Biomarker-focused Conference Call

April 30, 2026

NYSE American: OSTX

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This document contains forward-looking statements. In addition, from time to time, we or our representatives may make forward-looking statements orally or in writing. We base these forward-looking statements on our expectations and projections about future events, which we derive from the information currently available to us. Such forward-looking statements relate to future events or our future performance, including: our financial performance and projections; our growth in revenue and earnings; and our business prospects and opportunities. You can identify forward-looking statements by those that are not historical in nature, particularly those that use terminology such as “may,” “should,” “expects,” “anticipates,” “contemplates,” “estimates,” “believes,” “plans,” “projected,” “predicts,” “potential,” or “hopes” or the negative of these or similar terms. In evaluating these forward-looking statements, you should consider various factors, including: our ability to change the direction of the Company; our ability to keep pace with new technology and changing market needs; and the competitive environment of our business. These and other factors may cause our actual results to differ materially from any forward-looking statement. Forward-looking statements are only predictions. The forward-looking events discussed in this document and other statements made from time to time by us or our representatives, may not occur, and actual events and results may differ materially and are subject to risks, uncertainties and assumptions about us. We are not obligated to publicly update or revise any forward-looking statement, whether as a result of uncertainties and assumptions, the forward-looking events discussed in this document and other statements made from time to time by us or our representatives might not occur.

Agenda

1. **Introduction – Harrison Seidner, PhD**
2. Corporate Update – Paul Romness, MPH
3. Biotech Innovation Curve – Dr. Robert Langer
4. Clinical, Biomarker and Safety Data – Andrew Exley, MD, FRCP, FRCPath
5. Regulatory status by Jurisdiction (Europe, Australia, U.K. and U.S.) – David Brindley, PhD
6. Insights on developing treatments for rare pediatric cancers – Dr. Craig Eagle
7. Questions

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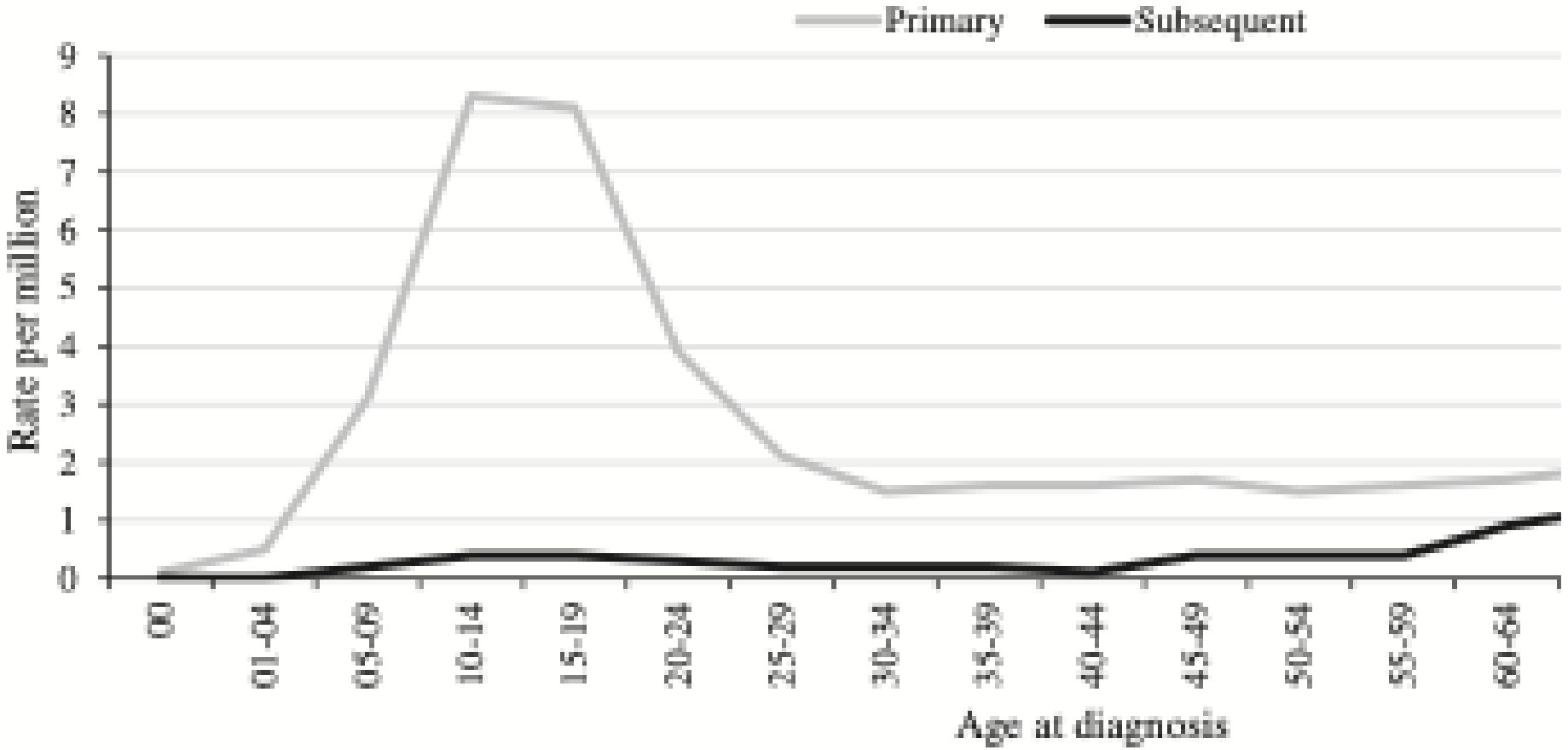
Osteosarcoma: Clinical Outline

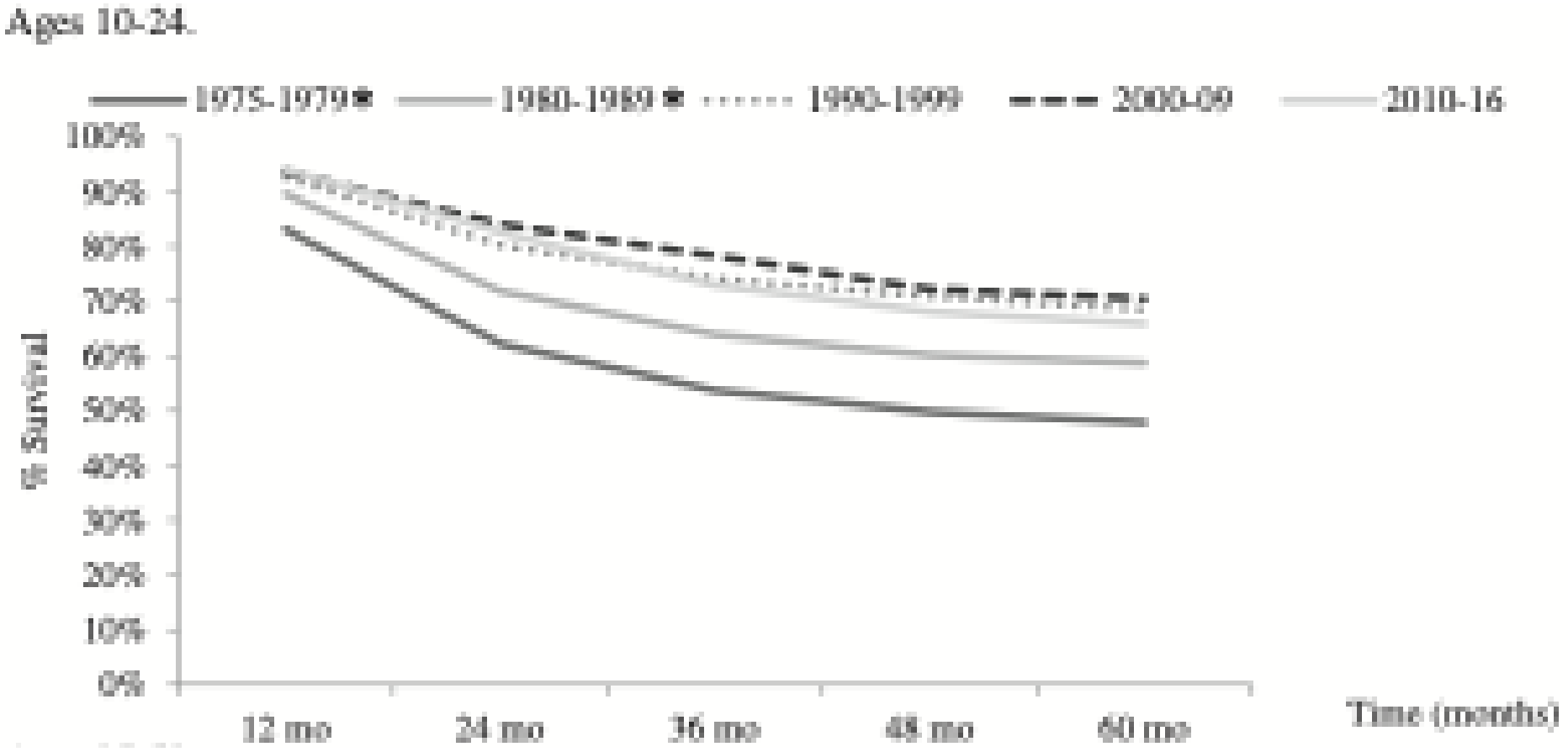
- Major form of pediatric bone cancer
- ~1,000 cases diagnosed annually in US
- Primarily affects adolescents & young adults: 12 – 39 yrs
- Localized disease
  - Chemotherapy & Surgery can sometimes achieve remission
- Recurrent / Metastatic disease e.g. in Lungs
  - No FDA-approved treatment options for recurrent, resected lung metastases
  - Systematic reviews highlight dearth of new therapies (Gazouli 2021, Biermann 2025)
  - Some progress on disease mechanisms BUT
  - Prognosis is dire with little improvement over the last 30 years (Cole 2022)
  - *Justifies use of historical control data*

Age-Related Incidence of Primary & Subsequent Osteosarcoma



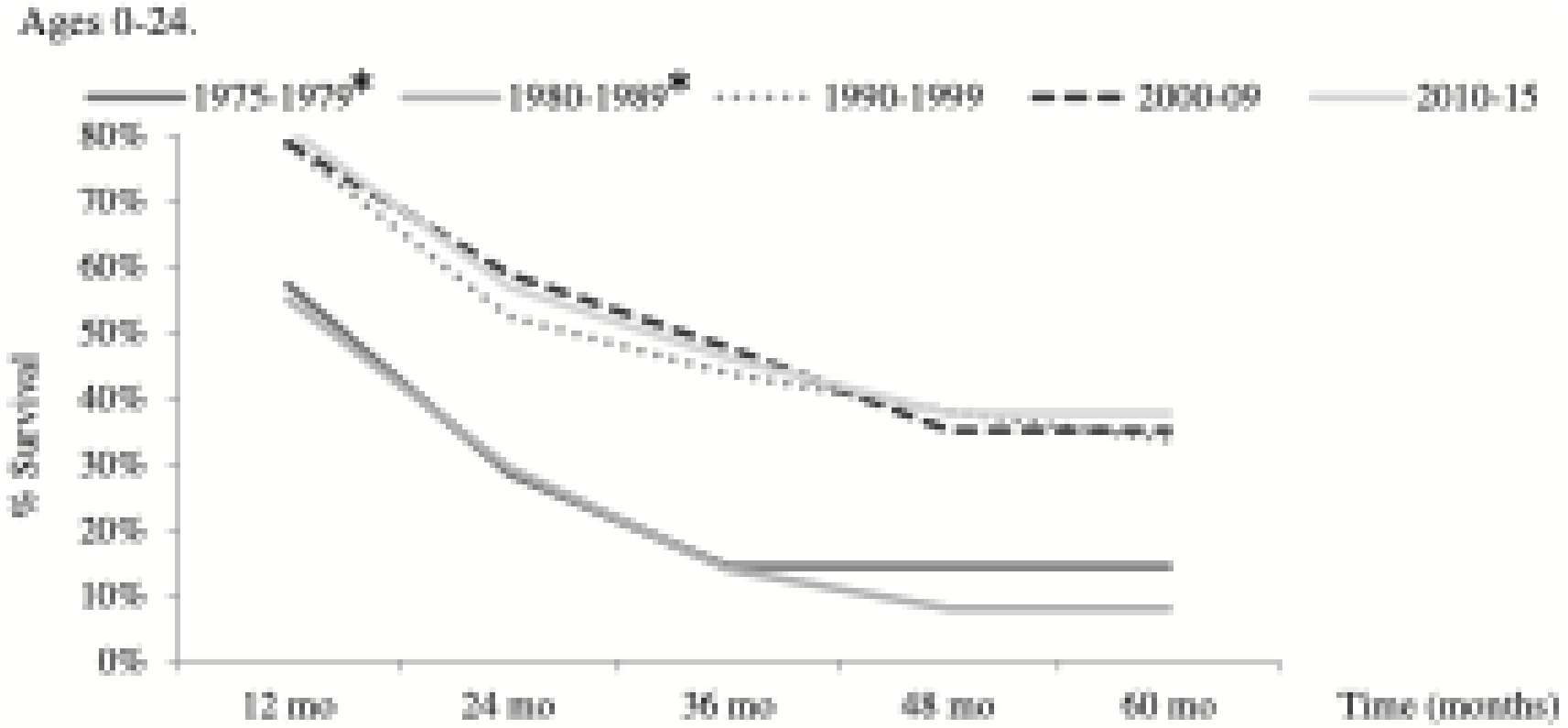
Cole 2022

Overall Survival in Primary Osteosarcoma: No Improvement in 30 years



Cole 2022

Overall Survival in Metastatic Osteosarcoma: No Improvement in 30 years



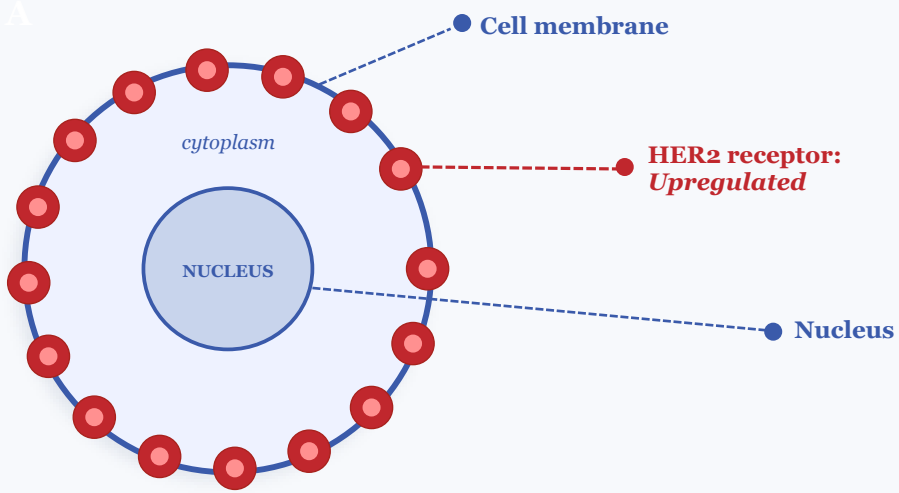
Cole 2022

OST31-164: Innovation – Novel Immunotherapy

1. 1st in class microbial vector gene therapy (MVGT)
   - Attenuated Listeria (Lm) bearing plasmids encoding chimeric fusion protein
     - Truncated Listerolysin: *promotes Ag presentation* & *acts as adjuvant* *
     - Tumour-associated antigen (TAA): Her2
2. Triggers a multi-modal anti-tumour immune response
   - Induces Her2 specific T cells
   - Boosts specific T cells to *structurally unrelated* TAAs *
   - Intratumoral *Lm* induces anti-tumour immunity as a cytosolic bacterium *
   - Boosts innate immune response to tumor – DCs, M1 monocytes, NK cells
   - Modulates tumour microenvironment – reduces MDSCs & Tregs

How OST-HER2 works

Her2 Expression in BREAST & OVARIAN CANCER

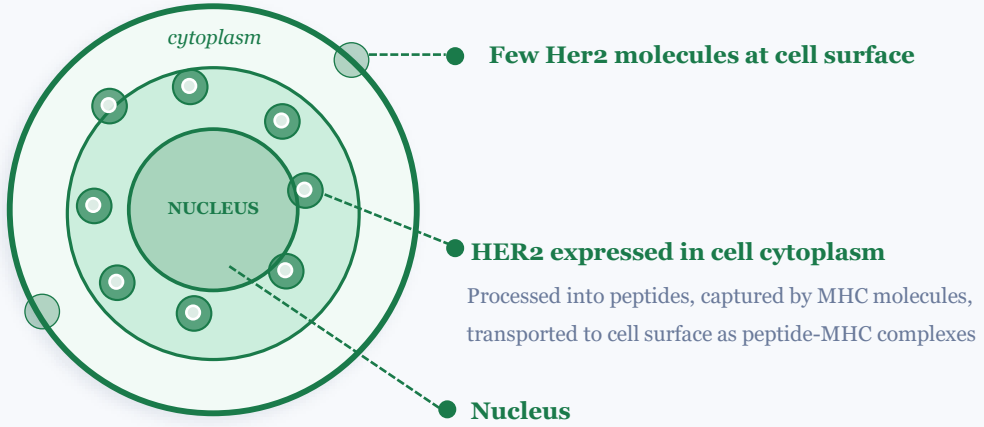


What this means:

- **HER2 is an "oncogenic driver"**
  It actively causes the cancer to grow and spread.
- **Upregulated: increased levels of Her2 expressed at cell surface**
- **Targetable by Antibodies (Ab): Ab-Drug conjugates (ADCs) or CAR-T cells**
- **Clinical Efficacy of ADCs: Trastuzumab-emtansine, Trastuzumab-duocarmycin**

VS

Her2 Expression in OSTEOSARCOMA (BONE CANCER)

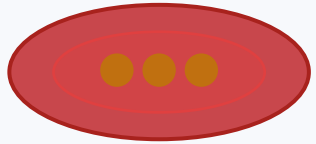


What this means:

- **Not an oncogenic driver: expression not mechanistically linked to cancer**
- **~80% express HER2 but mostly cytoplasmic, low intensity, variable density**
- **Antibody-based detection (ADCs / CAR-T cells) limited by sensitivity**
- **Highly-sensitive T cells detect even low levels of HER2-peptide-MHC complexes**
- **OST31-164: multi-modal action including T cells against Her2 and other TAAs**

How OST-HER2 works

1



L. monocytogenes
(*Lm*) Attenuated

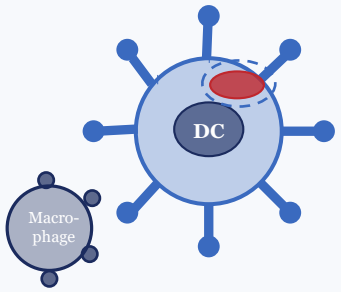
HER2-tLLO payload

The Construct

Attenuated *Lm* carrying plasmids encoding chimeric fusion protein
- truncated listerolysin tLLO (a potent innate immune adjuvant)
- HER2 sequences

Administered by iv Infusion

2



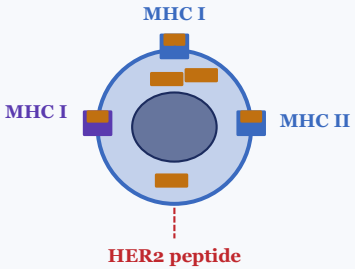
Trojan Horse Entry

Lm naturally targets professional antigen presenting cells = dendritic cells (DCs).

Lm intracellular cytosolic pathogen generates anti-tumour immunity to multiple TAAs

Antigen-presenting cells

3



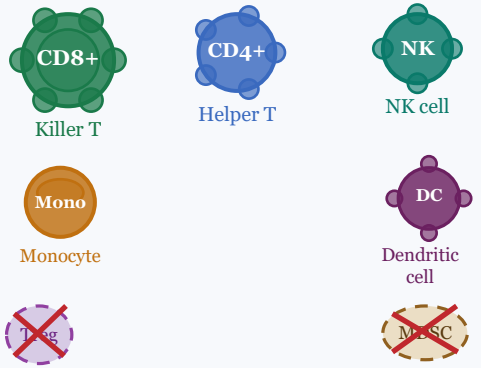
Peptide-MHC Array

DCs process & present TAA derived peptides as complexes with MHC I & MHC II receptors.

Dual-pathway presentation primes CD8+ & CD4+ T cells

Activates CD8+ and CD4+

4



Suppressors neutralised ×

Immune Activation

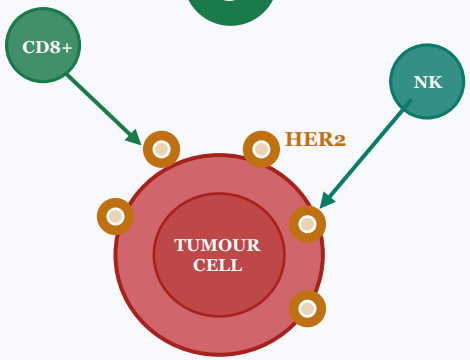
CD8+ & CD4+ T cells primed against HER2 & other TAAs

NK cells & M1 Monocytes activated

Tumour immune-evasion mediators, Tregs & MDSCs, suppressed

Multi-modal immune response: T cells + NK cells + Monocytes

5



tLLO Adjuvant Effect

Immune activation of HER2 specific & TAAs specific T cells
i.e. broadens anti-tumour effect

Tumour Destruction

NK cells target cancer stem cells

Cytotoxic CD8+ T cells kill cancer cells

CD4+ T cells promote memory

Osteosarcoma cells in Micro Metastases eliminated

Biomarker strategy and trial findings

Gene transcript modulation as the preferred biomarker of response to OST-HER2 (OST31-164)

Why Not ELiSpot Alone?

- Canine trials: clinical benefit but no correlation with HER2-specific T cells by ELiSpot
- Logistically challenging: requires viable blood samples from multiple centres and assays for multiple TAAs
- Misses the multi-modal (innate + adaptive) nature of the immune response to OST-HER2

ELISpot = T cell antigen-specific IFN-γ assay — sensitive but narrow in scope

Why Gene Transcript Modulation?

1 Captures full response

Reveals modulation across monocyte, NK, T cell, and Ag presentation pathways *simultaneously*.

Multi-modal by design

2 Operationally practical

Routine sampling techniques sufficient

Scalable across centres

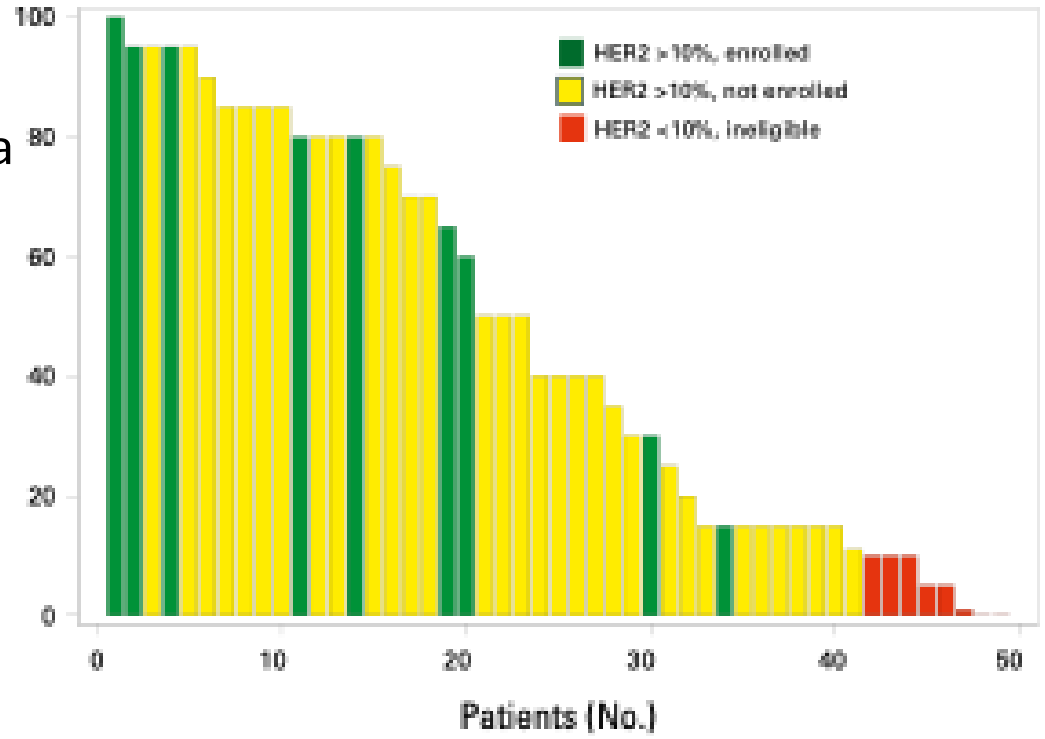
3 Evidenced

Transcript upregulation after 3 doses of OST31-164 correlates with outcomes in canine & human trials.

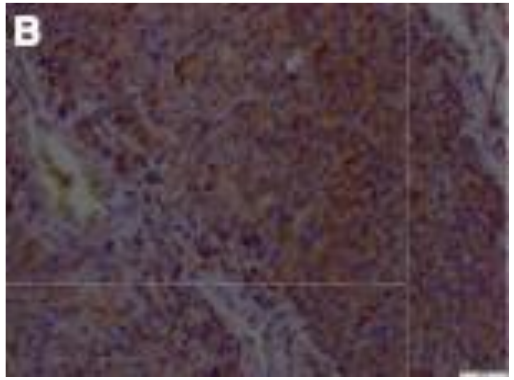
Canine + human correlation

Her2 Expression by ImmunoHistoChemistry (CB11 murine mAb to intracellular domain AA 1244–1249) in Relapsed Osteosarcoma

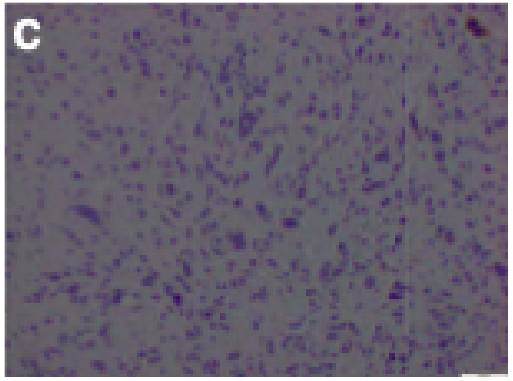
Osteosarcoma Tumour Cells Her2 positive (Percent)



85% Her2 +ve



Her2 -ve



Reed 2025

OST31-164: Proof of Principle: Comparative Oncology

3. NIH supported collaboration with comparative oncology experts demonstrates efficacy of OST31-164 in spontaneous osteosarcoma in canines

Canine Osteosarcoma: Parallels with Human Osteosarcoma

I. Spontaneous onset in immunocompetent dogs: rate >10x human rate

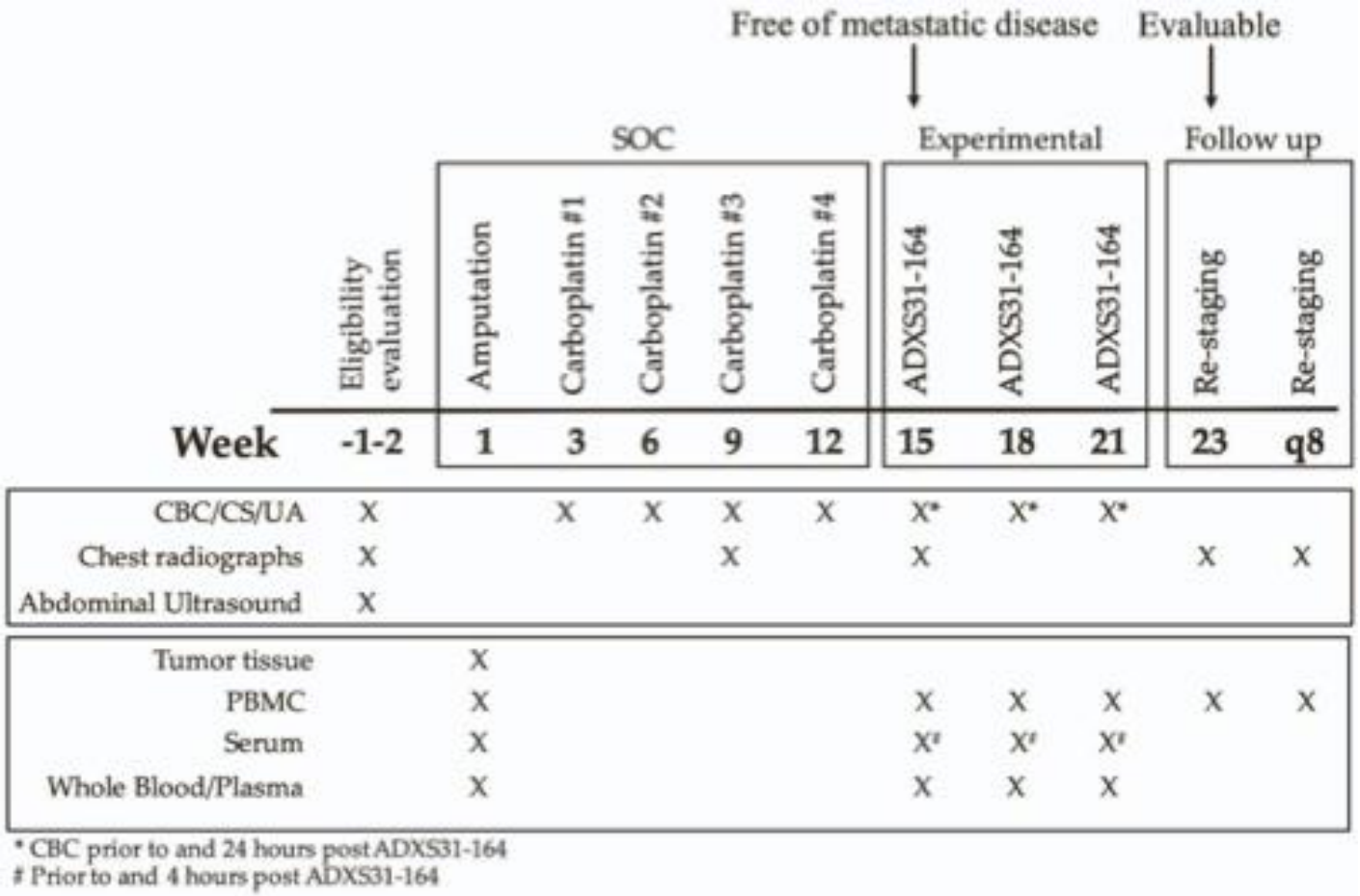
II. Many clinical, biological, and molecular features in common
   i. Primary lesion: typically, high-grade tumours in long bones
   ii. Standard treatment: chemotherapy & radical surgery
   iii. Disease course: metastatic disease often in the lungs
   iv. Highly rearranged genomes often affecting TP53, CDKN2A, RB1 genes

III. Similar molecular pathway alterations of prognostic significance
   - TH_1 & TH_2 immune cell signalling, Interferon signalling, Inflammatory responses

IV. Share 3 distinct TME subtypes – independent predictors of PFS
   - Immune Enriched [IE]; IE dense extracellular matrix-like; Immune Desert

Makielski 2019, Mannheimer 2023, Mason 2025, Patkar 2024

Immunological responses and clinical outcomes in dogs with osteosarcoma receiving SOC + ADXS31-164



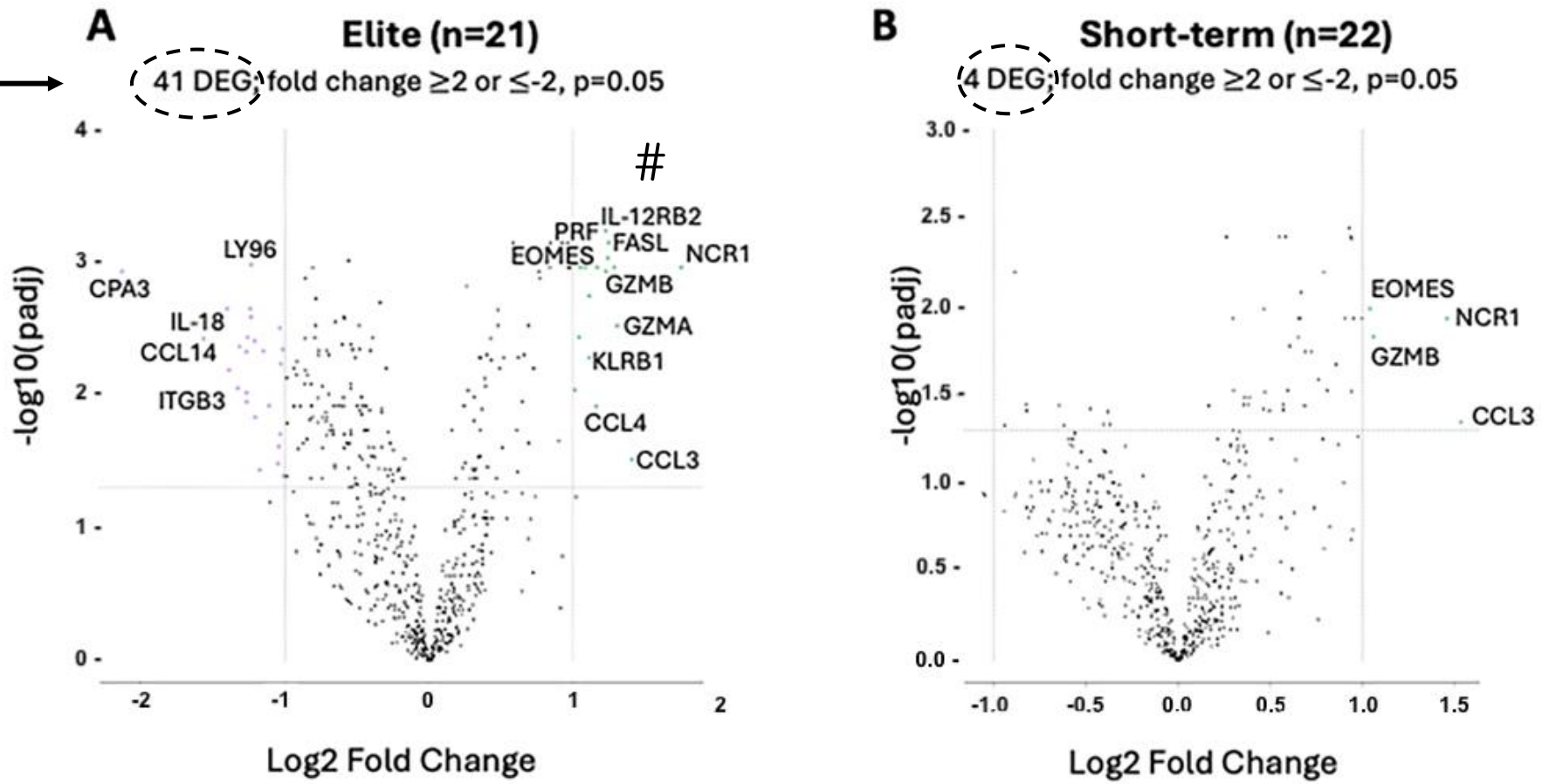
							Free of metastatic disease ↓			Evaluable ↓	
			SOC				Experimental			Follow up	
	Eligibility evaluation	Amputation	Carboplatin #1	Carboplatin #2	Carboplatin #3	Carboplatin #4	ADXS31-164	ADXS31-164	ADXS31-164	Re-staging	Re-staging
Week	**-1-2**	**1**	**3**	**6**	**9**	**12**	**15**	**18**	**21**	**23**	**q8**
CBC/CS/UA	X		X	X	X	X	X*	X*	X*		
Chest radiographs	X				X		X			X	X
Abdominal Ultrasound	X										
Tumor tissue		X									
PBMC		X					X	X	X	X	X
Serum		X					X#	X#	X#		
Whole Blood/Plasma		X					X	X	X		

* CBC prior to and 24 hours post ADXS31-164
\# Prior to and 4 hours post ADXS31-164

Mason NJ 2025

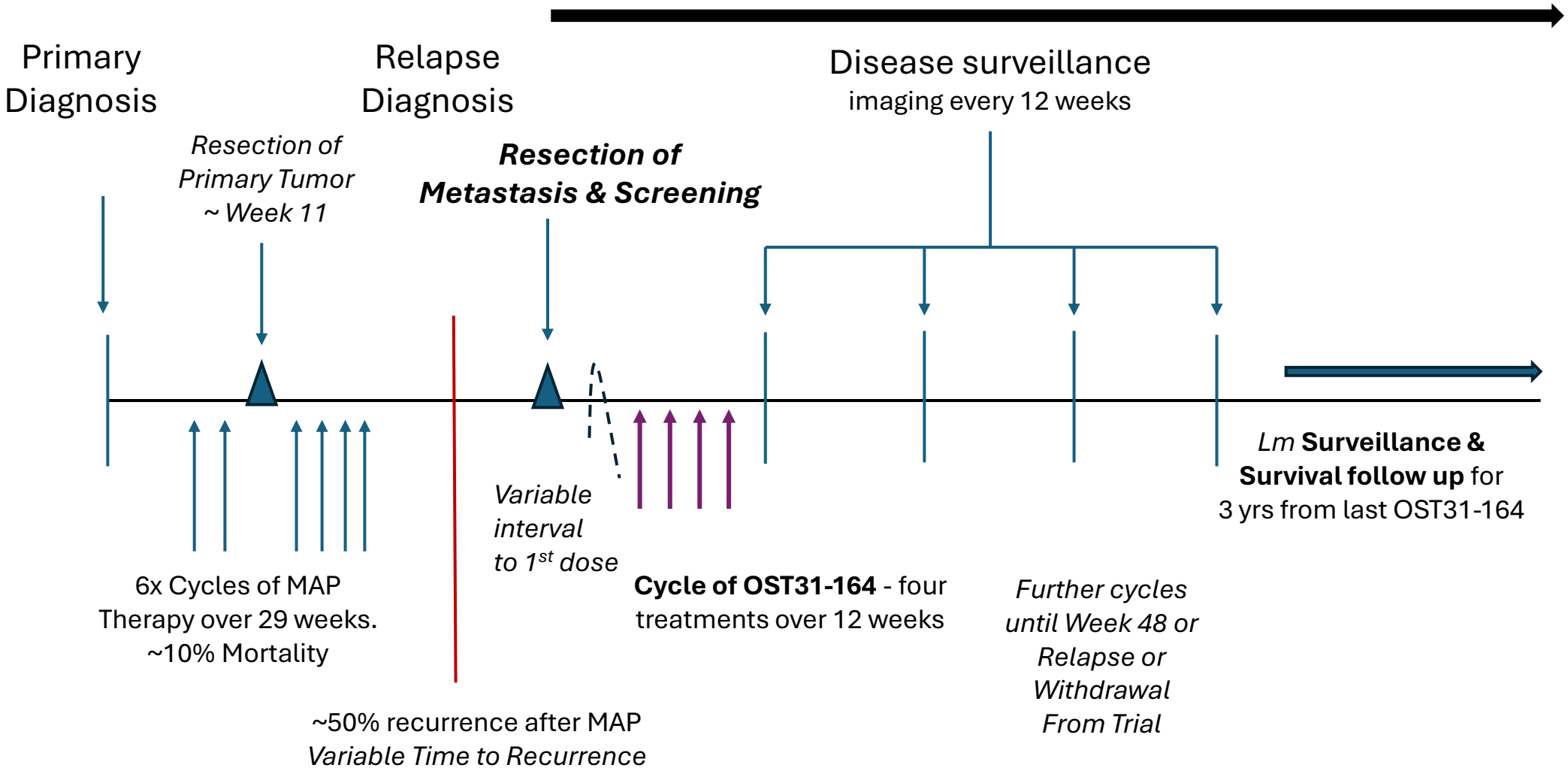
Canine Osteosarcoma Elite vs Short-term Survivors: PBMCs **D**ifferentially **E**xpressed **G**enes – Baseline vs last ADXS31-164

 # Up-regulation of Cytotoxic T cell, NK cell, & Ag presenting cell gene transcripts



Mason NJ 2025

OST31-164-01: Clinical Trial in Recurrent (Pulmonary) Osteosarcoma



OST31-164: Innovation – Historic Controls

4. Justification for use of Historic Controls
    i. Lack of improvement in OS (Cole 2022)
        i. Reduces risk of bias thru improvements in Standard Of Care (SOC)
    ii. *Systematic identification* of published trials
    iii. *Systematic screening* for comparable populations
    iv. *Conservative approach*: treatment effect of chemotherapy +/- IND in controls
    v. *Systematic extraction* of data from comparable populations

Rationale for EFS vs Objective Response Rate (ORR)

I. Radiographic response may not reflect critical cellular effect

II. Surgical resection is standard approach to pulmonary recurrence i.e. no lesion to determine ORR

III. Likely difference in drug activity in microscopic vs macroscopic disease

IV. Propose EFS vs historical benchmark

A. Measurable, unresectable osteosarcoma

- EFS ≤4 months vs >4 months = disease control failure v success

B. **Completely resected osteosarcoma**

- EFS ≤12 months vs >12 months

Lagmay 2016

Rationale for Preferring Overall Survival to Event Free Survival in the Assessment of Immunotherapies for Osteosarcoma

1. Patients value Overall survival over Event Free Survival (Tregear 2024)

2. Regulators prefer Overall Survival as a Hard Endpoint

3. Delayed effect of immunotherapies reduces discriminating power of

   12month Event Free Survival

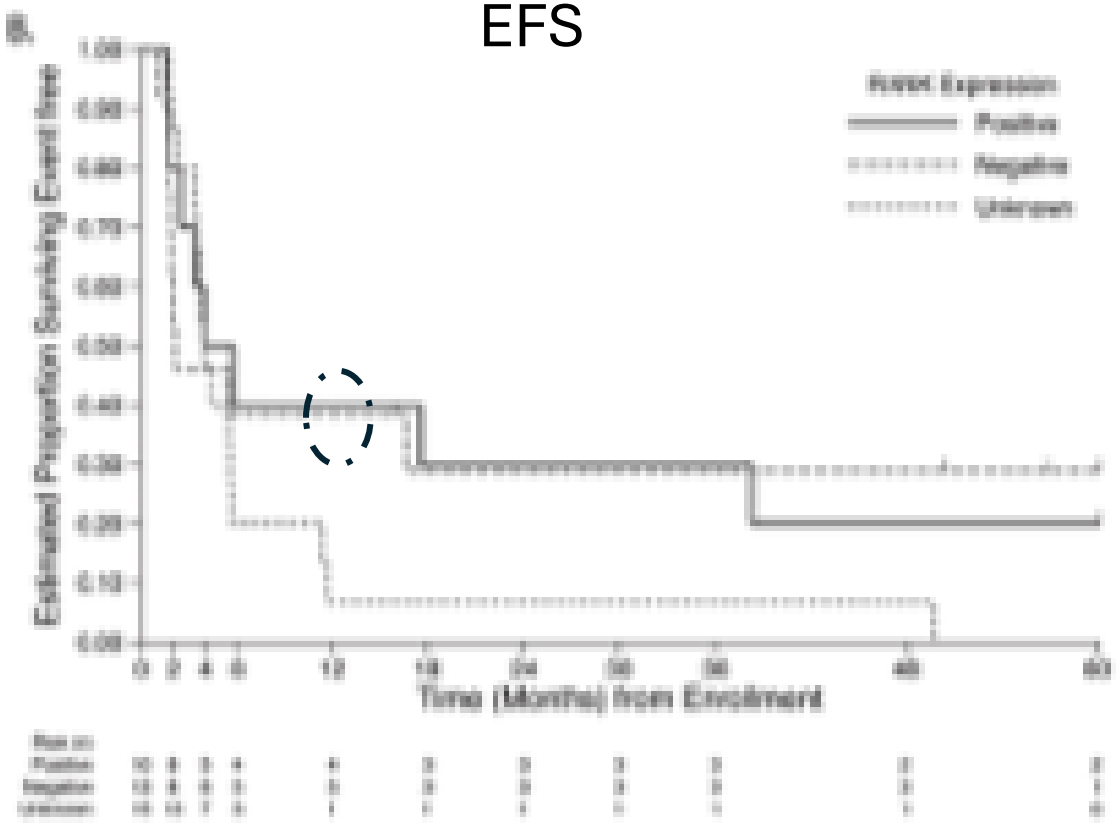
Measures Reducing Potential Bias in Single Arm Trial of OST31-164

Parameter	Measures Adopted to Reduce Potential bias
1. Assessment bias	Hard endpoints: Overall survival (OS)
2. Attrition bias	Overall survival preferred to Event-Free Survival; Sensitivity analyses
3. Pre-planning	Statistical analysis plan (SAP) pre-specified before data completion
4. Regression to mean	Standard criteria for patient selection
5. Variability in Disease History	Systematic selection of comparable control populations
6. Intercurrent events	Estimands defined in Statistical analysis plan
7. Selection bias with controls	Systematic selection of comparable control populations
8. Selection bias in study	Standard criteria for patient selection
9. Trial bias due to improved SOC	No improvement in Overall Survival in last 3 decades Controls include treatment effect of chemotherapy +/- IND in controls

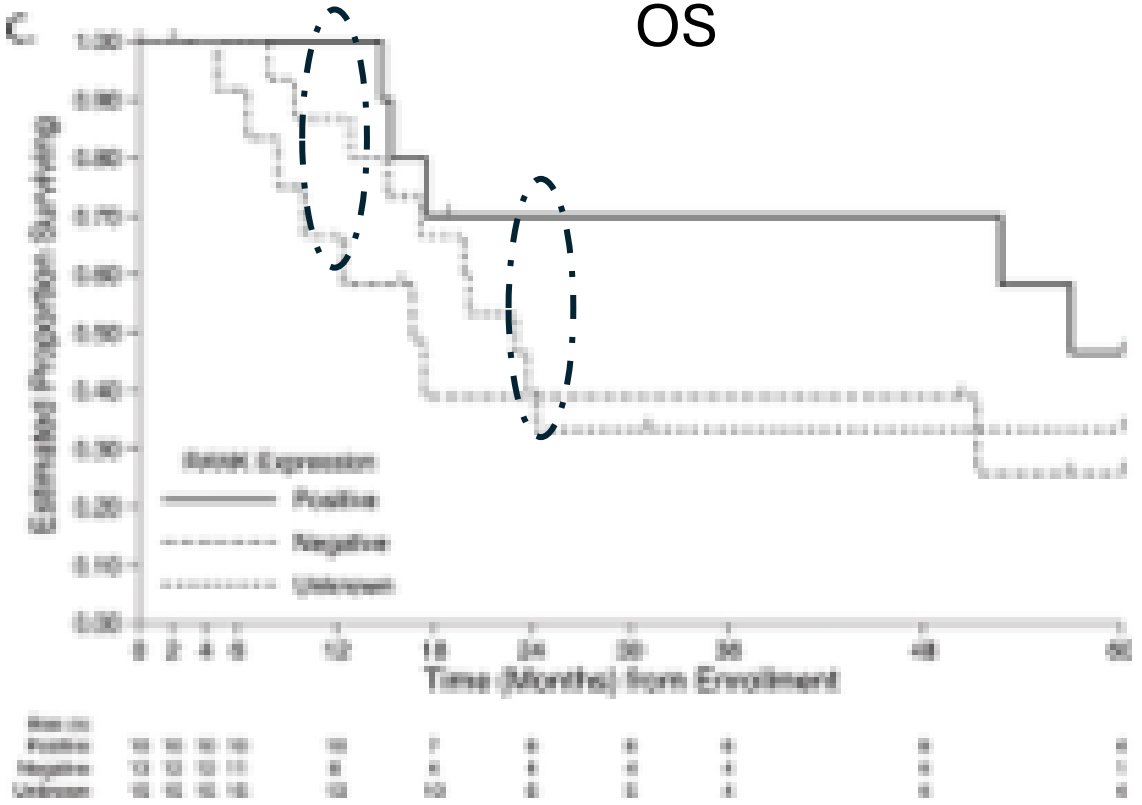
EMA/CHMP/458061/2024: Reflection paper on establishing efficacy based on single-arm trials

EFS vs OS after Immunotherapy: Single Arm Trial of Denosumab (RANKL mAb) in Patients with Recurrent / Refractory Osteosarcoma

EFS

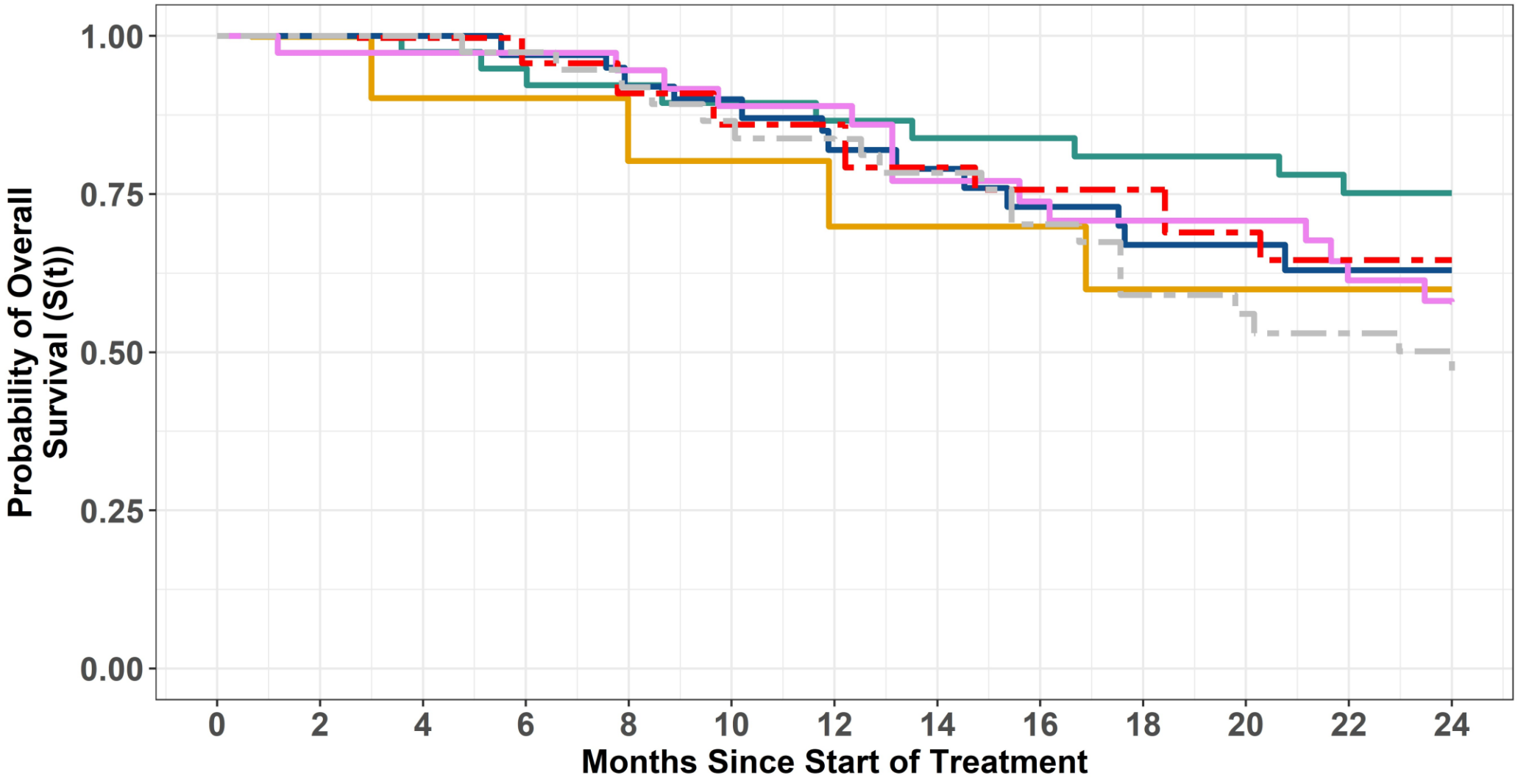


OS

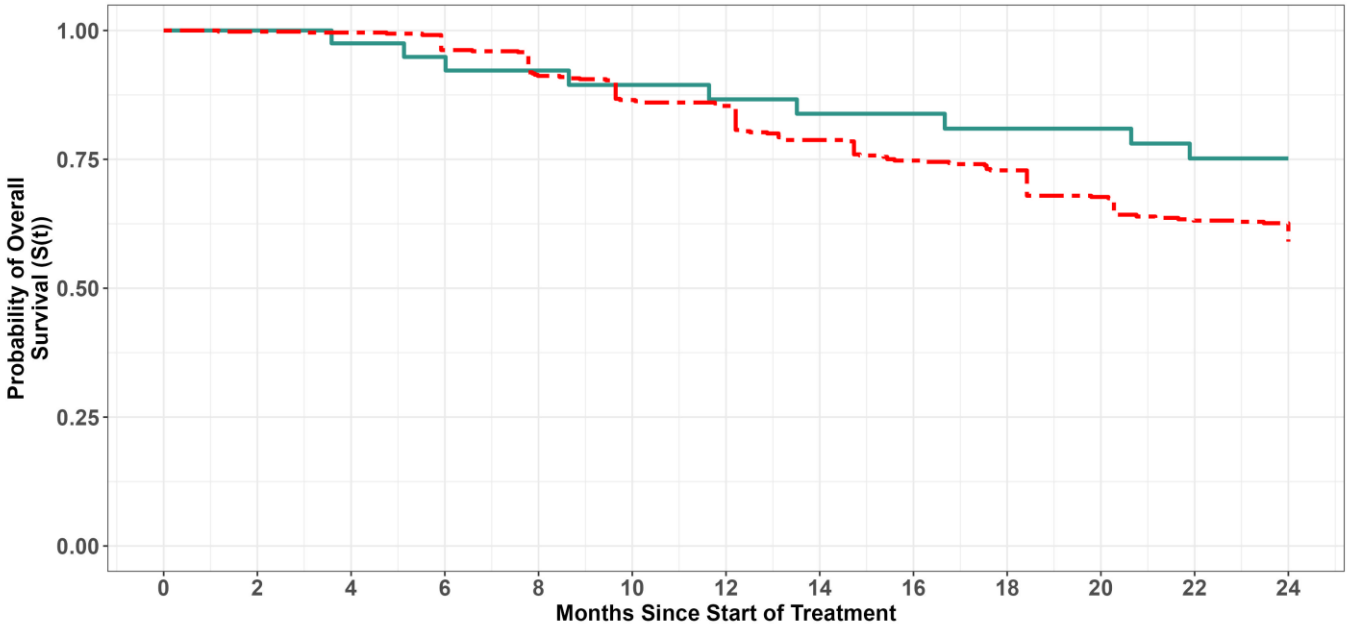


Janeway 2026

OS: OST-HER2 Phase 2b Trial vs. Historical Control



OS: OST-HER2 Phase 2b Trial vs. Pooled Historical Control



P=0.0344

Study	Population	Number of patients
OST-HER2	Recurrent, Completely Resected, Pulmonary	41
Pooled Historical Control	Recurrent, Completely Resected	467

Isolation of Treatment Effect

- Clinically significant improvement in Overall Survival & EFS

I. Highly significant link between Overall Survival & Immune Response Gene Signature (IRGS) after 3rd dose of OST31-164

II. IRGS includes cytotoxic effectors (NK/T cells) & T cell memory, and modulators of *Tumour MicroEnvironment (M1/M2, MDSCs)*

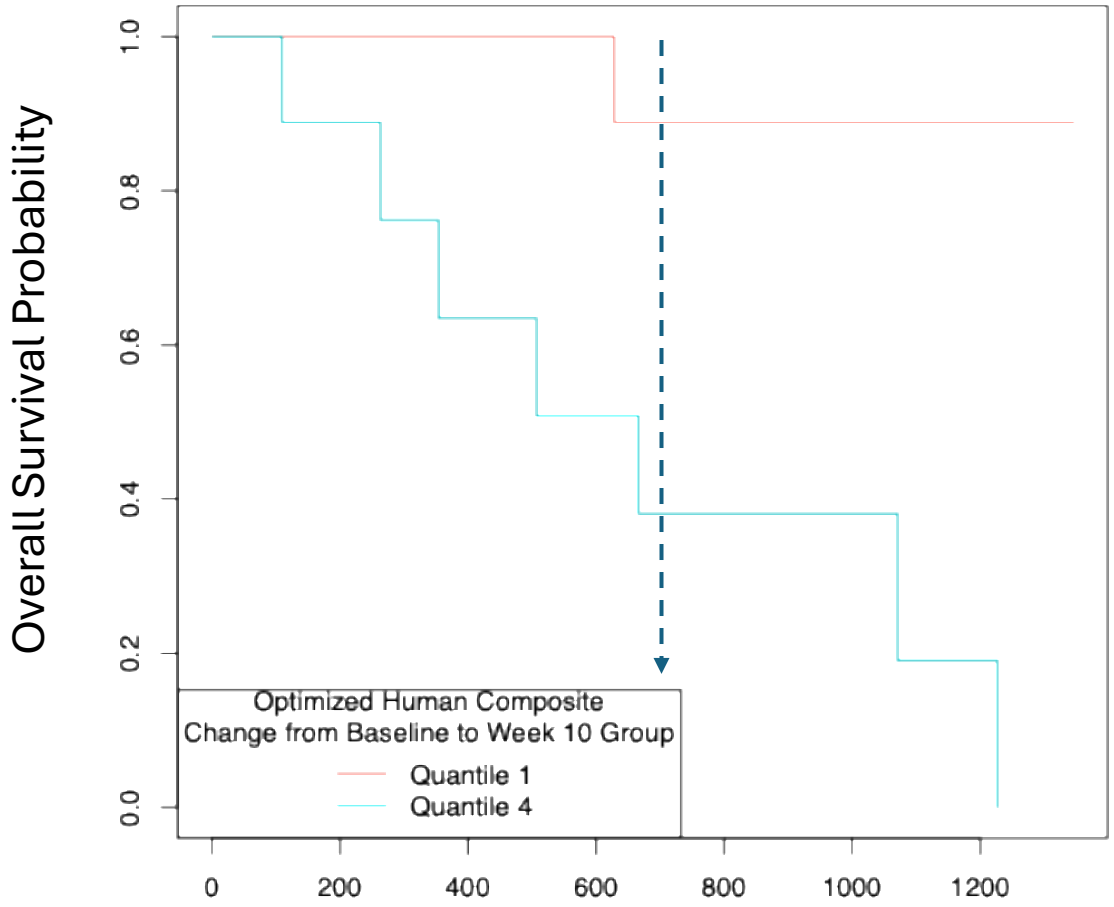
III. IRGS maps directly to the Mechanism of Action of OST31-164

IV. Clinical trial extends findings in parallel population of spontaneous osteosarcoma in canines: multi-modal immune response links Overall Survival to Mechanism of Action

Immune Response Gene Signatures after 3rd Dose of OST31-164 Link Mechanism of Action to OS in Canine & Human Osteosarcoma

- Cox Proportional Hazards Model
- Canine IRGS (optimized): p=10e-8 for Overall Survival
  - Beneficial: Ag presentation, NK cell activation, T cell activation
  - Detrimental: Type 1 IFN; M2 polarization; Myeloid Derived Suppressor Cells
- Human IRGS (optimized): p=10e-4 for Overall Survival
  - Beneficial: Ag presentation; NK cell activation; T cell activation/differentiation; M1 polarization
  - Detrimental: M2 polarization; failure to generate central memory CD8+ T cells

Kaplan Meier Analysis of Overall Survival by Immune Response Gene Composite (Baseline vs Post 3rd Dose)



Safety Profile

I. Infusion related cytokine release syndrome
- Frequency & severity reduced by pre-infusion regimen; no Rx discontinued
  - IV fluids, antihistamine, NSAID, antiemetic, H2-receptor antagonist

Cytokine release syndrome: maximum grade 2 intensity, 1st cycle

II. Infection risk
- Single episode of asymptomatic bacteraemia in subject with indwelling infusion port; responsive to antibiotics & removal of port

III. On-Target Off Tumor Effects
- Her2 widely expressed at low level including skeletal & cardiac muscle
- 1 episode of ?rhabdomyolysis: grade 3 *(*haematuria + raised CK) in body builder
- No signal in canine spontaneous osteosarcoma despite intensive monitoring

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OS Therapies, Inc. (NYSE American: OSTX)