Managing cancer patients during the COVID-19 pandemic: an ESMO multidisciplinary expert consensus

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We established an international consortium to review and discuss relevant clinical evidence in order to develop expert consensus statements related to cancer management during the severe acute respiratory syndrome coronavirus 2-related disease (COVID-19) pandemic. The steering committee prepared 10 working packages addressing significant clinical questions from diagnosis to surgery. During a virtual consensus meeting of 62 global experts and one patient advocate, led by the European Society for Medical Oncology, statements were discussed, amended and voted upon. When consensus could not be reached, the panel revised statements until a consensus was reached. Overall, the expert panel agreed on 28 consensus statements that can be used to overcome many of the clinical and technical areas of uncertainty ranging from diagnosis to therapeutic planning and treatment during the COVID-19 pandemic.

INTRODUCTION

The disease course of individuals contracting severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is phenotypically diverse. Many patients suffer only mild symptoms and it is becoming increasingly apparent from antibody (Ab) data that others suffer no symptoms at all but can actively carry and transmit the infection. However, at the other end of the spectrum, some individuals develop very severe symptoms and can follow an extreme phenotype with the development of respiratory failure, cytokine release syndrome and multi-organ failure.[1] Subgroups of SARS-CoV-2-related disease (COVID-19) patients have been identified who appear to be at increased risk of extreme

morbidity and mortality, including those of advancing age, male sex and those with comorbidities such as hypertension, chronic lung disease, diabetes and cancer.[1] Since the start of the global spread of COVID-19 in early 2020, patients with cancer were designated as a particularly vulnerable subgroup of the population. Cancer patients have been reported to be both at increased risk of contracting SARS-CoV-2 infection and of running a more severe disease course, with a higher proportion requiring greater levels of intensive care, having a more rapidly evolving disease and an increased risk of death.[2−4] However, the term 'cancer' encompasses a myriad of diseases with a diverse array of primary tumour subtypes and stages affecting a heterogeneous group of patients of all ages, all of which result in very different cancer prognoses and outcomes. Therefore, labeling all cancer patients as 'COVID-19 vulnerable' is probably neither reasonable nor informative. As a consequence of generic advice given to 'COVID-19 vulnerable' members of the population, cancer patients (of

any age, sex or tumour subtype and stage) have been labeled as high risk for COVID-19 and this has led to sweeping changes in cancer management for all cancer types over the last few months, including abbreviation of radiotherapy (RT), switching from intravenous (i.v.) to oral chemotherapy (ChT) regimens and the avoidance of immunotherapy.[5–7] These changes, perhaps reasonable in an acute pandemic situation, were instigated with very little evidence to support them. Based on the lack of evolving evidence, there has been little attempt to define the individualised risk for a given patient, taking into consideration their primary tumour type, stage, age and sex. A large, international and mutidisciplinary consortium was established to review and discuss clinical evidence in order to develop expert consensus statements on key areas of controversy and technical questions. These consensus statements provide clear recommendations for the management of cancer patients across the multidisciplinary team (MDT) in order to support physicians in optimising the cancer care pathway and improving clinical outcomes. The main goal is to help MDTs to deliver the best possible care during the COVID-19 pandemic.

METHODS

A steering committee (SC) prepared a series of questions to be voted upon at the consensus meeting. The multidisciplinary expert panel was compiled based on nominations from the European Society for Medical Oncology (ESMO) Guidelines Committee Chair G. Pentheroudakis and Co-Chair G. Curigliano. The SC consisted of 15 members (manuscript authors) with expertise across a wide range of malignant diseases. In order to develop the clinical questions to be addressed at the consensus meeting, the SC reviewed relevant clinical evidence and basic research in cancer patient management. Insights from the literature review were supplemented with expert clinical opinion to develop 10 working packages (WPs) (outlined in Table 1) with draft consensus statements included in the toolbox. The final Member Panel (including the SC members) consisted of 62 experts (including two individuals—J.Y. Douillard and D. Trapani—who did not participate in the voting of consensus recommendations) and 1 patient advocate. A modified Delphi process was conducted, including preparation, consensus and reporting. A feedback procedure by the SC panel was implemented via e-mail. Background information including the WPs were sent to panellists twice between 29 May 2020 and 3 June 2020. The SC incorporated all comments and suggestions and any disagreements were discussed and resolved. WPs were then sent for a second anonymous review to all panellists.

RESULTS: CLINICAL QUESTIONS AND STATEMENTS

Which groups of patients should be offered face-to-face consultations if feasible during the COVID-19 pandemic?

STATEMENT 1: Telehealth and digital health in oncology can be an excellent tool for real-time video consultations for primary care triage and interventions such as counselling, medication prescribing and management, management of long-term treatment and post-discharge coordination supported by remote-monitoring capabilities. It can also be an excellent tool for wellness interventions and in areas such as health education, physical activity, diet monitoring, health risk assessment, medication adherence and cognitive fitness.

Face-to-face consultations covering the delivery of key cancer-related information (e.g. new cancer diagnosis/ treatment plan, disease relapse/progression and no further cancer treatment decisions) may be more effective and empathetic than remote consultations (video or telephone). In addition, patients with complex cancer needs should be considered for face-to-face consultation. The risks of travel for the patient and SARS-CoV-2 exposure need to be considered. If practical, measures in the clinic should be implemented for patients to be allowed one person with them for support during the face-to-face consultation.[8]

Is there a possibility to tailor the intensity of care and social measures for cancer patients according to local COVID-19 incidence rates?

STATEMENT 2: Cancer care prioritisation and cancer care intensity should be adapted to the pandemic scenario [from 1 to 4 according to the European Centre for Disease Prevention and Control (ECDC)], to local R0 index and to health facilities and resources.

R0 is the measure used to track how many people on average will be infected for every person who has the disease and is the most internationally used index. R0 may also be used locally to shape prioritisation of treatments and safety measures at a local level. Possible R0 cut-off levels are <0.5, 0.5–1, >1–2, >2–3 and >3.[9,10]

Important factors are the status of the viral outbreak in terms of availability of hospital technical and human resources as well as on-site intensive care unit (ICU) ventilation capacity.[11] Expert and specialised multidisciplinary discussion should be available to define the priority level of the cancer treatment.

In a situation where resources are not exhausted, the general rule is that operations planned for cancer patients that cannot be postponed for 3 months should be scheduled as soon as possible, taking the necessary precautions (including viral screening) so not to compromise the oncological prognosis of the patient. In situations where resources are exhausted, only emergency services can be provided and alternative cancer therapeutic modalities that are still available must be administered with a plan put in place in accordance with health authorities.

For thoracic surgery, surgical procedures should be done as soon as possible for solid or predominantly solid lung nodules or presumed lung cancer >2 cm or with positive nodes, symptomatic mediastinal tumours or oesophageal cancer ≥T1b; surgery may be deferred in cases of predominantly ground glass nodules, tumours <2 cm or tumours of indolent histology—carcinoid or thymoma—but also for high-risk patients likely to require prolonged ICU

Table 1. Overview of WPs and main statements

WP	Main statements
Strategies for patient management and follow-up	STATEMENT 1: Telehealth and digital health in oncology can be an excellent tool for real-time video consultations for primary care triage and interventions such as counselling, medication prescribing and management, management of long-term treatment and post-discharge coordination supported by remote-monitoring capabilities. It can also be an excellent tool for wellness interventions and in areas such as health education, physical activity, diet monitoring, health risk assessment, medication adherence and cognitive fitness.
Prevention of SARS-CoV-2 infection in cancer patients and prioritisation of cancer care	STATEMENT 2: Cancer care prioritisation and cancer care intensity should be adapted to the pandemic scenario (from 1 to 4 according to the ECDC), to local R0 index and to health facilities and resources. STATEMENT 3: When feasible in the context of available resources, cancer patients requiring admission to hospital for cancer treatment should be tested for SARS-CoV-2 regardless of symptoms or chest radiological findings if considered at high risk of mortality in case of SARS-CoV-2 infection. STATEMENT 4: Perform a point-of-care risk assessment to assess the likelihood of SARS-CoV-2 infection, including the clinical presentation of the patient and a review of clinical, epidemiological and travel history. This should aim to achieve a rapid evaluation of the risk of infectiousness based on signs, symptoms and the procedures likely to result in infectious respiratory droplets and aerosols. STATEMENT 5: PPE should be provided to all health care professionals and used meticulously. Health care workers in enclosed spaces should wear eye protection, a gown and a surgical mask or, if available, an FFP, and practice hand hygiene or protection (gloves). Swab testing should be offered to all symptomatic health professionals.
G-CSF use and thromboprophylaxis in cancer patients during the COVID-19 pandemic: benefits, risks and impact in COVID-19-negative and COVID-19-positive cancer patients	STATEMENT 6: To lower the risk of febrile neutropaenia, consider expanding the indication of G-CSF for patients with intermediate (10%—20%) and high risk of febrile neutropaenia (>20%) and specifically for elderly patients with comorbidities. STATEMENT 7: In patients with cancer and COVID-19, there is an increased risk of thromboembolic events and associated complications such as lung vessel obstructive thrombo-inflammatory syndrome. Prophylaxis using LMWH or NOACs is recommended.
COVID-19 testing: who, when and how (PCR, serology)	STATEMENT 8: Detection of SARS-CoV-2 RNA by means of RT-PCR is the current gold standard for diagnosis of acute infection with the causative organism of COVID-19. STATEMENT 9: Serological Ab tests cannot replace testing for the SARS-CoV-2 nucleic acid. They can be used for longitudinal detection of seroconversion and seroprevalence in individuals previously positive for SARS-CoV-2. STATEMENT 10: Patients' infectivity for SARS-CoV-2 is determined by the presence of the virus in different body fluids, secretions and excreta. The persistence and clearance of viral RNA from different specimens of patients with COVID-19 remain unclear. We need longitudinal studies to distinguish early asymptomatic patients testing positive from patients recovered from COVID-19 who still test positive by RT-PCR as their infectivity may differ.
Use of immunotherapy	STATEMENT 11: For the approved indication of (neo)adjuvant treatment, where there is a significant survival benefit, ICIs should not be withheld or delayed in the absence of SARS-CoV-2 infection. In patients who have tested positive for SARS-CoV-2, the (neo)adjuvant ICI should be postponed until recovery. STATEMENT 12: For patients with metastatic melanoma, intermediate/poor-risk mRCC, PD-L1-positive NSCLC and hepatocellular carcinoma, where there is a clear survival benefit, ICI treatment should be interrupted because of COVID-19. Restarting ICI treatment should be considered after complete resolution of COVID-19 following negative RT-PCR testing. A combination of ICI with cytotoxic ChT can be considered and discussed with patients when the cost—benefit ratio is favourable (OS gain) according to patient risk factors and preference. STATEMENT 13: High-dose steroids may represent a potential risk factor for mortality in cancer patients who are infected with SARS-CoV-2. In case of the need to manage a G3—4 irAE, if possible, switch to another immunosuppressant agent. STATEMENT 14: The combination of anti-CTLA4 plus anti-PD-(L)1 should be given if the patient's disease requires such ICI treatment (in case of an approved indication), in view of the lack of evidence that sequencing anti-PD-(L)1 and anti-CTLA4 agents is as effective or less toxic. STATEMENT 15: For the differential diagnosis of an irAE from SARS pneumonitis, a nasopharyngeal swab should be obtained for PCR and a high-resolution thoracic CT scan should be carried out. If negative, a BAL should be considered (increased risk for pulmonary oncology team) for differential diagnosis of irAEs versus COVID-19.
Use of targeted TKI therapies	STATEMENT 16: TKIs of the PI3K/AKT/mTOR or RAS/RAF/MEK axis can interfere with critical pathways involved in innate or adaptive immune responses. The decision to withhold therapy with these TKIs depends on the risk—benefit balance. Consequently, the magnitude of benefit (ESMO-MCBS) from the TKI should be considered in a tumour-specific context in the decision-making process until more clinical data are available. STATEMENT 17: Due to the acute kinetics of COVID-19, it is reasonable to withhold TKI therapy in patients with oncologically stable disease until the patient recovers. TKIs may not be interrupted in patients with less severe COVID-19 or in those with targetable, oncogene-addicted high-volume tumours at high risk of flare upon TKI discontinuation.
Implementation of adjuvant/neoadjuvant ChT	STATEMENT 18: For breast cancer patients in the curative setting, regimens and doses of adjuvant/neoadjuvant systemic therapies should be followed, always preceded by a multidisciplinary discussion, risk—benefit analysis and discussion with the patient. Significant delays should be avoided and protective/supportive measures implemented (growth factor support, less immunosuppressive regimen selection). STATEMENT 19: In stage II—III NSCLC, adjuvant ChT (with concurrent or sequential RT in stage III) is recommended for fit, young patients without significant comorbidities, after an informed discussion with the patient. In the event of lack of surgical resources, neoadjuvant ChT followed by surgery may be considered in highly selected subsets of patients. STATEMENT 20: Switching to SCPRT (5 × 5 Gy) in rectal cancer rather than standard long-course CRT schedules should be considered.
RT strategies during the COVID-19 pandemic	STATEMENT 21: Patients undergoing adjuvant or definitive lung RT are at risk of severe complications from COVID-19. In order to reduce the risks of treatment and hospital attendances during the COVID-19 pandemic, the use of reduced-fractionation RT should be discussed by the multidisciplinary tumour board as well as with the patient in order to balance the risk-benefit of the approach. STATEMENT 22: In the case of a diagnosed COVID-19 patient with lung cancer, we recommend continuing curative-intent thoracic RT, taking into consideration the severity of the COVID-19 clinical syndrome, the risk of tumour recurrence/progression with treatment interruption and the local resources.

Table 1. Continued	
WP	**Main statements**
Prioritisation of cancer care and ICU triage in cancer patients/ rehabilitation after COVID-19 infection	**STATEMENT 23:** Active and progressing status of cancer, advanced age, poor PS, smoking status, comorbidities and possibly type of cancer (haematological, thoracic malignancies) and administration of cytotoxic ChT have been initially identified as significant risk factors for severity and mortality of COVID-19. **STATEMENT 24:** A decision on ICU transfer depends on the ICU resource strain and is to be adapted according to the R0 index and ECDC pandemic scenario; the ethical value of maximising the number of patients who survive COVID-19 with a reasonable life expectancy has the highest priority.
Clinical trial activities in the COVID-19 era	**STATEMENT 25:** The risk—benefit profile for including an individual patient in a clinical trial should be adapted to the R0 index and case load of the pandemic as well as health care organisation characteristics and resources. **STATEMENT 26:** During the COVID-19 pandemic, deviations from a clinical trial protocol (for risk—benefit reasons) may be considered provided there is rigorous documentation in the medical record of the patient and that this is communicated as soon as possible to the sponsor. There are no acceptable deviations in safety reporting. **STATEMENT 27:** During the COVID-19 pandemic, we should continue lobbying for promoting clinical cancer research to find better therapeutic options for patients with neoplasms. Cancer is and will continue to be one of the most significant causes of morbidity and mortality. **STATEMENT 28:** While we globally continue promoting clinical cancer research as the only way to find better therapeutic options and to improve cancer prognosis, we should continue ranking priorities in terms of value for the most appropriate clinical research.

Ab, antibody; BAL, broncho-alveolar lavage; ChT, chemotherapy; COVID-19, severe acute respiratory syndrome coronavirus 2-related disease; CRT, chemoradiotherapy; CT, computed tomography; CTLA4, cytotoxic T-lymphocyte-associated protein 4; ECDC, European Centre for Disease Prevention and Control; ESMO-MCBS, ESMO-Magnitude of Clinical Benefit Scale; FFP, filtering face piece; G, grade; G-CSF, granulocyte colony-stimulating factor; ICI, immune checkpoint inhibitor; ICU, intensive care unit; irAE, immune-related adverse event; LMWH, low molecular weight heparin; mRCC, metastatic renal cell carcinoma; mTOR, mammalian target of rapamycin; NOAC, novel oral anticoagulant; NSCLC, non-small-cell lung cancer; OS, overall survival; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; PI3K, phosphoinositide 3-kinase; PPE, personal protective equipment; PS, performance status; RT, radiotherapy; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SCPRT, short-course preoperative radiotherapy; TKI, tyrosine kinase inhibitor; WP, working package.

admissions. Alternative non-surgical approaches may be considered for early-stage tumours including stereotactic ablative RT or other interventional procedures.

Do all cancer patients have to be tested for COVID-19 infection before hospital admittance?

STATEMENT 3: When feasible in the context of available resources, cancer patients requiring admission to hospital for cancer treatment should be tested for SARS-CoV-2 regardless of symptoms or chest radiological findings if considered at high risk of mortality in case of SARS-CoV-2 infection.

It is imperative that cancer patients requiring inpatient admission with fever and upper respiratory symptoms or chest radiographical findings with suspected COVID-19 (new peripheral opacities) should be segregated/isolated and have a COVID-19 swab carried out (unless done within the past 48 h). Once a negative COVID-19 swab is obtained, they can be transferred to a regular ward.

COVID-19 management wards need to be segregated, with airflow and health staff flow management. Patients that are confirmed as COVID-19 positive should be admitted to these wards. Patients under investigation for COVID-19 should also be segregated until a negative swab is obtained. Health care workers should wear full personal protective equipment (PPE) and be segregated until the patient has a negative swab.[12-14]

When necessary resources are available and in the context of a high local SARS-CoV-2 spread and case load, all cancer patients requiring hospital admission should be screened with a RT-PCR pharyngeal swab within 48 h. In all cases, even when universal PCR screening is not feasible, it is recommended to test cancer patients requiring admission for fever and symptoms at admission and to have as much

separation as possible from other patients and use of PPE for health care workers. A patient who is transferred across hospital wards/departments for examinations must wear proper PPE. Further investigations should be prioritised to those that are urgent or needed for life-threatening treatments until a negative COVID-19 swab is obtained.

Which preventive measures do you suggest for patients coming to outpatient cancer clinics?

STATEMENT 4: Perform a point-of-care risk assessment to assess the likelihood of SARS-CoV-2 infection, including the clinical presentation of the patient and a review of clinical, epidemiological and travel history. This should aim to achieve a rapid evaluation of the risk of infectiousness based on signs, symptoms and the procedures likely to result in infectious respiratory droplets and aerosols.

All cancer patients for outpatient treatment should be screened before entry for fever (temperature >37.5°C) and upper respiratory symptoms. If positive on symptom screen, the patient should not be allowed to enter the cancer centre and advised that a swab should be taken to test for COVID-19. Once a swab is confirmed as negative, the patient can proceed to enter the cancer centre.[15] Once point-of-care testing is readily available, all cancer patients entering an outpatient setting should be advised to have a negative test before entry. In the presence of available resources, we suggest carrying out a swab within 48 h before each treatment cycle, testing for fever and symptoms at the cancer centre entrance and to have as much separation as possible from other patients and health care workers with the use of PPE. Testing policies may vary according to local resources and policies. During treatment, the patient must wear PPE. In case of shortages of testing equipment, we suggest testing at least all patients undergoing ChT.

Which preventive measures do you suggest for health care workers?

STATEMENT 5: PPE should be provided to all health care professionals and used meticulously. Health care workers in enclosed spaces should wear eye protection, a gown and a surgical mask or, if available, a filtering face piece (FFP), and practice hand hygiene or protection (gloves). Swab testing should be offered to all symptomatic health professionals.

We recommend routinely testing health care workers if PCR tests are available according to testing intervals defined by local health authorities taking into consideration the epidemiological characteristics of SARS-CoV-2 spread. In every setting, all health care workers should wear surgical masks, glasses and practice hand hygiene. If health care workers screen positive for fever or respiratory symptoms, the consensus advice is firmly for swab testing and to abstain from work/home quarantine until a swab is negative.[16,17]

We suggest implementing serological evaluations of established validity in health care workers in order to depict an epidemiological landscape of the pandemic in this setting.

Is there any different value/indication for the use of granulocyte colony-stimulating factors during the COVID pandemic?

STATEMENT 6: To lower the risk of febrile neutropaenia, consider expanding the indication of granulocyte colony-stimulating factor (G-CSF) for patients with intermediate (10%−20%) and high risk for febrile neutropaenia (>20%) and specifically for elderly patients with comorbidities.

Given the COVID-19 infection risk specifically in patients with solid tumours not treated with curative intent, one should consider equally effective treatments unlikely to induce febrile neutropaenia. There should be clear evidence to support using ChT regimens with higher neutropaenia risk. Moreover, to lower the risk of febrile neutropaenia, the indication for G-CSF can be expanded.[18,19] The theoretical raised concern of acute respiratory failure due to G-CSF-induced leukocyte recovery in patients with a pulmonary infection due to COVID-19 does not outweigh the benefit. Of note, cyclin-dependent kinase 4/6- or poly-adenosine diphosphate ribose polymerase-inhibitor-induced neutropaenia has not yet demonstrated a clear increase in associated viral infections.

How to prevent and manage thromboembolic events in patients with COVID-19

STATEMENT 7: In patients with cancer and COVID-19, there is an increased risk of thromboembolic events and associated complications such as lung vessel obstructive thrombo-inflammatory syndrome. Prophylaxis using low molecular weight heparin (LMWH) or novel oral anticoagulants (NOACs) is recommended.

In general, prophylaxis of thromboembolic events should be continued according to existing guidelines. In unclear cases for prophylaxis according to guidelines, thromboembolic prophylaxis may be initiated rather than withheld.[20−22] Patients should receive careful monitoring to prevent possible bleeding complications. Patients hospitalised with a confirmed diagnosis of COVID-19 should receive prophylaxis of thromboembolic events using LMWH or fondaparinux or even unfractionated heparin if critically ill with a significantly reduced kidney function. When direct oral anticoagulants are used, possible drug interactions with medications that are tested for use against COVID-19 have to be considered. The role of full anticoagulation in severely ill patients with COVID-19 remains controversial at this time.

Which tests are standard for detection of SARS-CoV-2?

STATEMENT 8: Detection of SARS-CoV-2 RNA by means of RT-PCR is the current gold standard for diagnosis of acute infection with the causative organism of COVID-19.

Tests used in the diagnosis of COVID-19 include assays based on RT-PCR, isothermal nucleic acid amplification, viral culture, antigen testing and serology. The current gold standard and most widely used assays are based on RT-PCR.[23,24] Target genes tested include RNA-dependent RNA polymerase (RdRp), open reading frame (ORF1), Envelope (E) and nucleocapsid (N) genes of the SARS-CoV-2 genome. The turnaround time is usually 6 to 8 h but can be as rapid as 45 min.

False-negative results may be due to improper sampling, degradation of the viral RNA during shipping/storage, low viral loads, incorrect nucleic acid extraction, presence of amplification inhibitors and mutation(s) in the RT-PCR target region. A false positive is mostly due to sample cross contamination.[25]

A detection result proving the presence of viral RNA sequence in the sampling area, e.g. nasopharynx, is interpreted as the person having the potential to spread SARS-CoV-2 to other individuals. However, viability of SARS-CoV-2 can only be proven by viral culture. Thus, the interpretation of a positive detection should be carefully examined. Timing of sampling during the course of the disease, quantification of the detected sequence and method of detection may affect the biological consequence.

The role of computed tomography (CT) screening is controversial and may play a role in regions with a high prevalence of COVID-19[26] but it should not be used routinely to screen or diagnose COVID-19.[27]

Can a blood-derived Ab test (imunoglobulin M and/or imunoglobulin G) replace testing for SARS-CoV-2 nucleic acid?

STATEMENT 9: Serological Ab tests cannot replace testing for the SARS-CoV-2 nucleic acid. They can be used for longitudinal detection of seroconversion and seroprevalence in individuals previously positive for SARS-CoV-2.

SARS-CoV-2 Ab tests are intended for use as an aid in identifying individuals with an adaptive immune response to SARS-CoV-2, indicating recent or prior

infection by detecting Abs in human blood. The Abs are part of the body's immune response to exposure and not the virus itself; therefore, such testing is not used for diagnosis of active infection. RT-PCR currently remains the reference standard for diagnosing infections, with high sensitivity and accuracy in the acute phase of illness.[28−31]

However, serology tests can play a critical role in broad-based, public health surveillance, identifying individuals with prior exposure to SARS-CoV-2 virus and guiding the response to the pandemic.

A serology test can yield a negative test result during the early stage of disease, as Abs take several days to be generated after exposure to the virus. A false positive result may be due to cross-reactivity (to a coronavirus type other than the current pandemic novel strain), which heavily impacts the sensitivity and specificity of the test.

At this time, it is unknown how long Abs persist following infection and if the presence of Abs confers long-term protective immunity.

Should a patient without clinical infection signs/symptoms but with a positive SARS-CoV-2 PCR after COVID-19 be regarded as infected and infectious?

STATEMENT 10: Patients' infectivity for SARS-CoV-2 is determined by the presence of the virus in different body fluids, secretions and excreta. The persistence and clearance of viral RNA from different specimens of patients with COVID-19 remain unclear. We need longitudinal studies to distinguish early asymptomatic patients testing positive from patients recovered from COVID-19 who still test positive by RT-PCR as their infectivity may differ.

There is an urgent need for information on immunity and infectivity in specific sites of the body. Investigators have reported a detailed virological analysis of nine cases of COVID-19 that provides proof of active virus replication in tissues of the upper respiratory tract. Pharyngeal virus shedding was very high during the first week of symptoms, with a peak at 7.11×10^8 RNA copies per throat swab on day 4. Infectious virus was readily isolated from samples derived from the throat or lung but not from stool samples despite high concentrations of viral RNA. Blood and urine samples never yielded virus. Active replication in the throat was confirmed by the presence of viral replicative RNA intermediates in the throat samples. Investigators consistently detected sequence-distinct virus populations in throat and lung samples from one patient, proving independent replication. The shedding of viral RNA from sputum outlasted the end of symptoms. Seroconversion occurred after 7 days in 50% of patients (and by day 14 in all patients) but was not followed by a rapid decline in viral load. The confirmation of active viral replication in the upper respiratory tract has implications for the containment of COVID-19.[32]

However, the presence of nucleic acid alone cannot be used to define viral shedding or infection potential. For many viral diseases [SARS-CoV, Middle East respiratory syndrome coronavirus (MERS-CoV), influenza virus, Ebola virus and Zika virus], it is well known that viral RNA can be detected long after the disappearance of infectious virus. The immune system can neutralise viruses by lysing their envelope or aggregating virus particles; these processes prevent subsequent infection but do not eliminate nucleic acid, which degrades slowly over time.[33]

Is it safe to treat cancer patients who have tested positive for SARS-COV-2 with immune checkpoint inhibitors (single agent or combination)?

STATEMENT 11: For the approved indication of (neo)adjuvant treatment, where there is a significant survival benefit, immune checkpoint inhibitors (ICIs) should not be withheld or delayed in the absence of SARS-CoV-2 infection. In patients who have tested positive for SARS-CoV-2, the (neo)adjuvant ICI should be postponed until recovery.

STATEMENT 12: For patients with metastatic melanoma, intermediate/poor-risk metastatic renal cell carcinoma, programmed death-ligand 1 (PD-L1)-positive and non-small-cell lung cancer (NSCLC) and hepatocellular carcinoma, where there is a clear survival benefit, ICI treatment should be interrupted because of COVID-19. Restarting ICI treatment should be considered after complete resolution of COVID-19 following negative RT-PCR testing. A combination of ICI with cytotoxic ChT can be considered and discussed with patients when the cost−benefit ratio is favourable (overall survival gain) according to patient risk factors and preference.

In general, there is no convincing evidence that using ICIs is detrimental to patients, but data are somewhat conflicting. If there is a survival benefit for patients in either the maintenance, adjuvant or neoadjuvant setting, we consider the risk−benefit ratio is to treat with ICIs. One could argue about the duration of the treatment and consider stopping at 1 year. According to real-world data from registries (CCC19, TERAVOLT, UK), the combination of ChT with ICIs may be detrimental in SARS-CoV-2-infected patients.

Should we avoid giving COVID-19 patients or SARS-CoV-2-positive individuals high-dose steroids (for symptoms or grade 3−4 immune-related adverse events management)?

STATEMENT 13: High-dose steroids may represent a potential risk factor for mortality in cancer patients who are infected with SARS-CoV-2. In case of the need to manage a grade 3−4 immune-related adverse event (irAE), if possible, switch to another immunosuppressant agent.

Should we avoid giving combinations of anti-cytotoxic T-lymphocyte-associated protein 4 plus anti-PD-(L)1 checkpoint inhibitors in order to decrease the risk of grade 3−4 irAEs and prefer sequential administration?

STATEMENT 14: The combination of anti-cytotoxic T-lymphocyte-associated protein 4 (CTLA4) plus anti-PD-(L)1 should be given if the patient's disease requires such ICI treatment (in case of an approved indication), in

view of the lack of evidence that sequencing anti-PD-(L)1 and anti-CTLA4 agents is as effective or less toxic.

The risk assessment depends on the local prevalence of COVID-19. The risk of dying from cancer is higher than the risk of fatal COVID-19 disease, a fact that should be discussed with the patient. Reported real-world data from the CCC19, UK and TERAVOLT registries support the suggestion that immunotherapy is not associated with a risk of dying from COVID-19. Nevertheless, the same data from TERA-VOLT indicate that the combination of ChT with other therapies, including ICIs, may increase the risk of death in SARS-CoV-2-infected patients [hazard ratio (HR) for death 1.71; 95% confidence interval 1.12—2.63].[34—46]

What should the work-up be for patients with radiological evidence of pneumonitis/pulmonary abnormalities/dyspnoea while receiving ICI treatment during the SARS-CoV-2 pandemic?

STATEMENT 15: For the differential diagnosis of an irAE from SARS pneumonitis, a nasopharyngeal swab should be obtained for PCR and a high-resolution thoracic CT scan should be carried out. If negative, a broncho-alveolar lavage (BAL) should be considered (increased risk for pulmonary oncology team) for differential diagnosis of irAEs versus COVID-19.

The physician should take into account a range of epidemiological, clinical, tumour and treatment-related factors. One the one hand, if the clinical/radiological suspicion for pneumonitis due to ICI is high, immediate steroid-based therapy may be implemented before SARS-CoV-2 PCR test results are available. On the other hand, if a diagnosis of COVID-19-related pneumonitis is likely in the presence of a negative pharyngeal PCR test, repeating the swab and proceeding to BAL for PCR testing may be necessary. Of note, the risk of a BAL procedure to the health care worker is high; accordingly, it should be discussed with the pulmonology team and be implemented only when positive or negative results will have an epidemiologic or therapeutic impact, with appropriate risk-mitigating safety measures.

Can tyrosine kinase inhibitors of the phosphoinositide 3-kinase/AKT/mammalian target of rapamycin, RAS/RAF/MEK axis modulate our immune response and lower its ability to control COVID-19 infection?

STATEMENT 16: Tyrosine kinase inhibitors (TKIs) of the phosphoinositide 3-kinase (PI3K)/AKT/mammalian target of rapamycin (mTOR) or RAS/RAF/MEK axis can interfere with critical pathways involved in innate or adaptive immune responses. The decision to withhold therapy with these TKIs depends on the risk—benefit balance. Consequently, the magnitude of benefit (ESMO-Magnitude of Clinical Benefit Scale) from the TKI should be considered in a tumour-specific context in the decision-making process until more clinical data are available.

The PI3K/AKT/mTOR pathway is important for survival, proliferation and migration of macrophages, which are an essential component of the immune 'clean-up' process. Everolimus is known to be an immunosuppressant for solid organ transplant patients. There are conflicting preclinical data on the role of the mitogen-activated protein kinase (MAPK) pathway, some indicating an important role in adaptive and innate components of the immune system, while others involve MAPK in suppression of immune cell trafficking.[37—40] Consequently, although we may speculate that PI3K/AKT/mTOR or MAPK inhibitors might potentially compromise immune function and response to SARS-CoV-2 infection, preliminary data from the CCC19 and TERAVOLT registries did not establish an association of non-cytotoxic targeted therapies with COVID-19-related mortality (HR 1.04 in both registries).

The decision to withhold therapy with these TKIs depends on the balance between risk and benefit and might vary from one cancer type to another, so the magnitude of benefit from the TKI should be considered in a tumour-specific context in the decision-making process. Specifically, as the indication of PI3K/AKT/mTOR inhibition for lung cancer is minimal, not recommending these drugs for lung cancer management during the pandemic is a reasonable strategy. As for other indications such as breast cancer, mTOR inhibition is largely limited to later lines of therapy as, despite the positive study outcomes, the impact is relatively minor. In contrast, in melanoma, BRAF and MEK TKI combinations appear relatively safe without the risk of irAEs or the need to use high-dose steroids.

Should TKIs be suspended during a patient's active SARS-CoV-2 infection?

STATEMENT 17: Due to the acute kinetics of COVID-19, it is reasonable to withhold TKI therapy in patients with oncologically stable disease until the patient recovers. TKIs may not be interrupted in patients with less severe COVID-19 or in those with targetable oncogene-addicted, high-volume tumours at high risk of flare upon TKI discontinuation.

Most patients who have previously responded to TKIs would remain stable for a number of weeks. As COVID-19 is an acute illness during which most patients may recover or succumb within days, it is reasonable to withhold the TKI in oncologically stable patients until the patient recovers. The severity of the SARS-CoV-2 infectious syndrome should obviously be taken into consideration. Of note, preliminary data from the CCC19 and TERAVOLT registries did not establish an association of non-cytotoxic, targeted therapies with COVID-19-related mortality (HR 1.04 in both registries).[34,35] Consequently, TKIs should not be interrupted in patients who need them, such as those in the initial weeks of therapy and without a fully established antitumour beneficial response and those with targetable, oncogene-addicted tumours such as lung cancer in which there is a risk of a flare effect associated with TKI discontinuation (high-risk population for flare such as shorter time to disease progression, pleural effusion and central nervous system involvement).[41]

How do we prioritise adjuvant therapies in patients with solid tumours during the COVID-19 pandemic?

Breast cancer.

STATEMENT 18: For breast cancer patients in the curative setting, regimens and doses of adjuvant/neoadjuvant systemic therapies should be followed, always preceded by a multidisciplinary discussion, risk—benefit analysis and discussion with the patient. Significant delays should be avoided and protective/supportive measures implemented (growth factor support, less immunosuppressive regimen selection).

For cancers in the curative setting, the risk—benefit balance clearly favours maintaining systemic treatment according to guidelines during the COVID-19 pandemic and therefore standard indications, regimens and doses of adjuvant/neoadjuvant systemic therapies should always be followed, preceded by a multidisciplinary discussion and avoiding as much as possible significant delays. Some adjuvant/neoadjuvant systemic therapies are associated with a significant risk of immunosuppression, particularly ChT, which can increase the risk of severe complications of SARS-CoV-2 infection. Therefore, relevant supportive measures should be implemented such as prophylactic use of hematopoietic growth factors in all regimens with a medium/high risk of immunosuppression, the use of dose-dense (q2weeks) regimens when appropriate to decrease the number of visits to the hospital, or conversely, the use of weekly regimens with low risk of immunosuppression (despite being associated with a higher number of visits). Some types of adjuvant/neoadjuvant systemic therapies are in principle not associated with risk of complications of COVID-19 and should therefore be used as recommended by the guidelines, particularly anti-human epidermal growth factor receptor 2 and endocrine therapies. In situations where the risk—benefit of adjuvant/neoadjuvant systemic ChT is controversial or uncertain, it may be wiser to decide against that treatment during the COVID-19 pandemic, but always after careful discussion with the patient.[42]

Lung cancer.

STATEMENT 19: In stage II—III NSCLC, adjuvant ChT (with concurrent or sequential RT in stage III) is recommended for fit, young patients without significant comorbidities, after an informed discussion with the patient. In the event of lack of surgical resources, neoadjuvant ChT followed by surgery may be considered in highly selected subsets of patients.

Adjuvant ChT should be considered in the presence of pathological N1 or N2 disease and should be proposed in patients who are fit and younger than 70 years of age while it should be withheld in frail, elderly patients with significant comorbidities. Adjuvant ChT could start 6—10 weeks post-surgical resection. The COVID-19 local epidemic profile and intensity should be taken into consideration for the decision-making process since absolute survival benefits from adjuvant ChT in lung cancer patients is not as substantial as in breast cancer.

Neoadjuvant ChT (enabling deferral of surgery by 3 months) should be considered in clinical stage II patients suitable for a surgical approach with curative intent.

Rectal cancer.

STATEMENT 20: Switching to short-course preoperative RT (SCPRT) (5 × 5 Gy) in rectal cancer rather than standard long-course chemoradiotherapy (CRT) schedules should be considered.

A preference for SCPRT (5 × 5 Gy) is justifiable in rectal cancer patients during the COVID-19 pandemic rather than standard long-course CRT schedules. SCPRT (5 × 5 Gy) is flexible in timing and provides a reduced in-hospital footfall during the COVID-19 pandemic, allowing better adherence to social distancing recommendations while avoiding the need for concomitant ChT. For easily resectable cancers, when SCPRT with immediate surgery and long-course concurrent CRT have been directly compared in randomised phase III trials, no differences in oncological outcomes (local control, rate of metastases, disease-free survival) or late effects and quality of life (QoL) were demonstrated.[43,44] Recent clinical data may support administration of short-course RT followed by systemic ChT and deferral of surgery by a few weeks in the event of lack of surgical resources.

In lung cancer patients with no COVID-19 symptoms treated with curative-intent RT, should we reduce RT fractionation to minimise the number of hospital visits?

STATEMENT 21: Patients undergoing adjuvant or definitive lung RT are at risk of severe complications from COVID-19. In order to reduce the risks of treatment and hospital attendances during the COVID-19 pandemic, the use of reduced-fractionation RT should be discussed by the multidisciplinary tumour board as well as with the patient in order to balance the risk—benefit of the approach.

The global COVID-19 pandemic presents a challenge to the delivery of radical RT to patients with lung cancer. Patients undergoing lung RT are in the group at highest risk of severe complications and death from COVID-19 due to their age, comorbidities and side-effects of their anticancer treatments. Therefore, there is a need to reduce the risks of treatment and hospital attendances during the COVID-19 pandemic.

Limited clinical data indicate that it is feasible to identify reduced-fractionation and curative-intent RT regimes in lung cancer, while taking into careful consideration parameters such as organs-at-risk dose constraints, limitations and practicalities related to implementation. Requirements to implement such change in practice will depend on the local incidence of COVID-19 and staffing resources. Implementation should be discussed with other specialist lung MDT members and importantly with patients. The risks and benefits of treatment and uncertainties about toxicity from reduced fractionation where there is limited experience in a department should be an essential component of the consent process.[45,46]

Do we interrupt curative-intent adjuvant or definitive thoracic RT in a lung cancer patient with documented COVID-19?

STATEMENT 22: In the case of a diagnosed COVID-19 patient with lung cancer, we recommend continuing curative-intent thoracic RT, taking into consideration the severity of the COVID-19 clinical syndrome, the risk of tumour recurrence/progression with treatment interruption and the local resources.

Mature data on the impact of continuation of RT in patients with COVID-19 are lacking, though preliminary data from the CCC19 and the TERAVOLT registries did not establish an association between RT and COVID-19 mortality. Still, it is acknowledged that patients with cancer face a higher risk of morbidity and mortality related to COVID-19 for a multitude of reasons. Currently, we are unable to conclude if the different treatment modalities harbour equal risks, given the small cumulative number of patients who received RT in these studies and the short follow-up. Moreover, long-term data are awaited to appreciate the effect of treatment interruption on cancer control and survival in these patients. From retrospective series dating from the 1980s and 1990s, we know that breaks during RT are associated with a higher rate of locoregional recurrences in patients with head and neck cancer and NSCLC.[47] For COVID-19-positive patients, discussing the risks of worsening illness with continuing RT versus the risk of tumour recurrence/progression with treatment interruption is recommended. If a patient with mild COVID-19 consents to continuing with treatment and delivery of treatment is possible, we recommend considering a change in the fractionation schedule to a hypofractionated regimen to reach a tumour equivalent of 60 Gy. Available local resources are a key determinant of therapeutic strategies to be selected. Given the infectivity of the SARS-CoV-2 virus, regardless of the extent of infection control measures, COVID-19-positive patients will pose a health risk when in close proximity to other individuals. Ideally, these patients should be treated in dedicated COVID-19 RT treatment facilities, where they can be isolated to limit virus transmission. An alternative would be to schedule the treatment of such patients at the end of the working day followed by meticulous disinfection and sanitisation of the facility.[48,49]

Are cancer patients at highest risk of severe forms of COVID-19?

STATEMENT 23: Active and progressing status of cancer, advanced age, poor performance status (PS), smoking status, comorbidities and possibly type of cancer (haematological, thoracic malignancies) and administration of cytotoxic ChT have been initially identified as significant risk factors for severity and mortality of COVID-19.

There is plausible concern that diagnostic pathways and cancer treatment modalities may expose cancer patients to a greater risk of acquiring SARS-CoV-2 infection than would be the case if they were able to maintain effective social distancing at home. The limited experience reported to-date indicates that the risk of SARS-CoV-2 infection might be comparable with the global population (11% of cancer patients tested positive at Gustave Roussy in France).[50] This encouraging observation may reflect enhanced precautions, adoption of protective measures (such as social distancing, handwashing, masks) and reconfiguration of cancer care services to maximise patient safety.

It is unclear whether there is an increased risk of death associated with specific oncological scenarios. Early published case series from China suggested that cancer is comparable to poorly-controlled hypertension and diabetes as a risk factor for death from COVID-19. These data are not sufficiently detailed with regard to the granularity of medical conditions in order to derive generalisable and actionable conclusions. The over-representation of older people with comorbidities and other risk factors in the cancer population are highly likely to be confounders in this association.

Preliminary data derived from cohort studies (CCC19, TERAVOLT, UK) are now available but should be interpreted with caution.[34,35] Selection bias with major recruitment of patients presenting with cancer and symptomatic COVID-19 in hospital settings and under-representation of mild or asymptomatic patients in the community enriches the cohort for patients more likely to experience poor outcomes. These differences in cohort selection may explain the differences in the preliminary data suggesting 29% of 897 UK cancer patients with a diagnosis of COVID-19 died[50] compared with 14.6% in France.[51] Overall, data from these registries commonly identify advanced age, male sex, poor PS, presence of comorbidities and active/progressing malignancy as risk factors for increased COVID-19 mortality or severity. Immunotherapy or targeted therapies were not identified as risk factors whereas discordant results were observed for cytotoxic ChT: it was not correlated with mortality in the UK and CCC19 registries but was in the TERAVOLT study.

COVID-19-related mortality has been reported to be higher in cases of haematological malignancies and lung cancer.[52] In the TERAVOLT study, there was a 25% mortality rate among SARS-CoV-2-infected patients with an underlying diagnosis of lung cancer.[34] Perioperative infection with COVID-19 is associated with a higher risk of mortality, so preoperative screening with RT-PCR and chest imaging is routinely carried out.[53,54]

Which patients with cancer should or should not access ICUs?

STATEMENT 24: A decision on ICU transfer depends on the ICU resource strain and is to be adapted according to the R0 index and ECDC pandemic scenario; the ethical value of maximising the number of patients who survive COVID-19 with a reasonable life expectancy has the highest priority.

Neither stage nor specific diagnosis has been validated as a predictor of survival of a severe acute concurrent illness such as COVID-19. Staging alone should not be used for triage as patients with stage IV cancer are extremely heterogeneous in terms of prognosis and their degree of

physiological compromise or reserves. Some patients with advanced cancers have expressed advanced directives ruling out ventilation support. However, it would be unlikely that a subgroup of patients suffering from physiological compromise from their cancer would survive this kind of acute concurrent infection even with ventilation support. The decision relies on the availability of ICU resources and is to be adapted according to the evolution of the pandemic. The ethical value of maximising the number of patients who survive COVID-19 with a reasonable life expectancy has the highest priority during the pandemic. Patients with haematological malignancies and primary or metastatic tumours in the lung are at greater risk of ICU referral, development of severe critical illness and use of invasive ventilation. The oncology team has to discuss with patients and their caregivers the possibility of referral to the ICU, taking into consideration concomitant risk factors for adverse outcomes including: disease, stage, intent of the antitumour treatment and reasonable life expectancy. A shared decision has to be reached and documented. A triage system involving the oncology team must be set up to ensure a fair assessment of cancer patients in the event of admission to the ICU and in case of worsening of patients' clinical conditions while in the ICU.[55,56]

During the COVID-19 pandemic, has the risk—benefit profile for including an individual patient in a clinical trial changed?

STATEMENT 25: The risk—benefit profile for including an individual patient in a clinical trial should be adapted to the R0 index and case load of the pandemic as well as health care organisation characteristics and resources.

Clinical trial sponsors are accountable for conducting an updated risk assessment for all clinical trials, adjusting the conduct of clinical trials accordingly, and informing investigators and clinical trial participants of the updated risk assessment and any changes to be implemented. Investigators play an important role in the accuracy of the risk—benefit assessment by promptly informing the sponsor of new risks identified and by making individual decisions about the potential risks benefits to an individual patient based on their medical history and situation. It is imperative that the assessment of potential changes in risk—benefit take into account the specificities of each clinical trial population, the intervention under investigation and the local situation at each clinical trial site. The risk—benefit assessment may or may not change materially for each clinical situation and, depending on the aforementioned, not taking part in a cancer clinical trial may pose a bigger risk to some patients than entering the trial under precautions against the risk of COVID-19. Investigators should also keep in mind that cancer patients may be eligible for clinical trials for the prevention or treatment of COVID-19 or its complications and stay informed of such clinical trial opportunities. COVID-19 patients with cancer have substantially higher risk of severe outcomes compared with patients without cancer, particularly in those with

metastatic cancer. Patients should be thoroughly informed about potential changes arising from the outbreak by using web technology for communication with the investigator team, possible social isolation during COVID-19 outbreak and closer collaboration with general practitioners or local laboratories.[57,58]

How do we decide whether to deviate from a clinical trial protocol (for risk—benefit reasons) and how do we handle the deviations that take place?

STATEMENT 26: During the COVID-19 pandemic, deviations from a clinical trial protocol (for risk—benefit reasons) may be considered provided there is rigorous documentation in the medical record of the patient and that this is communicated as soon as possible to the sponsor. There are no acceptable deviations in safety reporting.

During the COVID-19 pandemic, deviations from clinical trial protocols seem unavoidable if only for logistical reasons. Treating physicians should remain as close as possible within the provisions of clinical trial protocols so that the risk—benefit balance of the clinical trial remains acceptable. Frequent and open communication between clinical trial sites and clinical trial sponsors is paramount. Documentation of any deviation and communication of deviations to the clinical trial sponsor are necessary so that sponsors can monitor changes in the risk—benefit balance of the clinical trial, declare such deviations to the appropriate authorities and plan amendments to the clinical trial protocols. Examples of such deviations include but are not limited to remote methods of patient monitoring, investigational drug delivery and change of laboratories for diagnostic tests due to travel restrictions and the need for social distancing. Regardless, adaptations to the pandemic should not change the processes and timelines of safety reporting and pharmacovigilance declaration, which should be done completely and promptly even when using remote methods of patient assessment.[56,57]

Patient-reported outcomes merit special attention as clinical trial end points. Although remote patient monitoring may not change the self-reporting ability of patients, measures such as QoL and physical functioning are likely to be impacted by the social distancing and other measures in response to the pandemic. Investigators and clinical trial sponsors should assess whether to continue collecting such measures and how to handle the effect of the pandemic in the analysis of the clinical trial data.

Do we continue to advocate and emphasise the need for cancer clinical trials for our patients to other stakeholders including but not limited to hospital systems, insurers and sponsors?

STATEMENT 27: During the COVID-19 pandemic, we should continue lobbying for promoting clinical cancer research to find better therapeutic options for patients with neoplasms. Cancer is and will continue to be one of the most significant causes of morbidity and mortality.

We must consider that clinical trials have extended the lives of cancer patients both for individuals participating in trials and through development of new drugs. Failure to invest in ongoing and future clinical trials may lead to 'collateral damage' from COVID-19 for individuals currently and collectively for cancer patients in the future. Within the hospital system, it is right and fully accepted that resources will be directed toward COVID-19-related activity and restructuring. However, cancer patients still require treatment even during the current pandemic. Cancer treatment is not elective or optional. The benefits of cancer clinical trial participation are broader than the benefits for an individual since they also raise clinical standards. It is well documented that even patients who are not active participants in clinical trials have better outcomes in a research-active environment. Furthermore, decreased cancer clinical trial activity and deskilling of clinical trial staff represents a loss of valuable experience in addition to financial investment.[58,59]

For academic and commercial sponsors, we must retain a long-term vision and a sense of proportionality. Cancer was one of the most significant causes of mortality pre-COVID-19 (9.6 million deaths globally in 2018) and whatever the shape of the post-COVID-19 era, this will not change. We can work with sponsors to harness the energy that has led to rapid and radical changes being enacted in health care systems. We should facilitate similar changes in clinical trial design and delivery to allow faster and more economical drug development. In order to maintain and strengthen sponsor relationships, we should demonstrate our commitment and capacity for delivering trials safely for patients and with ongoing high standards for data and biospecimen collection within clinical protocols, which have been adapted to an intra- and post-COVID-19 environment.

If clinical trial activities are restricted or resources are limited, how do we select the most relevant clinical trials for continuation or initiation?

STATEMENT 28: While we globally continue promoting clinical cancer research as the only way to find better therapeutic options and to improve cancer prognosis, we should continue ranking priorities in terms of value for the most appropriate clinical research.

Depending on the level of resource available for clinical trial activity, interventional studies with the following characteristics could be prioritised: (i) trials with a high likelihood of benefit (e.g. promising activity in early phase or molecularly-selected therapy), (ii) trials where the risk is lower in the experimental arm than standard of care (e.g. targeted or immunotherapy versus cytotoxic ChT), (iii) trials where treatment is of lower intensity than standard of care (e.g. monthly versus biweekly visits or oral rather than i.v. medication) and (iv) trials where there is no standard of care available in that setting. Finally, trials with a high risk of use of intensive care facilities in areas with high COVID-19 activity may temporarily be considered of lower priority.

CONCLUSIONS

Using a structured method and relying on a diverse panel of experts, we have developed a detailed set of clinical statements to guide health care professionals and assist them in overcoming many of the clinical and technical obstacles related to diagnosis, risk assessment, response assessment, surgical planning, RT and medical treatment during the COVID-19 pandemic. Ultimately, this set of statements will serve as a dynamic knowledge repository that will be better informed by accumulating data on SARS-CoV-2 biology, COVID-19 pandemic characteristics, the risks of COVID-19 and its modulating factors in cancer patients and, finally, on optimal cancer care in the presence of the virus.

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APPENDIX

Panel members

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