COVID-19 in oncological patients

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The increasing number of people with COVID-19 and the rapid change in healthcare organisation that this has incurred, presents oncologists with the difficult decision of continuing or modifying a number of targeted therapies in some of their patient groups.

We have tried our best to come up with up-to-date recommendations on the management of COVID-19 in cancer patients. However, the most urgent question is almost impossible to answer: which therapies should be administered/continued and which therapies should be deferred/stopped?

To address this question, we conducted a survey amongst experts in the respective fields to get a better understanding of the perceived risk-benefit analyses of each targeted therapy, which we present alongside a summary of expert opinion.

SARS-CoV-2 causes a respiratory infectious disease which has a protracted clinical course and may result in a hyperinflammation causing acute respiratory distress syndrome, usually in the second week of the disease. Patients with malignant disease should be assumed to be at higher risk of developing severe complications due to impaired immunity. Other risk factors which should be considered are neutropenia, lymphopenia, advanced age and comorbidities.

On the other hand, it is known that patients with controlled malignancy are at lower risk of infection than those with active disease.\textsuperscript{1} We therefore asked experts how they would manage certain substances in patients with symptoms of SARS-CoV-2 infection. Altogether, 188 experts provided answers in the survey, but as each only answered questions concerning their own field of practice, the denominator differs between treatment modalities.

Reference:


Results summary:

There was agreement (>90%) to continue: BCR-ABL TKI

There was a majority (>70%) in favour of continuing: ALK-TKI, EGFR-TKI, JAK-STAT inhibitors, HER2-neu antibodies, Hydroxyurea, low-dose steroids (<20mg/d prednisone for at least 4 weeks), PARP-inhibitors, VEGF-antibodies
There was a majority (>70%) in favour of discontinuing: CD20 antibodies, high-dose steroids (>20mg/d prednisone for at least 4 weeks),

There was no clear vote in favour of continuing or discontinuing (>30% for both options): BCL2-Inhibitors, BRAF-Inhibitors, BTK-inhibitors, CDK4/6 inhibitors, CD38 antibodies, demethylating agents, immune-checkpoint inhibitors, IMIDs, HDAC-inhibitors, mTOR inhibitors, Proteasome inhibitors.
Summary of results by substance class:

Anti-CD20 antibodies

123/170 (72.5%) experts would rather discontinue anti-CD20 antibodies. Reasons stated (multiple answers possible):

- Severe immunosuppression: 100 (59%)
- Risk of hypersensitivity: 6 (3.5%)
- Other reasons: 28 (16.5%), Typical examples:
  - Delay while patients have active signs of infection.
  - B cells seem very important in immune response towards SARS-CoV-2.
  - B lymphocyte block of antiviral specific IgG.
  - Depends on disease: continue in aggressive lymphoma chemotherapy, but discontinue in indolent lymphoma maintenance.
  - Discontinue in maintenance therapy – no evidence of survival benefit indolent lymphoma and it is immunosuppressive.
  - Risk of concomitant pneumonitis due to CD20 monoclonal.
  - Withhold just during COVID-19 infection; would not affect hematologic disease in most cases.

48/170 (28%) experts would rather continue anti-CD20 antibodies. Reasons stated (multiple answers possible):

- No severe immunosuppression: 19 (11%)
- Risk of flare when stopped: 9 (5.5%)
- Other reasons: 23 (13.5%),
  - Continue in younger patients who are isolating themselves after taking the drug.
  - Crucial for the infection is the amount of NK cells and neutrophil function. We are suggesting social distance and isolation, and to keep treatment (could delay the next cycle for now try to maintain cumulative dosage).
  - Balancing act between COVID-19 and disease relapse.
  - It depends on the indication whether to stop or to continue: for aggressive b cell tumors I would definitely continue.
  - It has a very long effect so stopping now won’t change anything for two or three months. Persistent immunosuppression for several months (>3 mo).
**ALK-TKI**

17/74 (23%) experts would rather discontinue ALK-TKI. Reasons stated (multiple answers possible):

- Severe immunosuppression: 11 (15%)
- Risk of hypersensitivity: 0 (0%)
- Other reasons: 3 (4%)
  - Discontinuation until resolution of symptoms of respiratory infection.
  - Interaction. Possible interference with treatment/course of infections.

57/74 (77%) experts would rather continue ALK-TKI. Reasons stated (multiple answers possible):

- No severe immunosuppression: 33 (44.5%)
- Risk of flare when stopped: 24 (32.5%)
- Other reasons: 3 (4%)
  - Weighing between basic malignant disease risk classification the existing immunosuppression.

**BCL2-Inhibitors**

46/130 (35.5%) experts would rather discontinue BCL2-Inhibitors. Reasons stated (multiple answers possible):

- Severe immunosuppression: 33 (25.5%)
- Risk of hypersensitivity: 0 (0%)
- Other reasons: 13 (10%), typical examples:
  - Haven’t had so far severe neutro/lymphopenia with patients on this drug. In general I would stop all chemotherapy agents in patients with COVID-19 w/o immediate/pressing need for chemotherapy due to malignancy.
  - in CLL stopping BCL inhibitor will not lead to rapid relapse of disease as evident from pts who had to stop for adverse effects
  - Interactions with chloroquine expected
  - Occurrence of respiratory infections in our experience, risk of concurrent bacterial pneumonia
  - severe neutropenia

4/130 (3%) experts would switch to another drug of the same substance class

85/130 (65.5%) experts would rather continue BCL2-Inhibitors. Reasons stated (multiple answers possible):
No severe immunosuppression: 35 (27%)
Risk of flare when stopped: 42 (32.5%)
Other reasons: 17 (13%), typical examples:
  o adapt dose to avoid neutropenia, consider stopping if underlying disease is well controlled with no risk of relapse
  o can prolong patients’ life significantly eg in p53 CLL; use only dosage that does not lead to neutropenia
  o Generally well tolerated and doesn’t have major impact on immunosuppression of and above underlying disease
  o The immune suppression already exists and does not worsens when you keep treating the pt. Also, the treatment is given orally: no special visit is required to the hospital. CBCs can be measured safely in lab and communication can be done with tel/e-mail

BCR-ABL tyrosine-kinase inhibitors (e.g. Imatinib)

12/157 (7.5%) experts would rather discontinue BCR-ABL tyrosine-kinase inhibitors. Reasons stated (multiple answers possible):
- Severe immunosuppression: 3 (2%)
- Risk of hypersensitivity: 1 (0.5%)
- Other reasons: 6 (4%), typical examples:
  o A stop of 2-3 weeks is probably not a problem
  o May cause immune suppression
  o risk of interaction with other drugs

145/157 (92.5%) experts would rather continue BCR-ABL tyrosine-kinase inhibitors. Reasons stated (multiple answers possible):
- No severe immunosuppression: 120 (76.5%)
- Risk of flare when stopped: 34 (21.5%)
- Other reasons: 14 (10%), Typical examples
  o anti-abl activity inhibits intracellular virus spread
  o Crucial for the infection is the amount of NK cells and neutrophil function, we are suggesting social distance and isolation, and to keep treatment (we could delay the next cycle but for now we try to maintain the cumulative dosage)
  o Depends on the reason for taking TKI. On ALL Ph+ I would try to continue until severe symptoms of infection, and closely monitor for them. For CML patients I would probably discontinue until even mild symptoms disappear.
  o in CML, Dasatinib is known for risk of CMV reactivation, may have increased risk for serious CoVID19?
  o no real evidence that these patients are more at risk
**BRAF inhibitors**

15/45 (33.5%) experts would rather discontinue BRAF inhibitors. Reasons stated (multiple answers possible):

- Severe immunosuppression: 11 (24.5%)
- Risk of hypersensitivity: 1 (2%)
- Other reasons: 0 (0%)

2/45 (4.5%) experts would switch to another drug of the same substance class

30/45 (66.5%) experts would rather continue BRAF inhibitors. Reasons stated (multiple answers possible):

- No severe immunosuppression: 18 (40%)
- Risk of flare when stopped: 12 (26.5%)
- Other reasons: 3 (6.5%)
  - Melanoma may progress. HCL probably with no problem stop for 2 – 3 weeks.
  - Weighing between basic malignant disease and risk classification of the existing immunosuppression.

**Bruton Tyrosine Kinase (BTK) inhibitors**

54/137 (39.5%) experts would rather discontinue BTK inhibitors. Reasons stated (multiple answers possible):

- Severe immunosuppression: 42 (30.5%)
- Risk of hypersensitivity: 2 (1.5%)
- Other reasons: 17 (12.5%), Typical examples
  - BTK signalling interacts with infection control
  - Ibrutinib enhances encephalitis due to west nile virus and such clinical manifestations might be evident with covid-19, if the patients survive the hyperinflammatory lung status
  - Inhibition of B cell function that may reverse with hold
  - Interactions with other drugs
  - Neutropenia
  - Occurrence of respiratory infections in our experience, risk of concurrent fungal infections (i.e. aspergillosis)
  - Stop of 2-3 weeks probably not a problem
  - Switch to drug of other class such as BCL-2 inhibitor
  - This is a difficult one because there is clearly an impact on immune response, but in some patients discontinuing will cause rapid progression
3/137 (2%) experts would switch to another drug of the same substance class

85/137 (62%) experts would rather continue BTK inhibitors. Reasons stated (multiple answers possible):

- No severe immunosuppression: 36 (26.5%)
- Risk of flare when stopped: 48 (35%)
- Other reasons: 14 (10%), Typical examples:
  - Disease control better / more important in my patients
  - Domestic setting
  - If no history of infections, continue
  - Immune suppression seems to be late (years), however in the case of neutropenia I would discontinue
  - Mild immunosuppression may limit SARS-Cov-2 infection
  - Oral therapy, less monitoring. Use only in desperate indications
  - Risk of loss of disease control
  - Safe class of drugs
  - The immune suppression already exists and does not worsens when you keep treating the pt. Also, the treatment is given orally: no special visit is required to the hospital. CBCs can be measured safely in lab and communication can be done with tel/e-mail

CDK4/6 inhibitors

11/30 (36.5%) experts would rather discontinue CDK4/6 inhibitors. Reasons stated (multiple answers possible):

- Severe immunosuppression: 6 (20%)
- Risk of hypersensitivity: 2 (6.5%)
- Other reasons: 1 (3.5%)
  - A stop of 2 - 3 weeks is probably not a problem.

3/30 (10%) experts would switch to another drug of the same substance class

19/30 (63.5%) experts would rather continue CDK4/6 inhibitors. Reasons stated (multiple answers possible):

- No severe immunosuppression: 12 (40%)
- Risk of flare when stopped: 4 (13.5%)
- Other reasons: 4 (13.5%)
  - Monitor closely.
  - Progression of disease.
  - Weighing between basic malignant disease and risk classification of the existing immunosuppression.
CD38 antibodies (e.g. Daratumumab)

76/133 (57%) experts would rather discontinue CD38 antibodies. Reasons stated (multiple answers possible):

- Severe immunosuppression: 41 (31%)
- Risk of hypersensitivity: 14 (10.5%)
- Other reasons: 22 (16.5%), Typical examples
  - activation of immune response resulting in enhanced reactivity to SARS-Cov-2
  - Discontinuation in patients with monthly administration in order to reduce hospital access
  - Pulmonary toxicities and increased rate of pneumonia
  - short time discontinuation until resolution of symptoms of respiratory infectious
  - Stop it even with mild symptoms due to possible lung toxicity with the antiCD38

7/133 (5.5%) experts would switch to another drug of the same substance class

59/133 (44.5%) experts would rather continue CD38 antibodies, reasons (multiple answers possible):

- No severe immunosuppression: 25 (19%)
- Risk of flare when stopped: 17 (13%)
- Other reasons: 16 (12%), Typical examples:
  - Crucial for the infection is the amount of NK cells and neutrophil function, we are suggesting social distance and isolation, and to keep treatment (we could delay the next cycle but for now we try to maintain the cumulative dosage)
  - depends on disease status and current control of myeloma
  - If no history of infection, continue
  - most often no other less immunosuppressive regimen eligible, progressive disease needs treatment

Demethylating Substances

58/152 (38%) experts would rather discontinue demethylating substances. Reasons stated (multiple answers possible):

- Severe immunosuppression: 36 (23.5%)
- Risk of hypersensitivity: 0 (0%)
- Other reasons: 22 (14.5%), Typical examples:
  - a heavy toxicity
  - critically evaluate benefit
  - deep neutropenia and the consequent high risk of bacterial infection
  - Interrupt while patient has active infection, continue as soon as patient clinically stable to avoid disease progression
- Mainly elderly patients with MDS/ transformation, safer away from the hospital at present.
- Not an urgent treatment, can be delayed
- Occurrence of severe neutropenia in most cases, high-risk of concurrent lung infections
- Stop of 2-3 weeks probably not a problem
- Stop until acute disease resolves as usual for other infections
- Usually in high risk population (elderly), minor OS improvement, but higher risk of infection transmission due to method of administration

3/152 (2%) experts would switch to another drug of the same substance class

95/152 (62.5%) experts would rather continue demethylating substances. Reasons stated (multiple answers possible):
- No severe immunosuppression: 46 (30.5%)
- Risk of flare when stopped: 36 (23.5%)
- Other reasons: 23 (15%), Typical examples:
  - Adjust dose
  - azacytidine, which I preferentially give, can be administered in an outpatient setting
  - Crucial for the infection is the amount of NK cells and neutrophil function, we are suggesting social distance and isolation, and to keep treatment (we could delay the next cycle but for now we try to maintain the cumulative dosage)
  - Depends on severity of infection and state of hematological disease. Would withhold treatment on patients in CR even with mild symptoms, but would probably continue on patients with SD/PR/new diagnosis until severe symptoms and monitor closely.
- Disease for which drugs are used at least as dangerous as drug itself
- In the case of AML: urgent therapy
- May be no alternative intervention for high risk MDS
- Safe
- We attempt to prolong the time interval between cycles (after the first 8)

**EGFR-TKI**

7/28 (25%) experts would rather discontinue EGFR-TKI. Reasons stated (multiple answers possible):
- Severe immunosuppression: 2 (7%)
- Risk of hypersensitivity: 2 (7%)
- Other reasons: 2 (7%)
  - Depends on tumor dynamics.
  - No experience in COVID-19.
0/28 (0%) experts would switch to another drug of the same substance class

21/28 (75%) experts would rather continue EGFR-TKI. Reasons stated (multiple answers possible):

- No severe immunosuppression: 17 (60.5%)
- Risk of flare when stopped: 3 (10.5%)
- Other reasons: 1 (3.5%)
  - Weighing between basic malignant disease and risk classification of the existing immunosuppression.

**Immune checkpoint inhibitors**

46/101 (45.5%) experts would rather discontinue immune checkpoint inhibitors. Reasons stated (multiple answers possible):

- Severe immunosuppression: 17 (17%)
- Risk of hypersensitivity: 15 (15%)
- Other reasons: 18 (18%), typical examples:
  - Activation of immune response resulting in enhanced reactivity to SARS-Cov-2
  - Could increase hyperinflammation
  - Interactions with other treatments
  - Not infrequent severe inflammatory responses such as MAS
  - PD1/PDL1 inhibitors have autoimmune adverse events that may mimic the symptoms of SARS-COV-2 or may worsen them. They have to be given in hospital and as mentioned this is a problem for viral transmission. I would wait 2 or 3 weeks
  - Risk of pneumonitis. Stop of a few weeks not a problem. Long half time.

3/101 (3%) experts would switch to another drug of the same substance class

55/101 (54.5%) experts would rather continue immune checkpoint inhibitors. Reasons stated (multiple answers possible):

- No severe immunosuppression: 31 (31%)
- Risk of flare when stopped: 18 (18%)
- Other reasons: 7 (7%), typical examples:
  - Brief interruption reasonable, also dosing is q2 or q3 weeks, so it could hold 2-3 doses during acute illness
  - Check often for infection
  - Crucial for the infection is the amount of NK cells and neutrophil function, we are suggesting social distance and isolation, and to keep
treatment (we could delay the next cycle but for now we try to maintain the cumulative dosage)

**Immune modulatory substances (e.g. Lenalidomid)**

49/156 (31.5%) experts would rather discontinue immune modulatory substances. Reasons stated (multiple answers possible):

- Severe immunosuppression: 29 (18.5%)
- Risk of hypersensitivity: 5 (3%)
- Other reasons: 15 (9.5%), typical examples:
  - activation of immune response resulting in enhanced reactivity to SARS-Cov-2
  - Could increase hyperinflammation
  - depending on disease status
  - high risk of neutropenia
  - if disease is well controlled (e.g. maintenance) consider temporary interruption

108/156 (69%) experts would rather continue immune modulatory substances. Reasons stated (multiple answers possible):

- No severe immunosuppression: 61 (39%)
- Risk of flare when stopped: 34 (22%)
- Other reasons: 25 (16%), typical examples:
  - Adjust dose or interrupt if patient is neutropenic
  - Crucial for the infection is the amount of NK cells and neutrophil function, we are suggesting social distance and isolation, and to keep treatment (we could delay the next cycle but for now we try to maintain the cumulative dosage)
  - Domestic setting
  - I am told anecdotal evidence may not be harmful or possibly beneficial. Stop concurrent steroids
  - Immunomodulation has pros and contras in COVID-19 infection
  - In responding patients without severe toxicity, it would be better to keep disease under control
  - Potential anti IL 6 effect
  - The immune suppression already exists and does not worsen when you keep treating the pt. Also, the treatment is given orally: no special visit is required to the hospital. CBCs can be measured safely in lab and communication can be done with tel/e-mail
**JAK-STAT inhibitors**

37/127 (29%) experts would rather discontinue JAK-STAT inhibitors. Reasons stated (multiple answers possible):

- Severe immunosuppression: 24 (19%)
- Risk of hypersensitivity: 1 (0.5%)
- Other reasons: 9 (7%), typical examples:
  - higher risk of viral reactivation
  - avoided only when its possible (low risk disease flare)
  - highly immunosuppressive
  - Myelotoxicity - lowers neutrophil counts
  - no experience in Covid
  - Stop of a few weeks probably not a problem
  - thrombocytopenia
  - Weighing between basic malignant disease and risk classification of the existing immunosuppression

5/127 (4%) experts would switch to another drug of the same substance class

90/127 (71%) experts would rather continue JAK-STAT inhibitors, reasons (multiple answers possible):

- No severe immunosuppression: 49 (38.5%)
- Risk of flare when stopped: 35 (27.5%)
- Other reasons: 15 (12%), typical examples:
  - Adjust dose or interrupt if patient is neutropenic
  - Could be beneficial e.g. Baricitinib
  - does give immune suppression, but will continue using in exceptional patients in whom it is essential
  - jak/stat is involved in Angiotensin II transduction pathway, involved in lung injury. This inhibition could protect the lung
  - possible anti-inflammatory drug
  - Since the drug has anti-IL6 properties patients could have lower risk of symptomatic infection, while the drug benefit for MF is very high.

**HDAC inhibitors**

26/65 (40%) experts would rather discontinue HDAC inhibitors, reasons (multiple answers possible):

- Severe immunosuppression: 17 (26%)
- Risk of hypersensitivity: 0 (0%)
- Other reasons: 6 (9%)
  - Active infection.
  - Depends on the disease’s dynamics.
Increases neutropenia.
- Rather toxic drug.
- Weighing between basic malignant disease and risk classification of the existing immunosuppression. Pulmonary toxicity.

2/65 (3%) experts would switch to another drug of the same substance class

40/65 (61.5%) experts would rather continue HDAC inhibitors. Reasons stated (multiple answers possible):
- No severe immunosuppression: 20 (31%)
- Risk of flare when stopped: 14 (21.5%)
- Other reasons: 2 (3%)
  - NO strong data about negative impact on immune response.

**Her2-neu antibodies (e.g. Trastuzumab)**

8/29 (27.5%) experts would rather discontinue HER2-neu antibodies. Reasons stated (multiple answers possible):
- Severe immunosuppression: 2 (7%)
- Risk of hypersensitivity: 3 (10.5%)
- Other reasons: 2 (7%)
  - Depends on the clinical picture. Short stop is probably not a problem.
  - Potential unexpected events.

0/29 (0%) experts would switch to another drug of the same substance class

21/29 (72.5%) experts would rather continue HER2-neu antibodies. Reasons stated (multiple answers possible):
- No severe immunosuppression: 20 (69%)
- Risk of flare when stopped: 2 (7%)
- Other reasons: 1 (3.5%)
  - Weighing between basic malignant disease and risk classification of the existing immunosuppression.
High dose steroids (>20mg/d prednisone for at least 4 weeks)

118/165 (71.5%) experts would rather discontinue high dose steroids. Reasons stated (multiple answers possible):

- Severe immunosuppression: 99 (60%)
- Risk of hypersensitivity: 0 (0%)
- Other reasons: 24 (14.5%), typical examples:
  - action via transcriptase viral domain proliferation
  - continuing or not depends on reason for steroid treatment
  - Discontinue independently of COVID-19 pandemic
  - dose reduction
  - Impairment of lymphocytes function
  - In my practice I do not use such prolonged prednisolone regimens except in a rare case of gvhd, and there it would be hard to discontinue
  - Poor outcome reported
  - Steroids can hide the fever. Pneumonia od COVID19 seems to worsens with steroids
  - to be evaluated on a case basis: in ARDS maybe helpful
  - unless indicated e.g. for aggressive lymphoid malignancies
  - Use pulsed dexamethasone
  - Weighing between immune-associated disease (auto-, alloimmune, serve GvHD = no stopped, tapering) and risk classification of the existing immunosuppression

12/165 (7.5%) experts would switch to another drug of the same substance class

48/165 (29%) experts would rather continue high dose steroids. Reasons stated(multiple answers possible):

- No severe immunosuppression: 6 (3.5%)
- Risk of flare when stopped: 22 (13.5%)
- Other reasons: 22 (13.5%), typical examples:
  - Cave: Addison crisis when stopped in pat. on long-term corticosteroids
  - Context specific - depends upon reason for steroids
  - Difficult. On a case by case basis. Are people more likely to die of the illness you're treating or from the covid-19 infection, IF they get infected in the first place...
  - discontinuation could be considered in stable hematologic disease until resolution of symptoms of respiratory infectious
  - I think it would help against the hyperinflammatory condition seen at covid, it reminds me of the CRS after CAR-T cell therapy
  - risk of flare, IRIS, taper if possible
  - we cannot stop any therapy for fear
with protective isolation

**Hydroxyurea**

17/163 (10.5%) experts would rather discontinue Hydroxyurea. Reasons stated (multiple answers possible):

- Severe immunosuppression: 6 (3.5%)
- Risk of hypersensitivity: 1 (0.5%)
- Other reasons: 6 (3.5%)
  - Increases neutropenia.
  - Low risk stopping short term.
  - Stop until acute disease resolves as usual for other serious infections.
  - Symptomatic/toxic.

1/163 (0.5%) experts would switch to another drug of the same substance class

146/163 (89.5%) experts would rather continue Hydroxyurea. Reasons stated (multiple answers possible):

- No severe immunosuppression: 119 (73%)
- Risk of flare when stopped: 31 (19%)
- Other reasons: 16 (10%), typical examples:
  - adjust dose
  - Avoiding hyperleukocytosis
  - can be discontinued in low malignancies
  - disease control more important, usually not very immunosuppressive
  - Hyperviscosity syndrome prophylaxis
  - if needed, e.g. for chronic MPN patients with high platelet counts
  - If no cytopenia the drug will probably be safe
  - It is safer if patients stay home and maintain social distance, to warrant supportive care
  - Risk of coming to harm from the illness treated probably higher than the additional risk of HU in the event of covid-19 infection.

**Low dose steroids (<20mg/d prednisone for at least 4 weeks)**

41/168 (24.5%) experts would rather discontinue low dose steroids. Reasons stated (multiple answers possible):

- Severe immunosuppression: 27 (16%)
- Risk of hypersensitivity: 0 (0%)
• Other reasons: 9 (5.5%), typical examples:
  o Discontinue or lower the dose for the course of the infection
  o it depends on the reason for steroid, if it is for GVH it cannot be discontinued
  o low dose steroids should be more easily discontinued than high dose steroids I guess
  o unless vital indication

4/168 (2.5%) experts would switch to another drug of the same substance class

127/168 (75.5%) experts would rather continue low dose steroids. Reasons stated (multiple answers possible):
  o No severe immunosuppression: 64 (38%)
  o Risk of flare when stopped: 43 (25.5%)
  o Other reasons: 20 (12%), typical examples:
    o Although there is some immune suppression there is a risk of adrenal insufficiency
    o Immunomodulatory effect
    o It depends on the indication
    o It is safer if patients stay home and maintain social distance, to warrant supportive care
    o might be helpful in reducing inflammation
    o More straightforward this time: benefit probably outweigths the additional risk in the event of covid-19 infection.
    o Try for early taper
    o with the lowest dose possible

mTOR inhibitors

14/42 (33.5%) experts would rather discontinue mTOR inhibitors. Reasons stated (multiple answers possible):
  • Severe immunosuppression: 9 (21.5%)
  • Risk of hypersensitivity: 0 (0%)
  • Other reasons: 3 (7%)
    o Active infection.
    o Stop of a few weeks probably not a problem. Depends on the condition of the patient.
    o Weighing between basic malignant disease and risk classification of the existing immunosuppression.

2/42 (5%) experts would switch to another drug of the same substance class
18/42 (66.5%) experts would rather continue mTOR inhibitors, reasons (multiple answers possible):
  - No severe immunosuppression: 9 (21.5%)
  - Risk of flare when stopped: 14 (33.5%)
  - Other reasons: 23 (7%)
    - Case by case.
    - Monitor.
    - Safe in low doses.

**PARP inhibitors**

3/18 (16.5%) experts would rather discontinue PARP inhibitors. Reasons stated (multiple answers possible):

- Severe immunosuppression: 1 (5.5%)
- Risk of hypersensitivity: 0 (0%)
- Other reasons: 0 (0%)

0/18 (0%) experts would switch to another drug of the same substance class

15/18 (83.5%) experts would rather continue PARP inhibitors. Reasons stated (multiple answers possible):

- No severe immunosuppression: 10 (55.5%)
- Risk of flare when stopped: 4 (22%)
- Other reasons: 2 (11%)
  - Weighing between basic malignant disease and risk classification of the existing immunosuppression.

**Proteasome inhibitors (e.g. Bortezomib)**

55/153 (36%) experts would rather discontinue proteasome inhibitors. Reasons stated (multiple answers possible):

- Severe immunosuppression: 31 (20.5%)
- Risk of hypersensitivity: 1 (0.5%)
- Other reasons: 18 (12%), typical examples:
  - active infection
  - Documented moderate/high risk of Herpesviridae family and CMV infection
  - I would interrupt for 2 or 3 weeks, until I see that the patient is Ok and the symptoms have regressed. I think that this interruption
period is safe for a patient. No flare possibility. Bortezomib is administered in the hospital and this is generally unsafe
  o induction can be suspended after a few cycles with good response, depending on the disease severity
  o stop until acute disease resolves as usual for other serious infections
  o T cell and NK toxicity

6/153 (4%) experts would switch to another drug of the same substance class

98/153 (64%) experts would rather continue proteasome inhibitors. Reasons stated (multiple answers possible):
  o No severe immunosuppression: 61 (40%)
  o Risk of flare when stopped: 25 (16.5%)
  o Other reasons: 21 (13.5%), typical examples:
    o Crucial for the infection is the amount of NK cells and neutrophil function, we are suggesting social distance and isolation, and to keep treatment (we could delay the next cycle but for now we try to maintain the cumulative dosage)
    o Depends on the patient’s condition and the dynamics of the disease
    o discontinuation could be considered in stable hematologic disease until resolution of symptoms of respiratory infectious
    o Have heard anecdotal reports may not be harmful
    o In induction and consolidation, I prefer to continue. For bortezomib maintenance and carfilzomib administration after 12 months of therapy I prefer to stop.
    o only in patients with active MM; otherwise I would just withhold during COVID course
    o Use with proper prophylaxis
    o Weighing between basic malignant disease and risk classification of the existing immunosuppression
    o would try to increase intervals, but would depend on MM status

VEGF/ VEGFR2 inhibitors (e.g. Bevazicumab)

9/31 (29%) experts would rather discontinue VEGF/ VEGFR2 inhibitors. Reasons stated (multiple answers possible):

  • Severe immunosuppression: 2 (6.5%)
  • Risk of hypersensitivity: 1 (3%)
  • Other reasons: 4 (13%)
    o I don’t know any data of interaction.
    o No experience in COVID-19.
    o No major additional effect, risk minimalization.
0/31 (0%) experts would switch to another drug of the same substance class

22/31 (71%) experts would rather continue VEGF/VEGFR2 inhibitors. Reasons stated (multiple answers possible):

- No severe immunosuppression: 18 (58%)
- Risk of flare when stopped: 3 (9.5%)
- Other reasons: 3 (9.5%)
  - Use in low doses.
  - Crucial for the infection is the amount of NK cells and neutrophil function, we are suggesting social distance and isolation and to keep treatment (we could delay the next cycle but for now we try to maintain the cumulative dosage).
  - Weighing between basic malignant disease and risk classification of the existing immunosuppression.