

Imclone's Erbitux shows modest benefit in patients with metastatic colorectal cancer, but physicians are hardly impressed

by Kimberly Ha in New York

Imclone's Erbitux has only shown a modest 6-week overall median survival in patients with metastatic colorectal cancer (mCRC), which was unimpressive to physicians interviewed by this news service.

Erbitux, an anti-EGFR monoclonal antibody, is also currently in trials in potential combination with Genentech's Avastin in the first-line treatment setting in patients with mCRC.

In response to suggestions that Imclone's ongoing CAIRO II trials may be met with potential failure as Amgen's Vectibix failed last year in combination with Avastin, a spokesperson for Imclone said the CAIRO study and Erbitux are fundamentally different from other previously conducted clinical trials and currently approved medicines. "It would be inappropriate to speculate on the potential outcome of clinical trials," she added.

In Amgen's PAACE trial last year, patients on the Vectibix and Avastin combination with current standard of care reported a faster rate of disease progression and experienced more treatment side-effects.

This may be due to the dual-inhibition of both the VEGF and EGFR pathway, as Genentech's Avastin is a VEG-F receptor and both Imclone's Erbitux and Amgen's Vectibix act on the EGFR pathway.

"We don't have any experience with multiple biologics," said Dr John Cromwell, Associate Professor of Surgery and Chief of Colon & Rectal Surgery at the University of Tennessee Health Science Center in Memphis. Cromwell said the combination of Avastin and Erbitux would also incur high costs from a reimbursement standpoint. "Of course the pricing, but blocking antigenesis, and blocking mitosis, and blocking receptors with other agents. We don't know what the ultimate downside of that will be," said Cromwell.

Dr Stephen Cohen, a colorectal surgeon with the Atlanta Colon & Rectal Surgery, P.A, said with Erbitux 30% of patients can live an additional two more months. The five-year survival rate for patients with mCRC is less than 10%.

Erbitux is currently approved for use only in third-line therapy in patients with mCRC. It is approved for use in combination with irinotecan in the treatment of patients with EGFR-expressing, metastatic colorectal cancer who are refractory to irinotecan-based chemotherapy and for use as a single agent in the treatment of patients with EGFR-expressing, metastatic colorectal cancer who are intolerant to irinotecan-based chemotherapy.

However, due to Erbitux's toxicity profile, the side-effects are "so bad" the decision to receive the drug should depend on the individual. "I don't know that we as physicians can make that decision for the patient. We would all make a different decision," he said.

"Erbitux has only helped shrink tumors, but does not improve overall survival," added Cohen. Even though Erbitux was statistically significant and got approved for mCRC, the clinical relevance was only meager, reporting a 0.9 month PFS improvement, he added.

Personally, Cohen said that he would not take Erbitux. "You can live an extra two months, but you're sick and throwing up in the hospital. I'm not signing up for that."

Patients on Erbitux can get serum sickness and all those other side-effects like nausea and vomiting, for a relatively minimal benefit in survival, he added.

However, in a small group of patients, Erbitux makes a difference because in those patients, the drug shrinks the tumor so that it can be resectable. For example, if the drug got the hepatic metastasis down from 8 cm to 3cm, it would take the tumor from being unresectable to resectable.

"I think there is a group of patients where there is a benefit. How many patients, we don't know," said Cromwell. Patients who are resectable have a 30% 5-yr survival, he added.

A 6-week median improvement for Erbitux is hard to justify with the cost of the drug. "Giving the old drugs that have major side-effects and minor improvements is archaic, so maybe that is what made Erbitux disappointing because it reminds you of that," said Cromwell.

"6-week improvement is not looking too great," he said.

The rash is also a significant issue with patients.

"The problem with chemotherapy is that it's poison. It's designed to kill rapidly dividing cancer cells, including the GI cells," said Cohen.

Imclone's ongoing CAIRO II trials test Erbitux in combination with Avastin and current standard of care. Trial data is expected by 1H08, but interim data has shown the drug has only modest survival benefit and higher grade 3-4 toxicity in patients.

Dr John Mariadason, a cancer researcher whose current work involves examination of how cell-line panels in CRC tumors respond to Erbitux said there are toxicities associated with Vectibix that are not seen with Erbitux. He speculated that it might come down to the difference in patient populations, and differences between individual trials. "I don't have a good reason why one is toxic and another isn't," added Mariadason.

Dr Alan Venook, a renowned expert in colorectal and liver cancers at UCSF Medical Center, said the median survival for advanced colorectal cancer (CRC) is 22-24 months, and is dependent on the patterns of care in different parts of the world.

As a clinician, Venook was "hardly impressed with 6 week improvement."