PRECISION ONCOLOGY NEWS

With Support From Lawmakers, WGS Becoming More Accessible to Netherlands' Cancer Patients

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NEW YORK – Lawmakers in the Netherlands are advancing a plan to make whole-genome sequencing (WGS) the standard of care for advanced cancer patients in the country.

Last month, the House of Representatives in the States General of the Netherlands discussed and extended unanimous support for a proposal to make WGS more broadly available to cancer patients and reimbursed by the healthcare system based on findings from a pilot program at the Netherlands Cancer Institute. WGS currently is not reimbursed by the nation's public healthcare system for cancer patients, but advocates hope the WGS proposal could standardize genetic profiling, make test access more equitable, and advance research.

The proposal was backed by data from the "Whole-genome sequencing implementation and standard of care diagnostics for every cancer patient," or WIDE, study conducted by researchers within the Netherlands Cancer Institute's Antoni van Leeuwenhoek Hospital. The study was a collaboration between the cancer institute, research nonprofit Hartwig Medical Foundation, and the Utrecht UMC academic hospital.

Last year, the researchers presented interim data from WIDE at the European Society for Medical Oncology's Virtual Congress from the first 800 patients with metastatic solid tumors out of 1,200 total patients, who had both WGS and standard-of-care sequencing using targeted next-generation sequencing panels, RNA-based NGS fusion analysis, Sanger sequencing, reverse transcription polymerase chain reaction, fluorescence *in situ* hybridization, and immunohistochemistry. The WGS testing for the WIDE study was performed in Hartwig Medical Foundation's labs.

The study found that the WGS test reported extra actionable biomarkers in 60 percent of patients when compared to standard testing. The study also determined that the turnaround time for WGS from biopsy to patient report was less than 10 days and that 70 percent of the biopsy procedures led to a complete WGS result, said Hans van Snellenberg, managing director of the Hartwig Medical Foundation and a collaborator in WIDE.

The researchers also valued that WGS provided a more comprehensive picture of patients' tumor genomics in a single test, which they said could improve doctors' ability to diagnose patients with cancers of unknown primary without needing to run multiple targeted tests. The comprehensive results could also increase patients' chances of matching to investigational treatments in clinical trials as new predictive biomarkers are validated.

According to van Snellenberg, he and his colleagues embarked on the WIDE study to demonstrate that WGS was comparable to standard-of-care NGS panels. Initially, there were concerns that WGS results wouldn't have the same quality as results from the more targeted NGS panels, van Snellenberg said.

"Although many people agreed that whole-genome sequencing would be the future, we did not have sufficient evidence that the WGS test would at least cover all other tests that were done in standard diagnostics," he said. "It was necessary to at least show that the whole-genome sequencing data could deliver at least the same results as a big NGS panel test."

After the WIDE study showed that WGS was comparable to NGS panels, the Netherlands Cancer Institute presented the data to the Parliament, and according to van Snellenberg, it was received "positively." The study showed "that a very large hospital in the Netherlands, which only treats cancer patients, finds it necessary to use this test, even though it was not yet reimbursed," he said.

Currently, patients can access standard genetic tests, such as targeted NGS panels, Sanger sequencing, FISH, and multiplex ligation-dependent probe amplification, through the Netherlands health insurance law, called Zorgverzekeringswet (ZvW) in Dutch. The law provides a universal health insurance package for all residents, regardless of age or health status, through private insurers. The program is financed through taxes and government grants, as well as premiums paid by the insured.

After experts from the cancer institute presented the WIDE study data, three Dutch lawmakers in the House of Representatives brought forward a proposal to integrate WGS as a standard test for cancer patients that would be funded under the health insurance law. The representatives discussed the proposal in February and gave unanimous support to begin the process to determine government reimbursement for the test.

The effort will first integrate WGS in cancer populations with unmet needs, including metastatic cancer patients, similar to the WIDE study population, patients with cancer of unknown primary, and those with relatively good medical fitness who lack standard treatment options.

The Ministry of Health, Welfare, and Sport will prepare a "reimbursement title" with the Netherlands Healthcare Institute, which advises the Ministry of Health on which products and services should be financed out of public health insurance budgets and subsequently reimbursed by insurance companies. The Institute considers outcome data, health technology assessment data, cost efficiency, and clinical study findings on safety and efficacy. Once the Netherlands Healthcare Institute finishes its analysis and insurers have completed price negotiations for providing WGS with hospitals, testing will be available to patients.

At another February meeting, a majority of House of Representatives lawmakers voted to create a provisional billing code for WGS testing for cancer patients with unmet needs that insurers could use to facilitate reimbursement.

Although this proposal to implement WGS will initially be restricted to advanced cancer patients, the goal, according to van Snellenberg, is to eventually make such testing available to all cancer patients, though this may take months or years to negotiate.

Prior to this year, WGS was only used in research settings or as a last resort test for patients with advanced disease who are out of other options and may qualify for a clinical trial or for an off-label treatment through the Netherlands Drug Rediscovery Protocol (DRUP trial). The health system did not reimburse the cost of the test in these cases, but groups like Hartwig Medical Foundation, which van Snellenberg leads, funded the test for research or patients paid out of pocket.

Lawmakers recognized the inequities of this system and supported the proposal to make WGS more widely accessible to avoid what they called "postal code diagnostics and treatment," where certain hospitals and patients living near them, usually in more affluent areas, have better access to new technology and treatments. Van Snellenberg and others supporting the WGS proposal are hoping it will mitigate these regional access disparities.

Beyond patient care, making WGS standard in the Netherlands could also advance research. The Hartwig Foundation established the country's first national genomic database for cancer research in 2015. The database includes anonymized genetic data from WGS and clinical data from metastatic cancer patients in the Netherlands. Hartwig and its partner hospitals have collected WGS data from more than 5,000 patients.

Lawmakers also adopted a motion supporting the safe collection, storage, processing, and use of data from cancer patients based on the protocols Hartwig and Netherlands Cancer Institute developed for its genomic database.

Van Snellenberg hopes that this move toward WGS in cancer care in the Netherlands will foster a "learning care system in oncology," where data on current treatment approaches and patients' genetic data can lead to new treatments and improvements in care. As the database grows, he noted that the information could help researchers find new therapeutically relevant biomarkers or improve understanding of previously validated biomarkers.

"Using data from patients you are currently treating to improve the treatment of patients of tomorrow is something we want to be institutionalized," van Snellenberg said. "Rather than having a closed box for treating the current patients and another system for doing clinical studies, we want to bring those closer together. We think having a database and collecting the genomic data in a structured way [with WGS] can speed up the cycle of research."

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