Nuclear Medicine Prepares for Greater ^{68}Ga Demand

Mary Beth Massat

When the US Food and Drug Administration (FDA) approved the use of Gallium-68 prostate-specific membrane antigen (PSMA)-11 (^{68}Ga PSMA-11) PET imaging for prostate cancer in December, nuclear medicine specialists were not the only ones excited by the development.

Several companies aligned with the production and supply chain for ^{68}Ga had been anticipating—and planning for—the FDA's approval and its subsequent expected impact on demand for ^{68}Ga, which can be used diagnostically when paired with PSMA-11, and therapeutically when paired with lutetium-177 or actinium -225.

"We made the investment in a GMP ^{68}Ga generator years before any drugs were approved, betting that the market was going to have a ^{68}Ga drug," says Jay Simon, general manager and managing director of Eckert & Ziegler Radiopharma (Berlin).

In its action, the FDA gave the University of California, San Francisco (UCSF) and University of California, San Diego (UCSD) approval to label the ^{68}Ga isotope with PSMA for PET Imaging of the prostate.

Researchers reported that clinical trials comparing PSMA PET imaging with 18F fluciclovine PET found that ^{68}Ga PSMA-11 PET detected significantly more prostate lesions than 18F fluciclovine PET imaging in cases of cancer recurrence following prostatectomy.[1] Peter Carroll, MD, a professor at the UCSF Helen Diller Family Comprehensive Cancer Center, called the development a "game changer" in a statement issued by UCSF.

In addition, there are nearly 400 clinical trials[2] currently underway involving the use of ^{68}Ga for both diagnosis and therapeutics for prostate, neuroendocrine tumors and other types of cancer. "The market is definitely growing, even beyond PSMA," says Lutz Helmke, PhD, Head of the Medical Radiopharma Segment at Eckert & Zeigler. "We believe there are many more tracers that will come to market and, therefore, we have done our utmost to increase capacity for this product."

Dr Helmke adds that after the 2017 shortage of germanium, which is used to make ^{68}Ga**,** Eckert & Ziegler further increased its generator production capacity. He believes the company can meet current world demand for ^{68}Ga generators; however, he said the company is also preparing for the increase in demand resulting from the anticipated regulatory clearance of ^{68}Ga PSMA-11 for general clinical use and will be looking for additional suppliers for its GMP grade germanium.

Dr Helmke says there is a trend in the US toward developing larger ^{68}Ga generators with higher activities, from 50 mCi to 100 mCi. Eckert & Ziegler has developed a higher activity/higher capacity generator and will be filing for FDA approval in the near future. The company has also opened a new production facility in the Boston area.

"We have a geo strategy to serve our clients regionally but more importantly, we will have CMO capabilities so we can produce our customers final product," Dr Helmke says.

Raw Material To Generator Development

IRE ELiT (Fleurus, Belgium), a division of IRE, is also taking action to increase its production of germanium and ^{68}Ga. With respect to the former, IRE is building its own cyclotron to produce germanium; it is also working to increase production of ^{68}Ga generators and higher-quality and capacity ^{68}Ga—up to 100 mCi.

"This is very important for us to have an independent source of germanium," says Jean Bonnet, IRE's head of strategy, sales, and marketing. "We expect that in the future there will be intense competition to source germanium due the anticipated increase in demand for

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^{68}Ga generators. This will preserve our independence and capacity to maintain our position in the future market."

The higher-capacity generators will offer more flexibility than 50 millicurie generators, Bonnet says.

"We know there will be a burst of demand for several months when there is approval for a new indication, such as with ^{68}Ga PSMA PET," Bonnet says. "So we are preparing for this flexibility with our partners."

Made in the USA

In 2018, after four years as a US distributor of ^{68}Ga generators for German-based Isotopen Technologien München AG (ITM), RadioMedix (Houston, TX) began preparing to manufacture its own ^{68}Ga generators, making it the only US manufacturer of the generators, says Ebrahim S Delpassand, MD, CEO, founder and chairman of the board.

"Our plan was to … increase the bandwidth, or output, of the ^{68}Ga generators," Dr Delpassand says. "This was in anticipation that ^{68}Ga usage will only increase."

A secondary goal was to help ITM file a drug master file (DMF) in the US, which occurred in June 2020 for ITM's next generation Germanium-68/Gallium-68 (^{68}Ge/^{68}Ga) generator, GeGant. GeGant generators are available in 30, 50, and 100 mCi.

"Now we have the capability to manufacture five generators every day. This is a significant for generator accessibility in the market," Dr. Delpassand says. "We don't anticipate any shortage of ^{68}Ga supply in the market for PSMA, or for future ^{68}Ga-labeled agents that will come to market."

Dr. Delpassand sees other opportunities to label ^{68}Ga with different ligands to address unmet needs in oncology, including targeted therapies for brain tumors, ovarian cancer, pancreatic adenocarcinoma and triple negative breast cancers.

A Solid Approach

Although ^{68}Ga is generally produced in generators, ARTMS (Burnaby, British Columbia) has developed a low-energy cyclotron, QUANTM Irradiation System (QIS), to produce ^{68}Ga from solid zinc-68 targets. ARTMS CEO Charles Conroy explains that the QIS is used to produce decentralized radiopharmaceuticals such as ^{68}Ga on-site at hospitals, radiopharmacies, universities, and the like. The QIS is compatible with existing and new cyclotrons.

"There are hundreds of cyclotrons in North America, and with the QIS we can get the production closer to the end user," says Conroy. "Additionally, we can create large volumes of radioisotopes by utilizing high-purity, solid-metal targets that are then irradiated, significantly amplifying the amount of ^{68}Ga that one can produce. Using that solid target, a non-radioactive material, and a process that results in fewer impurities gives us the ability to produce such large quantities without the need for a generator. Its completely different than what is on the market today."

Compared to ^{68}Ga generators that typically produce 50-100 mCi of ^{68}Ga, Conroy says the QIS can produce five curies each hour, enough for almost 100 patients. In December 2020, ARTMS received Health Canada clearance to use QIS to produce technetium-99m. The QIS can also perform a "split" run, where the beam can be used to make both copper and ^{68}Ga, for example, on a single production run.

"With the QIS, we are able to create enough material in one location, which would usually be a commercial radiopharmacy, to diagnose or treat patients across several different cities," Conroy adds.

"Our customers are really delighted that ARTMS technology gives them more supply chain control and enables them to treat more patients from product being supplied from a single site Conroy says.

In early January, ARTMS and Telix Pharmaceuticals (Melbourne, Australia) announced the successful preparation of Telix's TLX591-CDx (illumet™), a radiopharmaceutical cold kit containing the components needed to prepare ^{68}Ga-PSMA-11 at ambient temperature. The kit is being evaluated at several institutions in the US, including Emory University Hospital, Memorial Sloan Kettering Cancer Center, City of Hope, and Endocyte (Novartis). Further, Telix has established a network of US partners, including approximately 100 nuclear pharmacies, to prepare and distribute the kits for investigational use in qualified clinical trials.

"We anticipate every corner of America, Europe or any country we serve will be able to offer prostate imaging to their patients," says Telix CEO Chris Behrenbruch. It doesn't matter if it's a New York-area hospital or a hospital in a remote area, everybody's going to have access to this diagnostic technology."

References

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