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Platinum Opinion

Advice Regarding Systemic Therapy in Patients with Urological Cancers During the COVID-19 Pandemic

Silke Gillessen [a,*], *Thomas Powles MD* [b,**]

[a] *Istituto Oncologico della Svizzera Italiana, Bellinzona, Switzerland;* [b] *Barts Cancer Institute, Queen Mary University of London, London, UK*

Evidence suggests that cancer patients are at higher risk of death from COVID-19 [1]. Therefore, the risk/benefit ratio of a number of palliative and (neo)adjuvant treatments has to be reconsidered during this pandemic. The duration of this period and details of the risk remain to be determined. A number of factors such as age and comorbidities will also influence this risk, as will the additional visits to hospital associated with specific treatment [2,3].

The advice set out here gives suggestions during the period of risk. These should not be considered as rigid guidelines in the traditional sense, but rather as a pragmatic perspective on this risk/benefit ratio in specific clinical scenarios. In addition, this advice will not apply to all patients, as there are a number of variables, including the stage of the pandemic and the local health care capacity, the risk of infection to the individual, the status of the cancer, comorbidities, age, and details of the treatment [4]. Here we only focus on the last of these factors.

Minimising potential exposure to COVID-19 by reducing visits to hospital, particularly for intravenous or inpatient therapy, is relevant. This is particularly important during the initial phase of the pandemic, when incidence is increasing exponentially and the upcoming pressure on health care resources is unknown [4]. Predicting the status of health care facilities and the ability to deliver systemic therapy in the future requires consideration. These factors will vary by geographic region.

There are a number of factors that require consideration. Regimens with a clear survival advantage should be prioritised, with curative treatments remaining mandatory and others requiring consideration of the risk/benefit ratio. Treatments that have only shown a palliative effect for patients who are symptomatic require careful discussion. Delaying the start of therapy during periods of uncertainty or difficulty is an appropriate measure for many of the therapies in urology cancer.

For curative treatments, use of growth factors and prophylactic antibiotics should be considered to avoid hospitalisation. Palliative treatments should be given at a dose intensity that avoids febrile neutropenia. While we do not recommend suboptimal dosing, if neutropenia occurs the doses need to be reduced for each episode. Prophylactic antibiotics are recommended where appropriate. Immunosuppressive agents such as steroids should be avoided or reduced for antiemesis where possible. Prolonged steroid treatment for prostate cancer requires consideration. Agents reducing the incidence of skeletal-related events such as bisphosphonates are probably best postponed if administration of the therapy involves potential exposure to COVID-19 (Table 1).

Adjuvant and neoadjuvant treatments require particular attention. The risk/benefit ratio may favour not giving therapy if the survival benefits are modest or unproven, such as perioperative therapy in urothelial cancer. Conversely, neoadjuvant therapy may be attractive in delaying the need for surgery/radiotherapy in cases in which these services are interrupted.

Aspects of clinical trials may not be appropriate in this pandemic. Recruitment to clinical trials requires careful consideration. Halting recruitment to cancer trials to divert resources to fight the pandemic may be appropriate.

The landscape will change as the risk of infection alters and more is known about preventing and treating COVID-19. In addition, treatments for COVID-19, such as antiviral

* Corresponding author. Department of Medical Oncology, Istituto Oncologico della Svizzera Italiana, Via Ospedale, Bellinzona 6500, Switzerland.
E-mail addresses: silke.gillessen@eoc.ch (S. Gillessen), thomas.powles1@nhs.net (T. Powles).
** Corresponding author.
E-mail address: thomas.powles1@nhs.net (T. Powles).

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Table 1 – Overview of suggestions regarding systemic therapy.

	Prostate cancer	Renal cancer	Germ cell cancer cancer	Urothelial cancer
1. Treatment should be commenced where possible	Frontline treatment for metastatic disease	Treatment for frontline IMDC intermediate- and poor-risk disease metastatic disease[a]	Treatment with curative intent	First-line treatment for metastatic disease
2. Treatment should not be commenced without justification	CTx in patients at significant COVID-19–related risk[b]	Nephrectomy for metastatic disease	Adjuvant therapy after orchidectomy for stage I disease	CTx in platinum-refractory disease Perioperative CTx for operable disease[c]
3. Treatment should not be stopped without justification	AR-targeted therapy[d]	Treatment for frontline metastatic disease	First- and second-line treatment for metastatic disease	Treatment for front line metastatic disease
4. Treatment that can potentially be stopped or delayed after careful consideration[e]	Minimising the number of CTx cycles or prolonging cycle length may be justified Steroids as a cancer therapy	ICI or oral VEGF-targeted therapy after prolonged period (1–2 yr)[d]		CTx for platinum refractory patients who are not responding to therapy More than 3 CTx cycles in the perioperative stetting
5. Treatments that can be given preferentially compared to other options	Oral AR-targeted therapy rather than CTx[f]	Oral VEGF therapy rather than IV immune therapy	Conventional dose rather than high-dose therapy	ICIs rather than CTx in PD-L1–positive frontline metastatic disease

AR = androgen receptor; CTx = chemotherapy; ICI = immune checkpoint inhibitor; IMDC = International Metastatic Renal Cell Carcinoma Database Consortium; IV = intravenous.
[a] Oral VEGF-targeted therapy rather than IV ICIs may be attractive as it requires less health care interactions and resources.
[b] Younger cancer patients and those without comorbidities may be at lower risk, which should be considered.
[c] Neoadjuvant chemotherapy may be helpful in bridging time to surgery in cases in which elective surgery is not possible.
[d] Regimens with a longer interval (4-weekly nivolumab or 6-weekly pembrolizumab) should be used where possible.
[e] Palliative CTx was tested with a specific number of cycles. The risk associated with stopping before this has not been assessed, nor of the principles of delaying chemotherapy. There are subgroups of prostate and urothelial cancer patients for whom continuing CTx to the full number of cycles may be associated with more risk than benefit. Patients will need to participate in this discussion.
[f] Assuming similar efficacy between the regimens.

agents, may improve outcomes. It is hoped that the advice here will quickly become redundant.

Conflicts of interest: Silke Gillessen Sommer has received honoraria from Janssen; has acted in a consulting or advisory role for Astellas Pharma, Curevac, Novartis, Active Biotech, Bristol-Myers Squibb, Ferring, Janssen, Innocrin Pharma, Bayer, Clovis Oncology, and Menarini Silicon Biosystems on an institutional basis and for MaxiVax, Advanced Accelerator Applications, Roche, Sanofi, and Orion Pharma GmbH on a personal basis; holds an interest in a patent for a biomarker method (WO 3752009138392 A1); and has a relevant relationship with Nektar and ProteoMediX. Thomas Powles has received research funding from AstraZeneca and Roche, and honoraria from AstraZeneca, Bristol-Myers Squibb, Roche, MSD, Pfizer, Merck Serono, Exelexis, IPSEN, Seattle Genetics, Johnson & Johnson, and Ferring.

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