Does systemic anticancer treatment result in resolution of malignant pleural effusion in patients with pharmacologically sensitive tumors?

**THE CLINICAL QUESTION**
Is systemic anticancer treatment (SACT) associated with resolution of malignant pleural effusions (MPE) in patients with pharmacologically sensitive tumors?

**STUDY CONCLUSION**
There is no independent association between SACT and MPE resolution in pharmacologically sensitive tumors.

**STUDY BACKGROUND**
Malignant pleural effusion is the 2nd most common cause of exudative pleural effusion. Current estimates suggest that it affects more than 15% of cancer patients; however, the incidence is expected to increase due to overall improved cancer survival. Given the advanced stages in which patients with MPE present and the associated morbidity of MPE, treatment should focus on symptom palliation in a minimally invasive manner while minimizing repeated procedures. Several reports suggested that systemic anticancer therapy, in pharmacologically sensitive tumors, might resolve MPE and reduce the need for definitive pleural interventions. This study explored this possible association.
CURRENT PRACTICE

In 2018, ATS/STS/STR issued a statement recommending definitive pleural intervention to all patients with MPE using chemical pleurodesis or indwelling pleural catheter upon first recurrence when symptom palliation was achieved after initial large volume drainage.

ERS/EACTS statement on the management of MPE suggested there was insufficient evidence to determine the value of antitumor treatments in the management of MPE.

METHODS & RESULTS

STUDY DESIGN

Type of trial: Retrospective analysis of prospective observational cohort

N: 280

Study groups: 127 = pharmacologically sensitive tumor, 153 = non pharmacologically sensitive tumor

Definition of pharmacologically sensitive tumors:
- ER, PR, or Her2-neu positive breast or ovarian cancer
- EGFR, ALK, ROS1-positive NSCLC, or NSCLC with > 50% cell positivity for PD-L1
- Small cell lung cancer
- High-grade lymphoma

Setting: Single pleural center in the UK

Treatment Period: May 2008 through August 2017

Follow up: minimum follow up 602 days

Primary outcome: MPE resolution (Defined as radiologic resolution [no effusion or minor blunting of the costophrenic angle CXR, absent or minimal fluid on CT imaging, or absence of fluid with or without features of pleurodesis on thoracic ultrasound] with cessation of pleural intervention and/or removal of indwelling pleural catheter)

POPULATION

Inclusion criteria:
- Subjects diagnosed with the first episode of MPE from lung, breast, ovarian or hematologic malignancy.
Baseline Characteristics “presented as sensitive tumors vs non-sensitive tumors”

Median (range) age 73 (62-80) vs 75 (67-80)
Female gender 72% vs 47%

Tumor type

Hematologic malignancy 19% vs 0%
Breast cancer 44% vs 7%
Ovarian cancer 15% vs 9%
Small cell lung cancer 13% vs 0%
Adenocarcinoma 8% vs 52%
Squamous cell carcinoma 0% vs 18%

Cancer treatment received:
SACT therapy 88% vs 38%
Radiotherapy 47% vs 29%
Surgery 42% vs 12%

Pleural effusion size:
Blunting of costophrenic angle 3% vs 4%
Fluid occupying <25% of hemithorax 8% vs 12%
Fluid occupying 26-50% of hemithorax 37% vs 40%
Fluid occupying 51-75% of hemithorax 45% vs 27%
Fluid occupying >75% of hemithorax 7% vs 17%
Nonexpendable lung present 27% vs 29%

Pleural intervention:
Diagnostic/therapeutic aspiration 90% vs 88%
Medical thoracoscopy 11% vs 10%
Chest drain insertion 47% vs 53%
Indwelling pleural catheter 38% vs 35%
Chemical pleurodesis 35% vs 35%

Overall, two sub-cohorts are well balanced.

INTERVENTIONS

None (retrospective study)

OUTCOMES

Primary outcomes: MPE resolution

Secondary outcomes:
- Time to MPE resolution
- MPE resolution at 3 months
- Total number of pleural interventions

Adverse events: Not reported
STUDY STRENGTHS
Inclusion of a comparator group
Controlling confounders
Performing sensitivity analysis

STUDY LIMITATIONS & POTENTIAL FOR BIAS
- Single-center study
- Retrospective nature
- Lack of randomization
- Lack of follow-up algorithm
- No adverse effects/outcomes reported
- No representation of lung cancer patients who are treated with immunotherapy (given it’s a novel therapy).
- Long study duration which makes the study susceptible to temporal changes in care not accounted for

RESEARCH QUESTION
Is systemic anticancer treatment associated with higher rates of MPE resolution in people with pharmacologically sensitive tumors?

TAKE HOME MESSAGE
All patients with MPE should be offered early definitive pleural intervention in line with current guidelines, regardless of tumor sensitivity or treatment plan.

RCTs are needed to further confirm this and to investigate different types of cancer where the potential benefit of SACT may exist.


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