Grupo Português Génito - Urinário

GPGU – NOTÍCIAS

'Finally, Real Promise' for Prostate Cancers With No Therapy

20+-Month Improvement in Metastasis-Free Survival

Nick Mulcahy

February 05, 2018

Long-needed change appears to be coming to the management of a group of prostate cancer patients for whom there is no apparent standard of care — men with early-stage disease whose prostate-specific antigen (PSA) score is rapidly rising after surgery or radiotherapy despite androgen-deprivation therapy (ADT).

There are currently no approved treatments for these men, who are destined to develop metastatic disease and are at increased risk for death. There are currently about 100,000 such patients in the United States.

Now, two phase 3, placebo-controlled clinical trials have shown that there are drugs that significantly delay the onset of metastasis in these patients.

The trials, which will be fully presented later this week at the Genitourinary Cancers Symposium (GUCS) 2018, in San Francisco, feature two different androgen-receptor inhibitors that are orally administered.

The SPARTAN trial employed the next-generation investigational agent apalutamide (Janssen Biotech). The PROSPER trial employed the earlier-generation enzalutamide (Xtandi, Astellas/Pfizer), which is already approved for men who have metastatic prostate cancer.

Both trials showed that in the treatment of men with non metastatic castrate-resistant prostate cancer, daily administration of the respective agents reduced the relative risk for metastasis or death by more than 70% and prolonged metastasis-free survival (MFS) by more than 20 months compared to placebo. All patients, in both the treatment and placebo arms, also received ADT.

Both trials enrolled men who had undergone definitive treatment, either surgery or radiotherapy, for prostate cancer but whose PSA scores subsequently double within 10 months or less, despite ADT. For each trial, MFS was the primary endpoint. Each trial showed a trend toward improved overall survival in an early interim analysis.

"These trials are addressing a great clinical need for these patients, who currently generally only receive observation," said Alexander Kutikov, MD, chief of urologic oncology at Fox Chase Cancer Center in Philadelphia, Pennsylvania, who was not involved in the research.

"The reported results will undoubtedly disrupt the treatment paradigms for these patients, delay the time to metastatic disease, and, ultimately, hopefully prove to extend survival," he told Medscape Medical News.

The reported results will undoubtedly disrupt the treatment paradigms for these patients. Dr Alexander Kutikov

In the 1207-patient SPARTAN trial, which was discussed during a presscast today before the GUCS, which will be held later this week, apalutamide decreased the risk for distant metastasis or death by 72% (hazard ratio [HR] = 0.28; 95% confidence interval [CI], 0.23 - 0.35; P < .0001), with a median MFS of 40.5 vs 16.2 months in the placebo group (an improvement of 24.3 months)

Median follow-up was 20.3 months.

"These data suggest that apalutamide should be considered as a new standard of care for men with high-risk nonmetastatic castrate-resistant prostate cancer," lead study author Eric J. Small, MD, professor of medicine at the University of California, San Francisco, said at the presscast.

"Currently, there is no obvious standard of care for these patients," commented Sumanta K. Pal, MD, urologic oncologist at City of Hope in Duarte, California. He was moderating the presscast as an American Society of Clinical Oncology expert.

"These findings suggest there may finally be a treatment that holds real promise for extending their health and their lives," he added.

There may finally be a treatment that holds real promise for extending their health and their lives. Dr Sumanta Pal

In the 1401-patient PROSPER trial, enzalutamide decreased the risk for distant metastasis or death by 71% (HR = 0.29; 95% CI, 0.24 - 0.35; P < .0001), with a median MFS of 36.6 vs 14.7 months in the placebo group (an improvement of 21.9 months).

"In the PROSPER trial, treatment with enzalutamide plus ADT delayed the development of metastases compared to standard-of-care ADT alone and, if approved, may provide

men with nonmetastatic, castrate-resistant prostate cancer an important new treatment option," said lead author Maha Hussain, MD, professor of medicine, Northwestern University, Chicago, Illinois, in a press statement.

Both apalutamide and enzalutamide were well tolerated, with only about 10% of patients discontinuing treatment, compared to roughly 6% and 8%, respectively, of patients who received placebo in the trials.

Which therapy looks better? Dr Kutikov was cautious in answering.

He agreed that apalutamide appeared more effective. But he emphasized that "the results are similar" and advised "great caution in making comparisons between the two trials with regard to superiority or equivalency of one agent vs another."

Only a direct, prospective, randomized comparison can establish the superiority of one agent over another, he reminded.

Dr Pal suggested that enzalutamide might be favored by clinicians because of the "familiarity that oncologists already have" with the drug, "which may help with clinical adoption."

He also asserted that the nonmetastatic, castrate-resistant prostate cancer patient population may be "shrinking."

That's because newer and improved imaging modalities are detecting metastatic spread earlier than the current standards of CT and conventional bone scanning, which were used in the SPARTAN trial, Dr Pal observed. In short, the spread of disease may become apparent in conjunction with the rapid rise of PSA, he suggested.

More Details on Both Trials

The SPARTAN study was conducted at 332 institutions internationally. Patients were randomly assigned in a 2:1 ratio to receive either apalutamide 240 mg QD or placebo. Baseline PSA doubling time was <5 months in both groups.

The primary endpoint of MFS was defined as the time from randomization to first radiographic evidence of distant metastasis (determined on the basis of blinded central review) or death.

Patients were eligible to receive study-provided abiraterone acetate plus prednisone after developing distant metastases.

At the median follow-up of 20.3 months, 61% of patients who received apalutamide and 30% of patients who received placebo were still on treatment.

Mean baseline health-related quality-of-life scores were maintained in both study groups. There was "no decrement in quality of life on apalutamide," reported Dr Small. There was also no difference in serious adverse events between the two groups, he said.

Of those whose disease progressed, 80% of patients who were given placebo and 56% of patients who were given apalutamide received open-label abiraterone (Zytiga, Janssen-Cilag) for metastatic castrate-resistant prostate cancer.

In the PROSPER study, eligible men were also randomly assigned in a 2:1 ratio to receive either enzalutamide 160 mg or placebo.

Enzalutamide, compared to placebo, also significantly prolonged time to first use of new antineoplastic therapy (39.6 vs 17.7 months; P < .0001) and time to PSA progression (37.2 vs 3.9 months; P < .0001), the study authors report in their abstract.

However, adverse events were higher with enzalutamide than with placebo (any grade: 87% vs 77%; grades ≥3: 31% vs 23%; serious: 24% vs 18%).