Efficacy of Bioactive Tree Bark Extracts to Reverse Idiopathic Pulmonary Fibrosis

2019
Final Progress Report

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Sponsor: Pneumoconiosis Compensation Fund

The Chinese University of Hong Kong
School of Biomedical Sciences

1) Aims of our project

In the light of our successful endeavor to find a potential treatment for liver fibrosis, we want to establish whether consumption of our tree bark extract could also alleviate lung fibrosis – which is progressive and disabling disease. In this propose study, we have three specific aims:

(1) To establish the bioactivity of our tree bark extract on excess collagen and other ECM production in activated human lung fibroblast cell line (Mrc-5).
(2) To screen our extensive library of plant extracts on activated Mrc-5 cells to identify other antifibrotic agents.
(3) Validate the ability of our tree bark extract to inhibit lung fibrosis in a silica-induced fibrosis mouse model.

2) Schedule of the Project

Overall Schedule

Commencement date (dd/mm/yy)	:	01/08/17
Original completion date (dd/mm/yy)	:	31/01/19
Amended completion date (dd/mm/yy)	:	31/04/19
Project duration (month)	:	21

Project Schedule

Periods		Milestones
From (dd/mm/yy)	To (dd/mm/yy)	
01/08/17	31/10/17	Establish the bioactivity of our tree bark extract on excess collagen and other ECM production in activated human lung fibroblast (Mrc-5) cell line.
01/11/17	31/08/18	Validate the ability of our tree bark extract to inhibit lung fibrosis in a silica-induced fibrosis mouse model.
28/02/18	31/01/19	Screen our extensive library of plant extracts on activated Mrc-5 cells to identify other potential antifibrotic agents.

3) Investigators

- Professor Kenneth Lee (PI), Chief of Stem Cell and Regeneration Thematic Research Program, School of Biomedical Sciences, Chinese University of Hong Kong.
- Dr. Stanton Kok (Co-PI), Research Associate, Stem Cell and Regeneration Thematic Research Program, School of Biomedical Sciences, Chinese University of Hong Kong.
- Dr. Kevin Kok (Laboratory Manager), Research Assistant, Stem Cell and Regeneration Thematic Research Program, School of Biomedical Sciences, Chinese University of Hong.
- Ms Elaine Tsang (Researcher), PhD student, Stem Cell and Regeneration Thematic Research Program, School of Biomedical Sciences, Chinese University of Hong.

4) Background and Significance of the Project

Lung fibrosis

Idiopathic pulmonary fibrosis (IPF) is a progressive and irreversible lung disorder with a not fully known etiology. It is characterized by the formation of extensive scar tissues from excessive production and accumulation of collagen-rich extracellular matrix (ECM). Extensive pulmonary fibrosis will lead to loss of normal lung architecture, elasticity, compliance and respiratory function - as a result of failure of alveolar re-epithelialization.[1] The five-year survival rate for IPF is 44%, which is even more deadly than most of cancers[2] – accompanied by serious adverse effect of chronic treatment.[3] The prevalence and incidence of IPF increases with age that are predominantly higher among male.[4] The prevalence rate has been estimated in the USA to vary between 14 and 27.9 cases per 100,000 population using narrow case definitions, and 42.7 and 63 per 100,000 population using broad case definitions. In Europe, IPF prevalence ranged from 1.25 to 23.4 cases per 100,000 population. The annual incidence of IPF in the USA was estimated at 6.8-8.8 per 100,000 population using narrow case definitions and 16.3-17.4 per 100,000 population using broad case definitions. In Europe, the annual incidence ranged between 0.22 and 7.4 per 100,000 population.[5] To date, there have only been approved two therapies by the US FDA to treat pulmonary fibrosis in humans (Pirfenidone and Nintedanib, **Figure 1**) and most of all potential drugs are still in clinical trial phases (e.g. Bosentan, GKT-137831, Imatinib, Macitentan, etc.)[6]. Lung transplant is feasible but it is limited supply with serious matching problem together with high potential to IPF. In addition, the average survival rate is only 3 years after successful transplantation[7] and the cost of these treatments is very high. Compared with the sky-high cost of new drug development and the many years that it involves, traditional Chinese medicine (TCM) offers very low cost of production with an unlimited supply of raw materials from Mainland China and South East Asia. The average production cost for 4-weeks TCM treatment may be less than US$100 and no additional cost on oral formulation. This will reduce the burden of early drug development cost and improve the long-term profitability. In addition, TCM also offers a convenient oral administration route that will increase patient compliance compared with subcutaneous injection. Apart from the high cost of drug development, TCM may also offer a better chance of polypharmacological interventions, with multiple targets in comparison to limited success of highly selective molecules on a single target. Of course, earlier diagnosis of IPF has greater potential of improvement after treatment but the long-term clinical outcome of this progressive condition is ultimately death.[8]

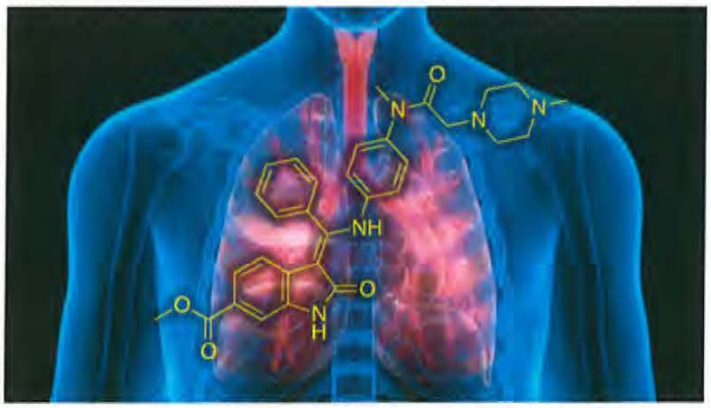

Figure 1 Nintedanib (tradename Ofev-Boehringer, 2014-Oct FDA approved formerly BIBF 1120; trade name Vargatef)