City of Hope

THIRD ANNUAL

ISSPP Congress 2022

International Society for the Study of Pleura and Peritoneum

PLENARY ABSTRACT | PLEURAL & PERITONEAL MESOTHELIOMA SESSION

Tumor Microenvironment in Peritoneal Mesothelioma Under Therapy

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Disclosures

- Other financial/material interests in Capnopharm GmbH (royalties).

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This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.

This presentation has been peer-reviewed and no conflicts were noted.

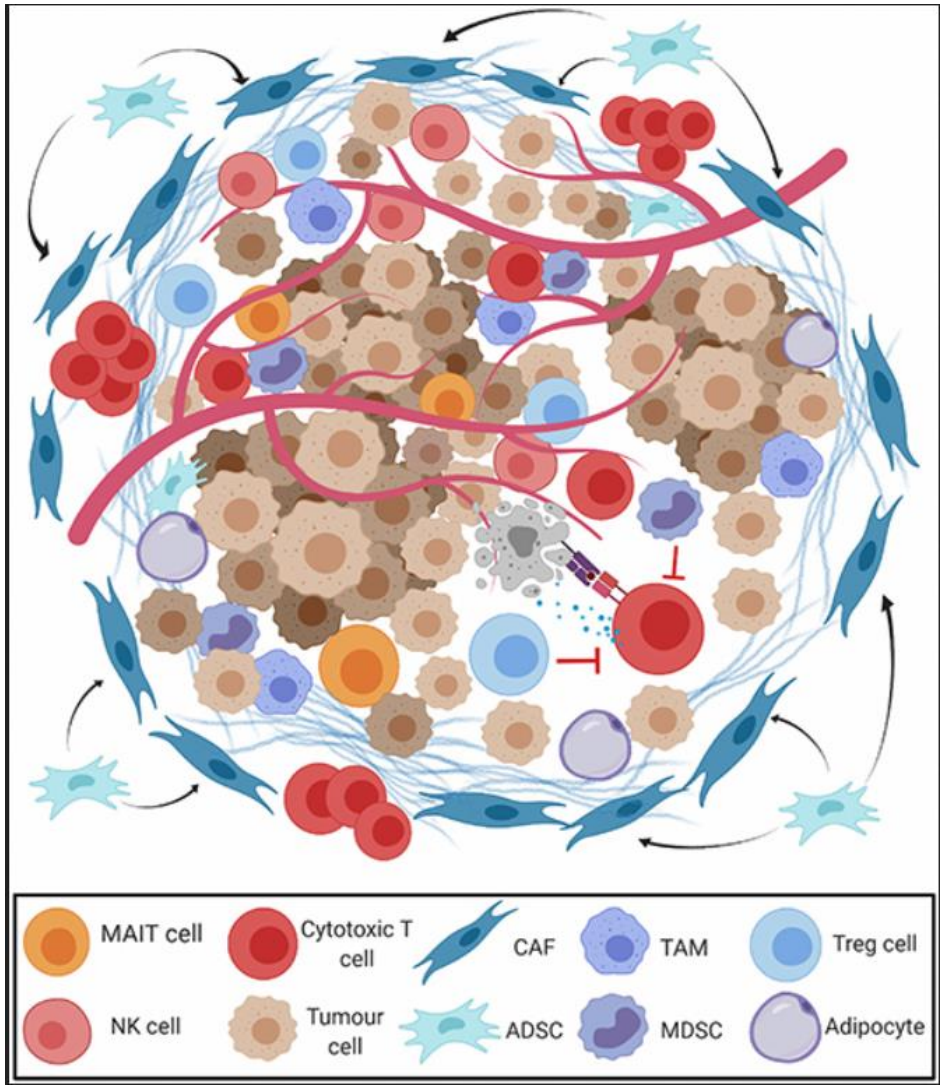
The off-label or investigational use of Cisplatin & Doxorubicin will be addressed.

Mesothelioma

- Peritoneal mesotheliomas 10–15%
- Resectable:
  - Trimodal therapy: chemotherapy, surgery, radiation therapy (pleural)
- Unresectable:
  - First-line chemotherapy (Cisplatin/pemetrexed)
  - Intraperitoneal chemotherapy

Tumor microenvironment

- Complex and changing interaction of
  - Tumor cells
  - Immune cells
  - Tumor-associated macrophages (TAMs)
  - Extracellular matrix
  - Nutrients
  - Cytokines
- Promote tumor growth and metastasis



Power R, et al. Front Oncol. 2020 Jun

TME in peritoneal mesothelioma

- The immune landscape is different in the histological subtypes (1)
- chemokines/cytokines levels/profiles are distinct in mesothelioma compared to those associated with inflammatory responses (2)
- Reflects an active reciprocal communication between tumor and associated stroma
- However, how systemic or intraperitoneal chemotherapy influences the TME has not been investigated

1: Tazzari et al. Journal of Immunology Research 2018
2: Judge et al. Ann Surg Oncol 2016

Knowledge Gap

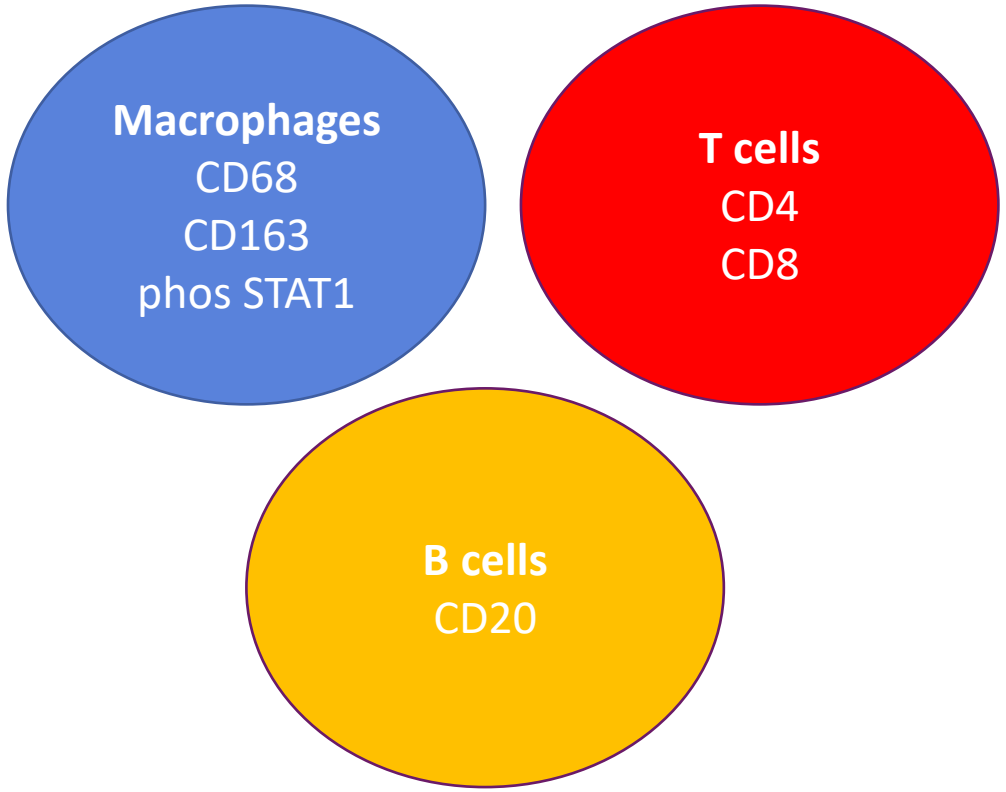
- Composition of the immune cell infiltrate:
  - peritumoral tissue (tumor microenvironment -TME)
  - central tumor area (CTA)
- Changes under therapy in both compartments
- Correlation with histological regression and clinical parameters

Material and Methods 1

- Retrospective study
- three patients with “epithelioid” peritoneal mesothelioma
- All receives prior systemic chemotherapy
- repetitive intraperitoneal chemotherapy (Cisplatin and Doxorubicin)
- Total of n= 19 procedures (max. 10; min. 4)

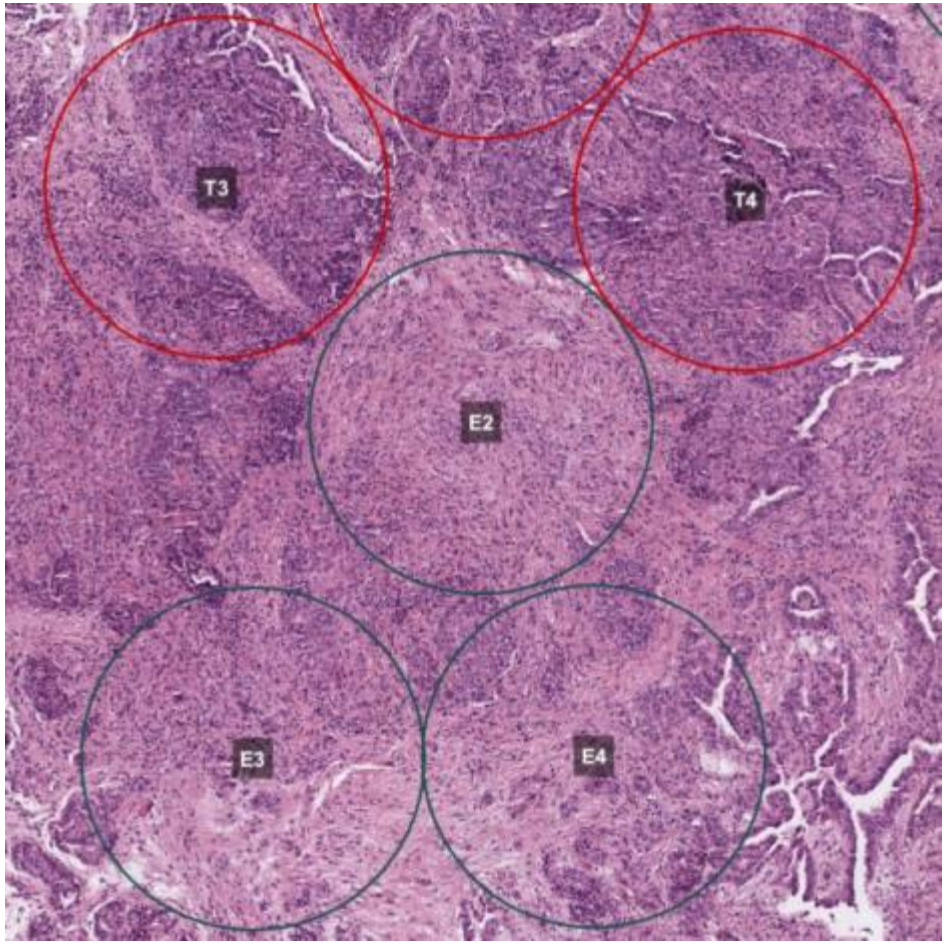
Material and Methods 2: Immunhistochemistry

- Choice of seven markers
- Macrophages: first immune defense
- T and B cells: adaptive immune response
- Other markers: proliferation index (Mib1/Ki67)

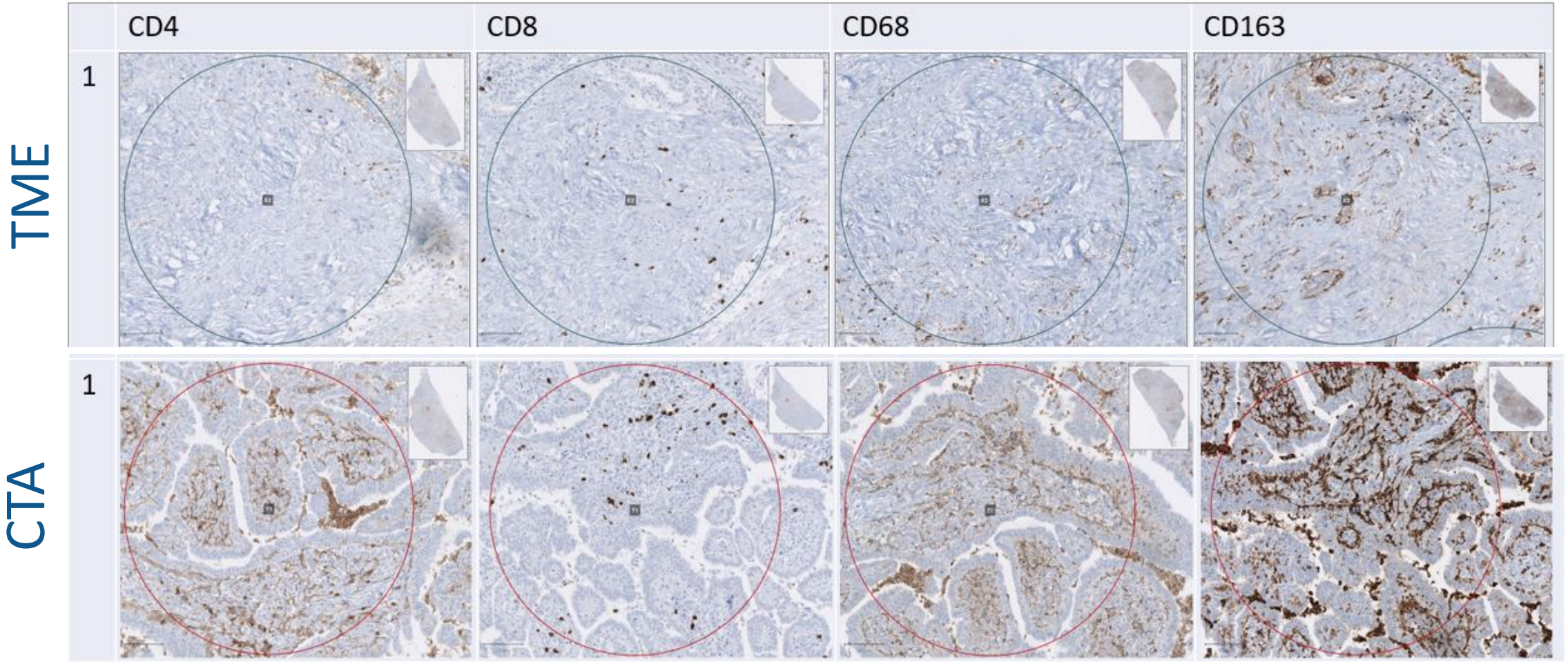


Material and Methods 3: Bioimage Analysis

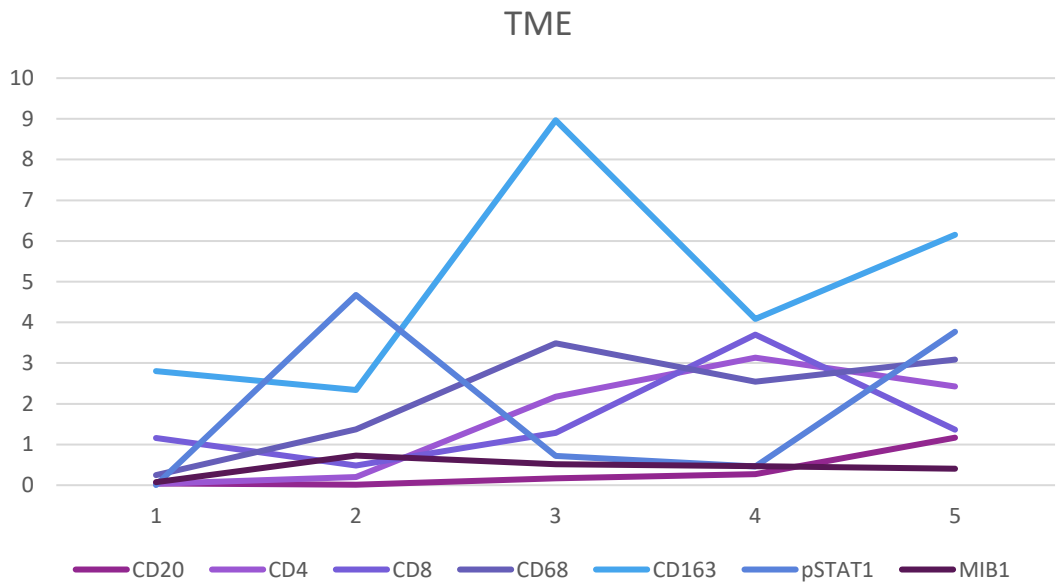
- QuPath (open-source software platform)
- Annotation of tumor (T) and environmental areas (E)
- defined radius to avoid analytical bias due to tissue size

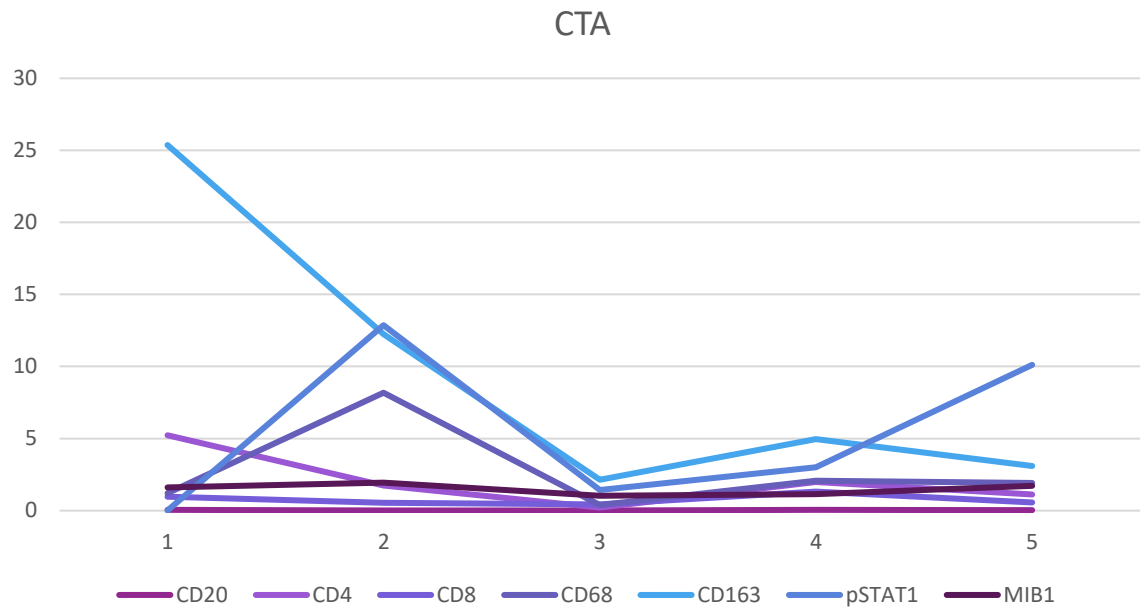


Results 1: immune cell infiltrate differs between the TME and CTA at beginning of therapy



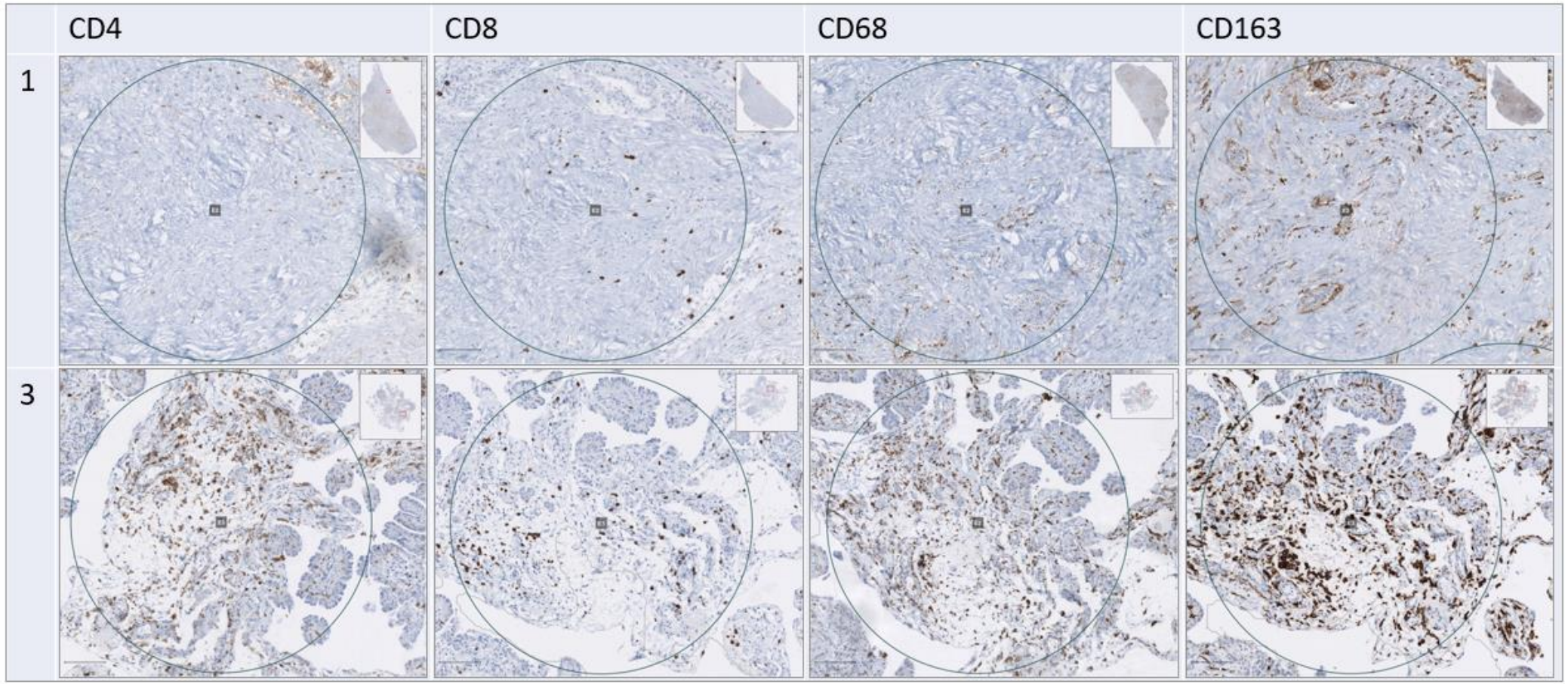
Result 2: Under the course of therapy the immune cell composition changes in both compartments



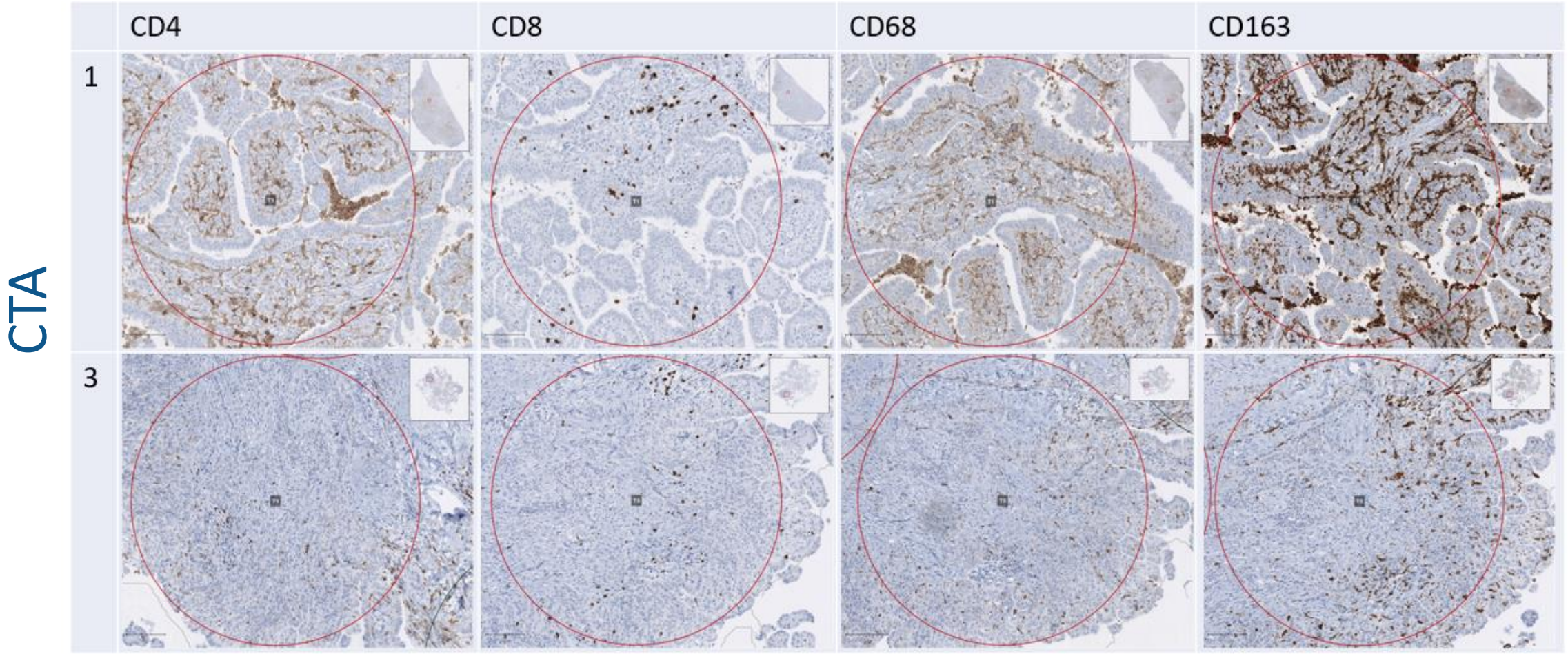


Result 3: Changes in the TME

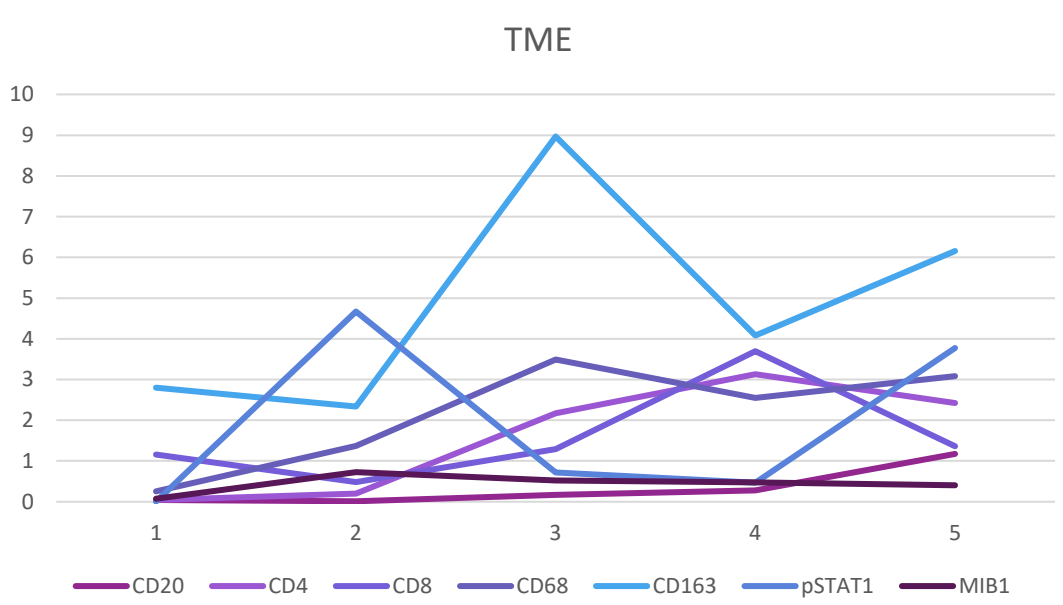
TME

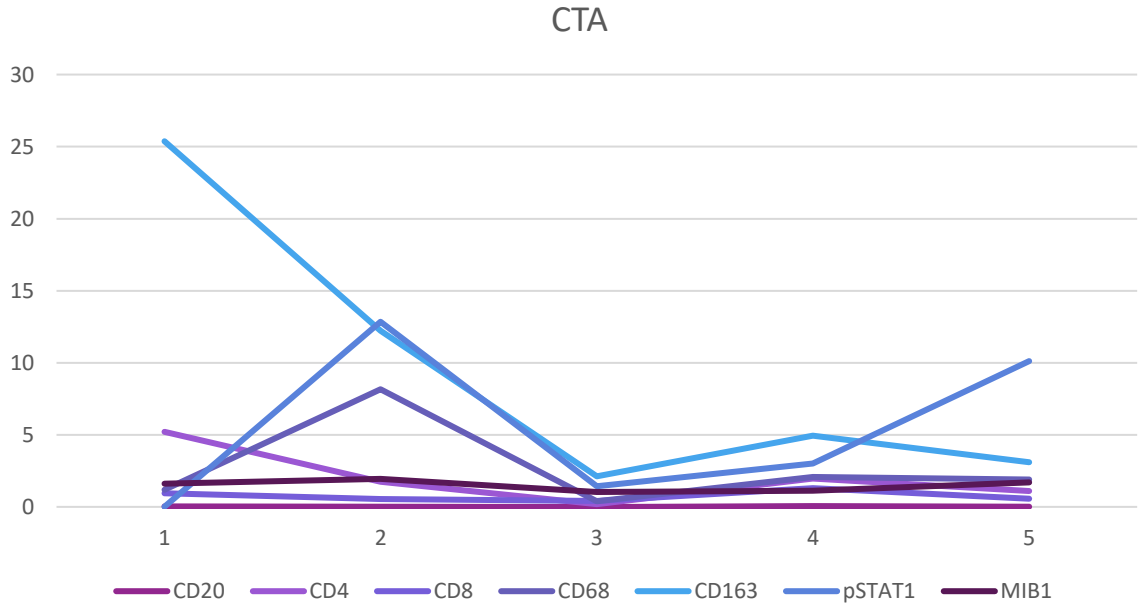


Result 4: Changes in the CTA



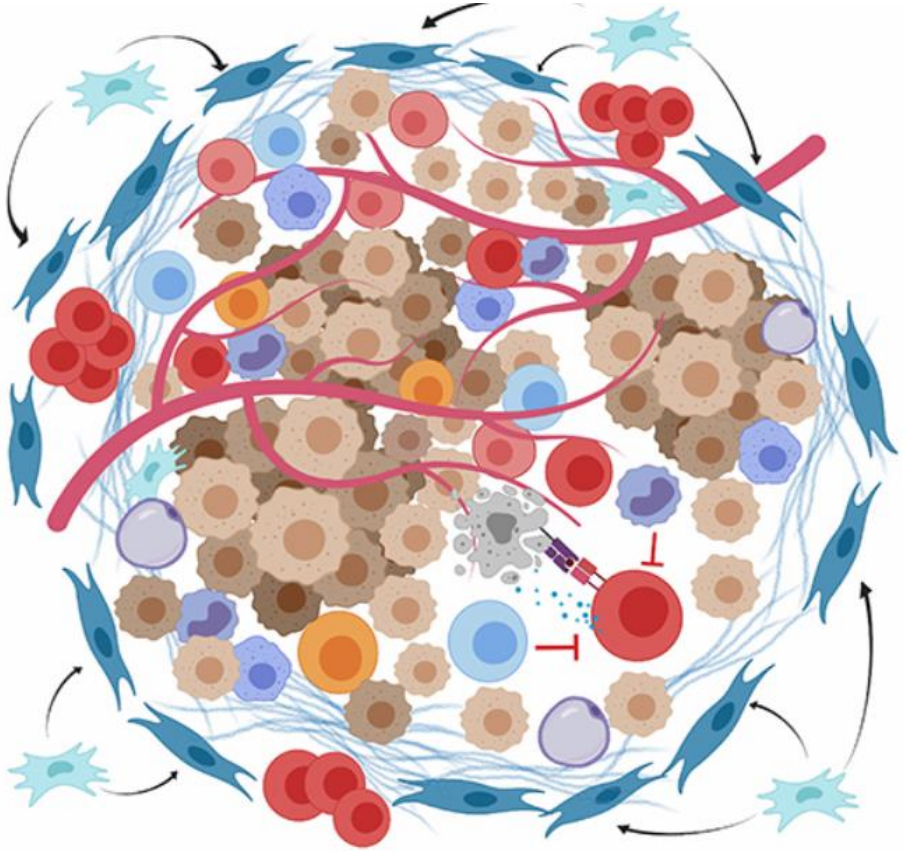
Result 5: With the progression of disease exhaustion of immune response occurs





Tumor microenvironment

- May offer potential drug targets via «immune editing.»
- Immune checkpoint inhibitors might overcome immune exhaustion.



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Conclusion

- Peritoneal mesotheliomas have a unique TME.
- Immune cell infiltrate differs between the TME and CTA.
- Intraperitoneal therapy has an impact on the composition of the TME.
- Exhaustion of the immune self-defense leads to re-establishing of the initial immune landscape.

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