Whole Tumor Expression Subtypes and Reclassification Resultant from Tumor Enrichmen

Abstract 39 Figure 1

Methods 87 fresh-frozen tumor specimens were selected from a cohort of over 630 patients to reflect a continuum of tumor purity balanced by progression and disease distribution. A whole tumor (WT) specimen and one enriched for tumor epithelium was prepared for each case using laser microdissection (LMD). Specimens were analyzed by whole genome sequencing (WGS), mRNA-seq, quantitative global/phosphoproteomics, and reverse phase protein array.

Results LMD enrichment increased median tumor purity estimated by WGS from 56% in WT to 79% ($P < 4 \times 10^{-11}$, MWW U test) and significantly enhanced identification of somatic single nucleotide variants (SNVs) (27%, $P < 3 \times 10^{-7}$) and short indels (16%, $P < 4 \times 10^{-4}$). Following LMD, 83% of cases characterized as mesenchymal expression subtype (C4) in WT samples were reclassified to other molecular subtypes ($P < 0.001$). LMD tumors with an immune expression subtype (C1) had improved progression-free survival (PFS) compared with other molecular subtypes ($p = 0.009$). Differential proteomic analyses focused on signaling alterations correlating with altered PFS, homologous recombination deficiency and immune signaling.

Conclusions These data demonstrate feasibility of cohort-level proteogenomic characterization of the tumor microenvironment and establishes a non-restrictive paradigm for patient inclusion and specimen prep in support of the prospective mission-scale analyses associated with APOLLO.

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SENTINEL LYMPH NODE MAPPING ALONE COMPARED TO MORE EXTENSIVE LYMPHADENECTOMY IN PATIENTS WITH UTERINE SEROUS CARCINOMA

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Objectives To assess survival among patients with uterine serous carcinoma (USC) who underwent sentinel lymph node (SLN) mapping alone, compared with patients who underwent systematic lymphadenectomy (LND).

Methods Newly diagnosed USC at our institution between 1/1/1996 and 12/31/2017 were reviewed. Patients were assigned to two cohorts: those who underwent SLN mapping alone (SLN Cohort); and those who underwent systematic [pelvic and paraaortic] LND without SLN mapping (LND Cohort). Progression-free survival (PFS) and overall survival (OS) were estimated using the Kaplan-Meier method.

Results In total, 245 patients were available for analysis. Of these, 79 (32.2%) underwent only SLN mapping and 166

(67.7%) underwent systematic LND. Patients in the SLN cohort had a median age of 66 years, compared to 68 years in the LND cohort ($p>0.05$). Median follow-up time was 23 months (range, 1–96) in the SLN cohort and 66 months (range, 4–265) in the LND cohort ($p<0.001$). In patients with stage I/II disease ($n=160$, 60.1%), the 2-year OS was 96.6% (SE ± 3.4) in the SLN cohort and 89.6% (SE ± 2.2) in the LND cohort ($p=0.8$). In patients with stage III disease ($n=77$), the 2-year OS was 73.6% (SE ± 10.2) in the SLN cohort and 77.3% (SE ± 5.8) in the LND cohort ($p=0.8$).

Conclusions SLN mapping alone and systematic pelvic and paraaortic nodal dissection (LND) led to similar survival outcomes in patients with stage I–III USC. In our practice, the SLN mapping algorithm has replaced systematic LND as the primary staging modality in the setting of apparent uterine-confined endometrial serous cancer.

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SENTINEL NODE MAPPING VS. LYMPHADENECTOMY IN ENDOMETRIAL CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Objectives Sentinel node mapping is increasingly being utilized for endometrial cancer staging. However, only limited evidence supporting the adoption of sentinel node mapping instead of conventional lymphadenectomy is still available. Here, we aimed to review the current evidence comparing sentinel node mapping and lymphadenectomy in endometrial cancer staging.

Methods This systematic review was registered in the International Prospective Register of Systematic Reviews. Der-Simonian and Laird random-effects models were used to pool log transformed event rates and estimated 95%CI for dichotomous outcomes between the two interventions for each study and we pooled the effect size using the same models.

Results Overall, 3,536 patients were included: 1,249 (35.3%) and 2,287 (64.7%), undergoing sentinel node mapping and lymphadenectomy, respectively. Pooled data suggested that positive pelvic nodes were detected in 184 out of 1,249 (14.7%) patients having sentinel node mapping and 228 out of 2,287 (9.9%) patients having lymphadenectomy (OR:2.03; (95% CI:1.30 to 3.18); $p=0.002$). No difference in detection of positive nodes located in the paraaortic was observed (OR:0.93 (95%CI:0.39 to 2.18); $p=0.86$). Overall recurrence rate was 4.3% and 7.3% after sentinel node mapping and lymphadenectomy, respectively (OR:0.90 (95%CI:0.58 to 1.38); $p=0.63$). Similarly, nodal recurrences were statistically similar between groups (1.2% vs. 1.7%; OR: 1.51 (95%CI:0.70 to 3.29); $p=0.29$).

Conclusions In conclusion, our meta-analysis underlines that sentinel node mapping is non-inferior to standard lymphadenectomy in term of detection of paraaortic nodal involvement and recurrence rates (any site and nodal recurrence); while, focusing on the ability to detect positive pelvic nodes,

sentinel node mapping could be consider superior to lymphadenectomy.

Regional Plenary

Latin America Regional Plenary

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SOCIAL AND ECONOMIC IMPACT OF CERVICAL CANCER IN BRAZIL: ANALYSIS OF EVA/EVITA COHORT STUDY (LACOG 0215)

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Objectives Compare marital status, household income and labor activity at diagnosis and at 1-year follow-up among cervical cancer (CC) patients in Brazil.

Methods LACOG 0215 EVITA is a prospective observational study, within 16 Brazilian sites, including 18 years-old, newly diagnosed, stage I to IV invasive CC patients. We present data collected at baseline and at 1-year follow-up regarding demography, histology, stage, marital status, household income and labor activity. Variables were compared using Chi-square test.

Results 593 patients were included in this analysis. 75 (12.6%) were diagnosed in stage I, 452 (76.2%) II–III and 66 (11.2%) IV. Mean age at diagnosis was 57.0, 56.4 and 50.5 years respectively. Squamous cell carcinoma was the most frequent histology. 34.2% of stage I, 30.6% of stage II–III and 24.6% of stage IV patients had 9 or more years of education. About 95% patients had a previous pregnancy history. At 1-year follow-up there was a decrease in the proportion of married patients in stage II–III patients only (53.3% to 47.5%; p -value <0.001). There was a reduction in the proportion of women engaged in labor activity in stage II–III (34.1% to 16.1%; p -value, <0.001) but not in stage I and IV. No difference was found in household income 1 year after diagnosis.

Conclusions CC may impact patients personal and work life long after diagnosis, even in those diagnosed with curable disease. In this cohort, stage II–III CC face more risk of divorce and job losses. Social support following diagnosis and treatment is essential for CC patients.