# IMMUNOGENICITY AND CLINICAL EFFICACY OF A HI-8™ PRIMEBOOST THERAPEUTIC VACCINE IN STAGE III/IV MELANOMA PATIENTS IN A PHASE I/II TRIAL

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OXXON THERAPEUTICS™

# Hi-8™ MEL: Melanoma Therapeutic Vaccine

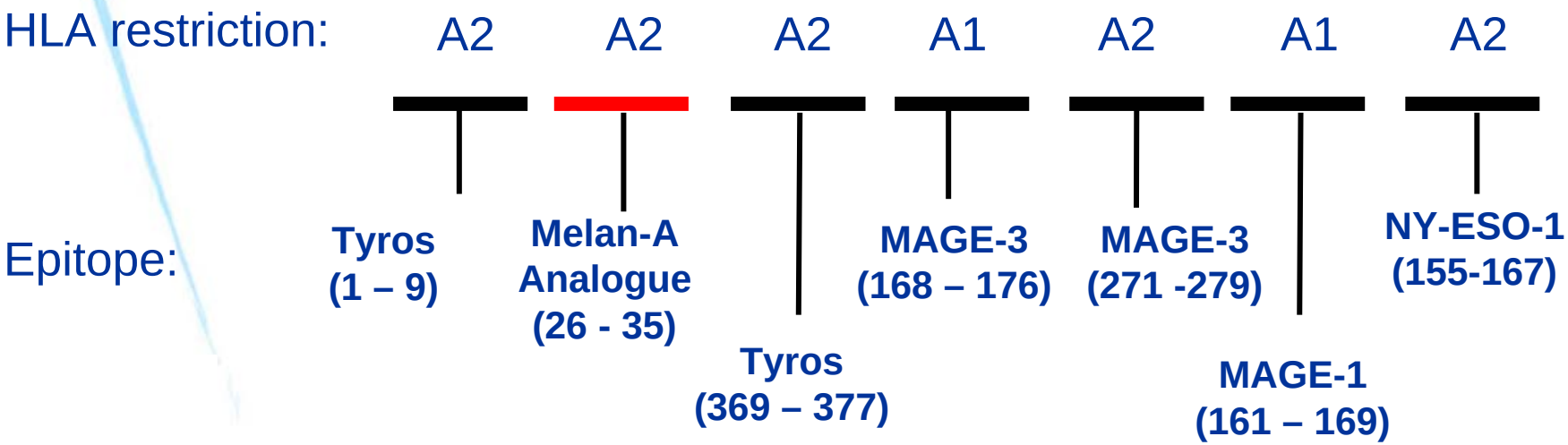
"Prime"

"Boost"

DNA vaccine

MVA viral vector

## Melanoma Epitope String



# Treatment Protocol

41 stage III/IV patients (UK and Germany) sequentially enrolled to 7 treatment groups

| Regimen | DDMM | | | | DMM | | MMMM |
|---|---|---|---|---|---|---|---|
| N | 8 | 5 | 7 | 6 | 5 | 5 | 5 |
| DNA.Mel3 (i.m.) | 2mg | 2mg | 2mg | 2mg | 4mg | 4mg | - |
| MVA.Mel3 (i.d.) | $5x10^7$ | $2x10^8$ | $5x10^8$ | $1x10^9$ | $5x10^7$ | $1x10^9$ | $1x10^9$ |

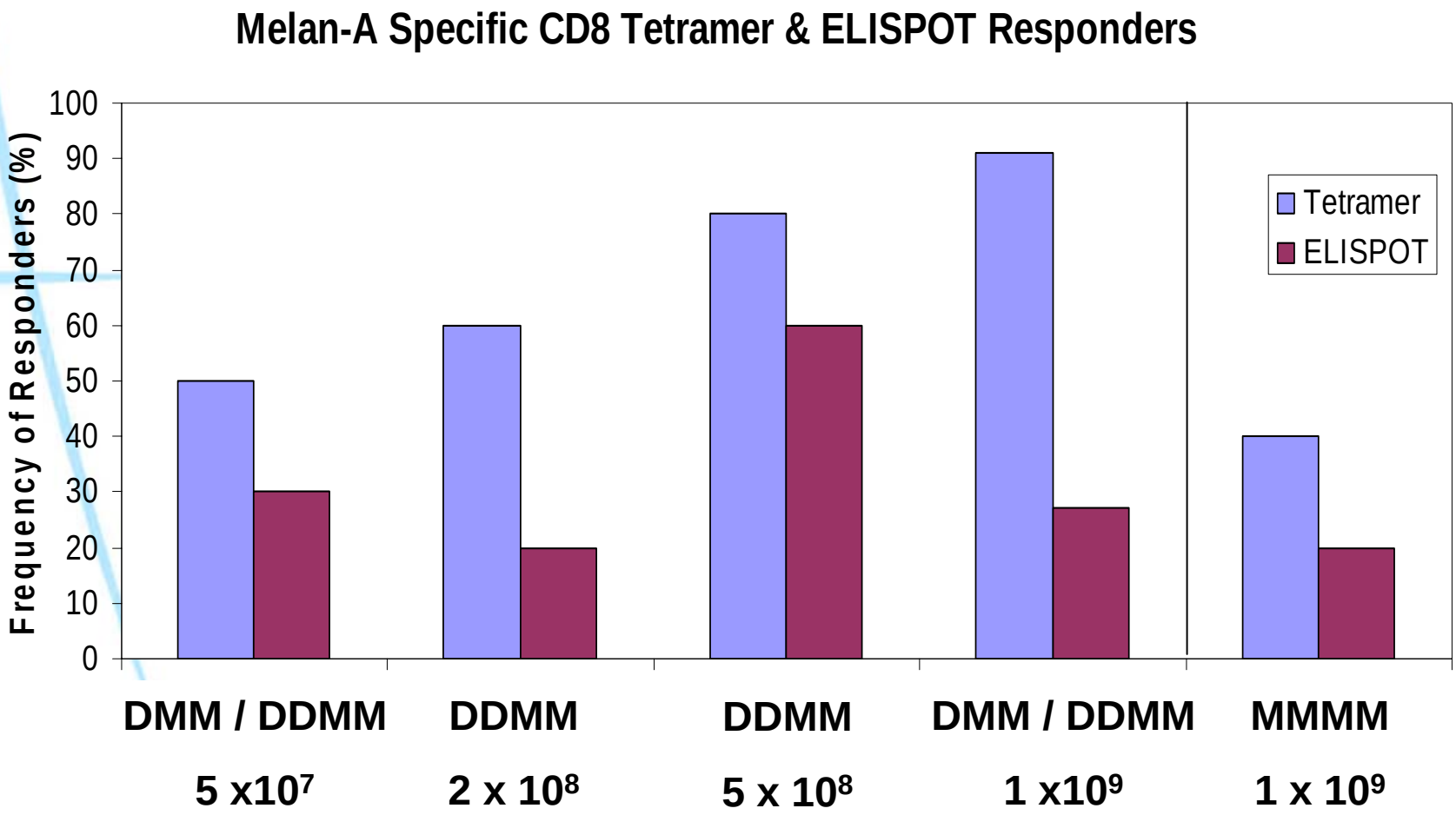
Vaccines administered 3 weeks apart

Additional MVA.Mel3 boosts given at weeks 16 and 24

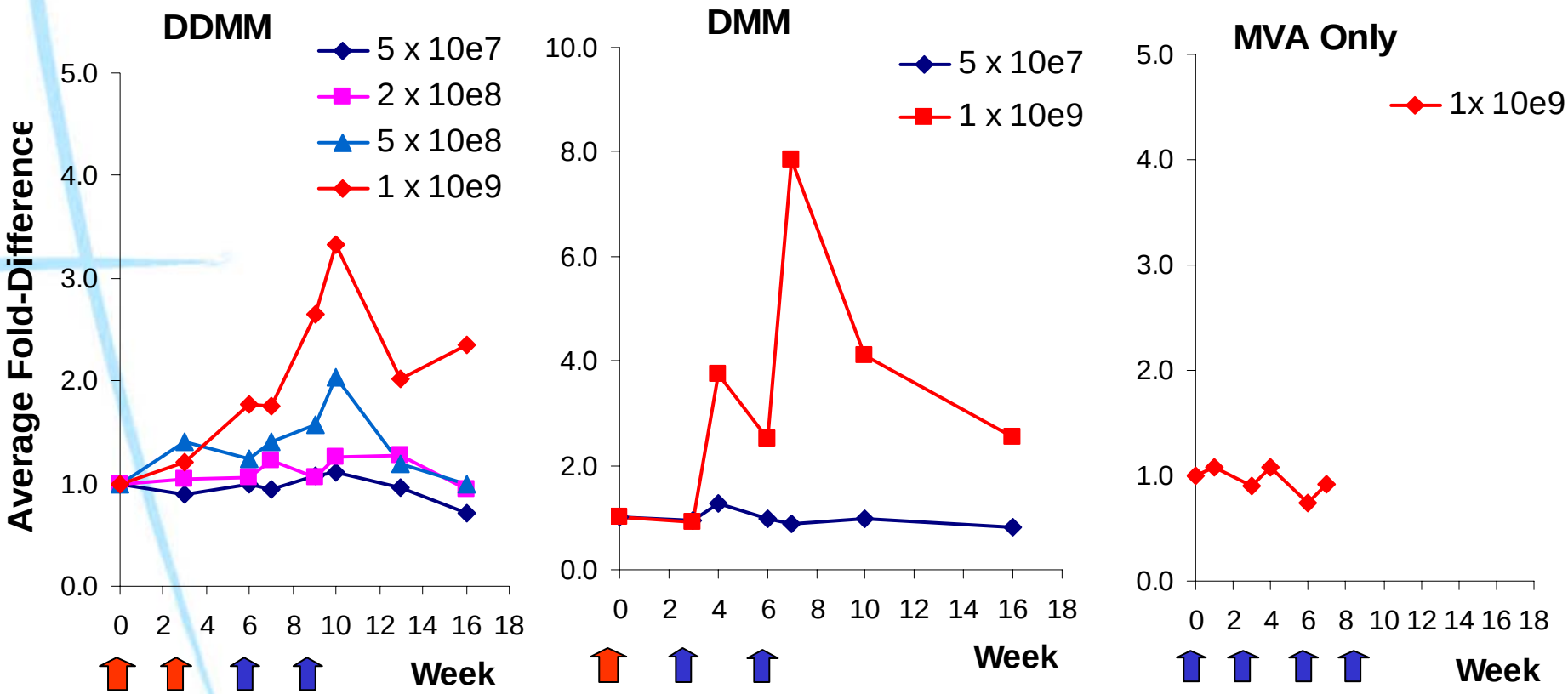
# Study Endpoints

- Immunogenicity
  - Melan-A epitope response by *ex vivo* Tetramer assay
  - All epitopes by *ex vivo* IFN-γ ELISPOT assay
  - Anti-MVA antibody by ELISA
- Clinical response
  - Tumour response (RECIST criteria)
  - Time-to-progression
  - Overall survival (to 12 months)
- *Safety and Tolerability*

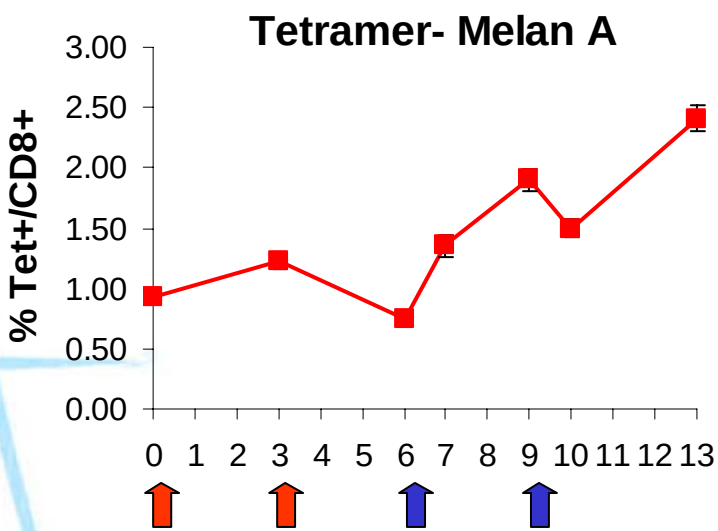
# Immune Response (Frequency)

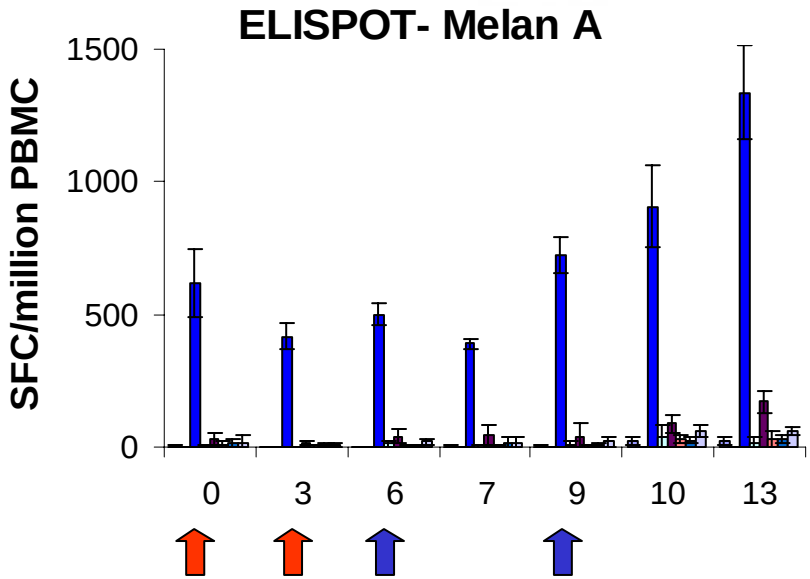


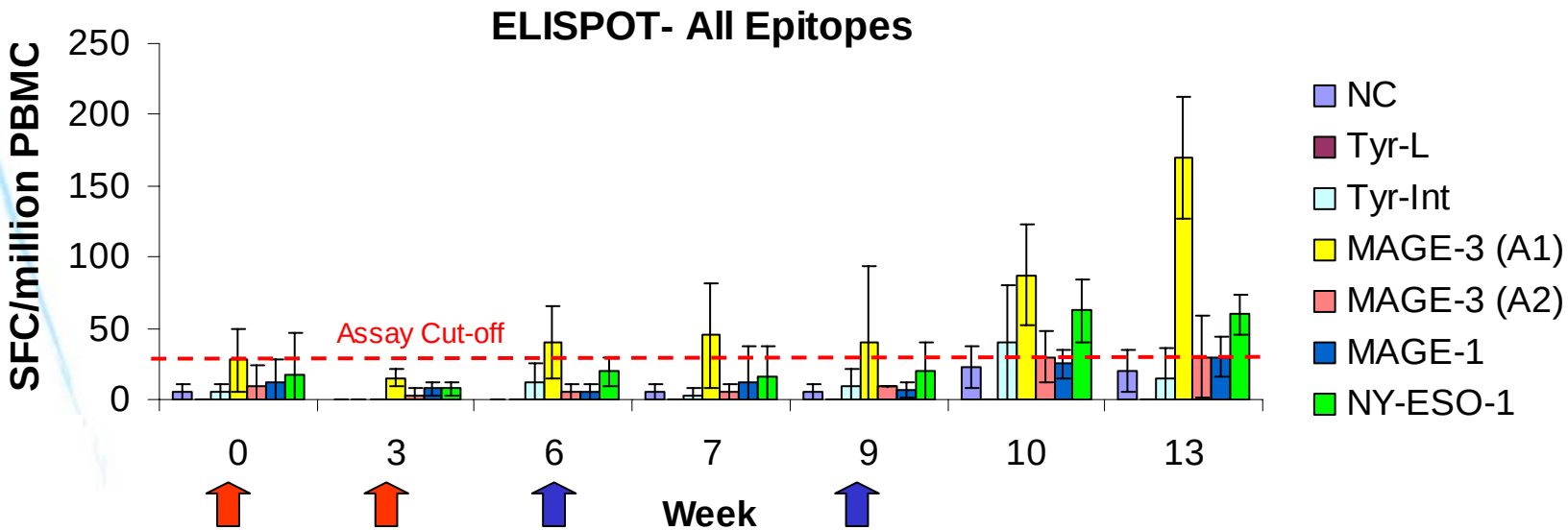
# Average Melan-A Tetramer Response



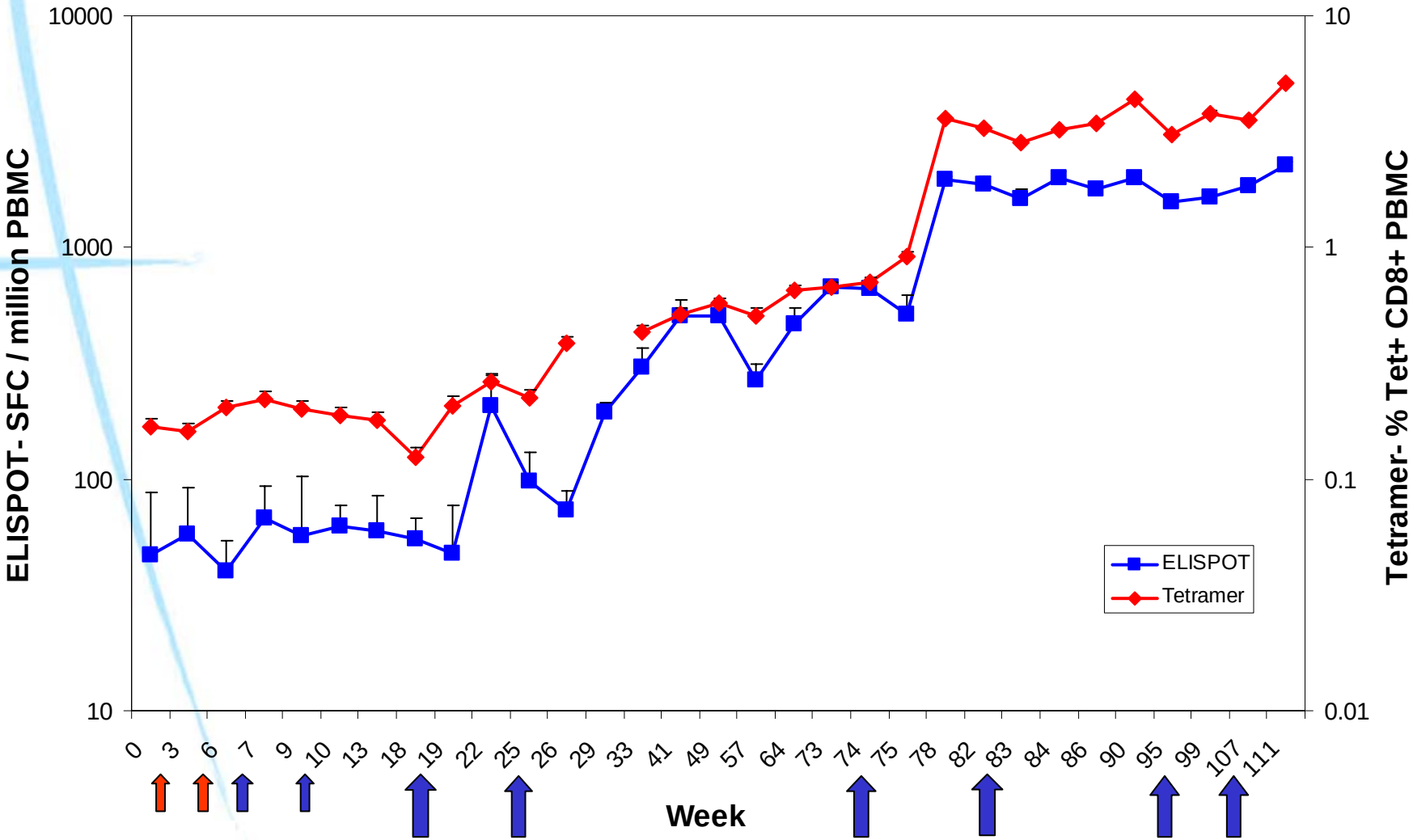
# Patient 047: Multi-Epitope Response



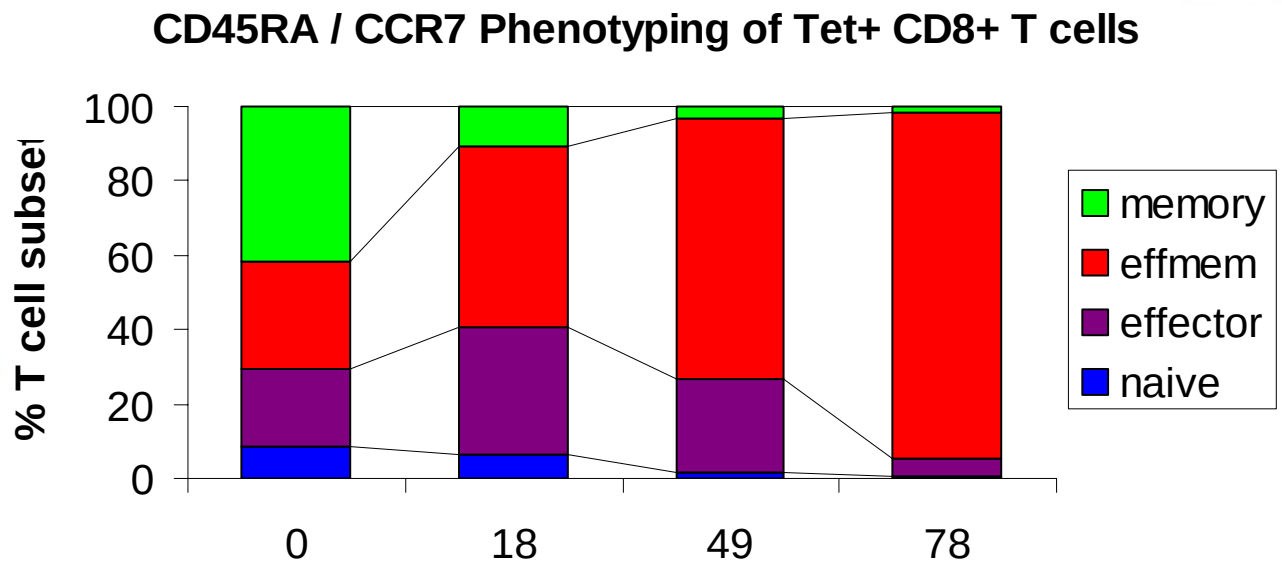



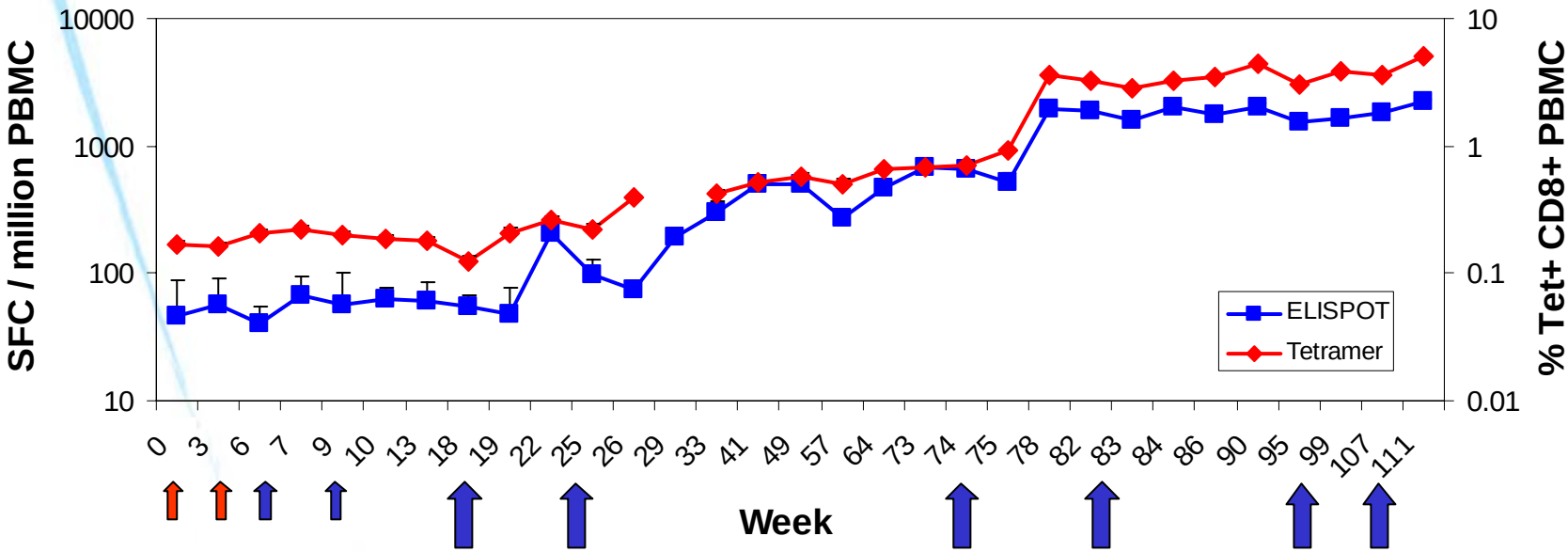



# Patient 033: Melan-A Response



# Patient 033: CCR7 / CD45RA Phenotyping



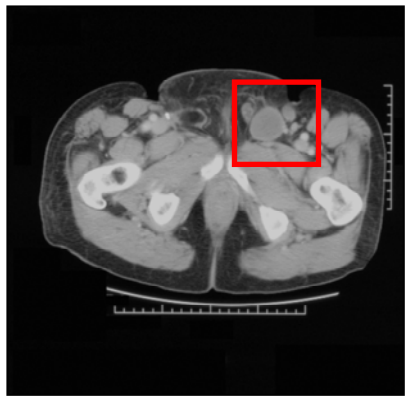
# Tumour Responses

- 1 PR >24 months
- 7 SD $\geq$ 6 months
- Tumour responses evident in subjects with all stages and sites of disease
- Tumour responses only seen following Hi-8™ PrimeBoost
- No tumour responses after MVA alone
- 87% of tumour responses were associated with immune response

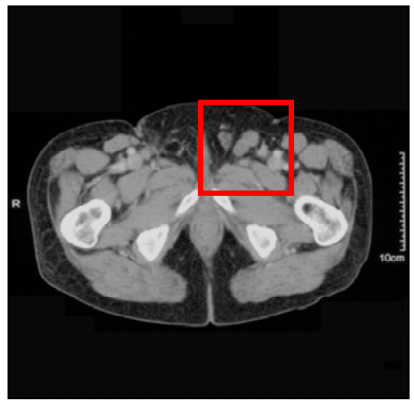
# Patient 033: Tumour Response

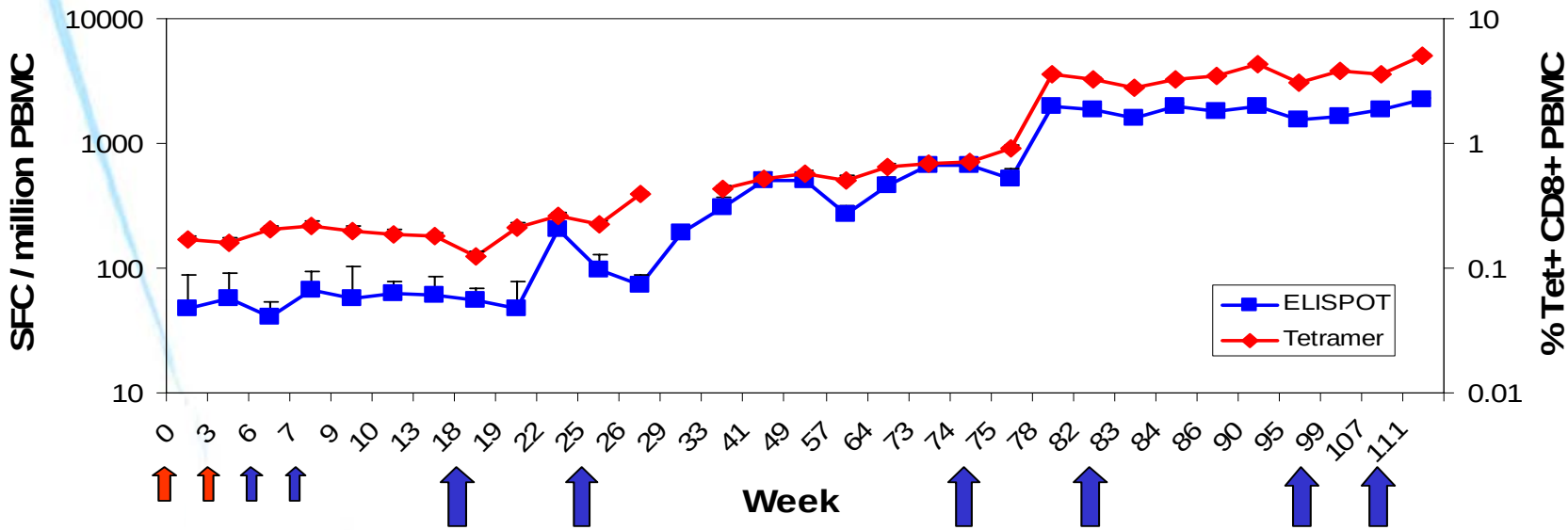
| Week | 8 | 16 | 24 | 28 | 40 | 48 | 56 | 64 | 72 | 108 |
|---|---|---|---|---|---|---|---|---|---|---|
| Δ LDsum | -15% | -25% | -30% | -30% | -37% | -37% | -48% | -52% | -48% | -51% |

**Baseline**

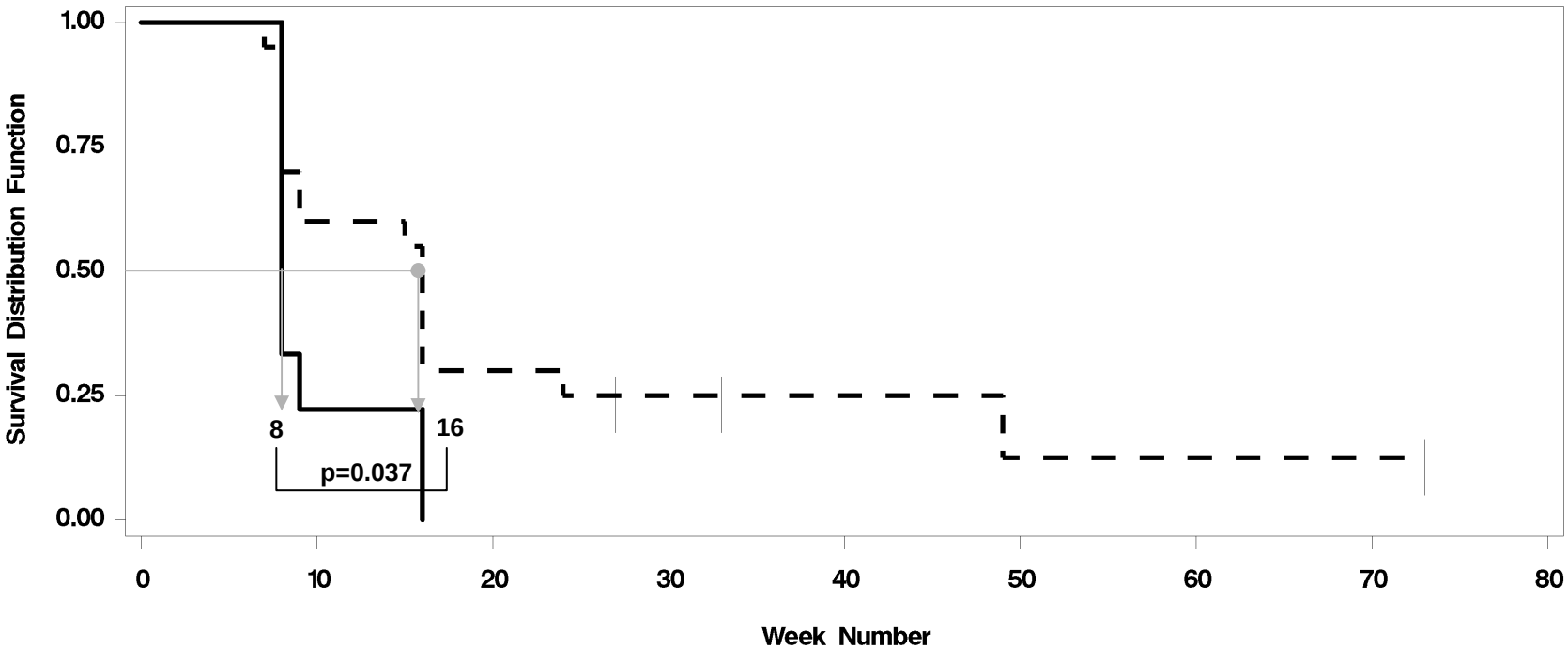


**Week 72**



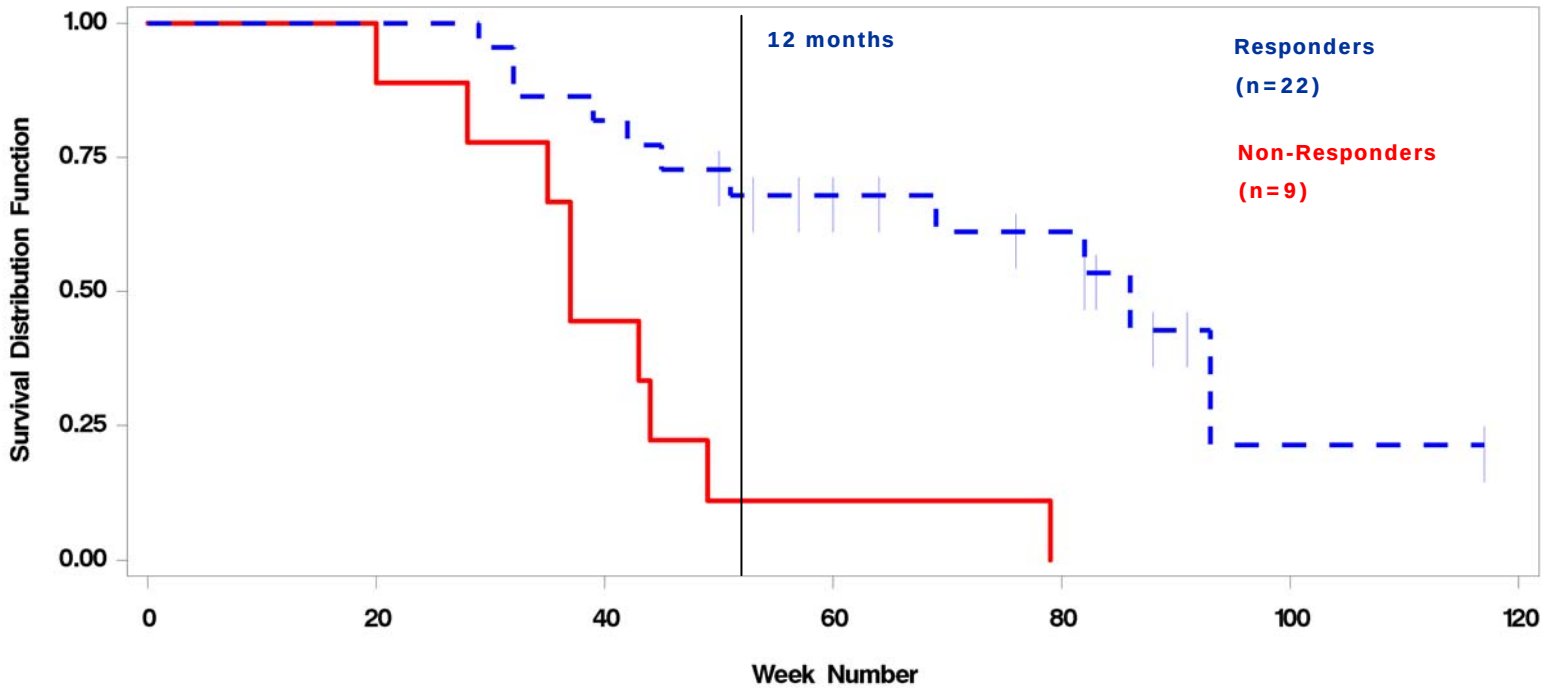


# Time-to-Progression: Immune Responders




Evaluable Per protocol population (N=34) excluding MVA alone treatment arm (N=5)

# Survival Analysis




- Median survival for stage III/IV tetramer responders was **86 weeks** compared to **37 weeks** for non-responders **(p<0.001).**
- Median survival for stage IV tetramer responders was **82 weeks (p<0.001).**

# Conclusions

- Immune response
  - 91% Melanoma-specific immune responders at highest dose
  - Multi-epitope responses in 3 subjects
  - Effector Memory response after treatment
  - Multiple MVA boosts effective
- Tumour responses associated with immune responses
- Immune responders → survival benefit
- Hi-8™ MEL to be evaluated in a Phase III clinical trial

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