5. Byrd D, Christopfel R, Buatti J, et al. Multicenter survey of PET/CT protocol parameters that affect standardized uptake values. *J Med Imaging (Bellingham).* 2018;5:011012.
6. Kesner A. The cultivation of supply side data science in medical imaging: an opportunity to define the future of global health. *Eur J Nucl Med Mol Imaging*. October 23, 2021 [Epub ahead of print].

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A VISION of ALSYMPCA

TO THE EDITOR: I just read the 2 editorials written by Hofman (*1*) and by Czernin and Calais (*2*) commenting on the use of ^{177}Lu-PSMA-617 therapy in patients with metastatic castration-resistant prostate cancer (mCRPC), mainly on the results of the VISION trial (*3*). ^{177}Lu-PSMA-617 together with ^{68}Ga- or ^{18}F-labeled PSMA ligands are doubtless important theranostic technologies that provide a new perspective on mCRPC treatment, as stated in another recent editorial by Srinivas and Iagaru (*4*). However, I miss in the VISION trial a comparison with the results of another study performed a few years ago that analyzed the use of ^{223}Ra in the treatment of mCRPC patients, the ALSYMPCA trial (*5*). Although ^{223}Ra is used to treat patients with exclusive bone metastases, this group represents most patients with mCRPC. In some studies, the percentage of patients with bone metastatic disease, with or without concomitant lymph node disease but without visceral (lung and liver) disease, represents around 70% of cases (*6*), and in this group the presence of concomitant lymph node disease does not appear to change the overall survival (this high percentage was also confirmed in the VISION trial, in which 91% of patients had bone metastases, 50% had lymph node metastases, 9% had lung metastases, and 12% had liver metastases) (*6*). Therefore, ^{223}Ra could represent an adequate option to treat most patients with mCRPC. In this sense, it will be useful if the authors of the VISION study, as well as of other future studies on this issue, also present the survival results for the distinct groups of metastatic lesions or, at least, separate the results of the ones with bone metastatic disease without visceral disease from the group with visceral disease. This separation would be useful to indirectly compare the effects of ^{177}Lu-PSMA-617 with the effects of ^{223}Ra in the group without visceral metastases and also to assess the effect of ^{177}Lu-PSMA-617 in the group of patients with visceral metastases, who certainly are not candidates for ^{223}Ra therapy.

In this line of reasoning, it is interesting to note that median survival differences between groups receiving or not receiving the radionuclide therapy are similar in both trials: 4 mo (15.3 mo vs. 11.3 mo for patients receiving or not receiving the therapy, respectively) in VISION and 3.6 mo (14.9 mo vs. 11.3 mo) in ALSYMPCA. Besides, although the authors of the VISION study did not present the results of subgroups with and without visceral metastases, in the supplementary appendix of the study (*3*) the authors presented the survival results in subgroups with and without liver metastases and showed that there is no statistically significant difference in overall survival in the subgroup with liver metastases. These findings, in my opinion, are worrisome and suggest that the main effect of ^{177}Lu-PSMA-617 in overall survival could be due to its action on bone metastases and not on visceral metastases.

Therefore, presentation of the survival results by subgroups will be essential to define the patients who would most benefit from ^{177}Lu-PSMA-617 therapy and to further establish the best theranostic algorithm to treat these patients (e.g., patients with exclusive bone disease would first receive ^{223}Ra, and patients with visceral disease would first receive ^{177}Lu-PSMA-617). Last, it is important to say that ^{223}Ra therapy is already a reality in several places around the world whereas ^{177}Lu-PSMA-617 is a distant vision; thus, to move from ALSYMPCA to VISION, VISION has to show where it is really effective.

REFERENCES

1. Hofman MS. Bringing VISION to nuclear medicine: accelerating evidence and changing paradigms with theranostics. *J Nucl Med.* August 12, 2021 [Epub ahead of print].
2. Czernin J, Calais J. ^{177}Lu-PSMA617 and the VISION trial: one of the greatest success stories in the history of nuclear medicine. *J Nucl Med.* 2021;62:1025–1026.
3. Sartor O, de Bono J, Chi KN, et al. Lutetium-177-PSMA-617 for metastatic castration-resistant prostate cancer. *N Engl J Med.* 2021;385:1091–1103.
4. Srinivas S, Iagaru A. To scan or not to scan: an unnecessary dilemma for PSMA radioligand therapy. *J Nucl Med.* 2021;62:1487–1488.
5. Parker C, Nilsson S, Heinrich D, et al. Alpha emitter radium-223 and survival in metastatic prostate cancer. *N Engl J Med.* 2013;369:213–223.
6. Halabi S, Kelly WK, Ma H, et al. Meta-analysis evaluating the impact of site of metastasis on overall survival in men with castration-resistant prostate cancer. *J Clin Oncol.* 2016;34:1652–1659.

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Reply: A VISION of ALSYMPCA

REPLY: Dr. Duarte urges an analysis of the VISION trial in an effort to ascertain results in subsets of men with bone and visceral disease. He then suggests an indirect comparison between ^{177}Lu-PSMA-617 and ^{223}Ra.

I agree with the first point but disagree with the second. The VISION trial (*1*) can be analyzed in a multiplicity of new ways. Right now, just the prespecified primary analyses have been published (*1*). There are many analyses that will follow that include not only the distribution of the disease (as suggested by Duarte) but also the various biomarkers that are known to be prognostic in other settings. These biomarkers might include hemoglobin, neutrophil-to-lymphocyte ratio, prostate-specific antigen, alkaline phosphatase, lactate dehydrogenase, performance status, age, time since diagnosis, pain, and others. As it turns out, the dataset from VISION is rich and there is much more to explore.

On the second point, there is disagreement. The ALSYMPCA trial with ^{223}Ra (*2*) was conducted in a long-ago era, before the use of novel hormones such as abiraterone and enzalutamide and before the widespread use of cabazitaxel. Further, patients enrolled in ALSYMPCA were not required to progress after docetaxel (but approximately half did). All patients enrolled in VISION had progressed after either