

Results from a Roche Phase 1 trial of RG7916 in healthy individuals

Key points

- RG7916 is an investigational medicine in development for people with spinal muscular atrophy (SMA). RG7916 is now being studied in clinical trials in people with SMA.
- RG7916 is designed to help the *SMN2* gene produce more SMN protein. People with SMA have reduced levels of SMN protein.
- This Phase 1 clinical trial began on 7 January 2016 and lasted until 4 August 2016. The trial investigated RG7916 in healthy volunteers and found:
 - RG7916 was well tolerated in healthy people. The most frequent side effects were headache and diarrhoea
 - RG7916 increased *SMN2* mRNA in healthy people compared with the start of the study. mRNA conveys information from a gene to make proteins.

What was this clinical trial?

In this Phase 1 clinical trial¹, 40 healthy adult male volunteers received different doses of RG7916. This was the first time RG7916 had been given to humans. Trials of investigational medicines are usually conducted in healthy people first, before people with diseases. This clinical trial was done to find out how much RG7916 is safe to give and if it has any side effects.

Healthy adult male volunteers were given a single dose of RG7916 (at 4 different doses) or placebo. The first few volunteers received very small dose of RG7916. If the doctors saw no concerning side effects, the next groups received slightly higher doses of RG7916. This was continued up to the highest dose.



Phase 1 clinical trial: An investigational medicine is first given to healthy people to evaluate safety.

What were the side effects?

No safety concerns related to RG7916 were seen during this trial. There were no serious drug-related side effects and no one stopped the trial due to RG7916-related side effects.² The most frequent side effects were headache and diarrhoea.

What else did this clinical trial show?

RG7916 was designed to help the *SMN2* gene produce more SMN protein. People with SMA have reduced levels of SMN protein. The template for making SMN protein is carried on molecules called mRNA. In this clinical trial, RG7916 both increased the amount of full-length *SMN2* mRNA and decreased the amount of the shorter, unstable *SMN2* mRNA in the blood of the healthy volunteers. This effect was dependent on the dose of RG7916, with higher doses of RG7916 causing greater increases in the amount of the full-length *SMN2* mRNA.²

As RG7916 is taken by mouth (or G-tube when necessary), food may influence how it works. However, when RG7916 was given with or without food, there was no relevant change to how the body processed RG7916. This means RG7916 can be taken at any time of day, either with or without food.²

What does this mean for people with SMA?

The results of this Phase 1 clinical trial in healthy people support the further development of RG7916 for people with SMA. Three trials, called **FIREFISH**,³ **SUNFISH**⁴ and **JEWELFISH**⁵ are currently recruiting. For more information, please visit: <http://www.roche-sma-clinicaltrials.com>.

SMA background

SMA is caused by reduced levels of functional SMN (Survival of Motor Neuron) protein. Recently, more and more evidence points to SMA being a whole-body disease, because SMN protein seems to be important for lots of different cells in the body, not just for motor neurons.

In healthy individuals, the *SMN1* gene produces full-length *SMN1* mRNA, which serves as the template for making SMN protein.

In people with SMA, due to loss of the *SMN1* gene, SMN protein is only produced by a related gene called *SMN2*. However, the *SMN2* gene mainly produces *SMN2* mRNA that is too short. Thus, only a small amount of functional SMN protein is formed.

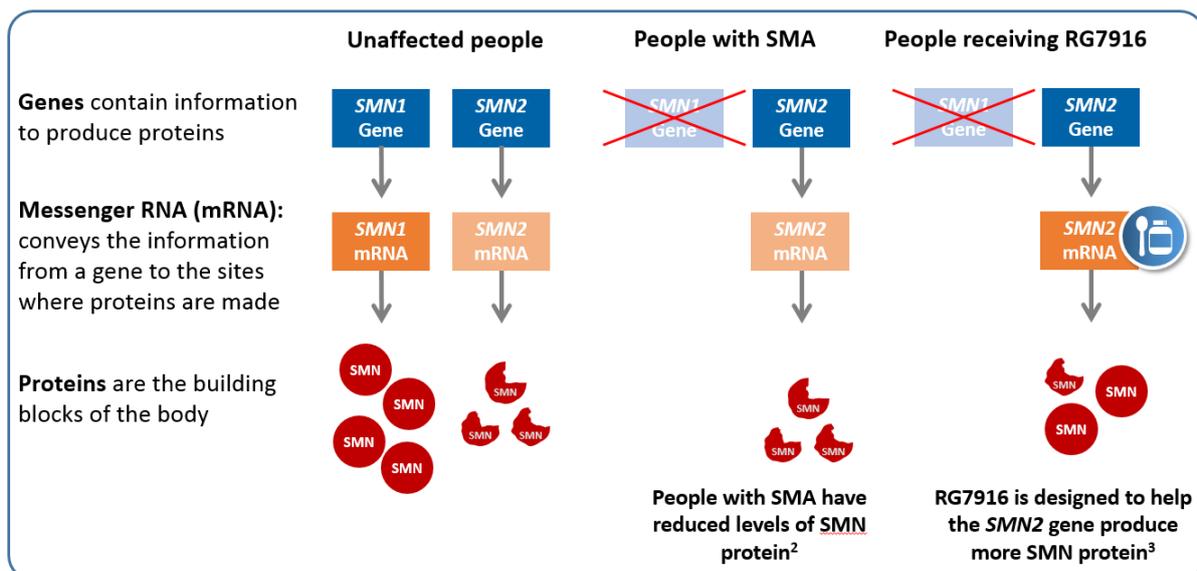
People have different numbers of *SMN2* genes. The more copies of the *SMN2* gene a person has, the less severe their SMA tends to be, as more functional SMN protein can be formed.⁶

RG7916 background

RG7916 is designed to increase the amount of full-length *SMN2* mRNA produced, with the aim of increasing the amount of functional SMN protein (see figure below).

Roche/Genentech, PTC Therapeutics and the SMA Foundation are collaborating to develop RG7916, an investigational medicine for SMA (spinal muscular atrophy) that is taken by mouth (or g-tube when necessary).

RG7916 is widely distributed throughout the body, not just in the central nervous system (CNS), and is small enough to pass from the blood into the brain.⁷



References

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