進行性腎細胞がん治療の進歩

RECORD-1トライアルの結果、everolimusは標準治療が無効だった進行した転移性腎細胞がん患者の無増悪生存期間を有意に延長させることが示された

RECORD-1 trial shows that everolimus significantly lengthens time to progression in patients with advanced kidney cancer who failed standard therapies

Everolimusは標準治療が無効だった進行した転移性腎細胞がん患者に有意に有益である、とAmerican Society of Clinical Oncology学会で発表された。RECORD-1トライアルは、ソラフェニブ、スニチニブまたはその両者を含む治療を行ったにもかかわらず悪化した患者400人以上を無作為化した。無増悪生存期間はeverolimusにおいてプラセボと比較し有意に改善した（中央値はそれぞれ4ヵ月対1.9ヵ月）。標的病変における最大腫瘍変化率は、評価可能な患者（everolimusとプラセボでそれぞれ223人および107人）の判定結果から、初回の二重盲検試験期間中にeverolimusを投与された患者の50%に腫瘍の縮小が認められたのに対し、プラセボ群におけるその割合は8%であった。この試験では疾患の進行が確認された時点で非盲検化され、プラセボ群の患者は実薬治療に切り換えられた。中間解析結果が完了した後、試験の二重盲検部分は中止された。

Full Text

Everolimus (RAD001) significantly lengthens progression-free survival in patients with metastatic renal cell carcinoma who have failed standard therapies, according to trial results presented at the annual meeting of the American Society of Clinical Oncology.

"This is the first study to show clinical benefit in patients with advanced kidney cancer who have experienced treatment failure with the most commonly used first-line therapies," said Robert J. Motzer, MD, attending physician, Memorial Sloan-Kettering Cancer Center, New York, and principal investigator of the RECORD-1 trial. "The results show RAD001 extended progression-free survival in patients regardless of their prior treatments, risk status, age, or gender."

The RECORD-1 trial (REnal Cell cancer treatment with Oral RAD001 given Daily) is the largest Phase III trial to evaluate an oral mTOR inhibitor in the setting of metastatic renal cell carcinoma, randomizing more than 400 patients with disease that worsened despite prior treatment, including sorafenib, or sunitinib, or both. In addition, eligible patients were allowed to have had prior therapy with bevacizumab, interferon, or interleukin-2.

Primary endpoint was progression-free survival assessed via a blinded, independent central review and defined as the time between randomization and first documented disease progression or death due to any cause. There was a statistically significant improvement for RAD001 compared with placebo (median progression-free survival 4 months versus 1.9 months, respectively).

Secondary endpoints included comparison of overall survival, objective response rate, quality of life, safety, and pharmacokinetics. There was no significant difference in overall survival between groups. Study design allowed patients to be unblinded at the time of radiological disease progression; patients receiving placebo were allowed to cross over to receive active treatment. There was no significant difference in objective response rate between the RAD001 and placebo groups (1 percent versus 0 percent).

However, in a central review among patients evaluable for best percentage change in target lesions (223 and 107 patients in RAD001 and placebo arms, respectively), tumor shrinkage was observed in 50 percent of patients receiving RAD001 during the double-blind portion of the study versus 8 percent of patients receiving placebo. Quality of life measurements taken throughout the study showed no significant difference between groups.

Safety findings were consistent with those in prior Phase II studies. The most frequent adverse events in patients who took RAD001 included mouth sores (40 percent), feelings of weakness (37 percent), and rash (25 percent). The trial had a low rate of adverse drug reactions leading to discontinuation among patients who took RAD001 (6 percent).

The interim study findings demonstrated that RAD001 significantly extended progression-free survival from 1.9 to 4 months and reduced the risk of cancer progression by 70 percent. Earlier this year, an independent data monitoring committee stopped the RECORD-1 trial after interim results showed that patients receiving RAD001 had significantly longer progression-free survival compared with patients receiving placebo.

RAD001 is a once-daily oral therapy that may offer a new approach to cancer treatment by continuously inhibiting the mTOR protein, a central regulator of tumor cell division and blood vessel growth in malignant cells.

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