Constant cooling
for the prevention or treatment of CIPN with Hilotherm ChemoCare® (HILOTHERAPY®)

HILOTHERM®

ChemoCare CIPN / CIA Gerät

Aufbau und Inbetriebnahme

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Düsseldorf
Patient representative, Chairman ISI e.V.

CIPN (Chemotherapy- induced polyneuropathy) – the problem is well known.

High incidence rates CIPN

Jones et al, JCO 2005: **60% CIPN**; 4,1% ≥ Grade 3 - 4

Seidman et al, JCO 2008: **33% grade 2-3** bei q3w Taxol; **51% grade 2-3 bei q1w Paclitaxel**

Sparano JA et al., N Engl J Med 2008: **27% ≥ grade 2** bei Paclitaxel weekly

Eckhoff L, Knoop AS et al 2013: Breast Cancer Res Treat: **16-23% ≥ grade 2**;

Goreishi Z et al. 2018: BMC Cancer 18: **42% CIPN** – icidence rate

The medical consequences:

- Due to CIPN ≥ grade 2 we see treatment delay and dose reductions
- sometimes permanent treatment discontinuation necessary
- That means decrease of healthy outcome and worsening of longterm prognosis

CIPN persists for years: Eckhoff L, Knoop AS et al 2013: Breast Cancer Res Treat: **persistent CIPN for 1-3 years in 34% of patients;**

Hershman DL, Lacchetti C, Dworkin RH, et al.; J Clin Oncol 2014: **67%-80%** persisting CIPN after one year

Ewertz et al.: CIPN, induced by taxanes, persists for several years in about **30% of patients**

What is the consequence of all these facts? What have oncologists to do?

We need to avoid CIPN grade 2 and 3!

- to make shure that patients can get their oncological therapies without dose reduction
- We should focuse of the life quality for our cancer survivors

Hilotherm ChemoCare: The effective approach to avoid side effects in oncological therapies

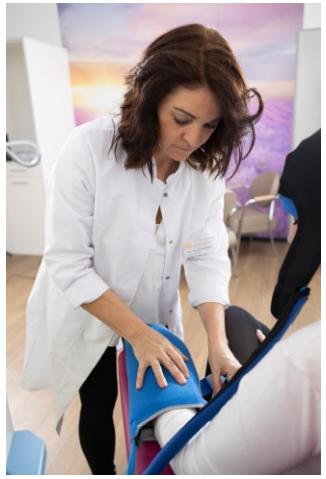
Hilotherm ChemoCare® (HILOTHERAPY®)

- Hilotherm device cool water to a specific temperature and pump it round a closed circuit with cuffs fitted to the part of the body requiring treatment
- The device not ice-based and can be used safely for hours at a time without intervention
- **Hilotherm ChemoCare® devices** work by cooling hands and feet for 30 mins before, during and 30-60 mins after chemotherapy at a constant controlled temperature
- Controlled cooling reduces the amount of chemotherapeutic agents reaching the extremities (vasoconstriction) and being excreted from the sweat glands in hands and feet – thus we prevent chemotherapy induced polyneuropathy **(CIPN), hand-foot syndrome and nail toxicities**
- Treatment is most effective when used from the start of the first chemotherapy treatment **as a preventive measure**
- If patient has already developed symptoms it **will help to stop progression and improve symptoms** but the earlier it is used, the more effective this will be

Hilotherm ChemoCare® (2. generation) – practical use

The application is simple and does not involve much additional effort for the nursing staff

- Gloves / slippers fitted to hands and feet of patient
- Cooling temperature at 15℃ -17°C as standard
- If patient is uncomfortable with treatment at 15℃ this can be increased up to 16℃ or 17℃ or even more
- Cooling for 30 minutes prior, during and 30 minutes post chemotherapy treatment
- If patient has any symptoms of CIPN the post chemotherapy cooling is increased to 60 minutes



Dr. Trudi Schaper pilotstudy (1. generation of gloves / slippers)

Efficiency of controlled cryotherapy in prevention of chemotherapy induced peripheral neuropathy

- 151 breast cancer patients Oct 2017-Feb 2019
- 30 mins prior, during, 60 mins post chemotherapy – prophylactic use
- 10-12ºC (start at 10 increase on patient preference)

Highest grade of side effects during treatment:

93.4% (n =141) of the patients grade 0-1 CIPN

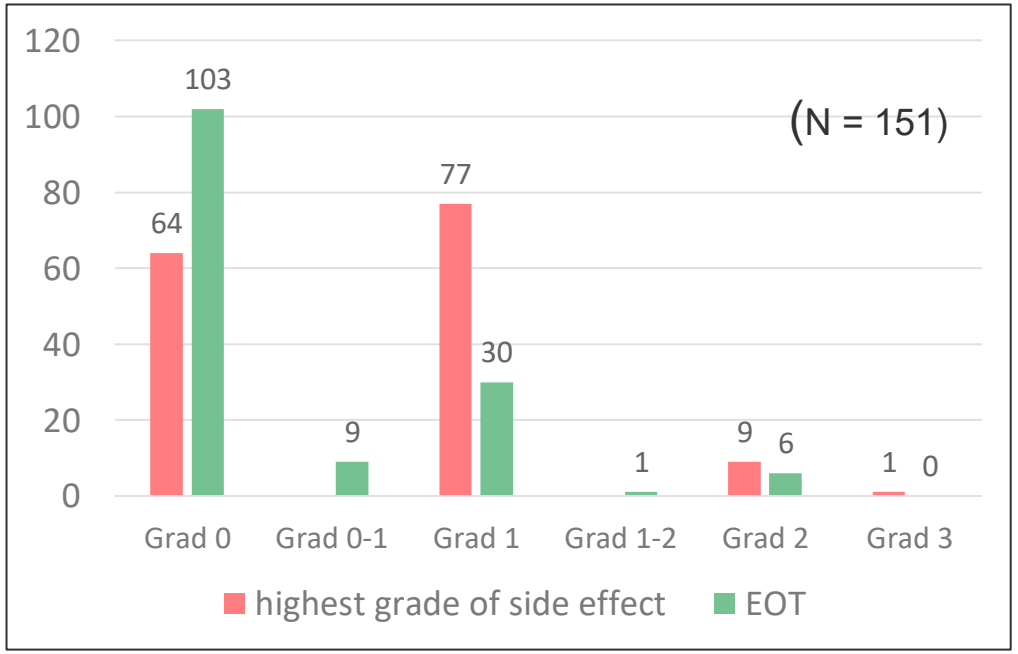
5.96% (n=9) grade 2; 0.66% (n=1) grade 3

EOT (4 wks after treatment) **no grade 3,**

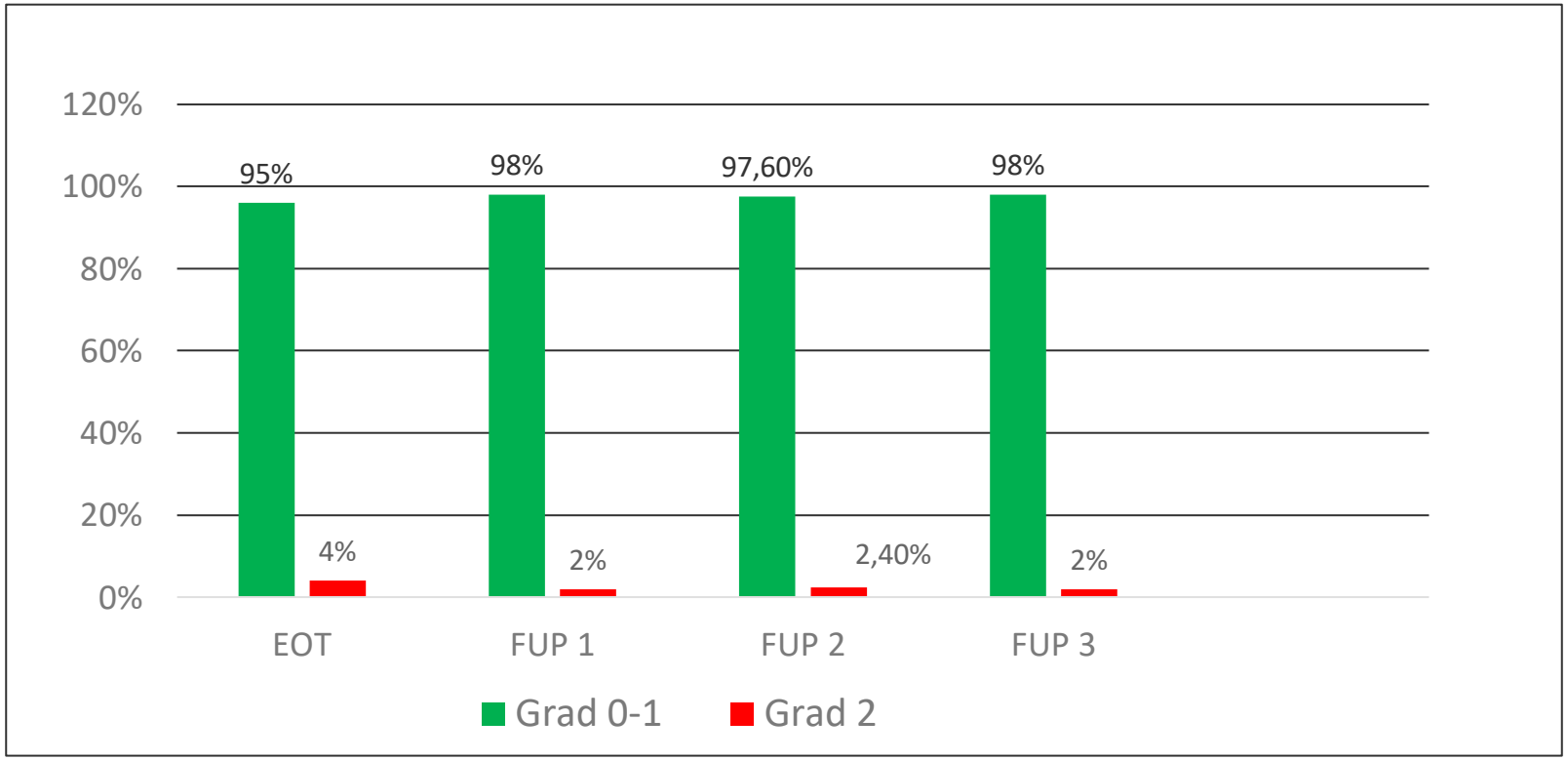
95,35% (n=142) 0-1; 4,6% (n=7)grade 2;

1. generation

Skin surface was cooled to approx. **25° C**

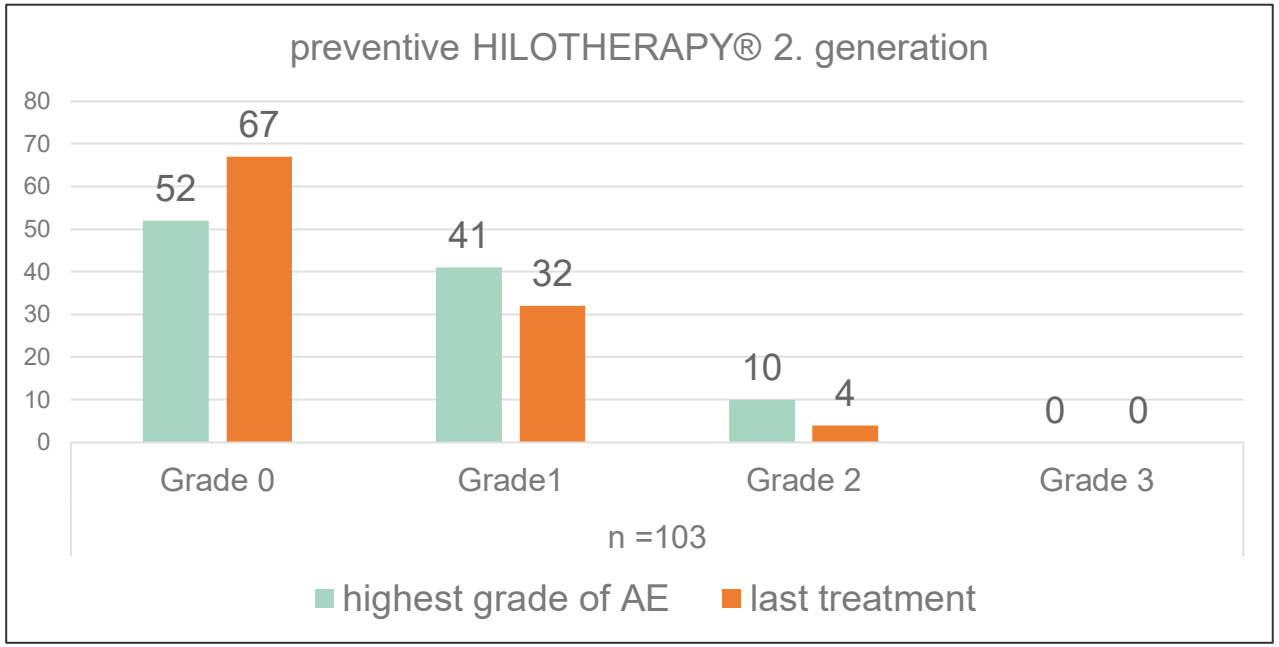


Long-term results preventive Hilotherapy®



EOT (n = 149):
4 weeks after treatment
FUP 1 (n =146):
4 mths after treatment
FUP 2 (n = 124):
7 mths after treatment
FUP 3 (n= 93):
10 mths after treatment

Dr. Athina Kostara GynOnco Düsseldof & Dr. Trudi Schaper data collection in process (2. generation of cuffs)



2. generation

Skin surface is cooled down to about 15-17 ° C

	2. generation Hilotherapy® 15-17°C			(n=103)
	Grade 0-1		Grade 2	Grade 3
hGAE	90,3%		9,7%	0
Last treatment	**96 %**		3,8%	0

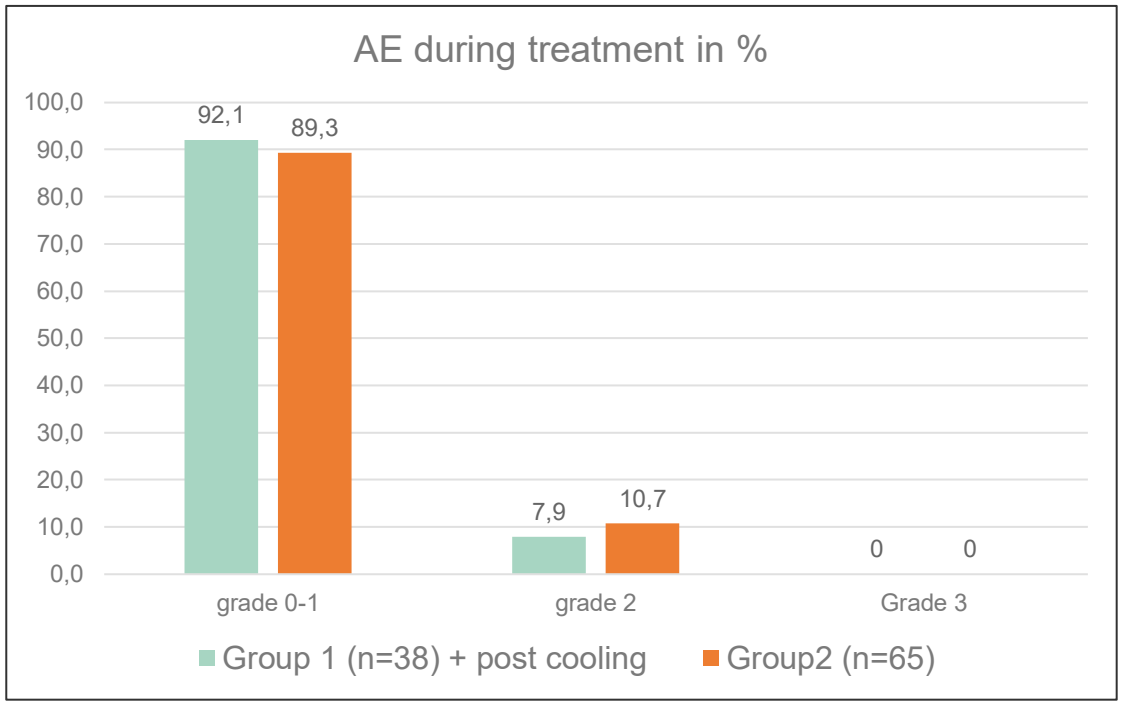
Comparison prophylactic cooling (HILOTHERAPY®)

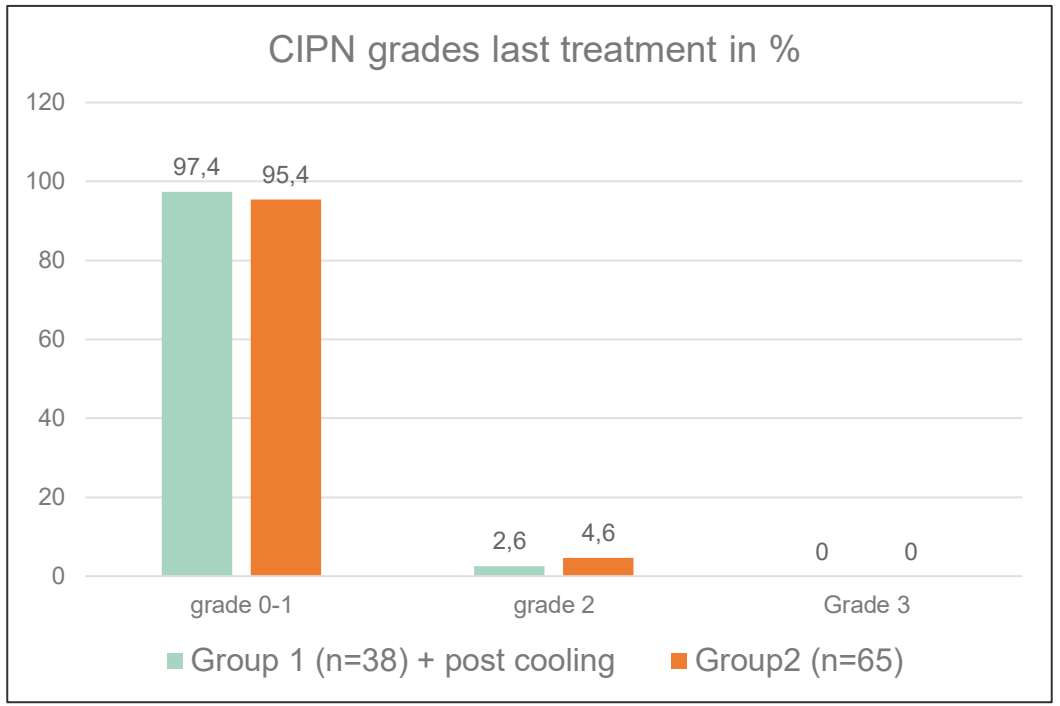
	without Hilotherapy®	gloves / slippers **1. generation** 10-12°C HILOTHERAPY last treatment	gloves / slippers **2. generation** 15-17°C HILOTHERAPY last treatment
Grade 0	9.5%	52,3%	**65%**
Grade 1	45.24%	40,4%	**31%**
Grade 2	40,5%	6,6%	4%
Grade 3	5,3%	0,6%	**0%**

With constant cooling (Hilotherapy) **93 – 96% of the patients remain without** CIPN symptoms > grade 1.
2. generation of HILOTHERAPY even more effective as 1.generation.

Current project in Düsseldorf:
Do we need the post-cooling time with the 2.generation of gloves / slippers?

Group1: 30 min pre-cooling – cooling during CTX – 30 min post-cooling
Group2: 30 min pre-cooling – cooling during CTX – **none** post-cooling





No significant differences in the results – new standard in Düsseldorf - **no postcooling time**
95 – 98 % grade 0-1

Other studies

- Gynecological oncology Scheibenberg – Dr Rene Schubert
  Comparison Hilotherm 12°C Vs ice gloves/boots (Posterpresentation 2019)

- Poliambulanza pilot study 2020 – Breast, ovarian & pancreatic cancer patients: Ester Oneda, MD1 et al., *Innovative approach for the prevention of chemotherapy induced peripheral neuropathy in cancer patients: a pilot study with the Hilotherm device, the Poliambulanza hospital experience (2020)*

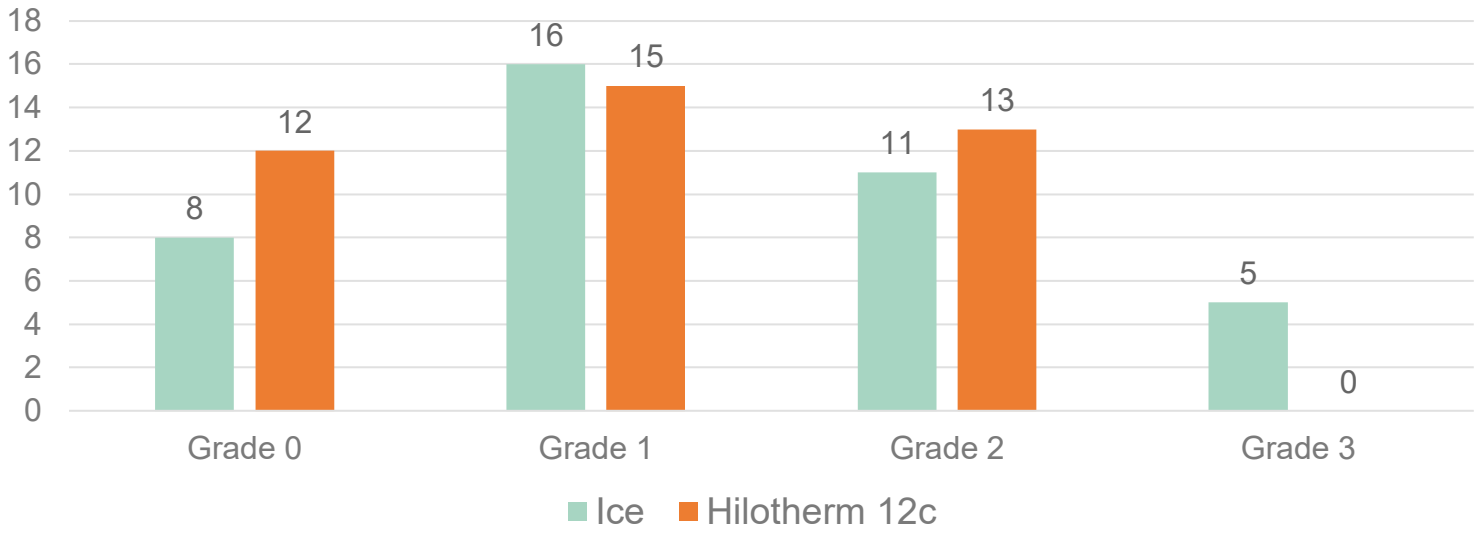
- Poliambulanza study of ovarian cancer patients 2021: Ester Oneda, MD1 et al., Chemotherapy-induced neurotoxicity in the treatment of gynecological cancers: State of art and an innovative approach for prevention

- Belgium Hilotherm vs Ice – Early breast cancer patients (2021): Annemarie Coolbrandt et al. *Preventing taxane-related peripheral neuropathy, pain and nail toxicity: a prospective self-controlled trial comparing hilotherapy with frozen gloves in early breast cancer*

- Belgium, Hilotherm Oxaliplatin (2022): Annemarie Coolbrandt et al. A randomized controlled trial of hand/foot-cooling by hilotherapy to prevent oxaliplatin-related peripheral neuropathy in patients with malignancies of the digestive system

- Questions

Gynecological oncology Scheibenberg – Dr Rene Schubert
Comparison Hilotherm 12℃ Vs ice gloves/boots (Posterpresentation 2019)



- 80 patients
- 40 HilothermChemoCare versus 40 ice gloves/boots
- Hilotherapy® more effective than cooling with ice gloves/boots
- no grade 3 toxicities with HilothermChemoCare

Poliambulanza pilot study

Innovative approach for the prevention of chemotherapy induced peripheral neuropathy in cancer patients: a pilot study with the Hilotherm device, the Poliambulanza hospital experience (2020)

- 64 patients undergoing chemotherapy for breast, gynaecological or pancreatic cancer. 54 finished all cycles at time of publication.
- Patients with weekly PTX, PTX/Carboplatin and nab-PTX/gemcitabine treatment
- Used Common Terminology Criteria for Adverse Events & European Organisation for Research & Treatment of Cancer Quality of Life questionnaire
- Hilotherm chemocare administered at 10ºC for 30 mins prior, during and 60 mins after chemotherapy
- **No patients developed higher than grade 2 CIPN symptoms**

Poliambulanza ovarian cancer study

Chemotherapy-induced neurotoxicity in the treatment of gynaecological cancers: state of art and an innovative approach for prevention (2021)

- Gynaecologic Oncology Group reported approx 20% of ovarian cancer patients treated with a combination of carboplatin & PTX at 175mg/mq every 3 weeks in first line therapy experienced grade 2 or higher neuropathy, and this percentage increased among older patients
- Patients treated at 10ºC for 30 mins prior, during and 60 mins post chemotherapy
- At the end of 6 cycles of chemotherapy:
  - 83.3% grade 0
  - 8.3% grade 1
  - 4.2% > grade 2 (1 patient)
- **Hilotherapy has proven to be a safe, well tolerated and effective method of preventing & treating CIPN**

Belgium Hilotherm vs ice study

Preventing taxane-related peripheral neuropathy, pain and nail toxicity: a prospective self-controlled trial comparing hilotherapy with frozen gloves in early breast cancer (2021)

- 62 patients, prospective self-controlled study, Patient-reported outcomes (NCI—PRO-CTCAE™ v1.0), June 2019 – November 2020
- Early breast cancer patients, treated with PTX 80 mg/m^2 weekly or three-weekly docetaxel 75 mg/m^2
- Right hand/foot Hilotherm ChemoCare – 30 mins prior, during and 30 mins post chemotherapy – 10-12ºC (patient preference)
- Left hand/foot Peters surgical frozen gloves 15 mins prior, during and 15 mins post chemotherapy
- Incidence of any grade symptoms – Hilotherm 85.5%; frozen gloves 90.3%
- Incidence of >grade 2 Hilotherm 43.6% vs 61.3% frozen gloves
- Patient comfort **significantly better with Hilotherm group**
- **Lower reported patient pain and nail toxicity in the Hilotherm group**

Belgium Hilotherm Oxaliplatin vs none cooling

A randomized controlled trial of hand/foot-cooling by hilotherapy to prevent oxaliplatin-related peripheral neuropathy in patients with malignancies of the digestive system (2023)

- 77 patients, monocentric, open-label phase II trial, patients with malignancies of the digestive system, May 2021 and January 2022,
- Patients receiving oxaliplatin-based chemotherapy,
- 39 patients receive continuous cooling of hands and feet (halotherapy) at 11°C during oxaliplatin infusion
- 38 patients with usual care (no cooling)
- the primary endpoint was grade 2 neuropathy-free rate in 12 weeks after initiation of chemotherapy.
- Secondary endpoints included OIPN-related treatment alterations, acute OIPN symptoms and perceived comfort of the intervention.
- The grade 2 neuropathy-free rate at 12 weeks was 100% in the experimental group versus 80.5% in the control group.
- Patients in the hilotherapy group experienced significantly less acute OIPN symptoms of numbness or tingling, pain and/or cold sensitivity in fingers or toes as well as less pharyngeal cold sensitivity

Conclusion: In this first study on hand/foot-cooling in oxaliplatin alone, hilotherapy significantly reduced the incidence of grade 2 OIPN at 12 and 24 weeks. Hilotherapy also reduced acute OIPN symptoms and was generally well tolerated.

Where do we find Hilotherm ChemoCare?

Boxer's 'ice pack' could knock out chemo nerve pain

By Ethan Ennals

AN 'ICE machine' that athletes use to speed up recovery from injuries could be rolled out on the NHS to tackle one of the most uncomfortable side effects of chemotherapy.

The hilotherapy device, used by former British world champion boxer David Haye to combat facial bruising and swelling after a fight, works in a similar way to an ice pack by constricting blood vessels and decreasing circulation to the affected area. When used during chemo, the highly controllable cooling cuts the risk of a nerve pain – called peripheral neuropathy – being triggered by the powerful drugs.

The condition affects as many as 85 per cent of chemo patients and leads to painful tingling, numbness and shooting pains in the hands and feet. It often continues after treatment has ended and, in some cases, can linger for several years.

But studies show hilotherapy, developed by German firm Hilotherm, can cut the risk of the side effect by as much as 90 per cent.

Although it is only available privately at the moment, it is hoped it will soon be on the NHS.

'Neuropathy is a debilitating side effect of chemo,' says Dr Russell Burcombe, consultant oncologist at Maidstone and Tunbridge Wells NHS Trust. 'Given the benefits of this therapy, hopefully the NHS will offer it to patients soon.'

About a third of UK cancer patients – roughly 100,000 people a year – undergo chemotherapy. The drugs work by killing off the rapidly dividing cancer cells, but they can also harm the body's healthy cells. This leads to the various side effects of the treatment, including nausea, diarrhoea and hair loss.

Peripheral neuropathy occurs when chemo damages nerve cells in the hands and feet, which can make walking and picking up objects difficult. Traditional painkillers, such as paracetamol and ibuprofen, are ineffective.

'This can be incredibly painful,' says Dr Burcombe. 'We are curing more cancer patients than ever before but we're leaving many with lingering side effects.'

Increasing evidence over the past decade has shown that cooling areas of the body protects them from the side effects of chemo, as the constriction of blood vessels reduces the amount of the drugs which can reach that area.

The NHS offers protection from hair loss during some chemo treatments using a cold cap – a special cap filled with a cold gel that reduces blood flow to the scalp.

With hilotherapy, patients are fitted with padded gloves and boots 30 minutes before they begin chemotherapy. Cold water is then pumped through channels in them, cooling the hands and feet throughout each chemo session and for about an hour afterwards.

Hilotherapy will be rolled out this year at private clinics run by the firm Genesis Care. Dr Burcombe, who also works at a Genesis Care centre in Maidstone, Kent, says the data collected will impact whether the NHS offers hilotherapy.

'This is an effective treatment,' he says. 'However, it means patients spend more time in hospital than a standard chemo patient does because they have to wear the device before and after treatment, and we know NHS resources are stretched.

'This is something every NHS cancer patient would want, so we want to find out how feasible that would be.'

ONE patient to benefit from hilotherapy is Bridget Schonbroich, 68, from Dusseldorf, Germany. Bridget, a doctor specialising in chronic pain, was diagnosed with breast cancer in October 2018 and began chemo two months later.

'I was really afraid of the chemotherapy,' she says. 'I knew it could cause neuropathy and hair loss.'

Along with a cold cap, Bridget underwent hilotherapy during each of her 12 chemotherapy sessions. 'It was a bit cold at first but you get used to it,' she says.

What's more, she says her symptoms of peripheral neuropathy were barely noticeable. 'I had tingling in my hands for the first few weeks but it wasn't too bad and it went away quickly,' she adds.

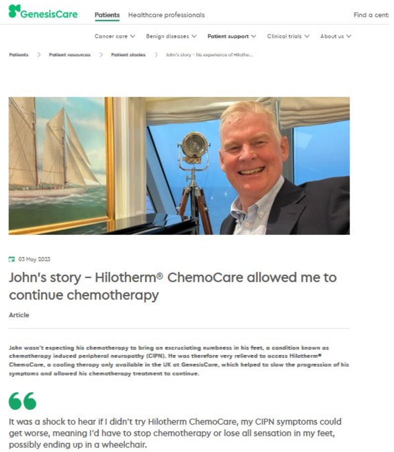
She is now cured of cancer and is once again working as a doctor.

Bridget says: 'If I'd developed bad neuropathy, I'm not sure I'd be back at work, as you need healthy hands to do this job. I feel very thankful I could get hilotherapy.'

COOL MOVES: The device treats debilitating pain in the hands and feet

- Hilotherm ChemoCare® system is used into **6 Genesis Care centres in UK**
- **GenesisCare first healthcare provider of ChemoCare® in the UK**
- Hilotherm ChemoCare® system in **60 Centers in Germany**
- Hilotherm ChemoCare® system available **in Belgium**, Austria, Brasil, Sweden, Swiss, France, **Italy**

Further Developments



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John's story – Hilotherm® ChemoCare allowed me to continue chemotherapy

Article

John wasn't expecting his chemotherapy to bring on excruciating numbness in his feet, a condition known as chemotherapy induced peripheral neuropathy (CIPN). He was therefore very relieved to access Hilotherm® ChemoCare, a cooling therapy only available in the UK at GenesisCare, which helped to slow the progression of his symptoms and allowed his chemotherapy treatment to continue.

It was a shock to hear if I didn't try Hilotherm ChemoCare, my CIPN symptoms could get worse, meaning I'd have to stop chemotherapy or lose all sensation in my feet, possibly ending up in a wheelchair.

- Significant improvements to cuff design following early trials have led to treatment now being administered at 15-17°C rather than 10-12°C and a reduction of standard post-chemotherapy cooling to 30 minutes **or none**
- On-going trials in Austria due to be published soon, Germany
- Health insurers in several European countries considering cover for Hilotherm ChemoCare® as standard treatment for patients

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What is Hilotherm ChemoCare?

Hilotherm ChemoCare is a cooling therapy used to prevent and manage chemotherapy-induced peripheral neuropathy and hand-foot syndrome. Special cuffs cool your hands and feet before, during and after your chemotherapy to 15 – 17°C. This reduces potential damage to your nerves and tissue in those areas, by slowing the blood flow and limiting how much chemotherapy can reach them.

If you're having a type of chemotherapy that can cause chemotherapy-induced peripheral neuropathy or hand-foot syndrome, we'll offer you Hilotherm ChemoCare alongside your treatment, so we can work on preventing these side effects from the very first step.

If you're already in the middle of your chemotherapy, you can still benefit from starting Hilotherm ChemoCare. It's never too late to start.

Improving our patients' outcomes and making treatment as comfortable as possible is important to us, that's why we're the first UK cancer care provider to offer Hilotherm ChemoCare.

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Contact us today

If you have any questions about chemotherapy related side effects, or Hilotherm ChemoCare, contact us today. We're here to help.

Contact us

What happens during my chemotherapy session?

- About 30 minutes before your treatment starts, your chemotherapy nurse will help you put on your cooling cuffs and boots. We'll then begin to cool your hands and feet to around 15 – 17°c
- It can take some getting used to and might feel uncomfortable to begin. We suggest wearing warm, comfortable clothing and taking paracetamol an hour beforehand. You can also bring heat pads and we have hot drinks to help you during the treatment
- You'll keep your cuffs and boots on during your treatment to maintain cooling at 15 – 17°c
- After your treatment finishes your cuffs and boots will need to stay on for 30 minutes. If you're already experiencing signs of chemotherapy-induced peripheral neuropathy or hand-foot syndrome this can sometimes extend to 60 minutes after your treatment

https://www.genesiscare.com/uk/patient-support/patient-stories/johns-story-hilotherm-chemocare

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"It was a shock to hear if I didn't try Hilotherm ChemoCare, my CIPN symptoms could get worse, meaning I'd have to stop chemotherapy or lose all sensation in my feet, possibly ending up in a wheelchair.

Also available: Scalp cooling to avoid Chemotherapy-induced Alopecia (CIA)

HILOTHERM ChemoCare CIA
Anwendung im Klinik-/
Praxisumfeld

Alopecia during chemotherapy:

- especially in young women, the most feared side effect of chemotherapy
- impairment of body and self-esteem
- reduction of quality of life (Lemieux J. et al. 2008)
- means stigma (Rosman S. et al. 2004), the disease becomes obvious
- associated with high negative psychological impact (Choi et al. 2014)
- sometimes represents such a great emotional burden that the Chemotherapy is refused

Thank you very much

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