

in novel genes or associated regulatory elements that would give us new biological insights into the etiology of these same tumor types in humans.”

Dogs possess several other features that make them ideal partners in cancer research. For example, dogs share their owners' environments and spontaneously develop tumors over time, as humans do. Like humans, they exhibit great phenotypic diversity. Furthermore, canine tumor progression often parallels cancer progression in people.

Even so, Daniel Gustafson, PhD, research director of the Flint Animal Cancer Center in Fort Collins, CO, warns that no one should expect canine cancer research to yield human-relevant results immediately.

“Dogs are not small furry people,” he says. “It may not make intuitive sense, but understanding the differences between cancer in dogs and humans is the only way to see the similarities.” He believes the initiative will be especially helpful in understanding the molecular basis of canine cancer, which will establish a foundation for comparative oncology.

The immediate beneficiaries of this research will most likely be dogs. “I have no doubt that the information garnered from these studies will also lead to incredible advances in personalized canine cancer therapy,” says Lee. —*Kristin Harper* ■

## Apalutamide OK'd for Some Prostate Cancers

The FDA approved the antiandrogen apalutamide (Erleada; Janssen) on February 14 for the treatment of men with nonmetastatic, castration-resistant prostate cancer (CRPC), the first drug for these patients greenlighted by the agency. It is also the first drug approved on the basis of a new trial endpoint: metastasis-free survival (Cancer Discov 2017;7:1053–4).

The approval was based on results of the phase III SPARTAN trial, in which 1,207 patients with nonmetastatic CRPC at high risk for developing metastatic disease were randomly assigned to receive androgen-deprivation therapy with either apalutamide or placebo in a 2:1 ratio (N Engl J Med 2018 February 8 [Epub ahead of print]). High risk was

defined as having a PSA doubling time of 10 months or less because “prior data have shown that these are the patients most at risk for developing metastases and death,” said Eric Small, MD, of the Helen Diller Family Comprehensive Cancer Center at the University of California, San Francisco, senior author of the study. Small also presented the study's findings at the 2018 Genitourinary Cancers Symposium, held in San Francisco, February 8–10.

Apalutamide decreased the risk of metastasis or death by 72%, Small reported. Median metastasis-free survival among men receiving the antiandrogen was 40.5 months compared with 16.2 months among those receiving placebo, an improvement of more than 2 years—evidence that the transition from nonmetastatic to metastatic CRPC can be slowed. Overall survival (OS) data is not yet mature, but an interim analysis showed a trend in favor of apalutamide, Small said.

Apalutamide was well tolerated, with 10.6% of men discontinuing its use due to side effects, compared with 7% of men receiving placebo. Rash, hypothyroidism, and fractures were more common in the apalutamide group.

A next-generation competitive inhibitor of the androgen receptor, apalutamide also prevents translocation of the androgen receptor to the nucleus and impedes androgen receptor-mediated DNA transcription, Small explained.

“There's been no obvious standard of care for these patients,” commented Sumanta K. Pal, MD, of City of Hope Comprehensive Cancer Center in Duarte, CA, making the findings “very clinically meaningful.”

Also at the symposium, Maha Hussain, MD, of Northwestern University in Chicago, IL, reported results of a phase III trial of a second antiandrogen, enzalutamide (Xtandi; Pfizer, Astellas), in patients with high-risk nonmetastatic CRPC. In that trial, dubbed PROSPER, researchers enrolled 1,401 men and randomly assigned them to receive enzalutamide or placebo in a 2:1 ratio. Like apalutamide, enzalutamide significantly prolonged metastasis-free survival compared with placebo—36.6 months versus 14.7 months, a difference of nearly 2 years. As with apalutamide, an early OS analysis favored enzalutamide.



In the phase III PROSPER trial, enzalutamide prolonged metastasis-free survival nearly 2 years longer than a placebo in men with castration-resistant prostate cancer, Maha Hussain, MD, reported.

“Enzalutamide is a drug familiar to the prostate cancer community, given existing approvals in the setting of more advanced disease,” said Pal. “The familiarity that oncologists already have with enzalutamide may help with clinical adoption.” Enzalutamide was approved in 2012 to treat metastatic CRPC.

The SPARTAN researchers and Pal noted that participants in the trials were deemed to have nonmetastatic disease based on conventional imaging techniques, such as CT and technetium bone scans. “While it's true that this is the current standard, imaging techniques such as... PET and PSMA PET may potentially improve our ability to detect disease earlier and thereby change our management strategy,” said Pal. —*Suzanne Rose* ■

## Arvinas, Pfizer Team Up on PROTACs

Taking an entirely different approach to fighting cancer, biotechnology start-up Arvinas (New Haven, CT) has spent the past 5 years developing proteolysis-targeting chimeras (PROTAC). The technology is based on a simple concept: Proteasomes break down proteins that have been tagged with ubiquitin by E3 ubiquitin ligases, so tagging oncogenic proteins for degradation will potentially stop their oncogenic signal.

Recently, Arvinas teamed up with Pfizer in a discovery-based deal worth up to \$830 million, while continuing to develop other promising PROTACs in its internal pipeline.

Craig Crews, PhD, founder and chief scientific advisor of Arvinas, started working on PROTAC technology at New Haven's Yale University during

# CANCER DISCOVERY

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