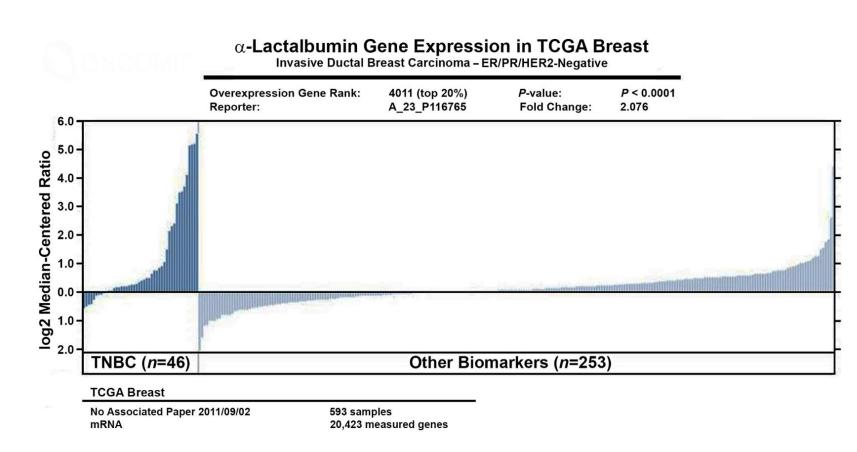
Phase I trial of an alpha-lactalbumin vaccine in patients with operable triple-negative breast cancer (TNBC)

G. Thomas Budd, Justin M. Johnson, Emily E. Rhoades, Halle C. F. Moore, Megan L. Kruse, Erin E. Roesch,

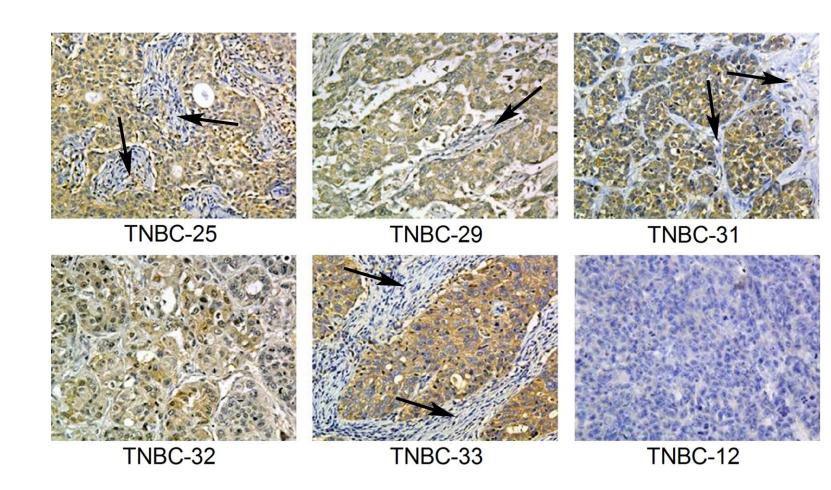
San Antonio Breast Cancer Symposium® December 6-10, 2022

OT2-10-02 **Abstract ID:1304814** Jame Abraham, Brenna Elliot, Elena Haury, Vincent K. Tuohy Cleveland Clinic, Cleveland, OH

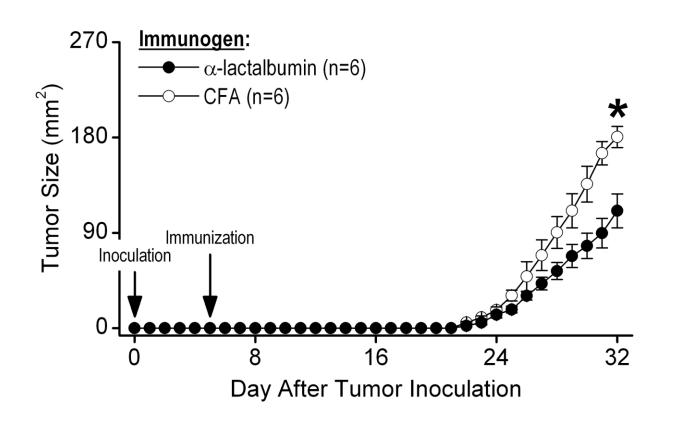
BACKGROUND



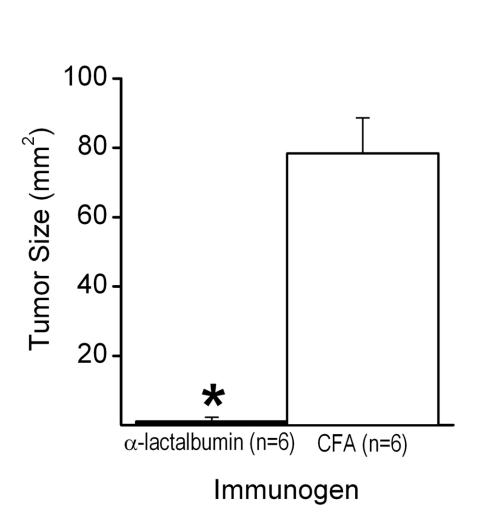
- α-lactalbumin normally expressed only in lactating breast tissue
- Oncomine database search of TCGA shows overexpression of α-lactalbumin gene in TNBC vs. other breast cancers



Immunohistochemical detection of α-lactalbumin protein in parenchyma of human TNBC tumors. 5/6 (83%) showed reactivity ranging from weak (TNBC-32) to moderate (TNBC-33). Arrows show no immunostaining in tumor stroma. Cancers PMID: 27322324



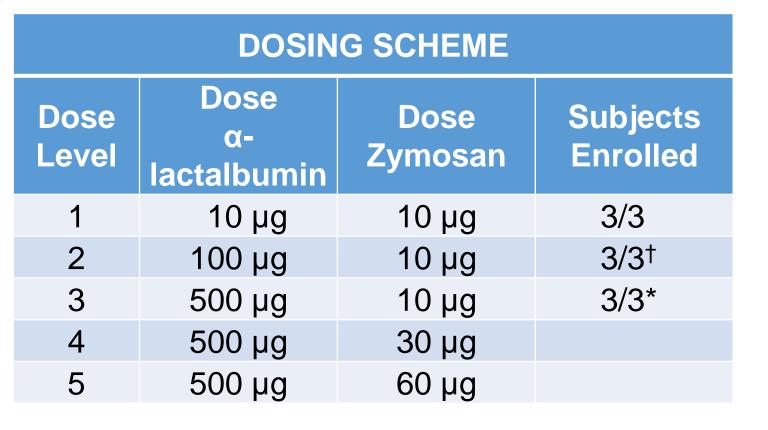
Inhibition of growth of 4T1 tumor growth with α-lactalbumin immunization 5 days after tumor inoculation (*P < 0.01). Nat Med PMID: 20512124



Growth of autochthonous breast tumors in 10-month-old MMTV-neu mice immunized with α-lactalbumin at 8 weeks of age (*P = 0.0004). Nat Med PMID: 20512124

STUDY DESIGN

- "3+3" Phase I trial design
- Vaccine contains α-lactalbumin antigen and zymosan adjuvant in Montanide ISA VG 51 vehicle
- Three vaccinations given at two-week intervals at Day 0, Day 14, and Day 28
- Toxicity monitored until Day 84 or resolution of toxicity
- CTCAE Grade ≥2 is dose limiting
- Immunologic monitoring from blood draw just prior to each immunization and at Day 56
- ❖ ELISpot assays for IFNy and IL-17
- * ELISA assays for α-lactalbumin antibody



†MTD established; cohort to be expanded to n=6 *Limiting toxicity observed in 1/3 subjects

Phase Ia TNBC Cohort Phase Ib Prevention Cohort Prophylactic End Mastectomy of Vaccination | Vaccination Vaccination | Vaccination | Vaccination | Study Subjects a Risk* for the Standard Of Care 28 56 (57-84) of TNBC undergoing prophylaction Breast Recurrence bilateral Toxicity Cancer mastectomy Assessment **Toxicity Assessment** Standard **Toxicity Assessment** Therapy for IHC Complete Draw Blood for Immunologic Monitoring **Draw Blood For Immunologic Monitoring** *Having ≥1 deleterious mutation (BRCA1, PALB2) *Stage IIA-IIIC or residual disease following neo-adjuvant chemotherapy

ELIGIBILITY CRITERIA

Phase Ia TNBC Cohort	Phase Ib Prevention Cohort
 Stage II-III TNBC Completed all standard therapy Within 3 years of diagnosis No evidence of recurrence 	 High-risk genetic mutation (<i>BRCA1</i>, <i>PALB2</i>) carriers planning to undergo prophylactic bilateral mastectomy No evidence of breast cancer

OBJECTIVES

For both Phase Ia TNBC and Phase Ib Prevention Cohorts

- Primary: Determine Maximum Tolerated Dose
- Secondary: Determine Lowest Immunologic Dose
- Exploratory: Establish Optimal Immunologic Dose
- Correlative: Examine the immune response to α-lactalbumin using ELISpot and ELISA

CURRENT STATUS

Phase la TNBC Cohort	Phase Ib Prevention Cohort
Currently enrolling Limiting toxicity reached at Dose Level 3 MTD established at Dose Level 2 Dose Level 2 to be expanded to n=6 Intermediate doses may be explored	 Open to accrual Subjects in the prevention cohort will be enrolled in dose levels at or below the maximum tolerated dose based on the TNBC cohort

FUTURE DIRECTIONS

- Expansion of Phase Ia MTD Dose Level 2 cohort
- Exploration of intermediate doses
- Add cohort to test vaccine adjuvant therapy with checkpoint inhibitor pembrolizumab

ACKNOWLEDGMENTS

Supported by Department of Defense Award Numbers: W81XWH-17-1-0592; W81XWH-17-1-0593

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Contact: buddg@ccf.org

