The preventive effect of DHL-HisZnNa, an α-lipoic acid derivative, for chemotherapy-induced alopecia: a single-arm phase 3 study

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Objective

Chemotherapy-induced alopecia (CIA) is one of the most distressing and unavoidable adverse events of chemotherapy in breast cancer patients. According to a questionnaire-based research in a population of Japanese patients who had received chemotherapy for breast cancer, the hair recovery rate in approximately 10% of patients was less than 50% after completing 1–2 years of chemotherapy. There is no drug to prevent CIA. The application of DHL-HisZnNa(Fig.1), an α-lipoic acid derivative, had a preventive effect on CIA in rodent models. ¹⁾ Therefore, we performed a multicenter clinical trial to assess whether the application of DHL-HisZnNa reduces CIA in breast cancer patients.

Fig.1 DHL-HisZnNa chemical structural formula

Methods

Trial design The clinical trial was a multicenter, single-arm study (Fig.2) on women planning to receive adjuvant chemotherapy.(Table1)

Number of patients 100 patients

Follow-up period: 1 year after chemotherapy completion

Fig.2 Study design

Inclusion criteria:	
	pathological diagnosis of breast cancer
	treatment plan including anthracycline and/or taxane chemotherapy
	20-80 year-old patient
	Performance Status(PS) : 0~1
Exclusion criteria:	
	previous history of severe drug hypersensitivity
	chemotherapy contraindication
	previous history of cosmetics or hair growth agent hypersensitivity
	severe complication
	pregnancy or lactation

Table1.Inclusion/exclusion criteria

End points The primary end point was the proportion of participants with grade 2 alopecia ($\geq 50\%$ hair loss, Common Terminology Criteria for Adverse Events version 4.0)(Table2).

The secondary end points were adverse events related to the study drug and symptoms associated with hair loss.

Alopecia	
grade 0	no hair loss
grade 1	hair loss of < 50% of normal
grade 2	hair loss of $\geq 50\%$ of normal

Table2 alopecia grade (CTCAE ver.4.0)

Procedure During chemotherapy, 4 ml of a topical product containing 1% DHL-HisZnNa was applied to the scalp four times a day.(Fig.2)

Fig.3 Intervention schedule

Evaluation methods The way to evaluate the alopecia grade is that 3 commissioners determine respectively the grade from 4-way photographs(Fig.3) of participant's head.

Fig.4 Patient's head photograph

Results

Patients characteristics

101 participants were enrolled from July 2014 to May 2015. The mean age was 50 years old; 34% of participants (n = 34) received 4 cycles of chemotherapy, and 66% (n = 67) received 8 cycles of chemotherapy. (Table2)

Age,y	median(range)	50(22-75)
Menstrual status,No.	premenopause	61
	postmenopause	40
PS,No.		0 99
		1 2
Breast cancer stage,No.	I	35
	II A	32
	II B	17
	III A	9
	III B	5
	III C	2
	IV	1
pretreatment,No.(%)		
operation	no	32(32)
	yes	69(68)
radiation (for breast)	no	100(99)
	yes	0
	unknown	1(1)
hormone	no	98(97)
	yes	2(2)
	unkown	1(1)
chemotherapy	no	100(99)
	yes	0
	unknouwn	1(1)
Trastuzumab	no	99(98)
	yes	1(1)
	unknown	1(1)

Table3. Patients charactaristics

Efficacy The rate of grade 2 alopecia was 100% (101/101), Grade 2 alopecia was occurred in all pts (101/101), but the recovered rate to less than G1 were 93% (94/101) and 100% at three and six months after the completion of chemotherapy, respectively.(Fig.5)

Fig.5 Alopecia grade change

Safety

All adverse events (n = 11, 11%) were grade 1 or grade 2,and these included scalp pain (n = 3), pruritus (n = 3), and rash (n = 5). Symptoms associated with hair loss were found in 53 patients (52%), including scalp pain in 25 patients and scalp itching in 35 patients.

Discussion

There is no complete prevention of CIA at present. There is no evidence about alopecia grade change after chemotherapy, but 41% of patients who had chemotherapy reported their hair regrowth occurred 6 weeks after chemotherapy. ²⁾ In our study, the rate of alopecia grade 1 or 0 3 months after chemotherapy is 81% (71/88).

We didn't set the control group and our endpoints are different, so we couldn't reach the conclusion, but application of α-lipoic acid might promote hair regrowth.

Conclusion

The results in our study suggested DHL-HisZnNa showed no preventive effect, but promoted the function of hair growth in CIA patients. We have a new study plan to confirm the interesting function of this application.

Reference

- 1) Surg Today. 2011 May;41(5):693-7.
- 2) Eur J Oncol Nurs. 2013 Oct;17(5):536-40.

COI: This study was funded by Aderans Co.,Ltd.