'Skipping' drug marks step forward for muscular dystrophy

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An experimental drug designed to fit a DNA patch in a flawed gene has cleared an important hurdle in tests on boys struck by a tragic muscle-wasting disease, a British study on Monday says.

The condition, Duchenne muscular dystrophy (DMD), occurs among roughly 1 one in 3,500 males.

It occurs because of a deletion in a gene that makes a protein called dystrophin, which helps provide a protective membrane around muscle fibres. Without this skin, muscle fibres become damaged and eventually die.

By they time they are aged eight to 12, boys with DMD become unable to walk and usually face a shortened life expectancy.

In DMD, the problem lies specifically in sections of DNA called exons that, like stepping stones, provide the pathway by which the gene makes dystrophin.

The new drug takes the approach of "exon skipping," or applying a tiny molecular patch over the deletion, so that the gene can produce a shorter but still functional version of the protein.

After successful tests on muscle cells cultured in a lab dish and on mice, the therapy was cautiously tested for safety on 19 ambulatory patients aged five to 15 at hospitals in London and Newcastle.

Seven out the 19 showed a "significant" response, with levels of dystrophin rising to as much as 18 percent of normal levels.

The volunteers, who were treated over 12 weeks, suffered no side effects.

They did not show any major improvement in a standard six-minute walking test, although this was not the goal of the mini-trial.

The drug, called AVI-4658, patches exon 51, which is deleted in about 15 percent of patients with DMD.

"On the basis of our data and recent pre-clinical data, we expect that extended administration of AVI-4658 at doses of 10 mg/kilo or higher will result in sufficient dystrophin expression to have a positive effect on the prevention of muscle degenation," says the study, which is published online by *The* Lancet.

The next step is to test it for efficacy, say the researchers, led by Francesco Muntoni of the Dubowitz Neuromuscular Centre at UCL Institute of Child Health, London.