Experimental drug works in resistant tuberculosis

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*Adding TMC207 made TB cocktail five time more effective

*Cleared TB in 48 percent of patients (Adds quotes, details and background)

By Gene Emery

BOSTON, June 3 (Reuters) - An experimental drug that starves the bacteria responsible for tuberculosis makes conventional therapy five times more effective against drug-resistant TB, doctors reported on Wednesday.

The company-run study found that the Johnson & Johnson (JNJ.N) drug TMC207, if added to a standard cocktail of five other TB medicines, cleared traces of the tuberculosis bacteria in the sputum of 48 percent of the volunteers after eight weeks. Only 9 percent of patients given the five older drugs alone showed that type of improvement.

TMC207 is being billed as the first new tuberculosis drug in 40 years. It works by interfering with the enzyme ATP synthase, which the bacteria need to store energy.

"It starves them. It's like cutting off your food supply," Dr. David McNeeley of Tibotec Inc., the subsidiary of Johnson & Johnson that developed the drug, said in a telephone interview. Other drugs attack TB in different ways.

The only notable side effect was nausea, experienced by 26 percent of volunteers in the TMC207 group, versus 4 percent among those getting the conventional cocktail plus a placebo, they reported in the New England Journal of Medicine.

The test involved 47 people in South Africa with newly diagnosed lung TB that was resistant to two standard drugs, isoniazid and rifampin.

About 1.8 million people die worldwide each year from tuberculosis and a third of the world's population -- 2 billion people -- are infected, according to the World Health Organization.

The WHO says that of 9 million new TB cases annually, about 490,000 are multiple-drug resistant TB or MDR-TB and about 40,000 are extensively drug resistant or XDR-TB.

HARD TO TREAT

Fewer than 3 percent of MDR-TB cases worldwide are being treated according to WHO recommendations.

The bacteria is extremely difficult to treat because it can remain dormant in the body, unresponsive to drugs. That means patients have to take medicine for a long time, and people often stop their therapy, allowing resistance to develop.

"It's like the bacteria are hibernating. They can go for 20 years and then there's a relapse," McNeeley said.

But even hibernating cells need to use some energy, he said. The new drug cuts off this lifeline. "So whether you're actively replicating or sleeping slowly, you strangle to death," he said.

The development of TMC207 represents an important advance in the chemotherapy of tuberculosis," Clifton Barry of the National Institute of Allergy and Infectious Diseases in Bethesda, Maryland, said in a commentary.

It represents "a new class of drugs that increase the therapeutic options for patients who have multidrug-resistant or extensively drug-resistant tuberculosis, for whom treatment options are often sparse, largely ineffective, and often highly toxic," Barry wrote.

McNeeley said another characteristic of the drug is that its effects show up later than conventional TB medicines, whose effectiveness may wane just as TMC207 is starting to have a real impact.

Asked if the drug, if approved, would be cheap enough for widespread use in the sometimes-poor countries where TB is the biggest problem, McNeeley said, "Johnson & Johnson is committed to bringing this out to the people who need it." (Editing by Doina Chiacu and Maggie Fox)