A new Norwegian-made anti-prostate cancer drug shows «unambiguously positive results». Time to open the champagne?

A stock-market upstart to prolong your life?

On Monday 6 June, the Norwegian biotechnology company Algeta announced the happy news. Trials of the drug Alpharadin on more than 900 patients suffering from prostate cancer had produced «unambiguously positive results». The study, which had been planned to run until 2012, was therefore terminated before the intended time (1). «We are proud and happy,» stated Thomas Ramdahl, Chief Technology Officer, to the *Aftenposten* daily. «This is very exciting for us, and not least for cancer patients who can be helped. They can live longer, and also avoid strong side effects,» he stated. «The market potential is of blockbuster format.» (1). The news triggered a stock-market hike of 37 per cent at Oslo Stock Exchange the same day. When the stock exchange closed, Algeta was valued at NOK 7.91 billion, and the eight leaders of the company could rejoice over options that would have paid profits of NOK 320 million (1). The next day, the newspapers bore headlines such as *Stock-market upstart prolongs your life* (Dagens Næringsliv) and *Filthy rich from cancer drug* (Aftenposten).

Three weeks later, the *Aftenposten* daily brought a five-page feature article on the case (2). The journalists reported from the decisive meeting in Chicago on 3 June 2011. «Thomas Ramdahl and Gillies O'Bryan-Tear from the Norwegian pharmaceutical company Algeta are sitting in a corridor. More than fifteen years of work and investments of NOK one billion have brought them to this corridor. And to a decision to be made behind closed doors. The hours pass as they are waiting. But they have already waited for many years. For three years, a total of 922 patients in 140 hospitals in 19 countries have taken part in the trials of the company's drug Alpharadin, a drug against prostate cancer that has spread to the skeleton. Just the last phase of the trials has cost half a billion NOK. This afternoon in Chicago, an expert committee of five medical academics will respond to whether the effects have been sufficiently documented. As Chief Technology Officer and Chief Medical Officer, they are very aware of what an affirmative answer will mean for the Norwegian company. The committee chairman opens the door, and they are invited in. Three of the experts are present in the room; the other two are on video link from London. The message from the experts is read aloud: The results stand up. The drug is effective and prolongs the life of terminally ill patients suffering from prostate cancer. You can terminate the trials one year ahead of schedule. Ramdahl quickly calls Andrew Kay, the company director, and then just as quickly cuts short his stay in Chicago, where he had only just arrived, and returns to Norway.»

The dramaturgy is cinematic, the conclusion is crystal clear – the stage is set for a stock-market bonanza! To be sure, Professor Sophie D. Fosså stated to the newspaper that she was not as confident about the new drug as Algeta. «I'm still sceptical about these results. I don't want to disparage the drug, but I just don't understand it,» Fosså said (2).

While those who received the placebo during the trials lived for 11.2 months (median value), the Alpharadin users survived for 14 months. In other words, the drug would prolong median life expectancy by a little less than three months. This may appear modest, but to the patient each additional day is precious. Most of the progress made in medical research is of this kind – taking small steps that cumulatively and over years produce larger effects. In addition, the researchers emphasised that the results could be improved «in several ways»: By identifying patients who are more susceptible to the treatment, starting treatment at an earlier stage in the course of the disease, and by combining Alpharadin with other drugs (1). In principle, Alpharadin can also be effective against other forms of cancer.

What is most important to the patients is the hope of a longer life and fewer side effects. Nor is it a daily occurrence to see Norwegian biotechnology companies enjoying a scientific and commercial success in this order of magnitude. But how could this really be achieved? According to the newspaper report, an expert committee of five medical academics had assessed the results and unanimously, we infer, come to the conclusion that the results stood up. Moreover, they stood up to such an extent that the study was discontinued ahead of schedule because the results were «so convincing that it is no longer defensible to give placebo to the participants in the trial» (3).

The Algeta case is not unique. It appears to be increasingly common to see results from ongoing studies published by way of press releases from the companies. The traditional way of doing this is for the researchers to publish scientific articles. Then the manuscripts undergo comprehensive scientific scrutiny and editorial processing. Researchers often have to describe their findings in more restrained terms, and the conclusions are toned down and sometimes even reversed. Scientific articles are scrutinised by researchers and other professionals, which most often sparks further debate and discussion in the journals' «Letters to the editor» column. Findings from one study usually need to be corroborated by other studies before they can be assumed to have general validity. The use of bevacizumab (Avastin) for the treatment of breast cancer is a recent example. The drug was registered following a single persuasive study showing a prolonged effect on the surrogate marker progression-free survival. Later studies, however, have shown smaller benefits for such survival, and none for overall survival. The Food and Drug Administration (FDA) is likely to withdraw its approval (4). Scientific publication procedures may appear unnecessarily laborious and time-consuming, which accords badly with the hectic pace of stock markets. This is not the problem, however. Stock exchanges can live well with rumours and insufficient information, whereas evidence-based medicine cannot. There are many ways in which science can be disseminated and debated. Press releases and stock-market quotations are not among them.

In late August 2011 it was reported that Algeta had seen a further stock-exchange hike, because Alpharadin had been granted a so-called fast-track procedure by the FDA. Thus, the drug may be ready for sale in the US in early 2012 (5). Of course we will hope that the «unambiguously positive results» from Alpharadin prove correct for patients, researchers and investors. Time will tell, however – after the results are published.

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