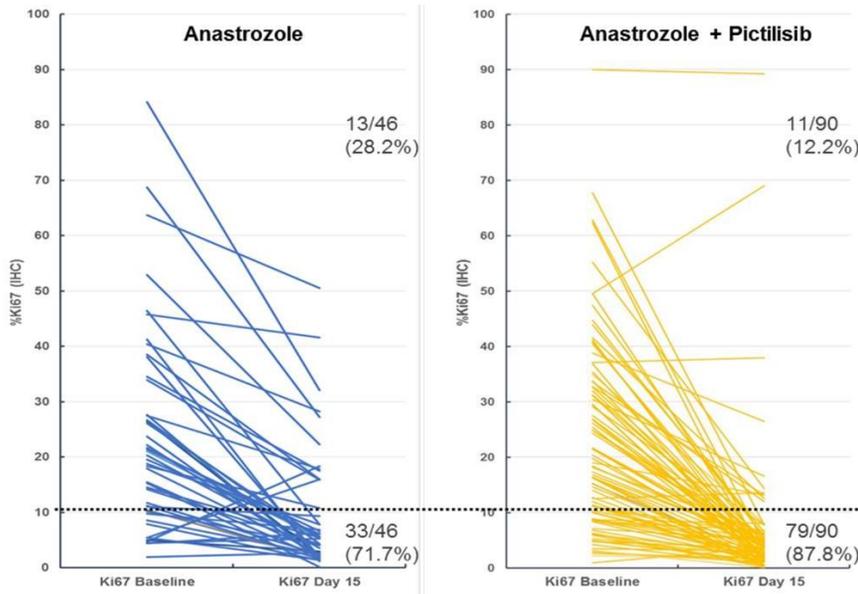


Figure 3: Individual changes in percentage Ki67 expression from baseline to Day 15; the number and percentage of patients achieving an end of treatment (EOT) Ki67 score of >10% or ≤10% are provided for each group.

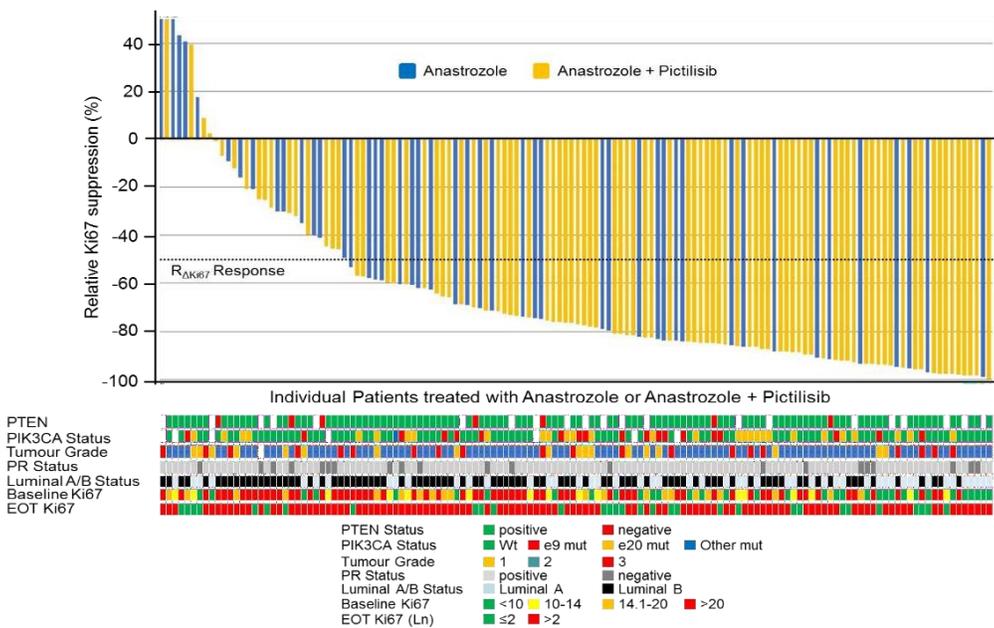


Figure 4: Individual relative Ki67 suppression sorted from low to high; relative Ki67 Suppression is defined as $\text{Ln}(\text{Ki67Day15}) - \text{Ln}(\text{Ki67baseline})$; results are displayed on their original scale by back transformation. Individual PTEN status, PIK3CA status, PR status, Luminal A/B status, tumour grade, Baseline and end of treatment (EOT) Ki67 expression are indicated as a coloured box under each patient.

Mean percentage suppression of Ki67 was 82.5% (95% CI, 78.3%-85.8%) for anastrozole plus pictilisib treated patients and 70.7% (61.0%-78.0%) for anastrozole treated patients (Table 2; Figure 5). The ratio (combination/anastrozole) of mean Ki67 suppression was 0.60 (0.58-0.85; $p=0.01$). The geometric mean end of treatment Ki67 expression was 6.3% (3.7%-8.8%) for anastrozole plus pictilisib and 9.5% (6.3%-12.8%) for anastrozole alone ($p=0.02$). The EOT response rate $R_{Ki67\text{-Day15}}$ was higher with the combination 83.3% (76.8%-90.9%) compared to anastrozole alone 65.2% (53.3%-77.1%; $p=0.02$).

	Anastrozole (n = 46)	Pictilisib plus Anastrozole (n = 90)	Relative Risk (combination/ anastrozole)	p-Value
Geometric mean Ki67 suppression [% (95% CI)]	70.7% (61.0%-78.0%)	82.5% (78.3%-85.8%)	0.60 ¹ (0.58-0.85)	$p=0.01$
The geometric mean EOT Ki67 expression [% (95% CI)]	9.5% (6.3%-12.8%)	6.3% (3.7%-8.8%)	0.66 ¹ (0.58-0.69)	$p=0.02$
$R_{\Delta Ki67}$ response rate [% (95% CI)]	69.6% (58.0%-81.1%)	81.1% (74.2%-88.0%)	1.17 (0.97-1.40)	$p=0.10$
$R_{Ki67\text{-Day15}}$ response rate [% (95% CI)]	65.2% (53.3%-77.1%)	83.3% (76.8%-90.9%)	1.36 (1.05-1.55)	$p=0.02$

Table 2: Anti-proliferative response to ANA or ANA+PIC. Geometric mean Ki67 suppression defined as $\text{Ln}(\text{Ki67Day15}) - \text{Ln}(\text{Ki67baseline})$; the ratio (combination/anastrozole) of geometric mean Ki67 suppression provided with 95% CI. Geometric mean end-of-treatment (EOT) Ki67 expression defined as $\text{Ln}(\text{Ki67Day15})$; individual EOT anti-proliferative response $R_{Ki67\text{-Day15}}$ defined as $\text{Ln}(\text{Ki67Day15}) \leq 2$; individual anti-proliferative response $R_{\Delta Ki67}$ defined as $\geq 50\%$ fall in Ki67 expression between baseline and Day 15.

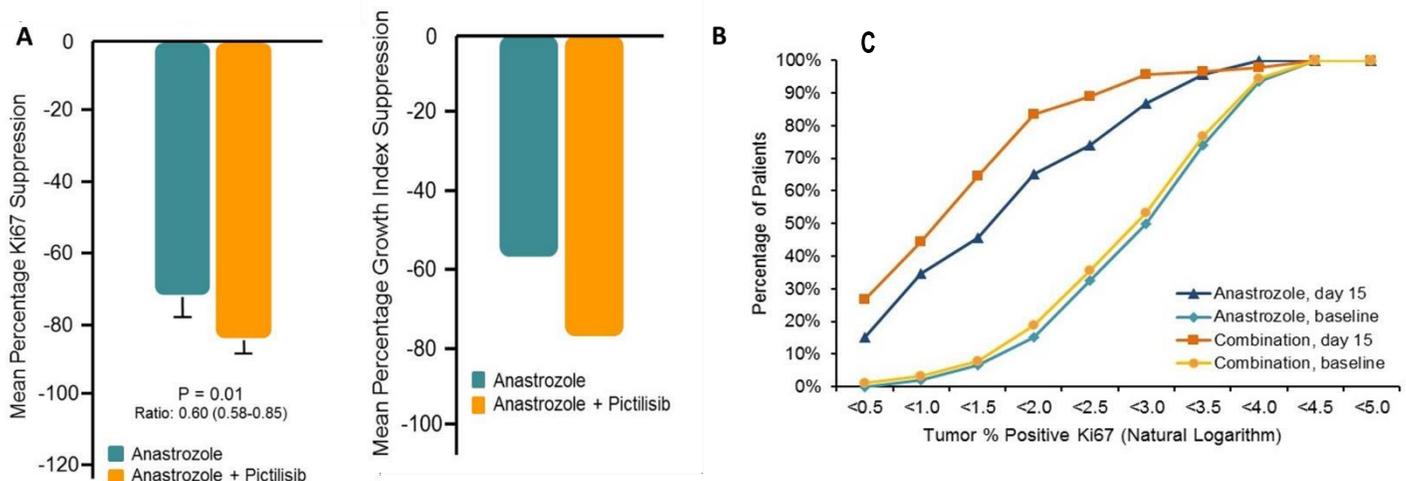


Figure 5: A) Anti-proliferative response expressed as the geometric mean Ki67 suppression in from baseline to day 15. B) Mean percentage Growth Index suppression. C) Figure 6: Cumulative proportion (by percentage) of patients who had tumours with %-positive Ki67 (expressed as natural logarithm) less than the value on the X axis is illustrated at BL and at D15