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Patient Portals: Use Increasing, along with Push to Reduce Problems

BY HEATHER LINDSEY

Researchers at the University of Texas Southwestern Medical Center have observed a sharp increase in the number of cancer patients using MyChart, a personal health record portal application of the EPIC electronic medical record system. Their study, they say, is the first to systematically evaluate portal use in the cancer community (*J Oncol Pract, doi: 10.1200/JOP.2013.001347*). "As a clinician on the faculty here who sees patients multiple days a week, I had suspected that MyChart or portal use was quite high and growing with time," said the lead author, David Gerber, MD, Associate Professor of Internal Medicine in the Hematology/Oncology Division and the Harold C. Simmons Cancer Center at UT Southwestern Medical Center.

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Metastatic Colorectal Cancer: Update Now Shows Higher Response for Cetuximab-Chemotherapy

BY ROBERT H. CARLSON

BARCELONA, Spain—An update for the CALGB/SWOG 80405 trial presented here at the ESMO World Congress on Gastrointestinal Cancer showed that patients in the chemotherapy-cetuximab arm had a significantly higher response rate than those in the chemotherapy-bevacizumab arm (*Abstract O-0019*).

Alan P. Venook, MD, Professor of Medical Oncology and Translational Research at the University of California, San Francisco, reported objective response rates, but with the caveat that they were based on two-thirds of the entire cohort, from investigator assessment of 369 patients on chemotherapy-bevacizumab and 364 on chemotherapy-cetuximab. The data were documented but not yet audited, he said.

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Good & Bad News about Prophylactic Thrombolysis in Cancer Patients

BY KURT SAMSON

Although hospitalized cancer patients receive anticoagulants to prevent venous thromboembolism (VTE) much more often than has been reported in the past, a new study shows that therapy is often prescribed without adherence to published recommendations on risk factors or by carefully assessing risk on a per-patient basis.

The prospective, multicenter, cross-sectional study (*JCO 2014;32:1792-1796*), assessed cancer patients admitted at hospitals for various procedures and found that more than 70 percent of individuals without contraindications received therapy. However, the hospitals in general did not follow published risk-evaluation guidelines in selecting which patients to treat—notably those by the American College of Chest Physicians (ACCP) and the American Society for Clinical Oncology.

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CALGB/SWOG 8045 UPDATE: HIGHER RESPONSE FOR CETUXIMAB-CHEMOTHERAPY

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The overall response rate was 57 percent for chemotherapy-bevacizumab versus 66 percent for chemotherapy-cetuximab.

There were a "surprisingly high" number of complete responses, Venook said—three percent for chemotherapy-bevacizumab and 7.4 percent for chemotherapy-cetuximab.

Partial response rates were 54 percent for chemotherapy-bevacizumab and 58 percent for chemotherapy-cetuximab; stable disease rates were 37 and 26 percent, respectively; and a small number of patients with refractory disease, with progressive disease rates of six and eight percent, respectively.

When Venook reported the initial results of the study at the plenary session at the American Society of Clinical Oncology this spring, the results showed no meaningful superiority of one regimen over the other (***OT 7/10/14 issue***). "The two antibodies added to chemotherapy consisting of either FOLFOX or FOLFIRI are both acceptable and similarly effective," he concluded at that time.

Eagerly Awaiting Expanded RAS Analysis

Confirmed response rates, depth of response, and expanded RAS analysis for the study are pending; Venook said these will be reported in September at the ESMO Congress in Madrid. Those data will hopefully explain a burning question: Why two similar trials, 80405 and FIRE-3, the Phase III trial presented at last year's ESMO GI meeting (***Ann Oncol 2013;24[suppl 4]: iv22-iv23***)–had different overall survival results with the same treatments.

As in 80405, FIRE-3 compared first-line chemotherapy-cetuximab with chemotherapy-bevacizumab in metastatic colorectal cancer. But unlike 80405, FIRE-3 showed a higher survival rate for chemotherapy-cetuximab than chemotherapy-bevacizumab.

ALAN P. VENOOK, MD, called the number of complete responses "surprisingly high"—3% for patients on chemotherapy-bevacizumab and 7.4% for those on chemotherapy-cetuximab.

Pending the final analyses, Venook stressed that similar studies "may have different results without being erroneous."

Congress Vice-Chair Josep Tabernero, MD, PhD, Head of Medical Oncology and Director of Clinical Research at Vall d'Hebron University Hospital and the Institute of Oncology in Barcelona, said the full analysis of 80405 is eagerly awaited: "We as physicians are really waiting for this data, because it was difficult to explain why the patients who received FOLFIRI-cetuximab [in FIRE-3] had an advantage in overall survival without any meaningful advantage in response rate and progression-free survival," he said in an interview.

"What we have seen now is that patients in the FOLFIRI-cetuximab arm had a more pronounced shrinkage of the tumor, so the objective response rate is higher, the depth of response is higher, and early tumor shrinkage is higher with FOLFIRI-cetuximab than with FOLFIRI-bevacizumab."

These factors, he said, suggest a good explanation of how this translates into an advantage in overall survival.

Biologicals May Not Require Cytotoxics

In a separate presentation here, Venook hypothesized that the best cytotoxic "backbone" on which to add a biological therapy for metastatic colorectal cancer may be no chemotherapy at all.

"The research on chemotherapy backbones and biologicals in these regimens is hindered because we do not always understand the mechanisms of action, but it is possible that less chemotherapy may be better," he said.

A chemotherapy backbone is not necessary in treating melanoma, and two biological agents work there very well together, he said.

In colorectal cancer, the randomized Phase II BOND-2 study of cetuximab-bevacizumab-irinotecan compared with cetuximab-bevacizumab alone in irinotecan-refractory colorectal cancer showed that the activity of bevacizumab-cetuximab and cetuximab-irinotecan appeared better as compared with historical controls of cetuximab or cetuximab-irinotecan in patients who had not previously received bevacizumab (***Saltz L et al: JCO 2007;25:4557-4561***).

Not all evidence points to the elimination of chemotherapy from regimens for metastatic colorectal cancer, however. Venook said the addition of panitumumab to bevacizumab and oxaliplatin- or irinotecan-based chemotherapy resulted in increased toxicity and decreased progression-free survival in the Phase III PACE study of metastatic colorectal cancer (***Hecht J et al: JCO 2009;27:672-680***).

"Without exception, patients [in that trial] who received double biologicals and chemotherapy did worse than patients who had a single biological," Venook said.

William Carlson

JOSEP TABERNERO, MD, PHD: "Patients in the FOLFIRI-cetuximab arm had a more pronounced shrinkage of the tumor, so the objective response, the depth of response, and early tumor shrinkage are all higher than with FOLFIRI-bevacizumab—all factors that suggest a good explanation of how this translates into an advantage in overall survival.

> Confirmed response rates, depth of response, and expanded RAS analysis are set to be reported in September at the ESMO Congress in Madrid.

But he added that KRAS status was just evolving at that time, and this was an example of the harm done when mutated KRAS patients get cetuximab or panitumomab.

Furthermore, in the CAIRO-2 trial, the addition of cetuximab to capecitabine-oxaliplatin-bevacizumab resulted in significantly shorter progression-free survival and inferior quality of life. "Patients who got double biologicals did worse than those who did not," he said.

Active Maintenance Beats No Maintenance

In another presentation here in the session on metastatic colorectal cancer, results from the Phase III AIO KRK 0207 trial were reported, showing

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> Reported were objective response rates but with the caveat that these were based on two-thirds of the entire cohort; the data were documented but not yet audited.

Gastric Cancer: RAINBOW Subanalysis Shows Paclitaxel-Ramucirumab Efficacy in Western Patients

BY ROBERT H. CARLSON

BARCELONA, Spain—In patients from Western countries, second-line treatment for advanced gastric and gastro-esophageal cancer with the combination of paclitaxel and the VEGF antagonist ramucirumab is safe and efficacious, significantly increasing overall and progression-free survival and response compared with use of paclitaxel alone.

The combination reduced the risk of death by 27 percent and increased survival from 5.9 to 8.6 months compared with paclitaxel alone, according to a subanalysis of 398 patients from Western countries in the randomized placebo-controlled RAINBOW trial who had disease progression on or after use of platinum and fluoropurimidine-containing chemotherapy.

The subanalysis data were presented here at the European Society for Medical Oncology World Congress on Gastrointestinal Cancer (the full analysis of all of RAINBOW's 665 patients was presented earlier this year at the Gastrointestinal Cancers Symposium (***Wilke H et al: Abstract LBA7***).

The results of the subanalysis had been eagerly awaited because some trials have shown significantly different outcomes between patients from Asian and Western countries. In an example cited by several speakers here, the AVAGAST study (***Ohtsu et al: JCO 2011;29:3968-3976***) of bevacizumab plus capecitabine-cisplatin as first-line treatment of patients with gastric cancer, the addition of bevacizumab provided no overall survival benefit for the Asian study population or the study population as a whole, but did improve survival rates in non-Asian patients with diffuse or distal tumors (***Van Cutsem et al: JCO 2012;30:2119-2127***).

In this RAINBOW subanalysis reported at the ESMO meeting, the efficacy and safety of ramucirumab, a vascular endothelial growth factor receptor-2 antagonist, were consistent with the overall study population results, said Eric Van Cutsem, MD, PhD, Professor of Internal Medicine at the University of Leuven and Head of the Digestive Oncology Unit at University Hospital Gasthuisberg in Belgium, first author of this study, and second author of the paper presented at the GI Cancers Symposium.

"Ramucirumab plus paclitaxel should be considered as a new standard in second-line treatment for advanced gastric cancer," he said.

> The results of the subanalysis had been eagerly awaited because some trials have shown significantly different outcomes between patients from Asian and Western countries.

Regional Differences at Baseline and in Outcome

He acknowledged that the goal of RAINBOW was not to formally compare Western versus Asian patients, but the subanalysis did show some small differences in patient outcomes between the entire RAINBOW cohort and patients in Region 1, comprising Europe (including Israel), Australia, and the United States.

Overall survival for all RAINBOW patients was a median of 9.6 months for the drug combination versus 7.4 months for paclitaxel alone, compared with 8.6 months versus 5.9 months, respectively, for the Western countries of Region 1.

And the objective response rates for all RAINBOW patients was 27.9 percent for the drug combination versus 16.1 percent for paclitaxel alone, compared with 26.8 percent versus 13.0 percent, respectively, for Region 1.

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ERIC VAN CUTSEM, MD, PhD: "We expect that the authorities will also approve the combination of paclitaxel plus ramucirumab, based on the RAINBOW study—That's an important breakthrough in second-line treatment."

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that maintenance therapy with bevacizumab alone is non-inferior to a fluoroupyrimidine-bevacizumab regimen, and that no active maintenance is inferior to either active regimen (***Abstract O-0027***).

Maintenance therapy for patients with metastatic colorectal cancer using fluoroupyrimidine plus bevacizumab after induction is a widely accepted standard, noted Dirk Arnold, MD, Medical Director of the Hubertus Wald Tumor Center, University Cancer Center Hamburg, Germany, who reported the trial that randomly assigned 473 patients to maintenance with fluoroupyrimidine-bevacizumab versus bevacizumab alone versus no maintenance, after a six-month induction with a fluoroupyrimidine-oxaliplatin-bevacizumab regimen.

"Progression-free survival after induction is better with active treatment—either fluoroupyrimidine-bevacizumab or bevacizumab—but preliminary overall survival data show no significant difference between the two active treatments and no treatment," he said.

Time to first progression from the start of induction was 11.7 months for the combination regimen, 10.2 months for bevacizumab alone, and 9.0 months for no maintenance. Overall survival was a median of 23.8 months for fluoroupyrimidine-bevacizumab, 26.2 months for bevacizumab alone, and 23.1 months for no maintenance.

But immediate re-induction with a fluoroupyrimidine-oxaliplatin-bevacizumab regimen after first progression did not work and cannot be recommended, he said. "De-escalation maintenance is confirmed as a standard for most patients, but the lack of a clear overall survival benefit allows individual approaches."

In the future a "moderately active" regimen—either de-escalation or a biologically defined "switch maintenance" strategies–should be evaluated, and that in fact is the next AIO Phase III project, he said.

> How can it be that the 80405 and FIRE-3 trials had different overall survival results with the same treatments?

DIRK ARNOLD, MD, said that in the future a "moderately active" regimen—either de-escalation or a biologically defined "switch maintenance" strategies—should be evaluated, and that in fact is now being planned for the next AIO Phase III project.