Potential Use of Radiolabeled Antibodies for Imaging and Treatment of COVID-19

TO THE EDITOR: I have read with interest the commentary by Pillarsetty et al. (*1*) in the December issue. Although the idea of investigating nuclear medicine–based solutions for treatment of coronavirus disease 2019 (COVID-19) is interesting and is potentially deserving of comment, the commentary by Pillarsetty et al. raises some concerns.

First, the only experimental data reported in the commentary are binding of the commercial antibody developed toward the spike protein of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) to that same commercial spike protein attached to magnetic beads. This piece of data, which is a simple quality control procedure for any antibody reagent received by a laboratory, does not prove the utility of detecting a virus such as SARS-CoV-2 in vivo.

Second, the authors did not use in their experiments a dead virus, a live virus, an attenuated strain, or a relevant in vivo model of COVID-19 infection, such as a ferret model (*2*). However, the title of their commentary promises not just one but several treatment options for COVID-19. The current situation, in which hundreds of thousands of COVID-19 patients are dying across the world, warrants proof of a therapeutic claim in at least one in vivo model of the disease.

Third, there is another issue with the title of the commentary. It states that the approach of targeting viral infections with radiolabeled antibodies for imaging or therapy is "oncology-inspired," when in fact at least 18 papers on targeting of viral infections for therapy with radiolabeled antibodies have been published since 2006 (*3*–*7*) and all of them have been listed on PubMed, presented at multiple nuclear medicine meetings and Department of Energy meetings, and covered by the press and Newsline. There have also been publications on radiolabeled-antibody imaging of viral infections in vivo in non-human primates (*8*,*9*).

Finally, the commentary does not discuss the enormous radioresistance of virions and the implications of such radioresistance for suggested therapy targeting the virus directly. For example, 18 kGy of radiation are required to sterilize bone grafts from HIV virions (*10*), which belong to the same RNA virus type as SARS-CoV-2.

DISCLOSURE

Ekaterina Dadachova is a consultant and received research support from Actinium Pharmaceuticals and RadImmune Therapeutics. No other potential conflict of interest relevant to this letter was reported.

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Published online May 7, 2021.
DOI: 10.2967/jnumed.120.261874

Reply: Potential Use of Radiolabeled Antibodies for Imaging and Treatment of COVID-19

REPLY: We are happy to respond to the 4 concerns raised by Dr. Ekaterina Dadachova in her letter to the editor commenting on our Brief Communication "Oncology-Inspired Treatment Options for COVID-19" (*1*).

Regarding the first 2 points, we would like to emphasize that these experiments were performed during the height of the devastating first COVID-19 peak in New York City, when very little was known about the etiology, transmission, and possible treatments for this virus. Without the ability to use animal models, we nevertheless recognized that the uncertainty, the general dearth of knowledge, and the rapidly evolving situation at that time merited publication of our data as a Brief Communication to provoke thought and discussion on a potential approach to treating this disease.

Regarding the third point: the suggested references, including some interesting papers authored by Dr. Dadachova, were not appropriate for this Brief Communication because they do not address Auger therapy. Future publication of the ongoing studies may warrant citation of this work.

Lastly, the critical advantage of Auger therapy, as described in our Brief Communication, is that Auger electron cascades are highly localized, providing potential advantages over other forms of ionizing radiation when it comes to destroying virions. The letter's final point references the "18 kGy of radiation" required for sterilization of bone

grafts from HIV virions (*2*); this figure of course applies to uniform external γ-irradiation. In the case of an Auger-emitting radionuclide bound to a virion, the locally absorbed energy must be considered; this may exceed megagray levels in small volumes near the decay site (*3*, *4*).

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Published online Apr. 23, 2021.
DOI: 10.2967/jnumed.121.261950

The Importance of an Adequate Surgical Template During Salvage Lymph Node Dissection for Node-Recurrent Prostate Cancer

TO THE EDITOR: We read with great interest the insightful article by Dr. Farolfi and colleagues (*1*) recently published in *The Journal of Nuclear Medicine* and describing patterns of prostate cancer recurrence after salvage lymph node dissection (sLND). Data provided by the authors add significantly to the current literature and improve our understanding of potential pitfalls that might determine suboptimal results after metastasis-directed therapies.

In a series of 16 men who had prostate-specific antigen persistence after sLND, Dr. Farolfi and colleagues compared the results of preoperative versus postoperative prostate-specific membrane antigen (PSMA) PET scans and found that 63% of patients had a postoperative scan positive for cancer recurrence in locations already described on preoperative imaging. Although the precise surgical template was not specified by the authors, all positive regions on the preoperative PSMA PET scan were surgically explored, with a median of 17 nodes removed. However, whereas preoperative PSMA PET scans identified 24 positive spots, the final pathologic report resulted in 88 positive nodes. This finding further underlines the likely underestimation of tumor burden on imaging (*2*, *3*) and reiterates the importance of a thorough surgical dissection, including the obturator and internal iliac nodes, which were the sites most often involved by PSMA PET persistence after sLND (*1*). In fact, an incomplete surgical resection might be among the reasons explaining the worse-than-expected outcomes of sLND at long-term follow-up (*4*, *5*). Therefore, while we await prospective evidence on this issue, an extended, bilateral surgical template should be recommended whenever pelvic sLND is contemplated, with the exception being men who have only a single spot on the preoperative PSMA PET scan and might safety undergo a unilateral (yet extended) surgical dissection (*6*).

The adoption of an adequate template is key to maximizing the potential benefit associated with metastasis-directed therapies, a rationale that pertains to sLND as well as to radiotherapy (*7–10*). This benefit was further confirmed by Dr. Farolfi and colleagues, who should be commended for their important contribution, which has relevant implications for clinical practice. Now more than ever, these data should be borne in mind whenever metastasis-directed therapies are contemplated, and physicians should be aware of the risk of unsuccessful metastasis-directed therapy in cases of a suboptimal treatment template.

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DOI: 10.2967/jnumed.121.262104