Phase III data in treatment of renal cell carcinoma reported

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New results from phase III trials exploring treatment options for patients with advanced renal cell carcinoma were released at the ESMO 2012 Congress of the European Society for Medical Oncology in Vienna.

Renal cell carcinoma is a type of kidney cancer that starts in the lining of very small tubes (tubules) in the kidney.

Prof Maria De Santis from Kaiser Franz Josef-Spital, Vienna, Chair of the ESMO 2012 Genitourinary program track (who was not involved in the studies) commented: "At this year's ESMO congress, three urgently awaited and highly ranked randomized phase III trials in the area of renal cell carcinoma are being presented. All three studies are important, although two of these studies are so called 'negative' studies (INTORACT and INTORSECT)."

"These studies are significant because they increase our knowledge about the use of targeted treatment options, in particular temsirolimus, sorafenib, bevacizumab and pazopanib," Prof De Santis said. "Most importantly, one of the studies, the COMPARZ trial, allows us to define a standard option in the front line treatment of renal cell carcinoma, because it was proven that pazopanib is non-inferior to sunitinib. In addition, being treated with pazopanib, patients experienced fewer troublesome side-effects and an increased quality of life."

COMPARZ trial: pazopanib and sunitinib similarly

effective in first line treatment of metastatic renal cell carcinoma

The new drug pazopanib has similar efficacy to sunitinib in controlling metastatic renal cell carcinoma, the results of the phase III randomized, open-label COMPARZ trial show.

Sunitinib and pazopanib are both targeted drugs available for first line treatment of metastatic renal cell carcinoma. Sunitinib has been considered as the reference standard, although non-randomized trials have suggested similar efficacy with pazopanib, and less incidence of some side effects found troublesome to patients.

Dr Robert Motzer from Memorial Sloan Kettering Cancer Center, New York, USA and colleagues set out to compare the efficacy, safety, and quality of life for pazopanib and sunitinib in a global, 1100-patient phase III trial. The primary endpoint was to establish non-inferiority of progression-free survival, and safety and quality of life were evaluated as secondary endpoints, as well.

"The trial showed that pazopanib had similar efficacy (i.e non-inferiority) compared to sunitinib in first-line treatment of metastatic renal cell carcinoma," Dr Motzer said. "The main endpoint for assessment was progression-free survival, and we looked at other endpoints as well, including response, overall survival, safety and quality of life."

For both drugs, the median progression-free survival by the treating physician's assessment was slightly more than 10 months.

Both drugs resulted in side effects, but some of those recognized to be troublesome to patients, such as fatigue and skin sores, occurred with

less frequency for pazopanib than with sunitinib, the researchers found.

"The quality-of-life questionnaires were in favor of pazopanib over sunitinib, and suggested improved tolerability for pazopanib over sunitinib," Dr Motzer said.

INTORSECT trial: Temsirolimus does not demonstrate superiority in survival over sorafenib in second-line treatment

The results of a phase III trial comparing two commonly used drugs in the second-line treatment of renal cell carcinoma suggest that temsirolimus does not improve survival over sorafenib in the second line setting.

The two drugs inhibit different cancer-associated molecules: temsirolimus targets mTOR, which regulates cell growth and proliferation, while sorafenib inhibits several tyrosine kinases, including VEGF receptors.

"This is the first head-to-head phase III trial comparing a VEGF inhibitor to an mTOR inhibitor in renal cell carcinoma, reporting final results. Hence, this trial will have important treatment implications for patients and physicians," said Dr Thomas Hutson from Texas Oncology-Baylor Charles A Sammons Cancer Center in Texas, USA.

Temsirolimus had demonstrated an overall survival benefit compared to interferon alfa in previously untreated patients with advanced renal cell carcinoma and poor prognostic features, but the drug's efficacy after treatment with a VEGF inhibitor was not known, Dr Hutson explained.

The INTORSECT Trial included 511 renal cell carcinoma patients from

112 sites, whose disease progressed after first-line sunitinib therapy and who had an ECOG performance status of 0 or 1. Median progression-free survival with temsirolimus was 4.28 months compared to 3.91 months with sorafenib. Median overall survival for the temsirolimus group was 12.27 months compared to 16.64 months for those who received sorafenib.

Based on these results, the researchers found that temsirolimus did not show superiority to sorafenib in the primary end point of progression-free survival or in the secondary end point of overall survival.

"This trial shows drugs that inhibit the VEGF pathway may be a better option than mTOR inhibitors for patients progressing on sunitinib," Dr Hutson said. "In addition, mTOR inhibitors may be appropriate for first line use for a select group of non-clear cell renal cell carcinoma patients and/or those patients with poor performance status."

INTORACT Trial: bevacizumab plus temsirolimus offers no advantage over bevacizumab plus interferon

A phase III trial has failed to confirm early clinical results with the combination of bevacizumab and temsirolimus in renal cell carcinoma, investigators from the INTORACT trial report.

The two drugs target separate molecular pathways involved in renal cell carcinoma, and early results had seemed promising, said Prof Brian Rini, a staff physician at the Cleveland Clinic's Taussig Cancer Institute in Cleveland, Ohio and Professor of Medicine at the Cleveland Clinic Lerner College of Medicine of Case Western Reserve University in Cleveland, Ohio.

The INTORACT trial, a global phase IIIb, randomized, open-label, multi-

center study, compared temsirolimus plus bevacizumab with interferon plus bevacizumab as first-line treatment in 791 patients with predominantly clear cell metastatic renal cell carcinoma.

At the data cutoff for final analysis, 489 patients had independently assessed progression-free survival events. Median progression-free survival with the temsirolimus combination was 9.1 months, compared to 9.3 months in the interferon group. Median overall survival was 25.8 months in the temsirolimus group and 25.5 months for the interferon group.

This study failed to find an advantage to the combination of bevacizumab and temsirolimus over bevacizumab and interferon, therefore did not confirm preliminary results of this combination," Prof Rini said.

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