Long-Term Survival of Patients with Stage III/IV Melanoma Receiving IMM-101

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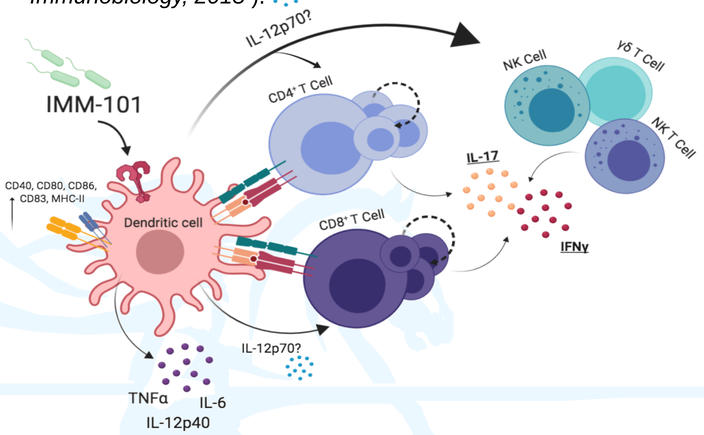
Background

- IMM-101 is a multimodal immunomodulator containing heat-killed, whole cell *Mycobacterium obuense* (NCTC13365), activating Pathogen Recognition Receptors (PRRs) including TLR-2.
- IMM-101 has shown to induce a protective $CD8^+$ response in clinically relevant models of pancreatic cancer (*Elia et al. J Immunother Cancer, 2013*).
- Recent animal data have shown that IMM-101 activates DCs in a dose-dependent manner, enabling these DCs to induce IFNγ production by a variety of immune cells *in vitro* and *in vivo (Galdon et al. FIFTH CRI-CIMT-EATI-AACR International Cancer Immunotherapy Conferences, 2019).*
- *In vitro* experiments with human PBMCs showed similar results (*Fowler et al. Cancer Immunol Immunother, 2012; Bazzi et al. Immunobiology, 2015*).



- IFNγ induction by IMM-101 DCs does not require their ability to produce IL-12, but is dependent on recipient IL-12 production *(Galdon et al. 2019*).
- Direct intradermal injection of IMM-101 initiates a Th1/Th17 adaptive immune response both locally and systemically *(Galdon et al. 2019*).

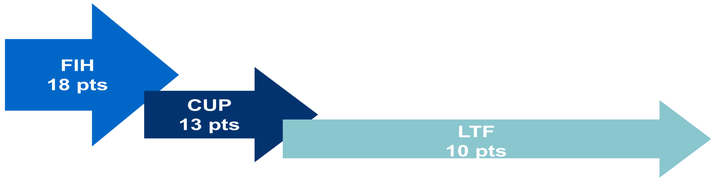
- In a randomised phase 2 study in combination with gemcitabine, IMM-101 showed improvement in PFS and OS in metastatic pancreatic cancer patients compared to gemcitabine alone without additional toxicity (*Dalgleish et al. Br J Cancer, 2016*)

- **Long term survival data are now available for patients with stage III/IV melanoma recruited into a Phase 1 placebo controlled, dose escalation study of IMM-101**

Methods

Between Mar and Sep 2010, 18 patients with Stage III/IV melanoma completed a first-in-human (FIH) study to evaluate the safety and tolerability of IMM-101 (NCT01308762).

Treatment with IMM-101 continued, initially on a compassionate use program (CUP) and then in an open label long term follow up (LTF) study, which closed in Dec 2018. Of the 18 patients (12 Stage IV, 3 Stage IIIB and 3 Stage IIIC) who completed the FIH study, 13 received subsequent treatment on a CUP and 10 were enrolled in the LTF study (9 Stage IV, 1 Stage IIIC at the time of enrolment to LTF), which started in Feb 2012.



First-in-human (FIH) study
To evaluate safety and tolerability of intra-dermal injections of IMM-101 in melanoma patients. Three doses of IMM-101 (0.1 mg, 0.5 mg or 1.0 mg) were given by intradermal injection at 2-weekly intervals after an initial placebo dose, each evaluated in sequential cohorts of 6 patients.

Long-term follow-up (LTF) study
To determine the long-term safety profile of IMM-101 over extended use. Intradermal injection of 1.0 mg IMM-101 (10 mg/mL solution) into skin overlying deltoid muscle, alternate arms at each dose. One dose every 4 weeks, with modification at investigator discretion (dosing interval ≥ 14 days). At start of LTF study, written informed consent was obtained to retrospectively collect disease and treatment history whilst on CUP.

Results

At time of LTF study closure, 6 of the 10 LTF study patients were alive with 4 of them still receiving treatment with IMM-101. The median time on treatment from first dose in the FIH study was 5.2 years (range 2.7 to 7.95, n= 10).

Two patients on the LTF study received immunotherapeutic agents other than IMM-101: one patient received IL-2 [A] and one patient IL-2 [A] and ipilimumab [B].

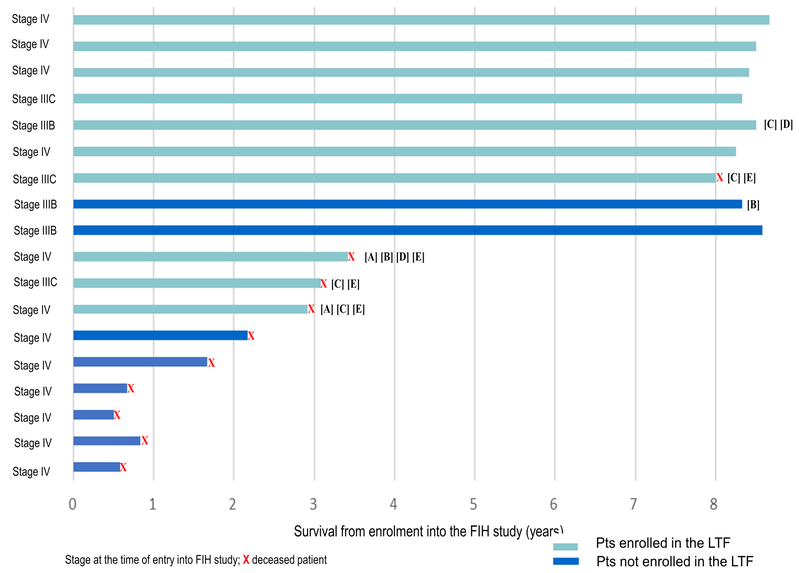
Other treatment included surgery [C] (4 patients), radiotherapy [D] (2 patients) and chemotherapy [E] (4 patients).

Two pts (both with stage IIIB disease at start of FIH study) who did not enter the LTF were also still alive in Dec 2018. One of these received further IMM-101 on a CUP followed by ipilimumab [B] at progression (patient 1 in *Dalgleish et al. J Trans Med 2018*)

Overall, IMM-101 was safe and well-tolerated and local reactions at the injection site were the most frequently reported adverse events.

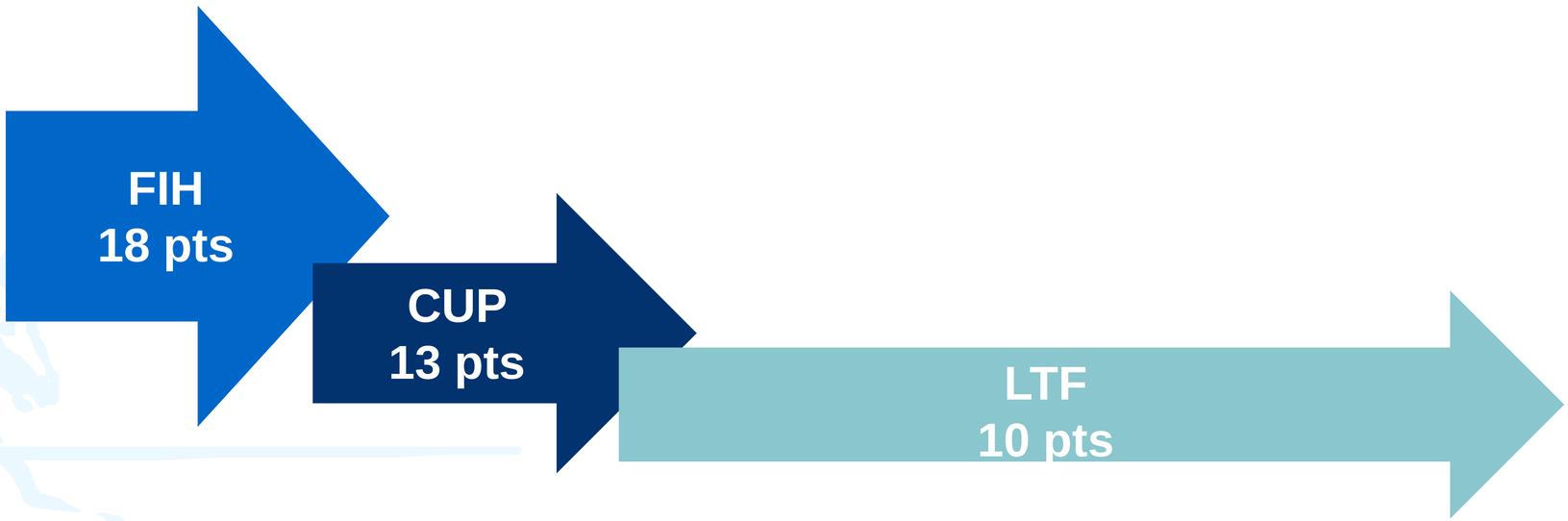
Patients characteristics at the time of enrolment into the FIH study

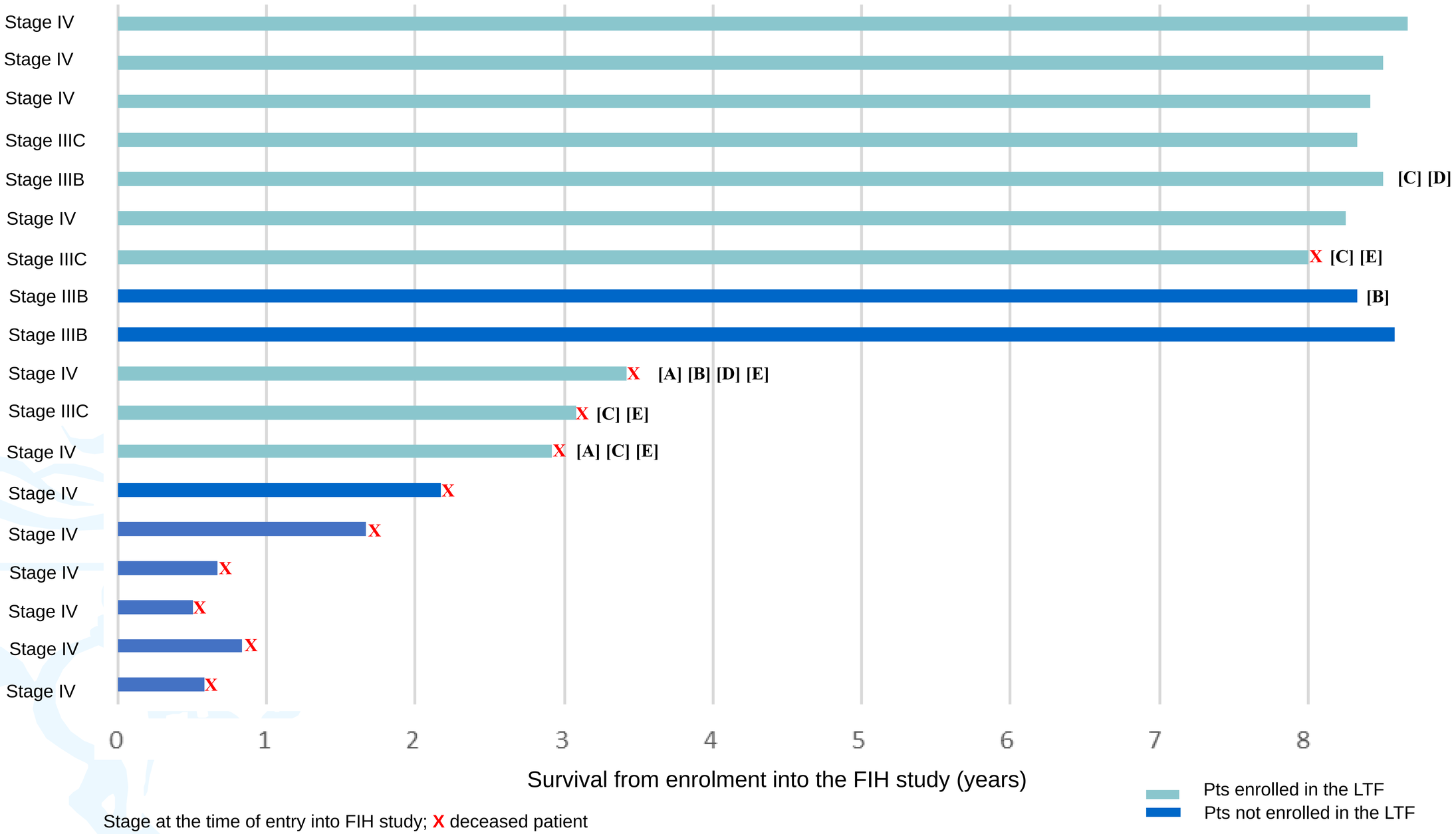
Age, median (range)		51 (26-69)
Gender	Male	10
	Female	8
AJCC 7 Stage	Stage IIIB	3 (16.7%)
	Stage IIIC	3 (16.7%)
	Stage IV	12 (66.6%)



Conclusion

Nine out of 18 (50%) patients with stage III/IV melanoma originally enrolled to the FIH study were alive at 5 years with 8/18 (44%) alive over 8 years. IMM-101 was well tolerated with no long-term adverse events seen.


FIH
18 pts
CUP
13 pts
LTF
10 pts



Stage at the time of entry into FIH study; **X** deceased patient