

COVID-19 in oncological patients

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The increasing number of people with COVID-19 presents oncologists with the difficult decision of continuation or modification of targeted therapies.

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 risks of respective (targeted) therapies and 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. 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 than those with active disease.

Based on this information we asked the question: how would you manage therapy **in a patient with controlled malignancy and proven SARS-CoV-2 infection?**

Would you rather discontinue or continue therapy with a respective drug?

Results by substance class:

Shown are the results of all experts who have answered a question. Altogether, 94 experts provided answers in the survey but not all to each drug.

Anti-CD20 antibodies

47/73 (64.5%) experts would rather discontinue anti-CD20 antibodies, reasons (multiple answer):

- Severe immunosuppression: 31 (42.5%)
- Risk of hypersensitivity: 2 (2.5%)
- Other reasons: 19 (26%)
 - Atypical pneumonia/pneumonitis most typical side effect; I would only stop until patient recovered.
 - Continue ritux in primary therapy, but stop maintenance.
 - Continue with chemo, stop when used for maintenance or non-malignant indications e.g. ITP. Swap IV to sc to minimise time in unit
 - delayed if possible.
 - Discontinue maintenance, make it possible to use vaccination further ahead.
 - Discontinue only for maintenance.
 - Discontinued as maintenance, (not all), not discontinued in combo with chemo (improves OS).
 - Especially during maintenance regimens.
 - For maintenance and for patients in good remissions, treatment can be postponed/stopped.
 - Generally can be delayed.
 - Hospital administration. Avoid patients in the hospital. Stay at home.
 - I discontinue antiCD20 only in the maintenance setting of Follicular Lymphoma.
 - I would definitely try to defer obinutuzumab in CLL, but not rituximab in aggressive b cell lymphoma.
 - If only PFS-benefit.
 - Immunosuppression potentially harmful under the current conditions, unless patient's situation does not permit treatment postponement.
 - Immunosuppression and not life-saving drugs usually.
 - Maintenance can be postponed.
 - Mild immunosuppression but no immediate adverse effects of postponing therapy until recovery.
 - Only in maintenance therapy.
 - Postpone after recovery.
 - Risk of significant lymphopaenia and hypogammaglobulinaemia.
 - To avoid contacts in hospital/ to diminish spread of COVID infections: quarantine.
 - Treatment can be safely delayed in indolent lymphomas.
 - Unknown effects in COVID context.
 - Unless curative setting.

0/73 (0%) experts would switch to another drug of the same substance class

26/73 (35.5%) experts would rather continue anti-CD20 antibodies, reasons (multiple answer):

- No severe immunosuppression: 13 (18%)
- Risk of flare when stopped: 10 (13.5%)
- Other reasons: 6 (8%)
 - Benefit usually higher than risk.
 - Continue with chemotherapy, delay maintenance.
 - COVID-19 acts through macrophages and not T cells.
 - During treatment such RCHOP.
 - For curative regimen.
 - For patients in 1st line treatment NHL ALL.
 - I continue Rituximab associated with chemotherapy in cases of aggressive lymphomas. In indolent lymphoma I try to defer treatment.
 - If OS-benefit.
 - Improves OS in combo with chemo.
 - Needed in the induction phase of therapy e.g. in DLBCL. When the patient is in maintenance phase of treatment of LOW-grade lymphomas, treatment should be postponed until the epidemic is gone.
 - Relapse.

ALK-TKI

2/32 (6%) experts would rather discontinue ALK-TKI, reasons (multiple answer):

- Severe immunosuppression: 1 (3%)
- Risk of hypersensitivity: 1 (3%)
- Other reasons: 1 (3%)
 - Depends on the TKI and the disease treated.
 - Risk of interaction with drugs used to treat COVID-19.

0/32 (0%) experts would switch to another drug of the same substance class

30/32 (94%) experts would rather continue ALK-TKI, reasons (multiple answer):

- No severe immunosuppression: 19 (59.5%)
- Risk of flare when stopped: 10 (31.5%)
- Other reasons: 1 (3%)
 - Progression of the disease – home quarantine (for ALK positive lymphomas).

BCL2-Inhibitors

20/64 (31.5%) experts would rather discontinue BCL2-Inhibitors, reasons (multiple answer):

- Severe immunosuppression: 10 (15.5%)
- Risk of hypersensitivity: 1 (1.5%)
- Other reasons: 6 (9.5%)
 - Bcl2 inhibitors can be interrupted in case of shoos be interrupted in case of.
 - I would discuss temporary discontinuation in select patients with good response on single agent BCL-2 inhibitor. I would also discuss discontinuation in patient's past month nine of the Murano protocol, due to lack of improvement of depth of response.
 - In case of well controlled hematologic malignancy.
 - neutropenia; I would only stop until patient recovered.
 - Postpone after recovery.
 - Risk of neutropenia, no flare reactions upon interruption.

2/64 (3%) experts would switch to another drug of the same substance class

44/64 (68.5%) experts would rather continue BCL2-Inhibitors, reasons (multiple answer):

- No severe immunosuppression: 16 (25%)
- Risk of flare when stopped: 22 (34.5%)
- Other reasons: 11 (17%)
 - Benefit vs risk mostly pro benefit.
 - Certainly after failure of BCR-inhibitors, consider earlier discontinuation in CLL MRD-negative and neutropenia.
 - good drugs!
 - I continue if the patient is already on treatment. I defer the start of treatment if possible.
 - I use in AML, risk of relapse and death whenever discontinued.
 - If uncontrolled hematologic malignancy.
 - mostly cause neutropenia that can be monitored and prevented/treated with growth factors.
 - Oral medication at home.
 - Relapse.
 - Used in severe cases - likely to have more problems with disease than COVID.
 - Usually on strict indication and needed.

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

6/76 (8%) experts would rather discontinue BCR-ABL tyrosine-kinase inhibitors, reasons (multiple answer):

- Severe immunosuppression: 1 (1.5%)
- Risk of hypersensitivity: 0 (0%)
- Other reasons: 5 (6.5%)
 - If the neoplasm is well controlled it is safer to stop the drug.
 - Postpone after recovery.
 - Potential interactions with antivirals.
 - Risk of interactions with drugs used to treat COVID19.
 - We can safely stop it if disease is controlled.

0/76 (0%) experts would switch to another drug of the same substance class

70/76 (92%) experts would rather continue BCR-ABL tyrosine-kinase inhibitors, reasons (multiple answer):

- No severe immunosuppression: 59 (77.5%)
- Risk of flare when stopped: 25 (33%)
- Other reasons: 7 (9.5%)
 - Discontinuation in eligible patients who did not wish to try a stop earlier could be reconsidered.
 - Discontinuation will require more visits.
 - Don't generally see lots of infectious problems in this group.
 - Not in-hospital treatment.
 - Oral medication at home.
 - risk of CML progression higher than the minimal risk for a severe COVID course.
 - It seems to be protective from preclinical data.

BRAF inhibitors

7/25 (28%) experts would rather discontinue BRAF inhibitors, reasons (multiple answer):

- Severe immunosuppression: 3 (12%)
- Risk of hypersensitivity: 1 (4%)

- Other reasons: 2 (8%)
 - Less immunosuppressive alternatives can be used.
 - I would only stop until patient is recovered.

0/25 (0%) experts would switch to another drug of the same substance class

18/25 (72%) experts would rather continue BRAF inhibitors, reasons (multiple answer):

- No severe immunosuppression: 8 (32%)
- Risk of flare when stopped: 8 (32%)
- Other reasons: 8 (8%)
 - Continue if tolerated by the patient.

Bruton Tyrosine Kinase (BTK) inhibitors

15/65 (23%) experts would rather discontinue BTK inhibitors, reasons (multiple answer):

- Severe immunosuppression: 11 (17%)
- Risk of hypersensitivity: 0 (0%)
- Other reasons: 6 (9%)
 - Atypical pneumonia/pneumonitis typical side effect; I would only stop until patient recovered.
 - Bleeding risk in patients with risk of alveolar haemorrhage.
 - Can cause immunosuppression and can be discontinued 1 week without significant risks.
 - If well controlled hematologic malignancy.
 - Postpone after recovery, if low risk for flare up of lymph node enlargement.
 - Risk of interactions with drugs used to treat COVID19.
 - We can safely stop it if disease is controlled.

0/65 (0%) experts would switch to another drug of the same substance class

50/65 (77%) experts would rather continue BTK inhibitors, reasons (multiple answer):

- No severe immunosuppression: 19 (29%)
- Risk of flare when stopped: 30 (46%)
- Other reasons: 12 (18.5%)
 - All the above plus potential immunomodulatory effects.
 - Alternatives cause more cytopenia and more infections.

- Degrees of immunosuppression attributable to the drug vs the disease is not clear.
- If still uncontrolled hematologic malignancy.
- Immunochemotherapy is more immunosuppressive; difficult to say about BCL2 inhibitors.
- May protect against cytokine storm during COVID infection.
- Might protect for ARDS.
- Often not many other options and at least they are oral.
- Oral medication at home.
- Potential benefit in controlling lung inflammation.
- Seems from limited data that T cell function would be more important, my one patient with Covid19 on ibrutinib is doing fine.
- Stop only if patient is in CR.

CDK4/6 inhibitors

6/15 (40%) experts would rather discontinue CDK4/6 inhibitors, reasons (multiple answer):

- Severe immunosuppression: 4 (26.5%)
- Risk of hypersensitivity: 1 (6.5%)
- Other reasons: 1 (6.5%)
 - Neutropenia is a frequent side effect. I would only stop until the patient is recovered.

0/15 (0%) experts would switch to another drug of the same substance class

9/15 (60%) experts would rather continue CDK4/6 inhibitors, reasons (multiple answer):

- No severe immunosuppression: 4 (26.5%)
- Risk of flare when stopped: 2 (13.5%)
- Other reasons: 2 (13.5%)
 - Relapse.

CD38 antibodies (e.g. Daratumumab)

24/63 (38%) experts would rather discontinue CD38 antibodies, reasons (multiple answer):

- Severe immunosuppression: 15 (24%)
- Risk of hypersensitivity: 1 (1.5%)

- Other reasons: 10 (16%)
 - For patients who have been on a long time, due to time needed to be in unit to receive.
 - Hospital administration.
 - I decide based on necessity and cocomitted drugs.
 - I would favour a temporary discontinuation if the patient status would allow it and this would lead to avoiding hospital visits.
 - If the patient is in CR and monitor closely.
 - Interrupt the treatment until recovery.
 - Postpone after recovery.
 - The risk/benefit is unclear in these circumstances.
 - We can safely stop it if disease is controlled.
 - I would only stop until patient recovered.

2/63 (3%) experts would switch to another drug of the same substance class

39/63 (62%) experts would rather continue CD38 antibodies, reasons (multiple answer):

- No severe immunosuppression: 17 (27%)
- Risk of flare when stopped: 16 (25.5%)
- Other reasons: 8 (12.5%)
 - It depends on the phase of the therapy - if in maintenance possibly to discontinue.
 - If the patient benefits from the drug, I would continue.
 - Improves OS.
 - Keep disease under control. If a patient is in the maintenance phase (CD38 Antibody monthly) and in stable remission than 1- or 2-month break should be considered.
 - Myeloma more likely to be a clinical problem in these cases.
 - Risk of disease is stronger than COVID.

Demethylating Substances

19/68 (28%) experts would rather discontinue demethylating substances, reasons (multiple answer):

- Severe immunosuppression: 10 (14.5%)
- Risk of hypersensitivity: 0 (0%)
- Other reasons: 9 (13%)
 - Because of transfusion need.
 - Delay start or continue if therapy has already started.

- I would hold temporarily or extend the cycle frequency. Risk of neutropenia.
- If well controlled hematologic malignancy.
- No data on the effect of demethylating substances in patients with COVID19.
- Palliative therapy, often relapse slow, reexposure often successful.
- Postpone after recovery.
- Quarantine for patients who are responsive and relatively normal haematologic parameters.
- Risk/benefit unclear.
- We can safely stop it if disease is controlled.

1/68 (1.5%) experts would switch to another drug of the same substance class

49/68 (72%) experts would rather continue demethylating substances, reasons (multiple answer):

- No severe immunosuppression: 22 (32.5%)
- Risk of flare when stopped: 25 (37%)
- Other reasons: 7 (10.5%)
 - Benefit vs risk mostly pro benefit.
 - If hematologic malignancy still uncontrolled.
 - Local hospital.
 - Only if substantial improvement of blood counts for MDS patients.
 - Risk of disease progression too significant.
 - Risk of relapse and death.
 - Risk of stopping or equivalent due to disease progression. We aim to reduce to 5-day schedules for azacytidine to avoid weekend visit to the outpatient treatment facility in both MDS and AML.
 - Will compromise treatment efficacy and no severe immunosuppression.

EGFR-TKI

4/15 (26.5%) experts would rather discontinue EGFR-TKI, reasons (multiple answer):

- Severe immunosuppression: 2 (13.5%)
- Risk of hypersensitivity: 1 (6.5%)
- Other reasons: 1 (6.5%)
 - Quarantine.

0/15 (0%) experts would switch to another drug of the same substance class

11/15 (73.5%) experts would rather continue EGFR-TKI, reasons (multiple answer):

- No severe immunosuppression: 5 (33.5%)
- Risk of flare when stopped: 3 (20%)
- Other reasons: 1 (6.5%)

Immune checkpoint inhibitors

21/43 (49%) experts would rather discontinue immune checkpoint inhibitors, reasons (multiple answer):

- Severe immunosuppression: 8 (18.5%)
- Risk of hypersensitivity: 8 (18.5%)
- Other reasons: 6 (14%)
 - Immune activation potentially worsening SARS-COV-2.
 - Immunological flare and risk of ARDS.
 - Pneumonitis typical side effect; would only stop until patient recovered.
 - Risk of severe lung lesions (COVID19 may trigger check point inhibitors pneumonitis?).
 - Risk pulmonary toxicity.
 - They can boost cytokine release syndrome in covid-19 positive patients.

0/43 (0%) experts would switch to another drug of the same substance class

22/43 (51%) experts would rather continue immune checkpoint inhibitors, reasons (multiple answer):

- No severe immunosuppression: 8 (18.5%)
- Risk of flare when stopped: 7 (16.5%)
- Other reasons: 6 (14%)
 - Continue if well tolerated.
 - No clear adverse effects.
 - Relapse.
 - This observation is for haematology patients, specifically for patients with HL progressive post ASCT, where the vital risk is too big to stop treatment.
 - Usually only high-risk patients with Hodgkin being treated, with no other Ro option.

Immune modulatory substances (e.g. Lenalidomid)

19/70 (27%) experts would rather discontinue immune modulatory substances, reasons (multiple answer):

- Severe immunosuppression: 9 (13%)
- Risk of hypersensitivity: 1 (1.5%)
- Other reasons: 9 (13%)
 - It can be delayed, at least in lymphomas.
 - It depends on necessity or alternative treatments.
 - If MDS del(5q) in response, delay new circles.
 - Immune activation potentially worsening SARS-COV-2.
 - In maintenance.
 - Neutropenia most frequent side effect; would only stop until patient recovered.
 - Often due to treated disease immunocompromised host + therapy related immunosuppression.
 - Only stop if stable disease.
 - Postpone after recovery.
 - We can safely stop it if disease is controlled.

0/70 (0%) experts would switch to another drug of the same substance class

51/70 (73%) experts would rather continue immune modulatory substances, reasons (multiple answer):

- No severe immunosuppression: 25 (35.5%)
- Risk of flare when stopped: 23 (33%)
- Other reasons: 9 (13%)
 - Better than iv treatment now.
 - Home quarantine and prescription by e-health visit way.
 - If no hematological toxicities, lenalidomide may decrease the hyperimmune stage of COVID, leading to a less severe disease? We have had a 70-year-old patient who had COVID while on lenalidomide for MM. He did not develop any lung complication.
 - If remission is needed.
 - In MM very effective drug and I would continue if the patient benefits from.
 - Oral medication at home.
 - Recovery of T cell function in MM, better to continue.

JAK-STAT inhibitors

5/60 (8.5%) experts would rather discontinue JAK-STAT inhibitors, reasons (multiple answer):

- Severe immunosuppression: 3 (5%)
- Risk of hypersensitivity: 0 (0%)
- Other reasons: 2 (3.5%)
 - Better wait for infection to pass.
 - Postpone after recovery.

0/60 (0%) experts would switch to another drug of the same substance class

55/60 (91.5%) experts would rather continue JAK-STAT inhibitors, reasons (multiple answer):

- No severe immunosuppression: 22 (36.5%)
- Risk of flare when stopped: 30 (50%)
- Other reasons: 11 (18.5%)
 - It depends on alternatives available.
 - It is possible a help.
 - Might mitigate cytokine storm.
 - Oral medication at home.
 - Possible effect on COVID infection.
 - Risk of recurrence of B symptoms.
 - It seems to be protective on Cyto-mediated damage.
 - To use in COVID19 pneumonia to reduce cytokine storm, it could be protective!!!
 - Unlikely to be a drawback from COVID perspective - there are anecdotal info that this could even be useful.
 - We had a heavily co-morbid 72 y lady (Hypertension, diabetes, obesity) with myelofibrosis who had COVID19 while on ruxolitinib. She did not develop any complication.

HDAC inhibitors

8/25 (32%) experts would rather discontinue HDAC inhibitors, reasons (multiple answer):

- Severe immunosuppression: 5 (20%)
- Risk of hypersensitivity: 1 (4%)
- Other reasons: 2 (8%)
 - Postpone after recovery.
 - We can safely stop it if disease is controlled.

0/25 (0%) experts would switch to another drug of the same substance class

17/25 (68%) experts would rather continue HDAC inhibitors, reasons (multiple answer):

- No severe immunosuppression: 7 (28%)
- Risk of flare when stopped: 8 (32%)
- Other reasons: 1 (4%)

Her2-neu antibodies (e.g. Trastuzumab)

2/14 (14.5%) experts would rather discontinue HER2-neu antibodies, reasons (multiple answer):

- Severe immunosuppression: 1 (7%)
- Risk of hypersensitivity: 0 (0%)
- Other reasons: 1 (7%)
 - Only one cycle or at home administration.

0/14 (0%) experts would switch to another drug of the same substance class

12/14 (85.5%) experts would rather continue HER2-neu antibodies, reasons (multiple answer):

- No severe immunosuppression: 8 (57%)
- Risk of flare when stopped: 2 (14.5%)
- Other reasons: 1 (7%)

High dose steroids (>20mg/d prednisone for at least 4 weeks)

54/79 (68.5%) experts would rather discontinue high dose steroids, reasons (multiple answer):

- Severe immunosuppression: 49 (62%)
- Risk of hypersensitivity: 0 (0%)
- Other reasons: 8 (10%)
 - Consider other treatment if less immunosuppressive.
 - I would actually reduce the dose, down to <0.5 mg/Kd/day.

- Possibility to find alternative regimens with lower doses.
- Possible adverse in Covid-19.
- risk of significant viral replication and secondary infections
- Risk/benefit unclear. Depends on circumstances.
- Stalker dose.
- They seem to do badly with COVID.
- Try to lower the dose.

4/79 (5%) experts would switch to another drug of the same substance class

25/79 (31.5%) experts would rather continue high dose steroids, reasons (multiple answer):

- No severe immunosuppression: 6 (7.5%)
- Risk of flare when stopped: 16 (20.5%)
- Other reasons: 8 (10%)
 - Depending on the indication.
 - Depends on which tumor and where the patient is in its trajectory.
 - Doses used in gvh, best Rex option.
 - If no other treatment available that is less immunosuppressive.
 - In particular in autoimmune conditions,
 - Might prevent or ameliorate ARDS.
 - Oral medication at home.
 - Short term usage.
 - Used in COVID therapy.

Hydroxyurea

6/78 (7.5%) experts would rather discontinue Hydroxyurea, reasons (multiple answer):

- Severe immunosuppression: 2 (2.5%)
- Risk of hypersensitivity: 0 (0%)
- Other reasons: 2 (2.5%)
 - If low risk disease.
 - We can safely stop it, if disease is controlled.
 - I would only stop until patient is recovered.

0/78 (0%) experts would switch to another drug of the same substance class

72/78 (92.5%) experts would rather continue Hydroxyurea, reasons (multiple answer):

- No severe immunosuppression: 63 (79%)

- Risk of flare when stopped: 20 (25.5%)
- Other reasons: 2 (2.5%)
 - If high risk disease.
 - Normally for palliative therapy.
 - Oral medication at home.

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

11/82 (13.5%) experts would rather discontinue low dose steroids, reasons (multiple answer):

- Severe immunosuppression: 5 (6%)
- Risk of hypersensitivity: 0 (0%)
- Other reasons: 4 (5%)
 - Depends on the treated pathology.
 - Need to assess the benefit/risk of discontinuation.
 - Risk/benefit in each case.
 - We can safely stop it if disease is controlled.

2/82 (2.5%) experts would switch to another drug of the same substance class

71/82 (86.5%) experts would rather continue low dose steroids, reasons (multiple answer):

- No severe immunosuppression: 42 (51%)
- Risk of flare when stopped: 25 (30.5%)
- Other reasons: 9 (11%)
 - Generally reduced from higher doses.
 - Often given in physiological maintenance doses.
 - On indication.
 - Oral medication at home.
 - Possibly beneficial in COVID-19-related pneumonitis.
 - Same as for high dose steroids.
 - Short term usage.

mTOR inhibitors

8/20 (40%) experts would rather discontinue mTOR inhibitors, reasons (multiple answer):

- Severe immunosuppression: 4 (20%)
- Risk of hypersensitivity: 1 (5%)
- Other reasons: 4 (20%)
 - Lung toxicity.
 - Neutropenia frequent side effect; would only stop until patient recovered.
 - No clear benefit in the majority of indications.
 - Postpone after recovery.

0/20 (0%) experts would switch to another drug of the same substance class

12/20 (60%) experts would rather continue mTOR inhibitors, reasons (multiple answer):

- No severe immunosuppression: 5 (25%)
- Risk of flare when stopped: 4 (20%)
- Other reasons: 3 (15%)
 - Seems to prevent severe reaction (ARDS).

Multi-Kinase inhibitors (e.g. Sorafenib, Sunitinib)

10/27 (37%) experts would rather discontinue Multi-Kinase inhibitors, reasons (multiple answer):

- Severe immunosuppression: 6 (22%)
- Risk of hypersensitivity: 1 (3.5%)
- Other reasons: 1 (3.5%)
 - Risk of interactions with drugs used to treat COVID-19.

0/27 (0%) experts would switch to another drug of the same substance class

17/27 (63%) experts would rather continue Multi-Kinase inhibitors, reasons (multiple answer):

- No severe immunosuppression: 6 (22%)
- Risk of flare when stopped: 11 (40.5%)
- Other reasons: 3 (11%)
 - For AML patients.
 - Relapse.

PARP inhibitors

2/12 (16.5%) experts would rather discontinue PARP inhibitors, reasons (multiple answer):

- Severe immunosuppression: 1 (8.5%)
- Risk of hypersensitivity: 0 (0%)
- Other reasons: 0 (0%)

0/12 (0%) experts would switch to another drug of the same substance class

10/12 (83.5%) experts would rather continue PARP inhibitors, reasons (multiple answer):

- No severe immunosuppression: 4 (33.5%)
- Risk of flare when stopped: 3 (25%)
- Other reasons: 2 (16.5%)
 - Indication.

Proteasome inhibitors (e.g. Bortezomib)

15/65 (23%) experts would rather discontinue proteasome inhibitors, reasons (multiple answer):

- Severe immunosuppression: 5 (7.5%)
- Risk of hypersensitivity: 0 (0%)
- Other reasons: 9 (14%)
 - Hospital administration.
 - If well controlled disease.
 - Many contacts with the health care workers, sometimes a weekly scheme.
 - Postpone after recovery.
 - Seems to do badly with CV19.
 - The problem is that the patient needs to go to the hospital twice a week. Maybe only one dose a week?
 - Unknown effects in combo with COVID.
 - We can safely stop it if disease is controlled.
 - I would only stop until patient recovered.

4/65 (6%) experts would switch to another drug of the same substance class

50/65 (77%) experts would rather continue proteasome inhibitors, reasons (multiple answer):

- No severe immunosuppression: 32 (49%)
- Risk of flare when stopped: 18 (28%)
- Other reasons: 5 (7.5%)
 - Benefit vs risk individually.
 - Consider / prefer once weekly regimens.
 - I would favour subcutaneous administration as outpatient.
 - If uncontrolled disease.
 - Might prevent hyper inflammation.
 - Myeloma probably more severe clinical problem.

VEGF/ VEGFR2 inhibitors (e.g. Bevacizumab)

3/13 (23%) experts would rather discontinue VEGF/ VEGFR2 inhibitors, reasons (multiple answer):

- Severe immunosuppression: 0 (0%)
- Risk of hypersensitivity: 1 (7.5%)
- Other reasons: 0 (0%)

0/13 (0%) experts would switch to another drug of the same substance class

10/13 (77%) experts would rather continue VEGF/ VEGFR2 inhibitors, reasons (multiple answer):

- No severe immunosuppression: 6 (46%)
- Risk of flare when stopped: 1 (7.5%)
- Other reasons: 1 (7.5%)

n= 94

Country

Austria 1 (1%)
Belgium 3 (3%)
Croatia 1 (1%)
Czechia 1 (1%)
Denmark 1 (1%)
Estonia 1 (1%)
France 2 (2%)
Germany 9 (9.5%)
Greece 7 (7.5%)
Ireland 1 (1%)
Israel 1 (1%)
Italy 19 (20%)
Malta 1 (1%)
Netherlands
Norway 1 (1%)
Poland 3 (3%)
Portugal 4 (4.5%)
Romania 2 (2%)
Russia 3 (3%)
Spain 7 (7.5%)
Sweden 5 (5.5%)
Switzerland 5 (5.5%)
Turkey 3 (3%)
Ukraine 2 (2%)
UK 6 (6.5%)
Unknown 2 (2%)

Specialization

Hematology 68 (72.5%)
Hemato-Oncology 25 (26.5%)

Gastrointestinal tumors 3 (3%)
Gynecological tumors 0 (0%)
Head and neck tumors 0 (0%)
Lung tumors 2 (2%)
Lymphatic neoplasias 73 (77.5%)
Myeloid neoplasias 59 (63%)
Sarcomas 2 (2%)
Urological tumors 3 (3.5%)
Other tumors 2 (2%)

Breast cancer 1 (1%)

Leukemia 1 (1%)

In your opinion what is the most urgent research question regarding COVID-19 in cancer patients?

- COVID testing.
- How to prevent infection?
- How to deal with short term risks of infection vs long term outcome of cancer treatment?
- Did we over-treat our patients before COVID-era or do we under-treat nowadays?
- approaches to alloSCT: Should be deferred high-dose therapy (autoSCT)?
- Are cancer patients more susceptible and is the treatment course different in cancer patients vs non-cancer?
- Can some of our drugs actually protect the patient from severe Covid-19 disease with CRS? How common is HLH in the severe cases and can we find ways to prevent it also in non-cancer patients?
- Clarify who are the patients at increased risk. Clarify the mechanism by which the virus causes most of the inflammation and organ damage since that can indicate with cancers and treatments constitute particular risk groups. Identify particular forms.
- Collection of real-life cases to better understand and know how COVID-19 infection impacts in morbidity and mortality in cancer patients.
- Continue or discontinue anti CD 20 agents.
- Control of the cytokine release syndrome, because at some point the viral replication does not matter.
- Convalescent plasma efficacy.
- Could immunocompromised patients be protected against severe pneumonitis?
- Define the risk category in patients with active therapy and recommendations of continue or delay their therapy.
- Define the risks of the different treatments.
- Developing efficacious preventive strategies.
- Do not forget that cancer kill even more than viruses.
- Effect of ongoing immunosuppression and COVID disease activity is most interesting. Do patients with immunosuppression are better protected from severe CRS/inflammatory cascade or do worse? What is optimum immunosuppression in this instance?
- Efficacy of vaccination, when this will become available.
- How much does the lower level of immunosuppression found in many drug classes impact outcome in covid-19 infection?
- I don't think that all Cancer patients have the same risk. Identification of risk groups (e.g. disease, treatment, comorbidity).
- Immunomodulators and their protective effect in COVID-19 in preventing severe cytokine storm damaging lungs
- Incidence and severity of infections in our patients, correlation with treatment and underlying disease. Is there any proof/ hint, that immunosuppressed patients do better (e.g. less ARDS) than other patients?
- Investigating an effective prophylaxis / treatment.

- Is low-dose immunosuppression or immunomodulation beneficial in severe cases?
- Is there a protective role of immunosuppression towards the SARS-CoV-2-induced hyper inflammation pattern? Are cancer patients at increased risk compared to the general population? Are there fewer cases compared with the general population (is it true?)
- Is there any targeted therapy that influence on outcome of patients infected with COVID-19? Which malignancy is associated with a worse outcome on COVID-19 infection?
- Logistic management.
- Markers of severe disease and targeted inhibitors of pathways involved.
- Molecular mechanisms of lung infiltration.
- Mortality in patients with hematological (oncological) disorder and covid-19.
- Most beautiful interaction of drug disease and viral infection.
- Naturally history of patients with lymphopenia, e.g. bmt, lymphoid malignant. Applicability of immune modulation to decrease cirr risk.
- No meeting it...
- Potential treatment to reduce ARDS and MOF.
- Guidelines on hematological patients on cure.
- Real impact on survival among hematological patients with specific diseases and the cost of delay treatment needed.
- Role of biological treatment in the pattern of the COVID-19 disease + role of immune system in the pattern of COVID-19 disease.
- Selection of COVID-19 positive patients who are asymptomatic and choice of the appropriate therapeutic program for them. The critical issue is finding a balance between need of continuing effective treatments of the hematologic neoplasia and not harming.
- Should treatment be withheld in cancer patients during the pandemic?
- So far, only minimal numbers of hematologic and oncologic cancer patients seem to demonstrate severe COVID courses. The infection seems to be comparable by risk to other respiratory viruses in this cohort of patients.
- Start or not a CIT urgently. Risk or benefit?
- Start therapy or not?
- The answers given above regard COVID19 negative patients. The most important point is how to treat patients if they become positive and in case the treatment cannot be postponed i.e. aggressive lymphomas, acute leukemias.
- The pathophysiology of hyperinflammatory syndrome as an immune response to COV-SARS-2 infection.
- There is a need to establish a scoring system to determine benefit/risk of discontinuation/continuation of therapy.
- To establish a profile of risk of each hemopathy and its specific treatment in comparison with standard population, in order to adapt the best possible treatment. The objective is of course to avoid toxicity in case of COVID.
- To find a vaccine.
- To identify patients with low NK cells, not able to sustain immune response against the virus, that should stop treatment, while all others should continue anti neoplastic treatment. Moreover, other coronaviruses could arrive later in the season.
- To stop or not to stop anti-CD20 monoclonal antibodies?
- Tocilizumab treatment option?
- Treatment.
- Try to find an efficient antiviral agent!

- Understanding who is at risk of developing SARS-COV-2 pneumonia.
- Up to now I have no patient with Covid-19.
- Vaccine.
- What are the predisposing factors to ARDS in cancer patients?
- What is the incidence of COVID 19 in hematology patients? What is the outcome of hematology patients undergoing therapy that are tested + for COVID 19? Do severely immunodepressed patients develop a severe disease when infected with coronavirus?
- When do we stop treatment in patients with curative treatment or with life threatening malignant disease? Only in case of overwhelmed hospitals?
- Which are the patients at higher risk of severe infection?
- Which are the therapeutic options in cancer patients with COVID-19?
- Which treatment should be stopped and which chemotherapy can be applied safely?