A new approach to prevent chemotherapy-induced Polyneuropathy (CIPN) - HILOTHERAPY®

Schaper T.[1,2], Darsow M.[1] ; [1] Luisenkrankenhaus Düsseldorf, [2] Internationale Senologie Initiative ISI e.V.

Background: Chemotherapy-induced peripheral neuropathy (CIPN) is an adverse effect of many commonly used chemotherapeutic agents (cisplatin, oxaliplatin, more rarely carboplatin, vinca alkaloids, especially vincristine, more rarely also vinblastine and vinorelbine, 5-fluoropyrimides (5-FU, capecitabine). CIPN in breast cancer is often caused by taxane-based regimen (Paclitaxel, nab-Paclitaxel, Docetaxel) carboplatin, eribulin and vinorelbine. Seidman et al (JCO 2008), reported incidence rates of CIPN grade 2-3 of 33% for three-week taxol administration and 51% grade 2-3 toxicities for weekly administration of paclitaxel. The peripheral neuropathy (PN) induced by taxanes may persist for several years and is negatively accociated with quality of life (Blackley et al, 2019). Often the CIPN results in dose delay, dose reduction or treatment discontinuation.
In our study we found that the prophylactic hand / foot cooling using a new processor - controlled thermotherapy device (Hilotherm Chemo Care Hilotherapy®) prevented the chemotherapy-induced-peripheral neuropathy (CIPN) in breast cancer patients.

Patients and Method: 189 breast cancer patients used the controlled, processor-controlled hand-foot cooling (Hilotherapy®) during chemotherapy to avoid CIPN toxicities. The extremities were cooled with a constant temperature setting (device setting 10-12°C) during each taxane-containing chemotherapy. Cooling took place 30 minutes before to 30 minutes after chemotherapy **(Fig. 1a&b).** After each chemotherapy treatment, symptoms of CIPN were recorded using CTCAE V.4 criteria, the sustainability of the effect was / is collected by follow-up data (patient contacts every 3 months). Group 1: prophylactic Hilotherapy® - pHT, (**Fig. 2**): 151 patients used Hilotherapy® primary prophylactically for each taxane-containing chemotherapy (Fig. 2-4). Group 2: secondary Hilotherapy® - rsHT, **(Fig. 2):** 38 patients use Hilotherapy® reactive-secondary (rsHT). The cooling of the extremities took place after the onset of the first CIPN symptoms. 4 patients remained in the observation group, without any cooling.

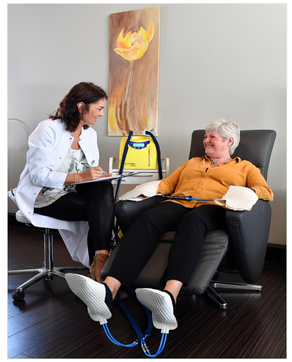

Fig 1a: Patient undergoing controlled cooling **Fig 1b:** Hilotherm ChemoCare device during chemotherapy treatment

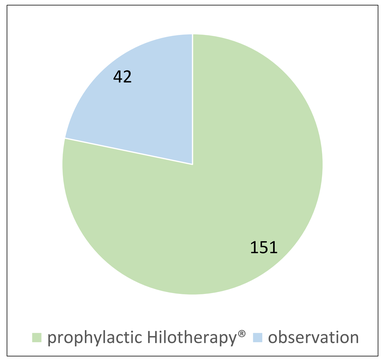

Fig. 2. Investigation Patientgroup

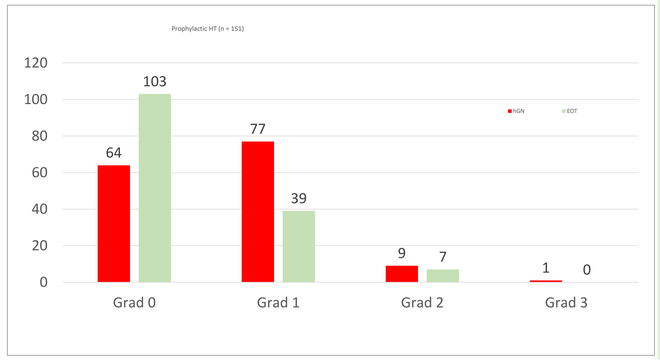

Fig. 3: Toxicity grades using prophylactic Hilotherapy®

Results: Group pHT1: Out of 151 patients using pHT, 141 patients (93.4%) developed none or mild symptoms of CIPN (grade 0: n = 64, grade 1: n = 77); 9 (6%) patients described a grade 2, 1 patient a grade 3 (0.7%) toxicity **(Fig. 3).** The symptoms were partially reversible: 4 weeks after the last chemotherapy treatment (EOT), none of the patients showed grade 3 toxicity, grade 2 toxicities decreased from 9 patients (6%) to 7 (4%) patients. 39 patients (26%) reported mild symptoms (grade 1), 103 patients (69%) had no ne symptoms (grade 0) anymore **(Fig. 3).** 10 months after last chemotherapy (FUP 3), 98% of the patients were without symptoms > grade 1. Follow Up data confirmed the sustainability of the results **(Fig. 4).**

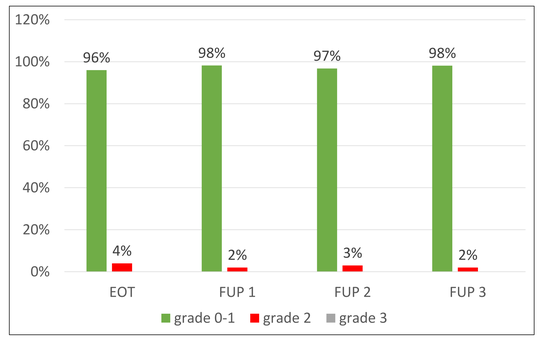

Fig 4: Long term reuslts after pHT®

EOT: 4 weeks after last chemo-therapy treatment (n = 125).
FUP 1: 4 months after last chemo-therapy treatment (n =113).
FUP 2: 7 months after last chemo-Therapy treatment (n = 96).
FUP 3: 10 months after last chemo-Therapy treatment (n= 54).

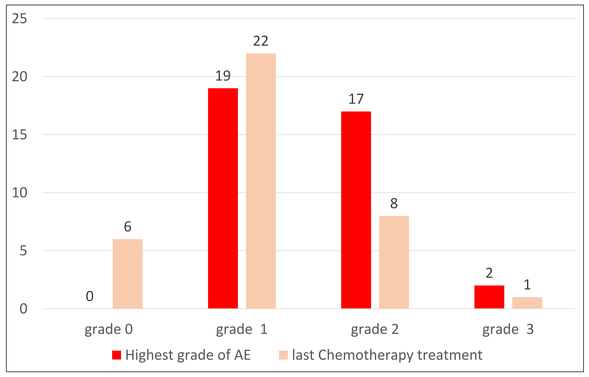

Fig. 5: Toxicities without prophylactic Hilotherapy®(n = 38)

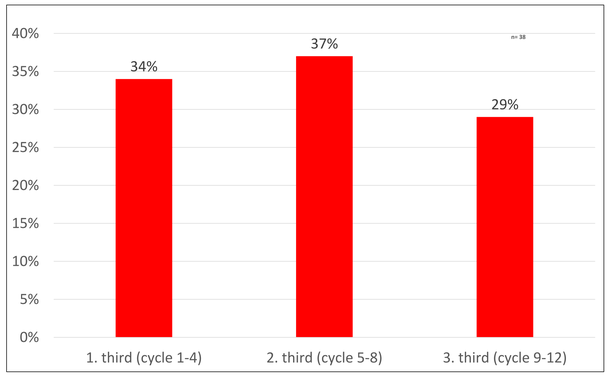

Fig. 6: Onset of CIPN without prophylactic Hilotherapy®

Results:
Group 2 rsHT: Initially 42 patients started chemotherapy without prophylactic cooling (Fig.2). 38 patients (90.5%) developed symptoms of CIPN (grade 1-3). 50% of these patients suffered grade 2 and 3 CIPN **(Fig. 5).** The onset of CIPN varied: 34% developed CIPN symptoms during the first 4 chemotherapy cycles, 37% during cycles 5-8 and 29% during cycles 9-12 **(Fig.6).** After the onset of CIPN the patients used secondary Hilotherapy (rsHT) reactively for all remaining chemotherapy treatments. RsHT stopped progression of CIPN and reduced first symptoms of CIPN **(Fig.5).**

	Prophylactic HILOTHERAPY	Without Hilotherapy
grade 0	42,4%	0
grade 1	51,0%	50%
grade 2	6%	44,7%
grade 3	0,6%	5,3%

Fig. 7: Comparison of CIPN grades using Hilotherapy® versus no Hilotherapy®.

Conclusions: Due to many new oncological therapeutic options, a significant improvement in the long-term prognosis and overall survival for oncological patients exist. Therefore maintaining quality of life and avoiding long term complications, such as CIPN, is becoming more important. Our investigations show, prophylactic Hilotherapy® (pHT) reduces CIPN symptoms > grade 1. Without pHT, 50 % of the patients developed CIPN grade 2&3. Prophylactic Hilotherapy® is a simple and practible technique to remain quality of life for cancer patients **(Fig.7).**