STOPFOP: A European phase II clinical trial using saracatinib to treat FOP

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Background: Fibrodysplasia ossificans progressiva (FOP) is a genetic, progressive and devastating disease characterized by severe heterotopic ossifications (HO), contractures and early death. There are no approved medications yet. Our STOPFOP team identified AZD0530 (saracatinib) as a potent inhibitor of the ALK2-kinase which plays a key role in this rare bone disease. AZD0530 was proven to be effective in FOP mouse models. The EU Innovative Medicines Initiative provided funding to investigate the repurposing of AZD0530, originally designed for ovarian cancer treatment, to treat patients with FOP.

Methods: This is a phase 2a study, designed as European, multicentre, 6-month double blind randomized controlled trial of AZD0530 versus placebo, followed by a 12 month trial comparing open-label extended AZD0530 treatment with control data from a previous trial. We will include 20 FOP patients, aged 18-65 years, with the classic FOP mutation (R206H). Endpoints are objective change in heterotopic bone volume measured by low-dose whole-body computer tomography (CT) , [18F] NaF PET activity and patient reported outcome measures.

Discussion: Drug repurposing - using existing clinical molecules for new disease indications - represents an ideal solution for limiting risks in early clinical studies. This is especially useful in rare diseases with limited study populations. Using existing assets may also allow more affordable pricing once an indication is approved. With positive study outcome, AZD0530 may provide a rapidly translatable therapy for FOP due to the availability of extensive safety data from 28 registered clinical trials with AZD0530 involving over 600 patients.

Trial registration: EudraCT number 2019-003324-20

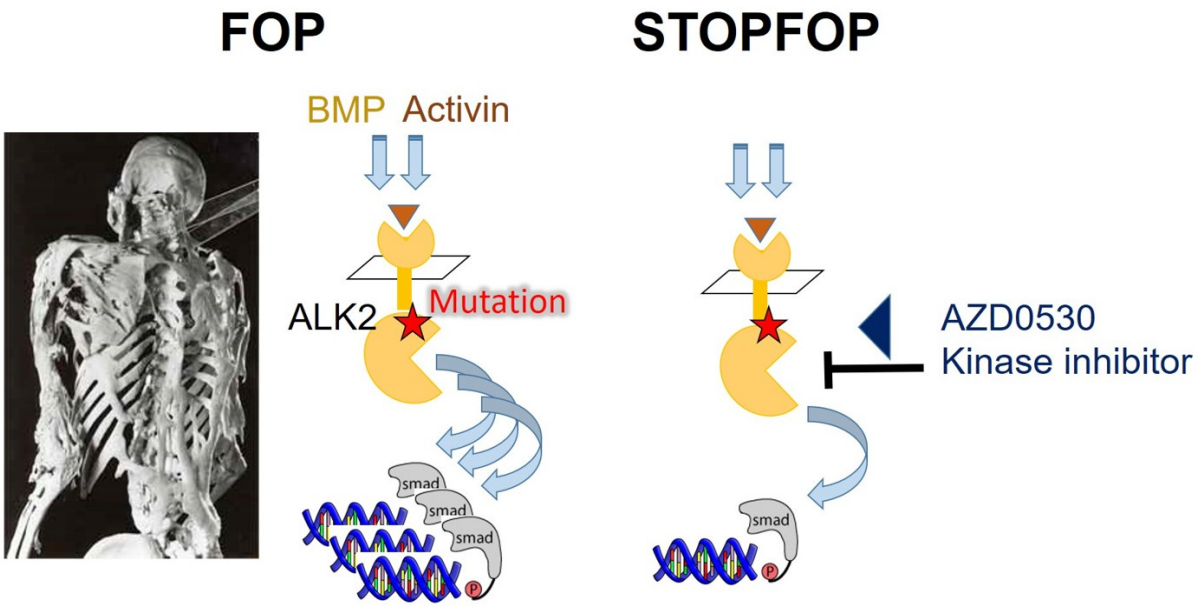

Fig. 1. Working mechanism of AZD0530 (saracatinib).