Multivariate survival analysis reveals RAD51 protein as a superior prognostic factor compared to tumor infiltrating lymphocytes and PD-L1 expression in patients with resected non-small-cell lung carcinoma
Conflicts of interest statement:

I declare no conflicts of interest
Background

DNA repair proteins have emerged as potential predictors for immunotherapy response alongside PD-L1 expression, tumor-infiltrating lymphocytes (TILs) and tumor mutational burden.


**DNA Repair Deficiency and Immunotherapy Response.**

Mouw KW¹, D'Andrea AD¹.


**DNA Damage and Repair Biomarkers of Immunotherapy Response.**

Mouw KW¹, Goldberg MS², Konstantinopoulos PA²,⁵,⁶, D'Andrea AD⁷,²,³,⁶.
**DDR/R and ImmR**

- ATM
- γH2AX
- Chk1
- Chk2
- RPA
- ATR
- CDK1
- CDK2
- p53
- p21
- Wee1
- Cdc25
- BRCA1
- BRCA2
- HRR
- DSB
- Interstrand crosslinks
- Replication fork collapse
- JAK/STAT/IRF1
- Type I interferon response
- Neoantigens
- MHCI
- PD-L1
- PD1
- NKG2D
- NK cells
- T cells

**Point Mutations, Indels**

**Neoantigens**
Objectives

➢ To analyze alterations in:
  ➢ PD-L1 expression in tumor cells and in TILs;
  ➢ TIL count;
  ➢ expression of the major homologous recombination (HR) protein RAD51

➢ To find:
  ➢ the relationship between above mentioned markers
  ➢ their potential prognostic value in patients with resected non-small-cell lung carcinoma (NSCLC).
Material & Methods

Tissue Microarrays:
- Training set – 96 NSCLC patients, Olomouc, CZ
- Validation set – 1109 NSCLC patients, Zurich, CH

Standard IHC (Ventana Benchmark Ultra)
- Markers: RAD51, CD3, CD8, CD68, PD-L1

TCGA DATA ANALYSIS

Lymphocyte and macrophage scoring

PD-L1 digital analysis algorithm
Results

Loss of nuclear RAD51 protein was associated with high TIL ($r=-0.25$, $p=0.01$) and PD-L1 (10.6 vs. 2.4, $p=0.012$) status in patients receiving neoadjuvant chemo-/radiotherapy (CT/RT).
Results

RAD51 low/PD-L1 high patients were clustered as separate entity in the replication set (A) and in TCGA dataset (B).
Results
## Cox regression

### Variables in the Equation

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<th>df</th>
<th>Sig.</th>
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Conclusions & Future Directions

➢ In conclusion, RAD51 nuclear loss is associated with high TIL and high PD-L1 expression at the time of surgery in curatively resected NSCLC and after prior exposure to neoadjuvant chemo- or radiotherapy;

➢ Both high TIL and RAD51 nuclear loss were confirmed as independent prognostic factors in curatively resected NSCLC, however only RAD51 was retained as an independent prognostic factor in both training and validation sets;

➢ RAD51 should be further explored as predictive factor for immunotherapy response in patients with NSCLC.
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