Ki67 as a predictor of response to PARP inhibitors in platinum sensitive BRCA Wild Type ovarian cancers: MITO 37 retrospective study

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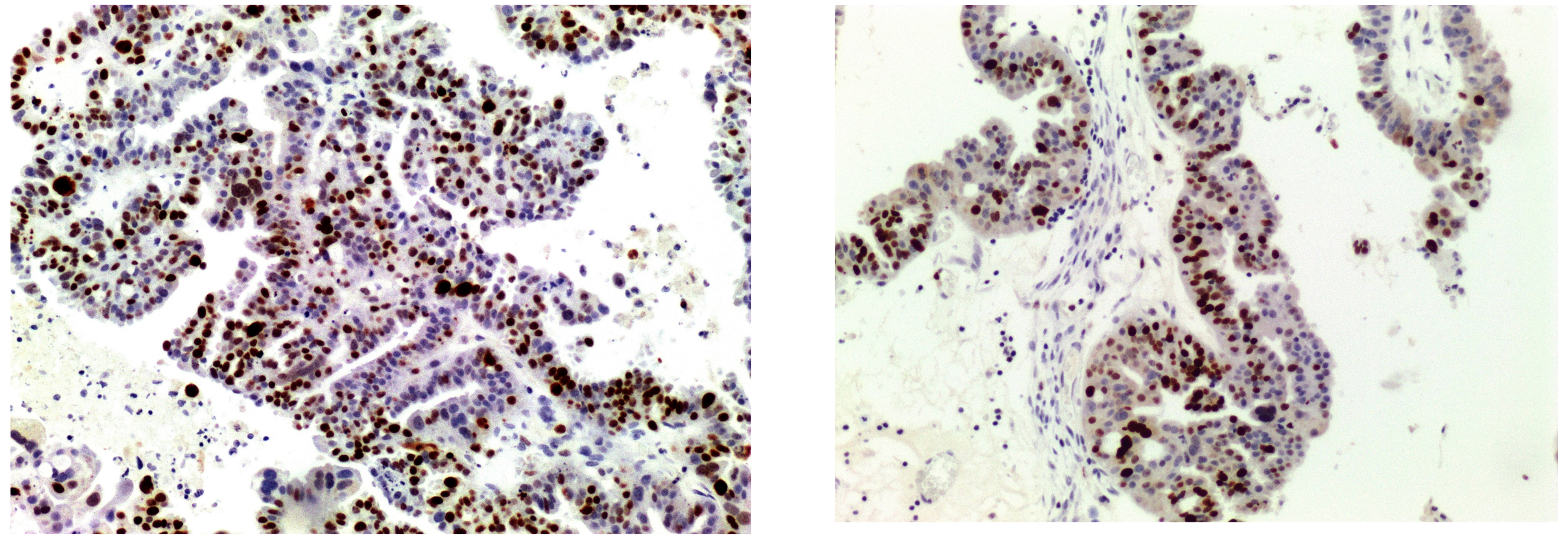
Background

Best predictor of response to PARP inhibitors (PARPi) in ovarian cancers (OC) is the presence of BRCA1 or BRCA2 mutations. However, also OC carrying other homologous recombination deficiency (HRD) can benefit from PARPi. HRD definition is still not standardized and no test is available to discriminate among BRCA wild type (WT) patients (pts) those who will benefit from PARPi. Since high Ki67 predicts sensitivity to alkylating agents, we hypothesized that Ki67 expression could also serve as a predictor of sensitivity to platinum salts and PARPi.

Methods

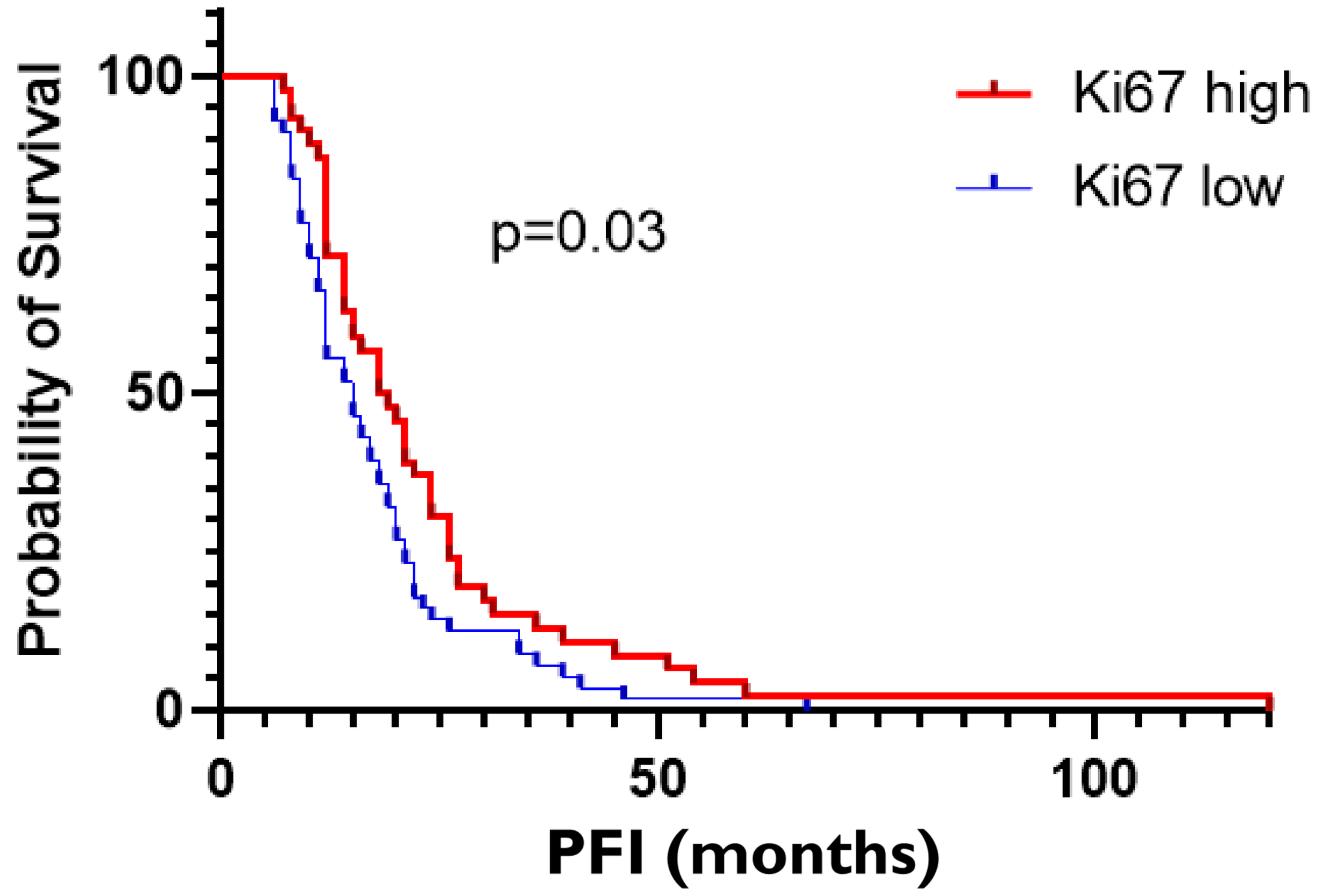
MITO 37 is a multicentre retrospective Italian study aiming at correlating Ki67 expression level with clinical outcome following platinum treatment and PARPi maintenance. Clinical data were collected from all pts with high grade serous or endometroid BRCA WT OC treated with niraparib or rucaparib maintenance between 2010-2021. Ki67 expression was assessed by certified pathologists on formalin-fixed paraffin embedded tumor at diagnosis and at relapse (if available) before PARPi.



Ki67 in high grade ovarian cancer. Original Magnification 200x

Results

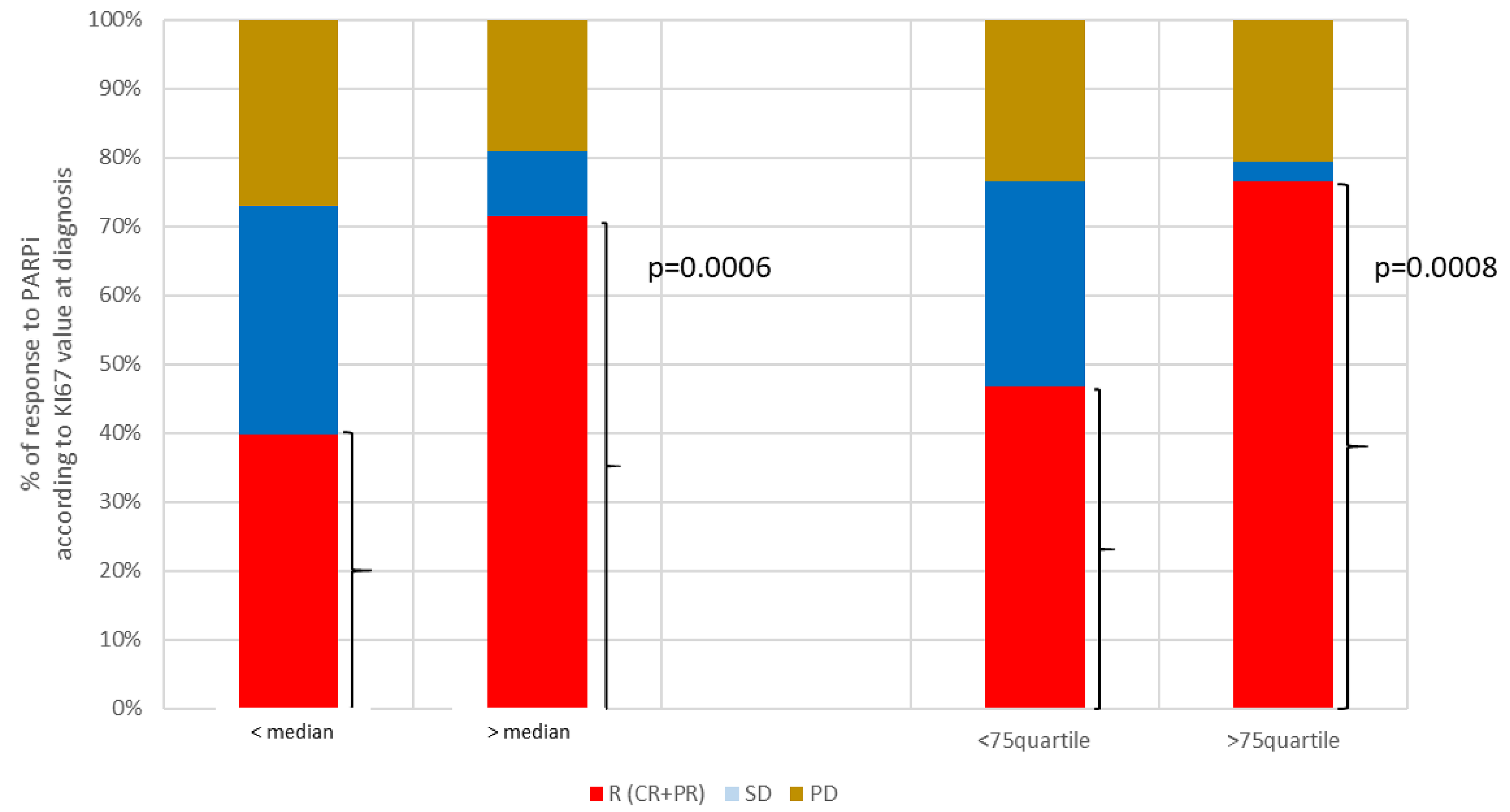
131 pts from 14 centres were included. Most pts were serous OC (93%, 121/131), advanced-stage (81%, 106/131 FIGO stage III-IV). The majority (71%, 93/131) had absence of residual disease (R0) at primary surgery. Median platinum free interval (PFI) at first relapse was 22.5 months (IQR 12-25.5) and median number of lines before PARPi was 2 (range 1-5). Niraparib was the most used PARPi (89%, 117/131). Best response to PARPi was: 30% (38/126) complete response (CR), 25% (31/126) partial response (PR), 21% (27/126) stable disease, 24% (27/126) progressive disease. Ki-67 was available for 129 pts at diagnosis and 22 at relapse. At diagnosis, median Ki67 was 49% (IQR 25%-70%). Higher Ki67 (using median as cut-off) was significantly associated with higher rate of R0 at surgery (100% vs 54.8%, p<0.001), longer first PFI (median 18.8 vs 27.2 months, p=0.03, Figure 1) and higher response to PARPi (71% vs 40% CR+PR, p<0.005, Figure 2). Similar results were observed using 75th percentile as Ki67 cut-off.



Hazard Ratio (logrank)

95% CI of ratio	0.4603 to 1.004

Figure 1



Fisher exact test

Figure 2

Conclusions

Preliminary results show that high Ki-67 at diagnosis potentially discriminates among BRCA WT responders to PARPi. Further analyses are ongoing

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