Real world data from everyday oncology clinical practice: prophylactic HILOTHERAPY® (degree-accurate, controlled hand-foot cooling) reduces the incidence rate of higher-grade chemotherapy-induced polyneuropathy (CIPN) and nail toxicity

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Background

Chemotherapy-induced polyneuropathy (CIPN) is a common side effect of antineoplastic systemic therapies. Grade-appropriate Hilotherapy® (used prophylactically) reduces high-grade CIPN and nail toxicity under oncological therapies (Oneda et al. 2020 & 2021, Coolbrandt et al 2022, Schaper et al ESMO 2019; DGS 2019 & 2023). Real world data from 151 breast cancer patients showed that with prophylactic Hilotherapy® (1st generation), CIPN ≥ grade 2 could be avoided in 93.4% of patients undergoing taxane-containing chemotherapy (Schaper et al. DGS, ESMO 2019). The 4-year follow-up data (130 breast cancer patients) confirmed the lasting effect of prophylactic Hilotherapy® for CIPN prophylaxis. It is already established as a supportive therapy in many oncology practices/clinics (Oneda et al. 2020 & 2021, Coolbrandt et al 2022, Schaper et al ESMO 2019).

The development of the 2nd generation of the cooling compression sleeve enables a controlled reduction of the skin surface temperature by a further 10°C. This raises the question of whether the effectiveness of Hilotherapy® can be further increased.

Patients and method

Prophylactic, processor-controlled hand-foot cooling (Hilotherapy® 2nd generation with cooling compression sleeves) is established as a standard supportive therapy at our institute. It is used for every oncology patient during taxane or platinum-containing chemotherapy to prevent CIPN and nail toxicity.

We present data from 257 breast cancer patients who used controlled hand-foot cooling (Hilotherapy® 2nd generation) in addition to their chemotherapy. Hilotherapy® is a processor-controlled, degree-accurate cooling method. The device (Hilotherm ChemoCare[CIPN]) is equipped with hand/foot cooling compression cuffs and enables constant cooling of the extremities. The device is operated with distilled water and electricity (**Fig. 1**).

The previous standard procedure recommends cooling hands and feet 30 minutes before, during and 30 minutes after the end of chemotherapy with a device temperature setting of 15°-17°C. The development of the 2nd generation of cooling compression sleeves has further optimized the cooling of the skin surface. We have now investigated the effectiveness of Hilotherapy® 2nd generation without post-cooling time. The symptoms of CIPN and nail toxicity were recorded according to the CTCAE criteria for each chemotherapy.

Our points of investigation were:

- Assessment of CIPN and nail toxicity (Hilotherapy 2nd generation, cooling compression sleeves) without the 30-minute post-cooling period
- Onset of CIPN ≥ grade 2
- Dose reductions due to CIPN ≥ grade 2.

Fig. 1: Hilotherm Chemo Care device with 2nd generation cooling pressure cuffs

Therapy regime	
q1w	N
12 x paclitaxel 80 mg/m² KOF q1w	64
12 x paclitaxel 80 mg/m² KOF + carboplatin AUC 2 q1w	34
12 x paclitaxel 80 mg/m² KOF + carboplatin AUC 1.5 q1w + pembrolizumab q3w	35
12 x paclitaxel 80 mg/m² KOF q1w + trastuzumab + pertuzumab q3w	32
12 x paclitaxel 80 mg/m² KOF q1w + trastuzumab q3w	8
18 x paclitaxel 80 mg/m² KOF q1w + bevacizumab q3w	3
6 x nabPaclitaxel 100 mg/m² KOF d1,8,15 q4w + Pembrolizumab q3w	3
6 x nabPaclitaxel 100 mg/m² KOF d1,8,15 q4w + Atezolizumab d1,15 q4w	1
12 x nabPaclitaxel 125 mg/m² KOF q1w + carboplatin AUC 2 q1w	3

q3w	
6 x docetaxel 75 mg/m² KOF + cyclophosphamide 600 mg/m² KOF q3w	30
6 x docetaxel 75 mg/m² KOF + trastuzumab + pertuzumab q3w	1
6 x docetaxel mg/m² KOF + carboplatin AUC 6 + trastuzumab + pertuzumab q3w	43

Table 1: Therapy regimen

onset CIPN grade 2 (n=21)									
	T3	T4	T6	T7	T8	T9	T10	T11	T12
q1w	1	2	3	1	1	3	6	3	1
onset CIPN grade 2 (n=8)									
	T3	T4	T5	T6					
q3w	1	1	3	3					

Table 2: Onset CIPN Grade 2

Results: Effectiveness of Hilotherapy® 2nd generation

We present the effectiveness data of 257 patients with breast cancer. Of these, 183 were treated with a weekly treatment regimen and 74 patients with a 3-week regimen. **Table 1** shows the detailed list of treatment regimens.

Of the total of 257 patients with Hilotherapy® prophylaxis, 228 patients (89%) developed no or only mild symptoms of CIPN (highest grade of neuropathy (hGAE): grade 0: n=82; grade 1: n= 146). 29 patients (11%) developed grade 2 toxicity, no patient showed grade 3 symptoms **(Fig. 2&3)**.

On EOT (day of last chemotherapy), 236 patients (94.4%) showed no or mild symptoms (grade 0: n=117; grade 1: n=119), while 14 patients (5.6%) reported grade 2 toxicity **(Fig. 2&3).**

Initial follow-up data from months 3, 6 and 12 are available, which show that Hilotherapy prophylaxis is sustainable **(Fig. 3)**.

Table 4a&b compares the individual CIPN incidence rates in the treatment regimens q1w and q3w.

A total of 29 patients developed CIPN grade 2 toxicity during their chemotherapy **(Table 2&3).** Of these, 21 patients were treated with a weekly regimen and 8 patients with a three-week regimen.

Table 2 shows the cycle in which grade 2 toxicity manifested itself.

In 24 patients, the dose of chemotherapy was reduced due to grade 2 CIPN **(Table 3).**

Nail toxicity: No nail toxicity was documented in any of the patients.

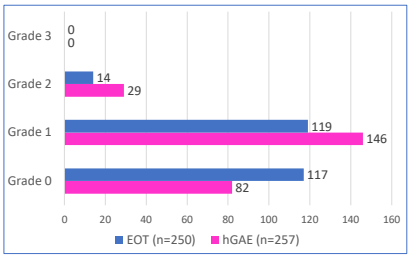

Fig. 2: CIPN development under Hilotherapy® prophylaxis

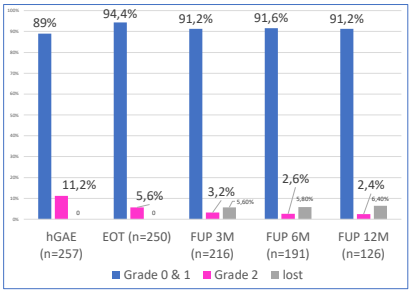

Fig. 3: CIPN development under Hilotherapy® prophylaxis

	Dose reductions (DR)	DR due to CIPN grade 2	DR other reasons
q1w (n=183)	25	**16**	9
q3w (n=74)	20	**8**	12

Table 3: CIPN-related dose reductions

	hGN (n=257)		
	Grade 0	Grade 1	Grade 2
q1w(n=183)	32,24%	56,28%	11,48%
q3w (74)	31,10%	58,10%	10,80%
total (n=257)	**32%**	**56,80%**	**11,20%**

	EOT (n=250)		
	Grade 0	Grade 1	Grade 2
q1w(n=179)	47%	48,60%	4,70%
q3w (71)	46,50%	45,00%	8,50%
total (n=250)	**46,80%**	**47,60%**	**5,60%**

Table 4a&b: Comparison of CIPN development q1w vs. q3w

Summary and discussion

With the controlled hand-foot cooling Hilotherapy® 1st & 2nd generation, CIPN toxicity ≥ grade 2 could be avoided in over 90% of patients during chemotherapy (Fig. 3 & Schaper et al. DGS, ESMO 2019**).** Grade 3 toxicity no longer occurred. The 2nd generation of cooling compression sleeves show a further optimization of the cooling effect**.** The previously conducted comparison of two groups with and without the 30-minute post-cooling period showed no differences in effectiveness (Kostara et al, Poster 121, DGS 2023). In both groups (with post-cooling time and without post-cooling time), 90% of patients were protected from CIPN > grade 1. At EOT (day of last chemotherapy), 94 - 97% of patients are without limiting CIPN symptoms > grade 1 (Kostara et al, Poster 121, DGS 2023)**.** The new standard at GynOnco Düsseldorf already integrates these results into everyday clinical practice - post-cooling is no longer required. This makes everyday practice in oncology easier. The first follow-up data show a lasting effect of the prophylactic use of Hilotherapy® with 2nd generation cooling pressure cuffs. Further follow-up data will be collected and updated accordingly.

The CIPN incidence rate depends on several factors: Type of chemotherapy, dose, BMI, lack of physical activity and concomitant diseases. Seidmann et al. (2018) reported a 50% incidence of grade 2&3 CIPN in patients receiving weekly paclitaxel (80mg/m²). CIPN can persist for many years (Blackley et al. 2019) and negatively affect the quality of life of oncology patients.

Modern oncological system therapies (individualized therapies, immunotherapies, targeted therapies, ADCs, etc.) lead to an improvement in the long-term prognosis of cancer patients - thus increasing the importance of maintaining quality of life. Controlled hand-foot cooling (Hilotherapy®) is a simple supportive therapy to prevent CIPN that is very well tolerated by patients. It is easy for nursing staff to implement and does not have a significant impact on everyday clinical practice.

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Conflicts of Interest:
A. Kostara: advisory board Hilotherm GmbH, not related to this investigation; T. Schaper: Lecture fees, advisory boards, consulting contracts Hilotherm GmbH; O-M. Opra: has nothing to declare.