Mateya Trinkaus m.d., frcp(c) — internal medicine

377 church street, suite 407,
markham, ontario l6b 1a1
tel. 905-472-7072
fax. 905-472-0529
mtrinkaus@msh.on.ca

medical oncology

February 13, 2014

CPSO

Re: Concern re: treatment for patient

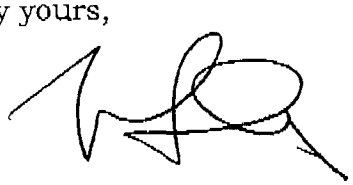
Fax: 416 967 2616

Please see the attached letters as requested.

I have not contacted this physician since sending documentation from February 7th 2014. I have not contacted the Berkeley Institute as suggested in his correspondence.

I am out of the country as of tomorrow until February 24th 2014. Please contact me via email as needed.

Sincerely yours,



Mateya Trinkaus MD

Dr. Mateya Trinkaus, m.d., frcp(c) *medical oncology*

377 church street, suite 407,
markham, ontario l6b 1a1
tel. 905-472-7072
fax. 905-472-0529

February 7, 2014

Dr. Akbar Khan
Suite 301
4576 Yonge Street
Toronto ON M2N 6N4
Fax: (416) 227-1915

Dear Dr. Khan:

Re:
DOB:

Thank you for speaking on the phone with me this evening. I did want to reinforce some of the concerns that I discussed over the telephone with you. Specifically, carboplatin is not an indicated use for colon cancer, and I would strongly advise that if you are going to continue to give this chemotherapy, to give it to cancer types where there is clear evidence of activity, such as ovarian cancer, lung cancer, breast cancer, and there is evidence for its use in head and neck and gastric/esophageal cancer. However, in this case, patients with an indicated use for carboplatin can also receive this chemotherapy at no charge in a cancer centre. Case reports or case series of activity for a chemotherapy like carboplatin for 'off label" uses in certain cancer types is not a good or appropriate use of chemotherapeutic agents given that they are almost always ineffective and would therefore cause unnecessary toxicity.

There are unfortunately countless examples in the cancer literature where clinicians have reported "activity" to chemotherapy or immune agents, leading to phase three trials where unfortunately hundreds of patients are exposed to a drug that in the end proves to be ineffective (and therefore even more harmful) – for example, the use of Interferon in colon cancer, the use of Avastin in breast cancer, the use of Cetuximab in breast cancer and in lung cancer, the use of sorafenib in melanoma/lung/breast cancer and the list unfortunately can go on for pages. The point that needs to be appreciated here, is that when offering toxic drugs to patients (ie. There is no such thing as "safe chemo"), the evidence for doing so must be compelling enough to use it; otherwise it truly is experimental and in the setting of a terminal malignancy where one's performance status and life span is already compromised, using the chemotherapy with the best chance of working and offering the least toxicity (so as to optimize the therapeutic index) should be the utmost priority.

I also think that when administering chemotherapy, it is very helpful to be fully aware of the potential consequences of using these toxic agents for your patients. Specifically, in the case of , it needed to be appreciated that this lady was heavily pretreated with oxaliplatin chemotherapy as part of the FOLFOX regimen, and therefore likely had platinum resistant disease to begin with, in addition to an already myelosuppressed bone marrow

given her chemo exposure and prior radiation to the pelvis. She now unfortunately has grade 3 myelosuppression, and worse functional status.

I also wanted to highlight an important point about cancer medications in general. It needs to be stressed that "activity" is not the same as "response". In fact, if a chemotherapy does not show any activity at all, then the rationale for augmenting the dose to try to induce a response is inaccurate, as if there is no activity, augmenting the dose from an AUC 3 for example to an AUC 5 of carboplatin will only augment toxicity, and have no benefit whatsoever in inducing a response. That is, chemotherapy will only induce a response rate when there is activity in the respective cancer cells in the first place. Unfortunately, blood work and clinical deterioration is and was in keeping with the fact that there was no response to her chemotherapy and therefore, I am thankful that you are in agreement that she should not have any more carboplatin; augmenting the dose in this case has no rationale and in fact is dangerous.

There is a very worth while three day clinical trial program workshop offered through Queen's University in August that could you improve your understanding for how to critically appraise data and scientific literature (http://www.ctg.queensu.ca/newinv/). This workshop would give any practicing clinician the fundamental understanding as to the pitfalls that have been inherent in clinical trials in the past, and a solid foundation for a general understanding of what is required when appraising data and applying the clinical literature data to individual patient care. I think that such a course would allow you to the opportunity to critically appraise the data supporting the Berkeley method – the level of evidence for this chemotherapeutic regimen is level 4 at best. We discussed that the reason why some patients are responding to this regimen is because carboplatin is an effective chemotherapy used for certain malignancies (ie lung, breast, ovarian).

It is a sobering thought that many of the treatments that we hope work for cancer care in fact do not work well, and therefore it is our responsibility that we protect our patients and also advocate for the most effective and safe treatments available.

There is much to be learned in treating our patients with cancer. Treating our patients needs to be done with the best evidence possible, and should be done in collaboration. I am happy to speak further about this as per your discretion.

Yours sincerely,

*Mateya Trinkaus, M.D.*MT/ceb

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February 7, 2014

Conversation with Dr. Akbar Khan

Re:
DOB:

Date of discussion: February 7, 2014
Time of discussion: Approximately 5:05 p.m. to 5:30 p.m.

Dr. Akbar Khan is a family physician who is currently monitoring chemotherapy for . She had been receiving carboplatin chemotherapy under his care for metastatic colon cancer. I was able to contact the physician today and we discussed the following points.

1. There is no evidence to use carboplatin for metastatic colon cancer or curative colon cancer.

2. There is no rationale to augment the dose of carboplatin if there is no activity shown in the first 1 to 2 cycles of treatment.

3. There is no evidence to suggest that there is any additional synergistic role for IV mesna with carboplatin.

4. I recommended that he contact whoever created the Berkeley carboplatin/mesna regimen for further evidence as trials from early phase II data or case reports are inadequate in order to provide toxic treatment that is off label for patients.

5. I tried my best to evoke the level of evidence required to offer toxic chemotherapeutic treatment. I also discussed that biologic rationale, preclinical data, and early phase II trials from particularly the 1980s and 1990s, which were not rigorous, are completely inappropriate in order to give assessments and recommendations for chemotherapy. Unfortunately, of the hundreds of targets that we find on cancer cells, only a few are actually targetable effectively with medications. That is, having a receptor on a target cell does not imply that a patient will respond to a medication that targets that receptor.

6. Apparently Dr. Khan has indicated that he has patients who tolerate carboplatin very well; he in fact cited a patient currently on his "tenth cycle of carboplatin" being administered on a q.2 weekly basis. With further questioning, there is no doubt that this patient is responding, given that he had lung cancer which is a sensitive tumor to carboplatin, and this is his first line of chemotherapy, and therefore he has not run into significant difficulties by way of myelosuppression and so forth.

February 7, 2014

7. It was very questionable to offer the current doses of carboplatin to this lady who was heavily pretreated with FOLFOX chemotherapy and with radiation to the pelvis. It is unclear whether Dr. Khan truly appreciated her overall clinical history and context of disease.

I invited Dr. Khan to learn more about evidence-based medicine and why we treat the way we do.

My plan of action will be to send Dr. Khan a letter outlining our discussion, and further contacting the CMPA for further guidance with respect to how to proceed with this plan.

ADDENDUM: February 10, 2014 - I spoke to the CMPA today. Given that the patient is not incapacitated to make a medical decision, and that the doctor himself is not incapacitated by way of substance abuse, for example, despite his poor reasoning for what to recommend for this patient, this is not a reportable offence to the CPSO. The advice was to document the conversation had with Dr. Khan, which had been already done, and also to contact the Royal College on an anonymous level, in order to ensure that the Medicor Clinic does have their QA and QC procedures in order for treating patients.

Overall, I am hopeful that my further corresponding with Dr. Khan will encourage him to stop giving ineffective chemotherapy, which in many ways is quite unsafe as well. Unfortunately, patients at the end of the day who are competent have to make the decision; however, my concern is that they are making an ill-informed decision as clinicians like Dr. Khan are not fully informed with how to safely administer chemotherapy and clearly need additional guidance with respect to evidence-based medicine practices.

Mateya Trinkaus, M.D.

MT/ceb