Chemotherapy of malignant pleural mesothelioma does not preclude use of check-point blockade

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Disclosure

No conflicts of interest
Mesothelioma

- Epitheloid
- Biphasic
- Sarcomatoid
Systemic treatment of mesothelioma

- 1st line: platin-based and pemetrexed
- 2nd line: gemcitabine, vinorelbine
- Small molecules: no clinical benefit
- Checkpoint point inhibitors

<table>
<thead>
<tr>
<th>Patients (N=29)</th>
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<tbody>
<tr>
<td>Complete response</td>
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<tr>
<td>Partial response</td>
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<tr>
<td>Stable disease</td>
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<tr>
<td>Progressive disease</td>
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<td>Disease control</td>
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Data are n (%) or n (%; 95% CI). Tumours were assessed at 70-90 days (RECIST 1.0 for peritoneal or modified RECIST for pleural malignant mesothelioma). RECIST—Response Evaluation Criteria in Solid Tumors.

Table 2: Best tumour response and disease control

Molecules involved in co-inhibition and co-stimulation determine the quality of T cell responses
Modulation of expression through hypoxia and IFN-gamma

Does chemotherapy modulate targets of checkpoint blockade?

**Tumor samples**
- **TMA (n=88)** before chemo
- **Whole tumor (n=10)** before - after chemotherapy

**Cell lines**
- before - after chemotherapy
TMA (n=88)

HLA I: 90% of cases positive

HLA II: 16% of cases positive
TMA (n=88)

ICOS-L: 90% of cases positive

B7-H3: 69% of cases positive
Whole tumor (n=10)

TUMOR

STROMA

BEFORE

PD-L1

FoxP3

AFTER
Does chemotherapy modulate targets of checkpoint blockade?

Cell lines derived from the 3 histological subtypes ZLT55, MSTO, SPC11

Chemotherapy:
Cisplatin /Pemetrexed
Gemcitabine
Stable expression upon treatment with gemcitabine
ZLT55: derived from epitheloid subtype
Stable expression upon treatment with gemcitabine
MSTO: derived from biphasic subtype
Stable expression upon treatment with gemcitabine

SPC11: derived from sarcomatoid subtype
Conclusions

• Frequent expression of HLA and immunomodulatory molecules

• The targets of immune checkpoint inhibitors are not downregulated by Gemcitabine or Cisplatin/Pemetrexed in vivo and in vitro

• Combining blockade of immune checkpoints with Gemcitabine or Cisplatin/Pemetrexed is rational
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