

# Targeted stem Cells expressing TRAIL as a therapy for lung Cancer

## TACTICAL: a phase I/II trial

### Introduction:

Current treatments for advanced NSCLC are associated with significant toxicities and only improve life expectancy by a few months. With over 70% of patients presenting with advanced disease there is a pressing need for novel therapies.

TNF-related apoptosis inducing ligand (TRAIL) is an anti-cancer therapy which causes apoptosis in tumour cells leaving healthy cells unaffected. We previously transduced mesenchymal stromal cells (MSCs) with a lentiviral vector to express TRAIL (MSCTRAIL). These cells home to tumours and induce apoptosis selectively in cancer cells resulting in a reduction in tumour growth in multiple *in vivo* models.

We have produced a viable working bank of MSCTRAIL and are now undertaking a first-in-man clinical trial to assess the therapeutic efficacy of this genetically modified cell therapy in the treatment of metastatic lung adenocarcinoma.

A key barrier to translation for cellular therapy is the understanding of the cell journey after delivery. <sup>111</sup>Indium-oxide is established for lymphocyte tracking but it has low sensitivity and is toxic to cells. <sup>89</sup>Zirconium-oxine is a novel PET tracer which has better sensitivity and lower toxicity. We have shown MSCTRAIL can be radiolabelled with <sup>89</sup>Zr without effecting viability or therapeutic efficacy.

### Trial design:

Phase I is a dose de-escalation study, phase II is multi-centre, single blinded, randomised, placebo controlled trial (figure 1a and 1b).

A first-in-man expansion cohort of 5 patients will received <sup>89</sup>ZrMSCTRAIL in cycles 1 and 3. They will undergo serial PET scanning allowing mapping of cell location and duration.

### Outcomes:

Phase I primary outcome is safety and tolerability of MSCTRAIL.

Phase II primary outcome is tumour response rate by RECIST (v 1.1) criteria 12 weeks

Secondary outcomes include, best overall response, duration of response, progression free survival and overall survival.

### Future Work:

If MSCTRAIL is safe and effective we plan to expand into larger phase III trials.

Figure 1a: Phase I Schema

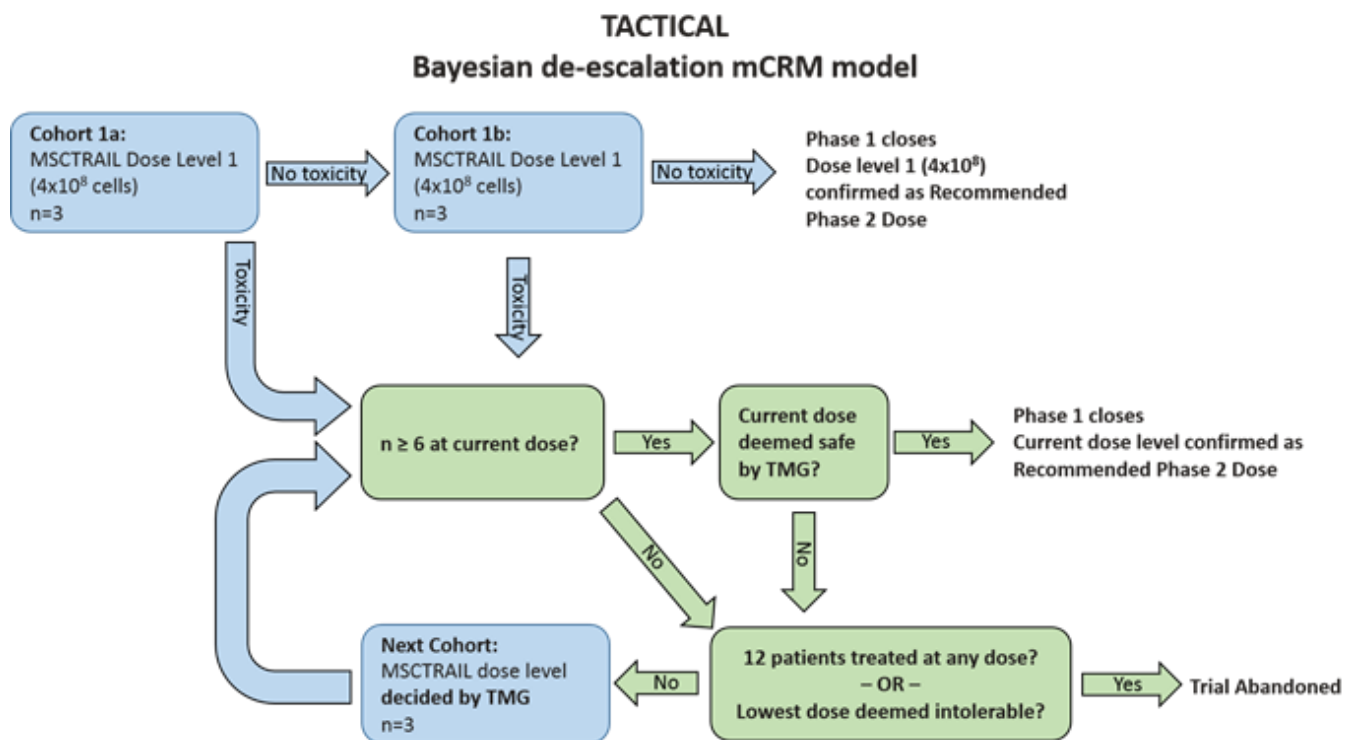


Figure 1b: Phase II Schema

