Evaluation of Tumor Infiltrating Lymphocytes (TILs) in Metastatic Tumor Deposits: Some breast carcinoma examples

Guidelines for TILs assessment from the “International Immuno-Oncology Biomarker Working Group”

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Define area for TILs evaluation

- TILs within the borders of the metastasis are evaluated
- The invasive edge of the metastasis is included in the evaluation, but not reported separately
- Immune infiltrates outside of the borders of the metastases (in the pre-existing tissue) are not included
Define area for TILs evaluation

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- Immune infiltrates outside of the borders of the metastasis are not included
- In some metastases the tumor border can be sharply delineated
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- Due to the extremely infiltrative (‘lobular-like’) growth pattern of some metastases, with only minimal disturbance of the pre-existing skin histology, the tumor border is difficult to discern.
Define area for TILs evaluation

Include TILs evaluation in (desmoplastic) stroma of the metastasis

Breast cancer peritoneal metastasis

Include TILs in this area = stromal TILs
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- In metastases, similar guidelines furthermore apply as in primary tumours:
  - Areas of necrosis or fibrosis are not included in the evaluation
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Determine the localization of inflammatory infiltrate

Breast cancer liver metastasis

Intraepithelial TILs

Stromal TILs
Determine the localization of inflammatory infiltrate

Intraepithelial TILs

Do not include TIL in this area

Breast cancer brain metastasis

Stromal TILs
Determine the localization of inflammatory infiltrate
Determine the localization of inflammatory infiltrate

In some metastasis, distinguishing between stromal and intratumoral TILs is very difficult, due to the infiltrative growth pattern. It can be even a challenge to distinguish between epithelial tumor cells and TILs.
Determine type of inflammatory infiltrate

Do not include granulocytic infiltrate in areas of tumor necrosis

Include only mononuclear infiltrate (lymphocytes & plasma cells)

Breast cancer brain metastasis

Do not include TIL in this area

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