

POSTER PRESENTATION

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# Matched T cell repertoire analysis of peripheral blood and tumor-infiltrating lymphocytes (TILs) in early stage breast cancer (ESBC) patients (pts) treated with pre-operative cryoablation (cryo) and/or Ipilimumab (Ipi)

David B Page<sup>1\*</sup>, Heather McArthur<sup>1</sup>, Zhiwan Dong<sup>2</sup>, Phillip Wong<sup>1</sup>, Ryan Emerson<sup>3</sup>, Zhenyu Mu<sup>2</sup>, Chunjun Zhao<sup>2</sup>, Christopher Comstock<sup>1</sup>, Elizabeth Morris<sup>1</sup>, Elizabeth Comen<sup>1</sup>, Alan Kotin<sup>1</sup>, Janice Sung<sup>1</sup>, Edi Brogi<sup>1</sup>, Monica Morrow<sup>1</sup>, Stephen Solomon<sup>1</sup>, Virgilio Sacchini<sup>1</sup>, Majid Maybody<sup>1</sup>, Deirdre Neville<sup>1</sup>, Adi Diab<sup>4</sup>, Padmanee Sharma<sup>4</sup>, Harlan Robins<sup>5</sup>, Sujata Patil<sup>1</sup>, Jedd D Wolchok<sup>1</sup>, Clifford Hudis<sup>1</sup>, Larry Norton<sup>1</sup>, James Allison<sup>4</sup>, Jianda Yuan<sup>6</sup>

From Society for Immunotherapy of Cancer 29th Annual Meeting  
National Harbor, MD, USA. 6-9 November 2014

## Background

Cryo plus anti-CTLA-4 therapy induces antigen-specific clonal T cell expansion, enhanced survival, and long-term anti-tumor immunity in mice [1]. We recently demonstrated that pre-operative cryo and/or anti-CTLA-4 therapy with Ipi is well tolerated and clinically feasible in women with ESBC. Furthermore, cryo with or without Ipi generates a polyclonal influx of novel T cell clones within the tumor bed [2,3]. Here, we utilize T cell repertoire analysis to explore the impact of cryo and/or Ipi on clonal expansion within peripheral blood and TILs.

## Methods

In a pilot study, women with ESBC were treated with cryo 7-10d before mastectomy (6 pts), single-dose Ipi (10 mg/kg) 8-15d before mastectomy (6 pts), or cryo+Ipi (6 pts). Peripheral blood mononuclear cells (PBMCs) and tumor tissue were obtained pre-mastectomy (immediately preceding cryo and/or 1-5d after Ipi), and at mastectomy. T cell repertoire analysis was conducted on extracted DNA using an Illumina<sup>®</sup> DNA deep sequencing platform and ImmunoSEQ<sup>™</sup> software. Clones comprising  $\geq 0.01\%$

of sample DNA were analyzed, and results are reported descriptively.

## Results

Cryo with or without Ipi was associated with decreases in absolute TIL count (median change: Ipi +6%, cryo -73%, cryo+Ipi -16%). However, cryo+Ipi was associated with the greatest expansion of TIL clones across the range of  $10^2$ - $10^4$  amplicons (table 1), although no difference was observed by group in PBMC clones. Across all samples, a median of 523 TIL clones increased by  $\geq 10^2$  amplicons, and a median of 4 TIL clones increased by  $\geq 10^3$  amplicons. The Ipi/cryo group exceeded the median in 80% (4/5) of cases. 21% of all TIL clones were detectable in time-matched PBMC, whereas 16% of expanding ( $\geq 10^2$ ) TIL clones were detectable in time-matched PBMC.

## Conclusion

Cryo plus Ipi expands more TIL clones than either strategy alone. Therapy-associated clonal expansion may be difficult to detect in PBMCs. These data highlight the potential importance of TIL repertoire analysis for the monitoring of pts treated with cryo and/or Ipi in the pre-operative setting. In a follow-up randomized study, we will evaluate whether TIL clonal expansion across the  $10^2$ - $10^4$  range can be used to predict recurrence-free survival.

<sup>1</sup>Memorial Sloan Kettering Cancer Center, New York, NY, USA  
Full list of author information is available at the end of the article

**Table 1 Therapy-associated T cell clonal expansion in TILs and PBMCs.**

	Median # TIL clones expanding by			Median # PBMC clones expanding by		
	$\geq 10^2$ amplicons	$\geq 10^3$ amplicons	$\geq 10^4$ amplicons	$\geq 10^2$ amplicons	$\geq 10^3$ amplicons	$\geq 10^4$ amplicons
<b>Cryo</b>	199	2	0	697	1	0
<b>Ipi</b>	750	22	1	545	5	0
<b>Cryo+Ipi</b>	2010	85	1	830	1	0

#### Authors' details

<sup>1</sup>Memorial Sloan Kettering Cancer Center, New York, NY, USA. <sup>2</sup>Sloan Kettering Institute, New York, NY, USA. <sup>3</sup>Adative Biotechnologies, Seattle, WA, USA. <sup>4</sup>MD Anderson Cancer Center, Houston, TX, USA. <sup>5</sup>Fred Hutchinson Cancer Center, Seattle, WA, USA. <sup>6</sup>Immune Monitoring Facility, Sloan Kettering Institute, New York, NY, USA.

Published: 6 November 2014

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doi:10.1186/2051-1426-2-S3-P138

**Cite this article as:** Page *et al*: Matched T cell repertoire analysis of peripheral blood and tumor-infiltrating lymphocytes (TILs) in early stage breast cancer (ESBC) patients (pts) treated with pre-operative cryoablation (cryo) and/or Ipilimumab (Ipi). *Journal for ImmunoTherapy of Cancer* 2014 **2**(Suppl 3):P138.

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