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

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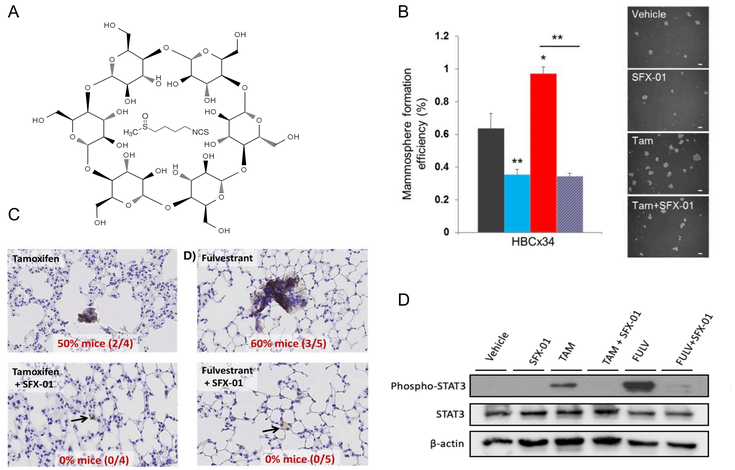
BACKGROUND

Sulforaphane (SFN) is a plant secondary metabolite that was first identified as an anti-cancer agent in 1992. SFN is a highly unstable compound and thus the development of a practical pharmaceutical has been challenging. Some exploratory clinical trials have used plant extracts that are enzymatically-treated to release SFN and then subsequently frozen. However, these formulations are not practical for larger trials or subsequent commercialization. SFX-01 is a novel pharmaceutical based upon synthetic SFN stabilized with cyclodextrin, solving the manufacturing and economic barriers to clinical development. Preclinical data show sulforaphane and SFX-01 inhibit breast cancer stem cells[1,2] and SFX-01 potently suppresses STAT3 in ER+ metastatic breast cancer (mBC) PDX tumours[3]. It is therefore hypothesised that SFX-01 could become a potential therapy for reducing resistance to hormone therapy in patients with mBC.

Figure 1: SFX-01 is a patented composition comprising sulforaphane stabilised in alpha-cyclodextrin (A). in patient-derived xenografts, SFX-01 reduces cancer stemness (mammosphere formation efficiency) which is increased by tamoxifen treatment[2] (B), reduces subsequent metastases to the lungs[3] (C), and eliminates the activated form of STAT3[3], a driver of therapy resistance, tumour renewal and metastases.

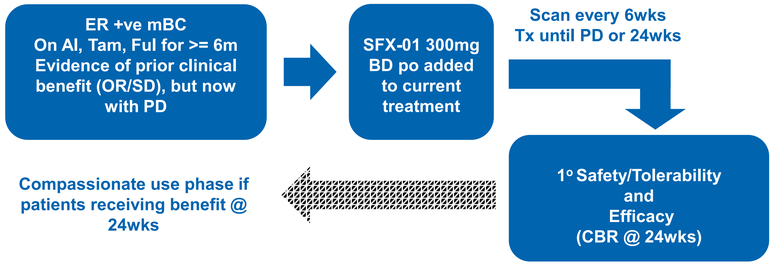


KEY ELIGIBILITY CRITERIA

- 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
- No more than 1 prior line of chemotherapy for metastatic/locally advanced breast cancer

TRIAL DESIGN

An open label trial with a maximum target of 60 patients with ER+, HER2-negative, mBC who are on a third generation aromatase inhibitor (AI), tamoxifen (Tam) or fulvestrant (Fulv) and have evidence of emerging secondary endocrine resistance. Participants remain on AI, Tam or Fulv and take this in combination with 300mg SFX-01 orally, twice-daily, and are scanned every 6 weeks (wks) until disease progression. Patients come off study upon progressive disease (PD) or at the full term of 24wks. Patients who are progression free as they approach 24wks can be enrolled in a compassionate use phase



SPECIFIC AIMS

The primary objectives of the study are:

- 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 are:

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

The exploratory objective is to evaluate the PK of SFX-01, AI, Tam & Fulv

ACCRUAL

Forty-six of the maximum 60 patients have been treated across 10 centres in Belgium, France, Spain and UK. Recruitment to the Tam and Fulv arms has been slower than anticipated, perhaps due to the widespread use of AIs in the treatment in ER+ mBC. Recruitment was stopped following a successful interim update in June this year.

STATISTICAL METHODS

Demographic, baseline characteristics, safety and efficacy data will primarily be summarised descriptively. The sample size of 20 patients in each treatment cohort is such that if the observed CBR on any arm is 15%, it will provide a 90% exact binomial confidence interval (CI) for the true CBR of 4.2% to 34.4%. Duration of response will be compared to duration of response on prior ET.

REFERENCES

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