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Treatment outcomes in TNBC patients undergoing neoadjuvant chemotherapy. The importance of Ki-67. BL Rapoport ^{1,2}, J Barnard-Tide ¹, RI Van Eeden ¹, T. Smit ¹, S Nayler ^{3,4}, C Benn ⁵

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Background

- Neoadjuvant chemotherapy (NAC) is widely used to downstage breast cancers prior to surgery.
- Pathologic complete response (pCR) rate is a strong predictor of outcome for breast cancer.
- TNBC often responsive to conventional NAC with good outcome similar to other subtypes.
- A non-pCR is an indication of a poorer outcome.

Figure 1. Responsiveness to Neoadjuvant Conventional Chemotherapy.

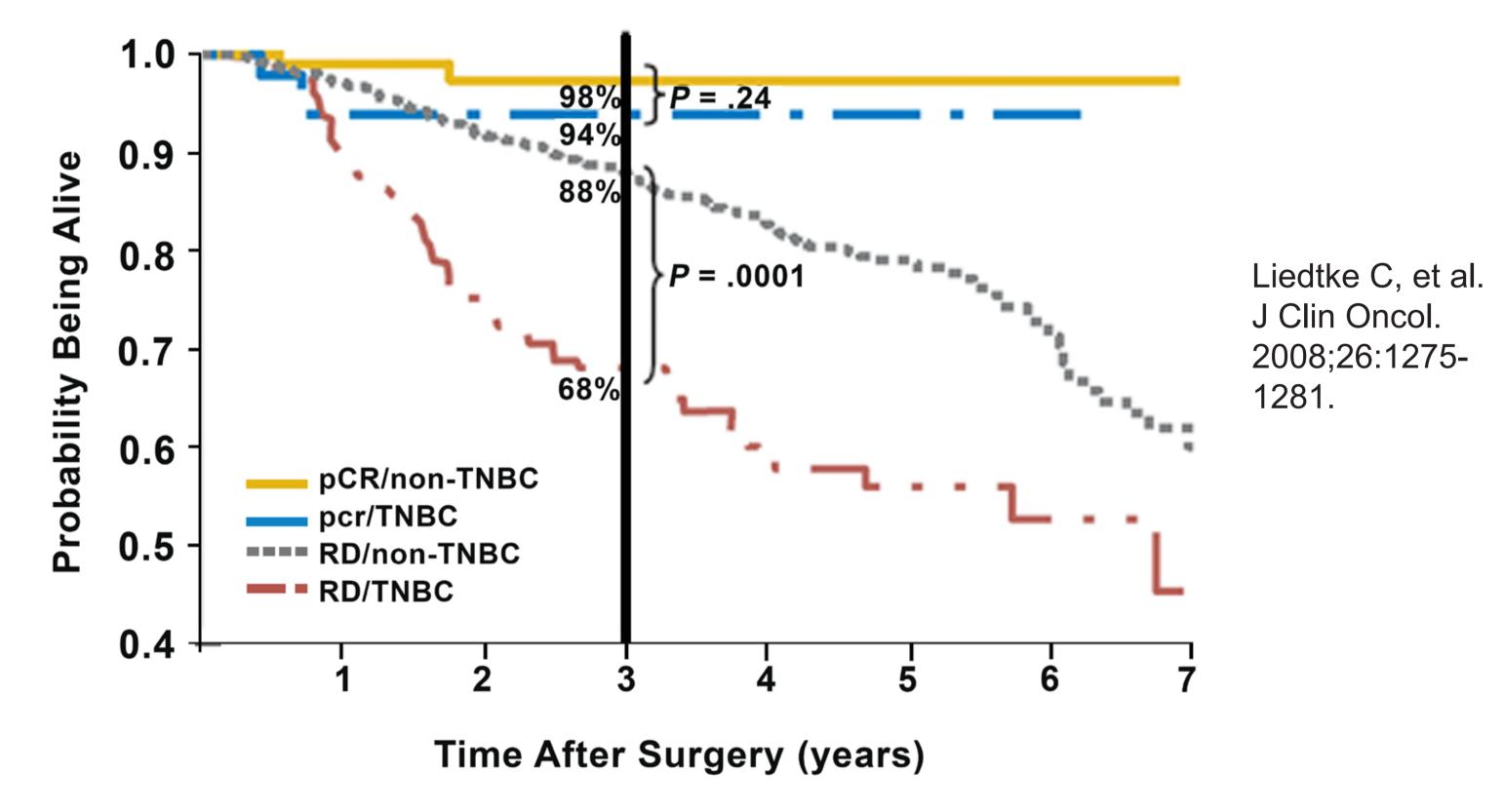
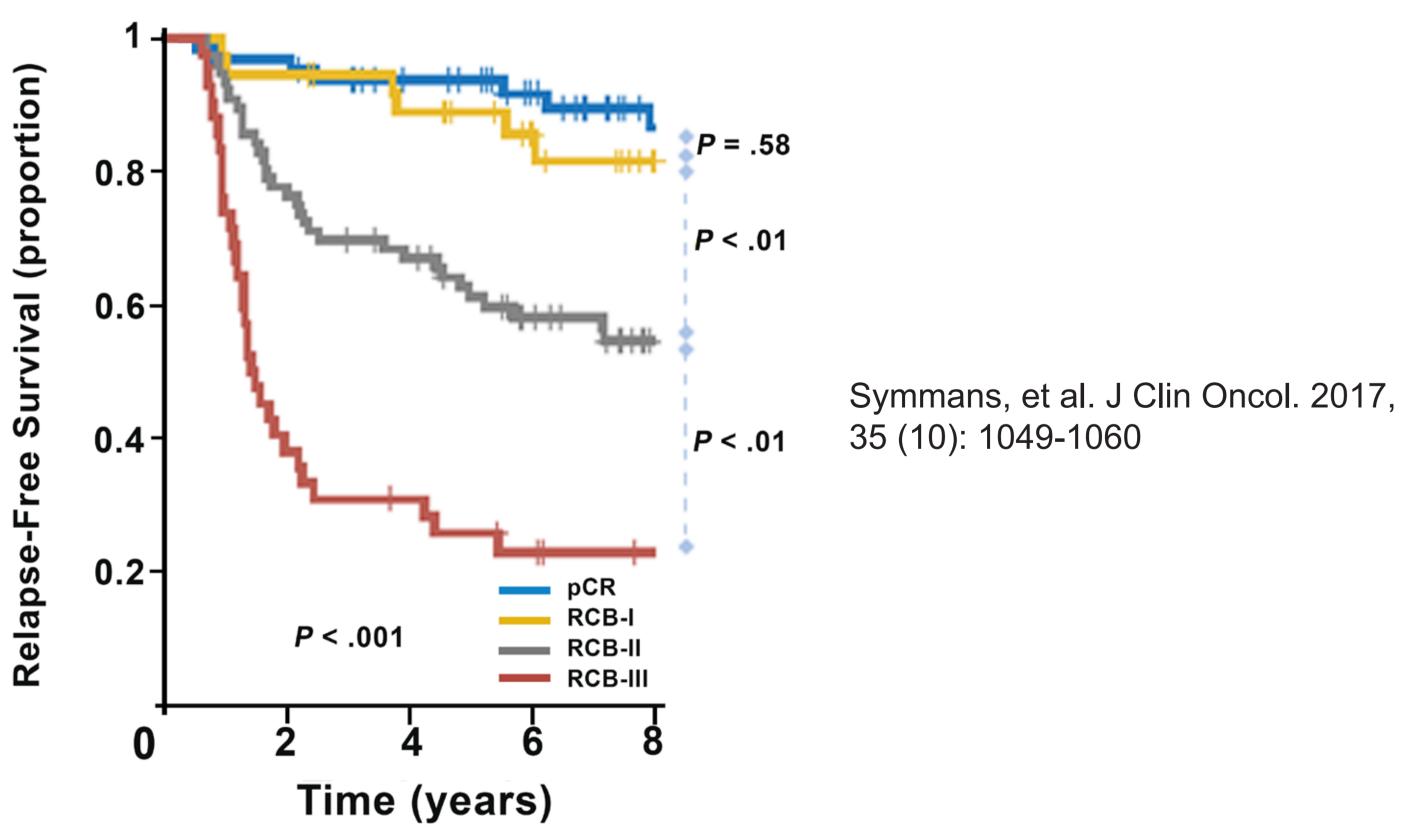


Figure 2. TNBC Response Free Survival by Residual Breast Cancer (MD Anderson Data).



- ▶ The Ki-67: two protein isoforms with molecular weights of 345 and 395 kDa.
- ▶ The Ki-67 protein has a half-life of only ~1–1.5 hours.
- Ki-67 is present during all active phases of the cell cycle (G1, S, G2 and M) but is absent in resting cells (G0).
- In later phases of mitosis (during anaphase and telophase), there is a sharp decrease in Ki-67 levels.
- The expression of the Ki-67 protein (pKi-67) is associated with the proliferative activity of intrinsic cell populations in malignant tumours.
- **Ki-67** is used as a marker of tumour aggressiveness.

Methods

- NAC.
- Outcome assessments: Associations of clinical and pathological characteristics including the Ki-67 with pCR and DFS.
- All patients were treated with anthracycline and/or taxane-based neoadjuvant chemotherapy.
- Immunohistochemical staining was performed for ER, PR, HER-2 and Ki-67. Fluoresce in situ hybridization (FISH) was used to confirm HER-2 positivity.
- Clinical assessment was made using bi-dimensional caliper measurements of the primary tumour and axillary lymph nodes.
- regularly
- nodes.

Statistical Methods

- Ki-67.
- variables.
- pCR (p < .1).

We analyzed date retrospectively/prospectively on 152 TNBC patients undergoing

Sonographic assessments of the primary tumour and lymph nodes were performed

Pathological complete response (pCR) was defined as the complete disappearance of the invasive cancer in the breast and absence of tumour in the axillary lymph

Ethics approval was obtained from Pharma-Ethics, Pretoria, South Africa (ethics committee working according to the South African Ethics regulations).

> Results Table 1. Patient Characteristics.

The primary hypothesis was that higher levels of Ki-67 would be associated with a better overall prognosis, independent of anti-cancer therapy.

Receiver-operating characteristic (ROC) curve analysis was used to determine the optimal cut-point for

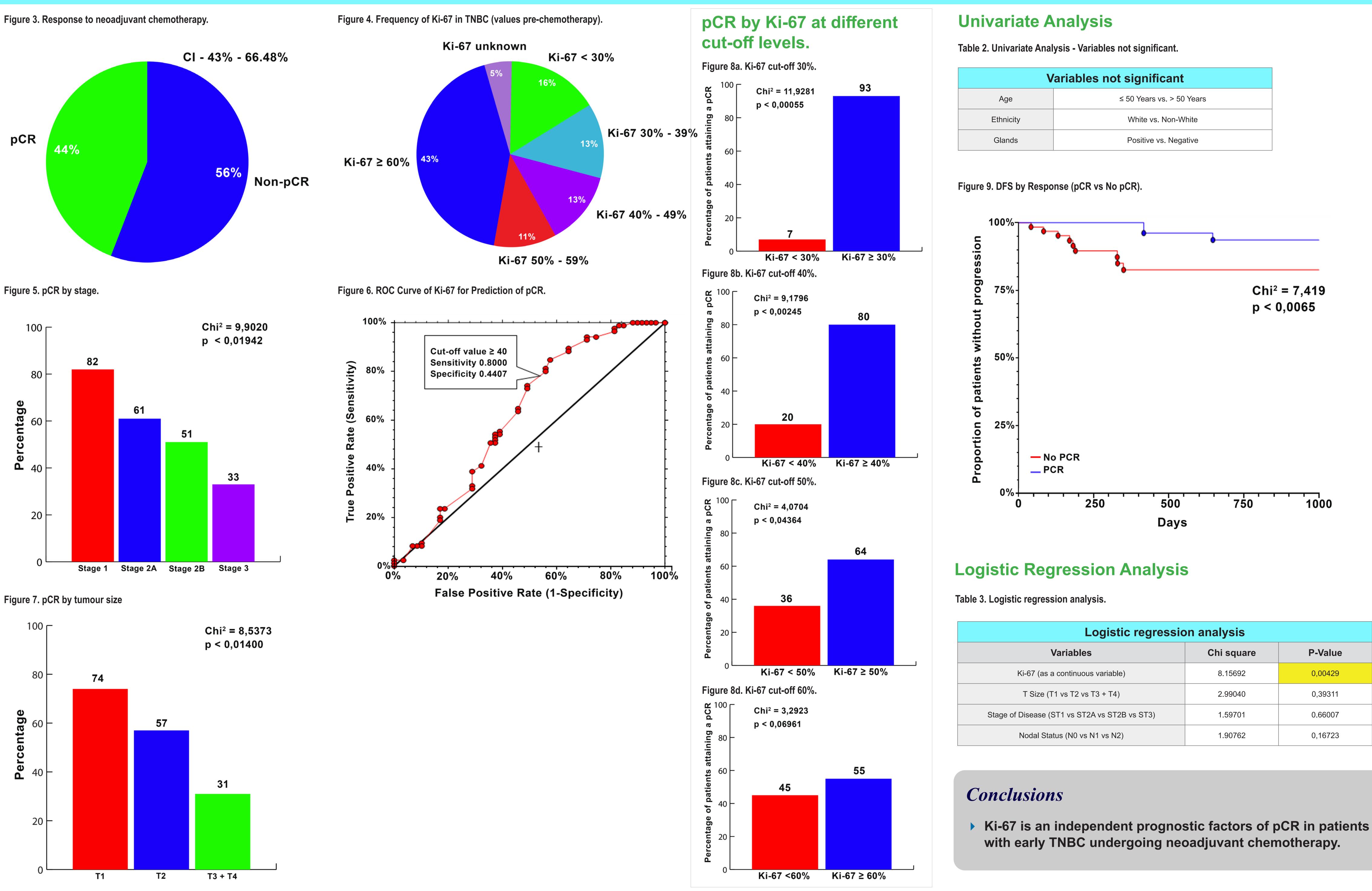
DFS was calculated from the time of diagnosis to first date of any documented disease recurrence, death, or date of last follow-up. DFS were estimated using the Kaplan-Meier method and compared using the log-rank test.

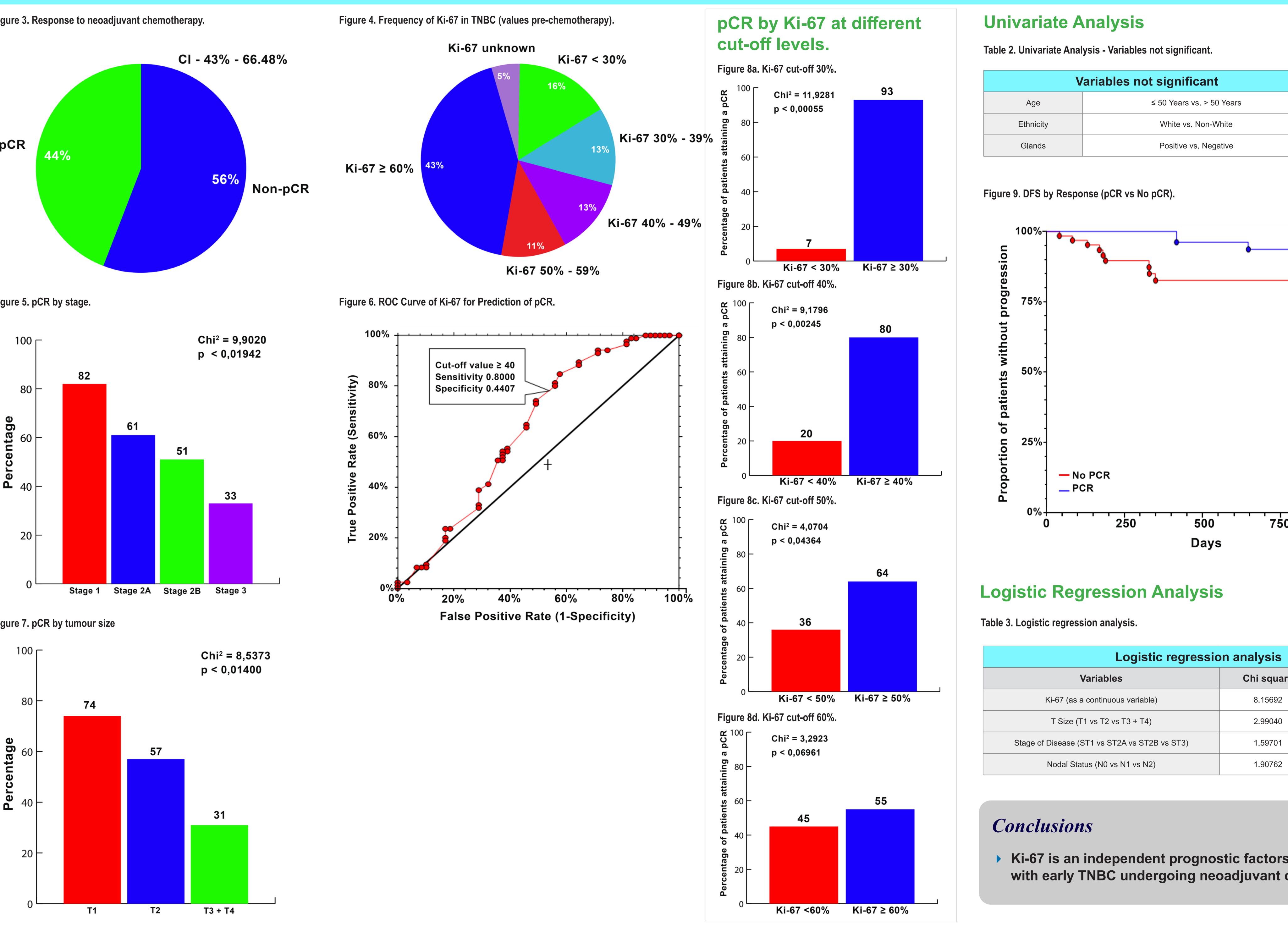
Fisher's exact or Chi- squared tests were used for the analysis of categorical

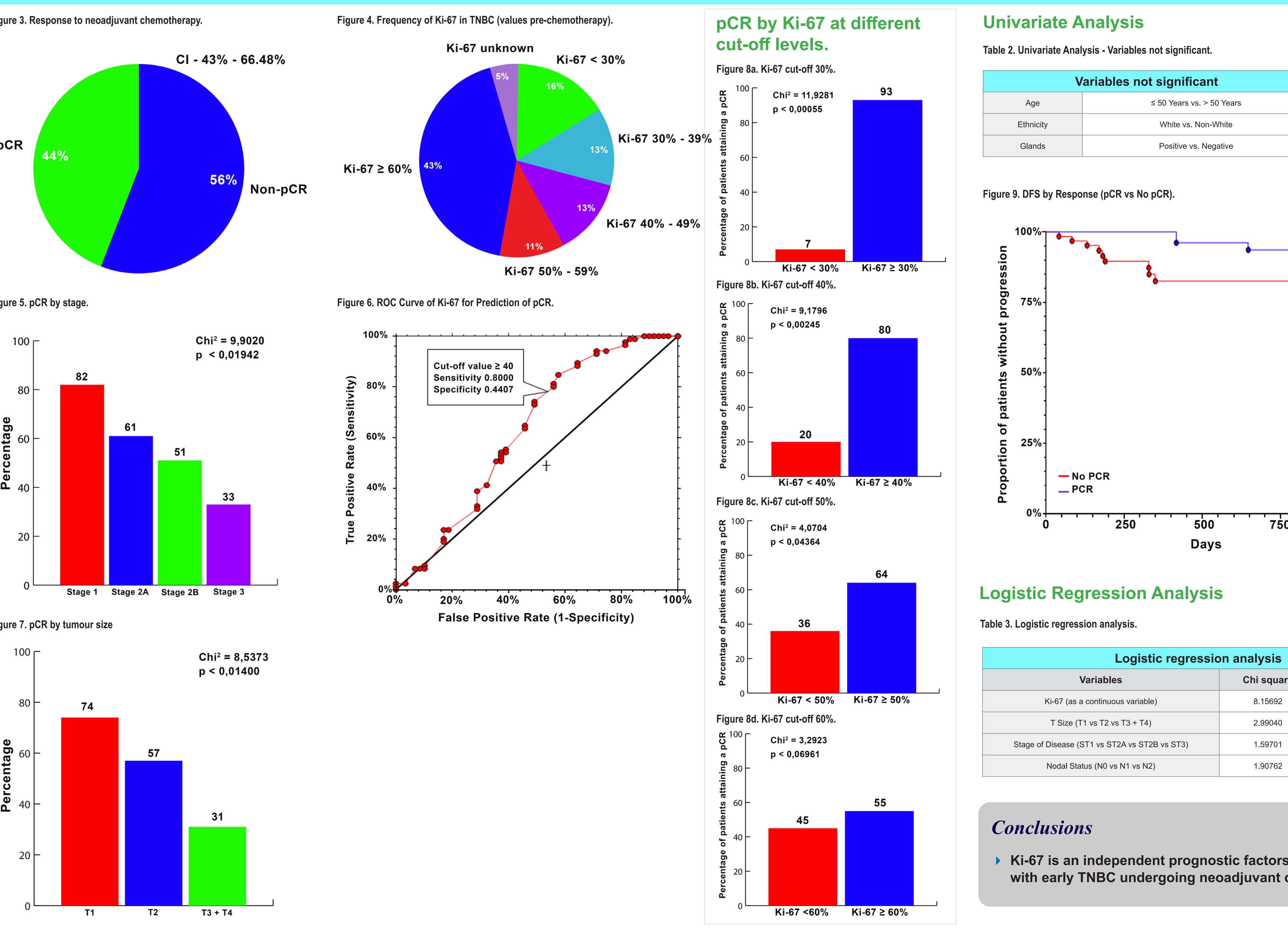
Multivariate models included only variables that exhibited a univariate association with the dependent variable,

NCSS software version 11 for Windows (USA) was used for statistical analyses.

Patient Characteristics Patient Characteristics n (%) Total (n) Median Age 50 (27-85) ≤ 50 years 76 (50%) > 50 years 76 (50%) **Menopausal Status** Pre-Menopausal 51 (37%) Post-Menopausal 86 (63%) **Tumour Siz** 35 (23%) 101 (66%) 13 (9%) 3 (2%) Nodal Status Negative 84 (55%) Positive 65 (43%) 3 (2%) Unknown Stage 19 (13%) 2 (1%) 75 (49%) 41 (27%) 11 (7%) 3 (2%) 1 (1%) Ethnicity 25 (17%) Black 106 (70%) White 15 (10%) Indian Coloured 5 (3%) Chemo-Groups 131 (86%) AC + Taxane 17 (11%) 1 (1%) Taxane 2 (1%) 1 (1%)







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P-Value

0,00429

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0.66007

0,16723



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