SAFETY PRELIMINARY EVALUATION
GIM30-RAPID

UPDATED TO 28/06/2024

Study objectives

Primary Objectives:

The primary objective of the study is to evaluate the safety of pertuzumab and trastuzumab (PH) fixed-dose combination (FDC) for subcutaneous (SC) administration in patients with HER-2 positive breast cancer who have completed concurrent chemotherapy combined with pertuzumab and trastuzumab administered intravenously (IV) and are currently receiving or will be receiving maintenance therapy with PH FDC SC.

Secondary Objectives:

The secondary exploratory objectives of the study are:

- To assess the patient's social cost saving by means of a specific questionnaire;
- To assess the patient's health related quality of life (HRQOL).

Investigational plan

Study design

This is a single arm prospective, observational multi-centre study in patients with HER-2 positive breast cancer who have completed concurrent chemotherapy with pertuzumab and trastuzumab administered IV and are currently receiving or will be receiving maintenance therapy with PH FDC SC and have at least 6 cycles of expected therapy with PH FDC SC to conclude pre-established oncological therapy.
Treatment of the patients will not be determined or assigned by study procedures but will be based on normal clinical practice. Only data available as per clinical practice will be collected within this study. The treatment decision must have been taken prior to and irrespective of the patient's enrollement in the study.

Primary endpoint

Number and percentage of patients with grade 3-4 adverse events (AEs), according to National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0 (NCI CTCAE v5.0).

Purpose of this partial evaluation

The purpose of this preliminary evaluation was to analyse the safety trend and to monitor the involved centers for the process of adverse events recording in the dedicated study platform (https://www.oncotech.org/gim30). Data will be updated during the trial.

Study population

Starting from Oct 11, 2023, sixty (60) patients were screened (n.1 screening failure + n.10 waiting for enrolment) and forty-nine (49) patients were treated within the study.

Initial Safety evaluations

Adverse events

Twenty-one (21) AEs were observed, involving twelve (12) different subjects (Table 1). The most common AEs were onychopathy (n=3; 6,12%), arthalgia (n=2; 4,08%) and nausea (n=2; 4,08%) Only one (1) event was graded as severe (Cardiac disorders - Other, specify: Reduction ejection fraction heart failure). All reported AEs were grade between I-II (max. Grade) except the SAE (notified as grade IV) which caused treatment discontinuation (please refer to "SAE Description"). No events caused death.

The observation time from the first dose until the last dose for each patient (current date for ongoing patients or end date + 30 days for dropouts) is shown in the table 3.

Treatment-Related Adverse events

From the total number of events, sixteen (16) treatment-related adverse events were observed, involving nine (9) different subjects (Table 2). The SAE (Cardiac disorders - Other, specify: Reduction ejection fraction heart failure) was identified as treatment-related.

The observation time from the first dose until the last dose (current date for ongoing patients or end date + 30 days for dropouts) is shown in the table 4.

SAE Description

The only serious adverse event observed has been the event "reduction ejection fraction - heart failure". It has been described as the evidence of heart failure with reduced ejection fraction occurring after the 6th cycle of adjuvant treatment with phesgo (PH FDC SC). The patient was treated with PH FDC SC in adjuvant setting before starting the trial. The SAE occurred at the first administration within the GIM30 Study and was graded as Life threatening/disabling - Grade 4 with a probable correlation to the treatment. The event occurred on the 25 oct 2023, with an echocardiogram dated 3 nov 2023 showing a left ventricular Ejection Fraction (LVEF) of 35%, and the SAE was declared resolved with sequelae on the 15 nov 2023. Initially, it was proposed the need of a cardioverter-defibrillator implantation, but, at further follow-up, it was no longer required because of spontaneous improvement of ejection fraction. The patient was admitted to cardiology from 19 march 2024 to 20 march 2024, with a loop recorder implantation. On the 09 may 2024 the patient was in good general condition, continuing cardiology follow-up, the latest on the 23 april 2024, with the echocardiogram showing a LVEF of 50% and blood chemistry in the normal range.

Table 1: Adverse Events

N°	DescriptionAE	Any Grade (Pt distinct)	%	Max Grade 1 (Pt distinct)	%	Max Grade 2 (Pt distinct)	%	Max Grade 3 (Pt distinct)	%	Max Grade 4 (Pt distinct)	%	DEAD	%
1	Skin and subcutaneous tissue disorders - Other, specify: onychopathy	3	6,12	3	6,12	0	0	0	0	0	0	0	0
2	Arthralgia	2	4,08	2	4,08	0	0	0	0	0	0	0	0
3	Nausea	2	4,08	1	2,04	1	2,04	0	0	0	0	0	0
4	Vertigo	1	2,04	1	2,04	0	0	0	0	0	0	0	0
5	Weight loss	1	2,04	1	2,04	0	0	0	0	0	0	0	0
6	Cardiac disorders - Other, specify: Reduction ejection fraction heart failure	1	2,04	0	0	0	0	0	0	1	2,04	0	0
7	Productive cough	1	2,04	0	0	1	2,04	0	0	0	0	0	0
8	Fatigue	1	2,04	0	0	1	2,04	0	0	0	0	0	0
9	Paresthesia	1	2,04	1	2,04	0	0	0	0	0	0	0	0
10	Respiratory, thoracic and mediastinal disorders - Other, specify: respiratory virus	1	2,04	1	2,04	0	0	0	0	0	0	0	0
11	Skin and subcutaneous tissue disorders - Other, specify: erythematous skin of the hands associated with periungual raghades	1	2,04	1	2,04	0	0	0	0	0	0	0	0
12	Cholesterol high	1	2,04	1	2,04	0	0	0	0	0	0	0	0
13	Constipation	1	2,04	1	2,04	0	0	0	0	0	0	0	0
14	Dyspnea	1	2,04	1	2,04	0	0	0	0	0	0	0	0
15	Eye disorders - Other, specify: vision loss (dx)	1	2,04	1	2,04	0	0	0	0	0	0	0	0
16	Fever	1	2,04	1	2,04	0	0	0	0	0	0	0	0
17	Gastrointestinal disorders - Other, specify: inappetence	1	2,04	1	2,04	0	0	0	0	0	0	0	0
18	Headache	1	2,04	1	2,04	0	0	0	0	0	0	0	0
19	Hematoma	1	2,04	1	2,04	0	0	0	0	0	0	0	0
20	Musculoskeletal and connective tissue disorder - Other, specify: low back pain	1	2,04	1	2,04	0	0	0	0	0	0	0	0
21	Anemia	1	2,04	1	2,04	0	0	0	0	0	0	0	0

Table 2: Related Adverse Event

N°	DescriptionAE	Any Grade (Pt distinct)	%	Max Grade 1 (Pt distinct)	%	Max Grade 2 (Pt distinct)	%	Max Grade 3 (Pt distinct)	%	Max Grade 4 (Pt distinct)	%	DEAD	%
1	Skin and subcutaneous tissue disorders - Other, specify: onychopathy	2	4,08	2	4,08	0	0	0	0	0	0	0	0
2	Nausea	2	4,08	1	2,04	1	2,04	0	0	0	0	0	0
3	Paresthesia	1	2,04	1	2,04	0	0	0	0	0	0	0	0
4	Skin and subcutaneous tissue disorders - Other, specify: erythematous skin of the hands associated with periungual raghades	1	2,04	1	2,04	0	0	0	0	0	0	0	0
5	Vertigo	1	2,04	1	2,04	0	0	0	0	0	0	0	0
6	Cardiac disorders - Other, specify: Reduction ejection fraction heart failure	1	2,04	0	0	0	0	0	0	1	2,04	0	0
7	Fatigue	1	2,04	0	0	1	2,04	0	0	0	0	0	0
8	Anemia	1	2,04	1	2,04	0	0	0	0	0	0	0	0
9	Arthralgia	1	2,04	1	2,04	0	0	0	0	0	0	0	0
10	Constipation	1	2,04	1	2,04	0	0	0	0	0	0	0	0
11	Dyspnea	1	2,04	1	2,04	0	0	0	0	0	0	0	0
12	Eye disorders - Other, specify: vision loss (dx)	1	2,04	1	2,04	0	0	0	0	0	0	0	0
13	Fever	1	2,04	1	2,04	0	0	0	0	0	0	0	0
14	Gastrointestinal disorders - Other, specify: inappetence	1	2,04	1	2,04	0	0	0	0	0	0	0	0
15	Hematoma	1	2,04	1	2,04	0	0	0	0	0	0	0	0
16	Musculoskeletal and connective tissue disorder - Other, specify: low back pain	1	2,04	1	2,04	0	0	0	0	0	0	0	0

Table 3: Observation Time for Adverse Event

N°Pt.	Age At Enrol	Phase	First Dose	Date EoT	Last Date	ObservationTime (Days)
1	58	ongoing	11/10/2023		28/06/2024	261
2	70	ongoing	24/10/2023		28/06/2024	248
3	49	ongoing	26/10/2023		28/06/2024	246
4	82	ongoing	13/12/2023		28/06/2024	198
5	50	ongoing	27/12/2023		28/06/2024	184
6	54	ongoing	01/02/2024		28/06/2024	148
7	57	ongoing	29/01/2024		28/06/2024	151
8	76	ongoing	22/02/2024		28/06/2024	127
9	41	ongoing	08/02/2024		28/06/2024	141
10	62	ongoing	03/04/2024		28/06/2024	86
11	53	EoT	11/03/2024	13/06/2024	13/07/2024	124
12	69	EoT	17/10/2023	25/10/2023	24/11/2023	38

Table 4: Observation Time for Related Adverse Event

N°Pt.	Age At Enrol	Phase	First Dose	Date EoT	Last Date	Observation Time (Days)
1	70	ongoing	24/10/2023		28/06/2024	248
2	82	ongoing	13/12/2023		28/06/2024	198
3	50	ongoing	27/12/2023		28/06/2024	184
4	54	ongoing	01/02/2024		28/06/2024	148
5	57	ongoing	29/01/2024		28/06/2024	151
6	76	ongoing	22/02/2024		28/06/2024	127
7	41	ongoing	08/02/2024		28/06/2024	141
8	53	EoT	11/03/2024	13/06/2024	13/07/2024	124
9	69	EoT	17/10/2023	25/10/2023	24/11/2023	38

Final considerations

As shown in this preliminary analyses involving the first 49 patients included in the trial (of the 80 planned to be enrolled) PH FDC SC demonstrated to be safe in a real-life cohort of patients with localized or advanced HER2 positive breast cancer, as most of AEs were grade 1-2.

No grade 3 and only one (1) grade 4 AEs were recorded. The SAE was related to acute heart failure, with reduction in the left ventricular ejection fraction, which represent a relatively common, described and usually reversible side effect of anti-HER2 treatments. The drug was permanently discontinued and the patient recovered ejection fraction from 35% to 50% on the latest echocardiogram of April 2024.

Importantly, no infusion-related AEs or hypersensitivity reaction were recorded.

The study is currently ongoing. In the final analysis, also patient's social cost and health related quality of life will be described.