Competence Center of SAKK
Effingerstrasse 33
CH-3008 Bern

Eribulin as first-line chemotherapy in advanced breast cancer for patients over 70 years (trial SAKK 25/14)

Information on the results of the trial

We report below on the key results of the trial «Eribulin as first-line chemotherapy in advanced breast cancer for patients over 70 years».

Trials are very important in enabling progress to be made in medicine and science. If you agree to be treated in the context of a clinical trial, you make a significant contribution to this end. By doing so, you help to answer health-related questions of other patients, to develop new treatments, or to improve existing ones. The Swiss Group for Clinical Cancer Research (SAKK) would like to express its sincere thanks for your participation and commitment.

1. Name of the trial

The original title of the trial is:

Eribulin as 1st line treatment in elderly patients ≥ 70 years with advanced breast cancer: a multicenter phase II trial.

Explanation of terms:

- *Eribulin* (Halaven®) is a drug that inhibits cell division and prevents the growth of cancer cells (chemotherapy agent).
- *"First-line"* in this context means that this is the first treatment offered for advanced disease.
- *"Chemotherapy"*: treatment with drugs that inhibit the growth of, or kill, cancer cells (in this case eribulin).
- *"Advanced breast cancer"* means that the cancer has spread so much in the breast that it is no longer operable, or that the cancer has formed metastases (secondaries) in other organs.
- *"Multicenter"* means that the trial was carried out in several hospitals.
- *"Phase II"*: The efficacy and tolerability of the investigated active substance were investigated in a relatively small number of patients.

Further explanations of technical terms can be found in the glossary at the end of this document.

2. Organization of the trial

The Swiss Group for Clinical Cancer Research (SAKK) planned and executed this trial. For more information about SAKK visit the website: www.sakk.ch.

3. General information about the trial

Various options exist for treating advanced breast cancer. One option is chemotherapy. However, many drugs used in chemotherapy cause serious side effects, particularly in elderly patients. Researchers are therefore looking for new chemotherapy agents that are both effective and better tolerated. Previous trials have shown that the active substance eribulin can trigger fewer side effects compared to other chemotherapy drugs, which is why the treatment with eribulin was investigated in this trial.

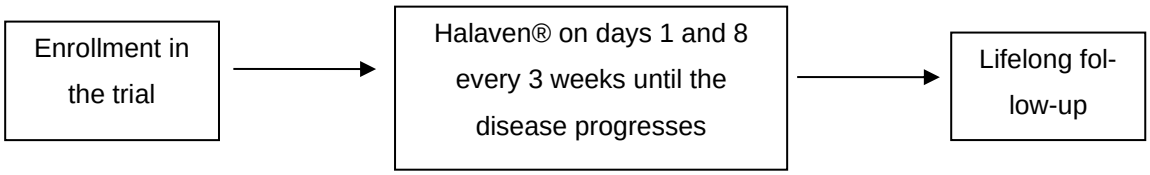
Eribulin is already approved in Switzerland for the treatment of advanced breast cancer. However, so far eribulin has only been used after previous chemotherapy, i.e.in the later stage of the disease. In this trial, by contrast, eribulin was administered as the first chemotherapy in advanced breast cancer (first-line chemotherapy). Not much is known about how eribulin works in women over 70, because most trials with eribulin tended to recruit younger patients. In this trial we wanted to find out how effective and well tolerated eribulin is in older patients.

4. Participants

77 women in 18 treatment sites in Switzerland took part in the trial. The patients were at least 70 years old with advanced breast cancer, and all were scheduled to receive chemotherapy.

5. Course of trial treatment

All participants received treatment with eribulin at a dosage of 1.1 mg per square meter of body surface area (mg/m^2). In previous trials, the patients had received a higher dose of 1.4 mg/m^2. The eribulin was administered to each participant as an infusion over 2–5 minutes. The treatments were given on day 1 and day 8 of a three-week period; these three weeks corresponded to a chemotherapy cycle.



The treatment with eribulin was continued either until the disease progressed or the patient was no longer able to tolerate the treatment. After completing the trial treatment, the patients were followed up at regular intervals. The trial lasted for around four years from the enrollment of the first participant until the last participant had completed the treatment.

6. Factors examined

The trial investigated various factor and aims that were to be achieved with the trial treatment, including:

- *Disease control: (no progression of the disease – in other words the treatment has a positive effect):* In how many patients does the tumor regress or at least remain stable for at least 24 weeks?
- *Response of the disease to the treatment*: In how many patients who benefited from the treatment does the disease regress completely or partially?
- *Safety and tolerability of the treatment:* What side effects does the treatment have and how intense are they? How many patients discontinue the treatment because of side effects?

7. Results of the trial

7.1 Disease control

Disease control was achieved in 31 of the 77 participants (40%). Before the start of the trial, and on the basis of the results of other trials, the researchers had expected that the treatment would produce disease control in 55% of the participants, which means that the results of this trial did not meet the expectations.

7.2 Response of the disease to the treatment

In the 31 participants who responded well to the treatment, the effect was as follows:

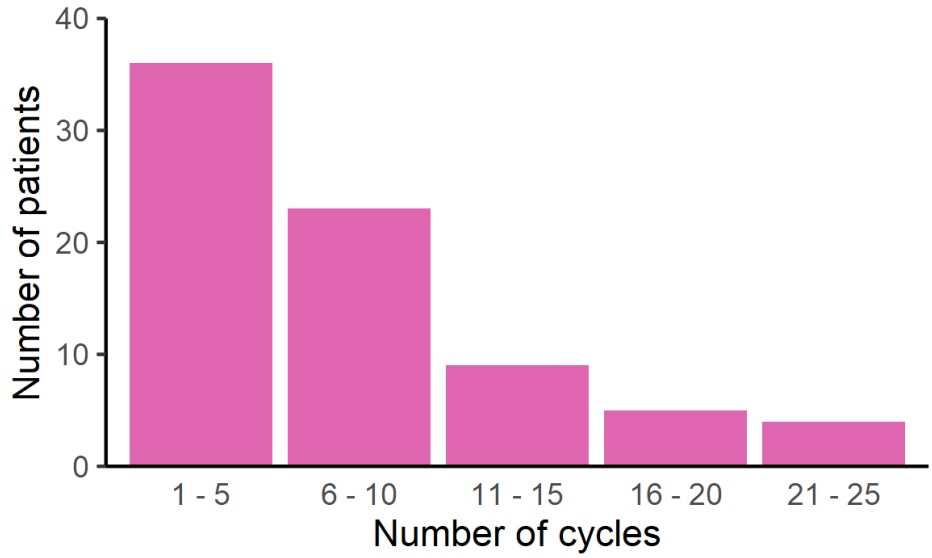
- In 2 of the 31 (6%), the tumor regressed completely temporarily.
- In 15 of the 31 (48%), the size of the tumor declined.
- In 5 of the 31 (16%), the disease remained stable for at least 24 weeks.
- In 9 of the 31 (29%), the disease remained stable for longer than 24 weeks.

When these results are viewed in relation to all participants in the trial, the effect was as follows:

- In 2 of the 77 (3%), the tumor regressed completely temporarily.
- In 15 of the 77 (19%) the size of the tumor declined.
- In 5 of the 77 (6%), the disease remained stable for at least 24 weeks.
- In 9 of the 77 (12%), the disease remained stable for longer than 24 weeks.
- In 46 of the 77 (60%), the treatment had no effect.

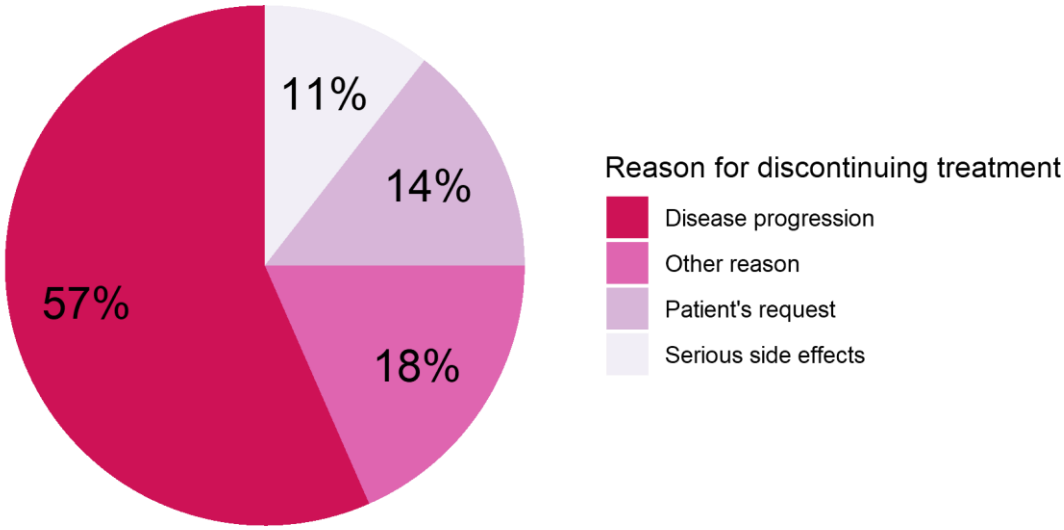
7.3 Duration of treatment

On average, the participants received the treatment for 7.7 cycles of 3 weeks each, i.e.for a total of 23 weeks. Nine of the 77 participants (12%) received 15 or more cycles, which means that their treatment lasted for 45 weeks or even longer. These patients tolerated the treatment very well.



The most common reasons for discontinuation of treatment were as follows:

- Progression of the disease (57%),
- Patient's request (14%),
- Serious side effects (11%).



7.4 Side effects

48 of the 77 participants (62%) experienced at least one serious or life-threatening side effect, although these side effects responded well to treatment in most cases.

- The most common side effect was neutropenia, i.e. a reduction in the number of white blood cells. Neutropenia can increase the risk of infectious diseases. Seven of the 77 participants (10%) experienced severe neutropenia, while 9 (12%) even had life-threatening neutropenia.
- In 27 of the 77 participants (35%), the dosage of eribulin had to be reduced during the trial, in most cases due to neutropenia.
- In 17 of the 77 participants (23%), the nerves were damaged, resulting in abnormal sensations in the hands and feet, including tingling, burning, or prickling (neuropathy). These symptoms were mild in most cases, but three of the patients discontinued the treatment as a result.

Especially vulnerable trial participants:
Vulnerable refers to someone who, due to previous illnesses, advanced age, or a poor state of health, is particularly susceptible to a worsening of disease or the occurrence of side effects of treatment.
23 of the 77 participants (30%) in this trial were considered to be vulnerable. In addition to the breast cancer, 47 participants (62%) were also suffering from other serious illnesses. However, disease control was achieved with the treatment just as frequently in the vulnerable women as in the other patients.

8. Significance of the trial results

The trial showed the following:

- A reduced starting dose of 1.1 mg/m^2 eribulin can safely be employed, including in older patients and over a prolonged period.
- Disease control was achieved in 31 of the 77 participants (40%) – that is fewer than had been hoped on the basis of other trial results.
- The dosage of eribulin cannot be reduced below 1.1 mg/m^2 since the drug is no longer effective at this level. In the trial, eribulin was no longer effective in those participants whose dosage had to be reduced to less than 1.1 mg/m^2.

Eribulin caused fewer cases of neuropathy in this trial than other chemotherapy drugs, particularly the "taxanes". During treatment with taxanes, more patients have to discontinue the treatment due to neuropathy than those who are treated with eribulin.

Whether a reduced dose of eribulin is the ideal treatment option for elderly patients cannot be concluded on the basis of these trial results. Further trials would be needed in order to answer this question. Thanks to this trial, we now know more about how eribulin works in older patients with advanced breast cancer.

These findings are important for future patients with this disease and their treating doctors. They now have better information to help them make decisions about treatment.

Annex: Glossar

- **Chemotherapy:** Treatment with drugs that inhibit the growth of, or kill, cancer cells.
- **Eribulin:** Drug that inhibits cell division and prevents the growth of cancer cells (chemotherapy agent).
- **First-line treatment:** Treatment that is the best option in a particular situation**.**
- **Disease control:** Disease control is said to occur when the disease regresses or remains stable.
- **Multicenter:** In many sites (in this case hospitals).
- **Neuropathy:** Damage to nerves that can lead to abnormal sensations in the hands and feet, for example tingling, burning, or prickling**.**
- **Neutropenia:** Reduction in the number of white blood cells.
- **Phase II trial:** Trial investigating the safety and efficacy of a treatment in a relatively small number of people. Differing dosages are also often investigated in a phase II trial.
- **Vulnerable:** from the Latin for "wounding"; in medicine, vulnerable means "susceptible" – for example, that someone who, due to previous illnesses or advanced age, is particularly susceptible to the occurrence of side effects of a treatment.