

Eosinophils in clear-cell renal cell carcinoma

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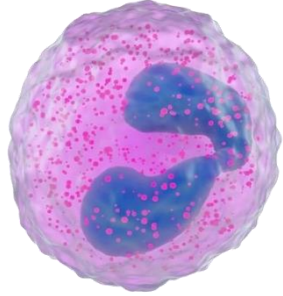


13th Belgian Multidisciplinary
Meeting on Urological Cancers

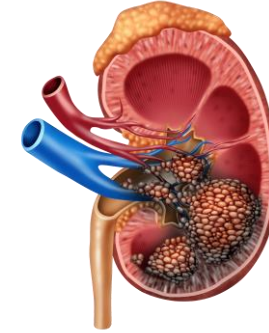
Disclosure

- I have no potential conflict of interest to report

Eosinophils in clear-cell renal cell carcinoma



?



- Rare cells (3%) but :
 - Protective
 - Prognostic
 - Predictive

- Direct toxicity :
 - Peroxidase
 - TNF-alpha
 - Granzyme

- Indirect toxicity :
 - CD8 T lymphocytes recruitment
 - Macrophages polarisation → M1
 - Vascularization normalisation

- 50% of relapse for intermediate-high risk localized ccRCC
- Need for adjuvant therapy
- KEYNOTE-564 :
 - ↗ DFS
 - ↗ OS
 - ↗ irAEs
- Need for more prognostic biomarkers

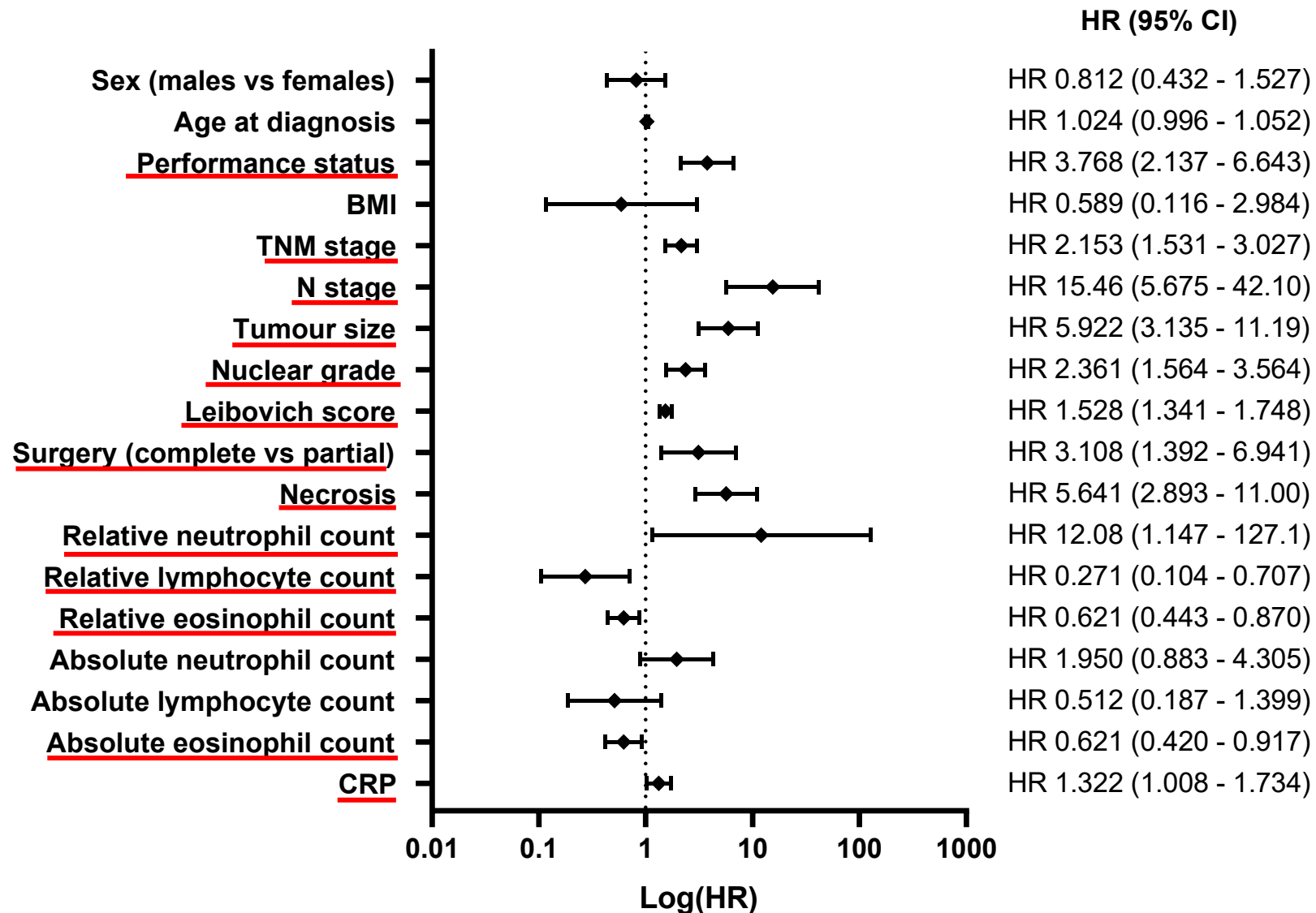
Methods

- Retrospective study including 169 patients with localized ccRCC from CHU Liège and CU Saint-Luc
- Exclusion criteria :
 - No surgery after diagnosis
 - Rhabdoid or sarcomatoid ccRCC
 - Another cancer 5 years before or after ccRCC
 - Any condition influencing immune system
 - Follow up < 2 years
- Collected data :
 - Demographic and clinical data
 - Anatomopathological characteristics
 - Survival outcomes
 - Haematological values at diagnosis, annually until 5y after diagnosis and at relapse
 - Eosinophil infiltration in tumoral tissue assessed by IHC

Results

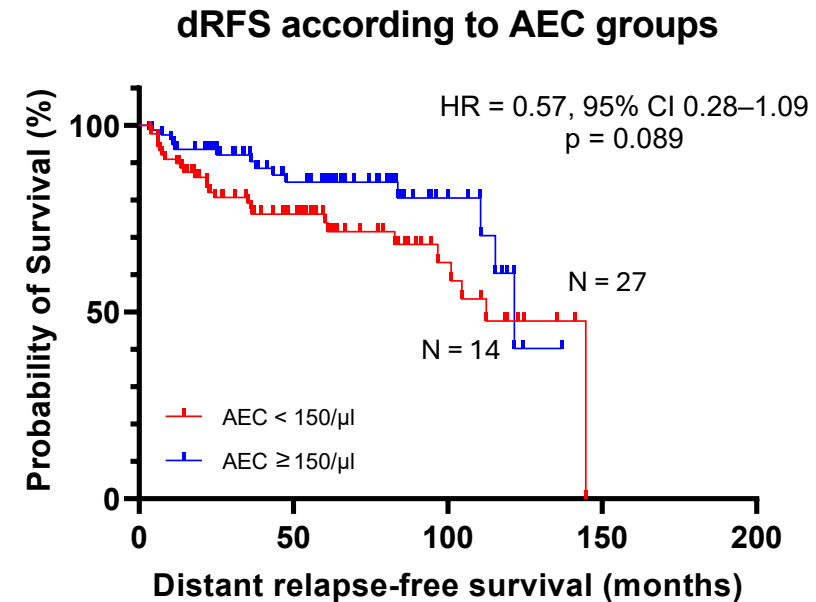
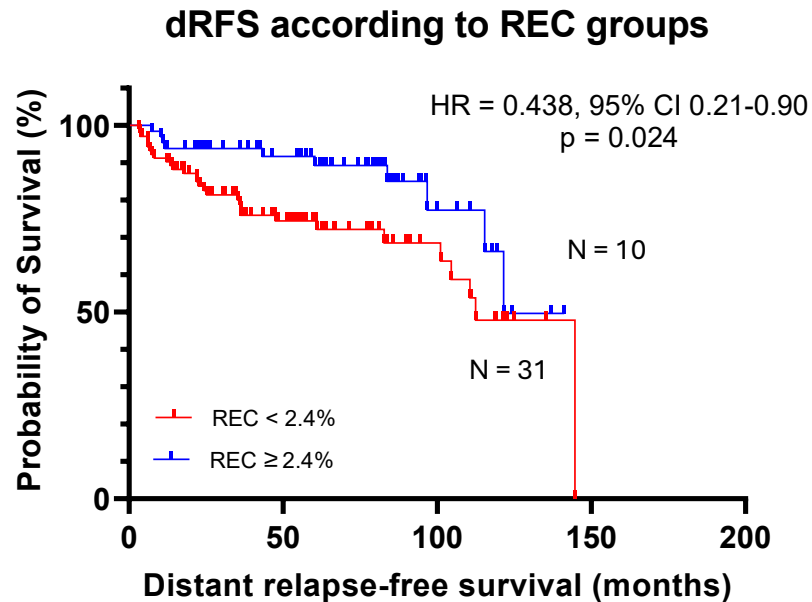
- Median follow up : 89.8 months
- Median age at diagnosis : 62.8y; sex ratio 2:1(M:F)
- Endpoints :
 - Distant relapse-free survival (dRFS) :
 - Relapse = 41 patients (24.3%)
 - Median dRFS : 122 months (83 – 145)
 - Cancer-specific survival (CSS) :
 - Death due to cancer = 14 patients (8.3%)
 - Median CSS : not reached

Factor associated with dRFS



Blood eosinophils and dRFS

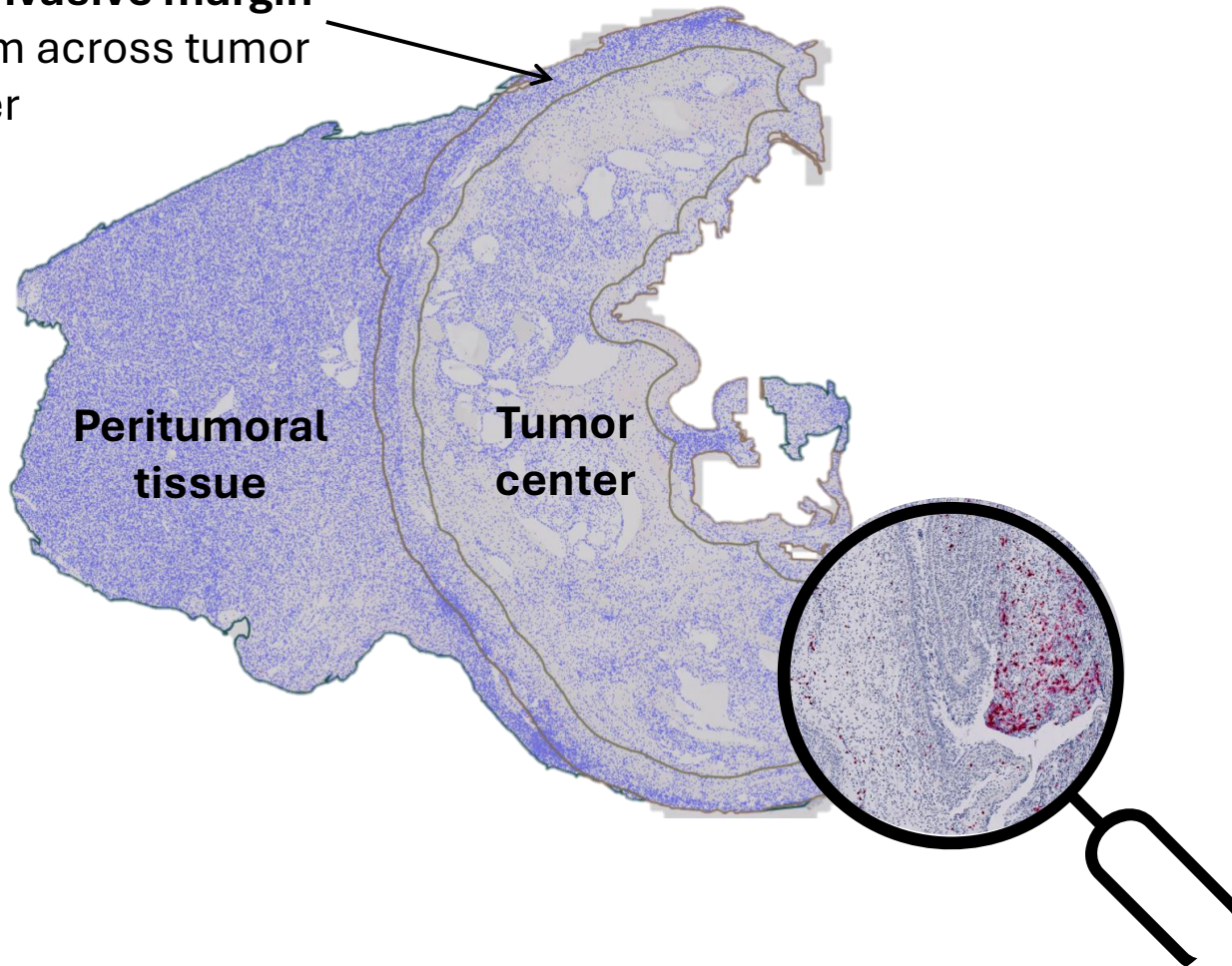
- A higher blood eosinophil count at diagnosis is correlated with a longer dRFS
 - Relative eosinophil count (REC) at diagnosis : HR = 0.621 (0.443 -0.87), p = 0.006
 - Absolute eosinophil count (AEC) at diagnosis : HR = 0.621 (0.42 – 0.917), p = 0.017



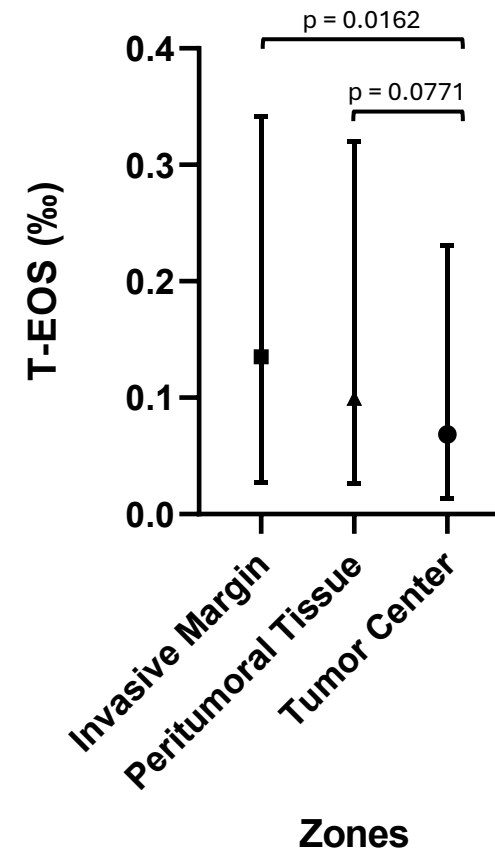
Eosinophil infiltration in tissue

- Eosinophil infiltration evaluated on tumoral and healthy tissue of 96 patients :

Invasive margin
= 1mm across tumor
border

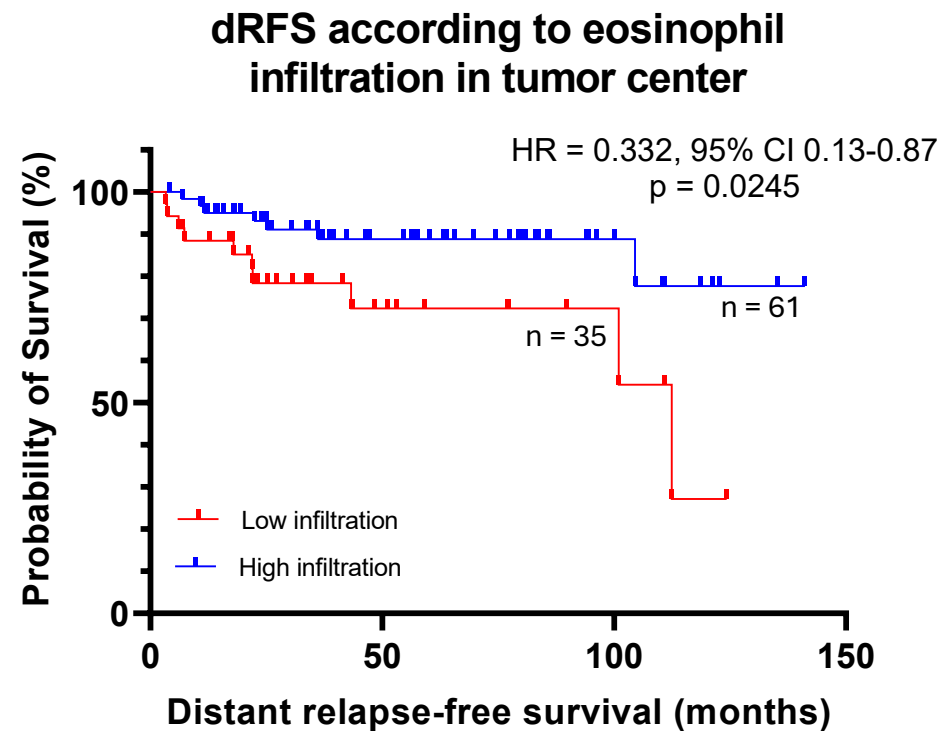
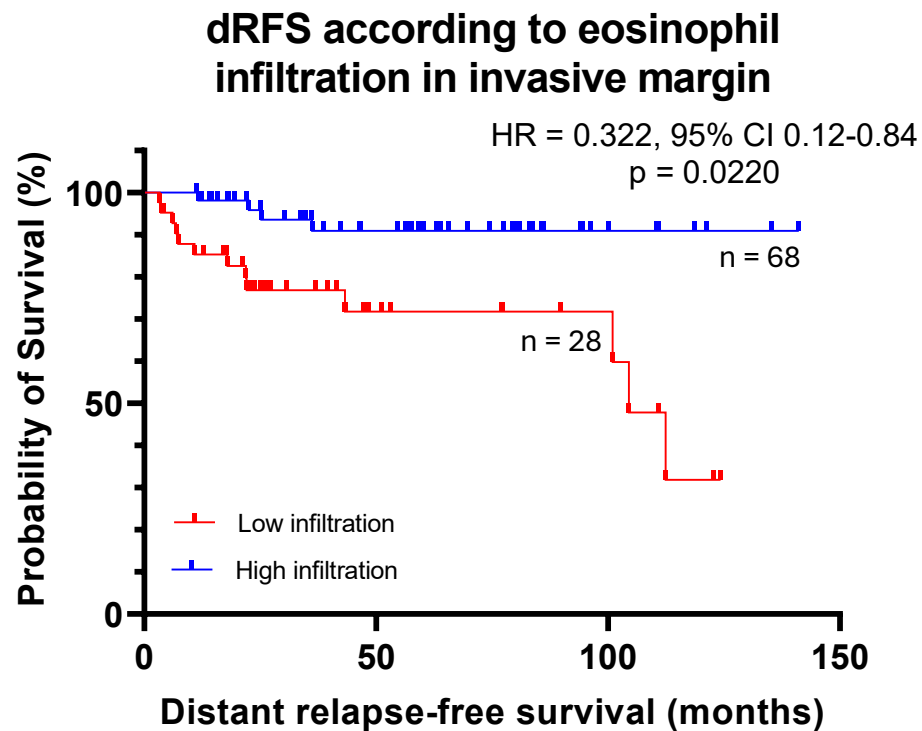


Eosinophil infiltration between zones

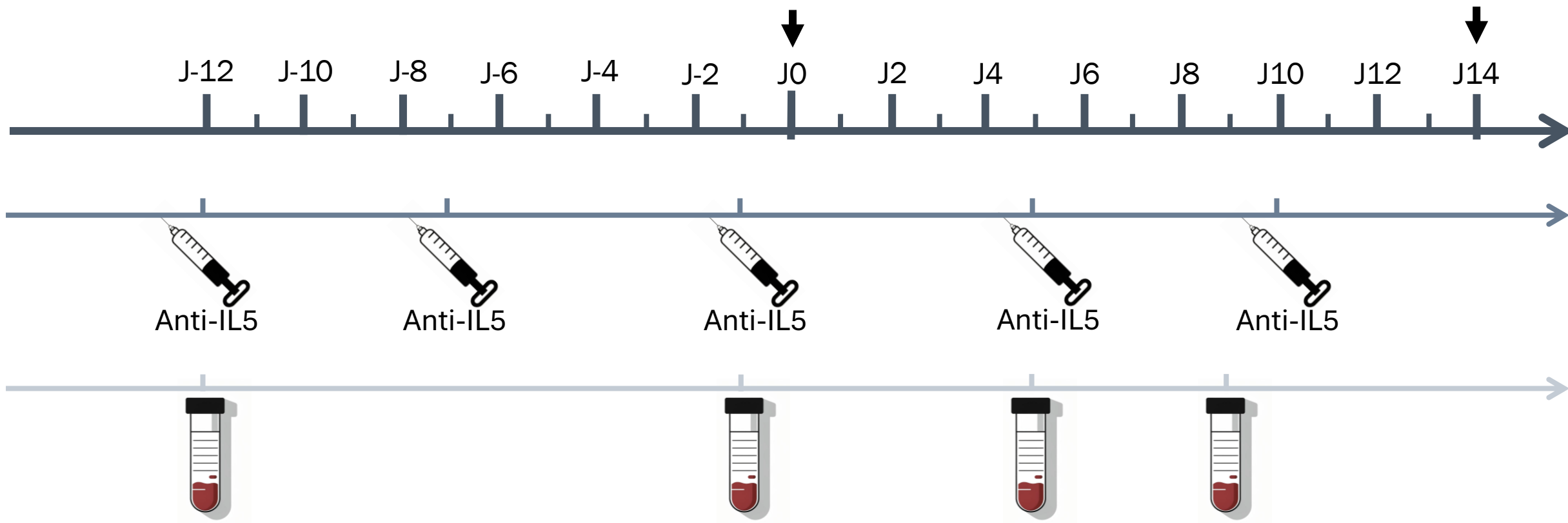
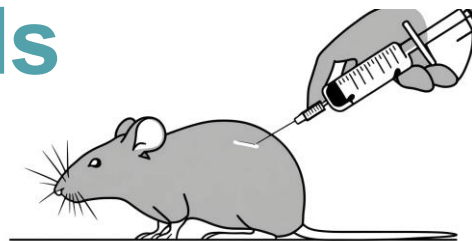


Eosinophil infiltration in tissue

- Higher eosinophil infiltration in invasive margin and tumor center is correlated with longer dRFS

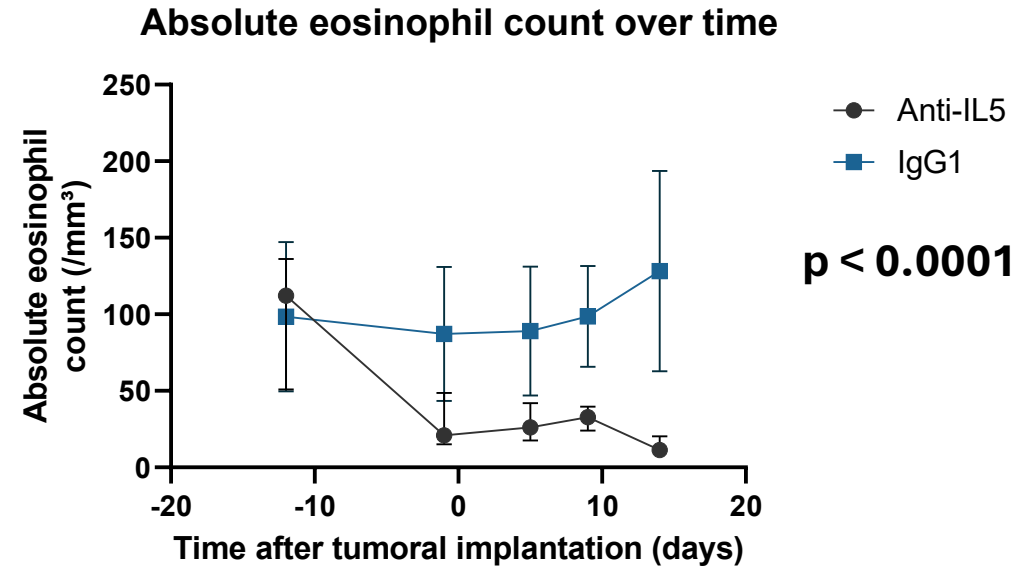
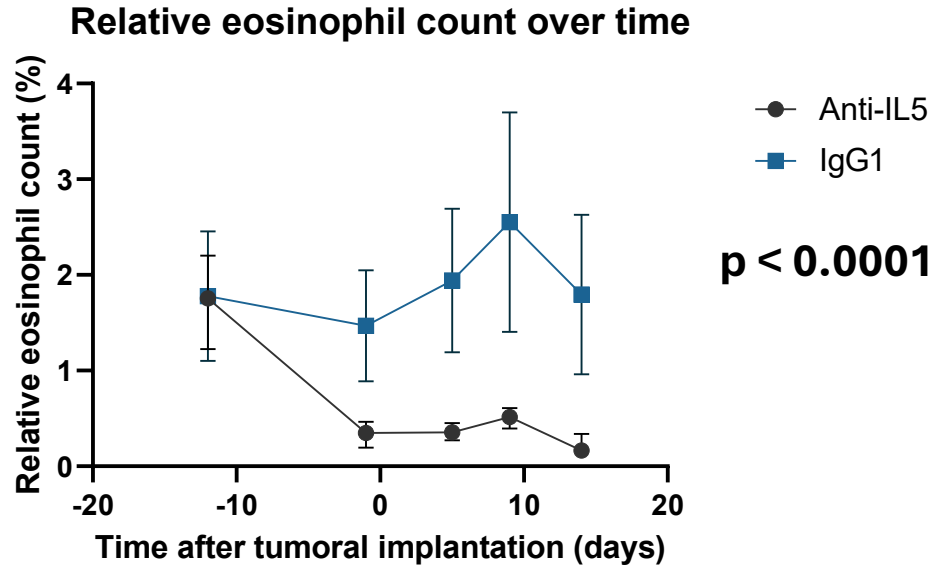


Material and methods



Effect of anti-IL5 on blood cells

- Anti-IL5 decreased eosinophil count

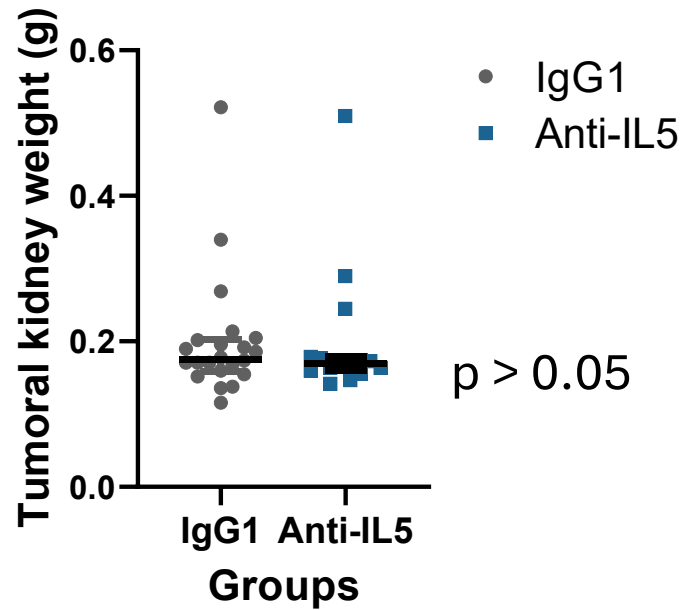


- No differences in total leucocytes, neutrophils, B and T lymphocytes

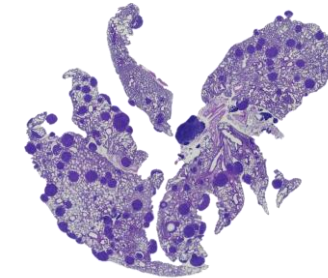
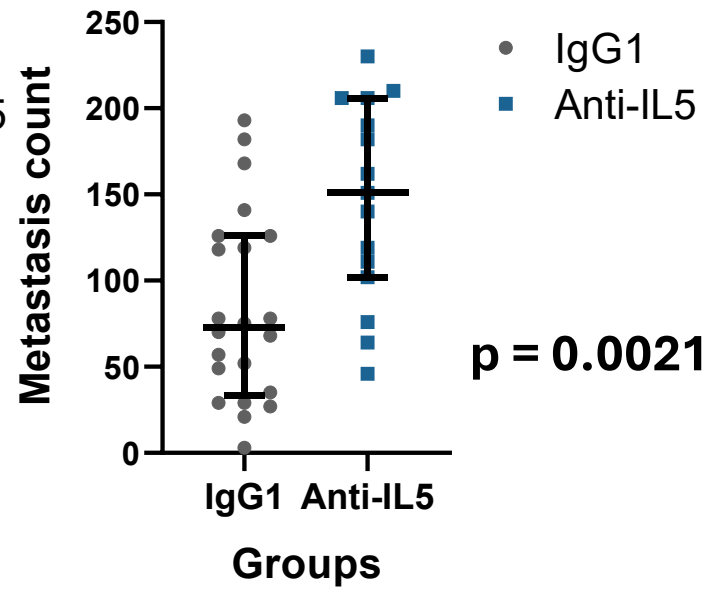
Anti-IL5 increased metastatic burden



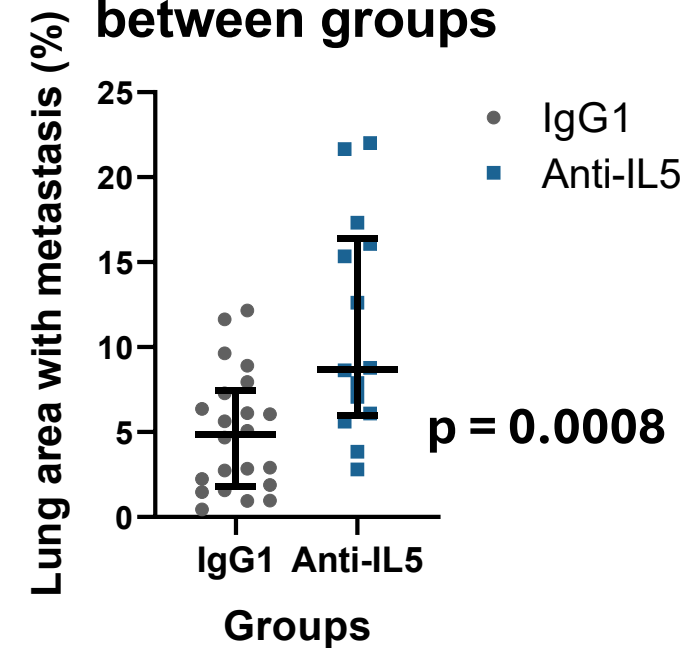
Tumoral kidney weight between groups



Metastasis count (on lung surface)



Lung area with metastases between groups



Conclusion and perspectives

- Higher blood and tissue eosinophil counts are associated with better prognosis
- In vivo study suggests a direct causal role, as eosinophil depletion result in increased metastatic dissemination
- Perspectives = elucidating eosinophil-mediated protective effect by :
 - Characterization of immune cell interactions (RNA seq, IHC, FACS)
 - Profiling of cytokine networks (ELISA)
 - Assessment of metabolic reprogramming (RNA seq)

Thanks to

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 - Pr Christine Gennigens (promoter)
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