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Original article

Safety profile of subcutaneous trastuzumab in patients with HER2-positive early breast cancer: The French HERmione non-interventional prospective study

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ABSTRACT

Objectives: HERmione study was conducted to assess, in human epidermal growth factor receptor 2 (HER2)-positive early breast cancer (eBC), the safety profile of subcutaneous (SC) formulation of trastuzumab in real-life in France.

Materials and methods: This prospective, non-interventional study included 511 patients planned to be treated in both neoadjuvant and adjuvant settings with a follow-up of 12 months maximum in 101 sites. The safety analyses concerned 505 patients. Primary endpoint was the description of systemic safety and local tolerability of the SC trastuzumab.

Results: The median age of patients was 58 years. Over the study, 2449 adverse events (AEs) occurred in 422 (83.6%) patients (asthenia, arthralgia, radiation skin injury, myalgia, hot flush and diarrhea in ≥10% of patients): 92 AEs (3.8%) were grade ≥3 (radiation skin injury in 1.8% of patients and febrile neutropenia in 1.4% of patients), 76 (3.1%) were serious (mainly febrile neutropenia in 1.4% of patients) and 336 (13.7%) were treatment-related (mainly injection site pain in 9.1% of patients). Congestive Heart Failure occurred in 58 (11.5%) patients and was related to treatment in 4.6% of patients. Only 34 AEs (1.4%) in 27 (5.4%) patients led to permanent treatment discontinuation. One death was assessed as not treatment-related. Quality of life (QoL) analyses showed no deterioration of global health status.

Conclusion: The HERmione study showed that, in a real-life setting, the safety of SC trastuzumab administered in HER2-positive eBC patients is consistent with data reported from previous clinical trials, without new safety concerns or QoL deterioration.

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Abbreviations

CHF	Congestive Heart Failure
HER-2	Human Epidermal growth factor Receptor 2
eBC	early Breast Cancer
SC	Subcutaneous
IV	Intravenous
AE	Adverse Events
SAE	Serious Adverse Events
QoL	Quality of Life

1. Introduction

Trastuzumab (Herceptin®, Roche Registration Ltd) combined to chemotherapy, is the standard of care for human epidermal growth factor receptor 2 (HER2)-positive breast cancer (BC) [1–3].

The first developed formulation of trastuzumab was an intravenous administration (IV). Since 2014, it can also be given subcutaneously (SC). The fixed-dose SC formulation of trastuzumab (SC trastuzumab 600 mg; Roche Registration Ltd) is an alternative to the weight-adjusted dose IV trastuzumab to allow drug administration over a shorter time period, with the goal of improving convenience and compliance [4–8]. SC trastuzumab was approved by the European Medicines Agency based on data from the phase III HannaH study (NCT00950300) [9] which showed that the use of SC as neoadjuvant/adjuvant therapy in patients with an HER2-positive early BC (eBC) is non-inferior to IV trastuzumab with respect to efficacy and an equivalent tolerability profile [9–11]. These supportive safety data for SC trastuzumab was reinforced in the adjuvant setting in the international, open-label, randomized PrefHER study (NCT01401166) [12]. In terms of safety and tolerability, the non-randomized, multinational, phase III open-label SafeHER study (NCT01566721) was the largest trial (˃ 2500 patients) which confirms the safety and tolerability of adjuvant SC trastuzumab BC therapy [13]. Nevertheless, no data on the safety of SC trastuzumab in real life conditions is currently available.

HERmione study is the first prospective non-interventional study to assess the safety profile of SC trastuzumab in HER2-positive eBC patients treated in the neoadjuvant/adjuvant settings, in real life in France.

2. Patients and methods

2.1. Patients selection

Eligible patients were women, aged ≥18 years, with HER2-positive eBC (stage I to IIIA), naive or non-naive of any previous IV anti-HER2 treatment and considered suitable to receive neoadjuvant or adjuvant anti-HER2 treatment. Patients who received prior SC trastuzumab or included in a clinical trial assessing an anticancer therapy were not allowed to participate to HERmione study.

The study was conducted in compliance with the deontological guidelines and according to the Good Epidemiology Practices defined by the "Association des Epidémiologistes de Langue Française (ADELF 2007)" and the European Network of Centers for Pharmacoepidemiology and Pharmacovigilance (ENCePP). All patients provided written informed consent.

2.2. Study design

HERmione is a French multicenter, prospective, non-interventional study designed to assess the safety profile of SC trastuzumab in patients with HER2-positive eBC. Diagnostic methods, therapeutic decisions and routine follow-up visits were decided individually (*i.e.* around 3, 6, 9, and 12 months after inclusion) by the physicians according to local guidelines for practice.

For all the patients, *i.e.* naive or non-naive of IV anti-HER2 treatment, the time of inclusion was the date of 1st SC trastuzumab injection. According to trastuzumab summary of product characteristics [SmPC], patients with eBC should be treated with trastuzumab for 12 months in total (18 cycles) whatever the route of administration or until disease progression. Consistently, for non-naive patients, the duration of SC trastuzumab treatment was expected to be shorter than in naive patients. Non-naive patients were expected to discontinue the study for "End of planned treatment duration" reason.

2.3. Study objectives

The primary objective was to describe the systemic safety and local tolerability of SC trastuzumab in patients with HER2-positive eBC, naive and non-naive of IV anti-HER2 treatment, treated in the neoadjuvant and/or adjuvant settings in routine clinical practice use in France.

The secondary objective related to patient-reported outcomes (PRO) was to describe the quality of life (QoL) of patients. The other secondary objectives included the description of the baseline and disease characteristics of patients with HER2-positive eBC initiating a treatment with SC trastuzumab and the description of the use of SC trastuzumab (treatment duration, frequency of injections and sites of injections).

2.4. Assessment

No additional planned assessments were required from study site or patients. QoL was assessed using the European Organization for Research and Treatment of Cancer [EORTC] QLQ-C30 questionnaire [14].

2.5. Clinical outcomes

Data were prospectively collected during the routine follow-up visits scheduled by the participating physicians, *i.e.* at inclusion, then around month 3 (M3), M6, M9 and M12. In case of discontinuation for "end of planned treatment duration", data were collected at the last administration of SC trastuzumab.

The study required the collection of data that are usually assessed during the management of eBC and available in the patient's medical files for patients' and disease characteristics, biological data and therapeutic management. Safety data collected included all adverse events (AEs) occurring over the study from 1st administration of SC trastuzumab and until 30 days after the last dose. All AEs were graded according to the National Cancer Institute Common Toxicity Criteria for Adverse Events (NCI CTC-AE) version 4.03 and the New York Heart Association functional classification and were coded using the Medical Dictionary for Regulatory Activities (MedDRA) dictionary (version 20.0).

2.6. Statistics

All analyses were descriptive. For the primary objective, safety analyses were performed on the safety population (SAF population, defined as all patients having received at least one dose of SC trastuzumab), on the *per* protocol population (PP population, defined as all patients from the SAF population meeting eligibility criteria). Safety results were described on overall population and in

naive and non-naive subgroups.

For the secondary objectives, patients and disease characteristics, and modalities of SC trastuzumab, analyses were performed on the SAF population (overall and by subgroups). PROs were analyzed on the QoL population, defined as all patients of the SAF population having answered at least one question on baseline self-reported QLQ-C30 questionnaire allowing for calculating a subscale score.

Quantitative variables were described using number of available data, number of missing data (MD), mean, standard deviation, median, Q1, Q3, minimum and maximum. Qualitative variables were summarized using number of available data, number of MD, number and percentage of patients in each group. MD were not counted in percentage calculation. The statistical analysis was performed using SAS® software (SAS Institute, North Carolina), version 9.4.

3. Results

A total of 101 office-based and hospital-based oncologists, radiologists and gynecologists regularly prescribing Trastuzumab in eBC patients participated in the study. Between January and November 2015, 511 patients have been enrolled in the study (Fig. 1). As no statistically significant difference was reported in a sensitivity analysis between SAF and PP populations regarding occurrence of any events, safety results are here described only on the SAF population.

3.1. Patient characteristics

Of the 511 included patients, the median follow-up study duration was 9.7 months (range: 0–14.8). The analysis population corresponding to the SAF population included 505 patients (six patients did not receive a dose of SC trastuzumab).

Baseline characteristics of the SAF population are summarized in Table 1. Median age was 57.9 years (range: 25.3–91.8) and 301 (59.6%) patients were non-naive of IV anti-HER2 (IV trastuzumab only, as there was no biosimilar agents commercialized at the time of the study). Overall, 454 (90.4%) patients were diagnosed with invasive ductal carcinoma, half of them (50.3%) at stage T1N0M0, 97.7% had ECOG 0–1, and 264 (52.3%) reported at least one previous or current disease other than BC, mainly arterial hypertension in 124/264 (47.0%) patients. Previous CHF was documented in 3/264 (1.1%) patients: one Grade III CHF in naive patients and two Grade I CHF.

Major reason of study discontinuation, as expected for patient previously treated with IV trastuzumab, was “end of planned treatment duration”. Among all patients who discontinued the study (340/511, 66.5%), this reason was reported in 237/340 patients (69.7%). Others reasons were: eligibility criteria not met (10.9%), AE (7.6%), investigator’s decision (4.4%), patients changed medical team (2.6%), patients no longer wanted to participate (1.8%), disease recurrence or progression since the 1st SC trastuzumab injection (0.3%), or reason not specified (2.6%).

3.2. Trastuzumab therapy modalities

The median duration of SC trastuzumab exposure was 12.7 months (range: 1.0–14.3) in naive patients and 9.5 months (range: 1.0–13.3) in non-naive patients. In non-naive patients, the median duration of IV and SC trastuzumab administration was 12.8 months

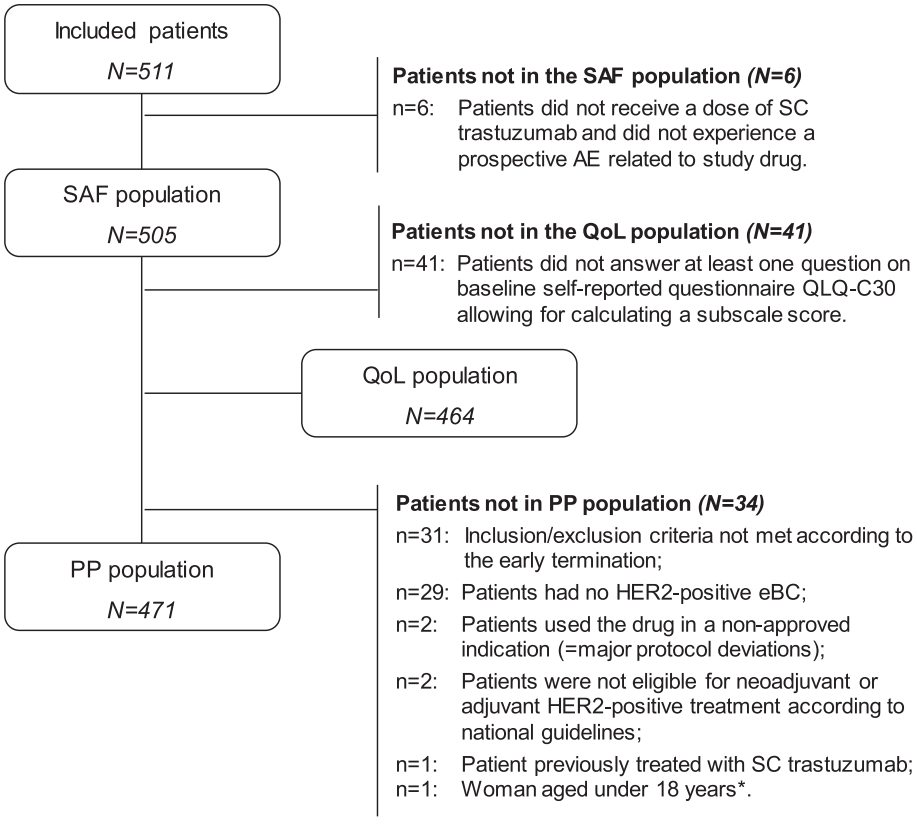

Fig. 1. Patient population – Flow Chart. Abbreviations: N, n = number; SAF = safety population; QoL = quality of life; PP=*Per* Protocol population; AE = adverse event; SC = subcutaneous; QLQ-C30 = quality of life-30 self-reported questionnaire; HER2 = human epidermal growth factor receptor 2; eBC = early breast cancer. *Note: “Woman aged under 18 years”: this patient was a man. As only women had to be included in the study, gender was not reported in the electronic case report form.

Table 1
Patients' demographic and clinical data at baseline according to naive/non-naive subgroups – SAF population *(N = 505)*.

	Naive *N = 204*	Non-naive *N = 301*	All *N = 505*
Median age (range), years	**57.9 (31.8–86.7)**	**58.1 (25.3–91.8)**	**57.9 (25.3–91.8)**
TNM classification at diagnosis, n (%)*			
Primary tumour	***N = 200***	***N = 297***	***N = 497***
T0	1 (0.5)	1 (0.3)	2 (0.4)
T1 (T1mi or T1a or T1b or T1c)	105 (52.5)	145 (48.8)	250 (50.3)
T2	68 (34.0)	111 (37.4)	179 (36.0)
T3	22 (11.0)	36 (12.1)	58 (11.7)
T4	4 (2.0)	4 (1.3)	8 (1.6)
Regional Lymph Nodes	***N = 199***	***N = 295***	***N = 494***
N0	126 (63.3)	179 (60.7)	305 (61.7)
N1	61 (30.7)	92 (31.2)	153 (31.0)
N2	10 (5.0)	17 (5.8)	27 (5.5)
N3	2 (1.0)	7 (2.4)	9 (1.8)
Distant Metastasis	***N = 191***	***N = 293***	***N = 484***
M0	190 (99.5)	290 (99.0)	480 (99.2)
M1	1 (0.5)	3 (1.0)	4 (0.8)
Prior therapy, n (%)			
Surgery	**170 (83.3)**	**281 (93.4)**	**451 (89.3)**
Chemotherapy	**142 (69.6)**	**290 (96.3)**	**432 (85.5)**
Cyclophosphamide	140 (98.6)	238 (82.1)	378 (87.5)
Anthracycline	139 (97.9)	185 (63.8)	324 (75.0)
5FU	111 (78.2)	147 (50.7)	258 (59.7)
Docetaxel	10 (7.0)	203 (70.0)	213 (49.3)
Paclitaxel	1 (0.7)	87 (30.0)	88 (20.4)
Carboplatine	0	20 (6.9)	20 (4.6)
Other	1 (0.7)	16 (5.5)	17 (3.9)
Radiotherapy	**2 (1.0)**	**75 (24.9)**	**77 (15.2)**
At least one previous or current disease other than BC, n (%)	**109 (53.4)**	**155 (51.5)**	**264 (52.3)**
Arterial hypertension	49 (45.0)	75 (48.4)	124 (47.0)
Type 2 diabetes	10 (9.2)	19 (12.3)	29 (11.0)
Dysrhythmia	6 (5.5)	12 (7.7)	18 (6.8)
Chronic inflammatory disease	8 (7.3)	6 (3.9)	14 (5.3)
Heart valve disease	3 (2.8)	3 (1.9)	6 (2.3)
Type 1 diabetes	3 (2.8)	2 (1.3)	5 (1.9)
Coronary heart disease	1 (0.9)	3 (1.9)	4 (1.5)
CHF	2 (1.8)	1 (0.6)	3 (1.1)
Other	88 (80.7)	98 (63.2)	186 (70.5)

Abbreviations: SAF = safety population receiving at least one dose of SC trastuzumab; SC = subcutaneous; IV = intravenous; BC = breast cancer; CHF = congestive heart failure; N, n = number of patients with available data; 5FU = 5 Fluorouracil. Naive patients were defined as patients with no previous IV trastuzumab treatment. Non-naive patients were defined as patients with previous IV trastuzumab treatment.

(range: 1.7–24.5). One hundred and sixty nine (82.8%) naive patients and 277 (92.0%) non-naive patients received SC trastuzumab in adjuvant setting only. The median number of injections was 18.0 (range: 1.0–19.0) in naive patients and 13.0 (range: 1.0–18.0) in non-naive patients. Sites of injection were equally distributed between right and left thigh in both groups of patients. All patients were treated according to local standard of care. Seven patients (1.4%; 6 naive-patients) received anthracycline combined-chemotherapy.

3.3. Safety analyses

Over the study, 2449 AEs occurred in 422 (83.6%) patients and 336 (13.7%) AEs were related to SC trastuzumab in 159 (31.5%) patients (Table 2). All-grade AEs of any category were similar between naive and non-naive patients. Most frequent AEs were mainly mild in severity (Table 3). Main grade ≥3 AEs in at least 1% of patients were: radiation skin injury (9 events in 9 (1.8%) patients), febrile neutropenia (7 events in 7 (1.4%) patients) and hypertension (5 events in 5 (1.0%) patients). Fifty-nine (11.7%) patients experienced at least one serious AE (SAE). Most frequently reported SAEs were febrile neutropenia in 7 (1.4%) patients and pulmonary embolism in 5 (1.0%) patients. Main local reaction related to SC trastuzumab was injection site pain: 66 (2.7%) events in 46 (9.1%) patients. Of all AEs, 87 (3.6%) were AESIs. Main AESI was CHF in 58 (11.5%) patients and was related to treatment only in 4.6% of patients (Table 3). Two patients (0.4%) experienced one serious related CHF: cardiac failure or ejection fraction decreased.

Only 34 AEs (1.4%) in 27 (5.4%) patients led to permanent treatment discontinuation; 8 SAEs in 7 patients led to permanent treatment discontinuation. Only one death assessed as not related to SC trastuzumab was reported (pulmonary thromboembolism).

3.4. Patient-reported outcome analyses

The subset of patients who returned their EORTC QLQ-C30 questionnaire at baseline (defined as QoL Population) was 464 (91.9%) and 121/464 (26.1%) at the M12 visit. Over the follow-up period, the mean global health status score remained stable until M12 (Fig. 2). Among the EORTC QLQ-C30 functioning scales, the scores for physical, social, role, cognitive and emotional function remained hight throughought the study (*higher scores show a better QoL*); of note, scores for social and role functioning were slightly improved. Among the EORTC QLQ-C30 symptom scales, the scores for insomnia, fatigue, pain, dyspnea, constipation, diarrhea, appetite loss, and nausea/vomiting remained low (*lower scores show a better QoL)* over the study; of note, scores for fatigue and appetite loss were slightly decreased. Similar trends were reported between naive and non-naive patients.

Table 2
Summary of AEs occurring during the treatment period according to naive/non-naive subgroups – SAF population *(N = 505)*.

	Naive *N = 204*		Non-naive *N = 301*		Overall *N = 505*	
	Events, n	Patients, n (%)	Events, n	Patients, n (%)	Events, n	Patients, n (%)
At least one AEs	1514	186 (91.2)	935	236 (78.4)	2449	422 (83.6)
Grade ≥ 3 AEs	64	44 (21.6)	28	26 (8.6)	92	70 (13.9)
Related^{+} AEs	138	68 (33.3)	198	91 (30.2)	336	159 (31.5)
SAEs*	53	40 (19.6)	23	19 (6.3)	76	59 (11.7)
Related^{+} SAEs*	6	6 (2.9)	1	1 (0.3)	7	7 (1.4)
SAEs* leading to temporary discontinuation	2	2 (1.0)	3	3 (1.0)	5	5 (1.0)
SAEs* leading to permanent discontinuation	6	5 (2.5)	2	2 (0.7)	8	7 (1.4%)
Death	1	1 (0.5)	0	0	1	1 (0.2)
At least one AESIs	59	45 (22.1)	28	22 (7.3)	87	67 (13.3)
Related^{+} AESIs	16	16 (7.8)	11	8 (2.7)	27	24 (4.8)
AESIs leading to temporary treatment discontinuation	2	2 (1.0)	3	3 (1.0)	5	5 (1.0)
AESIs leading to permanent treatment discontinuation	6	6 (2.9)	2	2 (0.7)	8	8 (1.6)
Serious AESIs*	3	3 (1.5)	1	1 (0.3)	4	4 (0.8)

Abbreviations: AE = adverse event; SAF = safety population receiving at least one dose of SC trastuzumab; SC = subcutaneous; IV = intravenous; n = number; SAE = serious adverse event; AESI = adverse event of special interest. Naive patients were defined as patients with no previous IV trastuzumab treatment. Non-naive patients were defined as patients with previous IV trastuzumab treatment. $^{+}$ Suspected to be related to the studied product or causality unknown. * As reported by the investigator or upgraded by the Sponsor.

Table 3
Most frequent AEs and treatment-related AESIs occurring during the treatment period according to naive/non-naive subgroups – SAF population (*N = 505*).

	Naive *N = 204*		Non-naive *N = 301*		All *N = 505*	
Patients, n (%)	Any grade	Grade≥ 3	Any grade	Grade≥ 3	Any grade	Grade≥ 3
Any AEs	186 (91.2)	44 (21.6)	236 (78.4)	26 (8.6)	422 (83.6)	70 (13.9)
AEs in > 10% of patients						
Asthenia	79 (38.7)	2 (1.0)	60 (19.9)	0	139 (27.5)	2 (0.4)
Arthralgia	65 (31.9)	2 (1.0)	54 (17.9)	0	119 (23.6)	2 (0.4)
Radiation skin injury	53 (26.0)	7 (3.4)	26 (8.6)	2 (0.7)	79 (15.6)	9 (1.8)
Myalgia	56 (27.5)	1 (0.5)	18 (6.0)	1 (0.3)	74 (14.7)	2 (0.4)
Hot flush	35 (17.2)	0	27 (9.0)	0	62 (12.3)	0
Diarrhea	48 (23.5)	2 (1.0)	10 (3.3)	0	58 (11.5)	2 (0.4)
Nausea	28 (13.7)	0	14 (4.7)	0	42 (8.3)	0
Neuropathy peripheral	26 (12.8)	1 (0.5)	10 (3.3)	0	36 (7.1)	1 (0.2)
Anaemia	24 (11.8)	2 (1.0)	3 (1.0)	0	27 (5.4)	2 (0.4)
Treatment-related^{+} AESIs*						
CHF	**16 (7.8)**	_	**7 (2.3)**	_	**23 (4.6)**	_
Ejection fraction deceased	11 (5.4)	0	5 (1.7)	0	16 (3.2)	0
Oedema peripheral	3 (1.5)	0	1 (0.3)	0	4 (0.8)	0
Left ventricular dysfunction	1 (0.5)	0	1 (0.3)	0	2 (0.4)	0
Cardiac failure	1 (0.5)	0	0	0	1 (0.2)	0
Ventricular dysfunction	0	0	1 (0.3)	0	1 (0.2)	0
Hepatobiliary toxicity						
GGT increased	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
Liver disorder	0	0	1 (0.3)	0	1 (0.2)	0

Abbreviations: AE = adverse event; SAF = safety population receiving at least one dose of SC trastuzumab; SC = subcutaneous; IV = intravenous; AESI = adverse event of special interest; N, n = number; CHF=Congestive Heart Failure; GGT = gamma-glutamyltransferase. Naive patients were defined as patients with no previous IV trastuzumab treatment. Non-naive patients were defined as patients with previous IV trastuzumab treatment.$^{+}$ Suspected to be related to the studied product or causality unknown.* Only sponsor AESI were described.

4. Discussion

To our knowledge, the present HERmione study is the first prospective non-interventional study to assess the systemic safety and local tolerability of SC trastuzumab in patients with HER2-positive eBC, naive or non-naive of any previous treatment with IV trastuzumab, treated in the neoadjuvant and adjuvant settings in current practice in France. The few limited eligibility criteria for patients and the absence of planned additional exams ensured that the HERmione study accurately reflected the “real life” conditions of use of SC trastuzumab in a population of eBC patients across France.

The HERmione study showed that in the real-life setting, the SC trastuzumab safety profile for the treatment of HER2-positive eBC is consistent with the known profile of SC trastuzumab in the clinical trials [9–13] without new safety concerns. Most frequent AEs (>10% of patients) were asthenia, arthralgia, radiation skin injury, myalgia, hot flush and diarrhea. The rate of SC trastuzumab-treated patients experiencing clinically important events was low: over the follow-up period only 92 AEs (3.8%) were grade ≥ 3 and 76 (3.1%) were serious. These include, accordingly to the timing of chemotherapy, the events related to chemotherapy when chemotherapy and SC trastuzumab were given concomitantly. A total of 336 AEs (13.7%) were assessed as related to SC trastuzumab during the study. The most frequently reported treatement-related AE was pain at site of injection in 9.1% of patients; no local reaction was assessed as serious.

Although trastuzumab is well tolerated, cardiotoxicity is known to be the most clinically relevant AE associated with trastuzumab. One major point of HERmione study was that patients with cardiac history could be enrolled while previous clinical trials usually excluded these patients [9–13]. In addition, in HERmione study, 7

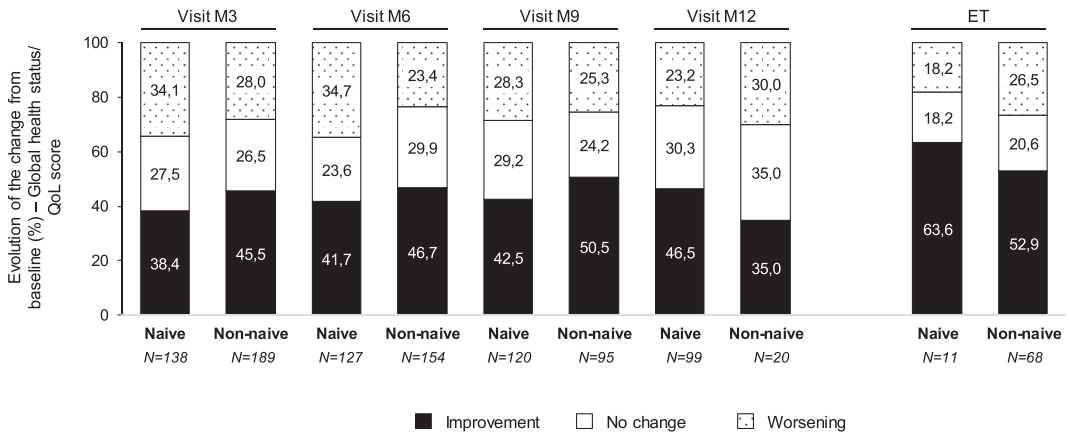

Fig. 2. Evolution of the change from baseline of Global health status during the period M3-M12 and at Early Termination by HER2-positive IV subgroup – QoL population ($N = 464$)
Abbreviations: QoL = quality of life; N = number of available data; M = month; ET = early termination; IV = intravenous; HER2 = human epidermal growth factor receptor 2. Naive patients were defined as patients with no previous IV trastuzumab treatment. Non-naive patients were defined as patients with previous IV trastuzumab treatment.

(1.4%) patients received concomitant anthracyclines, known to increase cardiotoxicity when combined with trastuzumab, and 324 (75%) before the 1st SC trastuzumab injection. The proportion of patients experiencing cardiac AEs in HERmione was low and in line with previous trials [9–13]: only 23/505 (4.6%) patients experienced at least one treatment-related CHF and only 2 (0.4%) patients experienced one serious treatment-related CHF (cardiac failure or ejection fraction decreased). The results showed no unexpected cardiotoxic effects.

Overall, HERmione study shows that the modalities of SC trastuzumab use in routine practice are consistent with the SmPC recommendations: treatment exposure (of about 12 months), injection frequency (*i.e.*, 18 injections over 12 months) and sites of injection (equally distributed between right and left thigh) were respected as well as cardiac assessments. However, regarding the debatable trastuzumab indications in subcentimetric tumors, we were not able to detail treatments among these patients as the initial questionnaire did not included T1 subclassification data.

Regarding quality of life, over one year of SC trastuzumab-based therapy in HERmione, the QoL of patients with HER2-positive eBC does not seem to be associated with clinically changes. Due to lack of data, conclusions and interpretations should be analyzed with caution. Nevertheless, these results, taking into account the good functional level of patients at baseline, are consistent with expectation: QoL analyses showed no deterioration of global health status. Recent reports also showed that patients without comorbidity receiving subcutaneous trastuzumab had less treatment side effects, less upset by hair loss, and higher emotional functioning [15].

HERmione confirms that the safety and tolerability of SC trastuzumab in real life conditions are consistent with the safety profile of SC trastuzumab reported from previous clinical trials [9–13] and with the known safety profile of IV trastuzumab. Comparing to IV infusion, the alternative SC form is considered less invasive and less time-consuming for both patients and the health care institutions. SC trastuzumab can be administered over 2–5 min instead of IV trastuzumab which requires a loading dose given over 90 min and subsequent infusions over 30 min. The shorter SC administration time could possibly lead to improve convenience for patients, which is particularly important when patients are treated for prolonged periods of time. Thus, considering patient experience and choice, costs trastuzumab administration, patient's survey has pointed out a strong preference for subcutaneous trastuzumab [16]. Furthermore, patients/health professionals (nurses, doctors and pharmacists) preferences and the organizational benefit of the subcutaneous trastuzumab form, has been also showed in the PrefHer study and MetaspHer reports [17–18].

Other potential benefits of SC administration include providing an alternative route of administration for patients with poor venous access as well as lower resource utilization.

5. Conclusion

The HERmione study showed that, in a real-life setting, the safety of SC trastuzumab administered in HER2-positive eBC patients is consistent with data reported from previous clinical trials, without new safety concerns or QoL deterioration.

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Declaration of competing interest

Y. Belkacemi: ROCHE National board of experts (HERmione study, Breast cancer) and FERRING board of experts (Prostate Cancer). F. Delaporte, N. Chalabi and S. Pibre: Full-time employees of ROCHE. All remaining authors have declared no conflicts of interest.

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