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oncology at the Abramson Cancer Center, both in Philadelphia (J Clin Oncol 2013;31:3303–6).

However, the findings about targeted therapies still leave clinicians pondering which one to choose, Langer says.

For years, the go-to drug for treatment-naïve NSCLC patients has been erlotinib (Tarceva; Astellas Pharma). The first-generation tyrosine kinase inhibitor (TKI) was used off-label until it was approved for first-line therapy by the U.S. Food and Drug Administration (FDA) in May 2013. In July, the FDA approved afatinib (Gilotrif; Boehringer Ingelheim), a second-generation TKI, for the same indication.

Afatinib is called a second-generation drug because it covalently binds to the receptor itself, as opposed to erlotinib, which is ATP-competitive at the binding site. Afatinib is also a pan-HER inhibitor, whereas erlotinib is specific for EGFR.

These two drugs have never been compared head to head, and investigators say that published results don't point to a clear advantage for afatinib over its predecessor.

Separate trials indicate that afatinib offers 11.1 months of PFS in this population (increasing to 13.6 months among patients who don't acquire TKI-resistance mutations) compared with 10.4 months with erlotinib.

However, clinical experience shows that afatinib can be more toxic. Side effects are manageable, but afatinib-treated patients are more likely to suffer from skin rashes, diarrhea, and mouth sores, says Alice Shaw, MD, PhD, a thoracic oncologist at Massachusetts General Hospital in Boston. "Choosing one or the other," she says, "boils down to what you think your patients can tolerate."

Roy Herbst, MD, PhD, chief of medical oncology at the Yale Cancer Center in New Haven, CT, raises another consideration—afatinib could be less susceptible to acquired resistance, potentially justifying second-line uses for which it is currently not approved. Preclinical studies have shown that when combined with cetuximab chemotherapy, afatinib remains effective in TKI-resistant mice.

Lecia Sequist, MD, an associate professor at Harvard Medical School in Boston, MA, comments, though, that evidence in humans doesn't support these preclinical findings. "Afatinib doesn't appear to have a lot of activity in human patients with acquired TKI resistance," she says.

Moreover, Sequist says, "it would be difficult to get the combination treatment outside of a clinical trial—afatinib isn't approved in combination with cetuximab, and cetuximab isn't approved in lung cancer. This would also be a very expensive regimen."

The four oncologists agree that third-generation TKIs now in phase I trials, such as Clovis Oncology's CO-1686, might offer greater benefits in TKI-resistant, EGFR-mutant–positive cancers. Unlike their first- and second-generation predecessors, these drugs are thought to bind only to mutated EGFR and not to the wild-type receptor in normal cells. "First- and second-generation TKIs are about the same," Langer concludes, "but this story is by no means over." ■

Project to Mesh Genomic, Patient Data

A new integrated database may offer a powerful resource for cancer genomics analysis by merging whole-genome sequencing data with clinical information.

Current efforts such as The Cancer Genome Atlas (TCGA) typically offer few details about the patients' responses to treatments, notes Anthony Tolcher, MD, director of clinical research for South Texas Accelerated Research Therapeutics (START) in San Antonio. For maximal use, genomic data need to be closely linked to detailed clinical treatment and outcome data, he says.

In September, START and BGI Tech Solutions of Shenzhen, China, announced that BGI will handle sequencing and analysis of genomic data that will be integrated with clinical data in the San Antonio 1000 Cancer Genome Project. Launched last year, the project is generating and studying sequences from 10 cancer types, using frozen tissue samples.

In addition to its focus on integrating clinical data, the initiative differs from most cancer genome efforts in the type of patients it is enrolling, Tolcher says. Patients come mainly from community-based hospitals in the San Antonio area, not from academic medical centers, and thus may be more representative of cancer patients in the general population. Software created by START gathers a variety of information from the participants' files, including tumor staging, treatments, survival, and lab results.

So far, about 1,200 patients have signed on. "Ideally, we want to get up to 10,000 patients," says Tolcher.

All of the genomic and patient information will be housed in a database that will be publicly accessible to researchers worldwide, and should be online next year, Tolcher says.

More than 200 San Antonio–area cancer surgeons, pathologists, researchers, and oncologists have joined the effort. Drawing heavily on time donated by these medical professionals, the project is projected to cost $5 million, all raised from donations.

"It is important to link the genomic data with clinical information," says Lynda Chin, MD, chair of the department of genomic medicine and scientific director of The University of Texas MD Anderson Cancer Center in Houston, who isn't involved in the project. "It's great that they are going to target community physicians, and it's great that they will use frozen tissues."

However, Chin is concerned that the project's small budget—just over 1% of the price tag for TCGA—might not support the careful specimen collection and meticulous quality control necessary to ensure the data's accuracy and usefulness. "I think they have underestimated the challenge of getting the samples," she suggests. ■

Oral Bacteria May Cause Colorectal Cancer

Scientists have long known that the oral microbe *Fusobacterium nucleatum* plays a role in plaque formation and various periodontal diseases, but it isn't confined to the mouth. The bacterium is prevalent in intrauterine infections that can cause complications during pregnancy. In addition, separate research teams reported in 2012 that levels of *F. nucleatum* and other *Fusobacterium* species were

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AACR American Association for Cancer Research

CANCER DISCOVERY

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