Immune response, safety, and survival impact from CMB305 in NY-ESO-1+ recurrent soft tissue sarcomas (C131 Study)

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Disclosures

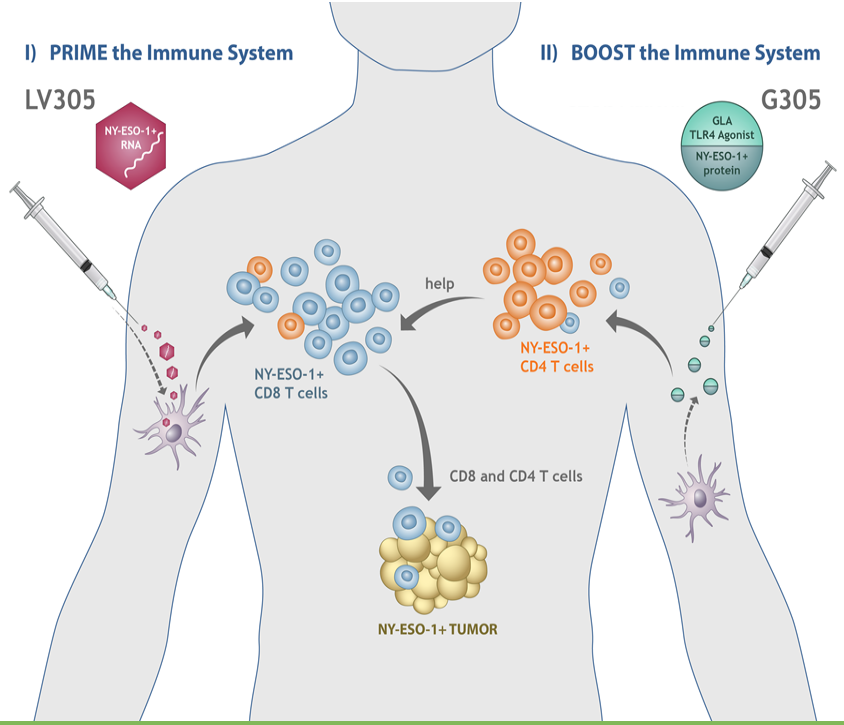
- Advisory board member
  - Deciphera
  - Immune Design
  - Bayer

Soft Tissue Sarcoma (STS), Immunotherapy and NY-ESO-1

- A group of rare malignancies with variable presentation, behavior, and outcome[1]
- The prognosis of advanced or metastatic STS is limited[2]
  - Overall survival in the second line and beyond is 11.7 – 13.5 months[3-6]
- Limited response (subtype specific) to single agent checkpoint blockade[7]
- There remains an urgent need to develop subtype specific or biomarker driven therapies
- Cancer testes antigen NY-ESO-1 is frequently expressed in certain STS[8] and high expression may be associated with poor prognosis[9]
- Effective targeting of NY-ESO-1 with novel immunotherapy in the right patient population could lead to prolonged benefit[10]

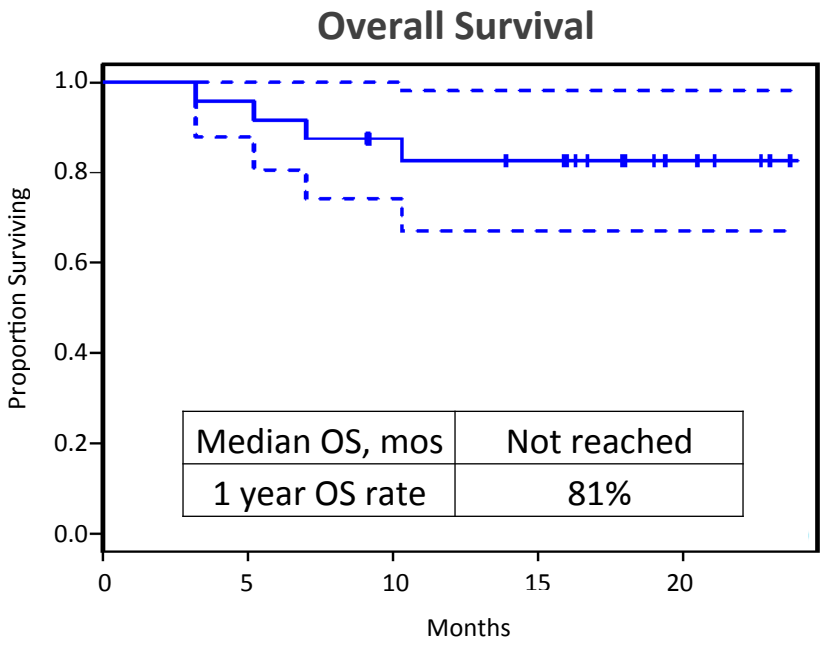
[1] Brennan, M., et al., 2014, [2] Schoffski, P. et al, 2014, [3] van def Graaf, M., et al., 2012, [4] Schoffski, P. et al, 2016, [5] Demetri, G. et al, [6]Savina, M., et al., 2017 (synovial sarcoma), [7]Tawbi, H., et al., 2016, [8]Endo, M., et al., 2015, [9]Iura, M., et al., 2017, [10]D'Angelo, S. 2016

CMB305: Prime-Boost Immunotherapy Targeting NY-ESO-1



- LV305 Priming:
  - Dendritic cell (DC) targeting NY-ESO-1 lentiviral vector encoding full length NY-ESO-1 RNA
  - Integration deficient, replication incompetent
  - Induces and expands NY-ESO-1 specific CD8 and CD4 T Cells
- G305 boosting:
  - Potent TLR-4 agonist co-formulated with NY-ESO-1 full length protein
  - Enhances LV305 T cell immunogenicity and triggers anti-NY-ESO-1 antibodies
- No ex vivo manipulation or HLA matching required

Single Agent Activity of LV305 in Sarcoma Patients[1]



- Sarcoma patients (n=24) including 13 (54%) synovial sarcoma, 6 (25%) myxoid round cell liposarcoma (MRCL); tumor burden ≤10 cm

Best Response by irRECIST	1/24 (4%) PR; 13/24 (54%) SD
Median PFS, mos [95% CI]	4.6 [2.6 – 14.4]

- LV305 induced anti-NY-ESO-1 T cells
- Delayed response was observed consistent with immune based mechanism
- LV305 was safe and well tolerated with no Grade 3/4 AEs

[1] Presented by Neeta Somaiah, et al. at ASCO Annual Meeting 2016

C131 Study: Phase 1 of CMB305

Eligibility:

- Recurrent locally advanced, relapsed and/or metastatic solid tumors, limited tumor burden (<10 cm)
- ECOG PS 0-1
- NY-ESO-1+ by IHC
- Received prior therapy

Part 1 Dose Escalation

Cohort	LV305 Dose (vg per dose)	G305 Dose (GLA/Ag)
1	10^9 ID	5 µg/250 µg IM
2	10^{10} ID	5 µg/250 µg IM

- **Primary Objective**: Safety and tolerability

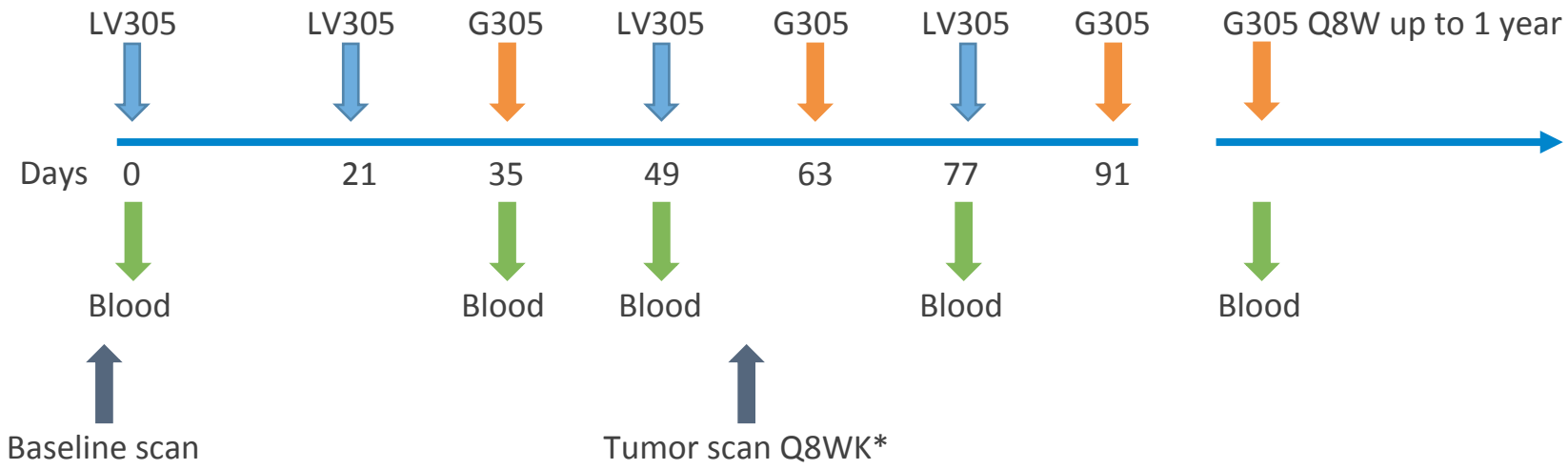
ID=Intradermal; IM=Intramuscular; SC=Subcutaneous

Part 2 Expansion

- **Arm A**: Up to 9 each NSCLC*, ovarian cancer*, synovial sarcoma or MRCL
- **Arm B*:** SQ route, 9 synovial or MRCL
- **Objectives**:
  - Safety
  - Efficacy
  - Immune response and biomarkers

* Biomarker analysis only

C131 Study: CMB305 Treatment and Biomarker Schedule



* Immune related RECIST criteria

C131 Study: Patient Population

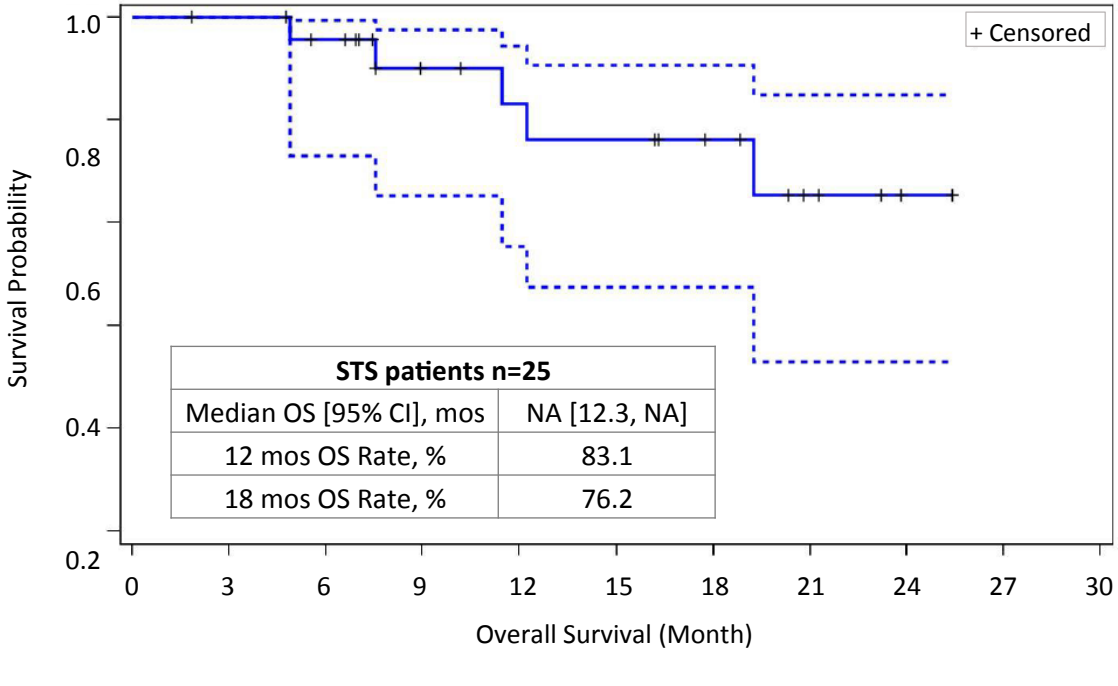
Safety population	49
STS[1], including	25
Synovial sarcoma	14
MRCL	9
Other sarcoma	2

[1] Arm B SQ dose excluded

C131 Study: STS Patient Demographics and Disease Characteristics

	STS (n=25)
Median age, (range)	42 years (20-76, years)
Female	32 %
ECOG PS1	56 %
Metastatic disease	92 %
Median time from diagnosis, (range)	34 months (10-131 months)
Prior chemotherapy	92 %
Median lines of chemotherapy	2.0
≥2 prior lines of chemotherapy	52 %
Disease progression at study entry	56 %
NY-ESO-1 expression 50-100 %, pt (%)	80 %

C131 Study: Overall Survival (OS) in STS pts



March 31, 2017 data cut; median duration of observation 11.4 months

Standard Therapy for 2nd Line STS	
Study	OS
Pazopanib[1]	12.5 months
Eribulin[2]	13.5 months
Trabectedin[3]	12.4 months

[1] van def Graaf, et al., 2012, [2] Schoffski, P. et al, 2016, [3] Demetri, G. et al, 2016

Standard Therapy for 2nd Line Synovial Sarcoma	
Study	OS
METASARC[1]	11.7 months

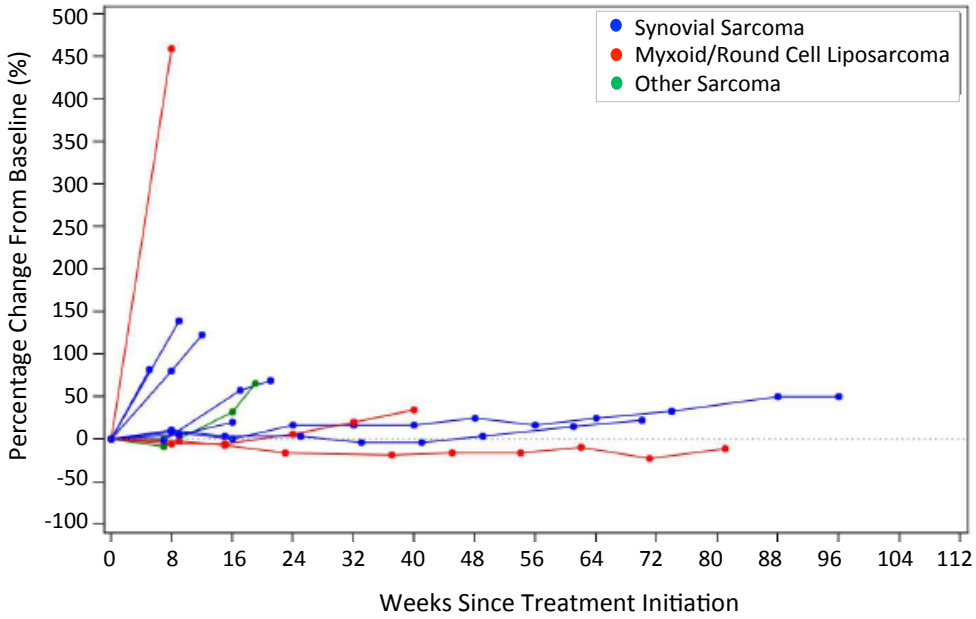
[1] Savina, et al., 2017 (synovial sarcoma)

C131 Study: Disease Control in STS Patients

STS Patients n=25	
ORR, pt (%)	0
SD, pt (%)	16 (64)
DCR, pt (%)	16 (64)
Median PFS, mos	4.7
95% CI	2.1 – 7.8
6 mos PFS Rate, %	36.4

March 31, 2017 data cut

STS patients with **<u>disease progression at study entry</u>** experienced durable tumor growth arrest



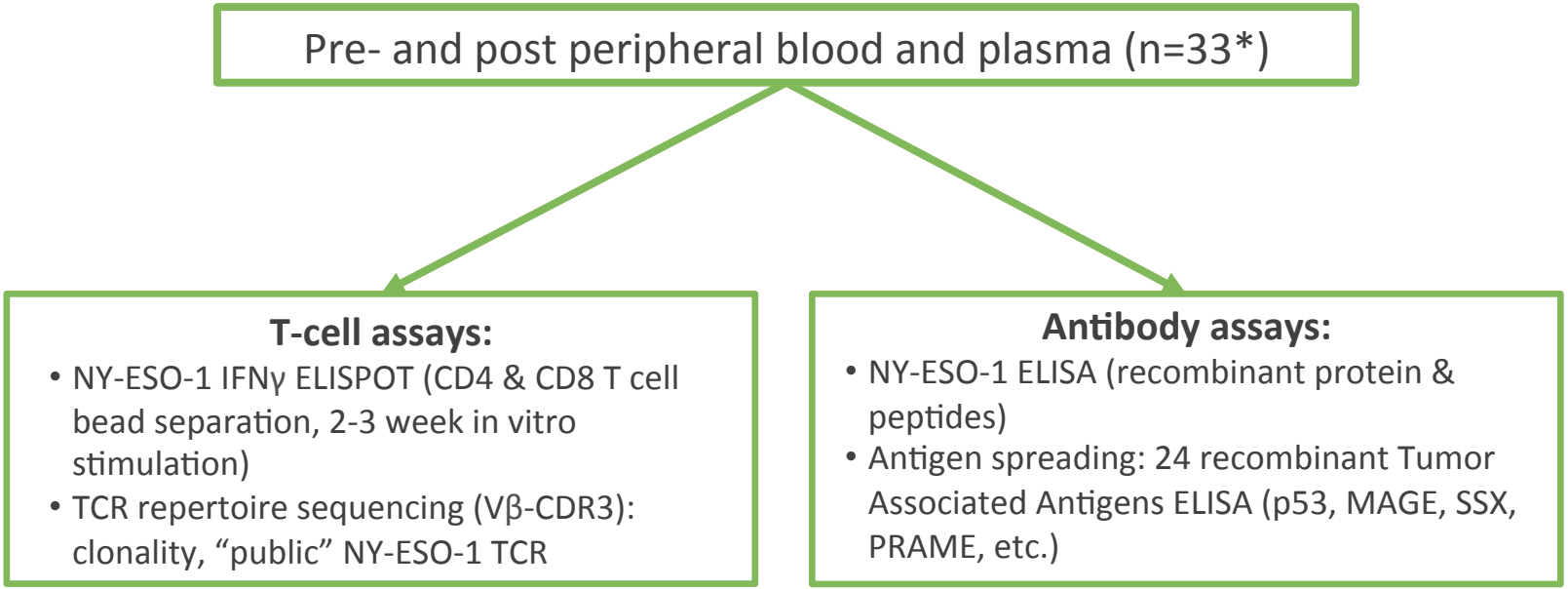
C131 Study: Summary of Safety – All Patients

Patients with at least one*	All patients (N=49)	
	N (%)	
	All TEAEs	**Related TEAEs**
TEAEs (all grades)	45 (92)	36 (74)
Grade 1-2	27 (55)	33 (67)
Grade 3	18 (37)	3 (6.1)
Grade 4	0	0
Grade 5	0	0
Serious TEAEs	11 (22)	2 (4)
Most common treatment related TEAEs: fatigue, injection site pain, influenza like illness, myalgia, injection site reaction (all self-limited)		

TEAE – treatment emergent adverse event; percentages are based on N; * worst grade

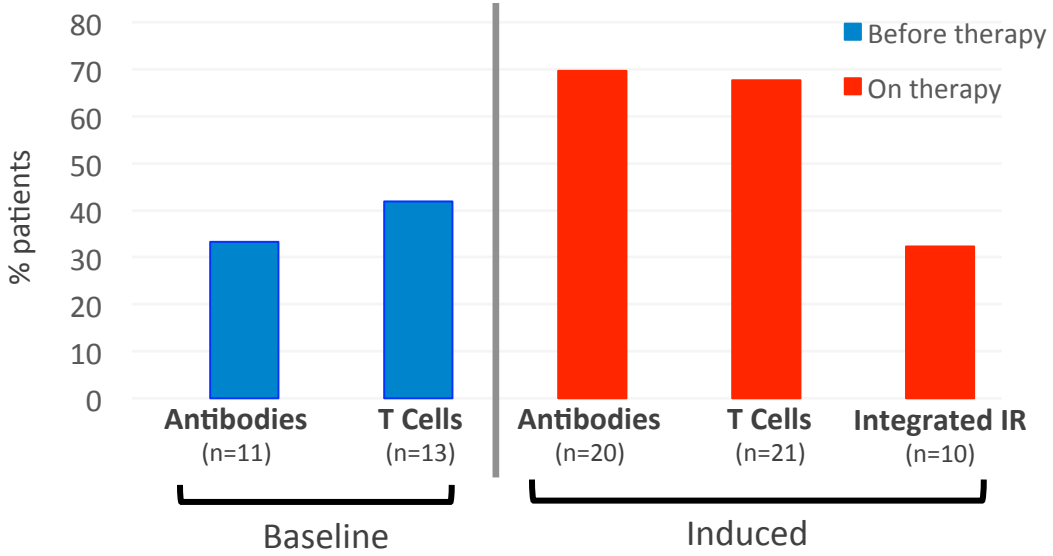
March 31, 2017 data cut

NY-ESO-1 Immune Response (IR) Assessment



* Exploratory biomarker analysis performed in all patients with biomarker samples; 24 sarcoma pts, 9 ovarian pts
more details in **Poster 3090 on Monday, June 5th**

C131 Study: Anti-NY-ESO-1 Baseline and CMB305 Induced Immunity

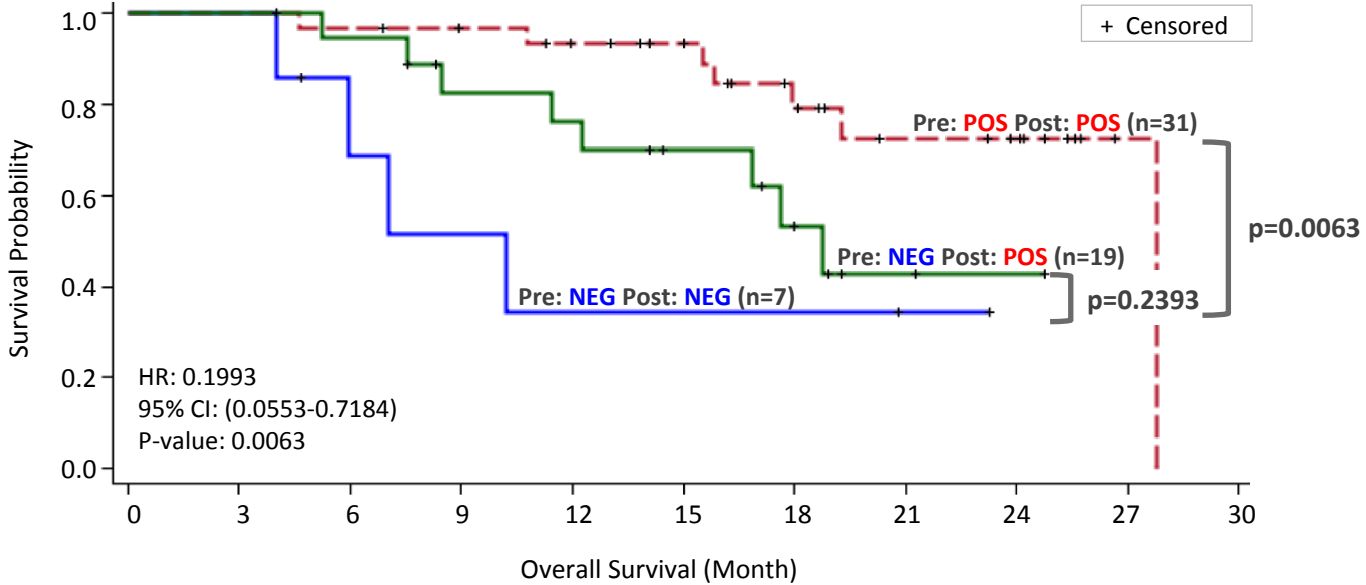


- CMB305 generates strong and broad anti-NY-ESO-1 IR:
  - Stronger T cell response (ELISPOT)
  - Antibody induction
  - 32% pts with induction of integrated IR
  - Evidence of antigen spreading in 4/12 (33%) patients

All tumor types (n=33): 24 sarcoma pts, 9 ovarian pts
Integrated IR: Antibodies, CD4 and CD8 T-cells are present post-Tx

NY-ESO-1 Immunity and Patient Survival

Induction of anti-NY-ESO-1 IR is associated with a better overall survival*



*All patients treated with LV305 or CMB305 (ID/IM and SQ dosing) and who had biomarker samples were analyzed (n=64)
50/64 pts (78%) of patients had an induced anti-NY-ESO-1 immune response on LV305 or CMB305 therapy (assessed by one of the antibody or T cell assays)

Conclusions

- Therapy with CMB305 is safe and well tolerated
- Overall survival compares favorably for patients with recurrent/metastatic STS
  - Median OS has not been reached
- Disease control was observed in more than half of STS patients, including durable tumor growth arrest in patients who had disease progression prior to CMB305 therapy
- CMB305 generates broad anti-NY-ESO-1 immune responses (T cells and antibodies) and triggers antigen spreading
- Anti-NY-ESO-1 immune biomarkers identify cancer patients who have prolonged survival following CMB305 therapy (additional data **Abstract #3090, Monday June 5th**)
- Randomized study of CMB305 and Atezolizumab in synovial sarcoma and MRCL is ongoing
- Immune biomarkers will inform a pivotal randomized study design of CMB305 in STS patients

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