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3rd National Meeting 2020 – 16/12/2020 – Virtual debate on COVID-19

Managing lung cancer patients in the era of COVID-19

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Disclosures [update 11/2020, alphabetical]

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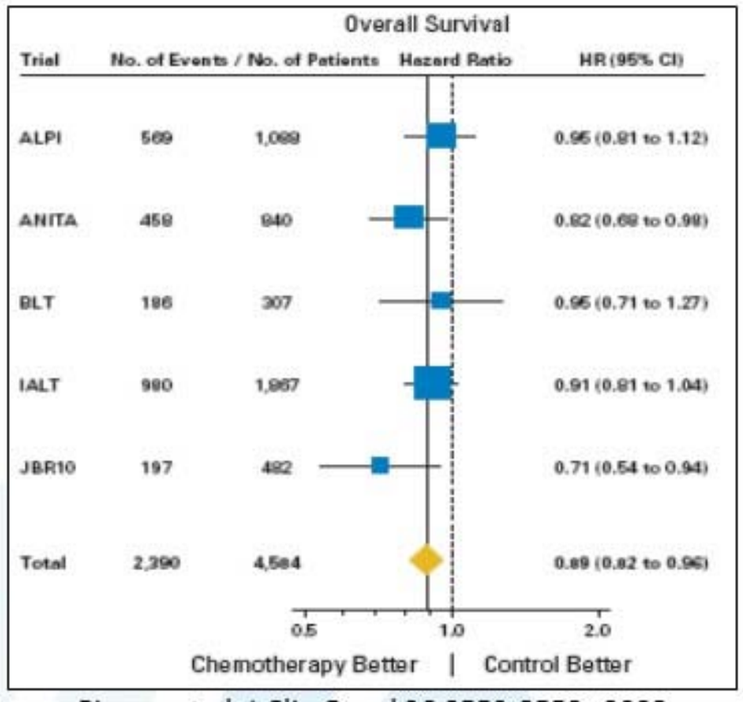
- **Research funding at University Hospitals KU Leuven**
  - **MSD**
- **Advisory functions**
  - **AstraZeneca, BMS, Boehringer, MSD, Novartis, Pfizer, Roche, Sanofi**
- **Lectures**
  - **AstraZeneca, BMS, Eli-Lilly, MSD**
- **Others**
  - **None**

Disclosures



Pignon et al, J Clin Oncol 26:3552-3559, 2008

Evidence based medicine
- **RCTs / meta-analyses**

Expert based medicine
- **COVID-19**

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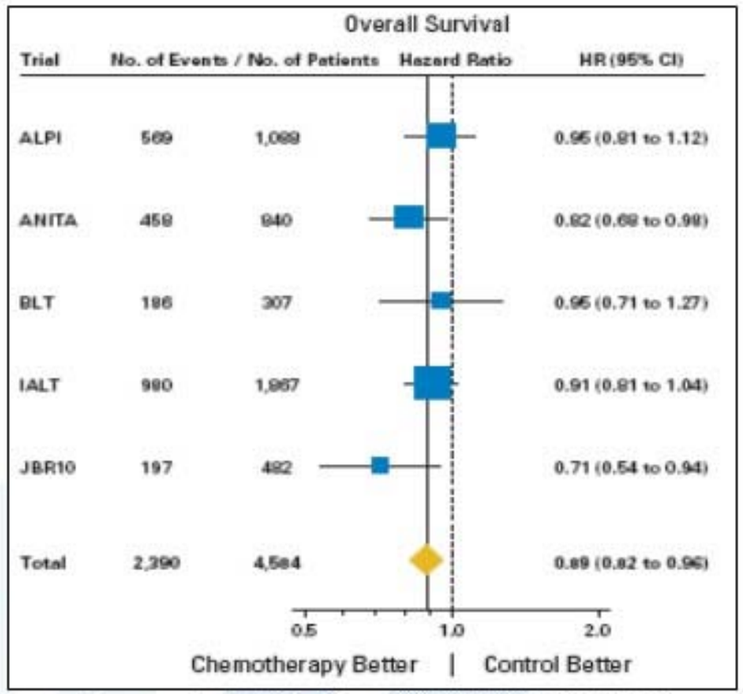

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Evidence based medicine
- **RCTs / meta-analyses**

Expert based medicine
- **COVID-19**

Fake-news based medicine

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Lung cancer in COVID-19 era

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- Practical cases
- What does lung cancer mean for COVID-19?
  - Increased susceptibility and severity
- What does COVID-19 mean for lung cancer?
  - Diagnosis
  - Local treatment
  - Systemic treatment
- Practical cases discussion

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What does lung cancer mean for COVID-19?

> case 1: 70-year old male

- **My patient is a 70 years-old smoker, PS = 2, and undergoing therapy with Docetaxel for a relapsed stage IV squamous NSCLC**
- **Presents with fever, cough and dyspnea. His PCR-test is positive for COVID-19 disease.**

<u>The risk that this is fatal is</u>:

1. **40-49%**
2. **50-59%**
3. **60-69%**
4. **70% or more**

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What does COVID-19 mean for lung cancer?

> case 2: 68-year old male

- **Jan 2020: diagnosis cT2N3M0 (stage IIIB) adenocarcinoma (KRAS+; PD-L1 60%).**
- **Profound partial response after concurrent chemoradiotherapy (cCRT). Indication for ICI consolidation with Durvalumab 10 mg/kg, q2w, for 1 year.**

<u>April 2020: I propose</u>:

1. **Start with Durvalumab consolidation, 10 mg/kg q2w; asap, but within 6 weeks**
2. **Start with Durvalumab consolidation, 20 mg/kg q4w; asap, but within 6 weeks**
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What does COVID-19 mean for lung cancer?

> case 3: 58-year old female

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- **History: COPD/emphysema (FEV1 66% - DLco 36%)**
- **Dec 2018: lung adenocarcinoma, cTxN2M1c (abdominal mass infiltrating m. ileopsoas and iliac vein, spleen, pancreas). Pulmonary emboli. PS = 2**
  - **V. cava superior stenting, antalgic RT on iliopsoas mass (5x4Gy), anticoagulation**
  - **KRAS-mutation. PD-L1 100%. Start carboplatin/pemetrexed & pembrolizumab**
- **July 2020: undergoing maintenance pembrolizumab**
- **01 Oct 2020: more dyspnea: pulmonary emboli? -> CT-scan COVID-19 suspect, PCR confirmed**
  - **O2 sat 84%, CRP 32mg/L, increased D-dimers**
  - **O2 6L/min, anticoagulation, corticosteroids**
  - **Favorable course, discharge after 13 days with O2 2L/min**

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Lung cancer in COVID-19 era

> case 3: 58-year old female

- **Five weeks post positive test, 3 weeks post hospital discharge, 6 weeks post previous ICI therapy**
- **O2sat at home 94% without supplement, a few episodes of 90% (2L/min O2 use)**
- **Dyspnea on exertion, e.g. lawn mowing**

<u>At this time, I will</u>:

1. **Resume ICI therapy q6 weeks**
2. **Wait 3 to 6 more weeks**
3. **Discontinue ICI therapy**
4. **Other**

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Lung cancer in COVID-19 era

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- **Practical cases**
- **What does lung cancer mean for COVID-19?**
  - **Increased susceptibility and severity**
- **What does COVID-19 mean for lung cancer?**
  - **Diagnosis**
  - **Local treatment**
  - **Systemic treatment**
- **Practical cases discussion**

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COVID-19

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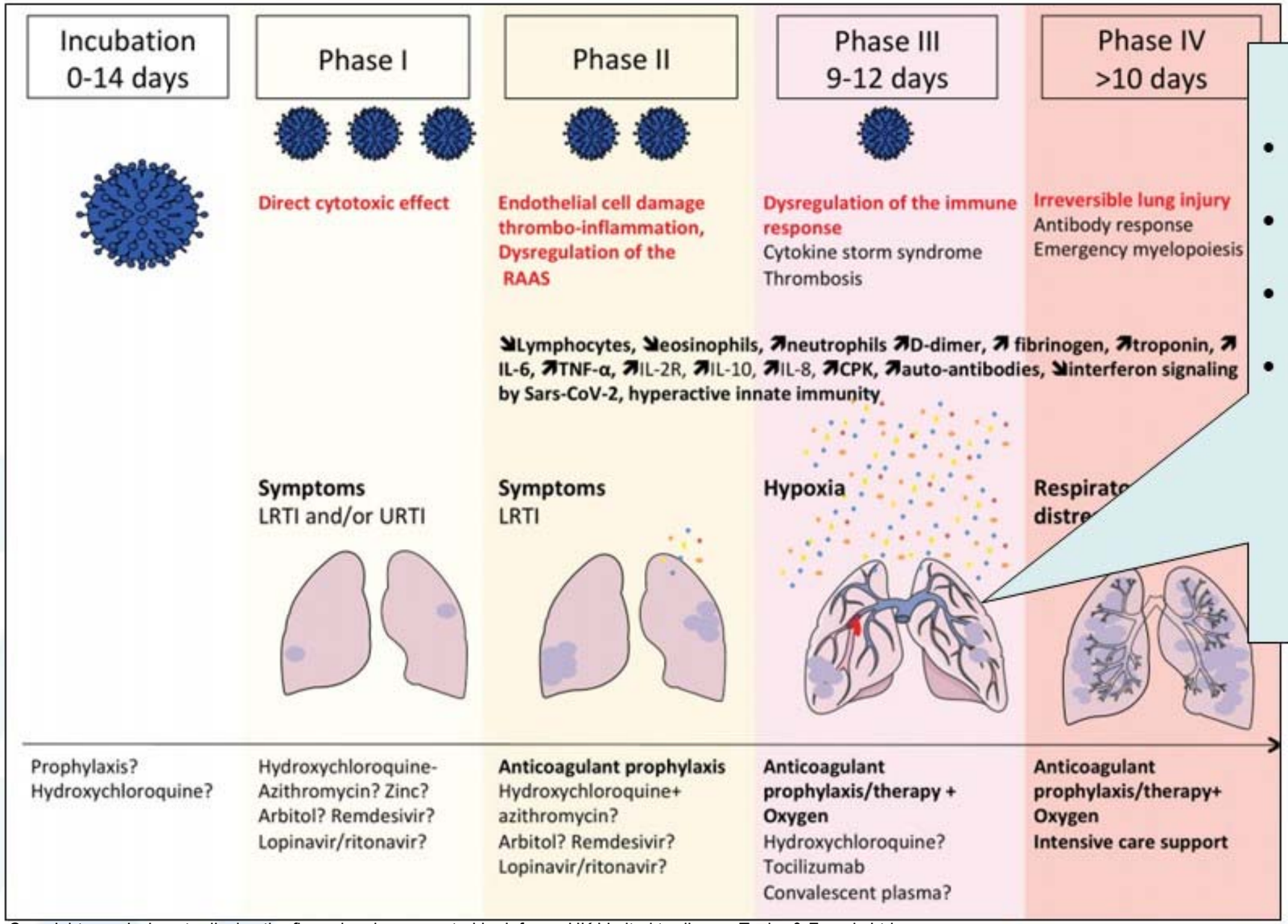

Immune system disrupted by:

- Lung cancer itself
- Age & immuno-senescence
- Smoking & related co-morbidities
- Lung cancer therapy
  - Chemotherapy
  - Immunotherapy
  - (Targeted therapy ≈ ILD)

Melenotte et al, Oncoimmunology 9: e1807836, August 2020

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> TERAVOLT

COVID-19 in patients with thoracic malignancies (TERAVOLT): first results of an international, registry-based, cohort study

Lancet Oncol 2020; 21: 914–22

- **Global consortium on patients with thoracic cancer who had COVID-19 (91% laboratory-confirmed)**
  - **Assess risk factors for death and hospitalisation in patients with thoracic malignancies who develop COVID-19, follow the clinical course, and to evaluate the long-term impact**
- **Initial report (N=200)**
  - **Median age 68, 70% male, 81% current/former smokers**
  - **76% NSCLC, 74% stage IV, 74% undergoing treatment (57% 1L treatment, all types)**
- **Results**
  - **152 admitted to hospital, only 13 to ICU – 66 died (52 COVID related)**
  - **Type of systemic therapy (TKI, ChT, ICI, ChT+ICI) did not influence outcome**
  - **TKI: decreased risk for hospitalisation – ICI: no worsening of outcome of COVID-19**

Garassino et al, Lancet Oncol 21:914-922, 2020

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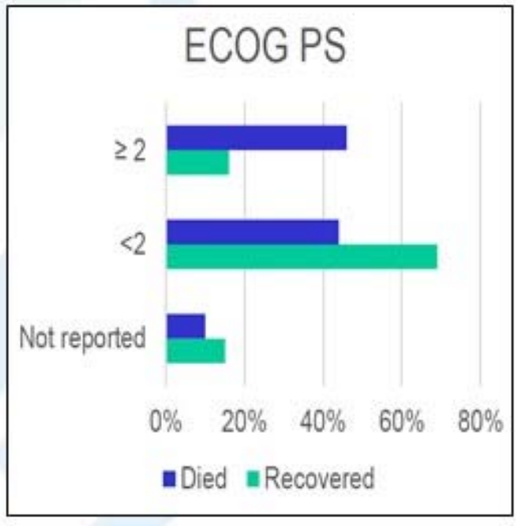
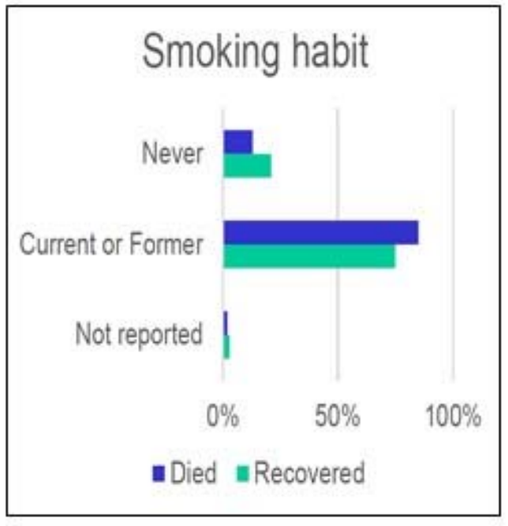
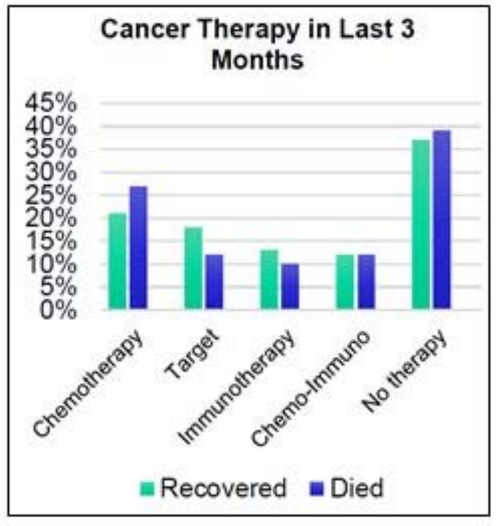
What does COVID-19 mean for lung cancer?

> TERAVOLT update ESMO 2020 [N=1012]: outcome

Outcome	Proportion	Numbers
Hospitalization [median stay 10 d]	72%	733
ICU stay [median stay 7 d]	12%	118
Invasive ventilation	7%	69
Non-invasive ventilation	18%	179







Espinar et al, ESMO 2020 LBA75

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> TERAVOLT update ESMO 2020 [N=1012]: multiple logistic regression

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Multivariate analysis of risk factors associated with COVID-19 mortality

Variable	Reference levels	OR (95%CI)	*P*-value
PS	≥2 vs. <2	3.6 (2.7-5.0)	<0.001
Stage at COVID-19 Dx	IV vs. ≤III	1.9 (1.4-2.7)	<0.001
Smoker	Former/current vs. never	1.8 (1.2-2.7)	<0.01
Steroids prior to COVID-19	Yes vs. no	1.7 (1.1-2.0)	<0.01
Age	>65 vs. ≤65 years	1.5 (1.1-2.0)	0.01
Oncologic therapy	None/chemo vs. ICI/ChT-ICI or targeted	1.4 (1.02-2.0)	0.03

- **Risk factors of general population (hypertension, obesity, heart disease) not significant**

Espinar et al, ESMO 2020 LBA75

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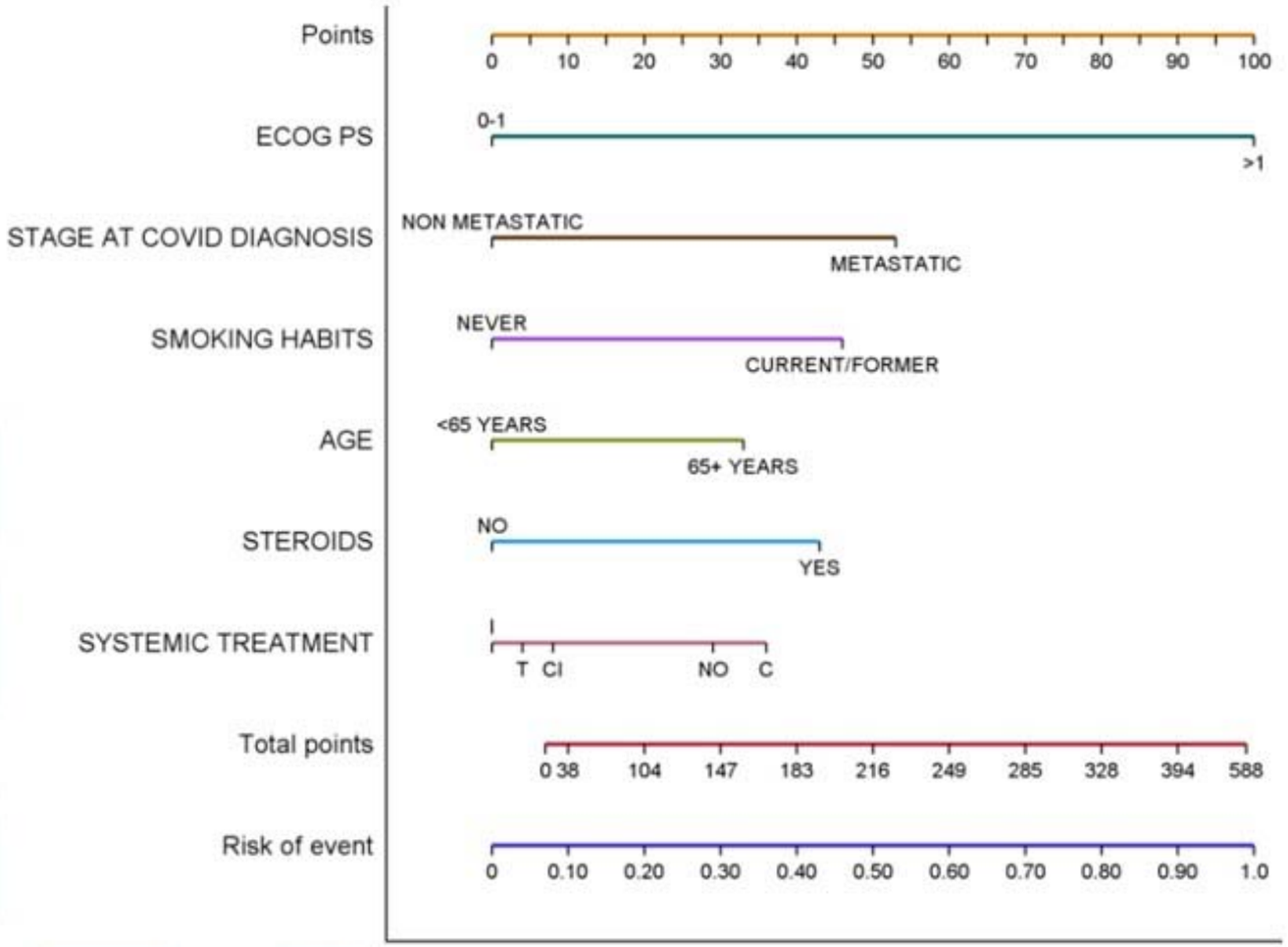
> TERAVOLT update ESMO 2020 [N=1012]: risk nomogram



Espinar et al, ESMO 2020 LBA75

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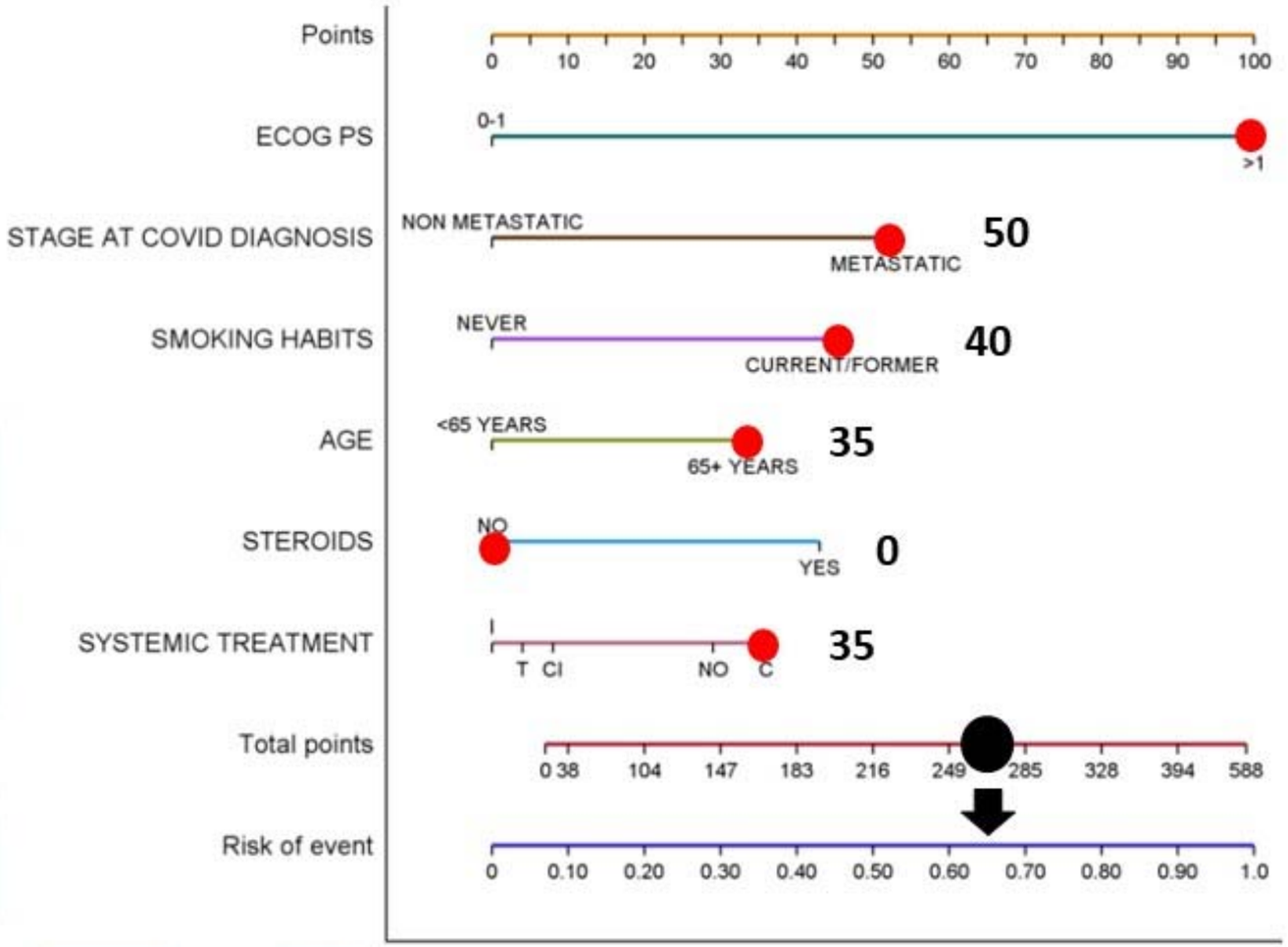

Espinar et al, ESMO 2020 LBA75

Display voting results case 1

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Lung cancer in COVID-19 era

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What does COVID-19 mean for lung cancer?

> general principles

Level of evidence
Grade of recommendation

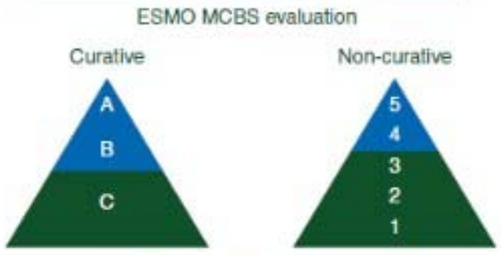
Levels of evidence

- I Evidence from at least one large randomised, controlled trial of good methodological quality (low potential for bias) or meta-analyses of well-conducted randomised trials without heterogeneity
- II Small randomised trials or large randomised trials with a suspicion of bias (lower methodological quality) or meta-analyses of such trials or of trials with demonstrated heterogeneity
- III Prospective cohort studies
- IV Retrospective cohort studies or case–control studies
- V Studies without control group, case reports, experts opinions

Grades of recommendation

- A Strong evidence for efficacy with a substantial clinical benefit, strongly recommended
- B Strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended
- C Insufficient evidence for efficacy or benefit does not outweigh the risk or the disadvantages (adverse events, costs, ...), optional
- D Moderate evidence against efficacy or for adverse outcome, generally not recommended
- E Strong evidence against efficacy or for adverse outcome, never recommended

ESMO-MCBS



Cherny et al, Ann Oncol 28:2340-2366, 2017

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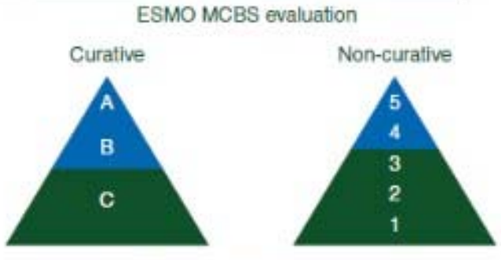
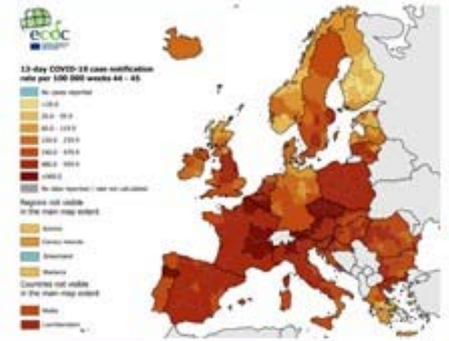


Infection risk: R0 index
Local epidemic situation



Available facilities [ICU]
Risk assessment [testing]

Cherny et al, Ann Oncol 28:2340-2366, 2017
https://www.ecdc.europa.eu/en/cases-2019-ncov-eueea

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What does COVID-19 mean for lung cancer?

> general principles

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Level of evidence
Grade of recommendation

Infection risk: R0 index
Local epidemic situation

Multidisciplinary tumor board

ESMO-MCBS

Local available facilities
Risk assessment [testing]

High priority
- **Clinically unstable**
- **High MCBS (e.g. OS gain)**

Medium priority
- **Delay 6-8 weeks**
- **Moderate MCBS**

Low priority
- **Delay until post COVID-19**
- **Low MCBS**

Curigliano et al, Ann Oncol 31: e-pub July 31, 2020
Passaro et al, ESMOopen 5:e000820, 2020

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> general principles

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Level of evidence
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Local available facilities
Risk assessment [testing]

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High priority
- **Clinically unstable**
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Medium priority
- **Delay 6-8 weeks**
- **Moderate MCBS**

Low priority
- **Delay until post COVID-19**
- **Low MCBS**

Insert telemedicine if feasible
- **YES: counseling, oral therapy, follow-up post-therapy**
- **NO: new diagnosis, post-MDT treatment planning, BSC setting**

Curigliano et al, Ann Oncol 31: e-pub July 31, 2020
Passaro et al, ESMOopen 5:e000820, 2020

What does COVID-19 mean for lung cancer?

> outpatient visits (diagnostic work-up/treatment/follow-up)

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- **Diagnostic work-up**
  - New diagnosis with symptoms or suspected stage II-III-IV
  - New nodule diagnosis (stage I)
- **Treatment**
  - Visits for treatment administration (also see below)
- **Follow-up**
  - Suspect nodule follow-up – Other nodule follow-up*
  - Evaluation of response
  - **Post-therapy:** High risk of relapse – Low risk of relapse/Long-term

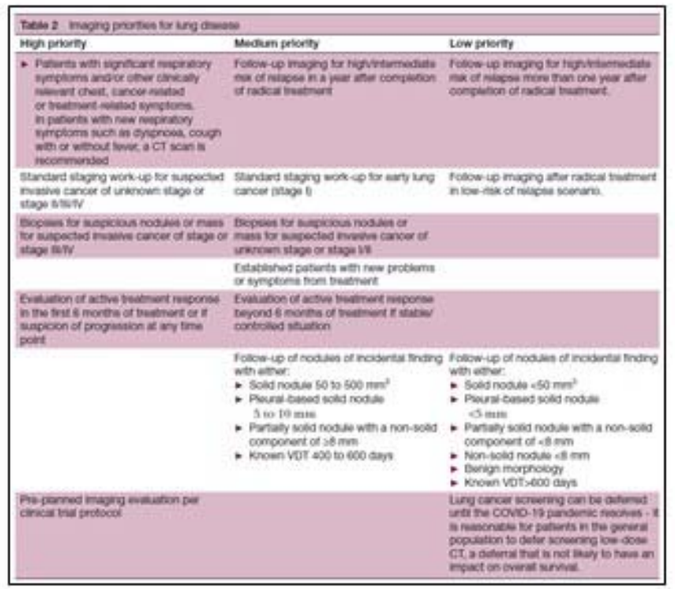

Table 2 Imaging priorities for lung disease

High priority	Medium priority	Low priority
▸ Patients with significant respiratory symptoms and/or other clinically relevant chest, cancer-related or treatment-related symptoms. In patients with new respiratory symptoms such as dyspnoea, cough with or without fever, a CT scan is recommended	Follow-up imaging for high/intermediate risk of relapse in a year after completion of radical treatment	Follow-up imaging for high/intermediate risk of relapse more than one year after completion of radical treatment.
Standard staging work-up for suspected invasive cancer of unknown stage or stage II/III/IV	Standard staging work-up for early lung cancer (stage I)	Follow-up imaging after radical treatment in low-risk of relapse scenario.
Biopsies for suspicious nodules or mass for suspected invasive cancer of stage or stage III/IV	Biopsies for suspicious nodules or mass for suspected invasive cancer of unknown stage or stage I/II	
	Established patients with new problems or symptoms from treatment	
Evaluation of active treatment response in the first 6 months of treatment or if suspicion of progression at any time point	Evaluation of active treatment response beyond 6 months of treatment if stable/ controlled situation	
	Follow-up of nodules of incidental finding with either: ▸ Solid nodule 50 to 500 mm³ ▸ Pleural-based solid nodule 5 to 10 mm ▸ Partially solid nodule with a non-solid component of ≥8 mm ▸ Known VDT 400 to 600 days	Follow-up of nodules of incidental finding with either: ▸ Solid nodule <50 mm³ ▸ Pleural-based solid nodule <5 mm ▸ Partially solid nodule with a non-solid component of <8 mm ▸ Non-solid nodule <8 mm ▸ Benign morphology ▸ Known VDT>600 days
Pre-planned imaging evaluation per clinical trial protocol		Lung cancer screening can be deferred until the COVID-19 pandemic resolves - it is reasonable for patients in the general population to defer screening low-dose CT, a deferral that is not likely to have an impact on overall survival.

*based on solid/part-solid/GGO aspect, volume, volume doubling time

Passaro et al, ESMOopen 5:e000820, 2020

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What does COVID-19 mean for lung cancer?

> early-stage (surgical) lung cancer

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- **Diagnostic/Therapeutic procedures (EBUS, mediastinoscopy, pleural fluid, …)**
- **Resection**
  - **Resectable stage II/IIIA – delay resection by use of induction rather than adjuvant chemotherapy**
  - **Resectable stage I resection – replace/delay resection by SABR**
  - **Suspect nodule resection**
  - **Other nodule resection***
- **Adjuvant chemotherapy**
  - **For T4 or N2 patients in fit condition** (liberal use of G-CSF)
  - **For T2b-3 or N1 patients to be discussed**
  - **Patients with major comorbidities**

*based on solid/part-solid/GGO aspect, volume, volume doubling time

Passaro et al, ESMOopen 5:e000820, 2020

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What does COVID-19 mean for lung cancer?

> locally advanced lung cancer

- **Concurrent chemoradiotherapy** (liberal use of G-CSF)
- **Sequential chemoradiotherapy** (liberal use of G-CSF) (use of hypofractionated RT)
- **Durvalumab consolidation if PD-L1 + tumor**

Passaro et al, ESMOopen 5:e000820, 2020

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What does COVID-19 mean for lung cancer?

> advanced lung cancer

- **First-line**
  - **Start of (chemo)immunotherapy, start of TKI to improve prognosis and/or symptoms** (liberal use of G-CSF)
- **Second-line**
  - **Start of 2L TKI**
  - **Start of 2L chemo- or immunotherapy for symptomatic progression**
  - **Start of 2L or beyond chemo- or immunotherapy for aymptomatic or low-volume progression**
- **Note: Immunotherapy**
  - **Consider larger interval (e.g. 4/6 weeks instead of 2/3 weeks)**
  - **Delay restart of ICI in patients stopped for toxicity and without progression**
- **Note: Antiresorptive therapy**
  - **Postpone unless for hypercalcemia**

Passaro et al, ESMOopen 5:e000820, 2020

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Display voting results case 2

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Lung cancer in COVID-19 era

> case 3: 58-year old female

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- **O2sat at home 94% without supplement, a few episodes of 90% (2L/min O2 use)**
- **Dyspnea on exertion, e.g. lawn mowing**

<u>At this time, I will</u>:

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2. **Wait 3 to 6 more weeks**
3. **Discontinue ICI therapy**
4. **Other**

Display voting results case 3

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Thank you for your kind attention

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