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Early View

Correspondence

CANCER IN THE TIME OF COVID: Expert opinion on how to adapt current practice

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CANCER IN THE TIME OF COVID:

Expert opinion on how to adapt current practice

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To the editor:

The susceptibility of cancer patients to adverse outcome of viral infections is well known from past experiences, e.g. Influenza increasing the risk of hospital admission with respiratory distress four times, and the risk of death ten times, compared to patients without cancer [1]. This risk is particularly elevated in patients with neutropenia or lymphopenia, which is often the case in patients treated with chemotherapy. In Wuhan, 1% of patients with SARS-CoV-2 were reported to suffer from cancer, which is more than three times the incidence of cancer in the Chinese population [2]. In addition, in 39% of cancer patients (compared to 8% of patients without cancer) transfer to the intensive care unit was necessary, with their illness deteriorating more rapidly (13 vs 43 days to severe event) [2]. Chemotherapy or surgery <1 month before was an important risk factor (OR 5.34, p=0.0026).

There is no doubt that patients with lung cancer or mesothelioma, who are often older and with concurrent obstructive or restrictive lung disease, are even more at risk for unfavourable outcomes in case of infection with SARS-CoV-2. Therefore, we have to reconsider our current clinical practice, in order to limit time-in-hospital, promote telemedicine, avoid unnecessary contact with medical personnel, and reduce severe neutropenia.

The British Thoracic Society (BTS) recently published recommendations on Covid and lung cancer/mesothelioma [3]; the French Haut Conseil de la Santé Publique (HCSP) on cancer in general [4-5]. This letter describes the viewpoint of the authors on these general recommendations (not always agreeing!) and tries to translate them into practical advice for clinicians (note: may not be feasible due to reimbursement issues), starting from the current standard of care. In all patients we propose to use video consultation as much as possible instead of face to face consultation [3,5].

RECOMMENDATIONS FOR TREATMENT OF SMALL-CELL LUNG CANCER (SCLC)

Stages I-III:

- Standard of care in most patients is chemoradiotherapy with 4 cycles of cisplatin/etoposide as preferred chemotherapy regimen.
- Replacing intravenous with oral etoposide to reduce time-in-hospital should be weighed against its lower biological availability and variable pharmacodynamics in a curative setting [6]
- In patients with stage I SCLC surgical resection of the tumour, followed by adjuvant chemotherapy (4 cycles of cisplatin/etoposide) is indicated.
- In selected patients, accelerated hyperfractionation of radiotherapy (twice-daily) remains an option to decrease the number of hospital visits.

Stage IV or not eligible for chemoradiotherapy:

- Palliative chemotherapy with platinum/etoposide is recommended.
- Replacing intravenous with oral etoposide to reduce time-in-hospital may be considered, providing attention is given to its lower biological availability and variable pharmacodynamics [6].
- In patients with increased risk of febrile neutropenia (FN) dose reduction might be an alternative to primary prophylactic use of G-CSF in all patients, given the palliative setting [7].

- Given the limited improvement in overall survival and the need for triweekly clinic visits during the maintenance phase, the addition of a checkpoint inhibitor (atezolizumab or durvalumab) can be omitted.
- The indication for second-line systemic therapy should be reviewed with extra care. In platinum-sensitive relapse, rechallenge with first-line chemotherapy is recommended. In platinum-refractory relapse, oral topotecan is the preferred regimen. Cyclophosphamide/doxorubicin/vincristine is not recommended as an alternative to topotecan in view of the need to hospitalize the patient.
- Any third-line chemotherapy should be considered only in fit patients with low risk of complications.

RECOMMENDATIONS FOR TREATMENT OF NON-SMALL-CELL LUNG CANCER (NSCLC)

Surgery

- Consider delaying surgery for up to 3 months in small tumours that appear not to grow fast; follow up of growth rate with chest CT is recommended [3].
- Consider stereotactic radiotherapy as an alternative in patients who are marginally fit for surgery, due to comorbidity or limited pulmonary reserve [3].
- Minimal invasive approaches are preferred over thoracotomy to limit time-in-hospital [3].

Adjuvant chemotherapy:

- Adjuvant chemotherapy in stage II and III and in some patients with high-risk stage IB leads to 5% improvement in 5-year survival and is therefore recommended.
- In elderly patients, patients with significant comorbidity or decreased performance (PS ≥ 2), the possible benefits of adjuvant chemotherapy may be outweighed by the increased risk of complications. Consider omitting adjuvant chemotherapy or stopping early (e.g. after 3 cycles) [3].
- Consider giving cisplatin/docetaxel to limit time-in-hospital, as it avoids day 8 administration of gemcitabine or vinorelbine, and has equivalent efficacy. In non-squamous NSCLC, cisplatin/pemetrexed is an equally efficacious alternative [8].
- In patients with an activating EGFR mutation, consider a 1 year course of daily oral EGFR-TKI as an alternative to adjuvant chemotherapy (currently no phase 3 evidence of superiority available).

Radiotherapy

- Consider delaying curative radiotherapy for small tumours that appear not to grow fast; follow up of growth rate with chest CT is recommended [3].

Concurrent chemoradiotherapy:

- Consider giving cisplatin/pemetrexed instead of cisplatin/etoposide, or weekly carboplatin/paclitaxel in non-squamous NSCLC to limit time-in-hospital [9].
- Consider giving adjuvant durvalumab at a dose of 20 mg/kg every 4 weeks instead of 10 mg/kg every 2 weeks to limit time-in-hospital. Phase 1b data have not shown an increase in adverse events [3, 10]

Systemic therapy:

- Evaluate the indication for palliative chemotherapy, immunotherapy or both with extra care in elderly patients or patients with significant comorbidity, decreased performance (PS ≥2), social isolation, decubitus, urinary catheters, … especially in second or further lines [3].
- Consider delaying chemotherapy or immunotherapy in patients who are asymptomatic and have indolent disease [3].
- Usual recommendations for chemotherapy, immunotherapy and targeted therapy apply.
- In patients with increased risk of febrile neutropenia (FN) dose reduction might be an alternative to primary prophylactic use of G-CSF in all patients, given the palliative setting [7].
- Keep in mind that pneumonitis may also be drug-induced (e.g. chemotherapy, TKI's) or immune-mediated (checkpoint inhibitors).
- Triweekly chemotherapy is preferred over weekly regimens (e.g. docetaxel) to limit time-in-hospital [4].
- Consider limiting palliative chemotherapy to 4 cycles and omitting pemetrexed maintenance therapy [3].
- In patients who are PD-L1 >50%, first-line pembrolizumab monotherapy is preferred over pembrolizumab plus chemotherapy [3].
- Consider giving nivolumab at a dose of 480 mg every 4 weeks instead of 240 mg every 2 weeks to limit time-in-hospital [3, 11].
- Immunotherapy in second-line is preferred over chemotherapy in patients who did not receive immunotherapy in first line.
- In case of lack of response to immunotherapy or significant toxicity, early discontinuation should be considered.
- Third-line chemotherapy is not advisable [3].
- Consider evaluating the response to immunotherapy or TKI less often in clinically stable patients.

<u>Supportive therapy/other:</u>

- Advance care planning should be discussed with all patients in order to avoid admission to hospital [3].
- Do not resuscitate (DNR) status should be available for all stage 4 patients.
- Patients receiving denosumab or low-molecular-weight heparin should be taught to self-administer [3].
- Patients receiving denosumab should not routinely consult a dentist before starting.
- Avoid transfusion of blood or platelets by using dose reduction or early discontinuation of chemotherapy in palliative patients.

RECOMMENDATIONS FOR TREATMENT OF MALIGNANT PLEURAL MESOTHELIOMA (MPM)

- In case of early-stage disease in a fit patient, evaluate for multimodality treatment including surgery (preferably extended pleurectomy/decortication) and chemotherapy.
- Palliative chemotherapy with 4 cycles of platinum/pemetrexed is recommended in all other cases of PS 0-1 patients.
- Evaluate the indication for palliative chemotherapy with extra care in elderly patients, patients with significant comorbidity or poorer performance (PS ≥2),
- Consider delaying chemotherapy in patients who are asymptomatic [3].

- Pemetrexed maintenance therapy is not recommended due to lack of efficiency data.
- Be reluctant with second-line chemotherapy with either vinorelbine, gemcitabine or doxorubicin.
- A home-managed indwelling pleural catheter is preferred over procedures that require a clinic visit [3].

RECOMMENDATIONS FOR TREATMENT OF THYMIC EPITHELIAL TUMOURS (TET)

- Platinum/etoposide is preferred over more haematotoxic regimens such as ADOC, CAP or VIP.

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