Summary of trial EudraCT: 2015-000658-39

Background: This randomized multicenter trial consisted of SNP guided antiemetics in chemotherapy treated patients with breast cancer. The trial was based on previous not randomized data where risk SNPs for nausea were identified (the SNPs of interest are shown in table below). The cytostatic regimens examined in the study included EC_{60} (Epirubicin 60 mg/m^2 and Cyclophosphamide 600 mg/m^2), FEC_{75} (Fluorouracil 600 mg/m^2, Epirubicin 75 mg/m^2 and Cyclophosphamide 600 mg/m^2), EC_{75} (Epirubicin 75 mg/m^2 and Cyclophosphamide 600 mg/m^2) and EC_{90} (Epirubicin 90 mg/m^2 and Cyclophosphamide 600 mg/m$^{2)}$. The Epirubicin dose was determined on clinical grounds.

The randomization was either antiemetics according to standard guidelines (control group) och antiemetics depending on presence of known risk SNPs. (experimental group). If the patients had one or more of the known risk SNPs for nausea they received standard antiemetics but if all of these were absent, the steroid dose was reduced to half.

The trial started 2017 with the first patient included. We planned to include 880 patients in order to identify a 14% difference between the two groups concerning nausea.

Early termination: Due to changes in the treatment modalities for breast cancer depending on new science, the study became less relevant for many patients. The chemotherapy drugs named in the protocol and reported to the Swedish medical products agency (Läkemedelsverket) were changed in clinical practice thus preventing inclusion of subject. On top of that, the Covid pandemic induced severe lack of resources both at the clinic as well as in the lab analyzing the SNPs. This resulted in an early termination of the study. The study was stopped the 31 December 2020. Number of patients included was 188, thus far from the intended number.

Serious adverse events: Eleven serious adverse events were reported. Among them 2 were reported to have possible relation to the study drug (chemotherapy). The two patients had chest pain after the first treatment. One was reported to probably be related to study drugs. It was a patient with anxiety due to the steroid administered in the antiemetic treatment.

Results: The early termination resulted in only partial results expressed in the two tables below

SNP genotype and CINV stratified on genotype of the three analysed SNPs.

Vomiting, any day			**Nausea, any day**		
FAS-CD95-genotyp rs2234978					
SNP genotype	Yes	No	SNP genotype	Yes	No
AA	1	10	AA	12	1
AG	8	65	AG	58	14
GG	4	66	GG	59	6
Total	13	141		129	21
RB1-LPAR6 genotype rs2854344					
AG	1	24	AG	24	3
GG	12	117	GG	105	18
Total	13	141		129	21
CCL2 genotype rs2530797					
AA	4	59	AA	52	12
AG	6	72	AG	59	9
GG	3	10	GG	18	0
Total	13	141		129	21

Nausea stratified on SNP genotype of the three analysed SNPs, on the evening of day 1 according to the diary					
	FAS-CD95-genotyp rs2234978				
SNP genotype	None	Mild	Moderate	Severe	Total
AA	7	3	2	1	13
AG	41	26	6	4	77
GG	35	29	9	7	80
					170*
	RB1_LPAR6 genotype rs2854344				
AG	17	7	1	4	29
GG	66	51	16	8	141
					170
	CCL2 genotype rs2530797				
AA	37	25	3	6	71
AG	42	28	9	4	83
GG	4	5	5	2	16
					170

* Missing 11 patients where the analysis failed

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Freddi Lewin, MD, PhD

Department of Oncology, County Hospital Ryhov, 551 85 Jönköping, Sweden.