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,
Jame Abraham, Brenna Elliot, Elena Haury, Vincent K. Tuohy
Cleveland Clinic, Cleveland, OH

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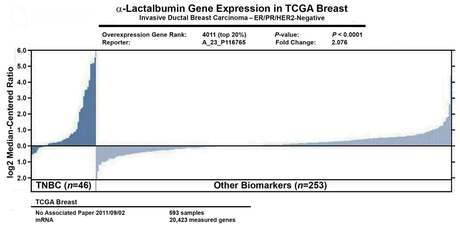
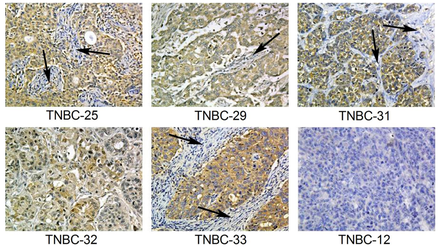
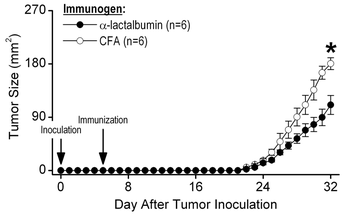
BACKGROUND



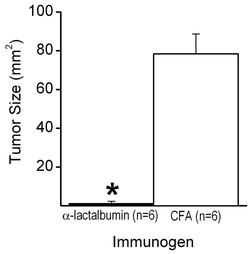
- α-lactalbumin normally expressed only in lactating breast tissue
- Oncomine database search of TCGA shows overexpression of α-lactalbumin gene in TNBC *vs.* other breast cancers



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

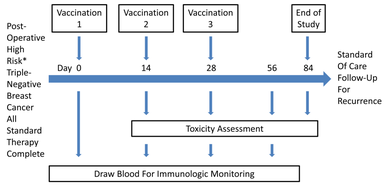
STUDY DESIGN

- "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 IFNγ and IL-17
  - ELISA assays for α-lactalbumin antibody

DOSING SCHEME			
Dose Level	Dose α-lactalbumin	Dose Zymosan	Subjects Enrolled
1	10 µg	10 µg	3/3
2	100 µg	10 µg	3/3†
3	500 µg	10 µg	3/3*
4	500 µg	30 µg	
5	500 µg	60 µg	

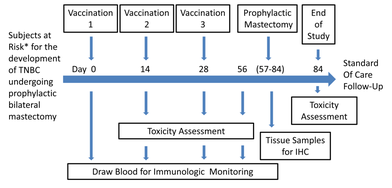
†MTD established; cohort to be expanded to n=6
*Limiting toxicity observed in 1/3 subjects

Phase Ia TNBC Cohort



*Stage IIA-IIIC or residual disease following neo-adjuvant chemotherapy

Phase Ib Prevention Cohort



*Having ≥1 deleterious mutation (BRCA1, PALB2)

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 (*BRCA1, PALB2*) 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 Ia 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

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Contact: buddg@ccf.org

Cleveland Clinic