They found that 49 percent of such patients who got both drugs survived five years, compared with 37 percent of such patients who got no drug treatment after surgery. They detail their findings in the October JOURNAL OF CLINICAL ONCOLOGY.

Preliminary results from a second study confirm those findings. Moertel, who also directed this study of 1,296 colon cancer patients, says he won't release full details until the results are formally published. He did reveal at the press conference, however, that the postsurgical combination treatment reduced the death rate by at least one-third for Dukes' C patients.

So far, Moertel says, the larger study shows no clear benefit from the double drug treatment for people with Dukes' B colon cancer, in which the cancer has not spread past the colon wall. "We don't know the best way to treat these patients yet," admits Michael A. Friedman of NCI. Further research may show they do benefit from the combination regimen, Moertel says.

NCI officials who reviewed data from both studies recommend that physicians treating patients with Dukes' C colon cancer consider postsurgical treatment with levamisole and 5-fluorouracil. Levamisole, commonly used in the United States to kill worms in animals, is not federally approved for human use. NCI advises physicians to enroll Dukes' C patients in research trials offering the experimental treatment. For those who can't get into a clinical trial, Janssen Pharmaceutica, Inc., a subsidiary of Johnson & Johnson, will provide levamisole to NCI free for distribution through physicians. This week, NCI mailed cancer specialists a clinical alert detailing the treatment advance.

Scientists don't understand how the two drugs work together, but they speculate that levamisole stimulates the immune system and somehow interacts with 5-fluorouracil to destroy cancer cells. Moertel says his team initially tried the double drug experiment in a "desperate search" for an effective chemical weapon against colon cancer. The second leading cause of cancer deaths in the United States, colon cancer kills nearly half those who get it.

Prior to Moertel's studies, small-scale European studies had suggested the drug combination showed activity against colon cancer. But because levamisole has a checkered history — showing early promise as an anticancer agent but until now failing the test of confirmation — Moertel expressed surprise at his group's results. NCI officials say the two new studies, taken together, yield strong evidence that the drug combination helps keep Dukes' C colon cancer patients alive longer than any other treatment tested. "We've never had this much data showing this consistent a benefit," Friedman notes. — *K.A. Fackelmann*

Tracing living signs of ancient life forms

Like cosmologists who construct speculative models of the early universe, some chemists and molecular biologists build intellectual models of ancient life. With a harvest of biochemical clues from contemporary cells and bacteria, three such researchers have assembled a theoretical model of what they call a "breakthrough organism." This archaic life form, they argue, stood on the evolutionary brink between even earlier organisms, which got by without genetically encoded proteins, and all modern organisms, whose existence rests on such proteins.

"We are attempting to reconstruct an ancient dinosaur using the few bones that are left to us," says molecular biologist Andrew D. Ellington of Massachusetts General Hospital in Boston. Those bones take the form of biochemical "fossils," some originating more than 3 billion years ago, that have survived as shadowy vestiges in modern organisms. Ellington compares the task to examining a palimpsest — a parchment inscribed more than once — with the previous writing only partially erased and still somewhat legible.

In the September PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES (Vol. 86, No. 18), Ellington and chemists Steven A. Benner and Andreas Tauer of the Swiss Federal Institute of Technology in Zurich describe their partial reconstruction of ancient life.

They assume life on Earth has passed through three phases, beginning with a so-called "RNA world" in which RNA-based genes within cell-like systems coded for catalytic forms of RNA — not of proteins — to do most metabolic chores. In the next phase, breakthrough organisms — still relying on RNA-based catalysts — started to evolve the biochemical machinery for translating DNA-based genetic code into catalytic proteins (enzymes). The third, ongoing phase began with the so-called "progenote," a protein-run organism that many biologists believe was the most recent common ancestor of all modern forms of life. Although many scientists think the evidence is strong for the first and third phases of this scenario, some have passionate doubts regarding the second.

As a first step toward modeling their breakthrough organism, the researchers reconstructed some of the biochemical features of the progenote. To do so, they analyzed the biochemical personalities of the progenote's own descendants — today's archaebacteria and eubacteria (the two kingdoms of bacteria) and the eukaryotes (organisms whose cells have defined nuclei), which include animals and plants. The team assigned to the progenote specific traits common to members of all three lineages and unlikely to have evolved relatively recently.

Because this exercise left the scientists with a single ancestral line, the progenote, they could no longer use the same common-trait tactic to peer farther back to pre-progenote organisms. For reconstructing their breakthrough organism from the progenote, they turned to a set of chemical criteria derived from assumptions about the RNA world, findings from decades of biochemical experimentation, and logical criteria regarding evolutionary mechanisms on the molecular scale.

The result: a partial and arguable picture of a breakthrough organism. The scientists suggest this organism appeared sometime more recent than 2.5 billion years ago and may have at one time been a contemporary of its descendant, the progenote. They also suggest the ancient organism probably had a complex metabolism involving RNA-based catalysts, used DNA for storing genetic information, synthesized porphyrin molecules for an energy-generating system fueled by either sunlight or chemicals, and made terpene molecules as its lipid component (for example, as membrane components) instead of the fatty acids now used by most organisms.

As a logical reconstruction guided by chemical and evolutionary plausibility, almost all aspects of the model are open to debate. "This idea of a breakthrough organism I find intellectually offensive," comments biochemist Alan M. Weiner of Yale University. For one thing, he says, talk of a breakthrough creates the impression that protein metabolism entered the evolutionary scene all at once. Weiner also argues that certain RNA structures found in the genomes of many viruses probably reflect ancient life more accurately than do features deduced from chemical and evolutionary assumptions. On the other hand, Frank H. Westheimer, emeritus professor of chemistry at Harvard University, points out that the plurality of theories helps to refine ideas about ancient life and points the way toward experiments.

Ellington and Benner acknowledge the speculative nature of the work. "I actually sit and wonder about events that I could never observe, never even prove, in the sense that I can show it must have happened that way," Ellington told SCIENCE NEWS. Still, Benner says such evolutionary stories can lead to testable questions. "If you have a model of [an ancestral organism], you make predictions about where you expect to find certain metabolic pathways or compounds in modern organisms." In one case, he says, this brand of reasoning has led to the discovery of a naturally occurring RNA compound that appears to have anticancer properties. — *I. Amato*