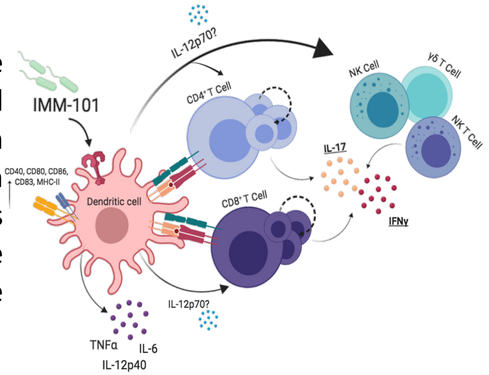
Abstract #9554: A phase II study to evaluate the safety and efficacy of IMM-101 in combination with checkpoint inhibitors in patients with advanced melanoma: Final results of the IMM-101-015 trial

Alberto Fusi, Avinash Gupta, Paul Lorigan, Peter L Smith, Mike Bowles

Background:

- IMM-101 is a multimodal immunomodulator containing heat-killed, whole cell *Mycobacterium obuense* (NCTC13365)
- It has shown to induce a protective $CD8^+$ response in clinically relevant models of pancreatic cancer (1) and to activate DCs in a dose-dependent manner, enabling these DCs to induce IFNγ (2)
- Direct Intradermal injection of IMM-101 initiates an adaptive Th1/Th17 immune response both locally and systemically (2)
- Pre-clinical works have showed improved activity of IMM-101 in combination with checkpoint blockades compared to the activity of either single agent (3)



Methods:

- Open-label Phase 2a study of the combination of IMM-101 with nivolumab in patients (pts) with advanced melanoma who were either treatment-naive (cohort A) or who had progressed during PD-1 blockade (cohort B)
- Patients in cohort B had the option to change to ipilimumab and IMM-101 if their disease continued to progress
- Primary Endpoints: Overall Response Rate (ORR) after a maximum of 18 months of treatment by RECIST 1.1 and safety/tolerability of the combination nivolumab + IMM-101

Patients:

Sixteen pts (11 Cohort A and 5 Cohort B) were treated between October 2018 and May 2021 at two UK centres

Main Takeaway

IMM-101 in combination with nivolumab is safe and shows encouraging antitumor activity in treatment-naïve patients with advanced melanoma

Future directions:

- Biomarkers analysis ongoing
- Larger trials needed

Contact information
Dr Alberto Fusi (alberto.fusi@stgeorges.nhs.uk; afusi@sgul.ac.uk)

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Patients characteristics		Cohort A (N=11)	Cohort B (N=5)	Overall (N=16)
Age	Median (range)	72.0 (36 – 92)	68.0 (61 – 74)	5. (36 – 92)
Gender n (%)	Male	8 (73)	3 (60)	11 (69)
	Female	3 (27)	2 (40)	5 (31)
ECOG ps n (%)	0	6 (55)	3 (60)	9 (56)
	1	5 (45)	2 (40)	7 (44)
AJCC staging n (%)	III	3 (27)	1 (20)	4 (25)
	IV	8 (73)	4 (80)	12 (75)
M staging n (%)	M0	3 (27)	1 (20)	4 (25)
	M1b	5 (45)	1 (20)	6 (38)
	M1c	3 (27)	3 (60)	6 (38)

Response rate:

Pts in cohort A were on study for a median time of 8.5 months (range 1.5 - 19.1) and those in cohort B for 3.0 months (range 1.5 - 7.4). The ORR was 73% (95% CI 39.03, 93.98) in cohort A whereas all pts in cohort B reported progressive disease

ORR in Cohort A (N=11)	PD-L1 Status		M Disease Staging			BRAF Status		LDH at Baseline	
	Positive	Negative/indeterminate	M0	M1a/M1b	M1c	WT	Mutant	≤ UNL	> UNL
Best objective response n (%)									
CR	2 (18)	0	0	2 (18)	0	2 (18)	0	1 (9)	1 (9)
PR	3 (27)	3 (27)	2 (18)	2 (18)	2 (18)	6 (55)	0	5 (46)	1 (9)
SD	0	0	0	0	0	0	1 (9)	1 (9)	0
PD	1 (9)	1 (9)	1 (9)	1 (9)	1 (9)	0	2 (18)	1 (9)	1 (9)
Objective response rate									
n (%)	5 (45)	3 (27)	2 (18)	4 (36)	2 (18)	8 (73)	0	6 (55)	2 (18)

Safety:

Ten (63%) of the patients had a TEAE of NCI CTCAE ≥Grade 3, but the majority of adverse events were Grade 1 or 2 with only 18.2% of events being Grade 3.

Most common drug related Treatment Emergent Adverse Events (>10%)	Patients, N (%) (N=16)	
	All grades	Grade 3 and 4
Total patients with drug related TEAEs		
Injection site reaction		
Skin rash		
Pruritus		
Fatigue		
Diarrhoea		
Transaminitis		
There were not reports grade 4 or grade 5 drug-related treatment emergent adverse events		

References:
1. Elia et al. J Immunother Cancer, 2013; 2. Galdon et al. British Society for Immunology Congress, Liverpool (UK), 2019; 3. Crooks J et al. SITC Annual Meeting, National Harbour (USA), 2016