STEM: SFX-01 in the Treatment and Evaluation of Metastatic breast cancer

#5696

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BACKGROUND

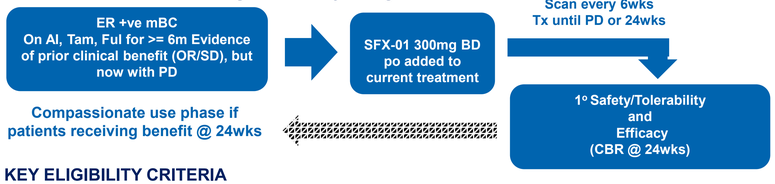
SFX-01 is a proprietary synthetic pharmaceutical product based upon a stabilised sulforaphane. In preclinical models SFX-01 inhibits the activity of cancer stem-like cells and reverses resistance to endocrine therapies (ET) tamoxifen (Tam) and fulvestrant (Fulv). The STEM study investigated the potential of SFX-01 to reverse acquired resistance to Tam, Fulv and third generation aromatase inhibitor (AI) therapy.

METHODS

STUDY DESIGN

- A Phase II, open label exploratory trial in 3 cohorts of patients with ER-positive MBC, to study the effects of SFX-01 in combination with AI, tamoxifen or fulvestrant in patients who have developed secondary resistance* to the current therapy
- The intention was to enrol approximately 60 patients (approx. 20 patients per arm) across the 3 different treatment arms: Arm A Aromatase Inhibitor +SFX-01; Arm B Tamoxifen + SFX-01; Arm C Fulvestrant + SFX-01

Figure 1. Study Design Schematic



KEY ELIGIBILITY CRITERIA

- Male or female patients 18yrs or older
- Histological confirmation of ER+ HER2-negative breast cancer
- Clinical or histological confirmation of metastatic or locally advanced disease not amenable to curative surgical resection
- At least 1 site of measurable disease
- Must be on a third generation AI, Tam or Fulv and have evidence of emerging secondary endocrine resistance as evidenced by either:
  a) Progressive disease while on adjuvant ET but after the first 2 years, or b) Progressive disease within 12 months of completing adjuvant ET, or c) Progressive disease while on ET, ≥6 months after initiating ET for metastatic breast cancer
- No more than 3 lines of endocrine therapy including the treatment at the time of study entry and
- No more than 1 prior line of chemotherapy for metastatic/locally advanced breast cancer

OBJECTIVES

The primary objectives of the study were:

- To determine the safety & tolerability of SFX-01 in combination with AI Tam or Fulv
- To determine the clinical benefit rate (CBR) at 24wks using RECIST 1.1

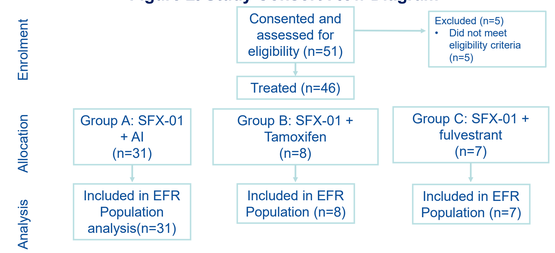
The key secondary objectives were:

- To determine objective response rate (ORR) at 24wks using RECIST 1.1
- To determine progression free survival at 24wks
- To determine overall survival at 24wks

RESULTS

- 46 patients were treated across 10 centres in Belgium, France, Spain and UK
- Recruitment to the Tam and Fulv arms was slower than anticipated, and recruitment was stopped following a successful interim update in June 2018
- 35/46 patients had visceral involvement
- Prior lines of ET were 1 =17/46 (37%); 2 =17/46 (37%) and ≥3 =12 (26%)
- 8/46 patients had prior chemotherapy

Figure 2. Study Consort Flow Diagram



EFR = Evaluable for Response: all subjects from the FAS population who receive study drug, who have a baseline disease assessment with measurable disease and one of the following: (1) at least one post-baseline disease assessment, or (2) withdrawn from study treatment before post-baseline disease assessment due to clinical progression or death

SAFETY

- 45 /46 patients had an averse event (AE).
- 10/46 patients had a serious adverse event (SAE).
  - 2/46 patients had SAEs that were considered to be possibly drug related.
  - This included one patient with 3 grade SAEs of anaemia, abdominal distention and should have been removed, as they were found to be due to disease progression.
  - The second patient had 2 SAEs of Fibrin D dimer increased and pleuritic pain

EFFICACY

- 2 /46 patients had partial responses
  - one patient with shrinkage of 27% at wk, increasing to 63.6% shrinkage at wk 18 and maintained at 54.5% at week 24
  - One patient narrowly missed a confirmed response by 0.2% with shrinkage of 29.8% followed by 48.9%
- 12/46 patients had clinical benefit, giving a CBR of 24%

CONCLUSIONS

- SFX-01 300mg BID is well tolerated with no safety concerns in patients with ER+ and HER2- MBC
- SFX-01 in combination with ET demonstrated both anti-tumour activity and prolonged disease stabilisation in heavily pre-treated patients who were pgrogressing on the ET at entry to the study
- Further development of SFX-01 in mBC is warranted

Figure 3. Most Common Adverse Events ≥10% with any causality

Adverse Event	Total Number of Patients (%) (N=46)	Patients with Grade 3 or 4 Adverse Event
Nausea	25 (54.3%)	0
Dyspepsia	15 (32.6%)	0
Diarrhoea	12 (26.1%)	0
Abdominal Pain + Abdominal Pain Upper + Gastrointestinal Pain	11 (23.9%)	0
Back Pain	10 (21.7)	0
Vomiting	10 (21.7%)	0
Fatigue	9 (19.6%)	1 (2.2%)
Asthenia	8 (17.4%)	0
Blood alkaline phosphatase increased	6 (13%)	0
Decreased appetite	6 (13%)	0
Alanine aminotransferase increased	5 (10.9%)	1 (2.2%)
Arthralgia	5 (10.9%)	0
Pain in extremity	5 (10.9%)	0

Figure 4. Best % change from Baseline in Target Lesions over time

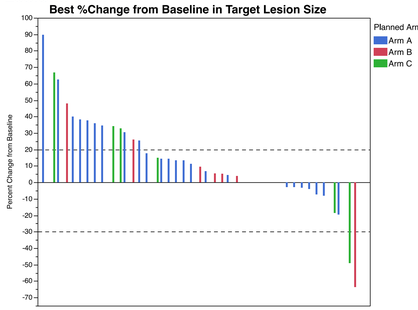
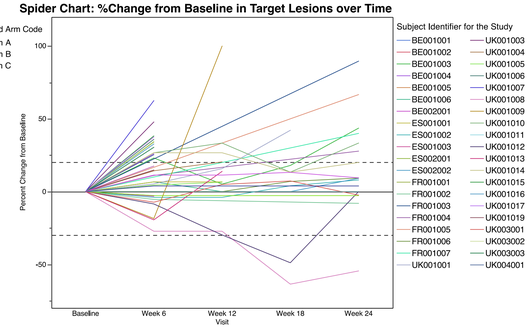


Figure 5. % change from Baseline in Target Lesions over time



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Acknowledgements and Special Thanks:
With thanks to all of the Investigators and site staff who contributed to the study. In addition to the authors: Dr Canon, Clinique Universitaires Saint-Luc, Belgium; Dr Altintas, Antwerp University Hospital, Belgium; Dr Perez, Hospital Quiron Barcelona, Spain: Dr Hickish, Royal Bournemouth and Christchurch Hospitals NHS Foundation Trust; Dr Takeuchi, Royal Albert and Edward Infirmary; Dr Anwar, University Hospitals Birmingham NHS Foundation Trust

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