Medicine Matters Oncology

20-09-2021 | ESMO 2021 | Conference coverage | News

PEACE-1: Upfront triplet therapy gives OS advantage to men with mCSPC

Author: Shreeya Nanda

medwireNews: The addition of abiraterone acetate to standard therapy with docetaxel plus androgen deprivation therapy (ADT) significantly improves the overall survival (OS) of patients with de novo metastatic castration-sensitive prostate cancer (mCSPC), report the PEACE-1 investigators.

Speaking at the ESMO Congress 2021, researcher Karim Fizazi (Institut Gustave Roussy, Villejuif, France) highlighted that "the treatment of metastatic prostate cancer has changed dramatically in the last 5 years after several decades with no significant progress," but questions remain regarding combinatorial approaches involving local and systemic therapies, and the trial aims to address these.

He explained that the phase 3 study, which has a 2x2 factorial design, is evaluating the efficacy and safety of adding abiraterone acetate plus prednisone and/or local radiotherapy to standard of care (SOC) in the mCSPC setting. But due to the "rapidly evolving" SOC in this setting, 710 of the 1173 participants received docetaxel plus ADT as SOC, which allowed the assessment of outcomes with the triplet regimen of abiraterone, docetaxel, and ADT, added Fizazi.

The investigators on the co-primary endpoint of radiographic progression-free survival, the risk for which was halved with the addition of abiraterone to docetaxel–ADT, with median durations of 4.5 and 2.0 years with and without abiraterone, respectively.

The current presentation focused on the second primary endpoint of OS. As reported by Fizazi, the median duration was unreached for the 355 participants who were randomly assigned to receive abiraterone 1000 mg/day plus prednisone 5 mg twice daily alongside six cycles of docetaxel 75 mg/m^2 every 3 weeks plus continuous ADT (with or without radiotherapy).

This was significantly better than the median of 4.4 years observed among their 355 counterparts who received just docetaxel plus ADT (with or without radiotherapy), and equated to a 25% reduction in the risk for death with the addition of abiraterone.

The presenter pointed out that the OS benefit offered by abiraterone was observed even though 84% of control participants received subsequent life-prolonging therapy, compared with 74% of those given the experimental regimen.

The findings were consistent in the approximately three-quarters of patients with high-volume disease, as defined by the CHAARTED criteria, with median OS times with and without abiraterone of 5.1 and 3.5 years, respectively, and a significant 28% decrease in the risk for death.

However, although the hazard ratio favored the addition of abiraterone in those with low-volume disease, the difference between treatments was not statistically significant at the time of analysis, which Fizazi suggested could be due to the immaturity of the dataset.

He also noted that the addition of abiraterone to SOC significantly improved OS in the full trial population of 1173 participants treated with any SOC, with a significant 18% lower risk for death relative to SOC alone, and respective median OS durations of 5.7 and 4.7 years.

“Side effects from abiraterone were as expected, with no evidence of synergistic toxicity with ADT plus docetaxel,” said the investigator.

The incidence of grade 3–5 neutropenia and febrile neutropenia was comparable between the abiraterone and control groups, at 10% versus 9% and 5% versus 5%, respectively, but the rates of hypertension and transaminase elevations were higher, at 22% versus 13% and 6% versus 1%, respectively.

“We believe this data is practice changing,” said Fizazi, adding that “at least men with de novo high-volume metastatic prostate cancer should be offered ADT plus docetaxel plus abiraterone.”

He added: “On the other hand, defining how best to combine systemic treatments with local radiotherapy, especially in men with oligometastatic disease, will require a longer follow-up of PEACE-1.”

Discussant Eleni Efstathiou (Houston Methodist Cancer Center in Texas, USA) agrees that the trial is practice changing, with “positive outcomes that are clinically meaningful.”

Querying how the triplet will fare in comparison with ADT plus abiraterone, she noted that the safety of the triplet will require more rigorous monitoring in practice.

But Efstathiou emphasized that based on all the data available in the mCSPC setting, physicians should not be using ADT alone for these patients anymore.

ESMO Congress 2021; 16–21 September