Immuno-FIELT: The role of Tumor Infiltrating Lymphocytes and PD-L1 expression in NSCLC adenocarcinoma in little to non-smokers and its relationship with driver mutations and clinical outcome parameters.

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Materials and Methods

- **Patient selection**: FIELT study population (De Grève et al. PloS One 2016)
  - Advanced adenocarcinoma of the lung
  - Little to non-smokers

- **Mutation analysis:**
  - EGFR
  - KRAS
  - (HER2 and BRAF: too few subjects)

- **TILs scoring:**
  - Scoring method on H&E validated in breast cancer (Salgado et al. Ann Oncol 2015)
  - Still needs to be validated in other solid tumors

- **PD-1/PD-L1 expression**
  - PD-1/PD-L1 double staining (Buisseret et al. Oncoimmunology - in press)

TILs- Results

Interobserver variability for TIL scoring

	ICC stromal TILs	ICC intratumoral TILs
All observers	0,74	0,16

Correlation of sTILs with mutation status

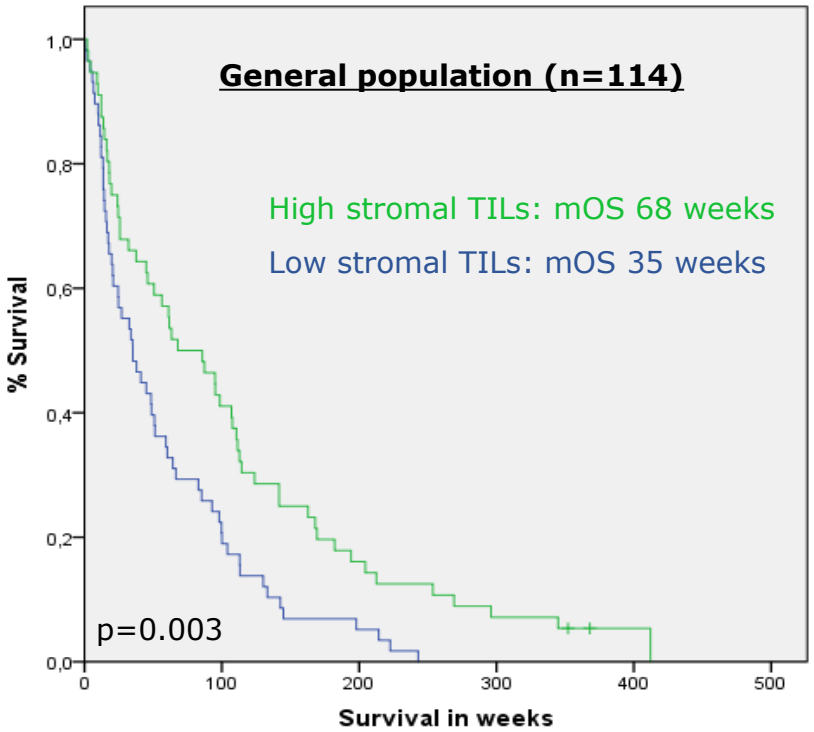
No correlation between sTILs levels and mutation status

TILs - Results

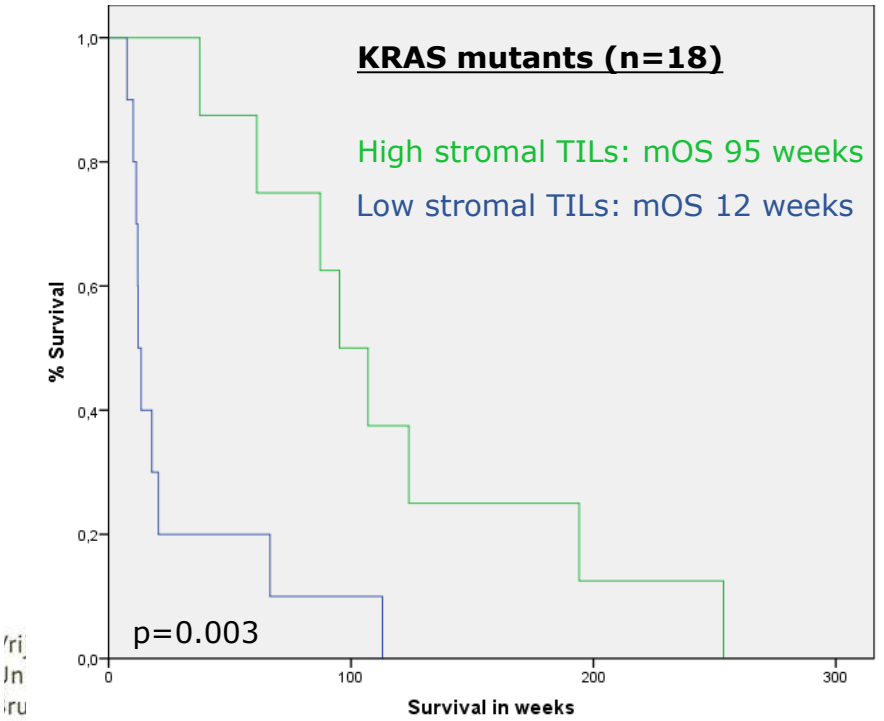
Correlation of sTILs with OS

- mOS general population 49 weeks
- No difference in mOS in the EGFR mutants (n=34; p=0,065)

- General population



- KRAS mutants



TILs - Results

Hypothesis: the immune response in EGFR mutants is of a different order, characterized by differences in the immune micro-environment.

→IHC to distinguish immune subsets will provide additional information.

Alternative hypothesis: Erlotinib is highly efficient in EGFR mutants → minimal impact of additional anti-tumor immune response.

PD-1/PD-L1 - Results

Interobserver variability

ICC > 0,80 for all analysis

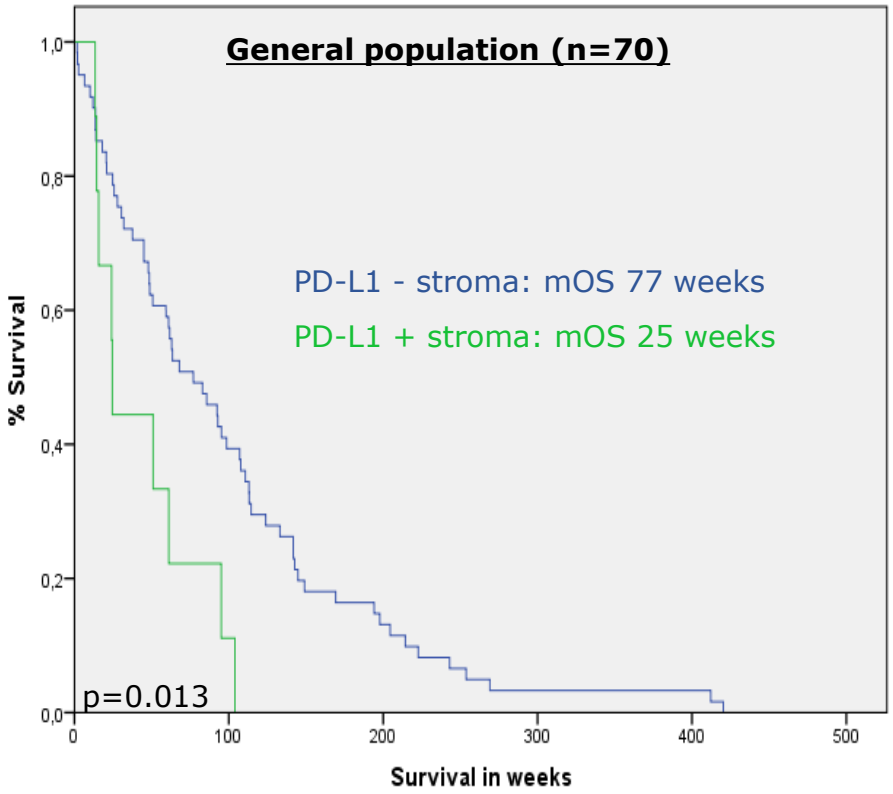
Association of expression with mutation status

Mean expression	General population	EGFR mutants			KRAS mutants			EGFR vs. KRAS mutants
		Mutant	WT	p-value	Mutant	WT	p-value	p-value
PD-L1 stroma	1.2%	0.2%	1.7%	0.129	1.9%	1.1%	0.652	0.564
PD-L1 tumor	4.4%	1.9%	5.7%	0.072	6.7%	3.9%	0.675	0.377
PD-L1 TILs	3.6%	3.1%	3.9%.	0.246	3.7%	3.6%	0.698	0.543
PD-1 TILs	0.7%	1.4%	0.3%	0.078	0%	0.9%	0.242	0.429

PD-1/PD-L1 - Results

Correlation of PD-1/PD-L1 expression with OS

- Only PD-L1 expression on stromal cells influenced OS



PD-1/PD-L1: Results

Association of PD-1/PD-L1 expression and sTILs levels:

- High sTILs are associated with
  - Higher PD-L1 expression on tumor cells (p=0,017)
  - Higher PD-L1 expression on TILs (p=0,001)

  ➔Dynamic expression of PD-L1 (He et al. Sci rep 2015)
  - No association with PD-1 expression nor with PD-L1 expression on stromal cells

Predictive value of PD-L1 expression on stromal cells?

Conclusion

1. Validation of standardized method for scoring sTILs in NSCLC.
2. sTILs are prognostic for longer OS in the general population and KRAS mutants, but not in EGFR mutants.
3. Prognostic value of PD-L1 expression on stromal cells.

References

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