Novartis 177Lu-PSMA-617 significantly improves overall survival and radiographic progression-free survival for men with metastatic castration-resistant prostate cancer in Phase III VISION study

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- Men who received 177Lu-PSMA-617 plus best standard of care had a 38% reduction in risk of death (median OS benefit of 4 months) and a 60% reduction in the risk of radiographic disease progression or death (median rPFS benefit of 5 months) compared to best standard of care alone[1]
- Significant improvement demonstrated in all key secondary endpoints, including time to first symptomatic skeletal event, overall response rate and disease control rate[1]
- VISION study findings to be presented during 2021 ASCO plenary; regulatory submissions to US and EU Health Authorities on track for 2H21; two additional pivotal studies in earlier lines of treatment for metastatic prostate cancer to start 1H21, goal to move into earlier stages of disease
- Novartis commitment to leadership in radioligand therapy (RLT) further strengthened by recent partnerships and investments; more than 15 ongoing research and discovery programs to identify and accelerate next wave of RLTs for cancer

EAST HANOVER, N.J., June 3, 2021 /PRNewswire/ -- Novartis today announced that results of the Phase III VISION study evaluating 177Lu-PSMA-617, a targeted radioligand therapy, plus best standard of care (SOC) demonstrated significant improvement in overall survival (OS) compared to SOC alone, in patients with progressive PSMA-positive metastatic castration-resistant prostate cancer (mCRPC)1. The difference in OS between study arms was statistically significant (one-sided p<0.001), with an estimated 38% reduction in risk of death in the 177Lu-PSMA-617 arm (n=551) compared to the best standard of care only arm (n=280) (hazard ratio: 0.62 with 95% confidence interval (CI): (0.52, 0.74))1. These results will be presented during the 2021 American Society of Clinical Oncology (ASCO) Annual Meeting plenary session on June 6.

Patients receiving 177Lu-PSMA-617 also demonstrated a statistically significant (one-sided p<0.001) 60% risk reduction for radiographic progression-free survival or death (rPFS), compared to the best standard of care only arm (hazard ratio: 0.40 with 99.2% CI: (0.29 0.57))1. There was a higher rate of drug-related treatment emergent adverse events reported in the 177Lu-PSMA-617 treatment arm (85.3%) compared to standard of care alone (28.8%)1.

Across both arms of the study, rates of treatment discontinuation associated with treatment-emergent adverse events occurred as follows: In the 177Lu-PSMA-617 plus standard of care (SOC) arm, 11.9% of patients discontinued 177Lu-PSMA-617 and 8.5% discontinued SOC; while in the SOC alone arm 7.8% of patients discontinued treatment1.

"Patients suffering from metastatic CRPC who have progressed through contemporary hormonal treatments and chemotherapy have few meaningful therapeutic options," said Michael J. Morris, MD, who chaired the study's Scientific Committee and is the Prostate Cancer Section Head, Genitourinary Oncology Service, Division of Solid Tumor Oncology at Memorial Sloan Kettering Cancer Center. "The study demonstrated that 177Lu-PSMA-617 improves disease progression and prolongs survival, which are key measures of clinical benefit in the mCRPC population. I am grateful to be a part of this study that may lead to additional therapeutic options for these patients."

"Men with metastatic prostate cancer have an approximately 3 in 10 chance of surviving 5 years2. These data from the first Phase III study of a radioligand therapy in this advanced prostate cancer setting confirm the potential of 177Lu-PSMA-617 targeted therapy to improve clinical outcomes," said John Tsai, Head of Global Drug Development and Chief Medical Officer for Novartis. "Our comprehensive development program for this targeted therapy seeks to reach eligible patients with advanced prostate cancer, who express the PSMA biomarker1,3-6. And, we won't stop with prostate cancer, our team is exploring next generation RLT across a number of tumor types."

Two additional studies with 177Lu-PSMA-617 radioligand therapy in earlier lines of treatment for metastatic prostate cancer are planned to start in the first half of 2021, investigating potential clinical utility in the mCRPC pre-taxane setting (PSMAfore) and in the metastatic hormone-sensitive setting (PSMAddition).

Additional VISION data

Median OS (95% CI) for the 177Lu-PSMA-617 plus best standard of care arm in the VISION study was 15.3 months (14.2, 16.9), compared to 11.3 months (9.8, 13.5) in the best standard of care arm only1. The median rPFS (99.2% CI) was 8.7 months (7.9, 10.8) for the 177Lu-PSMA-617 arm compared to 3.4 months (2.4, 4.0) for the best standard of care only arm1.

Key secondary endpoints were also met. The median time to first symptomatic skeletal event was 11.5 months (95% CI: 10.3, 13.2) in 177Lu-PSMA-617 arm compared to 6.8 months (95% CI: 5.2, 8.5) in the best standard of care only arm (hazard ratio: 0.50 (95%CI: 0.40, 0.62)); two-sided p-value: <0.0011. Significant differences were also seen in overall response rate in patients with measurable or non-measurable disease at baseline (29.8% partial or complete response in the 177Lu-PSMA-617 arm compared to 1.7% partial response in the best standard of care only arm (two-sided p-value: <0.001)) and disease control rate (89.0% in 177Lu-PSMA-617 arm compared to 66.7% in the best standard of care only arm (two-sided p-value: <0.001))1.

Grade ≥3 drug-related treatment emergent adverse events occurred in 28.4% of the 177Lu-PSMA-617 arm compared to 3.9% in the best standard of care only arm1. The most common treatment emergent adverse events regardless of drug relatedness (above 2% respectively for the 177Lu-PSMA-617 and best standard of care arm) were anemia (12.9% vs. 4.9%), thrombocytopenia (7.9% vs. 1%), lymphopenia (7.8% vs. 0.5%), fatigue (5.9% vs. 1.5%), urinary tract infection (3.8% vs 0.5%), neutropenia (3.4% vs 0.5%), hypertension (3.2% vs 1.5%), back pain (3.2% vs. 3.4%), acute kidney injury (3.0% vs 2.4%), leukopenia (2.5% vs. 0.5%), bone pain (2.5% vs. 2.4%), hematuria (2.5% vs 0.5%), and spinal cord compression (1.3% vs. 5.4%)1.

Serious drug-related treatment emergent adverse events occurred in 9.3% of patients in the 177Lu-PSMA-617 arm compared to 2.4% in the best standard of care only arm1.

Visit https://www.hcp.novartis.com/virtual-congress/a-2021/ for the latest information from Novartis, including our commitment to the Oncology community, and access to our ASCO21 Virtual Scientific Program data presentations (for registered participants).

About Advanced Prostate Cancer

Prostate cancer is a form of cancer that develops in the prostate gland, a small walnut shaped gland in the pelvis of men. In castration resistant prostate cancer (CRPC), the tumor shows signs of growth, such as rising Prostate Specific Antigen (PSA) levels, despite the use of hormone treatments that lower testosterone7. In metastatic CRPC (mCRPC), the tumor spreads to other parts of the body, such as neighboring organs or bones and remains unresponsive to hormone treatment7. The five-year survival rate for patients with metastatic prostate cancer is approximately 30%2.

About Phenotypic Precision Medicine in Advanced Prostate Cancer

Despite advances in prostate cancer care, there is a high unmet need for new targeted treatment options to improve outcomes for patients with mCRPC. More than 80% of prostate cancer tumors highly express a phenotypic biomarker6 called Prostate Specific Membrane Antigen (PSMA) 3-5,8-9, making it a promising diagnostic (through positron emission tomography (PET) scan imaging) and potential therapeutic target for radioligand therapy10. This differs from 'genotypic' precision medicine which targets specific genetic alterations in cancer cells6.

About 177Lu-PSMA-61

177Lu-PSMA-617 is an investigational PSMA-targeted radioligand therapy for metastatic castration-resistant prostate cancer. It is a type of precision cancer treatment combining a targeting compound (ligand) with a therapeutic radioisotope (a radioactive particle)11-13. After administration into the bloodstream, 177Lu-PSMA-617 binds to prostate cancer cells that express PSMA14, a transmembrane protein, with high tumor-to-normal tissue uptake11,15,16. Once bound, emissions from the radioisotope damage tumor cells, disrupting their ability to replicate and/or triggering cell death17-19. The radiation from the radioisotope works over very short distances to limit damage to surrounding cells10,11,15.

About VISION

VISION is an international, prospective, randomized, open-label, multicenter, phase III study to assess the efficacy and safety of 177Lu-PSMA-617 (7.4 GBq administered by intravenous infusion every 6 weeks for a maximum of 6 cycles) plus investigator-chosen best standard of care in the investigational arm, versus best standard of care in the control arm20. Patients with PSMA PET-scan positive mCRPC, and progression after prior taxane and androgen receptor pathway inhibitors, were randomized in a 2:1 ratio in favor of the investigational arm20. The alternate primary endpoints were rPFS and OS20. The study enrolled 831 patients1.

About Novartis

Novartis is reimagining medicine to improve and extend people's lives. As a leading global medicines company, we use innovative science and digital technologies to create transformative treatments in areas of great medical need. In our quest to find new medicines, we consistently rank among the world's top companies investing in research and development. Novartis products reach nearly 800 million people globally and we are finding innovative ways to expand access to our latest treatments. About 110,000 people of more than 140 nationalities work at Novartis around the world. Find out more at https://www.novartis.com.

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