A Cancer Research UK First Time in Human Phase I Trial of IMA950 (Novel Multi-Peptide Therapeutic Vaccine) in Patients with Newly Diagnosed Glioblastoma

Supplementary Tables and Figures

Table S1. TUMAPs contained in IMA950 and associated source antigens.

Peptide ID	Source antigen	Gene Symbol	Expression (%)*
IMA-BCA-002	Brevican	BCAN	10
IMA-BIR-002	Baculoviral IAP repeat-containing 5 (Survivin)	BIRC5	N/A
IMA-CSP-001	Chondroitin sulfate proteoglycan 4	CSPG4	100
IMA-FABP7-001	Fatty acid binding protein 7, brain	FABP7	20
IMA-HBV-001	Hepatitis B virus, core antigen	N/A	N/A
IMA-IGF2BP3-001	Insulin-like growth factor 2 mRNA binding protein 3	IGF2BP3	17
IMA-MET-005	Met proto-oncogene (hepatocyte growth factor receptor)	MET	N/A
IMA-NLGN4X-001	Neuroligin 4, X-linked	NLGN4X	20
IMA-NRCAM-001	Neuronal cell adhesion molecule	NRCAM	27
IMA-PTP-003	Protein tyrosine phosphatase, receptor-type, Z polypeptide 1	PTPRZ1	97
IMA-PTP-005			40
IMA-TNC-001	Tenascin C	TNC	83

* Values given indicate the percentage of primary GBM tumors on which the 9 HLA-A*02 TUMAPs were identified by mass spectrometry (n=30 analyzed tumor samples). These results indicate that the vast majority of GBM patients can be expected to express at least two of the IMA950 TUMAPs.

Abbreviations: N/A, not applicable; TUMAP, tumor associated peptide.

Table S2. Statistical analysis underlying the recruitment of 20 immune evaluable patients per cohort.

Number of single TUMAP responders from 20 immune evaluable patients	**Interpretation**	**Recommendation for further development of IMA950 plus GM-CSF based on immunogenicity results**
≤3	The true response rate is unlikely to be >40% (if there are 3 responders, the upper 95% CI is 34%)*	No further development
4 to 7	The true response rate could be above 40% and up to 60% (for 7 responders, upper 95% CI is 56%)*	Some evidence of immunogenicity, but consider supporting clinical evidence to decide whether further development is justified
8 to 12	The true response rate could be above 40% but also at least 60% (for 8 responders, the upper 95% CI is 61%)*	Moderate evidence of immunogenicity but consider supporting clinical evidence
≥13	The true response rate is highly likely to be at least 40% and could be at least 60% (for 13 responders, the exact two-sided 95% CI is 41% to 85%)	Good evidence of immunogenicity; positive outcome

*based on examining the upper one-sided 95% CI. A two-sided exact limit for ≤12 out of 20 patients would still include the possibility of the true response rate being <40%, but a one-sided limit is used in these three scenarios to promote further development of the IMPs.

In addition, when the trial design was conceived and, based on prior experience with other related vaccines developed by Immatics Biotechnologies, a very positive result was considered to be 30% or greater multi-TUMAP responders from 20 enrolled patients within a single cohort (1).

Table S3. Reasons for HLA-A*02 positive patients not entering the clinical trial.

Number of HLA-A*02 positive patients	Reason for non-entry
12	Patient declined consent for entry into the full trial
4	Decreased performance status and/or progression of disease
3	Tumor or patient not suitable for chemoradiotherapy
3	Timing or logistical issues during screening
2	Lymphocytes counts below threshold for entry
1	Gliadel wafers implanted
1	History of prior auto-immune disease

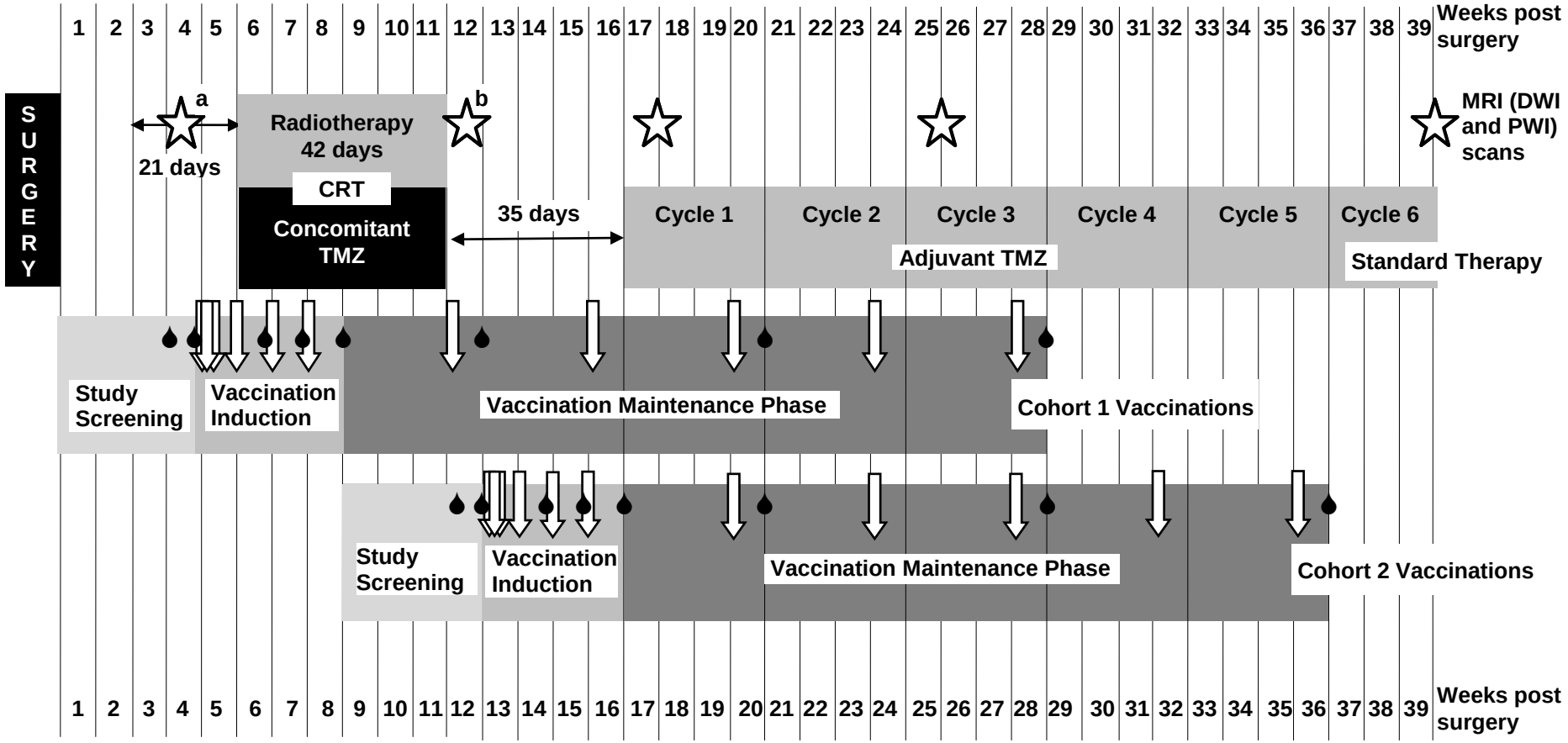
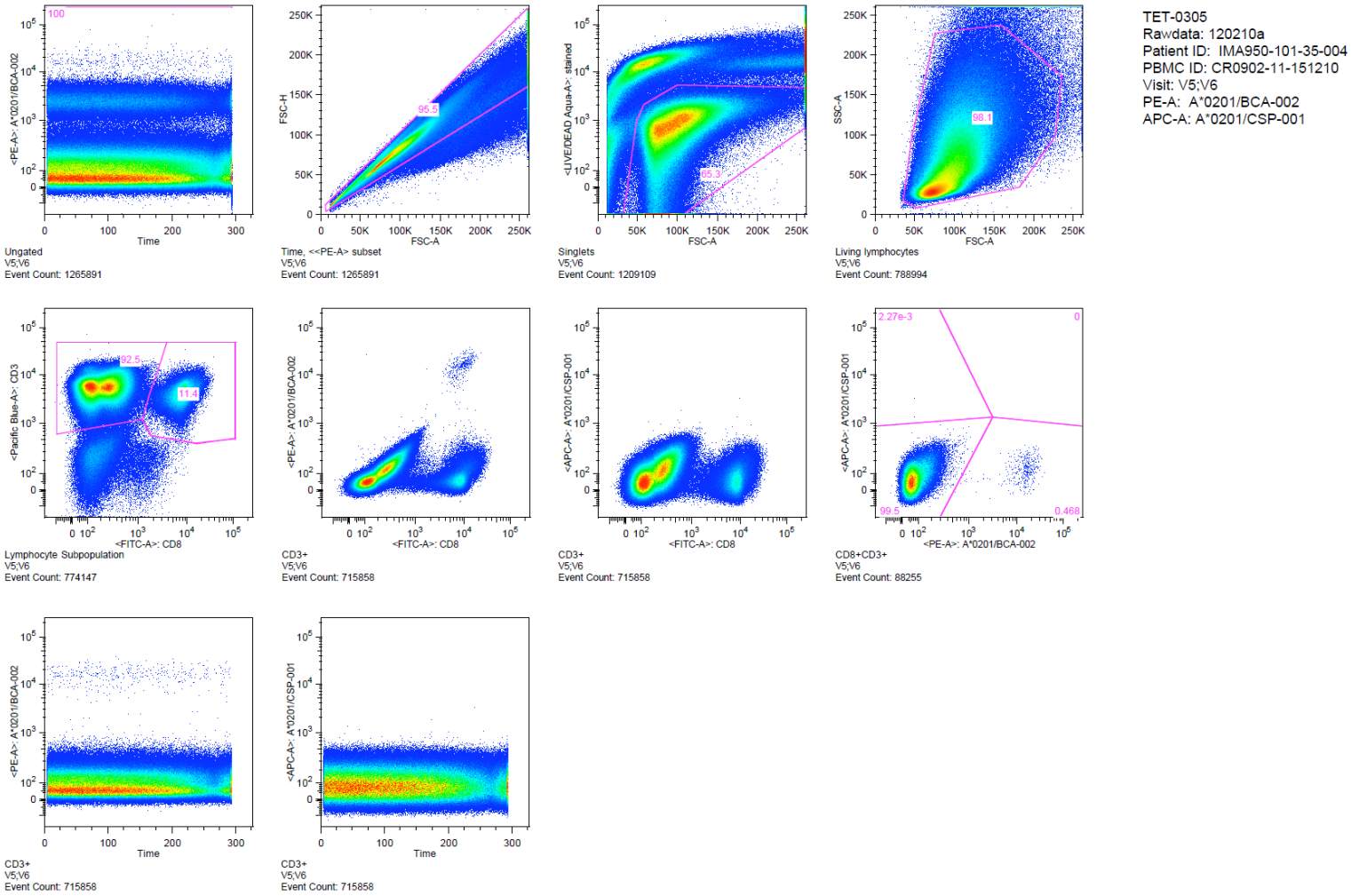


Figure S1. Study Schedule. Eight **i**mmunomonitoring PBMC samples (🩸) were taken pre-treatment on Day -7 to -3 (SCR) and Day 1 (V1), during the Vaccination Induction Phase on Day 15 (±1 day; V5), Day 22 (±1 day; V6) and Day 29 (±1 day; PV6), then seven days (±1 day) after first (PV7), third (PV9) and fifth (PV11) vaccinations (⇩) in the Vaccination Maintenance Phase. MRI scans (☆； including research DWI and PWI) were performed within 21 days prior to start of CRT for Cohort 1 (a), post completion of CRT and within 7 days before first vaccination for Cohort 2 (b) then within 7 days (±14 days) after the first dose of adjuvant TMZ therapy on Day 1 (approximately Week 16), at 25 weeks (±14 days) and at 40 weeks (±14 days) post-resection.

Abbreviations: CRT, chemoradiotherapy; DWI, diffusion weighted imaging; MRI, magnetic resonance imaging; PBMC, peripheral blood mononuclear cells; PV, post-vaccination; PWI, perfusion weighted imaging; TMZ, temozolomide; V, vaccination; VIP, vaccination induction phase.



TET-0305
Rawdata: 120210a
Patient ID: IMA950-101-35-004
PBMC ID: CR0902-11-151210
Visit: V5;V6
PE-A: A*0201/BCA-002
APC-A: A*0201/CSP-001

Figure S2. Exemplary gating strategy used for the primary multimer assay. A representative example of hierarchical gating is shown for patient 35-004, time point pool V5/V6 (post-vaccination 2). Consistent flow-performance is checked, duplets are excluded, vital cells are gated prior to defining lymphocytes (FSC/SSC), CD3 and CD8 positive T cells and finally cells stained by the multimers BCA-002 PE or CSP-001 APC.
Abbreviations: FSC, forward scatter channel; SSC, side scatter channel; PE, phycoerythrin; APC, allophycocyanin.

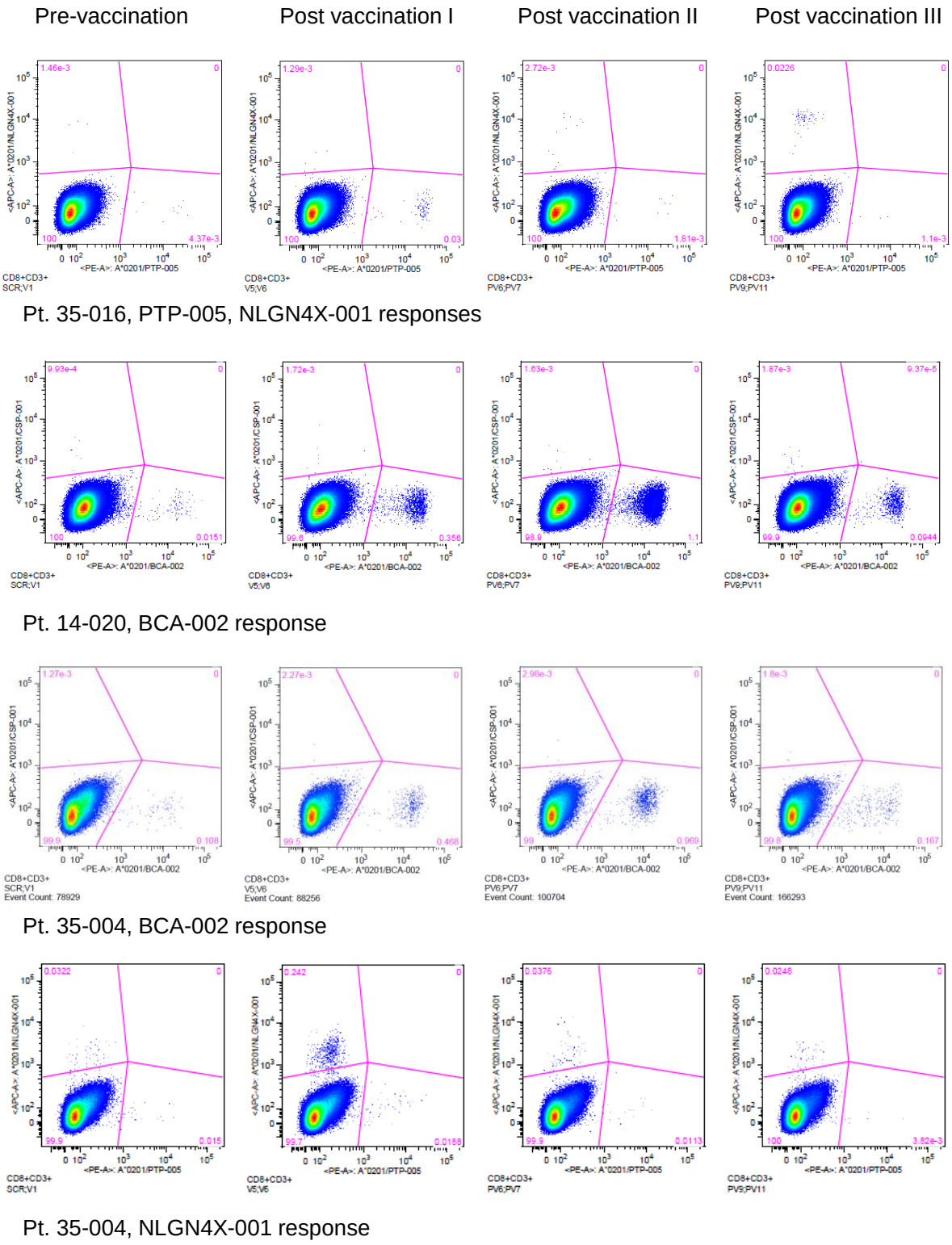


Figure S3. Exemplary immune responses in patients as determined by multimer assay after in vitro sensitization. Representative examples are shown for four patients and all four analyzed time point pools. The left panel represent pre-vaccination blood drawings while the three panels are post-vaccine time points. All samples were stained with two different peptide-major histocompatibility complex multimers coupled to two different fluorochromes (phycoerythrin / allophycocyanin).

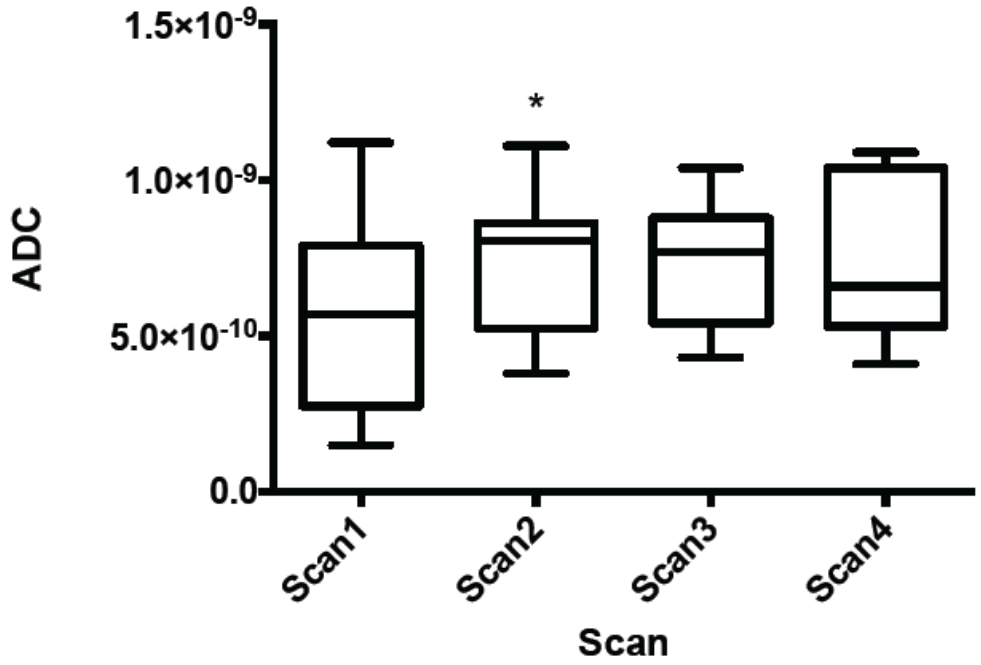


Figure S4. Apparent diffusion coefficient (ADC) in Cohort 1 at each of the four scan points. A significant increase in ADC was found between the initial and second scan points ($p < 0.05$; determined using one-way ANOVA analysis with post hoc intergroup analysis by Tukey's test) corresponding to the initiation of chemoradiotherapy.

REFERENCE

1. Walter S, Weinschenk T, Stenzl A, Zdrojowy R, Pluzanska A, Szczylik C, et al. Multipeptide immune response to cancer vaccine IMA901 after single-dose cyclophosphamide associates with longer patient survival. Nature medicine. 2012;18:1254-61.